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Exploring the Economic Case for Universal and Targeted Mindfulness-Based Approaches to Prevention: the trial feasibility stage

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Exploring the Economic Case for Universal and Targeted Mindfulness-Based Approaches to Prevention: the trial feasibility stage

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Thesis abstract

Background

In public health, there is an economic case for targeted and universal preventative interventions to prevent depression. There is a growing evidence-base for Mindfulness Based Programmes (MBPs) but less evidence of their cost-effectiveness. Within the context of a translational research framework, which aims to increase the transferability of research findings into practice, there are lessons to be learnt from early-stage trials to develop robust methodologies to evaluate MBPs as complex interventions delivered within complex systems. This thesis aims to explore the economic case for investment in MBPs with both targeted and universal prevention of poor health considered by identifying the evidence, conducting feasibility research, and appraising methodological guidance and health economic tools.

Methods

Multiple methods are employed through this thesis including a societal perspective systematic review (PROSPERO 2017 CRD42017074848) (Chapter 2); a micro-costing study to establish intervention costs across 9 MBPs (Chapter 3); a randomised feasibility trial (ISRCTN23380065) and concurrent service evaluation study of MBCT-Ca, a targeted MBP for cancer patients (Chapter 4); and a non-randomised matched cohort feasibility study (ISRCTN89407829) of a universal Mindfulness in Schools project programme for Sixth Form students aged 16-18 years (Chapter 5).

Results

Chapter 2: 25 economic evaluations of MBPs were identified in a societal perspective systematic review of major medical and economics literature databases and grey literature. Cost-utility analysis (*N=8*) was the most common form of economic evaluation (converted and inflated to 2019 pounds results ranged from £3,125 to £54,327 per QALY), closely followed by cost-effectiveness analysis (*N=7*). Social return on investment study results (*N=2*) indicated between £3.65 and £10.12 of social value is generated for every £1 investment in MBPs.

Chapter 3: MBP group courses in the UK (consisting of between 4-10 sessions, with between 8 and 30 group participants) costed between £2,786.48 and £6,301.70 per course (between £111 - £645 per participant per course).

Chapter 4: Mixed methods evaluation of a randomised feasibility trial of targeted MBCT-Ca (*N=39*) and concurrent service evaluation (*N=24*) indicated that MBCT-Ca was acceptable to patients who attended however there are important barriers to recruitment identified. Clinical and economic outcome

measures were piloted including the EQ-5D-3L (this study was conducted prior to the availability of value sets for the EQ-5D-5L), as a preference-based health related quality of life measure and the ICECAP-A as a measure of capabilities.

Chapter 5: A non-randomised matched cohort study of a universal Mindfulness in Schools program (*N=98*; complete case *N=38*) explores ceiling effects of measures such as the EQ-5D-5L as a primary economic outcome and the General Health Questionnaire as a screening tool for early signs of mental health problems. Feasibility of collecting resource use information from participants including school absenteeism and GP attendance was confirmed. However wider reaching resource use data is needed for a full societal perspective analysis.

Chapter 6: This methodological discussion chapter highlights the extensive health economics toolkit available to researchers looking to conduct economic evaluations of MBPs. This chapter offers a checklist for health economics within the feasibility stage and offers some insights about where public health practitioners might intervene to promote better mental health at a population level

Discussion

This thesis provides the first substantive review of MBP economic evaluations across public and private sectors. There is a need for more evidence on the economics of targeted and universal prevention interventions and future research which considers a precision public health approach should justify the approach taken. Embedding health economics into the entire translational process of complex intervention evaluation can help bridge the gaps to improve evidence-based practice.

Contents

Table of figures

Table of tables

Table of equations

Table of appendices

List of Abbreviations

ACT	Acceptance and Commitment Therapy
ADHD	Attention Deficit Hyperactivity Disorder
BDS	Bodily distress syndrome
CBT	Cognitive Behaviour Therapy
CBA	Cost-benefit analysis
CCA	Cost-consequence analysis
CEA	Cost-effectiveness analysis
CHEC	Consensus on Health Economic Criteria
CHEERS	Consolidated health economic evaluation reporting standards
DALY	Disability Adjusted Life Year
DBT	Dialectical Behaviour Therapy
FPIAFW	Finding Peace in a Frantic World
GBP	Great British Pounds Sterling
HRQoL	Health related quality of life
HTA	Health technology assessment
ICER	Incremental cost effectiveness ratio
ICUR	Incremental cost-utility ratio
m-ADM	maintenance Antidepressant Medication
MBCT	Mindfulness-Based Cognitive Therapy
MBCT-Ca	Mindfulness-Based Cognitive Therapy for Cancer
MBEI	Mindfulness Based emotional intelligence
MBP	Mindfulness Based programme
MBPBS	Mindfulness Based Positive Behavior Support
MBSR	Mindfulness Based Stress Reduction
MDD	Major Depressive Disorder
MID	Minimally important difference
NICE	National Institute for Health and Care Excellence
NHS	National Health Service
PAH	Pulmonary arterial hypertension
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
QALY	Quality adjusted life year
ROI	Return on investment
RCT	Randomised controlled trial
SROI	Social Return on Investment
SUQ	Service utilisation questionnaire
TAU	Treatment as usual
TTO	Time-trade off
UC	Usual Care
WTP	Willingness to pay

Declaration

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Title: Exploring the Economic Case for Universal and Targeted Mindfulness-Based Approaches to Prevention: the trial feasibility stage

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PURE declaration

'Yr wyf drwy hyn yn datgan mai canlyniad fy ymchwil fy hun yw'r thesis hwn, ac eithrio lle nodir yn wahanol. Caiff ffynonellau eraill eu cydnabod gan droednodiadau yn rhoi cyfeiriadau eglur. Nid yw sylwedd y gwaith hwn wedi cael ei dderbyn o'r blaen ar gyfer unrhyw radd, ac nid yw'n cael ei gyflwyno ar yr un pryd mewn ymgeisiaeth am unrhyw radd oni bai ei fod, fel y cytunwyd gan y Brifysgol, am gymwysterau deuol cymeradwy.'

Rwy'n cadarnhau fy mod yn cyflwyno'r gwaith gyda chytundeb fy Ngrichwyliwr (Goruchwylwyr)'

'I hereby declare that this thesis is the results of my own investigations, except where otherwise stated. All other sources are acknowledged by bibliographic references. This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree unless, as agreed by the University, for approved dual awards.'

I confirm that I am submitting the work with the agreement of my Supervisor(s)'

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Preface and researcher positioning statement

This preface aims to provide a researcher positioning statement which reflects on some of my research training, education and professional experiences which have influenced the methodological approach adopted in this thesis.

As a BSc Psychology graduate (2007 – 2010) I received training in both quantitative and qualitative methods and undertook a module on 'Introduction to Mindfulness Based Approaches' which involved elements of 'intuitive knowledge' generation through learning from lived experience of practicing mindfulness alongside studying theory from sources of peer reviewed published 'authoritarian knowledge' (which I went on to lecture to BSc undergraduate students).

In 2011 I completed my MRes in Psychology working in partnership with business through a knowledge economy skills scholarship to evaluate Dialectical Behaviour Therapy programmes using a novel benchmarking website which piloted health economics questionnaires to monitor patient health states over time. I became interested in the methods to evaluate new technologies, the role of audit and service evaluation alongside clinical practice, and the growing need for managers to provide a financial business case for on-going funding to support programme delivery after initial implementation. This was what led me into health economics research. Between January 2015 and December 2020 I worked at the Centre for Health Economics and Medicines Evaluation at Bangor University most recently as a Research Officer on a range of clinical trials and commissioned research projects.

This thesis represents the culmination of almost a decade of part-time work in exploring the economic case for mindfulness programmes as a potential tool against depression. This PhD started with a relatively narrow focus which has grown substantially during this time into the broad thesis presented here. The systematic review was commenced when very few studies had been published on mindfulness and economics however after returning from two periods of maternity leave the landscape of literature had moved on substantially. This PhD was funded through the Tenovus Cancer Care charity in Wales (https://www.tenovuscancercare.org.uk/) in 2011 to evaluate MBCT for Cancer and build on local development and implementation of the programme in North Wales. This was in a time where research into cancer drugs was particularly prominent and much less attention was paid to mental health. While cancer was a topic I had little personal experience of I knew that it was a life changing event for far too many. I have a personal and professional interest in promoting resilience and managing mental health conditions. I began this study enthusiastic to conduct research which might support the mental health of people recovering from cancer. At the very beginning this work involved a plan to conduct a concurrent health economics evaluation alongside a separately funded clinical trial, however, when the funding application for the larger trial was unsuccessful, my plan was adapted into the pilot trial which is

presented in this thesis. In addition, an opportunity arose in 2015 to include a school-based health economics study and the scope of this work grew again enabling this exploration of research focusing on different stages of life course intervention.

I have developed a great deal as a researcher during this time, and the evidence base has also grown. I have updated this thesis throughout to reflect the changing literature to provide an up-to-date picture of the evidence today, while also acknowledging that much of this work was designed and completed several years ago and may not reflect current thinking if studies were to be conducted today.

Publications and presentations of this thesis research

Edwards, R. T., **Bryning, L.** & Crane, R. (2015). Design of economic evaluations of mindfulness-based interventions: ten methodological questions of which to be mindful. *Mindfulness, 6,* 490–500. doi:10.1007/s12671-014-0282-6

Bryning, L. Crane, R. & Edwards, R.T. (2015). *The cost of Mindfulness Based Approaches: A micro-costing analysis.* Presentation. Mindfulness in Society CMRP Conference (July 2015), Chester, UK.

Bryning, L. Crane, R. & Edwards, R.T. (2015). *Applying a Micro-costing framework to calculate the costs of Mindfulness Based Approaches.* School of Health Care Sciences PGR Conference, Forging Partnerships and Understanding Approaches (July 2015), Bangor University.

Bryning, L., Edwards, R. T., & Crane, R. (2013). Study Protocol: Exploring the Cost Effectiveness of Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca). *Psycho-Oncology, 22* (S1), p.28.

Bryning, L. & Edwards, R.T. (2013). *Designing the economic evaluation of Mindfulness Based Interventions: Ten factors of which to be mindful.* Presentation. Welsh Health Economics Study Group (WHEG) Summer Meeting (July, 2013), Cardiff, UK.

Edwards, R. T. & **Bryning, L.** (2013). Measuring the cost effectiveness of mindfulness - challenges and opportunities. Presentation. *OECD Welfare Economics Conference (July 2013),* Paris, France.

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Bryning, L. & Shannon, D. (2013). *Introduction to Mindfulness Meditation workshop*. Tenovus 70th Anniversary Research Conference (October 2013), Cardiff UK.

Bryning, L., Edwards, R. T., & Crane, R. (2012). *Exploring the Cost Effectiveness of Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca): A Tenovus PhD.* Poster Presentations. Tenovus Mobile Cancer Support Unit, Mobile Monday, Bangor. (23rd April 2012).

Bryning, L., Edwards, R. T., & Crane, R. (2012). *Exploring the Cost Effectiveness of Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca): A Tenovus PhD.* Poster Presentations. Mindfulness health and wellbeing: An International Mindfulness Research Conference with Jon Kabat Zinn, Glasgow University. (20th June 2012).

Chapter 1: Introduction

"An ounce of prevention is worth a pound of cure"

—Benjamin Franklin, 1735

Chapter preface

This introductory chapter sets out the present state of theory and application of health economics of preventative public health, specifically applied to mental health and wellbeing. It goes on to reflect on Mindfulness-Based Programmes (MBPs) as a means of protecting against and treating mental health conditions both as universal and targeted interventions. I put forward the foundations of health economics and economic evaluation highlighting factors such as 'positive time-preference' as one reason why less is invested in prevention than cure in health care systems. The chapter then turns to the specific challenges of evaluating the effectiveness and cost-effectiveness of MBPs as complex interventions, and to the need for a full continuum of the translational research, specifically feasibility stage health economics research. The chapter concludes with the structure of the thesis, data sources and my novel contributions to the fields of health economics and MBP research.

Introduction

The economic burden of poor mental health

Poor mental health has both short-term and long-term impacts across various points in the life course (Fergusson, John Horwood, & Ridder, 2005; Knapp, King, Healey, & Thomas, 2011). Globally, chronic, noncommunicable diseases including mental health disorders are a leading cause of death, and have a high disease burden with a wide range of functions affected and costly consequences (WHO, 2014, 2016). Poor mental health is associated with high utilisation of health care resources and has increased risk of negative outcomes such as lower quality of life (Public Health England, 2019), suicide, associated physical health problems, productivity losses in the workplace, poor life chances and opportunities, poor job outcomes, and also has an overall impact on the wider economy (Smit, Beekman, Cuijpers, de Graaf, & Vollebergh, 2004).

Mental health conditions such as depression and anxiety are a common manifestation of ill health and are estimated to effect approximately 15.7% of the UK population, with one in every six individuals

showing symptoms of one of the common mental disorders (Mcmanus, Bebbington, Jenkins, & Brugha, 2016). The prevalence of mental health conditions is increasing[1] (Public Health England, 2019).

Depression alone is estimated to effect between 4 and 10% of the general population (NICE, 2011; Public Health England, 2019), and is a leading cause of years lived with disability worldwide (one measurement of disease burden) (GBD 2017 Disease and Injury Incidence and Prevalence Collaborators, 2018; Reddy, 2010; Vos et al., 2004; World Health Organization, 2019). Depression relapse rates are reported to be as high as 85% after the first episode of depression (Mueller et al., 1999). Some groups of people may be more likely to experience mental disorders than others, at risk groups (with a higher prevalence of depression, anxiety and other mental disorders than the general population) include cancer patients and other individuals with chronic physical conditions (Egede, 2007; Linden, Vodermaier, MacKenzie, & Greig, 2012).

Mental health disorders pose a significant growing cost burden on health care services (McCrone, Dhanasiri, Patel, Knapp, & Lawton-Smith, 2008). Greater prioritisation of mental health has been emphasised in UK law by the Health and Social Care Act 2012 'parity of esteem' principle by which mental health must be given equal priority to physical health (Centre for Mental Health, 2019). However, mental health spending is estimated to be around £11.7 billion in England, representing approximately just 12% of the overall health budget (National Audit Office, 2016). Furthermore, estimates suggest mental health conditions account for 28% of disease burden (Centre for Mental Health, 2013). The costs of poor mental health fall much wider than the health sector with the impact on the overall UK economy estimated to be between £70 billion and £100 billion a year in 2015 (Mental Health Foundation, 2015). More recent reports indicate costs of mental ill health reached £119 billion a year in 2019 in England alone (O'shea & Bell, 2020).

The costs to public services and loss of earnings due to depression and anxiety disorders alone have been predicted to rise by £10 billion (from 2007 figures) and reach a cost of £26.44 billion by 2026[2] (McCrone et al., 2008). All public sectors have had recent substantial real-terms cuts to funding, in England cuts to areas such as the Public Health grant have resulted in spending on prevention reducing by nearly a quarter between 2014/15 and 2019/20 (Buck, Baylis, Dougall, & Robertson, 2018; Finch,

[1] Prevalence of common mental health conditions between 1993 and 2014 as recorded by the Adult Psychiatric Morbidity Survey.

[2] Costs to public services include direct health and social care costs, informal care, and criminal justice services.

Bibby, & Elwell-Sutton, 2018). There is increasing evidence that mental health services are facing significant pressures, with reductions in funding and increasing demand (The Kings Fund, 2015).

There is a large treatment gap in access to mental health treatment in developed countries with estimates that half of people with depression receive either no professional treatment or experience long delays in accessing support (Kohn, Saxena, Levav, & Saraceno, 2004; WHO, 2005). Negative attitudes towards treatments such as antidepressants are a potential contributing factor, in addition to low levels of treatment seeking behaviour (Jorm, 2000). Treatments for mental health disorders are limited in the scale of impacts they can achieve.

The economic case for prevention

It has long been acknowledged that premature death and poor health may be preventable through early intervention and behaviour change (NICE, 2015). Moreover, it is widely recognized that the treatment of mental health disorders is unlikely to be affordable and emphasis must be on prevention (Knapp, McDaid, & Parsonage, 2011; McCrone et al., 2008). The absence of mental health disorders arguably does not go far enough, with a call for a more positive approach to mental health focusing on public mental health promotion that enables enhancing mental resilience and competence rather than focusing on the lack of impairment alone (Fledderus, Bohlmeijer, Smit, & Westerhof, 2010). However there is very little investment in mental health promotion for adults, with spending representing only one tenth of 1% of NHS spending (McCrone et al., 2008).

While it is commonly accepted that prevention is important, it is underrepresented in health policy and health spending across the world (Srivastav, 2008). One reason for this may be that there are methodological challenges to evidence the case for prevention with benefits of preventative services often occurring far into the future, well outside the duration of a standard clinical trial (Drummond et al., 2007; Weatherly et al., 2009).

It is common for people to accord less worth to a future reward than an immediate one based on the behavioural economics theory of intertemporal choice (Loewenstein, Read, & Baumeister, 2003). This phenomenon is described and studied by both psychologists and economists and referred to as temporal discounting, delay discounting, and time preference (Green, Myerson, & McFadden, 1997; Loewenstein et al., 2003; Odum, 2011). Decisions to engage in health-related behaviours require individuals to trade-off of the immediate costs of undertaking the behaviour such as time, energy and sometimes money, with the promise of future benefits. As a result of this preference for benefits now (a cognitive bias rather than a conscious decision-making process), benefits occurring in the future are valued as being worth less than immediate benefits. In general the further away the benefits, the lower the value, due to a tendency for hyperbolic discounting (Frederick, Loewenstein, & O'Donoghue, 2003).

There are economic arguments for investment in prevention and government intervention to improve public health. The government goal to reduce or prevent mental health problems in the population is an 'allocative efficiency' question, while which is the most cost-effective way of achieving this goal is a 'technical efficiency' question. In health care government intervention is necessary to correct market failures (where resources are inefficiently allocated) in order to improve social welfare (Knapp, McDaid, et al., 2011). Economists draw parallels between market forces that shape choices to purchase goods and services and the drivers that shape health-related behaviours such as the consumption of commodities like food, physical activities and leisure time (McDaid, Sassi, & Merkur, 2015).

Markets can fail to operate efficiently due to information failures, where people do not have enough information about the short and long-term consequences of a particular choice. Public levels of mental health literacy are poor, with common misunderstandings about the causes, prognosis and possible treatments of mental health disorders prevalent in much of western society (Jorm, 2000, 2012). Furthermore, public knowledge is limited about possible preventative action that can be taken to avoid risk of mental health disorder onset or relapse (Jorm, 2000, 2012). In addition, market failures can be because of behaviours that are not rational, driven by cognitive biases for short-term gains or because of addiction or chronic habit-forming behaviour. For example, someone who is clinically obese may still eat high sugar and high fat foods and not engage in physical activities, knowing the risks of diabetes and other health conditions. There are many factors that influence these behaviours including (but not limited to) the high immediate reward of unhealthy eating, making it very difficult to behave against these cognitive processes built up over many years.

Prevention may be able to further tackle disease burden and help stem the unaffordable rising costs of treatment (Knapp, King, et al., 2011; Knapp, McDaid, et al., 2011; McDaid, 2011). The expanding knowledgebase around the physiology, psychology and mechanisms of depression have increased in recent years meaning that at risk groups can be targeted thus improving the effectiveness of preventative interventions (Mrazek & Haggerty, 1994).

Prevention initiatives include a range of support (see Figure 1), from often late stage intensive (and high cost) tertiary services which aim to slow down the progression of illness or disability, to secondary prevention where the aim is for early diagnosis and early intervention, and then early primary prevention where the focus is on promoting good health and wellbeing before symptoms and support needs arise (Department of Health, 2008).

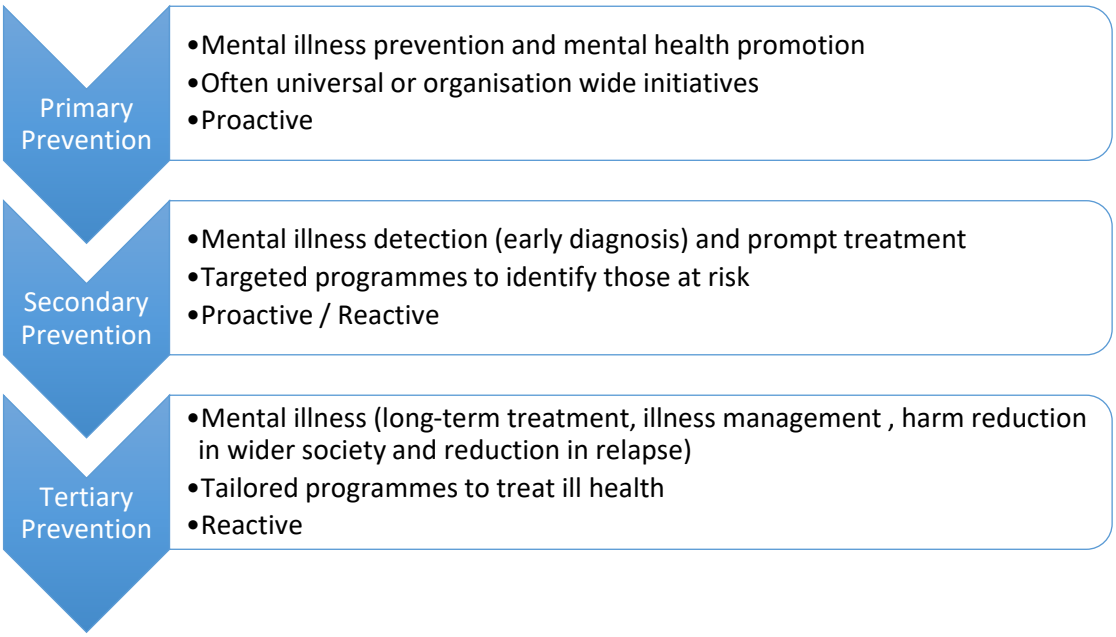


Figure 1: Levels of prevention in mental health

Health economics considerations for investment in mental health prevention

It is increasingly recognised that maximising population health should not focus on the treatment of physical health problems alone, but adopt a more holistic approach to health promotion with a focus on mental wellbeing at its core (WHO, 2005). Rather than focusing on the absence of disease or infirmity the World Health Organization defines health as complete physical, mental and social wellbeing (WHO, 1948). Definitions of mental health commonly encompass emotional wellbeing (affect/feeling); cognition (perception, thinking, reasoning); social functioning (relations with others and society); and coherence (sense of meaning and purpose in life) (Friedli, 2009).

Demand for health care generally is high, but with limited resources it is necessary to consider which services should be prioritised and made available. Health economists are concerned with decisions about resource use, which requires resources to be valued. Commonly this can be expressed in monetary terms and/or in health benefit, and in the compromises and trade-offs that are necessary to make the best use of scarce resources. Decision makers require accurate information on both the costs and benefits of interventions and treatments to effectively allocate scarce health care resources. The economic cost of a resource is different to the monetary cost that would be assigned by an accountant. Health economists are concerned with the 'opportunity cost'. This is the value of resources forgone by not selecting their best alternative use (Morris, Devlin, Spencer, & Parkin, 2013). In order to make decisions about how best to allocate resources (e.g., what to prioritise and on what basis), quality evidence on the demands, benefits and costs of innovations in health care is required (Beecham & Knapp, 2001). The role of the health economist is often therefore to provide evidence to inform these

necessary decisions around the potential trade-offs in resource allocation relating to the pursuit of overall societal goals.

It is necessary to weight costs and benefits appropriately reflecting the time in which they occur and the value people place on them, it is therefore recommended that in economic evaluations future costs and benefits (that occur more than 12 months in the future), should be discounted by a rate of 3.5%, as set by the HM treasury (HM Treasury, 2011). In the case of many public health interventions benefits may be observed along a longer time horizon compared to medicines or other treatments. NICE have argued that these discounting methods could result in a substantial undervaluation of preventative interventions (NICE Citizens Council, 2011). One argument to counter this potential undervaluation of public health interventions is to discount health benefits at a differential discount rate of 1.5% (Brouwer, Niessen, Postma, & Rutten, 2005). As cost-effectiveness estimates can be influenced by the discount rate selected, careful methodological considerations are needed (NICE, 2014a; O'Mahony et al., 2011; O'Mahony, Newall, & van Rosmalen, 2015). Current NICE guidance proposes sensitivity analysis where both costs and benefits are discounted at 1.5% and that this is presented alongside the reference case (at 3.5% discounting) for consideration in public health research (NICE, 2014a).

Health care can be a 'merit good' in that the true benefits are not always realised by the individual and there are often positive effects on others. For example, receiving an immunisation has positive externalities to both the individual and others through herd immunity. Poor mental health has considerable spillover effects or negative externalities, in that there is a significant impact on others going beyond the individual experiencing the direct burden of mental health disorders (Weatherly et al., 2009). These externalities are good justification for public sector investment in mental health protection (Smit, Cuijpers, Petrea, & McDaid, 2015). There is also an equity argument for investment in mental health intervention with a disproportionate amount of mental ill-health affecting the lowest socio-economic groups of society (Funk, Drew, & Knapp, 2012).

Early intervention: considering the critical time for investment.

In mental health interventions prevention can be made available to whole populations or targeted through selection or indicated criteria (see Figure 2). With limited health care resources and a growing number of innovative public health interventions, it is necessary to make choices about which intervention to provide to which population, in which context, and at what time. This is increasingly known as 'precision public health' (Khoury, Iademarco, & Riley, 2016; Olstad & McIntyre, 2019). This concept is applied further in Chapter 6 of this thesis.

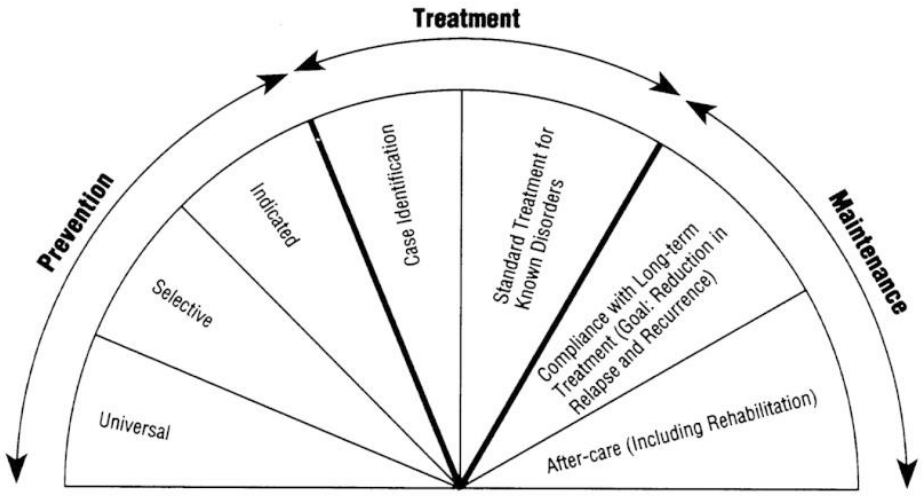


Figure 2: The mental health intervention spectrum (Mrazek & Haggerty, 1994).

In general terms, there is strong evidence supporting early intervention in the life course with evidence-based programmes able to deliver a high positive return on investment, offering benefits to society which are substantially greater than the costs of the programme (Karoly & Bigelow, 2005). Childhood offers a key intervention point for mental health promotion with action that focuses on developing social and emotional coping skills early and improving relationships with others. Half of all mental disorders are reported to develop by early adolescence, highlighting the need for preventative interventions targeted at children (Kessler et al., 2005). Poor mental health and its consequences in childhood can have an impact well into adulthood (Knapp, King, et al., 2011). Rates of depression in childhood are estimated to be around 2.5% rising to 8.3% in adolescence (Birmaher et al., 1996). Rates of sub-clinical levels of depression are even higher with up to 30% of adolescence experiencing signs of depression (Birmaher et al., 1996). Along with higher rates of comorbidity with other mental disorders, children with depression have higher vulnerability to relapse (Zisook et al., 2007), poorer educational outcomes (Birmaher et al., 1996) and poorer overall life trajectories across all personal social and economic domains (Knapp, King, et al., 2011).

The school environment offers an opportunity to reach many people at an early stage in the life course (McDaid et al., 2015). Overall the effectiveness and cost-effectiveness of school-based interventions vary but what appears to be critical to success is the need for appropriate implementation with fidelity (Smit et al., 2015). Economic evaluations of mental health prevention interventions delivered within school settings are discussed further in Chapter 5 of this thesis.

Developments in treatment, health promotion and prevention in mental health: psychological therapy

In the UK, the demand for psychological treatments is high and access is limited (Barrett & Byford, 2008; Bonin & Beecham, 2012). Additionally, psychological therapy has been argued to be “expensive and resource intensive” in comparison to alternative treatments such as antidepressants (Barrett & Byford,

2008, p. 15). It has also been argued that there is an insufficient number of trained therapists and services to meet demand (Barrett & Byford, 2008; Bonin & Beecham, 2012). There is increasing interest in group-based psychological therapies which may be cost-effective due to their high ratios of patient to therapist potentially offering a lower cost per patient compared to alternative treatments such as individual therapy (Barrett & Byford, 2008). However, there are many factors that can influence the cost of a group-based intervention such as the number of patients attending, the professional required to facilitate or run the group and the type of intervention itself.

Mindfulness Based Programmes (MBPs): application and effectiveness

There is an increasing body of evidence to support the effectiveness of Mindfulness Based Programmes (MBPs) (for reviews see Bohlmeijer et al., 2010; Chiesa & Serretti, 2009; Dimidjian & Segal, 2015; Kuyken et al., 2016)**.** Mindfulness can be defined as a non-judgemental but purposeful directing of attention to the present moment (Kabat-Zinn, 1990), and is learnt through practicing mindfulness meditation. Mindfulness meditation is typically taught by a trained MBP teacher to groups of between eight and 30, and is commonly based on a manualised programme of Mindfulness Based Stress Reduction (MBSR; Kabat-Zinn, 1990; Santorelli, Meleo-Meyer, & Koerbel, 2017) or Mindfulness Based Cognitive Therapy (MBCT; Segal, Williams, & Teasdale, 2013), which integrates features of cognitive behaviour therapy for depression (CBT; Beck, Rush, Shaw, Brian, & Emery, 1979) into the MBSR programme (Williams & Kuyken, 2012). MBPs commonly share a set of key characteristics (see Box 1); however, the underpinning framework has some flexibility and several adaptations of the core programmes may be considered in order to make the programmes more relevant or suitable for the specific target population (Crane et al., 2016).

Box 1: Mindfulness Based Programmes - Key Features

Recruitment: Self-referral, health professional referral or context derived (e.g., courses made available in schools or businesses).

Capacity: Group size can vary, rarely more than 30.

Location: Community, hospital, educational, and occupational settings.

Duration: One session (approx. 2-2.5 hours) per week, for approx. eight weeks.

Methods: Usually group sessions, led by a trained teacher. Home practice assignments.

Content:

- *Sustained practice in mindfulness meditation skills*
- *Teacher led dialogue integrating learning from mindfulness practice with life challenges*
- *Skill based and psycho-educative material integrated with experiential (e.g., depression, effects of avoidance, rumination).*

The National Institute for Health and Care Excellence (NICE) in the UK makes national clinical recommendations on which interventions have sufficiently robust evidence to be applied within the health service. MBCT has been evaluated as an effective intervention for preventing depression relapse and is recommended in UK clinical guidance (NICE, 2018). In 2004 MBCT was first recommended as a depression prevention treatment for people with a history of three or more episodes of depression, and in 2009 the guideline was updated and MBCT was highlighted as a key priority for implementation to be offered to people who are currently well but have a significant risk of depression relapse (NICE, 2009). In 2016 the provision of MBPs became a mandatory part of the Improving Access to Psychological Therapy (IAPT) programme aimed at supporting adults with anxiety disorder and depression (Rycroft-Malone et al., 2017). It has been argued that there is shortage of suitably trained MBP therapists to meet the delivery of MBPs through IAPT and there was a strong case made for ensuring funding is appropriately allocated to address this (Rycroft-Malone et al., 2017).

Meta-analyses indicate that MBCT is an effective treatment for reducing depressive relapse in patients with recurrent major depressive disorder (three or more previous episodes) (Kuyken et al., 2016; Piet & Hougaard, 2011). Recent studies have implicated specific vulnerabilities such as childhood trauma as more important mediating factors determining likely effectiveness, rather than number of episodes of depression alone (Williams et al., 2014). Over the last 40 years the evidence base on MBPs has increased considerably and internationally the application of mindfulness has been at a point of rapid expansion (Dimidjian & Segal, 2015; Williams & Kabat-Zinn, 2011). Further research is needed on the mechanisms for MBPs to help better understand when they may be most effective and cost-effective.

MBPs have been widely applied to various populations and several adaptations of the programmes now exist. MBSR is increasingly delivered to a wide range of population groups with varied physical and mental health conditions. Beyond the recommendations by NICE for the application of MBCT to the management of depression, there is an emerging evidence base in other clinical applications including anxiety (Evans et al., 2008), insomnia (Heidenreich, Tuin, Pflug, Michal, & Michalak, 2006), bipolar disorder (Williams, Alatiq, et al., 2008) and breast cancer (Haller et al., 2017). There is evidence to suggest that the real-world delivery of MBCT has broadened out from the target population of people at risk of depression relapse to include people currently experiencing depression (Tickell et al., 2019). MBPs delivered within the health sectors, often hospital based are used as a ‘clinical tool’ for treatment or prevention (Crane, 2017), while an increasing number of wider applications are becoming more commonplace including adaptations for workplaces (e.g., Chaskalson, 2011), and schools (e.g., Kuyken et al., 2013), where MBPs are delivered as ‘mental training tools’ to help build resilience and core coping skills (Crane, 2017). There are an increasing number of self-help options available to the general populations providing a potential tool for personal development (Crane, 2017). The recently published

Mindful Nation UK report recommends expanding NICE guidelines to consider other groups (The Mindfulness All-Party Parliamentary Group (MAPPG), 2015).

MBPs: do they offer value for money?

There is limited evidence on whether MBPs as a broad category of interventions are overall cost-effective and offer value for money in the context of scarce public resources (Edwards, Bryning, & Crane, 2015; Kabat-Zinn, 2013; Kuyken et al., 2016). In the last decade there have been a small but increasing number of publications with keywords “Mindfulness” and “Economics”, see Figure 3 below showing the numbers of published literature (in Science Direct as of September 2020) including keywords "mindfulness“ and “economic evaluation”. This is set alongside a rapid growth in the literature including the term “mindfulness” in the publication.

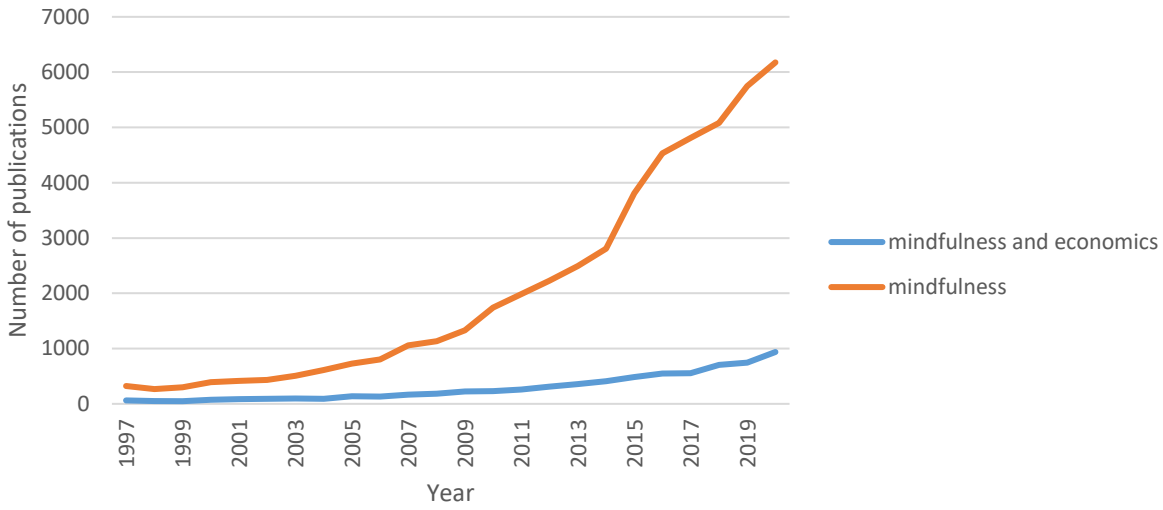


Figure 3: Comparison of the increasing number of publications over time on Mindfulness AND Economics

NICE guidance (NICE, 2018) recommended MBCT for the management of recurrent depression based on one available economic evaluation (NICE, 2010), where MBCT was likely to be cost-effective compared with maintenance antidepressants should societal willingness to pay levels rise above $1,000 (equivalent to £760) to prevent depression recurrence (Kuyken et al., 2008). However, in a subsequent trial these findings were not supported with the MBP incurring higher costs and poorer outcomes than maintenance antidepressant medication alone (Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Brejcha, et al., 2015). Chapter 2 in this thesis systematically reviews the available economic evidence for MBPs to evaluate whether MBPs or their comparators are likely to provide a cost-effective use of limited public resources.

MBPs as preventative targeted and universal interventions

Mental illness prevention is important from a public or population health perspective, particularly when you consider how improved mental health can "act as a protective factor for many physical illnesses" (British Medical Association, 2017, p. 3). In public health 'targeted' interventions are defined as interventions that "focus on groups with particular needs, or that are particularly likely to benefit (e.g., the provision of cancer screening to those who are at an increased risk)" (British Medical Association, 2017, p. 3), while 'universal' interventions are aimed at (although not always accessed by) the whole population.

MBPs are commonly delivered as preventative interventions, ranging from targeted programmes preventing recurrent depression to more universal programmes which aim to build resilience and promote positive mental health, for example within children (Kuyken et al., 2017). MBPs delivered within a school setting offers an opportunity for universal primary prevention, where a whole cohort of the population has the potential to access the intervention. More targeted approaches such as MBCT for depression or MBCT for Cancer (MBCT-Ca) identify individuals at greater risk of developing depression compared with the general population and aim to prevent onset of mental ill health or recurrence (see Figure 2).

Universal interventions, while commonly accessible to the whole population (or sometimes all members of a sub-section of society, for example, based on age group), if delivered on an opt-in basis are more likely to be used by those better off in society. For example, the NHS Health Check programme available to all people aged 40–74 years, does not always reach the people who need it the most, with programme generally benefiting those with better health and lower risks in the first place (Alageel & Gulliford, 2019). Furthermore, these individuals are likely to gain greater benefit from universal services which can as a result increase health inequality (NICE, 2012). This has implications for public health interventions that aim to reduce health inequalities and requires attention to be given to ways of implementing interventions to enable access and uptake to the full demographic of society.

Targeted programmes for individuals based on disadvantage or social exclusion can however be more difficult to implement and are argued to be often less cost-effective than universal programmes (NICE, 2012). For example, there is evidence that the provision of vitamins for young children and pregnant women is likely to be cost-effective when delivered on a universal basis, and not cost-effective when targeted based on receipt of qualifying income-related benefits or tax credits (NICE, 2014b; YHEC, 2015).

The decision to adopt a targeted or universal approach (or a combination) should be specific to the intervention and population of interest, and based on the evidence available about effectiveness, cost-effectiveness, and implementation.

Universal interventions delivered in schools setting have the benefit of being accessible to all rather than an opt-in basis. Advocates of MBPs applied in a universal prevention context argue that adopting a whole school approach helps overcome associated stigma around disadvantage and mental health which would be apparent through any efforts to target more vulnerable groups of students (Gouda, Luong, Schmidt, & Bauer, 2016).

The mindfulness literature highlights that MBPs have elements to target both universal and specific vulnerabilities (Williams, 2008). Many MBPs are tailored to enable individuals to become aware of shared general tendencies towards suffering, otherwise referred to as 'universal vulnerabilities' and identify 'specific vulnerabilities' that make individuals more likely to develop ill-health or disability. For example, MBCT includes a core element of mental health literacy, and teaches individuals about the processes that can both trigger and maintain depression and how to respond skilfully to these.

MBPs as complex interventions

MBPs are complex interventions (Demarzo, Cebolla, & Garcia-Campayo, 2015); they consist of many interacting component parts, can be delivered in range of different ways (e.g., varied contexts and populations), and they have a potential impact on a wide range of outcomes. In addition, they may be delivered within settings that are considered to be complex systems (Shiell, Hawe, & Gold, 2008). The evaluation of complex interventions requires considerable methodological consideration at the research design stage. The Medical Research Council (MRC) produces guidelines to inform the development, evaluation and implementation of complex interventions (Craig et al., 2008). The guidance provides a framework of steps and highlights the role of early research trials including both pilot and feasibility trials before full evaluations that can determine the effectiveness and cost-effectiveness can be conducted. Recent guidance also highlights the need for process evaluation to be embedded within trials evaluating the effectiveness and cost-effectiveness of complex interventions (Moore et al., 2015). There have been calls for more focus on economic outcomes with methodological rigor for MBPs (Edwards et al., 2015). Chapter 6 of this thesis discusses economic evaluations embedded into the complex interventions framework.

Economic theory informing methods of economic evaluation

When considering mental health services there is almost always a discrepancy between the demand for treatments and the available supply (Beecham & Knapp, 2001). Advances in technology and treatment innovations both contribute to an ageing population and place greater demands on already limited health care resources (Bevan Commission, 2011). The National Health Service (NHS) is under increasing pressure to allocate resources more productively (increasing efficiency) whilst still retaining its foundations of equity in access to health care (Department of Health, 2010). Health care resources,

which include doctors, nurses, drugs and so on, have a limited supply; there is no new money and therefore it is necessary to make choices.

Positive and normative economics: the roles of the health economist

There is a distinction in the foundations of economic analysis between positive economics and normative economics. Positive economics focuses on describing outcomes and predicting behaviours, for example exploring the relationship between two variables. Normative economics relies on value judgements, it is prescriptive in nature and provides information about the desirability of one option over another (Morris et al., 2013). In considering the appropriate methodology to use in economic evaluation, it is necessary to acknowledge that 'normative tensions' exist, i.e., that there are disagreements about what approach to take and why. The health economist is therefore required to appreciate both a positive and normative perspective, providing dispassionate evidence to inform decision makers; and yet they are faced with many choices themselves including those around how benefits and costs should be measured and valued (Culyer & Wagstaff, 1993).

When considering the ethical distribution of health care there are contrasting arguments based on principles of utilitarianism, delivering the greatest good for the greatest number (equality); or based on the egalitarian principle with distribution of goods in consideration of 'fairness' based on needs (equity) (Culyer & Wagstaff, 1993). It is the latter approach that the National Health Service in the UK is founded on. However, equity is rarely considered in evaluations of health technologies (Culyer, 2012). Savulescue and colleagues (2020) highlight that "utilitarianism requires consideration of the probability of success, length, and quality of life. Utilitarianism is at the heart of the NHS and the allocation of medical resources. The quality-adjusted life year (QALY) used by Clinical Commissioning Groups (CCGs) is a measure of the utility of medical treatments. It is a year of life adjusted by its quality. The cost per QALY of £20 000 to £30 000 limit is a utilitarian, not egalitarian, limit" (Savulescu, Cameron, & Wilkinson, 2020, p. 11). The NHS in the UK like many other health care systems, balances this tension between egalitarian and utilitarian approaches, while retaining its egalitarian foundations through continued provision of a universal, free at the point of access health care system, it has also embedded utilitarian systems which involve the distribution of resources that maximises utility (Gibbard, 1982).

Alternative approaches based on equity principles have more recently appeared in consideration of the rationing of ventilators in the COVID-19 pandemic and in raising the willingness to pay thresholds for high cost orphan drugs to treat rare diseases (Savulescu et al., 2020). By contrast, societal preferences indicate that very high spending on specific need is not always supported (Bourke, Plumpton, & Hughes, 2018; Linley & Hughes, 2013).

Welfarism

Welfarism is defined as a normative approach, where the primary function is to determine the relative social desirability of any set of arrangements in order to devise a strong decision rule to optimally allocate resources (Morris et al., 2013). Welfarism solely considers the outcomes and values of an individual, noting that individuals are the best judge of their own utility and that societal welfare can be the collective sum of all individuals' utility. In resource allocation, it is necessary to make utility trade-offs, and this requires a value judgement. Paretian analysis (underpinned by the 'Pareto principle') provides a framework for making this value judgement and enables the aggregation of individual preferences or utility in order to generate total societal welfare (Gibbard, 1982). A 'Pareto improvement' occurs when resource allocation results in the improvement of at least one person's utility, without reducing the utility of another. An allocation of resources becomes 'Pareto optimal' once no further improvements in utility can be achieved without resulting in a reduction in utility elsewhere. Where a dis-utility occurs it is no longer possible to use the Pareto principle to rank states and 'Pareto non-comparability' occurs. Kaldor-Hicks criterion and compensation tests can be applied in these cases where the worse off party can be hypothetically financially compensated (Bostani & Malekpoor, 2012). The application of Welfarism relies on cost-benefit analysis, where utility and costs are given a monetary value. Welfarism has faced significant criticism particularly in that the underpinning 'consumer choice theory', which states that individuals make rational choices in pursuit of the greatest utility (utility maximisation) (Levin & Milgrom, 2004). This is arguably not relevant to health markets, particularly where people may have limited information to make informed choices (Hanoch & Rice, 2011; Levin & Milgrom, 2004). It has further been argued that utility is a poor measure of individual wellbeing as it fails to consider individual differences (Sen, 1999).

Non-welfarism and extra-welfarism

Non-welfarism is a normative approach that rejects the welfarist focus on maximising individual utility alone. One form of non-welfarism is referred to as extra-welfarism. Extra-welfarism adopts a broader approach and supplements individual utilities with additional information about other factors. In extra-welfarism the societal objective is to maximise health output rather than maximising societal utility (the goal of welfarism). Cost-effectiveness analysis and cost-utility analysis are the analysis techniques used within the extra-welfarism paradigm.

Forms of economic evaluation and perspectives of analysis

There are several forms of economic evaluation analysis routinely used in health economic evaluation. These are most commonly cost–benefit analysis, which measures both costs and benefits in monetary terms; cost-effectiveness analysis, which measures outcomes in some appropriate natural unit,

commonly the primary clinical outcome of a trial; cost-utility analysis, which measures benefits in a universal unit of health gain, such as the quality adjusted life year (QALY); and cost-consequence analysis, which compares costs with a full range of disaggregated outcomes.

In consideration of the most appropriate method of economic evaluation it is necessary to first determine the perspective of the evaluation and identify which costs and benefits are important and merit inclusion in the study. In the UK NICE recommend economic evaluations of clinical intervention adopt a NHS and personal social services (PSS) perspective, with an appropriate range of costs and benefits selected to be most relevant in this context. In non-clinical settings, such as schools and workplaces, it is necessary to consider an alternative to the NHS perspective and adopt a wider perspective which extends across multiple public sectors which are likely to share a stake of investment in the range of potential costs and benefits (Edwards et al., 2015; Edwards, Hounsome, Linck, & Russell, 2008; Walker, Griffin, Asaria, Tsuchiya, & Sculpher, 2019).

Given the argument that "health is created largely outside the health sector" (de Leeuw, 2017, p. 1), health promotion is not the responsibility of the health sector alone but must be embedded into public policy and requires 'intersectoral action'(Jackson et al., 2006; Kumar & Preetha, 2012). A societal perspective or multi-agency public sector perspective adopts a broader approach with a wider range of costs and benefits (Edwards & McIntosh, 2019). It can be useful to monitor shifts between sectors (Byford & Raftery, 1998).

Cost-effectiveness, cost-utility analysis, QALYs and the EQ-5D

In cost-effectiveness analysis, one or more new interventions are compared against an existing treatment (e.g., standard of care) in terms of both effect and costs. The cost-effectiveness plane depicted in Figure 4 (Petrou & Gray, 2011) shows this dual outcomes comparison with the existing treatment occupying the center of the graph and the new treatment(s) plotted to indicate whether it is to the right or left (more or less effective), and above or below (more or less costly).

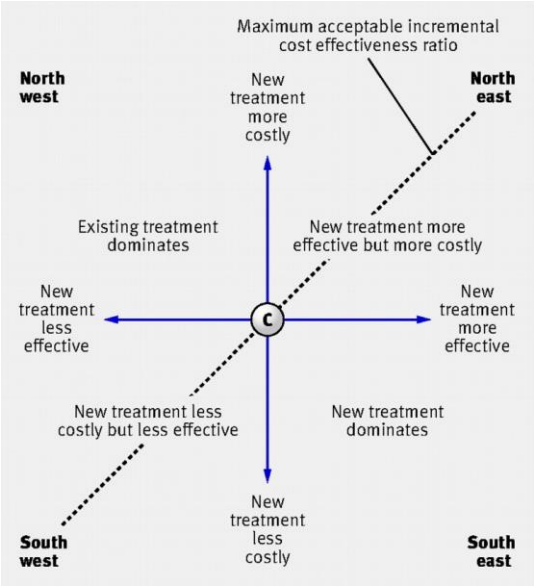


Figure 4: Incremental cost effectiveness plane (Petrou & Gray, 2011)

The four quadrants of the cost-effectiveness plane indicate how the new treatment(s) performs in relation to the comparator (e.g., standard care), the south east quadrant shows an intervention which has lower costs and is more effective making it the economically 'dominant' treatment; while the north west quadrant shows the opposite, with the new intervention costing more with less effectiveness than standard treatment; the new intervention is 'dominated' by standard care (Cohen & Reynolds, 2008). The north east quadrant indicates a new treatment which has improved clinical effectiveness however this comes at an increased cost. This requires judgements to be made and an incremental cost-effectiveness ratio to be calculated to assess whether the costs of these benefits are likely to be acceptable (Cohen & Reynolds, 2008).

When evaluating the cost-effectiveness of two treatments the CE ratio is calculated by dividing the difference in costs by the difference in effect (see Equation 1). Where C_1 is the cost of treatment using the new treatment, C_2 is the cost of regular standard treatment and E_1 and E_2 is the effectiveness of the respective treatment.

$$ICER = \frac{C_1 - C_2}{E_1 - E_2}$$

Equation 1: ICER calculation

In CEA the choice of effectiveness outcome can vary considerably from one study to another, with the measure of effect selected to be appropriate for the condition or population of interest. Although some limited comparisons have been demonstrated through the use of ICER league tables, it has been argued to raise challenges for decision makers who are required the make meaningful comparisons across diverse conditions (Mauskopf, Rutten, & Schonfeld, 2004; Weintraub & Cohen, 2009).

Cost-utility analysis, a subset of cost-effectiveness analysis, uses QALYs as the measure of benefit. NICE recommends that in the evaluation of new technologies health effects should be expressed in QALYs (NICE, 2013a). The QALY is an index of the combined gains in additional years of life gained from a medical or other intervention (a reduction in mortality), adjusted in some way to reflect health-related quality of life (a reduction in morbidity) (Robinson, 1993). Figure 5 depicts the QALYs gained from a treatment compared with no treatment in terms of both quality and quantity of life (Pettitt et al., 2016). Combining both quantity and quality of life generates a single index value and forms part of the utility concept that has foundations in welfare economics and utilitarianism. QALYs can be compared across conditions and time-points making it useful for decision makers considering the best use of limited resources.

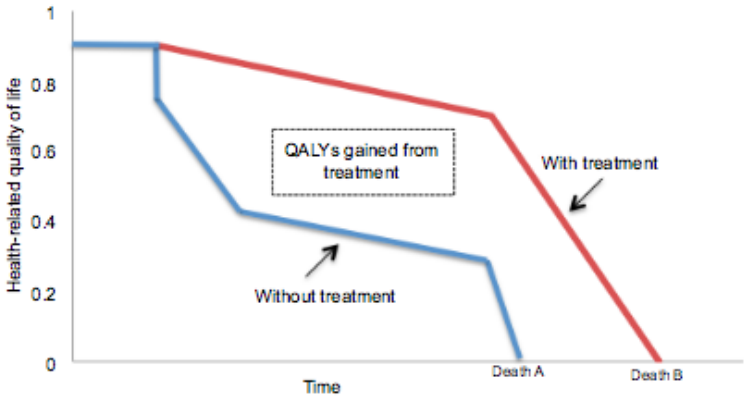


Figure 5: Chart showing QALYs gained from a treatment adapted from Pettitt et al., (2016).

NICE recommends the EQ-5D™ self-report outcome measure be used as the preferred measure of health-related quality of life in adults (NICE, 2013a). The EQ-5D is a measure of Health Related Quality of Life (HRQoL) which is both standardised and validated (van Agt, Essink-Bot, Krabbe, & Bonsel, 1994). As a generic measure rather than disease specific it is applicable and comparable across a wide range of health conditions and treatments. The EQ-5D provides a profile description of the health of an individual and is used to calculate a single index value or utility for each health state. NICE recommend that societal preferences derived using a choice based method such as time-trade off (TTO) should be used in the calculation of utilities (NICE, 2013a). It is from these public preferences, which indicate how much individuals value a particular hypothetical improvement in health (over another), that the health profiles can be appropriately weighted and converted from EQ-5D profiles into utility values. The EQ-5D utility scores can then provide the HRQoL gains that are required in the calculation of QALYs for cost-utility analysis of new health technologies.

QALYs are considered to be particularly appropriate for clinical evaluations where a threshold is relevant for a funding decision as in the case of NICE in the UK (NICE, 2012). “Every country has a limit on how much it spends on a treatment” (Savulescu et al., 2020, p. 3). The willingness to pay threshold for what

is considered reasonable varies considerably from nation to nation and is not always explicit. In the UK the NICE threshold of £20,000 to £30,000 per QALY gained is generally accepted to be the maximum willingness to pay for the additional benefit, with few exceptions as highlighted earlier. To aid interpretation of the ICER and to investigate the probability that the intervention is economically acceptable at a range of willingness to pay thresholds, results can be plotted on a cost-effectiveness acceptability curve (CEAC). This is most commonly conducted through bootstrapping resampling of the study results to help establish the uncertainty and to indicate levels of confidence in the cost-effectiveness ratio estimate. See Figure 6 for an example CEAC depicting the probability of internet-delivered cognitive behaviour therapy (iCBT) being cost-effective compared with a waitlist control condition at 8 weeks plus additional regression-based extrapolated scenarios at 6, 9 and 12 months (Richards et al., 2020). "Over 8-weeks the probability of cost-effectiveness was 46.6% if decision makers are willing to pay £30,000 per QALY, increasing to 91.2% when the control-arm's outcomes and costs were extrapolated over 12-months" (Richards et al., 2020, p. 85).

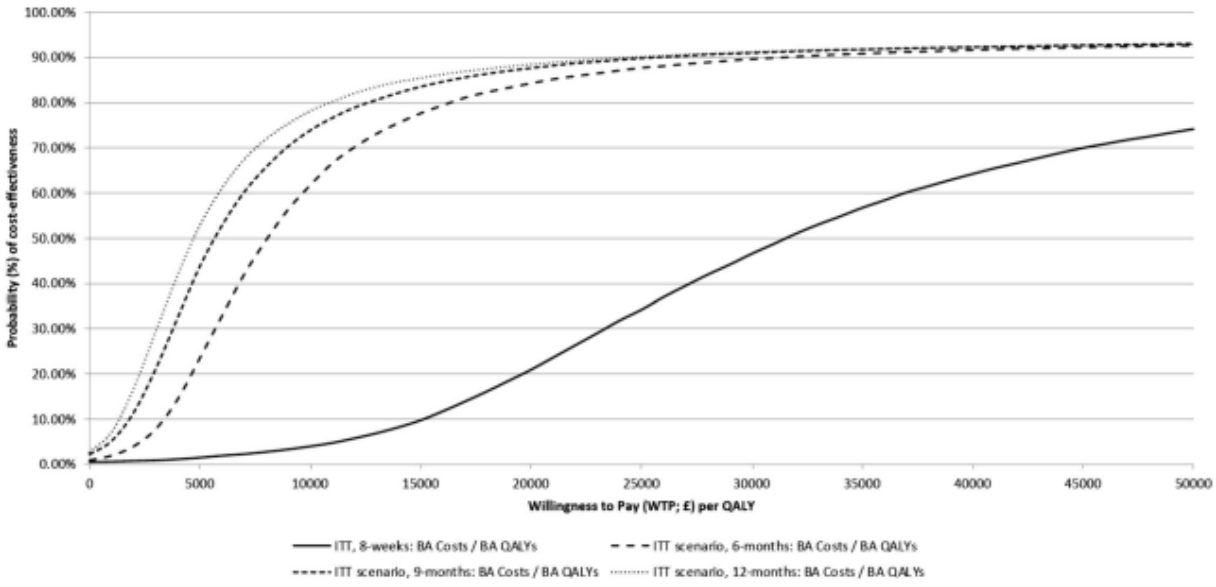


Figure 6: Cost-effectiveness acceptability curve example reproduced from Richards et al. (2020).

Opponents of the QALY system highlight that compared to short-term life-saving treatments, preventative or long-term interventions generally result in lower QALY values as the current calculations place too much emphasis on increasing length of life rather than interventions that improve quality of life (Pettitt et al., 2016). This has implications for condition specific evaluations such as in mental health where treatments are commonly focused on life enhancing outcomes, or in public health where preventative interventions result in outcomes that are commonly achieved over a longer time horizon (Edwards, Charles, & Lloyd-Williams, 2013; Pettitt et al., 2016). There are important equity considerations which traditionally may not be factored into economic evaluations using QALY gains (Whitehead & Ali, 2010). It has been advocated that an adapted QALY approach, commonly termed the

'super QALY', that builds on extra-welfarism and is weighted on equity considerations may be more appropriate for evaluating public health interventions (Anand & Wailoo, 2000; Johannesson, 2001).

Cost-benefit, Social Return on Investment and Cost-consequence analysis

Cost–benefit analysis and cost-consequence analysis have been implicated as useful tools for tackling the methodological challenges of evaluating complex public health interventions, offering a way of capturing a full range of benefits, to the individual, family, setting and wider society (Cordes, 2017; Drummond, Sculpher, Claxton, Stoddart, & Torrance, 2015; Drummond et al., 2007; Edwards et al., 2015; Kelly, McDaid, Ludbrook, & Powell, 2005; Weatherly et al., 2009). Cost-benefit analysis aims to weigh up a full range of costs and benefits, quantifying all outcomes in the same unit, most commonly in monetary terms, so that they can be weighed up on a 'social accounting framework' balance sheet (Cordes, 2017). Cost-benefit analysis aims to include both tangible and intangible costs and benefits. At its simplest, the decision rule for cost-benefit analysis is commonly considered to be in positive net-benefit terms, with the sum of social present value benefits outweighing the sum of present value costs, and when expressed as a benefit-cost ratio it is greater than 1. However, as decisions need to be made on how best to spend scarce resources, and it is necessary to choose between various investments, the decision rule in simplest terms would likely favour the higher cost benefit ratio. A criticism of CBA is that some items of importance are difficult to measure and quantify in monetary terms, leading some to argue that this may lead to a bias in favour of activities where outcomes are readily monetized (Cordes, 2017).

Unlike cost-benefit analysis where the focus is on positive net benefit, with 'profit' being a greater amount of present value benefits than the present value costs, return on investment analysis aims to establish the total financial returns as a 'payback' on the initial financial investment. Social Return on Investment (SROI) considers the 'triple bottom line' of economic, social and environmental benefits (Banke-Thomas, Madaj, Charles, & van den Broek, 2015). SROI has been compared with traditional cost-benefit analysis and is commonly seen as an extension to it which includes a broader set of outcomes including environmental and socio-economic factors (Banke-Thomas et al., 2015). Financial proxies are applied to complex outcomes (Banke-Thomas et al., 2015). SROI considers the 'impact' of interventions, which is becoming an increasingly important factor in determining the value for money of public health interventions (Banke-Thomas et al., 2015). While becoming increasingly popular, it is well recognised that there is little methodological consistency in SROI methods (Fujiwara, 2015). This limits the comparison across SROI estimates, particularly across sectors when methods may vary sufficiently to impact on the results (Lingane & Olsen, 2004; Nielsen, Lueg, & Van Liempd, 2021).

Cost-consequence analysis (CCA) has been recommended for the evaluation of public health interventions (NICE, 2013a). It offers a disaggregated approach to presenting costs and benefits which has been argued may be more acceptable and useful for decision makers (Hartfiel & Edwards, 2019; Hunter & Shearer, n.d.; Mauskopf, Paul, Grant, & Stergachis, 1998). A disadvantage of CCA is that there is limited guidance around how different outcomes included within CCA should be weighed against each other (Hartfiel & Edwards, 2019). CCA is a subjective process, with individual decision makers required to develop their own system to interpret the results, while this allows for the selection of components most relevant to their context, these results may not be generalisable to other contexts (Hartfiel & Edwards, 2019; Mauskopf et al., 1998).

Capabilities approach

Public health interventions often have a broad set of outcomes that go beyond health. These wider outcomes may also impact on multiple sectors including social care and education (Coast, Kinghorn, & Mitchell, 2015). It is therefore important to consider a broad approach to outcome measurement that goes beyond health and utility maximisation and ensure that non-health benefits can be captured in evaluations. The capabilities framework, while related to extra-welfarism, offers a broader approach that focuses on individuals' freedom and capability to function, rather than their actual level of functioning (Sen, 1999).

Several measurement tools have been developed including capability outcome measures for older people (Flynn, Chan, Coast, & Peters, 2011), public health (Lorgelly, 2015), mental health (Simon et al., 2013), and more routinely for a general adult population (Al-Janabi, N Flynn, & Coast, 2012). NICE and SCIE advocate the use of capability outcome measures for economic evaluations within social care (Francis & Byford, 2011; NICE, 2013b).

While the capability approach is increasingly being used within the field of health research, there appears to be large variation in the methods that are applied (Mitchell, Roberts, Barton, & Coast, 2016). There are methodological considerations that are involved in translating the capability approach from its conceptual roots to a consistent and meaningful methodology to be used within health economic evaluation (Coast, 2019; Coast et al., 2015). While capability measures such as the ICECAP-O (Flynn et al., 2011) have been suggested for use in economic evaluation in the UK, there is wide variation in the approach and little consensus about a decision rule that might apply (Proud, McLoughlin, & Kinghorn, 2019). To date the most promising option put forward for the purpose of use in evaluations that may influence decision making appears to be the measurement of minimum or sufficient capability, operationalised as Years of Sufficient Capability (YSC; Mitchell, Roberts, Barton, & Coast, 2015). Implications of this approach are discussed further in chapters 4 and 6.

Methodology for the economic evaluation of MBPs

The economic evaluation of MBPs should be informed by current best practice in the evaluation of both public health interventions and clinical interventions. Current guidance for the evaluation of public health interventions highlight methodological considerations such as whether QALYs are inadequate in a public health setting (Edwards, Charles, et al., 2013). Public health economics guidelines may be useful for determining the appropriate design of methodology for evaluating MBPs which aim to bring about population benefit through preventative action in mental health. There may be benefits from incorporating equity considerations in public health intervention economic evaluations (Cookson, Drummond, & Weatherly, 2009).

Many public health interventions have been shown to provide good value for money as either cost-effective interventions or cost-saving in the long term (Owen & Fischer, 2019). It has however been disputed whether public health interventions should always demonstrate net cost savings, however it is important to note that clinical interventions are rarely asked to demonstrate more than being simply cost-effective compared to alternative treatment (Edwards, Charles, et al., 2013; Woolf, Husten, Fielding, & Sanchez, 2009).

Role of pilot and feasibility studies in the economic evaluation of public health

As complex interventions, there is still a lot to be learnt about the potential benefits and costs of MBPs. Translational research as a concept has been widely used and applied in scientific literature for more than a decade. It is most broadly and simply defined as research steps to take discoveries “from the bench to the bedside and back again” (Fort, Herr, Shaw, Gutzman, & Starren, 2017, p. 60). This thesis sets MBP research within this translational research context, which is discussed further in Chapter 6. More translational research is needed to first develop early-stage studies with embedded health economics which can help shape the methodology for future clinical trials research and subsequent implementation.

MRC complex interventions guidelines state that economic evaluations are an important part of the full evaluation process of complex interventions (Medical Research Council, 2008). Methodological consideration is needed to consider the appropriate design of the economic component in an evaluation of a complex intervention and MRC guidance suggests that “it is best to involve health economists early in the planning of design of the evaluation, so that the economic evaluation is fully integrated” (Medical Research Council, 2008, p. 28). Beginning with basic clinical science studies, progressing to feasibility and pilot studies before definitive randomised controlled trials (RCTs) and finishing with implementation into routine clinical practice. Health economists have argued that “economic evaluation should be

iterative, generating progressively firmer estimates of cost-effectiveness and helping to maximise the efficiency of health care [research and development]" (Sculpher, Drummond, & Buxton, 1997, p. 1).

While feasibility and pilot studies do have differences, there are often parallels to be drawn and many references in the literature use these terms interchangeably (Arain, Campbell, Cooper, & Lancaster, 2010). Ultimately pilot and feasibility stage studies are often equivalent to a phase 1 or phase 2 clinical trial, sometimes referred to as proof of concept studies in pharmaceutical research (Arain et al., 2010). In pilot and feasibility research, various research aims exist (Arain et al., 2010). Aims of research should include first defining and then refining what data to collect and how, rather than analysis of 'outcomes' (Arain et al., 2010). However, many small randomised controlled trials are labelled as pilot as a result of their small sample size alone, with the research objectives containing inappropriate emphasis on hypothesis testing rather than appropriate pilot and feasibility research objectives (Arain et al., 2010).

Feasibility studies may also have other aims to further test the intervention(s), e.g., in human participants, to help establish its acceptability in addition to developing data collection tools. Pilot studies will often resemble a small version of a definitive phase 3 clinical trial, in fact many RCTs may embed an internal pilot into the larger study design to help assess whether the study should be halted or continue if certain progression criteria are met. External pilots can help evaluate the processes of a main trial, ensuring recruitment, randomisation and treatment all work as planned before commencing large RCTs (Arain et al., 2010; Gannon, 2017), and provide useful information about the necessary sample size for a main trial (Whitehead, Julious, Cooper, & Campbell, 2015).

Pilot and feasibility studies are particularly important where there may be significant uncertainty around the appropriate design of an economic evaluation, for example, in establishing the costs associated with new (and sometimes) existing treatments (Drummond & Coyle, 1998). Embedding health economics early can help inform the appropriate range of resource use data to be collected, the methods of data collection and the length of follow-up time (Coyle, Davies, & Drummond, 1998; Gannon, 2017). Early studies can develop and test data collection forms such as service utilisation questionnaires (SUQs) (Chisholm et al., 2002, 2000), which collect data on frequency of resource use to help to identify which key items of data collection are required in future research (Coyle et al., 1998). Determining appropriate outcome measures of quality of life assessment can be an important objective of feasibility trials, with generic measures such as the EQ-5D for the calculation of QALYs being compared with an alternative such as disease specific measures that can be mapped on to utility values (Gannon, 2017).

In all studies there are competing aims for both data collection comprehensiveness and concerns over data burden. In clinical trials there are often many secondary outcomes of interest; therefore, only collecting the outcomes that are really needed is a matter of both efficiency and ethics, particularly in

terms of not adding unnecessary burden on patient participants. Coyle and colleagues (1998) highlight that when designing an economic evaluation "decisions relating to which data should be collected alongside a trial and the length of follow-up are dependent both on the need to measure all relevant resource use and consideration of the opportunity costs of data collection. Thus, there is a need for a balance between comprehensiveness and data burden" (Coyle et al., 1998, p. 9). Resource use that does not differ between patient groups may not be required to be collected as part of a definitive trial while resources that are consumed by patients in just one treatment group need to be identified. Pilot studies provide an opportunity to identify resource items that were not expected to be used by the patients but could be important in future research (Coyle et al., 1998; Drummond & Coyle, 1998).

In addition, new data collection methods should be quality tested for accuracy in validity, consistency, reliability, and completeness, for example in the response rate of the forms assessed (Coyle et al., 1998; Gannon, 2017). If criteria are not met data collection forms can be adapted or designed and then repiloted. "If the pilot study indicates that there may be large amounts of missing data due to incomplete responses or nonresponse, consideration should be given to alternative designs and methods of data collection. A high percentage of missing data may result in biases in the data recorded, which may not be random between the study groups. This could lead to invalid results" (Coyle et al., 1998, p. 142).

According to Weatherly and colleagues (2009) who set out key recommendations for assessing the cost-effectiveness of public health interventions "there is an urgent need both for pilot studies and more methodological research" (Weatherly et al., 2009, p. 92). Chapter 6 of this thesis reflects on the lessons learnt from two early-stage evaluations (presented in Chapter 4 and 5) to build on the current 'toolkit' of resources available to health economists designing future evaluations of complex interventions.

Rationale for this thesis

Whilst MBPs have been applied in various sectors with various populations and the evidence of their effectiveness has been explored in many evaluations, the question of whether they can provide value for money in a context of limited public resources has not been explored as thoroughly. While MBCT has been recommended by NICE for the management of recurrent depression (based on a mixed economic evidence base), this does not translate to recommendations for public investment in other MBPs. More evidence on the cost-effectiveness of MBPs delivered to other targeted groups (such as vulnerable groups of individuals at increased risk of depression e.g., cancer survivors) or as a universal prevention initiative (e.g., in a school setting) is required.

Being recommended in NICE guidance also does not necessarily translate into the intervention being available on the ground. Despite high popular public and media interest and application within many

different settings, along with national recommendations in the UK, implementation of MBCT for the management of depression has been limited and it is unlikely to be sufficient to meet population demands (Kuyken, Crane, & Dalgleish, 2012; Rycroft-Malone et al., 2014). There are many issues which influence uptake and implementation (Rycroft-Malone et al., 2004). One potential barrier is the cost of the intervention (Chaudoir, Dugan, & Barr, 2013) and the available evidence on cost-effectiveness (Edwards et al., 2015). Consolidating the current evidence base on the cost-effectiveness of MBCT for depression management and other MBPs, may provide a useful resource for policy makers considering investment in public mental health promotion.

Preventative intervention can be effective at decreasing avoidable future health and social care costs; however, whether interventions may be best applied at a universal level or at a targeted level has not been explored in the case of MBPs. Future research could explore whether effective preventative MBPs are a better use of scarce resources than investments in treatments of mental health problems. This thesis aims to use feasibility studies to investigate the appropriate methods for the economic evaluation of MBPs as complex prevention interventions.

Thesis methods: Structure and objectives of this thesis

The structure and research objectives of this thesis are displayed in Figure 7. This introduction chapter has outlined key background literature relevant to the health economics evaluation of MBPs. This thesis adopts a multi-method approach to addressing the objectives of this PhD.

This thesis spans multiple disciplines (including public health, psychology, and health economics) and is underpinned by several epistemological frameworks. Psychology stemmed from sciences that are hypothesis driven and health economics which is question driven with a view to generate new 'logical knowledge' through analysis of primary data using a range of scientific methods (Ivlev & Ivlev, 2018). The 'positive' paradigm states that events can be measured and analysed (Kaboub, 2014), for example using scientific research methods such as clinical trials (often considered to be the 'gold standard' scientific method for evaluating health intervention). Research that leads to published peer reviewed 'empirical knowledge' to guide our understanding of reality. In health economics research aims to answer 'normative' questions about what the best use of scarce public resources is (McGuire, Parkin, Hughes, & Gerard, 1993). "The health economist must be objective and dispassionate and want to find out whether an intervention is effective and cost-effective, regardless of whether the results of the trial or economic evaluation end up positive or negative" (Edwards et al., 2015, p. 497). This is all set in the context of an evidence-based practice agenda prominent in a UK health care setting and a growing area of attention in other public sectors (Kennell, 1999).

Public health interventions can be complex and research to generate knowledge is not always as highly controlled in clinical trials as other medical evaluations (Long, McDermott, & Meadows, 2018). Following a secondary 'pragmatism' epistemology, qualitative methods and process evaluation are used to help make sense of these complex evaluations and offers real-world experience of patients (Hall, 2013; Long et al., 2018; Moore et al., 2015). Where 'early stage' research is conducted in pilot and feasibility trials, there can be valuable knowledge generated; however, appropriate caveats are needed with full transparency around limitations. In summary, through this thesis I adopt a mixed-methods approach to align with both positivist and pragmatist epistemologies, exploring through a series of empirical studies to help evaluate MBPs as a complex public health intervention.

Chapter 2 reports on a systematic review of published literature which outlines both existing and upcoming economic evidence for MBPs from a societal perspective, considering both public and private sector delivery of MBPs to a range of population and clinical groups.

Chapter 3 presents the conduct of a multi-programme micro costing evaluation of MBPs to assess the cost of delivering MBPs in different settings and to different populations. While MBP implementation is expanding there are barriers to implementation and there is a paucity of information available on critical issues such as the true cost of delivering programmes. Obtaining accurate cost information will enable further economic analysis of MBPs as a way of supporting and promoting good mental health and the implementation process. Future research with built-in measures of costs and resource use should enable robust economic evaluations and help inform national decision makers and local commissioners and managers who hope to successfully implement services. This empirical study was conducted between 2013 and 2014, I designed and collected data from a range of MBP practitioners about micro-level costs of delivering MBPs.

Chapter 4 reports on research on Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) evaluated through a randomised feasibility trial. This empirical study was funded by Tenovus Cancer Care, I designed and conducted the research between 2011 and 2015 to explore the feasibility of the research design, and to pilot the methods to explore whether MBCT-Ca is a cost-effective intervention compared with usual care at improving cancer patients' health and wellbeing. A range of costs and benefits relevant to a societal perspective are collected to explore the impact of MBCT-Ca as targeted intervention in supporting cancer survivors cope with the anxiety and stress related to cancer and to contribute to the prevention of depression. Patients' willingness to pay is evaluated and the appropriateness of the health economics tool kit (for example, condition specific and generic utility measures) is considered. Further methodological considerations for health economists wishing to evaluate the cost-effectiveness of targeted MBPs alongside randomised controlled trials or as part of routine service evaluation are discussed.

Chapter 5 reports on a concurrent economic evaluation alongside a pragmatic non-randomised study with matched control group of a school-based mindfulness curriculum for Sixth Form students (aged 16-18 years), delivered by trained in-house classroom teachers or assistants. The health economics feasibility study (embedded within an empirical study conducted in 2015) piloted methods for a primary cost-utility analysis using the EQ-5D-5L mapped to EQ-5D-3L, as a source of utility weights for the calculation of QALYs. Methods for a secondary cost-effectiveness analysis using GHQ-12 as a screening tool to identify cases of depression are discussed. As the assigned research officer for the health economics analysis, I refined the analysis plan, cleaned, and scored the economic data and completed the pilot analysis written up as presented in this thesis (Chapter 5).

Chapter 6 discusses how well the health economic toolkit works for the evaluation of MBPs and outlines what lessons can be learnt from the pilot and feasibility health economics research, with the aim of helping to address the challenges of evaluating complex interventions. This thesis highlights the need for essential pilot and feasibility studies to first establish the foundations of research into the cost-effectiveness of new treatments and preventative interventions such as MBPs. This chapter builds on two conference workshops that I co-facilitated in 2013 to discuss the methods of economic evaluation for MBPs with stakeholders, in addition to a co-authored journal article published in 2015, updated to reflect current thinking and considerations for feasibility studies.

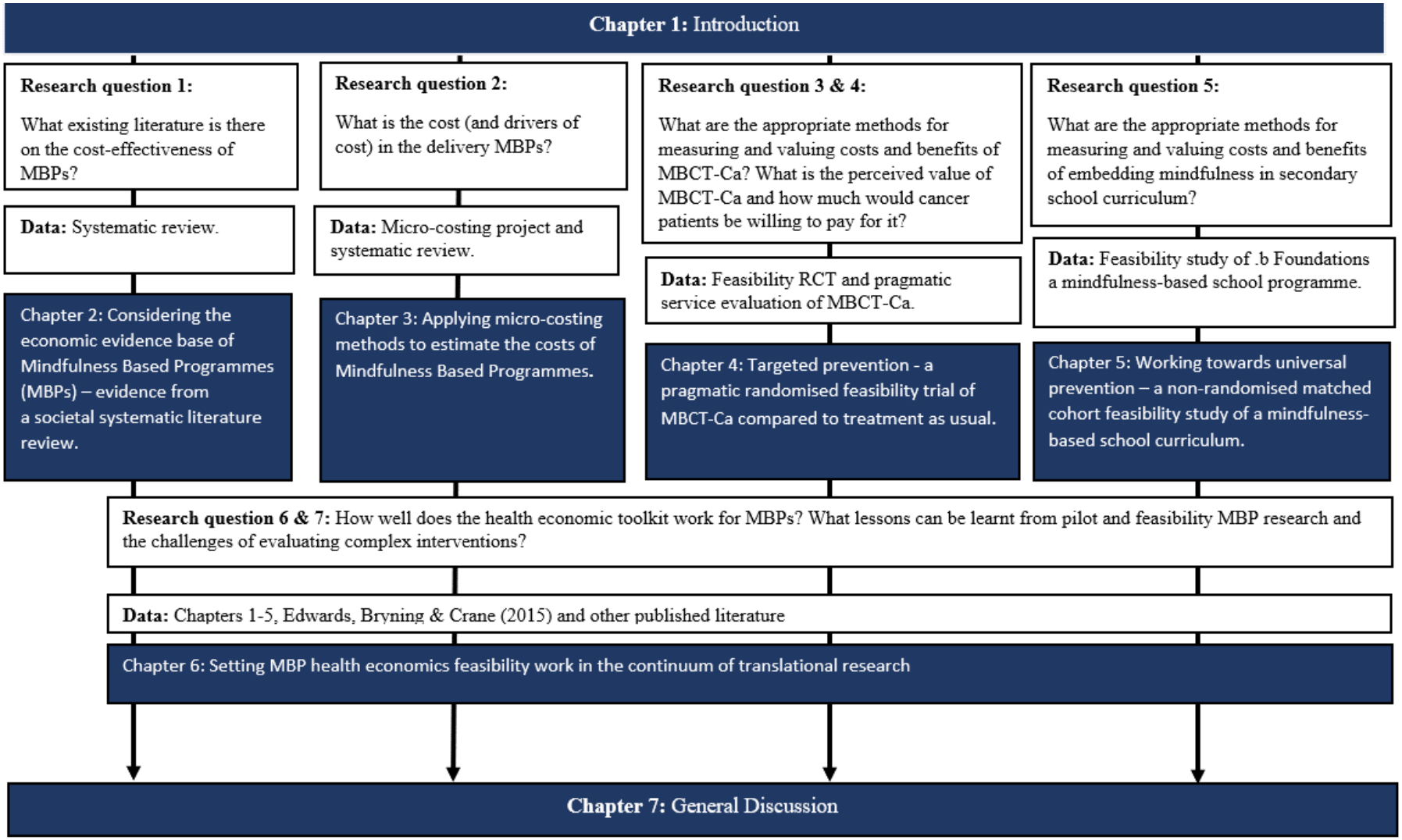
In conclusion this thesis explores the key methodological considerations for evaluating MBPs as complex interventions, commonly delivered within complex systems, from a health economics perspective, with a particular focus on the MBP economic evidence base to date across sectors (Chapter 2); the approach to costing of MBPs (Chapter 3); the role, design and conduct of MBP economic evaluation pilot and feasibility research with examples of both targeted and universal programme delivery (Chapters 4 & Chapter 5); and an exploration of the appropriate methods and outcome measures to capture a full range of costs and benefits (Chapter 6). This thesis concludes with a general discussion (Chapter 7) which provides an overview of the main thesis findings in relation to the original thesis research questions, practice and policy implications, comparisons with existing literature and areas for future research. The discussion chapter concludes with the original contributions of the thesis.

Thesis original contribution

This thesis consolidates the growing economic case for investment decisions in MBPs. There has been insufficient focus on the economic case for or against MBPs to date and little discussion about implementation of programmes without a robust evidence base to show they provide value for money, in the context of limited public resources. This thesis provides the first substantive review of MBP economic evaluations across public and private sectors and highlights lessons that can be learnt from

early economic evaluations to evaluate MBPs as complex interventions delivered within complex systems. This thesis sets MBP economic evaluation within the context of translational research framework to establish health economics research methods suitable to contribute to effective implementation of MBPs as public health prevention interventions across the life course. This thesis builds on the developing interest in precision public health, exploring targeted and universal delivery of MBPs and aiming to aid the development of robust methodologies that can establish what provides value for money in the context of limited public health resources. Both QALY and capability outcome measures are used in this thesis research, providing a novel pilot of the capabilities approach to evaluating MBPs in the UK. The conclusions of this thesis and original contribution to the field of health economics and public health are discussed further in Chapter 7.

Figure 7: Structure of thesis and research questions



Chapter 2: Considering the economic evidence base of Mindfulness Based Programmes (MBPs) – evidence from a societal systematic literature review.

Chapter preface

This thesis was undertaken part-time over an extended duration (including two maternity leave periods) and has been updated throughout this time to reflect the rapidly evolving picture of economic evidence in MBP research. The initial stage of this thesis chapter involved a literature review to reflect the availability of research at the start of commencing this work. A systematic scoping review was then conducted to increase the comprehensiveness of the initial evidence captured; finally, this review has been updated to reflect more recent publications prior to the completion of this thesis. The systematic scoping review had very broad aims to gather a comprehensive picture of the current evidence-base of MBP research and address the research question of "What existing literature is there on the cost-effectiveness of MBPs?"

Chapter 2 reports on the systematic review of published literature which outlines both existing and upcoming economic evidence for MBPs, considering both public and private sector delivery of MBPs to a range of population and clinical groups. This chapter consolidates a broad literature base, which is interpreted and critically appraised to generate new knowledge about the current strength of the economic evidence base for MBPs, the methods of health economics used to assess MBPs, and the evidence in progress through an embedded review of trial registration records and published protocols, to indicate the direction of travel for MBP health economics research.

Chapter 2 Abstract

Mindfulness Based Programmes (MBPs) are complex interventions consisting of many interacting component parts: they can be delivered in a range of different ways (e.g., varied modes of delivery, contexts, and populations) often within complex systems, and they have a potential impact on a wide range of outcomes, including the prevention of poor mental health. The evaluation of complex interventions requires considerable methodological consideration throughout the whole research process. MBPs are increasingly delivered outside health care contexts to non-clinical populations. However, the economic evidence of cost-effectiveness has not kept pace with effectiveness studies. With increasing wide-ranging implementation and delivery of MBPs, it is necessary to consider the benefits and costs that may fall both within and beyond the health care sector, and that appropriately designed research studies are required to capture this. No societal perspective systematic scoping review has been undertaken previously. This systematic scoping review aims first, to map out the

economic evidence of MBPs across all sectors and second, to compare methods used to evaluate cost-effectiveness at various points in the evaluation process.

Methods

The protocol for this systematic review was registered on PROSPERO (2017 CRD42017074848) and search strategies and reporting methods conforming to the published PRISMA statement were undertaken. Seven electronic bibliographic databases including specialist economic databases, technology assessment databases and general medical /psychological literature databases were searched to identify studies that included an economic evaluation of an MBP published up until 19 April 2019. A critical quality appraisal of the evidence was conducted using questions adapted from standardised checklists including 1) a risk of bias tool for clinical trials; 2) economic evaluation checklists for clinical trials, economic models, and social return on investment studies; and 3) MBP intervention integrity checklist to assess reporting of fidelity.

Results

Twenty-five completed economic evaluations were identified. Fourteen of the studies were full economic evaluations where both benefits and costs were assessed, while eleven of the studies were partial economic evaluations, for example where only costs or a single economic outcome were considered. Cost-utility analysis was the most common form of economic evaluation, followed by cost-effectiveness analysis. Perspectives of analysis included societal, health care, employer, or patient, with many of the economic evaluations using more than one perspective in their analysis. The MBPs included Mindfulness Based Stress Reduction (MBSR), Mindfulness Based Cognitive Therapy (MBCT) and programmes which had been adapted to meet the needs of a specific patient population (e.g., adults with Attention-deficit hyperactivity disorder [ADHD]), or specific delivery context (e.g., an employment setting). In terms of clinical populations, the most common economic evaluation focused on MBPs for the management of depression (*N=6*) and cancer recovery (*N=3*). Economic evaluations of more novel clinical applications included medically unexplained symptoms (*N=3*). There were few non-clinical setting studies that included an economic evaluation, with employment being the most common (*N=3*).

Discussion

The number of MBP economic evaluations has grown in the last 10 years and more studies are in progress indicated by a review of study protocols and trial registrations. However, the methods used in economic evaluations very considerably and there is limited scope for comparison across studies, interventions, populations, and sectors. Many of the studies rely on relatively small sample sizes

and several assumptions are made about the potential longer-term benefits of MBPs beyond the comparatively short period of most clinical trials. Rigorous economic modelling may help control for some of the uncertainty highlighted through this systematic scoping review. However, further trial-based studies with embedded economic evaluations building on this evidence base are required, with greater transparency in methods through improved adherence to economic evaluation reporting standards such as the Consolidated health economic evaluation reporting standards (CHEERS) checklist. Recognising MBPs as complex interventions, further highlights the role for pilot and feasibility trials to help develop definitive trials with high methodological rigour. To date few published studies focus on pilot objectives for economic evaluations. Social return on investment (a type of cost-benefit analysis), may offer a methodology capable of measuring broader outcomes relevant to a wide range of stakeholders. However, greater consistency in the methodology and interpretation of the results is required. Health care resources used are considered in a large proportion of the economic evaluations of MBPs. Recognising the most common focus of the MBP as a health improving or illness-preventing programme may also have the secondary benefit of reducing health care resources used. MBPs are often promoted as preventative interventions, with benefits observed in the future, but few studies capture a longer-term follow-up or extrapolation beyond the length of clinical trial. The time horizons of the studies identified through this review may be too short to identify the future costs averted and/or benefits gained, and assumptions are made about whether observed benefits are sustained over time.

Introduction

In the UK, economic evaluations of health care interventions form a core part of health care decision making and priority-setting in public policy (NICE, 2012b). Mindfulness Based Cognitive Therapy (MBCT) (Segal et al., 2013) is recommended by the National Institute for Health and Care Excellence (NICE) for the prevention of recurrent depression (NICE, 2004b, 2009a, 2018). Although there has been a substantial increase in the number of evaluation studies of Mindfulness Based Programmes (MBPs) including MBCT and Mindfulness Based Stress Reduction (MBSR; Santorelli et al., 2017), which MBCT is derived from, the number of studies which have considered both the costs and benefits and included a concurrent economic evaluation is limited (Edwards et al., 2015). To ensure investment in interventions provides value for money, particularly in the context of scarce public resources, there needs to be robust evidence on both the effectiveness and the cost-effectiveness of these interventions. In the case of MBP evaluation the economic evidence has not kept pace with evidence of effectiveness. More recently, novel applications of MBPs have been developed for workplaces (Lomas, Medina, Ivtzan, Rupprecht, & Eiroa-Orosa, 2019; Lomas et al., 2017) and schools (McKeering & Hwang, 2019). These are often pitched as interventions to boost performance or preventative interventions building resilience to future stressors (Crane, 2017). Although not delivered in a health care setting these interventions still have potential impacts on individual's health.

There are many different types of reviews which can be used to synthesis existing literature to answer research questions (Grant & Booth, 2009). Scoping reviews have broadly been defined as "a technique to 'map' relevant literature in the field of interest" (Arksey & O'Malley, 2005, p. 20). Scoping reviews are relatively new however they are increasingly being use to explore topics which are diverse and where limited previous review work has been undertaken (Pham et al., 2014). This systematic scoping review adopts a societal perspective to begin to explore the economic evidence base for MBPs delivered in both public and private sectors. As there has been little focus on the economic evidence base for MBPs, this chapter intends to synthesise existing literature on MBP evaluations which include an economic evaluation, to address the broad question of what is currently known about whether investment in MBPs are a cost-effective use of scarce public resources in the UK.

A post-hoc update on similar studies

Two recent systematic reviews have been published (Duarte, Lloyd, Kotas, Andronis, & White, 2019; Feliu-Soler et al., 2018) between the commencement and completion of this systematic review presented in this chapter. These have helped to highlight the economic impact of third-wave psychological therapies including MBPs delivered within the health sector. The systematic review by

Duarte et al (2018) focused on interventions for mental health alone. However, the full extent of the economic impact outside of the health sector or across public sectors has not yet been evaluated. The systematic review by Feliu-Soler et al (2018) focused on randomised controlled trials alone, excluding evidence from early-stage evaluations (e.g., pilot and feasibility trials) to minimise bias.

Aims of this review

This chapter offers a societal perspective systematic scoping review across public and private sectors of published literature on the cost-effectiveness and return on investment of MBPs, delivered across a range of population groups and settings. Through identifying and synthesising the body of published economic evaluations this review will help establish whether the delivery of MBPs provides a cost-effective use of societal, public, or private resources.

This review builds on the foundation that MBPs are complex interventions (Demarzo et al., 2015): i.e. consisting of many interacting component parts, can be delivered in a range of different ways (e.g., modes of delivery), may be delivered within settings that are considered to be complex systems (Shiell et al., 2008), and having a potential impact on a wide range of outcomes. The evaluation of complex interventions requires considerable methodological consideration at each stage of the evaluation process from pilot and feasibility trials to definitive randomised controlled trials and eventually implementation studies (Moore et al., 2015). Therefore, all study types and stages have been included within the scope of this review to help build a whole picture of economic evidence to date and identify lessons that can be learnt from pilot and feasibility evaluations of MBPs. This review will identify and discuss key methodological considerations for the design and conduct of future economic evaluations of MBPs as complex interventions at various stages of the evaluation process, including study design, pilot and feasibility trials and randomised controlled trials.

This review provides the first substantive review of all published economic evaluations of MBPs delivered in any public or private sector (health care, social care, education, employment) to any population (i.e., not exclusive to mental health contexts). In this systematic scoping study the review will be used to assess the amount of literature, the population groups of interest and range of MBPs evaluated, the methods of economic evaluation used and emerging trends in the results to indicate whether MBPs are likely to be cost-effective interventions.

Methods

The systematic scoping review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement for studies that evaluate health care

interventions (Liberati et al., 2009; Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2009). Figure 8 shows an overview of the systematic review process using the PRISMA statement (see also Appendix 1: PRISMA self-assessment checklist). Details of the protocol for this systematic review (Bryning, Crane, & Edwards, 2017) were registered on PROSPERO (2017 CRD42017074848) and can be accessed at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42017074848

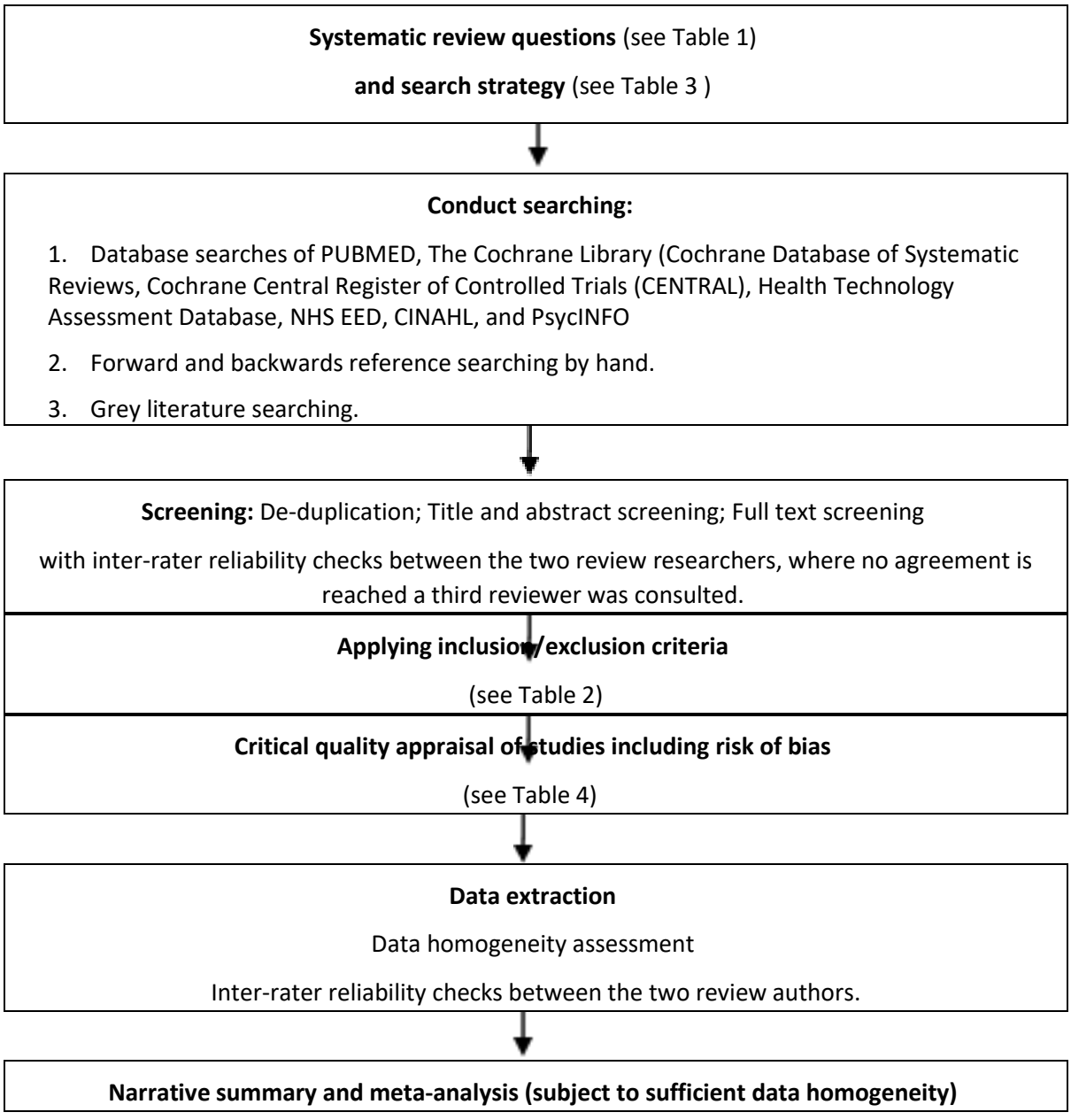


Figure 8: Overview of systematic review design using the PRISMA statement

Research question framework

The SPICE (Setting, Perspective, Intervention, Comparison and Evaluation) framework (Booth & Brice, 2003) was used to construct the search process and search terms directly from the review objectives by defining and focussing on the key attributes of the review topic (see Table 1).

Table 1: SPICE framework

Setting	Any setting including hospital, school, business/workplace, university, home, or community settings.
Population	Any population who has received the intervention of interest.
Intervention	Any MBP (specifically MBSR/MBCT or interventions largely based on or derived from these models).
Comparison	Any comparison of interest including Usual practice/usual care (UC); Active control; No control; Placebo.
Evaluation	Economic evaluation including cost-utility analysis; cost-consequence analysis; cost-minimisation analysis; cost-effectiveness analysis; Health care resource use and cost data; Health related quality of life; Return on investment; Incremental cost-effectiveness; Quality-adjusted life year gains

Eligibility criteria and exclusions

Eligibility inclusion and exclusion criteria is outline in Table 2. Studies which collect cost and effectiveness data, or cost data alone or an economic outcome of interest alone (such as QALYs or health and social care resource use) and investigate MBSR/MBCT or interventions largely based on or derived from these models, were included in this review.

Table 2: Eligibility inclusion and exclusion criteria

Inclusion	Exclusion
Participants: Any population who have received the intervention of interest. *Interventions:* Any MBSR or MBCT programme or an MBP which is largely based on or derived from these models. *Outcomes:* Cost and effectiveness or cost alone or economic outcome alone including but not limited to QALYs or resource use. *Evidence:* Any economic evaluation (full or partial) or published protocol of an economic evaluation of the interventions of interest.	*Participants:* Participants who have not received the intervention of interest. *Interventions:* Any intervention that is not based on MBSR / MBCT including those that have an element of mindfulness within the programme e.g., Dialectical Behaviour Therapy (DBT), Acceptance and Commitment Therapy (ACT). *Outcomes:* Any outcomes related to effectiveness alone that do not include some element of cost, resource use or other economic outcomes.

Database selection

To identify papers which met these inclusion criteria a range of electronic databases were searched for this review including:

1. Specialist economic databases (e.g., The NHS Economic Evaluation Database [NHS EED]),
2. Technology assessment databases (e.g., Health Technology Assessment [HTA] Database and Cochrane Central Register of Controlled Trials)
3. General medical /psychological literature databases (e.g., PubMed, CINAHL and PsycINFO).

It has been argued that searching within specialist economic databases combined with clinical evidence database will facilitate the identification of the majority of relevant economic evaluations (Wood, Arber, & Glanville, 2014). As the specialist economic database was discontinued in 2015, clinical trials database searching was added to this protocol to capture economic evaluations published after this date.. Therefore, a comprehensive search of published studies up to 19/04/2019 (beginning from the start of the database) was conducted using the following electronic databases: PubMed; The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials [CENTRAL], Health Technology Assessment Database, NHS EED), PsycINFO and CINAHL.

Search strategies (databases and keywords)

Two key term categories were identified during refinement of the review question and the scoping searches conducted between November 2017 and the final search date April 2019. These were words relating to the intervention i.e., 'mindfulness' terms, and words relating to the type of evaluation i.e.,

'economic' terms. Boolean operator 'OR' was used within search terms and the operator 'AND' was used to combine search term categories (see Table 3).

From the initial scoping searches 'mindfulness' and 'economics', terms were limited to title, abstract, and keywords (subject to database) search fields (see Table 3). Where appropriate words were truncated (as indicated by *) to allow for all word endings or beginnings to be included without repetition of the word in the search strategy. Limits used restricted articles to English language and studies involving humans.

Table 3: Search strategy

Search strategy Database: PubMed (19/04/19)	**Results**
1. Mindful* 2. Cognitive 3. Stress 4. 2 OR 3 5. 1 AND 4 6. MBCT 7. MBSR 8. MCBT 9. Mindfulness Based 10. Mindfulness-Based 11. Mindfulness [Mesh] 12. Mindfulness therapy 13. Mindfulness training 14. 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 15. "Economics" [Mesh] 16. economic* 17. "Costs and Cost Analysis" 18. cost 19. costs 20. costly 21. costing 22. cost outcome 23. return on investment 24. return-on-investment 25. health utilit* 26. budget* 27. impact analys* 28. 26 AND 27 29. price* 30. expenditure* 31. expense 32. financial 33. finance* 34. value for money 35. monetary value*	

36. models, economic [Mesh] 37. economic model* 38. markov chains [Mesh] 39. monte carlo method [Mesh] 40. monte carlo 41. Decision Theory [Mesh] 42. decision tree* 43. decision analy* 44. decision model* 45. 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 46. 14 AND 45	**266**

Screening

Screening was conducted blindly and independently by two reviewers using the cloud-based platform Rayyan QCRI by the Qatar Computing Research Institute (Ouzzani, Hammady, Fedorowicz, & Elmagarmid, 2016), with inter-rater reliability assessed and any conflicts resolved through discussion after each stage of screening. For the initial screening process, all identified paper titles and abstracts were assessed for relevance against the inclusion/exclusion criteria (see Table 2). If it was unclear whether a paper was relevant, the full paper was obtained and reviewed for inclusion. All studies that were considered relevant after initial screening were obtained in full and screened for inclusion. Multiple articles from the same study were linked together and the information used for the decision concerning which studies are eligible for inclusion.

Additional search strategies including grey literature and expert knowledge

Grey literature, including contemporary local government/agencies and charity reports, was included in the review to limit publication bias and ensure that all relevant literature was located. Relevant studies that may not be indexed in the major databases were searched for using the following search strategies:

1. Backward reference searching, also known as chain searching, was conducted to review the reference lists of key articles;
2. Forward reference searching was conducted to review articles which cite key papers identified during this review;
3. Hand-searching of Mindfulness Research Monthly or key journals identified as part of the review;

4. Hand-searching of grey literature from relevant organisations including the All-Party Parliamentary Groups UK Parliament relating to Mindfulness and NICE guidance which included recommendations for MBPs.

Critical quality appraisal, reporting and MBP intervention integrity assessments

Informed by guidelines on the conduct of systematic reviews of economic evaluations (Wijnen et al., 2016) a critical quality appraisal was conducted using forms designed for this study, using questions adapted from standardised checklists (see Table 4). Quality appraisal was not used to exclude studies, rather the findings were used to identify important shortcomings in the studies and to interpret the findings.

Table 4: Quality appraisal checklists

Checklist (authors, year)	**Rationale, description, and grading**
Economic evaluation reporting and methodology quality appraisal	
The British Medical Journal (BMJ) checklist for economic submissions (Drummond & Jefferson, 1996). The Consensus on Health Economics Criteria (CHEC) extended checklist (Evers, Goossens, de Vet, van Tulder, & Ament, 2005).	The BMJ checklist for appraising economic evaluations consisting of 35 questions under three headings (study design, data collection and analysis and interpretation) and the 19 question CHEC extended checklist were combined into a 28-question critical appraisal tool for economic evaluations (see Q1 – Q28 in Appendix 2 and Appendix 3). Each question was assessed as either a Yes, No, Unclear or Not applicable rating.
Risk of bias assessment	
Cochrane Collaboration Risk of bias tool (Higgins et al., 2011).	The risk of bias tool covers six bias domains: attrition bias, detection bias, performance bias, reporting bias, selection bias, and other bias. Three categorisation levels are used to indicate the risks of bias for each domain (high, low, or unclear). From this a composite grading is applied in this systematic review as follows: Studies showing high-levels of risk

Checklist (authors, year)	Rationale, description, and grading
	across all domains were reported to be of 'high' risk. Studies showing low levels of risk across most domains (5 or more) were reported to be of low risk. Where insufficient information was available to evaluate the risk of bias, or a mix of low and high-risk domains were observed the study was categorised as being 'unclear' (see Appendix 2 and Appendix 3 Q29).
SROI quality appraisal tool	
SROI quality assessment framework (Hutchinson et al., 2019b, 2019a; Hutchinson, Berndt, Gilbert-Hunt, George, & Ratcliffe, 2018).	As a supplement to the quality appraisal tool designed for this study SROI studies were deemed to be sufficiently methodologically different to warrant appraisal using questions from a specific SROI quality assessment framework. The SROI Quality Framework developed by Hutchinson and colleagues covers six categories and consists of 21 questions to assess the rigour of the SROI conduct and reporting. This work builds on earlier work to develop a five dimension 12-point quality assessment framework (Krlev, Münscher, & Mülbert, 2013) which has been previously used to critically appraise SROI evaluations of public health interventions (Banke-Thomas et al., 2015). Each question was answered with a Yes, No, Unclear grading. see Appendix 4 Q1- Q21
Economic modelling studies critical appraisal	
Good Practice Guidelines for Decision-Analytic Modelling in Health Technology Assessment: framework for quality assessment (Philips, Bojke, Sculpher, Claxton, & Golder, 2006).	The checklist recommended by NICE (NICE, 2013a) and the Cochrane Collaboration (Higgins et al., 2011) to appraise economic modelling studies consists of three major heading (structure, data and consistency) and sixty sub questions linked to attributes of good practice in decision analytic modelling.

Checklist (authors, year)	Rationale, description, and grading
Mindfulness Based Programmes intervention integrity and reporting	
The Template for Intervention Description and Replication (TIDieR) checklist (Crane & Hecht, 2018)	The MBPs were subject to an intervention integrity and reporting quality assessment based on the programme description provided in the economic evaluation paper supplemented with any cited papers or appendices where the programme was described in more detail. A brief check was designed to assess the quality of reporting on the MBP programme, particularly whether they contain the essential 'Warp' and flexible 'Weft' elements of MBPs presented (Crane et al., 2016). The Template for Intervention Description and Replication (TIDieR) checklist was used to screen the MBPs reporting (see Appendix 5). A high/moderate or low/unclear intervention integrity reporting grading was applied based on the information available in the paper and linked resources and recorded as part of the critical quality appraisal (see Appendix 2 and Appendix 3 Q30 & Appendix 4 Q23.)

Data extraction

Data was extracted from full-text articles by one reviewer (the candidate) and verified by the review team (candidate supervisors). A data extraction form was developed for this review capturing 1) bibliographic information (i.e., authors, publication year and country), 2) general information such as the intervention participant group including any clinical condition for inclusion, the MBP including details of any adaptations to MBSR / MBCT, 3) methodological information such as the study design, economic evaluation perspective and methods, economic costs and outcomes and results data.

Evidence synthesis and analysis

Health economics data is presented in tables which include the characteristics of the studies and the results of the included health economics studies (see Table 5 & Table 6). Costs are reported in country-of-origin local currency and converted to Great British Pounds Sterling to be most relevant to policy makers. All currency costs are converted to Pounds Sterling (£GBP), using daily exchange rate in the

Bank of England database (on 1st April 2019)[3], presented in 2019 cost year using the NHS cost inflation index (NHSCII) pay and prices inflation methodology outlined in the Personal Social Services Research Unit (PSSRU) Unit Costs of Health & Social Care 2019 guidance (Curtis & Burns, 2019).

Data homogeneity was initially assessed using the data extraction table. If heterogeneity was demonstrated in relation to the data, a narrative synthesis of the findings from identified studies was planned, structured around the type of economic analysis methodology and focus of intervention. It was anticipated that there would be limited scope for meta-analysis because of the scale of heterogeneity of different programmes and a range of different outcomes measured across a relatively small number of existing trials. Quantitative synthesis, using meta-analysis (on ICERs), was planned to be conducted if there was appropriate data that could be combined from similar studies.

Results

Results are presented in the PRISMA flowchart depicting the stages of study identification, screening, eligibility, and inclusion (see Figure 9 below). The systematic review identified 1,358 articles (1018 abstracts once duplicates were removed). During the initial title and abstract screening 814 records were excluded by the two independent reviewers. Two-hundred and four full text papers were retrieved and screened against the eligibility criteria. From this a total of 105 papers were considered relevant to this review, of which 25 were from papers on completed studies containing a full or partial economic evaluation.

The remaining papers were relevant background papers discussing economic evaluation methodology for MBPs, systematic reviews containing one or more study of an MBP evaluation which included an economic evaluation, trial registration records and study protocols which indicated inclusion of a planned economic evaluation, conference proceeding and abstracts of studies, including an MBP and an economic evaluation or student dissertations which included an MBP and an economic element.

[3] Rates available at: https://www.bankofengland.co.uk/boeapps/database/Rates.asp?TD=1&TM=Apr&TY=2019&into=GBP&rateview=D

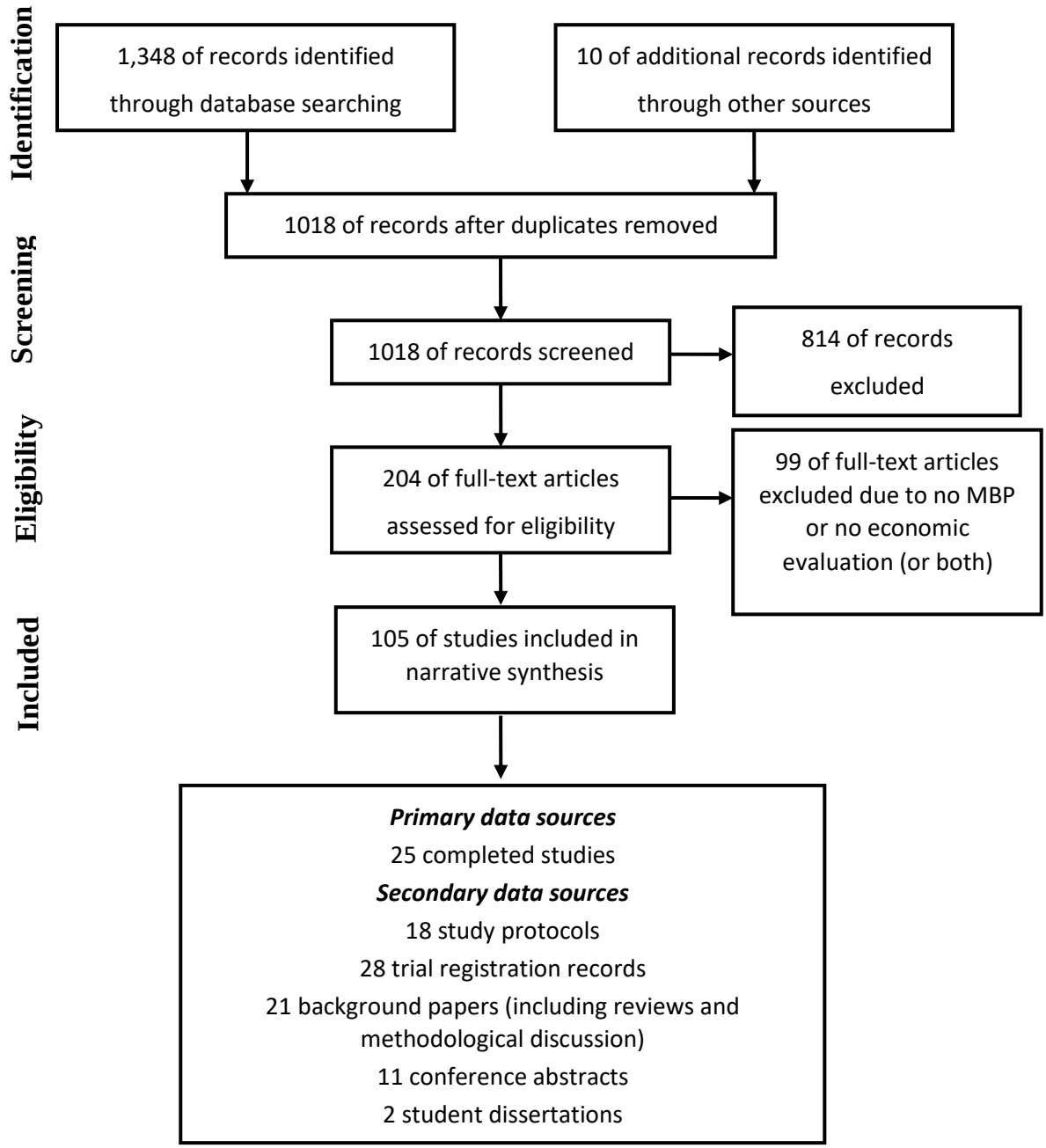


Figure 9: PRISMA flowchart

Overview of included studies

The completed economic evaluation studies are summarised in Table 5 providing an overview of the included studies including key characteristics of the MBP, population and delivery setting. The form of economic evaluation, perspective of analysis and main economic findings are presented in Table 6.

Twenty-five economic evaluations of MBPs were identified published between 2002 and 2019.

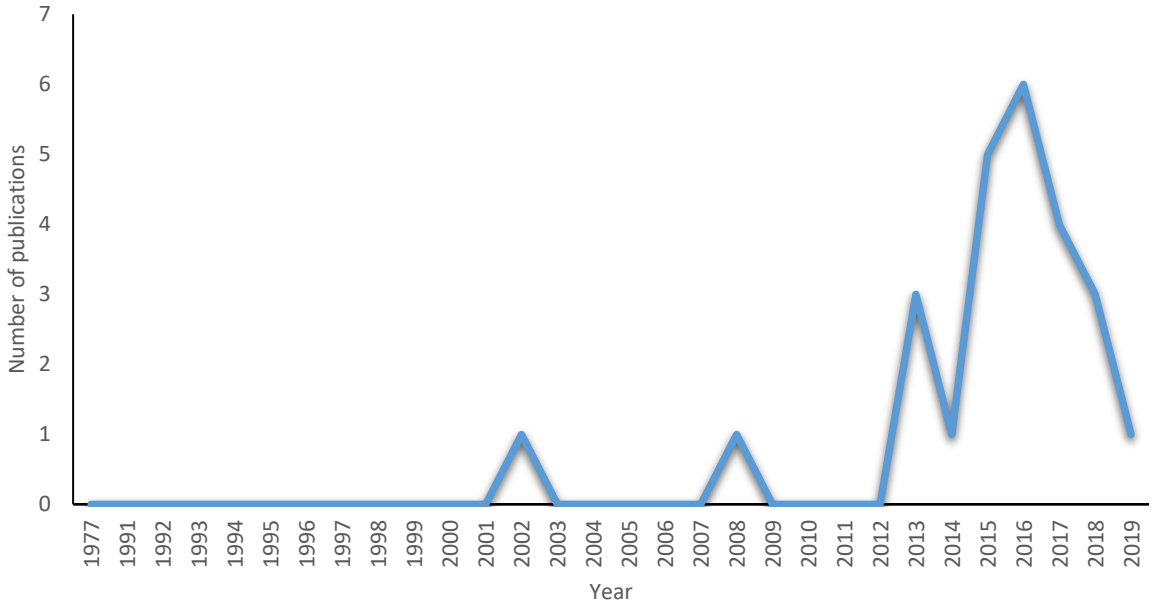


Figure 10: Number of publications over time including completed economic evaluations of mindfulness-based interventions as identified in this systematic review

Figure 10 shows the number of completed studies published each year between 1977 and 2019 which including an economic evaluation of an MBP. While the number of studies appears to decline in the last few years, in contrast to the scoping evidence reported in Chapter 1, it is important to reiterate that this only captures articles of published studies and that there is commonly a delay in publication of economic evaluations when compared with the clinical counterpart.

The MBPs included MBSR, MBCT, and programmes derived from these programmes that had been adapted to meet the needs of a specific patient population (e.g., adults with ADHD or specific delivery context such as an employment setting. In terms of clinical presentations, the most common economic evaluation focused on MBPs for the management of depression (*N=6*) and cancer recovery (*N=3*). Economic evaluations of more novel clinical applications were also included, for example, MBP for people with bodily distress syndrome (BDS) and medically unexplained symptoms (*N=3*). Non-clinical settings including MBPs in the workplace (*N=3*), prison (*N=1*) and parenting in the community (*N=1*)

Characteristic of economic evaluations

Fourteen of the studies were full economic evaluations where both benefits and costs were assessed, while eleven were partial economic evaluations (e.g., where only costs or a single economic outcome were considered). Substantial heterogeneity of studies was identified, and in line with current practice a narrative summary rather than meta-analysis is presented (Jacobsen, Boyers, & Avenell, 2020).

Critical appraisal of reporting and methodological quality

Results of the critical quality appraisal are presented in Appendix 2 for full economic evaluations. Partial economic evaluations met fewer criteria using the critical appraisal tools (see Appendix 3).

Results of the included economic evaluations by population: Narrative summary

Narrative results are grouped by population group and presented in alphabetical order.

Acute respiratory infection (N=1)

One study of a MBP for adults with acute respiratory infection reports on a United States of America (USA) societal cost comparison analysis of health care resource use (health care visits and medications) and lost wages (Rakel et al., 2013). Secondary data analysis from a RCT was used in a Monte Carlo bootstrapping analysis to compare the costs across two intervention conditions (MBP or exercise intervention) or a waitlist control. While the MBP group reported lower costs than exercise and the control condition and was concluded to be cost saving, the programme costs (estimated by the authors to be approximately $450, equivalent to £366 inflated to 2019) were not included in the analysis. No methods for the calculation of programme costs were provided, with these estimates reported in the discussion section of the paper as a limitation of the study. Inclusion of these costs would have resulted in higher total costs and the MBP was unlikely to be cost saving in the short term. See also one further record identified from secondary sources and described under trial registration records results.

ADHD (N=1)

One RCT of adults with ADHD was identified in the Netherlands receiving either Treatment as Usual (TAU) or adapted MBCT (in addition to TAU) which tailored psychoeducation to be specific to ADHD (Janssen et al., 2019). From a societal perspective cost-utility analysis (on an intention to treat basis) MBCT had a cost per QALY of €21,963 (equivalent to £19,820 converted and inflated to pounds in 2019). While the primary analysis indicated it may be more effective it was also more costly than TAU. The probability that it was the most cost-effective option was between 51% and 60%, with societal

willingness to pay between €30,000 and €80,000 per additional QALY (equivalent to a threshold in the UK of between £25,641 and £68,376). Per protocol (defined as an MBCT dose of 4 or more sessions) cost-utility analysis and cost-effectiveness analysis from a societal perspective indicated more favorable results for MBCT, which was dominant compared to TAU with lower costs and improved outcomes. Secondary analysis from a narrower health care perspective had a lower probability of being acceptable at all thresholds compared to the broader societal perspective analyses. The cost of MBCT was reported to be either €436 (complete case, intention to treat basis) or €445, with the authors stating they based these costs on the applied price from the Radboudumc Center for Mindfulness.

BDS or medically unexplained symptoms (N=3)

BDS is a more recent diagnostic label of medically unexplained symptoms (Budtz-Lilly, Vestergaard, Fink, Carlsen, & Rosendal, 2015; Rosendal et al., 2017) where the population are reported to be high utilisers of health care resources and have high rates of sickness absence (Rask, Ørnbøl, Rosendal, & Fink, 2017). Three economic evaluations of MBPs in this population were identified consisting of two MBSR (Fjorback et al., 2013; Rohricht, Zammit, & Papadopoulos, 2018) and one MBCT study (van Ravesteijn et al., 2013a).

The first study compared enhanced-TAU (2-hour specialist medical care and brief CBT for BDS), with an adapted MBSR course tailored to integrate elements of CBT for BDS for participants with Multi-organ BDS, consisting of Somatization disorder and functional somatic syndromes such as fibromyalgia and chronic fatigue syndrome (Fjorback et al., 2013). A cost-comparison study involving resource use and disability pension claims was conducted as part of the two arm RCT (*N=120*), in addition they included a retrospective data set comparison with a large, matched control cohort to provide a no treatment control condition (*N=5,950*). From a health care perspective both adapted MBSR and enhanced TAU were cost saving, compared to the no-treatment control condition, with the participants in the intervention conditions utilising fewer primary and secondary health care resources and fewer disability pension claims at the 15 months follow-up compared with the no treatment control condition. MBP intervention costs were reported to be an average of $3102 per patient however the methods for estimating these costs are not defined.

The second study on MBSR and body-oriented psychological therapy reports on an uncontrolled, open feasibility study (*N=93*) (Rohricht et al., 2018). Participants were patients with medically unexplained symptoms (patients meeting criteria for undifferentiated somatoform disorder and/or persistent bodily complaints not attributable to physical diseases and mild somatic symptoms). Health care resource use consisting of primary and secondary health care use reduced over the 6 months following the

interventions with an average reduction of £367 per patient. Based on an estimate of £57,000 per annum to deliver the care pathway the cost per patient of the MBP intervention was calculated to be £228 when taking into account the authors assumptions about rates of drop out and group capacity.

The final study in this population group reports on a RCT based economic evaluation (*N=96*) comparing MBCT (with unspecified minor modifications) with enhanced TAU which included a psychiatric interview in addition to all usual health care (van Ravesteijn et al., 2013a). Results from the societal perspective cost-utility analysis resulted in an incremental cost-utility ratio of €56,637 (equivalent to 2019 GBP £54,327) per QALY, with a 48% probability of cost-effectiveness at a €40,000 societal WTP threshold (equivalent to £34,188) and a 57% probability at a higher threshold of €80,000 (equivalent to a comparatively high threshold in UK terms of £68,376). MBP intervention costs are reported to be €450 mean cost per person, however the methods for costing programme are not described separate to other resources used where data was obtained from patient diaries.

Cancer (N=3)

One study evaluated MBSR (Lengacher et al., 2015) and two studies evaluated forms of MBCT (Compen, Bisseling, Donders, et al., 2017; Johannsen et al., 2017) with patients with cancer or in recovery.

The first study reports on a RCT (*N=96*) including cost-utility analysis of an adapted MBSR programme for breast cancer survivors compared with TAU (Lengacher et al., 2015). From a health care provider perspective results indicated MBSR had a cost of $22,200 per QALY (for the 12-week study period, equivalent to £17,918 in 2019). Scaling out to the first year resulted in a cost per QALY gained of $5,163 (results ranged between $3,872 and $7,744). From a patient perspective there was a cost per QALY of $4,589 per year. Longer-term high-level modelling projecting the potential cost per QALY estimated beyond the duration of the trial, indicated a reduced cost per QALY gained (QALYs discounted at 3% per annum) of $457 if a post-treatment 20-year life expectancy was achieved, and the benefits of MBSR and practice continued. The costs of MBSR reported was $666 per person based on the average number of participants attending through the course. Details of the costing was outlined in the paper including a breakdown of cost items and data collection methods. Direct costs included MBSR staff time, costs of the environment and course materials. Direct provider costs of the intervention are reported separate to patient opportunity costs from attending the intervention which averaged $592 per person during the course, consisting of participants time lost to travel and forgone employment, childcare costs and travel costs.

The second study reports on a RCT of MBCT tailored for breast cancer patients experiencing persistent pain (*N=84*) (Johannsen et al., 2017). The cost-effectiveness analysis conducted from a health care provider perspective indicates that MBCT was the dominant intervention with lower costs and better outcomes on average, and a high probability (results of primary and sensitivity analysis between 70 – 85%) of being a more cost-effective treatment compared with a waitlist control group in reducing pain intensity. The MBCT intervention costed €240 per participant, with costed items included staff salaries, room costs and materials. Material costs were depreciated over 3 years.

The third study compared health care utilisation (with no costs reported) in a population of patients with cancer and psychological distress as part of a three arm RCT (*N=245*) comparing group-based face-to-face delivered MBCT and internet e-MBCT, both tailored for the target population with a TAU control group (Compen, Bisseling, Donders, et al., 2017). There was no difference during the study period in health care resources used except for a higher rate of hospital outpatient visits (such as chemotherapy) observed in the TAU group. While the intervention was not costed, the authors highlight that the costs of e-MBCT are likely to be lower than traditional face-to-face MBCT (for example due to no travel costs and overheads), and that it could be a more cost-effective mode of delivery. MBCT and e-MBCT had promising clinical outcomes compared with TAU with a significant reduction in psychological distress and fear of cancer recurrence and health related quality of life (on mental health domains alone).

Chronic low back pain (N=2)

Two studies investigating MBPs in chronic low back pain populations included an economic evaluation (Herman et al., 2017; Zgierska, Ircink, Burzinski, & Mundt, 2017).

The first study provides evidence from a USA RCT investigating MBSR for adults with chronic low back pain (Herman et al., 2017). The economic evaluation indicated that from a societal perspective MBSR may be cost saving, as compared to usual care for adults with chronic low back pain with a net saving of £590 per participant. MBSR has a high probability of being cost-effective compared to TAU from both a societal and payer perspective. A breakdown of programme costings are reported, consisting of the hourly rate salary of therapist (inclusive of fringe benefits), number of hours of treatment time, materials per person, and average number of participants per course. The intervention costs of MBSR and CBT were reported to be equivalent and estimated to be $150 per participant irrespective of course attended. Exact course costs are not reported however the rounded estimate of $150 is applied. The authors considered it likely that the higher salary costs for CBT therapist balanced out the higher number of hours required to deliver the MBSR programme which included an addition 6 hours of treatment (the day of meditation practice retreat).

The second study was a small sample pilot RCT (*N=35*) conducted in the USA which investigated an adapted MBCT programme for adults with opioid-treated chronic low back pain, to compare the costs of health care use, medication use and productivity losses for participants receiving the MBP in addition to TAU compared with TAU alone (Zgierska et al., 2017). There was no significant impact on costs relating to opioid treated chronic low back pain when receiving the MBP in addition to usual care. The authors noted that they did not include the costs of the MBP in their analysis, nor did they report what the cost of the programme was, stating instead that longer term benefits of mindfulness practice reported in other studies are likely to offset the single fee associated with the course.

Depression (N=6)

Six economic evaluations of MBPs for depression were identified (Bota, Hazen, Tieu, & Novac, 2016; Knight, Bean, Wilton, & Lin, 2015; Kuyken et al., 2008; Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Brejcha, et al., 2015; Saha, 2018; Shawyer, Enticott, Özmen, Inder, & Meadows, 2016).

The first platform pilot RCT (*N=123*) of MBCT compared with the active control group of patients receiving maintenance antidepressant medication (m-ADM) (Kuyken et al., 2008), supplied promising but inconclusive evidence on whether MBCT was cost-effective. The probability of MBCT being the more cost-effective option was 42% at zero WTP. MBCT was however the more favourable option if society was willing to pay more than $1,000 (international dollars) equivalent to £763 (or £982 if the threshold rose with inflation to 2019 rates) to prevent relapse or recurrence. The average cost of MBCT was calculated to be $340 per participant (equivalent to £250), with intervention costs reported to include therapist salary for direct and indirect time and associated overhead expenses relating to administration, management, and capital.

In the second study, a larger RCT that followed (*N=414*) MBCT with support to taper m-ADM (MBCT-TS) was compared with m-ADM alone (Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Brejcha, et al., 2015; Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Morant, et al., 2015). The incremental cost per unit reduction in depression relapse rates was £4,955 from a health care perspective rising to £10,604 from a societal perspective. The probability of MBCT-TS being the most cost-effective option did not rise above 52% in any analysis and in the cost-utility analysis MBCT-TS was dominated, because of higher costs and lower QALY gains than the m-ADM control group on average. The average cost of an MBCT-TS session was reported to be £14 per participant, with group based costing based on allocation rather than attendance. For a typical course of eight sessions the total average cost was £112 per participant.

The third study reports on an Australian RCT (*N=203*) evaluating MBCT delivered in addition to depressive relapse active monitoring involving supported self-monitoring (Shawyer et al., 2016). Cost-utility analysis from a societal perspective indicated that MBCT was dominant, with lower costs and higher health gains (using DALYs as the primary outcome of effect). Analysis conducted from a range of perspectives indicated that MBCT was likely to be cost saving, with the incremental cost saving per averted DALY ranging from $14,040 (AUD) to $255,664 (AUD) (equivalent to between -£8,804 to -£160,310 in 2019 terms) from a societal perspective. MBCT programme costing methods are described, and focus on salary of therapist to deliver the programme and participant attendance at sessions, with the costs based on actual attendance rather than allocated. However, as the results do not separate programme costs from other resource use costings it is not possible to report the average cost of MBCT applied.

The fourth study, reports on a partial economic evaluation in the USA which compared health care resource use before and after an MBCT course for patients with recurrent major depressive disorder (MDD) (*N=142*, including 49 without MDD but with a mood disorder, bipolar disorder or depressive disorder) (Bota et al., 2016). They concluded that the patients with MDD receiving MBCT treatment had a reduction in follow-up psychiatric care visits. There was no significant difference in other health care resource use including medication use, primary care, and emergency care and hospitalizations. No monetary values are applied to resources used or MBCT programme costs.

The fifth study focused on MBSR for depression (Knight et al., 2015). In a matched cohort comparison study (*N=1730,* MBSR participants with 1:3 matched controls), a cost-comparison analysis indicated that MBSR resulted in a short-term reduction of health care resource use following the programme, with an average cost saving of $250 (CAD) per participant compared with the control group. However, these benefits were not sustained over time (by the 2-year follow-up). Intervention resources are described however no programme costs are reported.

The final study reports on a RCT in Sweden that evaluated a Mindfulness Group Therapy ([MGT] which they reported was based on MBSR and MBCT) compared with TAU consisting of pharmacological treatment or psychological therapy for patients with depression, anxiety or stress and adjustment disorder (MBT *N=110*; TAU *N=105*) (Saha, Jarl, Gerdtham, Sundquist, & Sundquist, 2018). Cost-utility analysis from both a health care provider perspective and a societal perspective analysis indicated that MGT resulted in significantly lower costs and was cost saving compared with TAU (mean savings of €115 [health care] per person and €112 [societal] in an 8-week period). At a societal willingness to pay threshold of €24 691 per additional QALY (equivalent to £22,809 in 2019), MGT has a 67% probability of

being cost-effective compared with TAU, rising to 70% probability at a health care perspective. Programme costing is described in full in the appendix of the authors paper, with costs per participant reported at 3,462 kr (Swedish Krona) based on participants allocated to attend rather than attendance of the sessions.

Employees (N=3)

Three studies provided an economic evaluation of an MBP delivered in the workplace to employees.

The first study reports on a workplace evaluation of the USA-based Dow Mindful Resilience Program reported to be adapted from MBSR; delivered over 7 weeks consisting of low dose taught sessions (1 hour live webinar sessions), and home practice (average 1.5 hours per week) (*N=89*) (Aikens et al., 2014). A high-level cost-benefit analysis, presented briefly in the discussion, indicated that the MBP resulted in a 20% reduction in burnout post-intervention compared to the self-reported burnout before the MBP, equating to potential employer savings of up to $22,580 per employee due to a reduction in employee presenteeism and absenteeism (equivalent to a saving of £18,591 in 2019). Although the study had a randomised waitlist control condition, this cohort of employees was offered the MBP after 7 weeks once the intervention cohort had completed the programme. As a result, the burnout results cannot be compared with a control cohort to observe for example what might have happened naturally over time.

The second study, a further USA study evaluated low dose MBSR delivered on site at the workplace consisting of 1 lunchtime hour per week over 8 consecutive weeks (*N=84*) (Klatt, Sieck, Gascon, Malarkey, & Huerta, 2016). A partial economic evaluation was conducted to compare the costs of health care utilisation with a retrospective matched cohort control condition (*N=258*, matched based on age, gender, relative risk score and pre baseline health care costs). Over a 5-year period post intervention the MBP participants had significantly less primary care visits but significantly more prescriptions compared with the matched control. The average total costs of all health care resources were lower by $6,196 (equivalent to £4984 in 2019) in the MBP condition than the control cohort, although this difference was not statistically significant.

The final study details a large RCT in the Netherlands (*N=257*) comparing the Mindful ‘‘Vitality in Practice’’ (VIP) programme (which included an adapted MBSR programme delivered in a moderate dose format), with enhanced-TAU (where staff had access to an employee health promotion web platform) (van Dongen et al., 2016b). Analysis was conducted from both a societal perspective and employers’ perspective with a primary CEA on four key employee outcomes: worker engagement, general vitality,

job satisfaction and work ability. The MBP was dominated by the control condition, with higher costs and lower outcomes, the maximum probabilities of cost-effectiveness did not rise above 0.25 irrespective of WTP in any analysis. From an employer perspective, the MBP did not have positive financial return on investment. Using a bottom-up micro-costing approach to costing the MBP costs were calculated as equivalent to €171 from a societal perspective and €464 from the employer's perspective.

Inner-city patient population (N=1)

Roth and Stanley (2002) conducted a pre-post design evaluation of a bilingual (English/Spanish) MBSR for inner city health center patients (in the USA) with a high proportion of participants receiving public welfare assistance and from ethnic minorities (Roth & Stanley, 2002). The annual average number of primary care visits was significantly lower after patients received MBSR. No costs of primary care resource use or programme costs are reported.

Multiple Sclerosis (MS) (N=1)

Bogosian et al. (2015) report on a UK based pilot RCT (*N=40*) economic evaluation comparing TAU with an adapted MBCT course delivered via Skype video conferencing to patients referred by public and third sector specialist MS services with Primary or Secondary Progressive MS who were also experiencing distress (Bogosian et al., 2015). The MBP was dominant with lower overall costs and better outcomes and had a high probability of being cost-effective (90% at a WTP threshold of £20,000) compared with TAU. While micro-costing methods are described the MBP intervention costs are not reported in study results.

Parents (N=1)

A UK based SROI evaluation evaluated the Nurturing Parents programme, based on MBSR and available for parents referred by their Family Support Worker due to a range of reasons including difficulties at home, parenting skills or health concerns (Social Value Cymru, 2016). The SROI concludes that the Nurturing Parents programme generated £3.65 of social value for every £1 invested (Social Value Cymru, 2016). The cost of delivering four programmes was reported to have a total financial input of £15,786.63 equivalent to £141 per stakeholder. The costs are further disaggregated to report the initial set up costs of staff training and course materials as £7,845.93 and course delivery costs as £7,940.70 consisting of project workers, venue hire, refreshments, course resources, transport, and childcare (which formed part of the programme).

Prisoners (N=1)

Ferszt et al (2015) reports on a pilot evaluation of an MBP in a USA public sector prison with incarcerated women (*N=33*) receiving mindfulness-based emotional intelligence (MBEI) training which integrates elements of social emotional learning and MBCT, delivered in 1.5-hour sessions over 12 weeks (Ferszt, Miller, Hickey, Maull, & Crisp, 2015). Although not a full economic evaluation this study concludes the MBP is low cost and provides a brief intervention costing, equating to costs of $42 per person for resources (CDs and CD player), plus staffing costs of the intervention facilitator (up to $100 per hour) equating to between $100 and $120 per participant (depending on group size of 15 or 18 women).

Pulmonary arterial hypertension (N=1)

Tulloh et al (2018) UK pilot study (MBSR, *N=18*; TAU, *N=16*) of an adapted MBSR programme delivered over 2 hour sessions for 8 weeks to small groups of 7 participants with Pulmonary arterial hypertension (PAH), compared with patients receiving TAU consisting of clinic and phone contact with specialist PAH health care professionals (Tulloh et al., 2018). The pilot study was used to test the response rates of outcomes including a measure of health and social care resource use, and health-related quality of life using SF-36 subset (SF-6D) to produce a single index preference-based utility value suitable for cost-utility analysis. Resource use outcomes and utility values are not reported, and no comparison is made between the arms as the study was not appropriately powered to detect differences. The mean cost of MBSR per person ranged between £372 and £1,538 (£393 and £1626 inflated to 2019) depending on costing approach, geographical location of course and the number of participants per group (expected attendance compared with actual attendance).

Social prescribing scheme patients referred for mental, social and/or emotional issues (N=1)

Fox Advising CIC (2016) SROI evaluated a social prescribing project for people with a variety of mental, social and emotional issues referred by primary care and third sector organisations with an embedded programme based on MBSR and concluded that the project generated 'a social profit' of £10.12 for every £1 invested (Fox Advising CIC, 2012). Financial inputs specific to the delivery of the MBSR programme are not reported.

Table 5: Key features of studies: country, population, sector, MBP and comparator

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
1	Aikens et al. (2014). USA.	Employees. Employment.	MBP: Mindful Resilience Programme adapted MBSR. Format: weekly live webinar plus email coaching and text message reminders. Duration / frequency: 7-weeks, 1-hour live sessions per week plus short home practice (average 1.5 hours per week). Group based (size): yes (45).	Waiting-list control
2	Bogosian et al. (2015). UK.	Patients with Primary or Secondary Progressive Multiple Sclerosis experiencing distress. Health [specialist MS services - third sector and public sector NHS MS centers]	MBP: Adapted MBCT course Format: Skype video conferences Duration/frequency: 8-weeks, 1-hour sessions per week plus audio track guided home practice. Group based (size): yes (5).	TAU (Waiting-list control)
3	Bota et al. (2016). USA.	Patients with Recurrent Major Depressive Disorder (MDD) or mood disorder, bipolar disorder, depressive disorder, but excluding patients with single-episode MDD	MBP: MBCT Format: no additional details provided. Duration/frequency: no additional details provided.	No intervention comparator

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
		Health [specialist mental health services]	Group based (size): not specified.	
4	Compen et al. (2017). The Netherlands.	Distressed cancer patients (with a score of more than 11 on the Hospital Anxiety and Depression Scale). Health [cancer services]	MBP1: MBCT with modifications to tailor the programme for patients with cancer (including cancer-related psychoeducation and adapted movement exercises). Format: face-to-face Duration/frequency: 8-weeks, 2.5-hour sessions per week plus a 6-hour silent day and audio track guided home practice. Group based (size): yes (not specified). MBP2: Internet-based MBCT (eMBCT) Format: email contact and website structured self help Duration/frequency: 8-weeks, weekly emails with therapist plus audio track guided home practice and home silent day. Group based (size): individual (not applicable).	TAU

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
5	Ferszt et al. (2015). USA.	Incarcerated Women Public sector [Prisons]	MBP: 'Path to Freedom' MBEI training integrating elements of social emotional learning and MBCT. Format: face-to-face Duration/frequency: 12-weeks, 1.5-hour sessions per week. Group based (size): yes (15-18).	No intervention comparator
6	Fjorback et al. (2013). Denmark.	Multi-organ BDS: Somatization disorder and functional somatic syndromes such as fibromyalgia and chronic fatigue syndrome. Health [Primary and secondary care - hospital & community GP].	MBP: adapted MBSR programme with integrated elements of CBT for BDS Format: face-to-face Duration/frequency: 8-weeks, 3.5-hour sessions per week. Group based (size): yes (12).	1) Enhanced TAU (2-hour specialist medical care and brief CBT for BDS). 2) No treatment – matched population cohort.
7	FOX ADVISING CIC (2016). UK	Local community users of GP practices Health [community – primary care]	MBP: MBSR Format: not specified Duration/frequency: 8-weeks, 2-hour sessions per week plus audio track guided home practice. Group based (size): yes (not specified).	No intervention comparator

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
8	Herman et al. (2017). USA.	Adults (members of a group health plan) with Chronic Low-Back Pain. Health [primary care – insurance based]	MBP: MBSR. Format: face-to-face. Duration/frequency: 8-weeks, 2-hour sessions per week. Group based (size): yes (12).	1) Cognitive Behavioral Therapy 2) TAU and £41 compensation
9	Janssen et al. (2019). The Netherlands.	Adults with ADHD. Health [specialized outpatient clinics]	MBP: MBCT (delivered in addition to TAU) with modifications to tailor the programme for patients with ADHD (including ADHD-related psychoeducation and a gradual increase in the duration of meditation exercises). Format: face-to-face. Duration/frequency: 8-weeks, 2.5-hour sessions per week plus audio track guided home practice. Group based (size): yes (9).	TAU consisted of pharmacotherapy and/or psychosocial treatments such as psychoeducation and skills training
10	Johannsen et al. (2017). Denmark.	Women treated for primary breast cancer experiencing persistent pain. Health [secondary care – hospital]	MBP: MBCT with modifications to tailor the programme for patients with breast cancer (including shorter meditation exercises ≤ 30 min, more gentle yoga exercises, and omission of the whole day 'retreat' session). Format: face-to-face.	TAU (Waiting-list control)

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
			Duration/frequency: 8-weeks, 2-hour sessions per week. Group based (size): yes (13-17).	
11	Klatt et al. (2016). USA.	Employees. Employment / Education [University]	MBP: adapted MBSR (low dose) limited yoga stretches with gentle background music, Format: Duration/frequency: 8-weeks, 1-hour (lunchtime) sessions per week plus shorter home practice ≤ 20 min and shorter 2-hour 'retreat'. Group based (size): yes (≤18).	1) Active control diet/exercise lifestyle intervention consisting of 8 weekly 1 hour education sessions plus 30 minutes reading homework. Group sizes of 18 or less. 2) Matched controls 5 years post intervention comparison
12	Knight et al. (2015). Canada.	Patients referred by their physician for a variety of physical and/or mental health issues. Health [primary / secondary]	MBP: MBSR. Format: face-to-face. Duration/frequency: 10-weeks, 3-hour sessions per week (for 9 weeks) plus one 7-hour 'retreat' class and audio track guided home practice. Group based (size): yes (30).	No intervention comparator Data comparison with matched cohort (receiving TAU).
13	Kuyken et al. (2008). UK.	Patients with recurrent depression. Health (community - Primary Care)	MBP: MBCT plus support from their primary care physician to taper and discontinue their m-ADM from week 4 of the MBCT course onwards.	m-ADM

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
			Format: face-to-face. Duration/frequency: 8-weeks, 2-hour sessions per week plus audio track guided home practice (40 min daily). Additional four follow-up 'booster' sessions in the following year. Group based (size): yes (9-15).	
14	Kuyken et al. (2015 a&b). UK.	Patients with recurrent depression. Health (community - Primary Care)	MBP: adapted MBCT including support to taper/ discontinue m-ADM (MBCT-TS) and tailored psychoeducation / integrated GP involvement Format: face-to-face. Duration/frequency: 8-weeks, 2.25-hour sessions per week. Additional four follow-up 'booster' sessions in the following year. Group based (size): yes (12-15).	m-ADM
15	Lengacher et al. (2015). USA.	Breast Cancer Survivors. Health [secondary care - cancer center]	MBP: MBSR adapted. Format: face-to-face. Duration/frequency: 6-weeks, 2-hour sessions per week plus audio track guided daily home practice (15-45 minutes).	TAU (waitlist control)

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
			Group based (size): yes (not specified).	
16	Rakel et al. (2013). USA.	Acute respiratory infection. Health [community]	MBP: MBSR Format: face-to-face. Duration/frequency: 8-weeks, 2.5-hour sessions per week plus home practice (duration unspecified). Group based (size): yes (not specified).	1) Moderate exercise intervention consisting of 2.5hr sessions led by exercise physiotherapists over an 8-week period, plus 45 minutes home exercise practice. 2) Waitlist control (choice of MBSR, Exercise support or $300 cash).
17	Rohricht et al. (2018). UK.	Patients with medically unexplained symptoms (patients meeting criteria for undifferentiated somatoform disorder and/or persistent bodily complaints not attributable to physical diseases and mild somatic symptoms) Health [Community – Primary Care]	MBP: MBSR (delivered as part of a primary care package involving assessment and psychoeducation) Format: face-to-face Duration/frequency: 8-weeks, 1.5-hour sessions per week. Group based (size): yes (5-12).	Body-orientated Psychological Therapy (delivered as part of a primary care package involving assessment and psychoeducation) delivered over 10 weeks (90-minute sessions) to groups of between 5 and 12 participants.
18	Roth & Stanley. (2002). USA.	Inner City health center patients (high proportion minority populations / receiving public welfare assistance) Health [Community]	MBP: Bilingual (English / Spanish) MBSR Format: face-to-face	No intervention comparator (pre-post)

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
			Duration/frequency: 8-weeks, 2-hour sessions per week plus home practice (duration not specified). Group based (size): yes (not specified).	
19	Saha et al (2018). Sweden.	Patients with depression, anxiety or stress and adjustment disorders Health [Community - Primary Care]	MBP: Mindfulness Group Therapy (MGT) reported to be based on MBSR and MBCT. Format: face-to-face. Duration/frequency: 8-weeks, 2-hour sessions per week plus audio track guided home practice (20 mins daily). Group based (size): yes (≤10).	TAU consisting of pharmacological treatment and psychotherapy (CBT) or counselling.
20	Shawyer et al. (2016). Australia.	Recurrent major depression (3 or more episodes) Health [Primary and secondary / specialist care]	MBP: MBCT plus depressive relapse active monitoring involving supported self-monitoring. Format: Duration/frequency: 8-weeks, 2-hour sessions per week plus 3-monthly optional 'booster sessions.' Group based (size): yes (8).	Depressive relapse active monitoring involving supported self-monitoring.

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
21	Social Value Cymru (2016). UK	Parents referred to Family Support Workers for various reasons including difficulties at home, parenting skills, health reasons. Social care [community]	MBP: Nurturing Parents mindfulness course based on MBSR Format: face-to-face Duration/frequency: 8-weeks, length of sessions per week not specified. Group based (size): yes / some one-to-one (average 7).	No intervention comparator
22	Tulloh et al. (2018). UK.	Pulmonary arterial hypertension (PAH): Health [secondary/ specialist clinic and hospital]	MBP: MBSR programme with 'gentle' content tailored to physical disability due to PAH patients Format: face-to-face. Duration/frequency: 8-weeks, 2-hour sessions per week. Group based (size): yes (7).	TAU consisting of clinic and phone contact with pulmonary hypertension nurses or doctors.
23	van Dongen et al. (2016). The Netherlands.	Employees. Employment [Government]	MBP: Mindful ''Vitality in Practice'' (VIP) programme Format: face-to-face plus on-going e-support Duration/frequency: 8-weeks, 1.5-hour sessions per week followed by 8 weeks of mindfulness e-coaching and referral to other work-based health services as required. Homework, peer	Control condition included having access to intranet webpage with links to health promotion activities.

	Author (Year) Country	Population / Sector	MBP(s) (including adaptations, format, duration, frequency, group size)	Comparator(s)
			support and an intranet-based repository of resources were accessible as part of the wider programme (delivered over a 6-month period). Group based (size): yes (4-17).	
24	van Ravesteijn et al. (2013). The Netherlands.	Patients with medically unexplained symptoms (patients meeting criteria for undifferentiated somatoform disorder) Health [community - primary care]	MBP: MBCT with minor adaptations (unspecified) were made to the MBCT training protocol to make it more suitable for patients with physical symptoms. Duration/frequency: 8-weeks, 2.5-hour sessions per week plus silent whole-day 'retreat' session and home practice for 6 days a week (45 min a day). Group based (size): yes (7-14).	Enhanced TAU consisting of a psychiatric interview delivered in addition to all usual health care contact.
25	Zgierska et al. (2017). USA.	Opioid-treated chronic low back pain Health [Outpatient setting]	MBP: Mindfulness meditation (MM) following an MBCT model adapted to include pain-specific CBT strategies delivered as adjunctive to usual care. Delivered in addition to TAU. Format: face-to-face. Duration/frequency: 8-weeks, 2-hour sessions per week plus home practice (30+ minutes 6 days a week). Group based (size): yes (21).	TAU for opioid-treated chronic low back pain consisting of "pharmacotherapy, safety, and treatment progress monitoring, treatment agreements, and referral to specialty care, including physical therapy, and complementary therapies for pain and/or mental health" (Zgierska et al., 2016, p. 1867).

Table 6: Summary of economic evidence included in MBP evaluation: key features and headline results

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
1	Aikens et al. (2014)	Not stated	Randomised partially controlled (7 weeks) trial with post-hoc economic evaluation (online adapted MBSR *N=44*; wait-list *N=45*) Cost-benefit analysis (high level)	6 months (no discounting)	**Primary outcome(s):** Life-style survey questionnaire (designed for study) including self-reported burnout measured as the "number of days per week a participant felt too burned out to work" (Aikens et al., 2014, p. 3). **Cost year (currency):** 2012 ($USD) **Summary result(s):** Savings of up to $22,580 per employee per year due to a 20% increase in worker productivity following the MBP. **MBP intervention costs:** No costs presented
2	Bogosian et al. (2015).	Not stated	Pilot randomised controlled trial-based economic evaluation (Skype adapted MBCT *N=19*; TAU waiting-list *N=21*) 1) Cost-effectiveness analysis 2) Cost-utility analysis	20 weeks (no discounting)	**Primary outcome(s):** 1) General Health Questionnaire (GHQ-12) clinical measure of distress 2) HRQoL measured using EQ-5D-3L to calculate QALYs **Cost year (currency):** 2012–2013 (£GBP) **Summary result(s):** MBCT was reported to be dominant with lower costs and better GHQ outcomes compared to the TAU waiting-list group, with an 87.4% probability that the intervention saves money and improves outcomes. At a WTP threshold of £20,000 Skype delivered MBCT has more than a 90% chance of being the most cost-effective option. **MBP intervention costs:** micro-costing methods described however intervention costs not reported in results.

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
3	Bota et al. (2016).	Not stated	Pre-post health care utilisation	1 year (No discounting)	**Primary outcome(s):** health care resource use **Cost year (currency):** N/A no costings were provided. **Summary result(s):** "Patients with a history of MDD who underwent MBCT treatment were less likely to be high utilizers of follow-up psychiatric care. However, the participants in MBCT did not have statistically significant changes in the need for primary care and other specialties" (Bota et al., 2016, p. 4). **MBP intervention costs:** No costs presented.
4	Compen et al. (2017).	Not stated	Randomised Controlled Trial Health Care Utilisation	3 months (no discounting)	**Primary outcome(s):** health care resource use **Cost year (currency):** N/A no costings were provided. **Summary result(s):** No significant differences in health care utilisation between groups were observed, except for the a higher proportion of patients in the TAU group receiving outpatient treatment (e.g., chemotherapy). **MBP intervention costs:** No costs presented.
5	Ferszt et al. (2015).	Not stated	Pilot study (pre-post non-experimental design) including a preliminary intervention costing	12 weeks (no discounting)	**Primary outcome(s):** intervention cost estimates **Cost year (currency):** not specified ($USD) **Summary result(s):** Authors headline economic discussion point: "Low-cost treatment approach offers potential utility for use in correctional settings and may lead to cost savings in treating stress, anxiety and depression in this population" (Ferszt et al., 2015, p. 11605) **MBP intervention costs:** Between $100 and $120 per participant (high level estimate).

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
6	Fjorback et al. (2013).	Not stated (health care / societal implied)	A randomised controlled trial-based economic evaluation and matched cohort control (*N=60* enhanced TAU; *N=60* MBSR; *N=5,950* matched population control participants) Cost-comparison study	15 months (no discounting)	**Primary outcome(s):** health care resource use and disability pension claims **Cost year (currency):** 2007 (Danish kroner converted to $USD at rate 100/544,5551). **Summary result(s):** "At 15-month follow-up, 25% from the mindfulness therapy group received disability pension compared with 45% from the specialized treatment group (p=.025)" (Fjorback et al., 2013, p. 41). "Both interventions saved money within the health care system. MBSR was significantly more expensive than enhanced TAU, in spite of these additional costs, MBSR appears to reduce the overall health care costs within the range of enhanced TAU" (Fjorback et al., 2013, p. 44). **MBP intervention costs:** mean cost per patient $3102 (methods undefined).
7	FOX ADVISING CIC (2016).	Societal perspective.	SROI (*N=19*)	15 days over 3 months with future outcomes estimated (discount rate of 2% was applied to the social return ratio.)	**Primary outcome(s):** social value generated **Cost year (currency):** 2015 (£ GBP) **Summary result(s):** £10.12:1. **MBP intervention costs:** not reported.

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
8	Herman et al. (2017).	1) Societal perspective 2) Payer perspective (health care costs)	a randomised trial-based economic evaluation (MBSR, *N=116*; CBT, *N=113*; or TAU, *N=113*). Cost-utility analysis	12 months (no discounting)	**Primary outcome(s):** HRQoL measured using SF-6D to calculate QALYs **Cost year (currency):** 2013 ($USD) **Summary result(s):** The average incremental cost per participant to society of CBT was $125 and of MBSR was −$724when compared with TAU i.e., a net saving of $724. Incremental costs per participant to the health plan were $495 for CBT over TAU and −$982 for MBSR, and incremental back-related costs per participant were −$984 for CBT over TAU and − $127 for MBSR. "These costs (and cost savings) were associated with statistically significant gains in QALYs over TAU: 0.041 (0.015, 0.067) for CBT and 0.034 (0.008, 0.060) for MBSR. Conclusions—In this setting CBT and MBSR have high probabilities of being cost-effective, and MBSR may be cost saving, as compared to TAU for adults with CLBP. These findings suggest that MBSR, and to a lesser extent CBT, may provide cost-effective treatment for CLBP for payers and society" (Herman et al., 2017, p. 1517). **MBP intervention costs:** $150 per person (rounded estimate).
9	Janssen et al. (2019).	1) Societal perspective 2) Health care perspective	A trial-based economic evaluation (*N=47,* MBCT+TAU; *N=49*, TAU) 1) Cost-utility analysis 2) Cost-effectiveness	9 months (no discounting)	**Primary outcome(s):** 1) HRQoL measured using SF-12 to calculate QALYs 2) disease-specific measure of treatment response based on ADHD rating scale (CAARS-INV: SV; Adler et al. 2007). **Cost year (currency):** 2015 (€Euros – converted from $USD at a rate of 1.11). **Summary result(s):** Societal ICER ITT cost per QALY of €21,963 and dominant in per protocol analysis.

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
					MBP intervention costs: €436 - €445 (applied price from the Radboudumc Center for Mindfulness, no further methods defined).
10	Johannsen et al. (2017).	Health care perspective	A randomised controlled trial-based economic evaluation (MBCT *N=36*; TAU *N=48*) Cost-effectiveness analysis	8 months (no discounting)	**Primary outcome(s):** minimal clinically important difference (MCID) on pain intensity. **Cost year (currency):** 2015-(Danish kroner DKK converted to Euro at rate (1 Euro = 7.50 DKK). **Summary result(s):** "MBCT was cost- effective with a probability of 85% with a value of an additional women achieving MCID [on pain intensity] set to zero remained cost-effective with a probability of 70% to 82% when smaller effect and higher MBCT costs were assumed" (Johannsen et al., 2017, p. 1). **MBP intervention costs:** €240 per participant (methods detailed items and salary assumptions).
11	Klatt et al. (2016).	Not stated	matched historical cohort (5 years post intervention) Cost-comparison study	5 years (no discounting)	**Primary outcome(s):** health care resource use consisting of primary care visits, hospital visits and prescriptions. **Cost year (currency):** not specified ($USD) **Summary result(s):** MBP reduction in primary care visits compared to controls. MBP had lower overall health care utilisation after five years (although difference not significant). Pharmacy costs and number of prescriptions were significantly higher for MBP compared to controls over the five years ($p < 0.05$).

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
					MBP intervention costs: Programme costs used are not reported.
12	Knight et al. (2015).	Third-party payer	Matched cohort comparison study (*N=1730* MBP participants with 1:3 match controls) Cost-comparison study	2 years (no discounting)	**Primary outcome(s):** resource use **Cost year (currency):** not specified ($ unspecified, study country currency Canadian dollars $CAD) **Summary result(s):** "Participation in an MBSR program resulted in consistent decreases in utilisation across all outcome variables at the 1-year pre/post interval. These decreases were significantly different than the patterns shown by the matched comparisons. Assuming 1500 MBSR participants (close to the number in the closest match) times an average savings of $250 would result in $375,000 [equivalent to £226,871] in savings. These differences disappeared at the 2-year pre/post interval with the exception of laboratory utilisation. Our findings suggest that mindfulness training is effective for short-term reductions in health care use among a group complex and heavy users. Anecdotal reports suggest MBSR participants stop their formal mindfulness practice within months of completing the program. It may well be that continuing the formal practice of mindfulness is a necessary prerequisite for maintaining the reductions in health care utilisation" (Knight et al., 2015, p. 1379). **MBP intervention costs:** No programme costs presented.
13	Kuyken et al. (2008).	1) Health care perspective 2) Societal perspective	A randomised controlled trial-based economic evaluation Cost-effectiveness analysis	15 months (no discounting)	**Primary outcome(s):** Depression relapse (SCID-I) **Cost year (currency):** 2005–2006 (All costs "converted to international dollars using a purchasing power parity exchange rate of 0.6 as recommended by the World Bank (2006 World Development Indicators available at http://www.worldbank.org/)."

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
					Summary result(s): Societal perspective CEA ICER= $962 per relapse prevented; $50 per depression free day. Health care perspective CEA ICER=$439 per relapse prevented; $23 per depression free day. Probability MBCT was more cost-effective than m-ADM was 42% ($0 WTP threshold) and more than 80% at a societal WTP threshold $10,000 . **MBP intervention costs:** The average cost of MBCT was $340 per participant.
14	Kuyken et al. (2015 a & b).	1) Health care perspective 2) Societal perspective	A randomised controlled trial-based economic evaluation 1) Cost-effectiveness analysis 2) Cost-utility analysis	24 months (3.5% discount rate)	**Primary outcome(s):** 1) HRQoL measured using EQ-5D-3L to calculate QALYs 2) Depression relapse (SCID-I) **Cost year (currency):** 2011/12 (£GBP) **Summary result(s):** MBCT-TS QALY analysis dominated (costs were higher and outcomes worse). ICER of £4,955 (Health care perspective) per unit reduction in depression relapse rates. ICER of £10,604 (societal perspective) per unit reduction in depression relapse rates.

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
					Probability MBCT-TS was more cost-effective than m-ADM was 43% or lower (at a range of WTP thresholds). **MBP intervention costs:** average cost was £112 per participant.
15	Lengacher et al. (2015).	1) societal perspective 2) patient perspective 3) health care perspective	A randomised controlled trial-based economic evaluation MBSR(BC) (*N=49*) TAU (*N=47*) Cost-utility analysis	18 weeks plus 20-year projection (3% QALY discount rate)	**Primary outcome(s):** HRQoL measured using SF-36 to calculate QALYs **Cost year (currency):** cost year unspecified ($ unspecified, study country currency USD$) **Summary result(s):** Provider perspective $22,200 per QALY (12-week QALY gain of 0.03) equating to an annual QALY gain of 0.13 and first year cost per QALY of $5,163. **MBP intervention costs:** direct costs of $666 per person (costing clearly outlined in paper including breakdown of cost items and data collection methods).
16	Rakel et al. (2013).	Societal perspective	Secondary data analysis of randomised controlled trial (RCT) data on resource use and lost work time to generate probability data based on Monte Carlo boot strap analysis. Cost comparison study	1 year (no discounting)	**Primary outcome(s):** mean costs from lost work time, health care visits and medications. **Cost year (currency):** 2013 (USD$) **Summary result(s):** "Comparing the meditation group ($65 per person) with the control group ($214 per person) there was a significant reduction in total cost. If these findings were extrapolated to the general population, assuming Fendrick's estimate of $40 billion spent annually on ARI, the cost savings could amount to $28 billion a year" (Rakel et al., 2013, p. 394). **MBP intervention costs:** $450 (estimated, methods undefined)

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
17	Rohricht et al. (2018).	Not stated (societal implied)	a cohort intervention study Cost comparison study	12 months (no discounting)	**Primary outcome(s):** primary and secondary health care use, prescribed medication and social care including informal care from family/friends, employment rates and state benefits. **Cost year (currency):** 2015 (£GBP) **Summary result(s):** Mean reduction was £3867 per patient over the 6 months post intervention. No difference in social care, employment, or benefits. **MBP intervention costs:** (BOPT and MBSR) calculated as £228 per person (costing using study high level study information, with estimated values outlined in paper).
18	Roth & Stanley. (2002).	Not stated	1 group pre-post design (*N=47*) Primary health care resource use	26 months (12 months pre-8-week MBSR course and 12 months post (no discounting)	**Primary outcome(s):** primary care resource use **Cost year (currency):** no costs. **Summary result(s):** The annual average number of primary care visits was significantly lower after patients received MBSR. **MBP intervention costs:** No costs are reported.
19	Saha et al (2018).	1) Health care perspective 2) Societal perspective	Randomised Controlled Trial-based economic evaluation (MBT *N=110*; TAU *N=105*).	8 weeks (no discounting)	**Primary outcome(s):** HRQoL measured using EQ-5D-5L to calculate QALYs **Cost year (currency):** using the 2012 (Swedish Kronor, SEK, converted to euros, EUR, using the 2012 exchange rate of 8.705 SEK/EUR.15

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
			Cost-utility analysis		**Summary result(s):** MGT cost per person €398. No significant difference between groups in terms of QALYs however, MGT was cost saving to health care and society with savings of €115 (health care) per person and €112 (societal) in an 8-week period. MGT has a 70% probability of being cost-effective from the health care perspective and 67% probability of cost-effectiveness from a societal perspective. **MBP intervention costs:** 3,462 kr (Swedish Krona) per participant (costing methods described in full in Saha et al (2018) supplementary material.
20	Shawyer et al. (2016).	1) Mental health care perspective 2) Health care perspective 3) Societal perspective	Trial-based economic evaluation 1) Cost-effectiveness analysis 2) Cost-utility analysis	24 months (3% discount rate)	**Primary outcome(s):** DALYs calculated as length of life and quality of life (number of days in a major depressive episode during the previous 12 months weighted by depression severity) **Cost year (currency):** 2009 first quarter (Australian dollars AUD) **Summary result(s):** "From a whole-of-society perspective, analyses of patients receiving usual care from all sectors of the health-care system demonstrated dominance (reduced costs, demonstrable health gains). From a mental health-care perspective, the incremental gain per DALY for MBCT was AUD83,744 net benefit, with an overall annual cost saving of AUD143,511 for people in specialist care" (Shawyer et al., 2016, p. 1001). **MBP intervention costs:** Programme costs used are not clearly reported as not presented separate to wider resource use costs. Methods outline the source of unit costs as the Australian Government Medicare Benefits Schedule.

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
21	Social Value Cymru (2016).	Societal perspective.	SROI (stakeholders - *N=9* parents; *N=78* children; *N=7* professional staff)	10 months study duration (3.5% discount rate).	**Primary outcome(s):** social value generated **Cost year (currency):** 2015 (£ GBP) **Summary result(s):** £3.65:1 **MBP intervention costs:** Four courses delivered with a total financial input of £15,786.63 equivalent to £141 per stakeholder.
22	Tulloh et al. (2018).	Not stated	A pilot randomised controlled trial-based economic evaluation (MBSR *N=18*; TAU *N=16*) Intervention cost analysis	15 months (no discounting)	**Primary outcome(s):** Intervention costs. **Cost year (currency):** 2015 (£ GBP) **Summary result(s):** A range of feasibility outcomes are reported including qualitative findings on intervention acceptability. **MBP intervention costs:** Mean cost of MBSR per person ranged between £372 and £1538) depending on costing approach and number of participants per group (available attendance and actual attendance).
23	van Dongen et al. (2016).	1) Societal perspective 2) Employers' perspective	randomised controlled trial based economic evaluation (*N=257*), 1) Cost-effectiveness analysis 2) Return on investment analysis	12 months (no discounting)	**Primary outcome(s):** Resource use (health care and employer costs), work engagement, general vitality, job satisfaction and work ability **Cost year (currency):** 2011 (Euros). **Summary result(s):** Societal perspective CEA: • Work engagement ICER of €-7321 (Dominated) • General vitality ICER €-470 (Dominated) Employers' perspective CEA: • Work engagement ICER of €-8593 (Dominated) • Job satisfaction ICER of €-8593

	Author (Year)	Perspective(s)	Type of economic evaluation (study design and stage e.g., pilot / total number of participants)	Time horizon (discount rate)	Outcomes / Results
					• Work ability ICER of €-5081 (Dominated) Employer perspective financial returns analysis (95% CI) • NB -1635 (€- 4268 to €973) • BCR -2.51 (€ -8.19 to €3.10) • ROI -315% (€-919 to €210) **MBP intervention costs:** €171 per participant (societal perspectives); €464 per participant (employer perspective). Micro-costing methods used to cost MBP from a societal perspective and market prices applied for course costs from an employer perspective.
24	van Ravesteijn et al. (2013).	1) Health care perspective 2) Societal perspective	Randomised controlled trial-based economic evaluation (*N=125*: MBCT; *N=64*; enhanced TAU *N=61*) Cost-utility analysis	12 months (no discounting)	**Primary outcome(s):** HRQoL measured using SF-6D to calculate QALYs **Cost year (currency):** 2010 (Euros) **Summary result(s):** ICUR = €56,637 per QALY. A 48% probability of cost-effective at Euro €40,000 societal WTP threshold / 57% at Euro €80,000. **MBP intervention costs:** €450 mean cost per person (methods not clearly defined, data from resource use diaries and attendance records)
25	Zgierska et al. (2017).	Not stated	An un-blinded pilot randomised controlled trial-based economic evaluation (MM+TAU *N=21*; TAU *N=14*). Cost-comparison study	26-week (no discounting)	**Primary outcome(s):** Costs related to self-reported health care utilisation, medication use (direct costs), lost productivity (indirect costs). **Cost year (currency):** 2013 (US dollars) **Summary result(s):** No statistically significant impact of MM+TAU on costs related to opioid-treated chronic back pain. **MBP intervention costs:** Not reported or included within analysis.

Upcoming evidence

Eighteen trial protocol publications were identified in the review (Bogosian et al., 2017; Bryning, Edwards, & Crane, 2013; Carlson et al., 2017; Castro et al., 2015; Cherkin et al., 2014; Compen et al., 2015; Dowsey et al., 2014a; Feliu-Soler et al., 2016; Fletcher et al., 2018; Huijbers et al., 2012; L. Janssen et al., 2015; Kuyken, Byford, et al., 2010; Kuyken et al., 2017; Meppelink, de Bruin, & Bögels, 2016; Schellekens et al., 2014; Shawyer et al., 2012; van Berkel, Proper, Boot, Bongers, & van der Beek, 2011; Veringa et al., 2016).

Six of the protocols were for studies that had been complete and have already been included in the results of this systematic review:

1. Cherkin et al., 2014 (Herman et al., 2017)
2. Compen et al., 2015 (Compen, Bisseling, Donders, et al., 2017)
3. Janssen et al., 2015 (Janssen et al., 2019)
4. Kuyken et al., 2010 (Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Brejcha, et al., 2015)
5. Shawyer et al., 2012 (Shawyer et al., 2016)
6. van Berkel et al., 2011 (van Dongen et al., 2016a)

One final protocol paper identified (Feliu-Soler et al., 2016) has been published following the inclusion date of this systematic review (Pérez-Aranda et al., 2019). Pérez-Aranda and colleagues evaluate the cost-utility of MBSR for fibromyalgia, a chronic syndrome with symptoms including high pain, and often incurring high health care costs. The economic evaluation was conducted alongside a 12-month RCT comparing MBSR with an active control and a treatment as usual condition. Analysis was conducted from both a Catalonia government and public health care system perspective. MBSR resulted in a reduction of health care costs compared with control conditions, however, the difference was not significant in all the analyses performed. MBSR was the dominant treatment compared with TAU and the active control FibroQoL in all analysis except for one. In the complete case analysis comparing MBSR and FibroQoL the cost-utility analysis with EQ-5D as the source of utility indicated a cost per QALY of €385,400 (equivalent to £340,571 in 2019 terms) which is unlikely to be considered cost-effective.

Two protocol publications were identified with completed trial papers published; however, they did not report on the economic evaluation as outlined in their protocol:

1. Preventing relapse in recurrent depression using mindfulness-based cognitive therapy, antidepressant medication or the combination: Trial design and protocol of the MOMENT study (Huijbers et al., 2012). While a completed randomised controlled trial publication was identified (Huijbers et al., 2015), the study reported no significant differences in effectiveness and the authors highlighted it was underpowered for an economic evaluation. The protocol paper outlined a societal perspective cost-utility analysis.
2. Study protocol of a randomised controlled trial comparing Mindfulness-Based Stress Reduction with treatment as usual in reducing psychological distress in patients with lung cancer and their partners: the MILON study (Schellekens et al., 2014). A completed pilot trial publication was identified where no significant differences in effectiveness were recorded (van den Hurk, Schellekens, Molema, Speckens, & Van Der Drift, 2015). However, no economic evaluation was reported despite the protocol paper outlining a societal perspective cost-effectiveness analysis.

In addition, 9 further protocol publications had not published completed results papers to date:

1. Distant delivery of a mindfulness-based intervention for people with Parkinson's disease: the study protocol of a randomised pilot trial (Bogosian et al., 2017).
2. Study Protocol: Exploring the Cost-Effectiveness of Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) (Bryning et al., 2013). This study is reported on in Chapter 4.
3. Protocol for the MATCH study (Mindfulness and Tai Chi for cancer health): a preference-based multi-site randomised comparative effectiveness trial (CET) of Mindfulness-Based Cancer Recovery (MBCR) vs. Tai Chi/Qigong (TCQ) for cancer survivors (Carlson et al., 2017).
4. Efficacy of low-intensity psychological intervention applied by ICTs for the treatment of depression in primary care: a controlled trial (Castro et al., 2015).
5. The effect of mindfulness training prior to total joint arthroplasty on post-operative pain and physical function: study protocol for a randomised controlled trial (Dowsey et al., 2014a).
6. Web-based intervention to improve quality of life in late stage bipolar disorder (ORBIT): randomised controlled trial protocol (Fletcher et al., 2018).
7. The effectiveness and cost-effectiveness of a mindfulness training programme in schools compared with normal school provision (MYRIAD): study protocol for a randomised controlled trial (Kuyken et al., 2017).
8. Meditation or Medication? Mindfulness training versus medication in the treatment of childhood ADHD: a randomised controlled trial (Meppelink et al., 2016).

9. ‘I’ve Changed My Mind’, Mindfulness-Based Childbirth and Parenting (MBCP) for pregnant women with a high level of fear of childbirth and their partners: study protocol of the quasi-experimental controlled trial (Veringa et al., 2016).

Trial registration records

Twenty-eight trial registration records were identified as part of the review from 5 trial registration databases (see Appendix 6 for summary of trial registrations and overview of planned economic evaluation methods). The records were screened to identify planned economic evaluations key features, however, most of the trial registration records contained limited details about the methods to enable detailed analysis and critical appraisal of the studies. Cost-utility analysis and cost-effectiveness analysis were most often listed as the planned form of economic evaluation. While partial economic evaluations were planned considering productivity losses and resource use cost comparison between study arms. Linked publications (e.g., protocol papers) were searched for further details on economic methods and any resulting outcome papers were screened for economic evaluation results. Even when studies had been completed and main outcomes published in several cases there remain no published health economics evaluations. It is anticipated that some of these papers are likely to be in progress or submitted and pending publication.

One publication identified reported on the completed economic evaluation in the Meditation or exercise for preventing acute respiratory infection (MEPARI-2) randomised controlled trial was identified (Barrett et al., 2018). This study follows on from the results of the MEPARI trial reported above (Rakel et al., 2013) (see study number 16 in Table 5 and Table 6). The findings from this large (*N=413*) three-arm RCT comparing MBSR, moderate intensity exercise (EX) and a waitlist control condition were as follows:

“There were 73 ARI-related days-of-missed-work and 22 ARI-related health care visits in the MBSR group, 81 days and 21 visits for EX, and 105 days and 24 visits for control. Mean ARI-related economic costs (including the cost of absenteeism) were $140 ($83, $197) for MBSR, $119 ($62, $175) for EX, and $163 ($95, $231) for control. Trends towards reduced absenteeism and ARI-related costs for both EX and MBSR were not statistically significant. On average, controls used 2.9 (2.6, 3.2) medications per ARI episode, similar to 2.8 (2.3, 3.2) medications for those in the MBSR condition. Exercisers used fewer medications than controls during ARI episodes (2.2 vs. 2.9; p = 0.001). Total ARI-related economic costs were slightly lower in both EX and MBSR groups compared to control” (Barrett et al., 2018, p. 8).

Discussion

Synthesis of findings

There is a small but growing evidence base of economic evaluations of MBPs with the number of economic evaluations published during the last decade growing, however, not keeping pace with the rapid increase of publications on MBPs in general (see Chapter 1). This is commonly observed with a preference towards publications on effectiveness compared with cost-effectiveness. Particularly as the economic evaluation may not get published or progress if the intervention is not first established to be effective (Huijbers et al., 2012, 2015; Schellekens et al., 2014; van den Hurk et al., 2015).

Twenty-five completed economic evaluations were identified. Fourteen of the studies were full economic evaluations where both benefits and costs were assessed, while eleven of the studies were partial economic evaluations for example where only costs or a single economic outcome were considered. Cost-utility analysis was the most common form of economic evaluation, followed by cost-effectiveness analysis. Cost-comparison studies were the most common form of partial economic evaluation. Perspectives of analysis included societal, health care, employer, patient, with many of the economic evaluations using more than one perspective in their analysis. The MBPs included MBSR, MBCT and programmes which had been adapted to be tailored to meet the needs of a specific patient population (e.g., for adults with ADHD) or specific delivery context (e.g., in an employment setting). In terms of clinical populations, the most common economic evaluation focused on MBPs for the management of depression (*N=6*) and cancer recovery (*N=3*). Economic evaluations of more novel clinical applications included medically unexplained symptoms and BDS (*N=3*). There were only a few non-clinical setting studies including an economic evaluation, with employment being the most common (*N=3*).

Synthesis of the main economic evaluation evidence

MBP for management of depression

MBPs for the management of recurrent depression were the most common evaluations to include an economic evaluation (*N=6*). As MBCT is recommended by NICE in the UK for the management of depression (NICE, 2018) this was not unexpected. NICE guidance in the UK included the cost-effectiveness evidence from Kuyken et al (2008) in their guidance and health economics appendix of evidence (NICE, 2010; 2018), however, no further economic evidence of MBP for depression management has been included in NICE evidence reviews.

The review highlights that evidence from the UK on whether MBCT is cost-effective for the management of depression is limited, with one pilot study (*N=123*) and one larger RCT (*N=414*) providing mixed findings (Kuyken et al., 2008; Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Morant, et al., 2015). Kuyken et al 2008 "suggest that the additional cost of MBCT may be justified in terms of improvements in the proportion of patients who relapse" (NICE, 2018, p. 239).

There is more support in favour of MBCT as "a best buy" for public health when considering international economic evidence e.g. the Australian RCT (*N=203*) which included a 2 year follow-up and conducted economic evaluation from a range of perspectives concluding MBCT compared to control condition (depressive relapse active monitoring) was likely to be cost saving to society (Shawyer et al., 2016). There may be important differences in target populations, settings and health care systems between UK and Australia that limit the comparison of these studies.

MBP for other populations and settings

There was limited evidence of economic evaluation in other population areas and a total absence of economic evaluations of MBPs for many other conditions, although published protocols and trial registrations records identified as part of this review indicate that more evidence is upcoming. MBPs in cancer populations were identified in three completed economic evaluations, two protocol papers of research in progress, and six trial registration records, including the pilot evaluation which is discussed further in Chapter 4.

Although there were three employment-based studies there was limited evidence from non-health sector despite increasing implementation of MBPs outside of health care services in schools and private settings.

This review found that all economic evaluations published to date focused on MBPs for adult population groups. Except the SROI of the Nurturing Parents mindfulness programme which included impacts on children as stakeholders. With a trend for national implementation of MBPs in some UK schools, the economic case for investing in these programmes warrants further economic evaluation (see Chapter 5). The Myriad trial protocol (Kuyken et al., 2017) highlighted in upcoming research, outlines a planned cost-effectiveness analysis from a societal perspective and includes plans for longer term costs and outcomes economic modelling outside the 2-year time horizon trial.

Health economics methodological considerations

Defining MBPs, target population, settings, and location

This systematic review has highlighted that MBPs cover a broad category of interventions and there is substantial heterogeneity with the programmes, population groups, and outcomes of interest differing considerably, making meta-analysis of data inappropriate and generalizability of the findings difficult. MBPs varied both between populations and within populations for example of the three employment-based programmes:

1. 8 week moderate dose (1.5hr sessions) Mindful ‘‘Vitality in Practice’’ (VIP) programme (adapted from MBSR) integrated within a wider health promotion programme including intranet access, e-coaching, fruit and veg available over a 6 month period (van Dongen et al., 2016a)
2. 8 week low dose (1hr sessions) adapted MBSR (Klatt et al., 2016).
3. 7 week low dose (1hr sessions) Mindful Resilience programme adapted MBSR (Aikens et al., 2014).

All share the trend for a lower weekly dose of MBSR which appears to be popular in certain setting such as busy workplaces (Bartlett et al., 2019; Lomas et al., 2019).

Although this review covers varied MBPs, it was limited to interventions which were derived from MBSR/MBCT models. This was to provide clear boundaries for the inclusion and exclusion of studies, to aid the comparison across research identified through the review and the scope would have been too broad had a broader definition of MBP been adopted. It is important to acknowledge however, that this excluded some studies of MBPs and mindfulness-informed programmes, such as the work by Nirbhay Singh and colleagues evaluating the benefits and costs of Mindfulness interventions in the field of intellectual and developmental disability (IDD), including the Soles of the Feet intervention for adults with IDD (Roberts et al., 2020; Singh et al., 2008) and the Mindfulness-Based Positive Behaviour Support (MBPBS) intervention for caregivers of people with IDD (Singh, Lancioni, Karazsia, Chan, & Winton, 2016; Singh, Lancioni, Karazsia, & Myers, 2016; Singh et al., 2015, 2018). MBPBS includes elements of mindfulness and other meditation practice as part of the core training received over three days, however, the programme varies significantly from MBCT/MBSR models. For the purpose of this thesis research MBPBS was considered in the same category as programmes such as DBT and ACT which include mindfulness but are not based on them, nor are derived from MBSR/MBCT models. This evidence base warrants further exploration to establish the potential cost-effectiveness of mindfulness and acceptance based psychological therapy in the field of IDD.

Not all programmes provided sufficient details of the MBP, improving the reporting of the intervention integrity of the MBP being researched is an important consideration (Crane et al., 2016; Crane & Hecht, 2018). Few studies provide enough information to assess the quality of intervention integrity in full,

which in turn means that a critical variable in the research process is not clearly accounted for. Evidence of adequate teacher training and assessment of teacher competence were often missing completely or poorly reported. Where there was limited information on the details of the MBP (Table 5) full fidelity to the programme could not be assessed using the Template for Intervention Description and Replication (TIDieR) checklist adapted for application in MBP research (Crane & Hecht, 2018; Hoffmann et al., 2014) (See Appendix 5). Providing full details of adaptations including 'slight modification' allow for replicability of research and aid future implementation of programmes.

Study design: the role of early economic evaluation studies

MBPs are both complex interventions and may be delivered as part of a portfolio of programmes within complex systems, making it difficult to untangle findings. Recognising MBPs as complex interventions, further highlights the role for pilot and feasibility trials to help develop definitive trials with high methodological rigour. The role of pilot and feasibility trials of complex interventions is to establish the suitability of research measures to capture the economic costs and benefits. Not all studies identified themselves as 'pilot' or stage ii clinical trials; however, the small sample size and limited previous evidence in these areas indicates the early stage of some of the evaluations. Process evaluation and qualitative methods to explore early economic methodological considerations may help improve the design of future trials and help untangle the findings in trials (Byford & Sefton, 2003; Moore et al., 2015).

While previous systematic reviews excluded non-randomised studies "owing to their susceptibility to bias" (Feliu-Soler et al., 2018, p. 143), this review aimed to include all economic evidence to help explore the role of pilot and feasibility research in economic evaluations of MBPs.

This study included small studies despite criticism of low internal validity of the results (Duarte et al., 2019). One example of good practice employed in pilot studies that included economic outcomes, comes from the UK pilot study of MBSR (*N=18*) compared with TAU (*N=16*) (Tulloh et al., 2018). This study acknowledges the sample size would be underpowered for comparison across groups and uses the study to pilot the MBP and the economic evaluation outcome measures to help inform a full trial, and to cost the intervention. However, this review also highlights other studies which would be considered pilot; however, full economic analysis is conducted. The sample sizes vary considerably in these studies and the interpretation of an ICER in an underpowered study warrants caution.

In addition, unlike previous reviews where "Unpublished studies were also excluded as numbers enrolled may vary between unpublished data and final publications" (Feliu-Soler et al., 2018, p. 143),

this review included trial registration records to help provide an indicator of upcoming economic evaluations and methodologies. In parallel with the findings from the review of completed research, cost-utility analysis and cost-effectiveness analysis were the most popular planned form of economic evaluation reported in trial registration records. In addition, a few partial economic evaluations were planned considering productivity losses and resource use cost comparison between study arms. Unfortunately, due to limited details provided in most trial registration records it was not possible to identify any emerging trends around perspectives of analysis or outcome measurement methods.

In cases where effectiveness was not established the planned economic evaluations were not always reported (Huijbers et al., 2012, 2015; Schellekens et al., 2014; van den Hurk et al., 2015). A meta-analysis of cost-effectiveness evidence may be skewed by the availability of data and publication bias for positive results alone, and it may not provide a complete picture of value for money. The findings from this review highlighted that where studies had progressed from protocol to completed research that the planned health economics was not always reported in comparison with main study outcomes. However, it is anticipated that number of health economics publications may be forthcoming as standalone publications.

Forms of economic evaluation

Cost-utility analysis was the most commonly used method of analysis, being used in 32% (*N=8*) of the economic evaluations (*N=25*). Of these studies half also conducted cost-effectiveness analysis as another method of analysis. Cost-effectiveness analysis was used in 28% (*N=7*) of the studies (5 of which also conducted a second method of analysis). Six studies (24%) involved cost-comparison analysis reporting on the costs of resource used. Three further studies (12%) reported on resource use but did not apply any costs. Two studies used SROI methodology (see below for further discussion). One study calculated ROI to demonstrate financial returns (which was in addition to the primary CEA). One study reported to use cost-benefit analysis. Two studies reported intervention costs alone.

The two studies that used SROI methodology (Fox Advising CIC, 2012; Social Value Cymru, 2016) were identified in grey literature rather than published peer-review papers. The results indicated £3.65 (Social Value Cymru, 2016) and £10.12 (Fox Advising CIC, 2012) of social value was generated for every £1 invested in the MBP. The critical quality appraisal of the two SROI studies was useful in the interpretation of these findings: while the Social Value Cymru (2016) indicated that the study was of high quality, the quality appraisal of Fox Advising CIC (2012) was inhibited by the impact map being unavailable for assessment indicating the results should be interpreted with caution as the study is of potentially low quality.

While comparisons with other studies is difficult due to different ROI methodologies and different interventions of interest, the ROI from mental health interventions more generally has been reported to be between £1.57 to £11.91 for every £1 invested (Banke-Thomas et al., 2015). Investing in workplace mental health is reported to generate a good return on investment of £9 for every £1 invested (Knapp, McDaid, et al., 2011).

Local authorities along with non-government organisations, charities and voluntary providers of services are increasingly looking to ROI and SROI as a means of quantifying social value generated and potential financial returns of investment (West, 2016). SROI is increasingly popular in public health and mental health evaluations which some argue offer a methodology capable of measuring broader outcomes relevant to a wide range of stakeholder (Banke-Thomas et al., 2015). While SROI studies have the potential to capture wider economic benefits, they raise a number of methodological challenges, in part because there is little standardisation (Fujiwara, 2015). Greater consistency in the methodology and interpretation of the results is required, and researchers should take note of available quality appraisal frameworks (Hutchinson et al., 2019a) which could be a useful tool comparable to the PRISMA self-assessment checklist for systematic reviews (see Appendix 1).

Trials of MBPs which have included a concurrent economic evaluation have commonly adopted a cost-utility or cost-effectiveness approach in a clinical setting (Kuyken et al., 2008; Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Brejcha, et al., 2015; van Ravesteijn et al., 2013a). It has been argued that MBPs delivered in non-clinical settings such as schools and workplaces should be evaluated with cost-benefit or cost-consequence analysis in order to capture a full range of potential benefits including non-health benefits such as the financial impact of improving educational standards or reducing absenteeism (Edwards et al., 2015).

Study perspective

Several studies failed to state the perspective of analysis. NICE recommends a NHS and personal social services perspective within a UK clinical context, and in certain contexts advocates for alternatives such as in public health contexts where a societal perspective may be more appropriate. Where the perspectives of analysis was reported in the systematic review papers these included a health care perspective, societal perspective, patient perspective, and employer perspective, with many of the economic evaluations using more than one perspective in their analysis.

In the context of management of depression (in Australia) the case for considering a 'mental health care' perspective is put forward with the authors highlighting that "commissioners or managers need to make decisions based on a narrower budgetary perspective" (Shawyer et al., 2016, p. 1010).

Time horizon

Most of the studies had a time horizon of 1 year or less (60%, *N=15*). Of the remaining studies, only two of the evaluations had a time horizon of more than 2-years: one study which had a projected time horizon of 20-years (Lengacher et al., 2015), and one study with a 5-year time horizon (Klatt et al., 2016). Few studies considered the potential for costs and benefits to continue, and whether follow-up MBP sessions are necessary to sustain benefits outside of the short trial duration.

MBPs have been promoted as a preventative intervention; however, the time horizons of the studies identified through this review may be too short to identify the future costs averted and/or benefits gained. The potential use of economic modelling to explore longer term impacts of prevention warrants further consideration in the economic evaluation of MBPs.

Discount rate

Most of the studies adopted a short time horizon of under one year and neither costs nor benefits were discounted. With a study period of more than 12 months Kuyken et al (2015) discounted costs and benefits at 3.5%, while Shawyer et al (2016) discounted at 3%. Lengacher et al (2015) include a 3% discount rate for QALYs gained for each additional year extrapolated (up to 20 years in total). Within SROI methodology the discount rate adopted was 2% (Fox Advising CIC, 2012) and 3.5% (Social Value Cymru, 2016). For public health interventions and prevention evaluations there has been discussion in recent years about whether the discount rate should be varied.

Estimating resources and costs

Health care resources used are considered in a large proportion of the economic evaluations of MBPs, recognising the most common focus of the MBP as a health improving programme, which may also have the secondary benefit of reducing health care resources used. There are a number of methods available for collecting information on resources used such as resource use questionnaires, or direct from medical notes or hospital records, few studies provided clear information about the methods for the collection of resource use data and how resources were valued.

The cost of the MBP varied considerably and not all programmes reported them. For those that did the methods for costing were rarely specified. Social Value Cymru (2016) reported the cost of the

programme as £141 per stakeholder and note for comparison a typical fee for the general population as provided by a UK Mindfulness Centre as £225 per person for an 8-week course. There are example of good practice which clearly evidence a bottom-up micro-costing (van Dongen et al., 2016b), and studies which give consideration to MBP cost uncertainty, for example, accounting for variation in group size when considering participants actual attendance compared with participants allocated to attend (Tulloh et al., 2018). A diversity of methods for costing and poor reporting in methods of costings result raises for challenges for comparing across studies. Improved reporting on the costs and attention to the appropriate methods for costing is needed, Chapter 3 of this thesis will consider the methods of costing MBPs further.

Update to systematic review with recent publications

One additional paper was identified following the completion of this systematic review and finalising this thesis. A German based non-randomised propensity score matched trial evaluated the cost-effectiveness of a universal 'mindfulness based mental health promotion program' compared with usual care. From a societal perspective the MBP had "an ICER of €-29 (savings) per unit improvement" on the Hospital Anxiety and Depression Scale (HADS), while from a health care perspective the MBP yielded "an ICER of €91 per unit improvement"(Müller, Pfinder, Schmahl, Bohus, & Lyssenko, 2019, p. 1). The authors of the study highlight the variation in results depending on perspective of analysis and that there is a case for multiple stakeholder investment in preventive services. This study provides a good example of a pragmatic evaluation of a universal health promotion and mental ill health prevention programmes delivered in community settings. However, the 12 month time horizon means that longer term outcomes may not be reflected in analysis due to "time lag of effects" and that benefits of prevention may be underestimated (Müller et al., 2019, p. 10).

Strengths and weaknesses of the study

As the first substantive societal perspective review, a strength of this study is that it consolidates a varied and growing literature base. Limitations include that the scope of the review and the range of MBPs identified resulted in a large but heterogeneous evidence base, making more narrow definitive comparisons difficult. While this limited the interpretation around cost-effectiveness of MBPs it is also an important finding highlighting that there needs to be a more joined up approach to data collection and methodology so that larger scale interpretation of the evidence becomes possible. The MBPs included within this review had both treatment and prevention focus and the programmes vary sufficiently to highlight caution in generalisation from one MBP to another.

Possible implications for clinicians, policymakers, and researchers

NICE guidance for depression warrants greater inclusion of economic evidence to fully inform the case for investment in the UK NHS. While this review has highlighted mixed evidence on the cost-effectiveness of MBPs in depression, further research is required to help explore the potential long-term benefits and costs of preventing depression relapse.

This review builds on previous work which highlights the need to improve the reporting of economic evaluations (Jacobsen et al., 2020), using recommended checklist on reporting e.g. CHEERS (Husereau et al., 2013).

Unanswered questions and future research

It was not possible to comprehensively compare economic methodology across sectors. There may be important lessons learnt from health care economic evaluations than can inform evaluations in other sectors such as education. This is discussed further in Chapter 6.

More evidence of what works best, for whom and when is needed to enable a precision public health approach to achieving better mental health in the population. The cost-effectiveness of MBPs delivered with fidelity to targeted populations at increased risk of poor mental health requires further investigation. Economic evaluation of MBPs delivered with a universal prevention focus, at an early stage of intervention, for example in schools is needed.

Conclusions

This review provides the first substantive review conducted from a societal perspective to explore the published literature on the cost-effectiveness and return on investment of MBPs delivered in any public or private sector (health care, social care, education, employment) to any population (i.e., not exclusive to mental health).

Through identifying and synthesising the body of published economic evaluations this review aimed to help establish whether the delivery of MBPs provides a cost-effective use of societal, public, or private resources. Although there is a growing evidence base in some areas of application, there is a need for further high-quality economic evaluations with improvements needed in reporting of both the MBP features and the methods of analysis.

Through this systematic review, several key methodological considerations are highlighted for the design, conduct and reporting of economic evaluations of MBPs as complex interventions at various

stages of the evaluation process including study design, pilot and feasibility trials and randomised controlled trials. The following chapters in this thesis go on to discuss these methodological considerations further, particularly methods for MBP intervention costing (see Chapter 3 on micro-costing MBPs), and economic outcome measures to assess health care resource use and societal impacts across sectors (see Chapter 4 on pilot evaluation of a MBP in cancer care and Chapter 5 on pilot evaluation of a MBP in a school setting).

Chapter 3: Applying micro-costing methods to estimate the costs of Mindfulness Based Programmes

Chapter preface

Chapter 3 focuses on exploring the costs of implementing MBPs and to address the second thesis research question of "What is the cost (and drivers of cost) in the delivery of MBPs?" As highlighted in Chapter 2 the cost of MBPs is not always reported in the publication of MBP economic evaluations, and there remain logical questions about the appropriate methods for costing MBPs. This chapter presents a multi-programme micro costing evaluation of MBPs to assess the cost of delivering MBPs in different settings and to different populations. This empirical study was conducted between 2013 and 2014, I designed the study, recruited participants, and collected data from a range of MBP practitioners about micro-level costs of delivering MBPs. I independently conducted the analysis and wrote up the findings in this thesis chapter format. While MBP implementation is expanding there are barriers to implementation and there is a paucity of information available on critical issues such as the true cost of delivering programmes. Obtaining accurate cost information will enable further economic analysis of MBPs as a way of supporting and promoting good mental health and the implementation process. Future research with built-in measures of costs and resource use should enable robust economic evaluations and help inform national decision makers and local commissioners and managers who hope to successfully implement services.

Chapter 3 Abstract

Overview

The costing of interventions can be conducted by using various methods, and different costing methodologies can produce significant variations of unit costs. The chosen methodology can influence the economic analysis outputs sufficiently to alter policy recommendations and the subsequent adoption or otherwise of new interventions. It is necessary to obtain accurate costs at a micro-level to perform robust economic analysis such as cost-effectiveness or cost benefit analysis. MBPs vary in terms of the target population, the setting and how they are tailored to meet the needs of service users – these factors may impact the cost of the intervention. A standardised methodology (specific to MBPs) for the collection of cost information alongside clinical trials could help aid researchers wishing to evaluate the cost-effectiveness of MBPs. This thesis chapter sets out a framework for the collection of detailed resources required for the delivery of MBPs in a range of settings. Micro-costing methods can be applied both alongside research trials and within routine practice delivery to estimate the economic cost of programme delivery. This chapter builds on previous work on developing a practical set of steps

for costing complex public health or psycho-social interventions for the purpose of economic evaluations.

Methods

This micro-costing was undertaken in a range of settings and client populations between October 2012 and January 2014 . The study aimed to capture the variety of MBP courses delivered in the UK including targeted prevention programmes aimed at managing depression relapse in high-risk groups (i.e., cancer patients) and universal prevention programmes aimed at promoting mental health resilience in children and young people (i.e., through schools and university settings). This study employed a combined micro-costing technique (both bottom-up and top-down) for the collection of detailed cost information of the delivery of MBPs from both research and 'real world' routine practice contexts. Micro-costing methods were employed through the collection of data directly from MBP teachers through the completion of a resource use diary developed as part of this study. The top-down construction of initial MBP teacher training was undertaken to estimate initial set up costs that weren't otherwise included in the cost diaries (e.g., if the MBP teacher had been trained for more than one year, which was outside the range of the costing diary).

MBPs may have costs and benefits that span multiple sectors. It is necessary to collect a full range of costs and benefits relevant to the perspective of analysis. This micro-costing analysis was conducted from a public sector multi-agency perspective to be applicable to the range of MBPs evaluated.

Due to the nature of MBPs operating with a limited capacity most commonly as 'closed groups' where new participants cannot join after the start date or take a place following a drop out, the costs were shared amongst the number of spaces in a group that were allocated rather than amongst those that attended each session. Unit costs were applied where appropriate from national reference costs and all costs are reported in GBP£ 2013/2014 cost year. Costs were annuitized and discounted to reflect that the resources were used more than once in each year and used over a period of more than one year. Sensitivity analysis was used to test the core assumptions used within the analysis i.e., inclusion of initial development and implementation costs; number of treatment sessions delivered; participants in each course; the number of courses delivered each year; discount rate used; period of annuitisation.

Results

A total of ten MBP courses were costed as part of this micro-costing study. The different settings were categorised as Hospital, Hospice, Community Centre, Private residence, University, School, or Workplace. In the base case analysis the total costs ranged from £2,786 to £6,302 per MBP course. This

equated to between £111 and £645 per participant. The highest cost per participant (£645) was obtained in a clinical setting where there was a low number of participants in each group (*N=8*). While the lowest cost per participant (£111) was obtained in a general population context where there were a high number of participants in each group (*N=25*).

Discussion

This micro-costing study illustrates for the first time the costs for a range of MBPs delivered both as part of normal service delivery and within a research trial. MBPs included targeted programmes for a specific patient group (e.g. people recovering from cancer) and more universal programmes delivered in a range of settings (universities, workplaces, and schools). If cost estimates are based on insufficient details, then this may result in poor cost-effectiveness analysis and threaten accurate evidence-based service commissioning and policy development and inhibit the likely success of implementation and sustainability. This chapter concludes that as a core part of future economic evaluations researchers collect detailed information on the resources for implementation and delivery to establish a full range of costs and benefits of the interventions and help determine whether the intervention could be cost-effective against an alternative treatment. A standardised resource use data collection tool and costing schema specific to MBPs are outlined as part of this chapter to support future research. Future research with built-in measures of costs and resource use should enable robust economic evaluations and help inform national decision makers and local commissioners and managers that hope to successfully implement services.

Introduction

The cost of MBPs

There is increasing interest in group-based psychological therapies which may offer a low cost per patient due to high ratios of patients to therapist(s), in comparison to alternative treatments such as individual therapy (Barrett & Byford, 2008). Indeed, some authors have argued that MBPs[4] are likely to be cost-effective because they are most commonly delivered in a group context (Teasdale et al., 2000). However, it is important not to make assumptions as many factors can influence the cost of a group-based intervention, such as, the number of patients attending, the professional required to facilitate the group, and the type of intervention itself (Edwards et al., 2015). For MBPs the population groups can vary considerably, and several adaptations of the core programmes may be considered to make the programmes more relevant or suitable for the specific target population and/or context. Therefore, the costs and effects of one MBP may not be generalisable to other contexts. With an increasing number of MBP adaptations and applications it is important to establish, along with the possible benefits, what the costs are, and whether a framework for the collection of detailed costs could be employed to capture any variation across courses that could have an impact on a full economic evaluation.

Costing complex interventions

MBPs are considered complex interventions as defined in the Medical Research Council (MRC) guidelines (Craig et al., 2008; Moore et al., 2015). They are complex due to the number of component parts that may operate independently of one another, and this means special consideration is required in terms of the analysis and evaluation. The MRC guidelines outline a framework for the development and evaluation of complex interventions and identify the need to consider cost at multiple stages of the development-evaluation-implementation process. Despite the advances in evaluating MBPs in terms of the potential benefit there has been little focus on the costs of interventions and the evaluation of whether they are cost-effective interventions compared with alternative treatments.

Costing complex interventions is challenging which may explain this gap (Bonin & Beecham, 2012). The complexity of the costing increases with the complexity of the intervention (e.g., group based, multiple component interventions) and context (e.g., clinical practice or multi-site randomised control trials). The costing of multi-site group-based interventions alongside clinical research is particularly challenging as it

[4] I use the term MBPs here to describe interventions that share key mindfulness components (Crane et al., 2016), these are most commonly MBCT and MBSR and other closely aligned group interventions.

involves identifying any research costs which should not be included in the cost calculation (Bonin & Beecham, 2012). Many factors can affect the cost of the group, such as the type of group and the number of participants attending (Barrett & Byford, 2008). It is important to collect information about the individual program and assess how the cost changes, for example as the number of participants change (Glick, Doshi, Sonnad, & Polsky, 2014). Other factors such as the professional delivering the group, including their experience, training, and supervision, and also group information, such as the location, travel time, and number of people who attend may influence the cost.

Methods of costing: micro, macro, or a combination

The costing of interventions can be conducted using various methods, most commonly by utilising either macro-costing or micro-costing techniques (Wolff, 1998). Macro-costing (sometimes also referred to as gross-costing) is most commonly the top-down construction of the costs of a programme where aggregate statistics are used to estimate the average costs of reimbursement amounts or charges. In contrast, micro-costing traditionally adopts a bottom-up approach where specific individual level information is collected about a programme. In addition to the cost approach adopted there are different levels of accuracy that can be obtained within each approach (Drummond et al., 2015). While a comprehensive bottom-up micro-costing is normally considered to be the gold standard of estimating the costs of interventions, it is time consuming and individual level data may not always be available (Tan, 2009). A micro-costing approach is particularly appropriate alongside a clinical trial where information at a patient level is available (Drummond et al., 2015). It has been argued that a 'confined' bottom-up micro-costing approach could be adopted, where the bottom-up construction is restricted to costs that are likely to have a large impact on the total costs, for example interventions with high staff resources and overheads (Drummond et al., 2015; Tan, 2009).

It has been shown that different costing methodologies can produce significant variations of unit costs (Riewpaiboon, Malaroje, & Kongsawatt, 2007). Further evidence suggests the chosen methodology can influence the economic analysis outputs sufficiently to alter policy recommendations and the subsequent adoption of new interventions (Clement (Nee Shrive), Ghali, Donaldson, & Manns, 2009). It is necessary to obtain accurate costs at a micro-level to perform robust future economic analysis such as cost-effectiveness or cost-benefit analysis.

Micro-costing techniques have been employed successfully to capture detailed costs of other complex psycho-social group-based interventions (Charles, Edwards, Bywater, & Hutchings, 2013). They are considered to be the gold standard for costing detailed resource use information (Clement (Nee Shrive) et al., 2009), and treatment innovations in health care (Frick, 2009). Cost information about a

programme can be obtained using programme specific instruments that record information on the resources used (Glick et al., 2014). It is necessary to identify a range of costs and record all the resources allocated to an intervention, this includes resources such as the staff involved in a programme, the time spent on programme activities and the materials distributed as part of the programme. Micro-costing resource diaries kept by programme facilitators is one method of collecting detailed cost information about resources utilised and the value of those resources (Frick, 2009). Conducting a micro-costing alongside clinical trials has been proposed as the preferred method which enables the accurate recording of detailed cost data (Bryning, Edwards, & Crane, 2015; Charles et al., 2013; Edwards et al., 2015).

Previous costing analyses of MBPs

There are few studies where costs were included as part of the evaluation, with most evaluations focusing on effectiveness alone. Studies which include an economic evaluation and consider the costs of the MBP are outlined in full in Chapter 2 of this thesis. Not all the economic evaluations included the costs of the programme in the evaluation. Those that did include costs did not all include details of methods used to calculate them.

As an example of an evaluation which included a micro-costing analysis, MBCT for depression was calculated to cost be between £165 and £172 per 2-hour group session or £14 per service user per session (Curtis & Beecham, 2014; Kuyken et al., 2008). The Kuyken et al (2008) study represents one type of MBCT delivery, within a trial design, and based on information presented in the publication with a course delivered by full-time salaried and already trained staff. It has not been explored before whether, due to the varied nature of MBPs, these unit costs would be generalisable across all MBPs, including those offered outside of clinical settings and with other populations. In order to best inform future policy and practice relating to MBPs, well designed studies should include relevant economic outcomes in order to capture a full range of costs and benefits (Bryning et al., 2015; Edwards et al., 2015; Kabat-Zinn, 2013).

Study Objectives

This chapter reports on the use of a micro-costing framework to cost a range of MBPs from a service provider perspective. This micro-costing was undertaken in a range of settings and client populations and aims to capture the variety of MBP courses delivered in the UK. Both clinical and non-clinical settings (e.g., university, health care, business, and community) and client populations (e.g., members of local communities, students, cancer patients, carers, parents, and patients with depression and/or

anxiety) were included. This study also aims to explore whether variations across courses result in significant variations in costs and if so, what specific factors explain this variation. This chapter reports on findings of a costing exercise of mindfulness as an integrated intervention, delivered in routine practice in various settings. It has not been conducted before and as indicated in the systematic review (Chapter 2), there are limited economic cost estimates for delivering MBPs outside health care settings. Estimating the cost of MBPs is the first step in conducting a full economic evaluation and establishing whether it could prove to be a cost-effective alternative to other treatments.

Methods

Study design

To evaluate the costs of delivering MBPs in a real world setting this study included both a costing exercise alongside a randomised feasibility trial, and a concurrent costing survey of mindfulness teachers working in routine practice contexts. This study used both pragmatic, real-time data collection within groups delivered in routine practice, and (in some cases) retrospective data collection with teachers recalling information from their most recent course (delivered within the last 4 months).

Determining the micro-costing approach (top-down or bottom-up)

This study employed a combined micro-costing technique (both bottom-up and top-down) for the collection of detailed cost information of the delivery of MBPs. Micro-costing methods were employed through the collection of data directly from mindfulness teachers through the completion of a resource use diary developed as part of this study (described in detail on pages 120 – 124). Mindfulness teachers were asked to report their own costs under different headings and to distinguish between the initial set-up costs and the subsequent running costs. The top-down construction of initial teacher training was undertaken to estimate initial set up costs that were not otherwise included in the cost diaries (e.g., if the teacher had been trained for more than one year). One additional retrospective top-down costing of an MBP was conducted where limited resource use data was available.

Group costing approach

To allocate the costs of the course between course participants, it was necessary to consider whether this should be based on the number of participants who attended each session, or the number of participants allocated to attend each session. Due to the nature of MBPs operating as 'closed groups' (i.e., where new participants cannot join after the start date or take a place following a drop out), the costs were shared amongst the number of allocated spaces in a group i.e., registered participants,

rather than amongst the number that attended each session. In the case of closed groups, costs should be based on the resources that are allocated to an individual when entering a group rather than based on their level of consumption and whether they attend the course or not (Barrett & Byford, 2008).

The approach developed by Barrett and Byford (2008) to cost group-based CBT was applied (Equation 2) to estimate the unit cost of group-based interventions at the individual level.

Equation 2: Estimating the unit cost of MBPs

$$TC_{MBP} = \left(\frac{\left(\left((wages + overheads) / \left(workingtime \right) \right) * ratio \right) * duration}{number\_allocated\_group} \right) * number\_sessions\_allocated$$

Based on Barrett & Byford (2008) approach to the estimation of group therapy

The approach was adapted to include the cost of equipment and materials where appropriate. Furthermore, the calculation of staff time factored in whether an MBP included additional sessions such as an all-day meditation practice session, an orientation session, or any follow-up sessions as standard. Overheads were broadened to also include any premises rental fees for when courses were externally provided.

Process of micro-costing a framework for public health interventions

Figure 11 shows the process of micro-costing adapted from the Charles et al (2013) framework used for costing public health interventions.

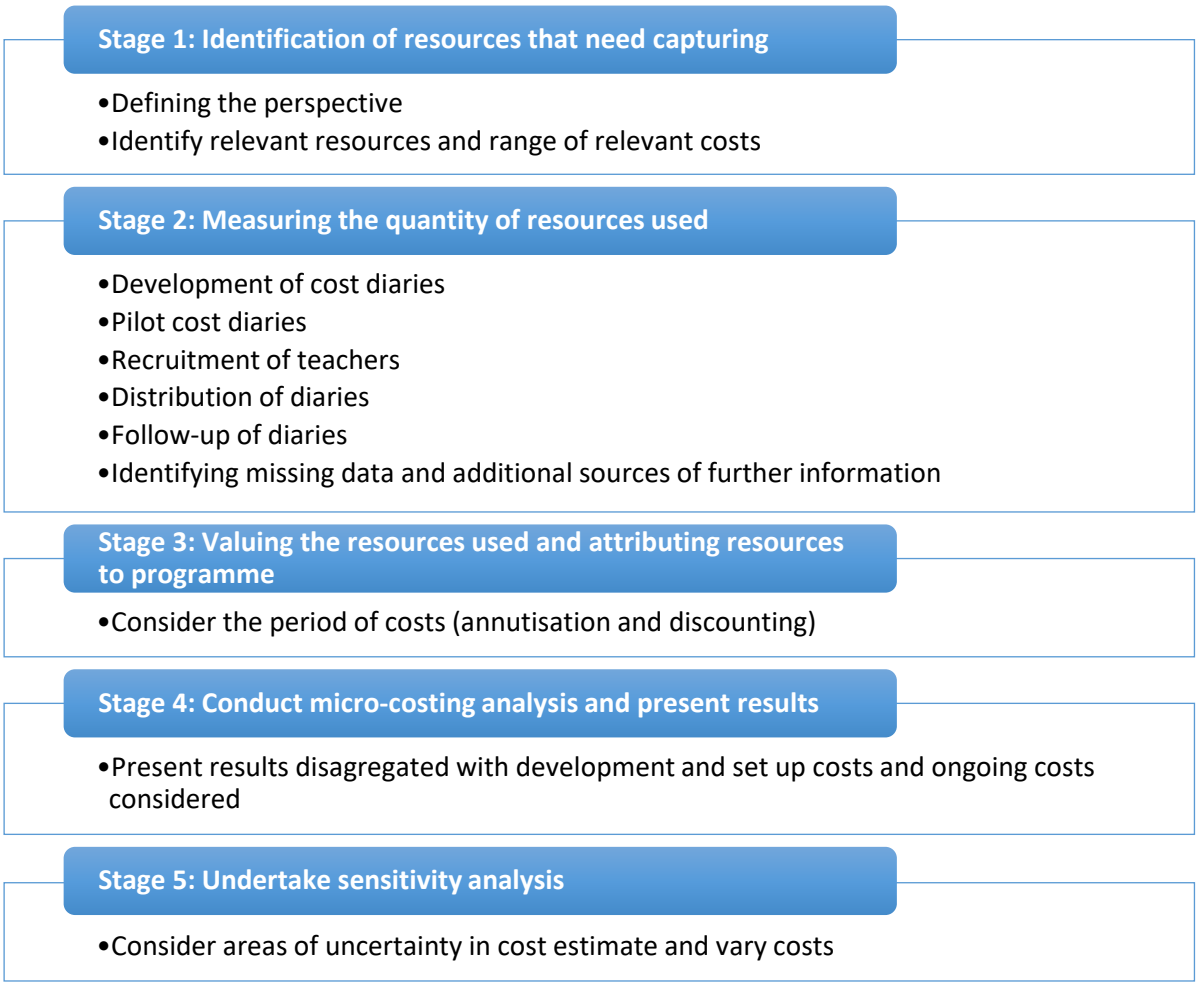


Figure 11: Process of micro-costing

Stage 1: Identification of resources that need capturing

Defining the perspective

In order to establish the range of costs to be assessed, the perspective that the study is being conducted from must first be defined (Charles et al., 2013). Commonly in health care settings in the UK the perspective would be the NHS perspective, while public health interventions which aim to impact across all multiple public sectors (e.g., health, social, education, criminal justice) would more commonly adopt a public sector multi-agency or societal perspective.

MBPs are increasingly being integrated into practice beyond the health service and delivered in community settings, in the workplace, and in schools. It is therefore necessary to collect detailed cost information about a range of MBPs to explore the possible variations in costs across settings and populations. This micro-costing analysis was conducted from a public sector multi-agency perspective to be applicable to the range of courses evaluated.

Identifying relevant resources and range of costs

Identifying relevant resources to be collected was achieved through discussion with service providers and mindfulness professionals. Direct costs relevant to an MBP service provider were collected. Time resources for the course were measured to the nearest half hour. The monetary cost of resources was recorded and information about who bore the costs was obtained, and whether the costs were incurred by the teacher (even if waived), their employer or the service provider (if different).

The following resource categories were calculated:

A. Staff costs: teacher salaries and time, administration salaries and time.
B. Staff on-costs: Employer's National Insurance and contribution to superannuation
C. Training and supervision: mindfulness retreat or annual training and regular supervision as a core requirement of MBP delivery
D. Overheads: venue costs such as rent and/or capital overheads and staff overheads such as management, administration, and estates costs.
E. Material costs: consumables including participant course workbooks (or handouts), CDs and refreshments.
F. Equipment costs: reusable items such as exercise mats, meditation cushions, stools, blankets, and chairs.

Development and implementation costs including initial teacher training and registration were only recorded if they fell within the diary recall period (12 months). These costs were otherwise obtained through secondary sources (top-down) and were presented separate to the base case costing of the course as a sensitivity analysis.

While one of the courses costed were conducted as part of a RCT, research costs were separated from running costs and not included in the analysis.

Stage 2: Measurement of the quantity of resources used

Developing the cost diaries as a standardised resource use data collection tool for MBPs

Cost diaries were developed providing a standardised resource use data collection tool which included detailed information on the range of costs direct from the teachers (bottom-up). Diaries were constructed with four sections, covering course information, teacher information, pre-course and set up resources, and weekly resources.

Section 1: Course information

Background information was collected about the course. This included the type of course, length of course, population and setting, materials, and equipment.

- Type of course: Teachers were asked to self-define the type of MBP being conducted and whether it was 1) MBSR 2) MBCT or 3) other e.g., an adapted programme.
- Population: The 'target' population group and number of participants who attended each week was also collected.
- Setting: The location of the course was recorded and the rates or fees of hiring the room were recorded where applicable.
- Materials: Materials for the course included course workbooks or hand-outs, audio CDs or audio downloads.
- Equipment: Equipment for the course included mats, stools, meditation cushions, blankets. Whether equipment was new or used was recorded.

Section 2: Teacher information

Information about the teacher aimed to establish how many teachers led the delivery of the course and their associated salaries. In addition, ongoing training and supervision received over the previous 12-month period was recorded (training costs included course fee, travel cost and accommodation where applicable). Teachers were asked to indicate whether training or supervision was required for the delivery of this specific course or whether they considered it to be part of their own continuous personal and professional development (CPPD) requirement. Staff on-costs including employer pension and National Insurance contributions were applied at a rate of 38.2% (13.8% National Insurance and 24.4% pension contributions) unless otherwise stated.

Section 3: Pre course and set up resources

These included staff time for session preparation, room set up, and any administration. In addition, cost diaries recorded whether any staff support were available (e.g., admin support), and time information and salaries were recorded where applicable.

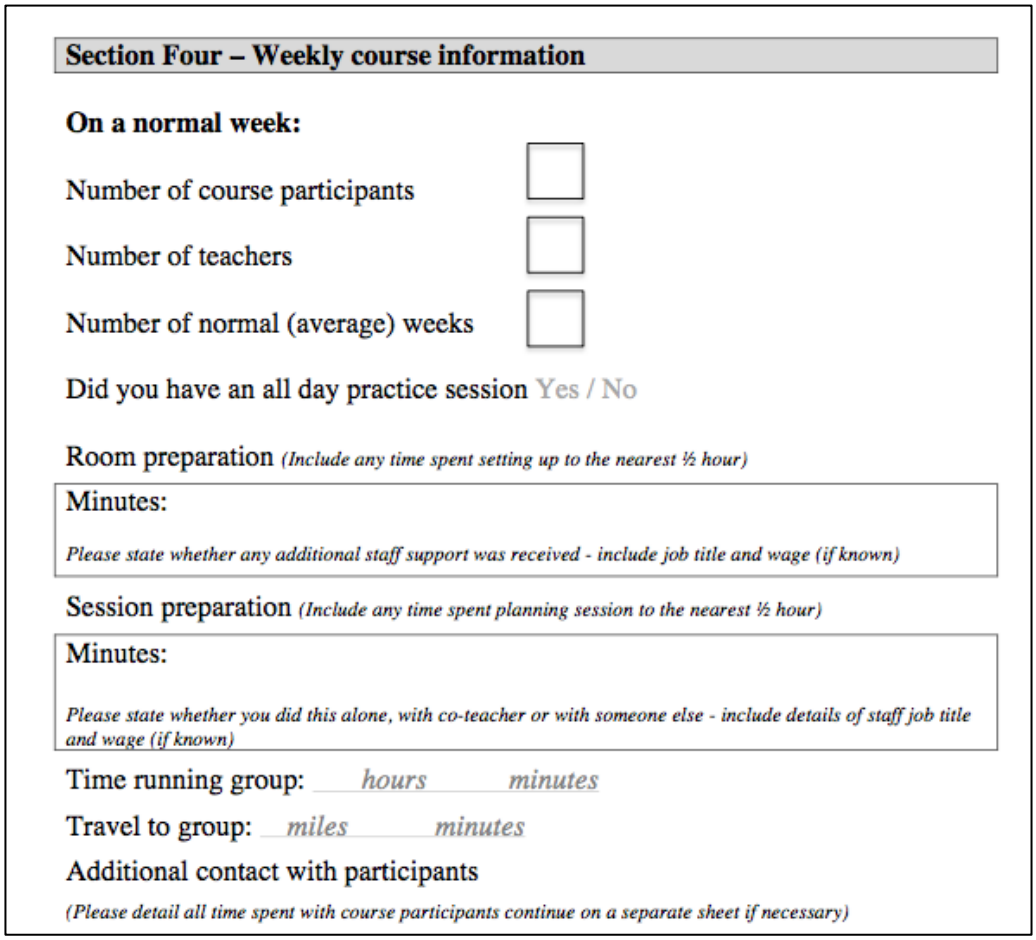
Section 4: Weekly resources

These included weekly records of staff time spent delivering sessions, travel time, and any out of session time spent speaking with participants.

The length of course was obtained in terms of number of weeks, session time and whether any orientation and practice day session was conducted (MBSR and MBCT typically include a day of guided mindfulness practice between sessions 6 and 7).

Piloting the measures

To ensure the diaries could collect a full range of relevant costs the cost diaries were piloted at a university-based mindfulness training and delivery centre in the UK with two staff members who had recently run MBP courses. Feedback from the pilot was that the weekly resource diaries were time consuming to complete, and not easy to complete if filled in retrospectively. It was concluded that MBP courses had a largely consistent resource pattern each week with some small variation that was unlikely to influence the estimated costs. To maximise completion rates and minimise missing data the diaries were adapted for the survey and trial to make them less resource intensive. The adaption revised to booklets to ask MBP teachers to report based on an average, 'normal week' where a standard course session was conducted (see Figure 12: Example of page from costing resource diary). In addition, to reflect the full range of resource use and to capture the anticipated variations to this 'normal week', information about any 'non-standard' weeks in terms of time and resources (e.g., weeks where an additional day long meditation session was delivered) was also collected within the adapted diary.



Section Four – Weekly course information

On a normal week:

Number of course participants

Number of teachers

Number of normal (average) weeks

Did you have an all day practice session Yes / No

Room preparation *(Include any time spent setting up to the nearest ½ hour)*

Minutes:

Please state whether any additional staff support was received - include job title and wage (if known)

Session preparation *(Include any time spent planning session to the nearest ½ hour)*

Minutes:

Please state whether you did this alone, with co-teacher or with someone else - include details of staff job title and wage (if known)

Time running group: *hours* *minutes*

Travel to group: *miles* *minutes*

Additional contact with participants

(Please detail all time spent with course participants continue on a separate sheet if necessary)

Figure 12: Example of page from costing resource diary

Recruitment of mindfulness teachers

MBP teachers from the UK were recruited from several sources for this study to obtain a wide range of MBP courses to contribute to this costing study. Initially, teachers were recruited from a database of teachers held by a university-based mindfulness training and delivery centre in the UK and through subsequent colleague referrals. This recruitment method led to micro-costing diaries being sent out to 18 teachers as part of a survey. Secondly, an opportunistic recruitment of delegates attending a UK based international scientific conference was conducted where booklets were made available at event registration. In both cases booklets were returned by post direct to the researcher. In addition, a costing exercise alongside a pilot RCT evaluating MBCT for Cancer (MBCT-Ca) was conducted.

The recruitment period was from February 2013 to November 2013. Teachers were eligible to participate if they were currently running an MBP or had recently run a course completed no more than 4 months prior to their participation in this study.

Collecting the data (distribution of diaries and follow-up)

Diaries were sent out by post or distributed in-person. A follow-up letter was sent to the postal recruitment sample. It was not possible to follow-up on the other recruitment method as participation was entirely voluntary and no contact details were kept for those invited to attend.

Primary information was provided directly by the MBP teacher. In this study information was drawn from a total of nine courses delivered between October 2012 and January 2014 in the UK.

Reviewing the data (dealing with missing or incomplete data)

Where information was incomplete or missing, secondary information was obtained from staff within a university-based mindfulness training and delivery centre in the UK for whom some of the teachers were working to inform assumptions. Finally, this was compared with unit costs reported in national Unit Costs of Health and Social Care (Curtis & Beecham, 2014) which was based on resource use data from three MBCT teachers in Kuyken et al. (2008). At times it was necessary to make assumptions where the available data was unclear or missing. All assumptions and estimates were noted and justified by a second author who is also an MBP teacher.

Measuring the quantity of resources used

The quantity of time resources was measured to the nearest half hour by teachers completing the resource use cost diaries. The quantity of other resources e.g., equipment was measured in terms of the number of units, while any monetary costs were measured to the nearest whole £ (pounds sterling).

Stage 3: Valuing the resources used and attributing resources to programme

Valuing the resources used

Time resources were valued based on the salary information provided directly by the teachers or by the employer on participant request. Where no salary information was available or teachers reported to volunteer their time at no monetary cost, the opportunity cost of time was valued by estimating an average salary of an equivalent professional within the context of course delivery.

Overheads and location costs (e.g., room hire fees) were obtained directly from the participant or from the employer on participant request. Where no overheads or location costs were available, or teachers reported use of a space with no monetary cost, the opportunity cost of the location was valued by

estimating the average rates of overhead for a comparable venue to the location of the course being costed.

Considering the period of costs (from annual resources to course resources)

To capture the range of costs attributed to an MBP, the resource cost diaries covered a 12-month period. While MBPs rarely exceed a period of 3 months, associated resources such as training and supervision fall beyond this period (e.g., equipment, training, and supervision). It is important to note that during the 12-month recall period the teacher may have run more than one course and some of the resources may arguably be attributed to multiple courses. To attribute the appropriate level of resources to each course it was necessary to identify resources and costs that were not solely used during the specific course being costed and estimate the number of courses delivered per year by an MBP teacher. Furthermore, where resources were reusable and had a shared usage across multiple courses, and/or the costs and benefits spanned a period of more than one year there was a need to annuitise and discount costs.

Annuitisation and Discounting

Costs were annuitised to reflect that the costs span more than one course delivered over a period of more than 12 months and discounted at a rate of 3.5% in accordance with NICE recommendations (NICE, 2013a). The total cost of the equipment was annuitised over an initial period of 3 years and discounted at a rate of 3.5% per year. Initial teacher training and development costs were annuitised at a longer period, due to their application spanning a longer period than other costs, as outlined in the sensitivity analysis. Annuitsation was calculated (see Equation 3) based on methodology detailed in the Guide to Community Preventive Services (The Community Guide, 2010)

$$C = \left[P - S * \frac{1}{(1+r)^t}\right] * (AF)^{-1}$$

where AF= $$\left[1 - \frac{1}{(1+r)^t}\right] r^{-1}$$

C= calculated equivalent annual cost of the unit
P= cost of purchasing the unit
S= scrap value of the unit after t years of service
r= discount rate
AF= annuity factor

Equation 3: Annuitisation factor

Ethical considerations and approval

This micro-costing study was reviewed and approved by Bangor University School of Psychology Ethics Committee (Reference: 2012-6444). The pilot MBCT-Ca RCT was reviewed and approved by the North Wales - West NHS REC and local R&D committees (Reference: 12/WA/0095). The school based MBP was reviewed and approved by Bangor University School of Psychology Ethics Committee (Reference: 2013-9304-A13893).

Results

Stage 4: Conduct micro-costing analysis and present results

Course features

A total of nine courses were costed as part of this study (with one additional course presented as a post hoc retrospective costing as part of sensitivity analysis). Table 7 shows the course features across the courses included. The different settings were categorised as university, hospital, hospice, community centre, private residence, or workplace. The population groups were categorised into three groups: health, business, and education. The type of course offered included standard MBSR and MBCT courses, Mindfulness in the Workplace course based on Finding Peace in a Frantic World (Williams & Penman, 2011), or another course programme that varied significantly from the 8-week manual e.g., a 4-week workplace course.

Number and length of sessions

The number of sessions in each course ranged from between four and eight sessions, some with an additional orientation session at the beginning and up to two additional follow-up classes at the end. Session length varied from 1.5 hours to 3 hours.

Some courses included a full day session towards the end of the course. For the course that included an orientation session, this was either conducted as a group session or as an individual orientation session. The latter was also combined with an assessment session in order to pre-screen participants against a set of exclusion criteria for participating.

Number of participants per group

The number of participants allocated to attend the courses ranged between 8 and 25 participants.

Number of staff

Most courses were taught by one MBP teacher, although some courses had either a second teacher or an assistant to support the teaching. Most courses received some admin support, although in some cases administration time was reported to be absorbed by the teacher.

Ongoing training and staff development

Annual training and supervision costs were estimated, based on top down information provided by a UK Centre for Mindfulness and provider of training courses. These equated to £1,000 per year for a one-week residential training retreat (with costs including course fee, travel costs and accommodation). In addition, monthly supervision was costed at £50 per month based on average supervision tariffs provided by the same UK Centre for Mindfulness. In order to meet UK recommendations of good practice for mindfulness teachers one annual retreat and monthly supervision was costed and considered appropriate to be attributed to and spread across the number of courses run during that year (BAMBA – British Association of Mindfulness-Based Approaches, 2015). Where more than one retreat or training was recorded, it was noted to be non-essential for the delivery of the course, and therefore was not included as a course cost.

Table 7: General features of MBP courses included within the micro-costing analysis

Type of course	Setting	Population	No. of participants	No. of weeks
MBCT	Hospital	Health - Cancer	8	8 (plus initial orientation session)
MBCT	Hospice	Health - Cancer	10	8
MBSR	University	Student	26	8 (plus initial orientation session)
MBSR	Private	General	13	8 (plus initial orientation session)
Undefined / Other	University	General	25	4
FPIAFW	Workplace	Business - Employees	24	8 (plus initial orientation session)
MBCT	University	Student	22	8 (plus initial orientation session and one follow-up session)
MBCT	University	Student	17	8 (plus initial orientation session and one follow-up session)
MBSR	Community	Health - Physical	12	8 (plus initial orientation session)

Staff costs

Reported staff salaries were estimated primarily from secondary sources as the self-report salaries did not represent paid time for the total number of hours worked or in some cases any of the hours worked (e.g., one teacher reported to run courses on a voluntary basis). In these cases, our assumption for the MBP teacher was to apply an equivalent academic salary from a University setting (e.g., grade 8 lecturer) or a clinical salary for a NHS setting (e.g., Band 8 NHS clinician). Administrative staff were costed using a University salary (e.g., grade 4 clerical) where data was otherwise unavailable or unrepresentative of the resources used.

Summary Results: Costs

Of the nine courses the total costs ranged from £2,786.48 to £6,301.70. This equated to between £111 - £645 per participant. The highest cost per participant (£645) was obtained in a clinical setting where there was a low number of participants in each group (*N=8*). The lowest cost per participant (£111) was obtained in a general population context where there were a high number of participants in each group (*N=25*).

The total base case costings, considering an average MBSR, MBCT and workplaces MBP based on Finding Peace in a Frantic World adapted programme, ranged from £2,865 - £3,781 per course equating to between £115 and £252 per participant.

The summary unit costs of the base case MBSR programme are presented in Table 8.

Table 8: Unit costs for base case costing of MBSR programme in non-clinical setting

	Cost per MBSR course (cost year 2013/2014)	Notes – base case costs assume 3 MBSR courses to be run per year with an average of 24 participants per course.
A. Wages 1. MBP teacher 2. Admin support role	 £1502.87 £176.58	Based on average salary of nine mindfulness teachers (equivalent to University Grade 8 University or Band 8 NHS clinician). Mean salary of £43,325 per year was applied, with an hourly rate calculated as £22.92 for MBP teacher hours. Admin support role costs were calculated as £9.81 per hour, based on an entry level University Grade 4 salary. Total costs are calculated based on the total number of hours worked by each staff role.
B. Salary oncosts	£641.55	On-costs were applied at a rate of 38.2% (13.8% National Insurance and 24.4% pension contributions).
C. Training and supervision - Ongoing training - Supervision	 £333.33 £200	Training and supervision costs were included to represented adherence to best practice guidelines for ongoing supervision and professional development. Annual training costs were reported as £1000 with costs based on one retreat per year, travel to venue and accommodation. Annual training costs were spread equally across the 3 courses conducted during the year. Supervision costs were based on one hour per month of supervision costed as £50 per session by telephone or Skype.
D. Overheads / room hire	£325	Room estimates vary, base case costing of university room hire.
E. & F. Materials and equipment		
- Refreshments	£12.24	Based on £0.51p per person for hot drink refreshments provided at all day practice session.
- Course materials (CDs and workbooks)	£204	Workbook and CD costed as £8.50 per person.
- Course equipment	£153.12	Costs of equipment for courses including yoga mats (£12 per unit), meditation stools (£10 per unit), zafus - meditation cushions (£13.50 per unit), blocks (£5 per unit), blankets (£5 per unit), cushions (£5 per unit). Costs are assumed to be re-used across courses and are annuitized and discounted at a rate of 3.5% over a three-year period.
G. Contact time	27.5 hours	MBP sessions lasted two and a half hours for eight sessions plus one initial orientation session of one and a half hours. An additional 'all day session' lasted six hours (one session).
H. Additional working time 1. MBP teacher 2. Admin support role	 38.07 hours 18 hours	 Including all planning, preparation, admin, training, and supervision time worked. Additional admin based on 2 hours of admin support role per week of course.
Total costs for 2013/2014: £3548.68 per course £147.86 per participant		

Planned sensitivity analysis

Stage 5: Undertake sensitivity analysis

Secondary sensitivity analysis was used to vary the core assumptions e.g., number of participants in each course, the number of courses delivered each year.

Sensitivity analysis enables researchers to explore whether variations to their core assumptions (the base case analysis) can influence the overall findings. This study included a set of planned sensitivity analyses to evaluate factors that might be capable of producing differential costs.

From the nine courses an average set of costs were applied to create a base case. It was based on these costs that the sensitivity analysis was conducted.

1. **Initial development and implementation costs (e.g., mindfulness teacher training)**

Initial development and implementation costs were not included as part of the base case costing. However, initial teacher training and registration costs were included in the sensitivity analysis (after being annuitized over a period of 5-years and discounted at a rate of 3.5%). Initial development costs (including teacher training) were estimated directly from staff at a university-based mindfulness training and delivery centre in the UK and modelled the cost of pursuing the teacher training pathway previously provided by Bangor University website (http://www.bangor.ac.uk/mindfulness/training-pathway/index.php.en). This included attendance on an initial eight-week MBSR course, completion of the teacher training programmes (at one UK university-based teacher training centre), Teacher Training Pathway registration and certification.

Initial training total costs were estimated to be £4465 per teacher, based on initial eight-week MBSR course, TTR1 & TTR2, Teacher Training Pathway registration and certification.

When including the resource costs of initial teacher training and development the total cost of courses increased from £2865 - £3781 per course to £3854 - £4770 per course equating to between £154 and £318 per participant.

2. **Number of sessions (e.g., follow-up sessions)**

MBPs are largely based on an eight-week course model. However, there may be more than eight sessions which make up the entire programme. Courses may also include an orientation session to introduce the course and to help ensure participants have a commitment to engage in the course and attend sessions. In addition, courses may offer a full day of guided mindfulness practice and even follow-

up sessions for graduates. More recent adaptations of MBPs have varied the number of sessions offered and the length of sessions. For the primary costing, the cost of all course sessions recorded in the course diaries was used to calculate the cost of the intervention. Most courses included a shorter orientation session, eight weekly session and one day of guided practice.

For the sensitivity analysis, the number of sessions was varied to include two possible scenarios, two additional follow-up sessions attended by course participants (from that course cohort only), or follow-up sessions attended by 'graduates' from more than one course, thus spreading the cost between a greater number of participants. Additional overheads and staff costs were applied to consider the additional resources to deliver two follow-up sessions.

When including the resource costs of two follow-up sessions, the total cost per courses ranged from £4,088 to £3,141 equating to £273 - £126 per participant. However, if the costs of the follow-up sessions were shared amongst other course graduated (estimated a maximum of double the current cohort), then the additional session costs reduced from £22.75 per session per participant to £13 per session per participant or from £12.60 per session per participant to £7.20 per session per participant. The total course costs would therefore be £4,361 to £3,267 equating to £299 - £140 per participant.

3. The number of participants

The number of participants attending the course varied: 10, 25 and 30 participants applied and are presented in Table 9 below:

Table 9: Sensitivity analysis on number of course participants.

Course type	No. of participants	Total course costs (£)	Cost per participant (£)
MBSR	10	3,288.78	328.88
MBCT	10	3,585.13	358.51
Finding peace	10	2,586.34	258.63
MBSR	24*	3548.58	147.86
MBSR	25	3,567.14	142.69
MBCT	25	4,172.33	166.89
Finding peace	25	2,864.71	114.59
MBSR	30	3,659.93	122.00
MBCT	30	4,368.07	145.60
Finding peace	30	2,957.50	98.58

*24 participants MBSR course representing base case analysis

4. **No. of courses delivered by the mindfulness teacher per year**

The total costs of annual ongoing training (including retreats), supervision, and equipment were divided by the estimated number of courses delivered each year. The base case assumption for the number of courses delivered each year was 3. A full-time equivalent MBP teacher would have the capacity to deliver significantly more courses than 3 per year as courses could be run concurrently. This analysis was built on the assumption that it would be unlikely for a teacher to deliver more than 2 courses concurrently and more than a total of 8 courses per year. To test these assumptions a range of scenarios were considered with the number of courses delivered per year: 1 course, 3 courses, 6 courses and 8 courses.

Table 10: Sensitivity analysis of number of courses delivered per year variation.

Course type	No. of courses delivered per year	Total course costs (£)	Cost per participant (£)
MBSR	1	5686.94	236.96
MBCT	1	5919.22	394.61
Finding peace	1	5011.06	200.44
MBSR	3*	3548.58	147.86
MBCT	3*	3780.87	252.06
Finding peace	3*	2864.71	114.59
MBSR	6	3014.00	125.58
MBCT	6	3246.28	216.42
Finding peace	6	2328.12	93.12
MBSR	8	2880.35	120.01
MBCT	8	3112.63	207.51
Finding peace	8	2193.97	87.76

*3 courses included representing base case analysis

5. Discount rate 0-6%

The discount rate of 3.5% used within the base case analysis was also varied with sensitivity analysis options of 0.5%, 1.5% and 6%.

Table 11: Sensitivity analysis of discount rate used for costs of MBPs.

Course type	Discount rate applied	Total course costs (£)	Cost per participant (£)
MBSR	0.5%	3539.89	147.50
MBCT	0.5%	3775.43	251.70
Finding peace	0.5%	2855.65	114.23
MBSR	1.5%	3542.77	147.62
MBCT	1.5%	3777.23	251.82
Finding peace	1.5%	2858.65	114.35
MBSR	3.5%*	3548.58	147.86
MBCT	3.5%*	3780.87	252.06
Finding peace	3.5%*	2864.71	114.59
MBSR	6%	3555.95	148.16
MBCT	6%	3785.47	252.36
Finding peace	6%	2872.38	114.90

*3.5% discount rate included representing base case analysis

6. Choice of period for annuitisation of costs

Annuitisation over the estimated working life of an MBP teacher was conducted as a planned sensitivity analysis. It is estimated that the average working life of an MBP teacher is likely to fall within a range of 10 - 40 years. Annuitisation was conducted based on 4 possible scenario estimates of 10, 20, 30 & 40 years.

Table 12: Sensitivity analysis of annuitisation period

Course type	Annuitisation period applied	Total course costs (inc. set up)	Cost per participant (inc. set up)
MBSR	5 years*	£4,537.50	£189.06
MBCT	5 years*	£4,769.78	£317.99
Finding peace	5 years*	£3,853.62	£154.14
MBSR	10 years	£4,085.46	£170.23
MBCT	10 years	£4,317.74	£287.85
Finding peace	10 years	£3,401.59	£136.06
MBSR	20 years	£3,862.75	£160.95
MBCT	20 years	£4,095.03	£273.00
Finding peace	20 years	£3,178.87	£127.15
MBSR	30 years	£3,791.35	£157.97
MBCT	30 years	£4,023.63	£268.24
Finding peace	30 years	£3,107.48	£124.30
MBSR	40 years	£3,757.67	£156.57
MBCT	40 years	£3,989.95	£266.00
Finding peace	40 years	£3,073.79	£122.95

*5-year period included representing base case analysis

Post-hoc schools-based costing case study

A retrospective costing of a schools based MBP was conducted in 2020 to consider a base case costing of delivering mindfulness as part of a national curriculum. The schools based MBP study (presented in Chapter 5) was reviewed and approved by Bangor University School of Psychology Ethics Committee. As no resource use diaries were collected during this study, a top-down indicative costing is conducted with cost estimates drawn from publicly available information on the likely costs of teacher training and assumptions around the number of course delivered each year following the same pattern as outlined through this chapter.

Teacher training cost estimates were obtained from the Mindfulness in Schools Project Website (https://mindfulnessinschools.org/) with a £720 course fee for training on the Teach .b Mindfulness for 11-18 year olds ("Mindfulness in Schools Project (MiSP)," 2020). The MISP estimates that teaching 30 pupils a year for 5 years would equate to a cost of £5 per pupil (MISP, 2020). This costing does not include any resources spent on delivering the programme but is based on training costs alone. With the annual salary of a teacher already accounted for within existing school budgets, the provision of an MBP within a school curriculum requires consideration of appropriate costing methods to capture the full economic cost of delivery, however, the opportunity cost of time spent on MBP teaching is important to capture.

Teacher salary costs were estimated from NASUWT, the Teachers' Union, Teachers' Pay Scales 2018-20, with a mid-spine point M3 classroom teacher gross annual salary of £27,652.55 (£34,863.55 including on-costs) in 2019 (NASUWT, 2020), used in the base case costing and total working hours of 1,265 hours per year, resulting in an hourly rate of £27.56 (including on-costs).

Teacher time allocations were estimated from the course schedule consisting of one introduction and 9 sessions between 40 minutes and 1 hour each week, rounded up to an hour per session. Planning, preparation, and other admin time spent outside the course sessions was estimated to be 2 hours per week. This may overestimate the amount of time teachers are allocated in practice with teachers' working time conditions of service only guaranteeing a minimum 10% of timetabled teaching time allocated to planning, preparation and assessment. Preparation time may reduce over time as teachers become more familiar with course sessions and the time allocation may need adjustment to reflect this.

This upper estimated total of 3 hours per week or 30 hours of teacher time per course would reduce if a teacher was to run multiple courses e.g., different year groups run simultaneously. Group sizes were estimated to be 30 pupils per course. However, some schools may operate smaller class sizes which could affect the cost estimates per pupil. Resource use diaries collected alongside future trials of MBPs in schools would help provide more accurate estimates of time allocated to delivering courses. What is

not known is whether implementation of MBPs within schools has any impact on workload allocation, and whether teachers are expected to deliver programmes on top of existing teaching.

No costs for course resources and consumables were identified. In addition, no overheads were included in the costing with the assumption that the school-based programme is delivered within existing classrooms. No additional training and MBP supervision costs are included in this base case costing, and it may underestimate the costs of ongoing training and support needed to continue to deliver the programme.

One-year time horizon estimated course cost (single course N=30 pupils):

The total cost over a one-year time horizon was £1586.80 per course based on 30 pupils allocated to attend. This equates to £52.89 per pupil (inclusive of initial training fees). When excluding initial teacher training fees, the total course costs were £826.80 equivalent to £27.56 per pupil.

Five-year time horizon estimated course cost (single course N=30 pupils per year; total pupils N=150)

Over a longer time-horizon of five years the total course costs were estimated to be £4975.65 (5-years), £995.13 per annum, equating to £33.17 per pupil (including annuitisation over 5 years and 3.5% discounted for training costs).

The teacher time undertaking the training or costs of substitute teachers were not included within this base case cost estimate, however, variations to costing assumptions are explored and discussed further in Chapter 5.

Discussion

Rigorous evidence on cost-effectiveness is not available in many popular areas of MBP application. Methods of evaluating benefits are continually developing, however, the methodology of evaluating costs has not kept pace. Furthermore, if cost estimates are based on insufficient detail then this may result in inaccurate cost-effectiveness analysis results, and inhibit the likely success of implementation and sustainability, or result in resources not being used in their best possible use. While mindfulness implementation is expanding there are still barriers to implementation and there is a paucity of information available on critical issues, such as the true cost of delivering programmes. Obtaining accurate cost information will improve further economic analysis of MBPs and support the implementation process and consideration of the likely budget impact (Charles et al., 2013; Edwards et al., 2015).

This chapter sets out a framework for the collection of detailed resources required for the delivery of MBPs in a range of settings. Micro-costing methods can be applied both alongside research trials and within routine practice delivery in order to estimate the economic cost of programme delivery. This chapter builds on previous work at developing a practical set of steps for costing complex public health or psycho-social interventions for the purpose of economic evaluation (Barrett & Byford, 2008; Charles et al., 2013; Drummond et al., 2015; Edwards et al., 2015; Kinsella, 2008).

Determining the perspective for range of costs to be collected

For the health economist, the perspective of analysis is commonly focused on the costs and benefits to the health service. However, this traditional model may not be appropriate for the evaluation of MBPs due to the broader applicability of the interventions, i.e., the wide-reaching application and implementation of programmes outside of the health sector. A broader perspective than a narrow payer perspective for example the NHS, Employer or Private Sector, may be more appropriate and reflect who bears the cost of programmes and where the benefit falls. Several of the cost diaries indicated that the costs were absorbed by the MBP teacher rather than the employer, and there may be scope for some of these costs to be shared between the stakeholders. Costs to participants attending the intervention may also be relevant if course fees are applicable or if there are wider costs to attendance (for example, considering travel costs, lost income, childcare costs).

Continuous personal and professional development

On occasion on-going mindfulness training was self-reported to not be essential for the delivery of the course, but instead was undertaken by the teacher for their own continuous personal and professional development (CPPD) requirement. Based on the cost diaries it appears that many of the teachers were absorbing the full cost of CPPD, ongoing training and supervision. This perhaps speaks to the way in which training in MBPs crosses the usual personal and professional boundaries. Many practitioners engage in mindfulness training because it confers significant personal benefit, and so are willing to take on some of the costs on a personal level. These additional costs did not appear to be reflected in the salary or rates of pay reported by teachers, especially those working freelance who on average had comparable hourly pay to other therapists. Costs of initial teacher training were obtained using top-down methods from national training provider information and applied to base case costings to best reflect the costs of implementation in new settings. More recent good practice guidelines developed by the British Association for Mindfulness-based Approaches provide further information about what are the essential criteria for delivering a range of MBPs and the costs included in this thesis chapter reflect the need to value all resources with an alternative use and to appropriately value to experience gained from training as essential parts of the MBPs delivered.

Disentangling research costs from programme costs

There is a need to disentangle research costs from delivery costs; however, there remains uncertainty around some resources, such as the recording group sessions. These could be viewed as a core part of ensuring fidelity of MBP delivery and a core part of ongoing service evaluation. Recruitment of participants may also be a cost usually considered to be associated with research. However, due to the nature of the courses, many teachers were responsible for recruiting participants into their classes, for example, where the teacher worked freelance and delivered classes in a community setting. When designing trial based economic evaluations these resources warrant consideration and sensitivity analysis to vary the costs of programme delivery may be appropriate to control for the uncertainty in intervention costs estimates.

Strengths and limitations of this thesis study

This micro-costing study illustrates for the first time the costs for a range of MBPs delivered both as part of normal service delivery and within a research trial. These findings highlight the differential costs depending on the delivery type, context, and setting along with the chosen methods of evaluation. Few studies have included the costs of MBPs in their evaluations, and those that have may not have captured a full range of costs relevant to a service provider interested in MBP implementation. Development and implementation costs should be included, even if these costs are annuitized over the average working life of a mindfulness teacher. Equipment costs should also be included but reflect the reusable nature rather than single use of the resources. While some may argue these are not essential to the delivery of an MBP as mindfulness meditation can be practiced anywhere, a supportive and conducive environment is often given significant consideration and these items are in practice made available. Therefore, they should be included to reflect the full costs of programmes when implemented.

While this study included a range of courses, delivered in a range of contexts and population groups, the sample size is small. This study has demonstrated that variations in the programme type can result in differential costs, limiting the generalisability of our findings to other MBPs. As a core part of future studies researchers should collect detailed MBP costs to help determine whether the intervention could be cost-effective against an alternative treatment.

This study adopted a condensed resource use diary based on a ‘normal’ week and an abnormal week to capture any variations in programme delivery, for example, the week where a silent all-day practice session may be included. The weekly completion of diaries would reduce the need for estimates of average resources per week. However, it is our assumption that the manualised nature of the programmes limits significant variation of resources within each ‘normal’ week and that additional

resource costs such as the orientation sessions can be collected in a less resource intensive way as part of our revised costing diaries.

Future research considerations and policy impact

In general, investment decisions when considering public health should not be based on cost outcome data alone, but instead should consider both costs and benefits (Beecham & Knapp, 2001). In order to make decisions about how best to allocate scarce health care resources, methodologically robust evidence on the demands for health, benefits of intervention and costs of innovations in health care is required (Beecham & Knapp, 2001). Future MBP research should build in measures of costs and resources used to enable economic evaluations and to help inform national decision makers and local commissioners and managers that hope to successfully implement services.

In this thesis study assumptions about costs were made to estimate a full economic base case cost of delivering the MBPs. This included the assumption that teachers adhered to best practice recommendations about ongoing training and supervision. In practice many MBPs may be embedded within existing services and these costs may be allocated across a larger programme budget or omitted entirely. What is not known is whether cost saving or cost sharing can impact on the effectiveness or cost-effectiveness of MBPs once implemented. Since completion of this work some of the resources to set up and deliver a MBP course have changed and this may impact on the future costs of MBP, for example, more recent training pathways developed through The Mindfulness Network (mindfulness-network.org). Variations in these costs of MBPs can be assessed through the concurrent collection of resources alongside future trial based economic evaluations.

The costs determined as part of this micro-costing may not all be additional to current spending within the NHS. If rolled out into routine practice some programme costs could be absorbed into existing programme budgets as they may be comparable with staff training and development. Economic evaluations of MBPs require a comparator control group in order to calculate the incremental cost of the MBP to help inform policy makers and service providers the potential cost impact to budgets. Since this research was conducted Health Education England (HEE) have put funding into their own version of a Teacher Training Pathway (TTP) which is delivered in a bespoke way for the NHS and has economies of scale.

There are unanswered questions for economic evaluations within other sectors including establishing the costs of school based MBPs where implementation may be at a whole school level rather than smaller cohorts. Costs will differ depending on method of implementation i.e., whether programme delivery is embedded within the national curriculum or additional to teaching and whether courses are delivered ‘in-house’ or by external organisations.

Survival analysis of programmes following implementation including information on staff turnover may help provide more detailed estimates for future budget impact analysis. Implementation of MBPs in general has been highlighted in recent publications, however, there has been less attention on the health economics perspective of implementation (Dimidjian & Segal, 2015; Rycroft-Malone et al., 2017).

In addition, to the group-based programmes there is increasing interest in other modes of course delivery including distance learning (telephone or internet) and easy to follow at home self-help books such as the best-selling book 'Mindfulness: a practical guide to finding peace in a frantic world' (Williams & Penman, 2011). These other manualised programmes (e.g., Finding Peace in a Frantic World) have increased access to MBPs outside of structured groups and have also expanded the number of programme types offered within groups beyond the traditional MBSR and MBCT manuals. The cost of these programmes is likely to vary from the costings outlined in this chapter. Upcoming evaluations using these MBP models including the effectiveness and cost-effectiveness is welcomed (Strauss et al., 2020). With the impacts of the current global COVID-19 pandemic resulting in many face-to-face services moving to more online provision, the costs (and benefits) of these alternative modes of delivery require further investigation (Moreno et al., 2020).

Conclusions

This micro-costing study illustrates for the first time the costs for a range of MBPs delivered both as part of normal service delivery and within a research trial, to a specific patient group (cancer) and in a more public settings (universities, workplaces, and schools). If cost estimates are based on insufficient details, then this may result in poor cost-effectiveness analysis and threaten accurate evidence-based service commissioning and policy development and inhibit the likely success of implementation and sustainability. This chapter concludes that as a core part of future economic evaluations researchers collect detailed information on the resources for implementation and delivery to establish a full range of costs and benefits of the interventions and help determine whether the intervention could be cost-effective against an alternative treatment. A standardised resource use data collection tool and costing schema specific to MBPs are outlined as part of this chapter to support future research. Future research with built-in measures of costs and resource use should enable robust economic evaluations and help inform national decision makers and local commissioners and managers that hope to successfully implement services. These costings are updated and applied to the evaluation of MBCT-Ca as a targeted intervention for population at heightened risk of depression in Chapter 4 before turning to the evaluation of an MBP embedded within the education curriculum in a school setting in Chapter 5.

Chapter 4: Targeted prevention - a pragmatic randomised feasibility trial of MBCT-Ca compared to treatment as usual.

Chapter preface

This chapter focuses on a targeted case for prevention focusing on patients recovering from cancer and at heightened risk of depression. The chapter provides an overview of the application of MBCT for cancer and reports on a pragmatic randomised feasibility trial (ISRCTN23380065) and concurrent service evaluation study both conducted as part of this thesis research. I worked independently to design and conduct this thesis research taking on the role chief investigator, primarily operating as the sole researcher on the project seeking and support from clinical and research advisors when needed. This research study turned out to be a very small feasibility trial, but it explored using mixed-methods in considerable depth many aspects of conducting a trial including identification and recruitment of cancer patients, randomisation to MBCT-Ca or a TAU control condition, choice of questionnaires and valuation of outcomes. This thesis research answers two principal research questions: 1) What are the appropriate methods for measuring and valuing costs and benefits of MBCT-Ca? and 2) What is the perceived value of MBCT-Ca and how much would cancer patients be willing to pay for it? This detailed feasibility study can inform the next stage of the MBP translational research process (discussed further in Chapter 6) and produce a Health Economics Analysis Plan (HEAP) for a definitive RCT. This chapter gives the space to explore many aspects of MBP evaluation from a health economics perspective in detail in a feasibility stage trial.

Chapter 4 Abstract

Background

There is an economic case for targeted intervention to prevent depression for groups at heightened risk of mental health problems. MBCT-Ca may be a useful targeted intervention in supporting cancer survivors cope with the anxiety and stress related to cancer. However, there is little evidence of economic evaluations of MBCT-Ca compared with alternatives for post-treatment cancer patients.

Methods

A pragmatic randomised feasibility trial of MBCT-Ca compared with TAU (*N=39*) with concurrent service evaluation (*N=24*) was conducted between 2011 and 2014. The study piloted elements of the design of an economic evaluation for a MBP delivered to populations who have previously received active cancer treatment. An embedded assessment of trial methods and qualitative component were included within this pragmatic trial to explore the feasibility of trial methods and acceptability of MBCT-Ca to

participants. A brief willingness to pay (WTP) exercise was completed to provide an indicator of the value of the course to participants and the potential for alternative options for funding of future course e.g. through cost sharing with participants. Outcome measures included the EQ-5D-3L as a primary economic outcome for calculating QALYs for cost-utility analysis and the HADS as a screening tool for anxiety and depression and outcome for cost-effectiveness analysis. Secondary outcome measures included the EORTC-QLQ-C30 as a cancer specific quality of life tool, the ICECAP-A as a measure of capabilities and the WHO-5 as a general wellbeing tool. A feasibility outcome assessment included consideration of floor and ceiling effects of outcomes, levels of missing data and impact of thresholds/cut-offs on interpretation of findings. A checklist for feasibility studies is proposed as a framework for evaluating early-stage health economics studies in MBP.

Results

The assessment of trial methods and qualitative study indicated that MBCT-Ca was generally acceptable to patients who attended. However, there were important barriers to running research groups and some barriers to participants attending. Barriers to recruitment are also discussed including clinician views and sufficiency of trial resources. Benefits reported by participants in the qualitative study included improvements in mental health, wellbeing and coping with cancer. The location of courses and the mix of participants attending MBCT-Ca may be important factors in the acceptability of MBCT-Ca.

An available case analysis of 39 participants (*N=22* in the MBP treatment group) is reported. Clinical and economic outcome measures were successfully piloted including the EQ-5D-3L as a preference-based health related quality of life measure. Ceiling effects and floor effects were not found in the majority of HRQoL measures at baseline, however, there were high ceiling effects on three out of the five EORTC-QLQ-C30 cancer specific function scales and the majority of cancer symptom scales and items.

There was a small incremental QALY gain *M=0.11* for the MBCT-Ca group compared with TAU mean QALYs over the 9-month trial duration.

HADS scores above 13 as a clinical cut-off was observed in 58% of all participants at baseline. When considering the higher general population threshold for abnormal anxiety and depression 42% of participants had scores higher than 16. The WHO-5 cut-off ≤50 indicated that 49% of the participants could benefit from addition investigation and potentially support with their mental health.

The feasibility of collecting a full range of health and social care resource use from across primary care, secondary care, and third sector services including charities direct from participants was confirmed as feasible. With a small sample size, it is difficult to observe any clear patterns of resource use. Instead, the data helps build a picture of ‘usual care’ and provides information of the types of services relevant

to the population. There was some variation amongst patients in where they accessed support for health problems including depression and some indicators of unmet need from the qualitative feedback and outcome data. The evaluation of trial methods highlighted key steps to improve the accuracy and completeness of outcome measurement in future trials of MBCT-Ca.

There were small, non-significant changes in health-related quality of life and depression over time, and no difference between feasibility trial groups detected in this pilot. A pragmatic trade-off was made with an amendment to randomisation methods helping enable MBCT-Ca courses to be delivered, as they required a minimum number of participants, however, this reduced the number of participants allocated to the control group. This was further confounded by higher rates of attrition observed in TAU control condition compared with MBCT-Ca group. Due to limited recruitment and loss to follow-up there was a very small control group limiting the appropriate analysis and interpretation of this research to inform a full RCT.

The mean WTP by feasibility trial participants for an MBCT-Ca course was £95. The total MBCT-Ca costs on an intention to treat basis was £15,180 for the 22 participants allocated to receive MBCT-Ca, equating to £690 per participant.

Discussion

This study provides indicators of both a demand and need for greater psycho-social support for people at risk of poor mental health after cancer. These findings are in support of the case for greater investment in effective and cost-effective psycho-social support more generally. Further research is needed to establish whether MBCT-Ca can be a cost-effective intervention to support this population. This chapter concludes with a set of recommendations relevant to MBP feasibility trials and future research in MBPs in cancer care.

Introduction

The unmet need for psychological services in cancer care

In the UK half of the population will experience some form of cancer in their lifetime (Cancer Research UK, 2020). It is normal for many patients with cancer to feel psychological distress, given the impact of diagnosis, uncertain survival and effects of treatment, it is a natural response to a traumatic and threatening experience (Ward, Salzano, Sampson, & Cowan, 2004). Cancer diagnosis and subsequent treatment can have a wide range of physical and psychological side-effects such as difficulty sleeping, problems with concentration, reduced social skills, memory impairment, sexual problems and anxiety and depression (Adler & Page, 2008; Die Trill, 2013). Prevalence of mental health problems amongst cancer patients varies widely, although it is generally recognised, on average that one in four cancer patients have depression or anxiety (Miovic & Block, 2007; NICE, 2004a). At the time of diagnosis, it is estimated that nearly 50% of cancer patients will experience high levels of anxiety and depression (Ward et al., 2004), this may not however provide a full picture as psychological symptoms are not always identified, with many people with cancer supported by family and relying on their inner resilience to deal with this distress (Ward et al., 2004). However, few front line cancer professionals feel equipped to identify and offer support for patients and carers in psychological distress (Ward et al., 2004). Only a small proportion of cancer patients at around 10% will need specialist intervention by psychological/psychiatric services in the year following diagnosis (NICE, 2004a; Ward et al., 2004). However, distress can be long-lasting with reports highlighting 54% of cancer survivors continue to experience one or more psychological issue after ten years (Macmillan Cancer Support, 2013). In addition to impacting on quality of life, depression has been linked to higher mortality rates in cancer patients (Satin, Linden, & Phillips, 2009) and greater use of health care services (Mausbach, Yeung, Bos, & Irwin, 2018).

Despite the UK governments law calling for 'parity of esteem', access to appropriate mental health services continues to be an issue in the UK with mental health rarely given equal attention or funding, with spending on mental health falling in many areas (Centre for Mental Health, 2013). There is an unmet need for mental health support for cancer patients both during and after treatment (Niedzwiedz, Knifton, Robb, Katikireddi, & Smith, 2019).

According to the latest economic review conducted in 2004 as part of the improving supportive and palliative care for adults with cancer NICE Cancer service guideline [CSG4] "current provision of psychological services is extremely limited in the majority of Cancer Networks. There are insufficient numbers of professionals available, so that psychological support services are neither available to – nor accessed by – many people with cancer who have psychological care needs" (Ward et al., 2004, p. 29).

Costs and cost-effectiveness of psychological services for cancer care

In 2004 the NICE economic review (Ward et al., 2004) highlighted the cost estimate of meeting psychological support services in cancer care represented 21.4% of total costs at £12.7million (England and Wales). The report indicated that as minimal service provision and limited staffing was available at the time that the cost impact would be high. However, the costs of not intervening are high with cancer patients who experience on-going psychological distress more likely to use primary and secondary health services, such as increased visits to GP, A&E, higher medication costs, and spend more time in hospital (Macmillan Cancer Support, 2013; Mausbach, Bos, & Irwin, 2018; Mausbach, Yeung, et al., 2018). According to Macmillan in 2010 the costs of excess bed days associated with preventable psychological illness in cancer patients in just one NHS trust was £366,000 each year (Macmillan Cancer Support, 2013). There has been limited updates to the provision of cancer services and whether these financial shortfalls have yet been met, however, reports indicate that there remains a shortfall in survivor support in terms of psychological services and rehabilitation care (Taylor, 2020).

Early and appropriate psychological support can improve health and has been argued to be a cost-effective use of scares public resources (Carlson & Bultz, 2004; Macmillan Cancer Support, 2013). In a review of the cost-effectiveness of a range of psychosocial care in cancer patients (Jansen, van Zwieten, Coupé, Leemans, & Verdonck-de Leeuw, 2016) six of the eight interventions were highlighted as likely to be cost-effective at UK NICE willingness-to-pay thresholds, however, that further research is needed, with methods capable of identifying potentially important cost drivers, such as informal care and/or productivity losses, when taking a societal perspective. This is particularly important when considering the personal financial impact of psychological illness following cancer which can result in lost employment, time off work and difficulty returning to employment after time of sick (Bell et al., 2006).

Mindfulness based programmes (MBPs) for cancer populations

MBCT being integrated with cognitive behaviour therapy (Beck et al., 1979) offers a framework which enables the therapist and the participants to link the learning of mindfulness to the particular cognitive vulnerability relevant to that population. The evidence for its efficacy in preventing depression (Teasdale et al., 2000; Ma & Teasdale, 2004) has resulted in the inclusion of MBCT in NICE guidelines for recurrent depression (NICE, 2009a, 2018). While MBCT was originally developed for people with recurrent depression, given that rumination and experiential avoidance are known to be common in many adverse mental health states and implicated in their maintenance (Hayes et al., 2004; Nolen-Hoeksema, 2000), there has been much clinical and research interest in adaptations of MBCT for other populations and contexts, including cancer care (Hulbert-Williams, Beatty, & Dhillon, 2018).

Early evidence of the efficacy of MBSR for improving psychological functioning in cancer patients was described by Speca, Carlson, Goodey and Angen (2000). Reported benefits for cancer patients include improvements in symptoms of stress, sleep, mental adjustment, pain and physical wellbeing, and significantly less mood disturbance and depression (Johannsen et al., 2016; Ledesma & Kumano, 2009; Mackenzie, Carlson, & Speca, 2005; Matchim & Armer, 2007; Matchim, Armer, & Stewart, 2011; Ott, Norris, & Bauer-Wu, 2006; Rush & Sharma, 2017; Smith, Richardson, Hoffman, & Pilkington, 2005; Speca et al., 2000). Since then, additional published studies delivering MBCT to cancer patients have continued to provide some evidence of a reduction in depression and anxiety symptoms (Foley, Baillie, Huxter, Price, & Sinclair, 2010; Sharplin et al., 2010). A more recent meta-analysis of MBSR and MBCT for women with breast cancer (published after this thesis research was completed) provides a more mixed result with a significant reduction in anxiety and depression outcomes at six months, although these effects did not reach a minimal clinically important differences threshold and only benefits on anxiety were maintained at the 12 month follow-up (Haller et al., 2017).

While MBPs are increasingly being adapted for cancer populations there are concerns raised about the methodological rigour of trials, benefits which are not sustained at follow-up and the inconsistent reporting of the interventions being delivered (Hulbert-Williams et al., 2018; Shaw, Sekelja, Frasca, Dhillon, & Price, 2018).

It is not yet well established whether offering a manualised tailored version of MBCT to people with cancer, where depressed mood is common, would be effective and cost-effective at preventing mental illness. This chapter aims to develop preliminary evidence on the targeted application of MBCT for cancer populations who are at a heightened risk of developing anxiety and depression. Following a methodological framework for the evaluation of complex interventions (discussed in Chapter 1), this thesis research begins with early-stage studies to explore the feasibility and acceptability of delivering the intervention and piloting the evaluation methods as part of a small sample randomised controlled trial.

Cost-effectiveness of MBPs for cancer – overview of economic evaluations from systematic review

At the time of conducting this thesis research there had been no economic evaluations of MBPs in cancer care published. Since then, as highlighted in Chapter 2 of this thesis there have been three published evaluations of MBPs delivered to cancer populations, either during cancer treatment or following as survivors of cancer. All the studies were published after the thesis research presented in this chapter was conducted. Greater discussion on contrasting findings and parallels with this thesis research are considered in the discussion section of this chapter.

Rationale for this feasibility study

Mindfulness-Based Cognitive Therapy for Cancer (MBCT-Ca; Bartley, 2011), is an adaptation of MBCT which has been designed and developed in North Wales specifically to meet the needs of cancer patients and their families. Those delivering the course have carefully adapted the programme to target the particular vulnerabilities of people with cancer (Bartley, 2011). These adaptations have been guided by ongoing course evaluations and feedback from participants. The approach offers people living with cancer the opportunity to learn to become less reactive to personal experience, thereby decreasing suffering and increasing wellbeing. It enables participants to become aware of their habits of mind and learn ways of responding to them differently. Mindfulness skills are developed through teaching, practice, reflection, dialogue, and group process within the class and through daily home practice schedules. In 2011, approximately 200 patients had attended the course at a North Wales hospital and clinical audit of the outcomes indicated that MBCT-Ca could improve overall wellbeing, self-compassion, and mindfulness skills (Soulsby, Morrison, Bartley, & Stuart, 2005). Whilst MBCT-Ca was available to some cancer patients in North Wales, no formal evaluation of its efficacy had been undertaken. Moreover, its implementation in 2011 across the North Wales Betsi Cadwaladr University Health Board (BCUHB) was at an early stage. A pilot and feasibility clinical trial to evaluate the implementation during this early phase of development aimed to provide valuable insight into the potential cost-effectiveness of the programme and to establish the feasibility of a large, randomised study to definitively evaluate the costs and benefits of MBCT-Ca for patients recovering from cancer. This study was conducted between 2011 and 2015 and was designed in the context of no previous economic evaluations of MBP for cancer and little available guidance on the methods for embedding health economics into pilot and feasibility trials. Since this study the research evidence has moved on (reflected in an update to the introduction above) and changes to best practice are discussed through the write up of this chapter where appropriate.

Overview of study aims

This feasibility study aimed to assess the proposed methods for conducting a full-scale multi-centre, randomised controlled trial to evaluate the effectiveness and cost-effectiveness of MBCT-Ca delivered in addition to Treatment as Usual (TAU) in a sample of patients with cancer who have previously received active cancer treatment as compared with TAU alone. This feasibility study aimed to achieve the following overarching study aims to:

1. Assess the study methods and processes for a full definitive trial to evaluate MBCT-Ca delivered alongside usual care compared to TAU alone,
2. Test the selection of outcome measures to consider a full range of costs and benefits relevant for economic evaluation of MBCT-Ca compared with TAU alone,

3. Assess patient experiences, perceived value and acceptability of support service options following cancer treatment.

Methods

Overview of study design

The core study design was a pragmatic two-arm randomised feasibility trial with embedded health economics pilot study and a concurrent service evaluation.

Trial processes and management

The trial was prospectively registered on ISRCTN registry clinical trials database (ISRCTN23380065, 2012). The study was designed by the candidate who undertook the role of chief investigator and primary researcher and supported by a Study Advisory Group (SAG) and Data Monitoring and Ethics Committee (DMEC).

The SAG and DMEC meetings constituted a key component of the feasibility study assessment of trial methods. The SAG meetings were held once every two months, chaired by the chief investigator (PhD candidate) and attended by academic supervisors and additional study advisors when needed. The chief investigator reported to the DMEC which were held every four months (or more regularly if required). Members of the DMEC included two Public and Patient Involvement (PPI) representatives, and senior independent research and clinical advisors. Both SAG and DMEC meetings were utilised to discuss and record important trial processes. The DMEC was independently chaired to ensure the trial was conducted as set out in the study protocol and in line with ethical approvals.

PPI is increasingly recognised as critical for successful research (Boivin et al., 2018). PPI representative assisted in the development of study documentation, for example, ensuring appropriate language was used and instructions were clear in the information sheet and consent form. PPI has been recently highlighted as important in health economics research (Al-Janabi et al., 2020).

The trial management and design of this study was a pragmatic and adaptive process. This meant that the methods for this study developed over time, with key milestones and practical requirements requiring changes to planned methods during the course of the study (Figure 13). To enable important lessons to be learned from this feasibility study these amendments are detailed in full through the methods and discussed further in the discussion section of this chapter.

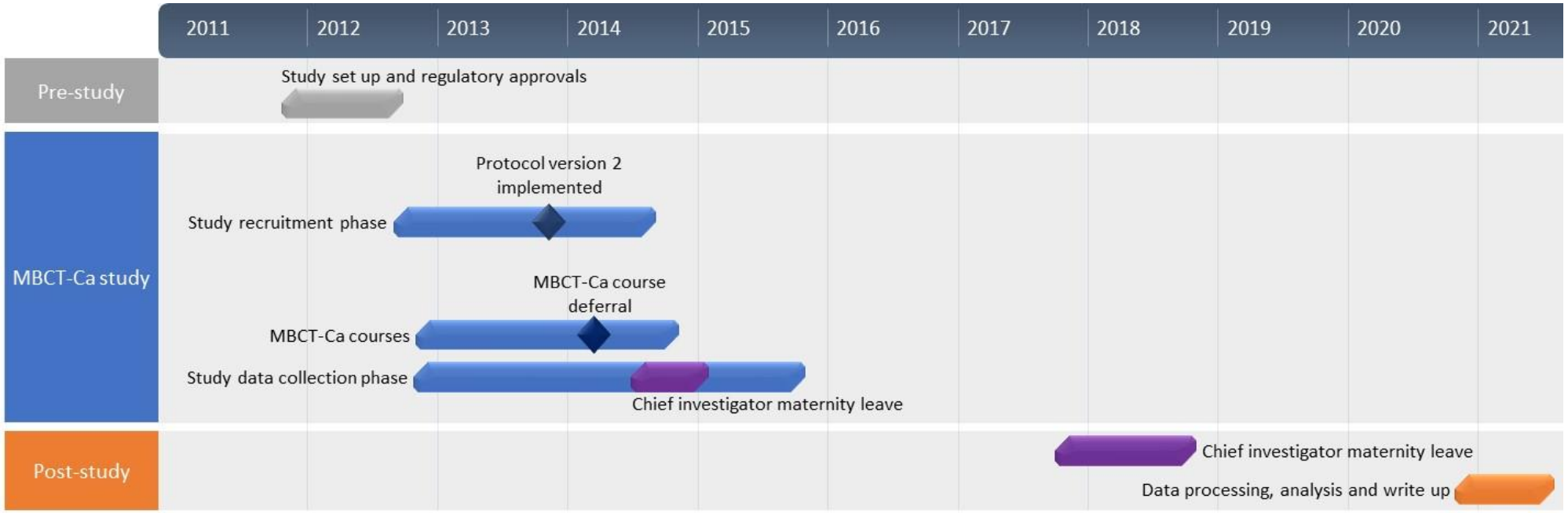


Figure 13: Timeline of trial phases and key milestones

This thesis research was funded as a Tenovus Charity PhD studentship however full research funding for the randomised feasibility trial was not available. This study was conducted with one core researcher (the candidate), who also undertook the role of chief investigator, and was supported by trial management groups (the SAG and DMEC). There was some limited additional support available for this study through key stakeholders including 1) the local health board who provided a site principal investigator and clinical advisor, 2) Bangor University who provided the randomisation systems through NWORTH and some admin support to facilitate chief investigator maternity leave and blinding procedures and, 3) the local providers of MBCT-Ca who predominantly delivered the intervention as part of their usual activities. Additional externally funded support that would typically facilitate the conduct of clinical trials was not available for this research for example through the scheme available at the commencement of this research delivered by the National Institute for Social Care and Health Research Clinical Research Centre (NISCHR CRC) in Wales to provide research infrastructure funded clinical research nurses to support portfolio trials.

The pragmatic but multicentre nature of the study meant that lining up recruitment and randomisation with the delivery of MBCT-Ca courses was challenging. Low participant recruitment levels meant the number of participants randomised to receive MBCT-Ca was insufficient to meet the minimum number of participants needed to run the MBCT-Ca groups. Due to delays in recruiting enough participants some MBCT-Ca courses were postponed. One MBCT-Ca course was deferred due to the availability of the MBCT-Ca therapist and a replacement therapist and course was set up. The impact of these factors was that some participants allocated to the intervention were unable to attend the revised course dates and this further reduced the number of participants within each course. A pragmatic response to ensure groups were viable to run was taken. This involved amending the study protocol to increase overall recruitment levels through the introduction of a secondary postal recruitment strategy to identify patients who had received surgical cancer treatment, alongside, widening the inclusion criteria to include patients receiving on-going active cancer treatment. In addition, the revised protocol aimed to increase recruitment specifically to the MBCT-Ca groups by amending the ratio of randomisation to be 2:1 in favor of the intervention compared with the control group. Finally, the introduction of a concurrent service evaluation study was employed to facilitate the inclusion of participants referred directly into the MBCT-Ca courses without randomisation.

All changes to study processes and methods were discussed and approved at the DMEC before implementation.

Overview of study methods and data sources to meet study objectives

This study adopted a mixed methods approach to evaluating MBCT-Ca as a complex intervention. A mixed methods approach has been argued to be appropriate for addressing complex questions in public health research (Kaur, 2016). The study methods and relevant sources of data were designed to meet a wide range of study objectives as detailed in Table 13:

Table 13: Study objectives and relevant sources of data

	Relevant sources of data 1 = Trial records, 2 = Quantitative data (trial), 3 = Quantitative data (service evaluation), 4 = Qualitative data and participant feedback form			
Study objective:	**1**	**2**	**3**	**4**
1. assess the methods for patient recruitment including identification, referral, enrolment	X			X
2. assess the randomisation processes	X			X
3. determine the acceptability of participants to receive the intervention or control condition	X			X
4. determine the willingness of participants to remain in the study	X	X		X
5. assess the acceptability of participants to complete the necessary study questionnaires for the duration of the study		X	X	X
6. collect service use information and build up a picture of typical health care, social care, and voluntary service use by patients		X	X	
7. obtain descriptive data on relevant outcome measure to assess the potential impact of MBCT-Ca		X	X	
8. conduct pilot assessments where appropriate to explore potentially meaningful differences between groups		X		
9. conduct pilot assessments where appropriate to explore potentially meaningful differences within groups over time		X	X	
10. assessment participant views and experiences relating to the study and support options following cancer treatment				X
11. measure the resources required to deliver MBCT-Ca	X			
12. estimate the cost of delivering the MBCT-Ca intervention, considering factors such as size of groups and course setting	X			
13. assess patient willingness to pay for MBCT-Ca				X

Within this feasibility study a formal assessment of the trial methods was undertaken. This included assessments of all aspects of the study protocol and involved collection of trial records which reported on the identification of eligible patients, referral rates by clinicians (objectives 1 &2), rates of conversions from referral to enrolment in the study and randomisation to receive wither MBCT-Ca alongside usual care or TAU alone (objective 2 & 3). Trial records relating to formal withdrawals from the research and completion of outcome measures as a proxy for continued participation were used to consider rates of attrition to determine participants willingness to remain in the study after enrolment and randomisation (objective 4).

To understand the potential impact of MBCT-Ca a pilot quantitative assessment of patient outcomes over time was undertaken. The acceptability of participants to complete the necessary study questionnaires for the duration of the study was assessed through the completion of the data booklets and the levels of missing data within each booklet (objective 5). The quantitative study aimed to collect service use information and build up a picture of typical health care, social care, and voluntary service use by patients (objective 6). In addition, obtaining descriptive data on relevant outcome measures was important to assess the potential impact of MBCT-Ca (objective 7). This study aimed to conduct pilot assessments where appropriate to explore meaningful differences between groups within the randomised feasibility study (objective 8). In addition, pilot assessments where appropriate to explore meaningful differences within groups over time were conducted (objective 9). A wide range of outcome measures were employed within this study to facilitate the inclusion of process evaluation involvement mediation and moderating factors analysis in a future large scale definitive research study. Embedding process evaluation in feasibility or full-scale clinical trials can help increase the transferability of research into practice, by considering contextual factors or mechanisms for an intervention working or failing (Cheng & Metcalfe, 2018). Process evaluation is argued to be a key component for evaluating complex interventions (Moore et al., 2015).

In addition, a feedback survey was employed for trial participants and an optional qualitative semi-structured interview was employed to explored patient experiences and views about support services following cancer treatment (objective 10) and help expand on the suitability of trial methods employed (objective 1-5).

Measurement of the resources required to deliver MBCT-Ca (objective 11) was achieved through micro-costing diaries collected as part of trial records and valued to provide an estimated cost of MBCT-Ca delivery (objective 12). Finally, the willingness of patients to share the cost of MBCT-Ca was assessed as part of this qualitative feedback process to explore the value of MBCT-Ca to patients following cancer treatment (objective 13).

Study setting and sample size

The randomised feasibility trial was conducted across BCUHB, which covers nearly a third of the landmass area of Wales (Public Health Observatory for Wales, 2009). The participants were patients receiving follow-up care after active cancer treatment across three hospital-based centres.

The study aimed to recruit up to 120 cancer patients post-treatment. As the first research study to formally evaluate MBCT-Ca, no prior evidence was available to indicate levels of effectiveness and calculate the sample size required to power definitive statistical analysis. This recruitment aim was pragmatic and opportunistic based on the number of planned MBCT-Ca courses and participant places available during the initial 2-year time of the study. During this time there were ten treatment clusters with each cluster linked to an MBCT-Ca course held across the three hospital-based centres.

The MBCT-Ca courses were taught across one large health board, with the research conducted across three counties each including one hospital based center. Tests for clustering by center were planned, however the size of each cluster ended up as very small and it was considered more appropriate for difference between centers to focus on participant numbers and to report on any recruitment factors that varied between hospital locations.

Participant eligibility criteria

Eligible patients were aged over 18 years, attending secondary hospital care having recently completed active cancer treatment; were able to attend the course venue weekly to undertake MBCT-Ca (if randomized to the intervention condition). Patients who were also receiving on-going hormone therapy and other on-going medication were still eligible to participate providing they were considered clinically stable by the inviting clinical team. Patients were excluded if they had:

1. not been offered active treatment for their cancer by their oncologist;
2. were unable or unwilling to complete treatment sessions and questionnaires in English for reasons of literacy, language, or cognitive impairment;
3. were lacking the capacity to give informed consent.

Participant identification and recruitment methods

There were four cohorts of recruitment into the randomised feasibility trial which occurred between December 2012 and May 2014. During this time patients were initially contacted by their oncology clinician at routine follow-up outpatient appointments. Clinicians were informed about the study by the researcher and principal investigator by word of mouth and by letter (see Appendix 7). Patients were given an invitation letter by the clinician with a self-referral response slip to return by post to request

more information about the research study should they choose to (Appendix 8). The number of patients approached was recorded by the researcher (through a clinical referral notification process shown in Appendix 9) and the clinician marked patient notes to ensure patients weren't approached more than once. A second recruitment strategy was introduced part way through the study to target eligible patients who had been discharged from surgery between June 2012 and June 2013. Eligible patients were identified through a database search of CANIS (National Health database of cancer patients in Wales), and recent patient records screened by the chief investigator researcher (the candidate) and principal investigator clinician who was a consultant oncologist. Patients were sent a letter by post inviting them to participate in the trial and return a self-referral response slip to receive more information about the study (see Appendix 10).

Recruitment commenced in December 2012 in two out of three treatment centres, where MBCT-Ca was more established. While roll out and recruitment into the third treatment centre was delayed until the final recruitment cohort which invited participants to take part in the study between October 2013 and May 2014.

At the end of the study all participants were contacted, and a self-selecting sample of participants were recruited to participate in the qualitative semi-structured interview and feedback form.

Randomisation methods

Consenting patients were randomised after baseline, via an online randomisation service provided by North Wales Organisation for Randomised Trials in Health (NWORTH) Clinical Trials Unit (CTU) to either receive the MBCT-Ca intervention or continue in the treatment as usual (TAU) control group on a 1:1 basis. The randomisation specification (Appendix 11) was amended part way through the trial to increase allocation to 2:1 in favour of the intervention (see milestone events detailed above in timeline).

Approach to blinding

Due to the nature of the intervention the participants could not be blinded to the assigned intervention. To minimise bias, the research was conducted by the chief investigator (the candidate) who was blinded to treatment allocation. The MBCT-Ca therapists were provided with details of participants allocated to the intervention. Limited admin support was available at points in the trial where research support was needed to gather information that would have revealed treatment allocation to the chief investigator, for example, to update intervention attendance registers. Participants were asked not to disclose their group allocation during the follow-up assessments. Group allocation and details of which group was which, was planned to be available to the chief investigator once the data had been entered into a database and locked.

Concurrent service evaluation

After 10 months of trial recruitment a concurrent service evaluation project was introduced in addition to the randomised feasibility trial. This was done for two reasons, firstly, to gather data on the demographic characteristics of patients receiving the intervention as part of routine clinical practice who had not been referred into the trial, and secondly, to help consider the costs and benefits of the full cohort of patients attending MBCT-Ca. Service evaluation project recruitment was opportunistic with participants of the MBCT-Ca course not already enrolled in the pilot RCT invited to participate in the service evaluation. Participants were provided with an information sheet (Appendix 21), consent form (Appendix 22) and baseline questionnaire booklet (Appendix 23) by the MBCT-Ca therapist to complete, with follow-up questionnaire booklets sent by post at the post intervention timepoint. The service evaluation study ran concurrently with cohort 4 of the randomised feasibility trial: routine service participants attended two MBCT-Ca courses alongside trial participants, and one further routine service course which was also attended by TAU control participants following completion of the active study period.

The intervention(s)

MBCT-Ca (in addition to Treatment as Usual)

The MBCT-Ca treatment condition has been fully described in the book by Trish Bartley (Bartley, 2011). The course consisted of an individual orientation and assessment session plus eight weeks of taught mindfulness practice sessions delivered in person to groups of up to 12 participants.

Each weekly class was two and a half hours long during which participants were taught guided mindfulness meditation. MBCT-Ca includes breathing exercises and gentle movement activities so participants become more aware of the present moment, including getting in touch with moment-to-moment changes in the mind and the body. It also included basic psych-education about depression and anxiety. In addition, the MBCT-Ca course involved homework assignments (consisting of up to an hour per day of home practice with audio CDs and a workbook).

All treatment sessions were delivered by a trained MBCT-Ca therapist as assessed by the developer of the training programme. Treatment sessions were video-recorded (with the camera focusing on the therapist alone) for a member of the SAG to conduct quantitative ratings of sessions to assess practitioner competency during treatment delivery using the Mindfulness-Based Interventions – Teaching Assessment Criteria (MBI-TAC; Crane et al., 2011).

MBCT-Ca was delivered in addition to Treatment as Usual (TAU). This was to ensure that participants were not restricted from accessing care that would normally be available to them. Health and social care and voluntary services were recorded (see below for details of the Service Utilisation Questionnaire; SUQ) for all participants to build a picture of treatment as usual. Hereafter, this group is referred to at the intervention condition or MBCT-Ca group. For participants attending MBCT-Ca but not enrolled into the randomised feasibility trial and instead recruited through the service evaluation referral route the group is referred to as the MBCT-Ca service evaluation cohort.

Control group: TAU alone

TAU served as a control condition, participants continued with their normal routine care in this condition and were informed that they would be offered the MBCT-Ca after a wait time of approximately 6-8 months once the study period was complete. Hereafter, this group is referred to as the control condition or TAU group. In the concurrent service evaluation study there was no control group comparison.

Ethical considerations

The randomised feasibility trial was reviewed and approved by the North Wales - West NHS REC and local R&D committees (Reference: 12/WA/0095, see Appendix 12) and the Bangor University School of Psychology ethics committee.

The main potential ethical issues thought to arise from the study was that it was a two-arm randomised study, and that participants are vulnerable. In the context of some existing limited access to MBCT-Ca in North Wales it was important to ensure that patients were not withheld a service that would normal have been available to them, however, to evaluate the efficacy and cost-effectiveness of MBCT-Ca, it was necessary to establish the course of quality of life and wellbeing when MBCT-Ca was not delivered. All those randomised to TAU were offered the MBCT-Ca course upon completion of all follow-up measures and the time horizon purposely kept short to ensure patients could access services in a timely fashion should they want to.

Following initial telephone contact made by the patient with the researcher, an in-person home visit appointment[5] was made to first provide patients with information about the study (Appendix 13), offer an opportunity to answer any questions and to obtain written informed consent (Appendix 14) before

[5] As an alternative to home visits a hospital-based appointment was available to any patients who preferred to conduct the assessment outside of their home or if any safety concerns were raised during pre-appointment contacts.

randomisation into the study. There was a risk that participants would find the pre course interview and parts of the assessment where they were asked to report on current symptoms distressing. This risk was minimised by 1) fully informing participants about the content of the interview and questionnaires so that they could prepare themselves and give fully informed consent to participate, 2) emphasising to participants that all questions were optional and that they could choose not to answer any questions they didn't want to, and 3) ensuring the researcher remained sensitive to signs of participant distress.

If patients disclosed significant distress at any stage of the study, these were planned for to be managed by a standard protocol developed by members of the team used in previous similar studies exploring MBCT. The interviewer was trained to terminate the interview if the participant became distressed, taking action to ensure participants safety and recording the adverse event in study records (Appendix 15). As an additional safety measure participants' GPs were informed of their involvement in the study (Appendix 16) and could be contacted if necessary. The limits of confidentiality and the procedures for dealing with significant distress were explained to all participants prior to obtaining consent. Where appropriate, concerns were referred to appropriate professionals as determined by the DMEC.

A substantial ethics amendment to include the secondary postal recruitment strategy and a concurrent service evaluation conducted alongside the RCT was reviewed and approved by the North Wales Research Ethics Committee - West (Reference: 12/WA/0095/AM01, see Appendix 17).

All data collected was kept confidential and stored in a locked filing cabinet with access only by the research team in accordance with the Data Protection legislation. Participants were allocated a unique numeric identifier to be used on all questionnaires to protect their anonymity. Electronic data was password protected and stored on encrypted computers. Patients were free to withdraw from the study at any time and at the end of the study were sent a debrief form (Appendix 18).

Lone worker policies and security procedures for lone working home visits were implemented to ensure safety of researcher. An honorary research contract and occupational health clearance was obtained by the researcher to enable research activities on NHS site (Appendix 19).

Study data collection points (timepoints)

The trial study time horizon was planned to be 6 months, with data collected at key timepoints through the study. See Appendix 24 for a flow chart of the planned study timeline and process. Timepoint zero (T0) provided the baseline assessment of outcomes (see below for a description of the measures completed at each timepoint). T0 was conducted immediately following a participants consent to participate and prior to their randomisation and allocation to treatment condition. Timepoint one (T1) provided a post-intervention phase assessment and the first follow up after T0. T1 was anchored on the

end of the MBCT-Ca course (for both the intervention group and the control condition). Timepoint two (T2) provided a further follow-up assessment, which was conducted 3 months after T1. It was intended that the MBCT course would commence within one month of a patient's T0 assessment and randomisation into the study, with T1 therefore occurring three months after T0. In a couple of cases there was a substantial delay in commencement of the MBCT-Ca course after completion of baseline outcomes and randomisation into the study and in these cases T0 was repeated to ensure comparability with the treatment cluster in which they had been allocated. A final mixed methods feedback form and opt-in qualitative interview was held at the end of the study (T3).

For the service evaluation sub-study data was collected at two timepoint prior to the intervention commencing (pre-intervention T0) and immediately after the 8-week MBCT-Ca course had finished (post-intervention T1).

Timing of follow up assessments

The follow-up time was pragmatically derived with T1 falling at the end of the intervention, and T2 to 3 months later. In some cases, a delay in the MBCT-Ca course commencing meant that the time between baseline and T1 was longer than planned. Where possible baseline assessments were repeated to capture health at a comparable point to the rest of the cluster. However, despite this the time between baseline, T1 and T2 varied between participants. Only 42% of follow up assessments were completed within one month of the planned assessment point, 3 months after baseline and 3 months after T1. As a result, for the pilot assessment a decision about how to calculate benefit over time needed to be made. Two options were considered 1) varying length of time between assessments on an individual basis, which would limit comparability of QALYs at a group level however adjustment for differential timing could be conducted; 2) taking an average length of time across the cohort at each timepoint as a proxy for the time between timepoints. The second option was adopted with the average length in time between baseline and T1 recorded as 4.4 months, while a delay in returning T2 booklets resulted in an average length between T1 and T2 of 4.6 months. The time between T0 and T1 as a proportion of 1 year was 0.37, while the time between T1 and T2 was 0.38. Where T1 was missing the time between T2 and T0 was calculated to be 0.75. The total duration of the study was 9 months. This research aimed to explore what the likely bounds of assessments points were to establish a clear apriori definition of what is considered 'within window', for example, whether follow-up assessments were completed within one month of the assessment date. Data was collected pre and post timepoints for the service evaluation sub-study. The average length of time between pre and post assessment points was 8.73 weeks (*M=61.13 days, SD=16.72 days*).

Materials

Quantitative outcome measures

Baseline demographic information

The inclusion of this measure served two important functions. Firstly, it provided data for assessment of equivalency between intervention and control groups and was used to explore indicators of potentially important covariates for inclusion within further research. Secondly, the baseline demographics interview was used to establish a rapport with participants, and, important in terms of assessment contiguity, for the participant to have an opportunity to express matters of concern prior to being asked to complete the subsequent questionnaires.

Self-reported outcome measures

A total of 7 previously validated questionnaires were used in this study at each timepoint. Each questionnaire was estimated to take between 2-5 minutes to complete.

The EQ-5D-3L

The EQ-5D-3L (The EuroQol Group, 1990) provided a measure of HRQoL. As a generic (rather than disease specific), preference-based measure, it is commonly considered the gold standard for the calculation of utility and subsequent QALYs for cost-utility analysis. The measure consisted of two parts, a five-item questionnaire, and a visual analogue scale (EQ-VAS). There were five domains, 1) Mobility, 2) Self-Care, 3) Usual activity, 4) Pain and Discomfort, and 5) Anxiety and Depression. The EQ-5D-3L had three levels of responses to each domain question, no problems scored as 1, some problems scored as 2, and extreme problems scored as 3. The three level scores provided one of 243 health profiles that have been valued and weighted by general population samples using time trade off methods (Dolan, 1997). The UK EQ-5D-3L population weightings were applied to each health profile to generate utility scores between -0.594 and 1, with 1 meaning full HRQoL. EQ-5D utility values were used to calculate QALYs (see analysis methods below for further methods). The EQ-VAS thermometer was scored between 0 (worst possible health) and 100 (best possible health), with respondents asked to mark their current HRQoL level. Ceiling effects of the EQ-5D-3L measure were explored in the form of the proportion of participants who answered no problems to all domains. Floor effects were considered the highest severity of responses to the questions, yielding scores of zero or lower (representing states worse than death).

The E0RTC-QLQ-C30 Version 3.0 (EORTC Quality of Life Group)

The QLQ-C30 (Aaronson et al., 1993) is a cancer specific health related quality of life questionnaire. The questionnaire consists of 30 questions and consists of multi-item scales and single item scores (see Table 14). The global health items are on a 7-point Likert scale with 1 representing very poor health and 7 representing excellent health. The functional scales and symptom scales / items have four possible responses "Not at all", "A little", "Quite a bit", and "Very much".

Table 14: EORTC-QLQ-C30 scales and items scoring

	Items(n)	Range*	Item numbers (Version 3)
Global health status / QoL			
Global health status/QoL	2	6	29, 30
Functional scales			
Physical functioning	5	3	1 to 5
Role functioning	2	3	6, 7
Emotional functioning	4	3	21 to 24
Cognitive functioning	2	3	20, 25
Social functioning	2	3	26, 27
Symptom scales / items			
Fatigue	3	3	10, 12, 18
Nausea and vomiting	2	3	14, 15
Pain	2	3	9, 19
Dyspnoea	1	3	8
Insomnia	1	3	11
Appetite loss	1	3	13
Constipation	1	3	16
Diarrhoea	1	3	17
Financial difficulties	1	3	28

** The item range is the difference between the possible maximum and the minimum response to individual items. Source: Adapted from the EORTC-QLQ-C30 scoring manual* (Fayers et al., 2001).

The scales include one global health status (quality of life) scale, five functional scales (covering physical, role, emotional, cognitive, and social functioning), three symptom scales (covering fatigue, nausea and vomiting, and pain), plus six single items. For all scales and single-item measures, a Raw Score (*RS)*, is calculated as the mean of the component items. The raw scores are then converted with linear transformation to standardise the raw score from 0 to 100. For the functional scales scores see Equation 4. For the Symptoms scales and global health status scales see Equation 5:

$$Score = {}^{1 - \frac{(RS - 1)}{Range}} \times 100$$

Equation 4: Functional scales score

$$Score \ = \{(RS \ - 1) \ \text{range}\} \times 100$$

Equation 5: Symptom scales / items and Global health status / QoL scores

A high score on the functional scales represents a high level of functioning, while a high score on the symptom scales and items represents a high level of symptoms. After reversing symptom scores to ensure a single direction of all scores, a composite summary score can be calculated as the mean of 13 of the 15 scales (excluding the financial difficulties item and the global health status scale).

The ICEpop CAPability measure for Adults (ICECAP-A) Version 2

The ICECAP-A (Al-Janabi & Coast, 2010) was used to measure capabilities and to provide a broader measure benefit for this study (see Chapter 1 for an introduction to the capabilities framework e.g. Sen, 1999). The reliability, validity and feasibility of ICECAP-A for use in a range of population groups has been well researched (Al-Janabi et al., 2012, 2013).

The ICECAP-A consisted of five attributes covering attachment, stability, achievement, enjoyment, and autonomy. Each attribute was addressed by a single question with response options scored from 1 to 4, with higher scores corresponding with higher quality of life. The best possible set of responses was a value of 4 scored on each attribute providing a profile score of 44444, while the worst possible profile of responses was 11111. A UK value set (scored using best worst scaling) was used to obtain an index value from 0 to 1, with 1 indicating the highest level of wellbeing and 0 equivalent to the worst possible wellbeing (Flynn et al., 2015).

The ICECAP-O, an earlier version of the ICECAP measure which was designed for older people, has previously highlighted that there are various possible options for valuing meaningful change on ICECAP outcomes, with competing evaluative frameworks which consider either maximisation of wellbeing or sufficiency of wellbeing. There has been work to identify a 'Threshold of Sufficient Capability', where it has been proposed that no value should be attributed to improvements above a sufficient threshold

(equivalent to an ICECAP profile score of 33333). Using this approach it is possible to generate a Sufficient Capability Score (SCS), and then using the AUC approach (as described to calculate QALYs) benefits over time can be used to calculate a Years of Sufficient Capability (YSC) score (Mitchell et al., 2015). In contrast, using the UK tariff for calculating index values from ICECAP-A and applying AUC approach method to combine capability scores over time allows for the calculation of Years of Full Capability (YFC) (Flynn et al., 2015). The later approach focuses on maximisation of capabilities; this was considered to be more comparable with the QALY maximisation approach, while considering sufficiency required a shift into a different conceptual framework. It is important to note that YFC and QALY approaches are distinctively different, particularly in terms of decision making where more work is needed to identify willingness to pay thresholds for a year of full capability (Proud et al., 2019).

For this pilot study, ICECAP-A was used to generate YFC (see analysis methods below for further methods), providing a comparable outcome to QALYs.

The WHO (Five) Well-Being Index (WHO-5)

The WHO-5 (sometimes also referred to in the literature as the WBI-5) (World Health Organisation, 1998) was used to measure participant subjective psychological wellbeing. The WHO-5 was comprised of five questions, has been validated as a simple screening tool for depression (Löwe et al., 2004) and has been proposed as a useful outcome measure for clinical trials (Topp, Østergaard, Søndergaard, & Bech, 2015). Each question was scored using a Likert scale of 0 to 5 with higher scores representing better wellbeing. Scores were summed and multiplied by 4 providing a total percentage score ranging from 0–100.

The WHO-5 is rarely used in the field of health economics (Topp et al., 2015). However, as subjective wellbeing is included as an outcome in national population monitoring in the UK and considered a strong indicator of economic performance, it is argued to be an important outcome to capture in evaluations (Hicks, Tinkler, & Allin, 2013; OECD, 2013; Social Impacts Task Force, 2014).

The Hospital Anxiety and Depression Scale (HADS)

The HADS questionnaire was used to screen for anxiety and depression symptoms (Zigmond & Snaith, 1983). The measure has a total of fourteen questions, consisting of seven items each relating to sub-scales of anxiety and depression. Each item has four possible responses indicating how the participant has been feeling in the past week. The responses are scored from 0 to 3 with low scores corresponding with no problems and high scores representing significant problems with each item. Subscale scores are summed to provide a score between 0 and 21, with higher scores indicating a higher severity of anxiety or depression. Scores are banded to indicate thresholds for normal levels of functioning between 0 and

7, borderline abnormal levels (borderline case) with scores between 8 and 10 and abnormal (case) with scores of 11 or higher. Total scores (anxiety and depression subscales combined) indicating overall levels of distress with a lower threshold ⩾13 in cancer populations have been proposed as being a useful indicator of patients who may require further support (Singer et al., 2009). The HADS has been validated for use with both patients and non-clinical general population samples (Bjelland, Dahl, Haug, & Neckelmann, 2002).

Five Facet Mindfulness Questionnaire – Short form (FFMQ-SF)

The FFMQ-SF provided a measure of trait mindfulness. The 24 item short form (Bohlmeijer, Klooster, Fledderus, Veehof, & Baer, 2011) has been developed from the original 29 item questionnaire (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006) which has been validated within both meditating and non-meditating samples (Baer et al., 2008). The FFMQ-SF has been confirmed to be "highly sensitive to change" and to be "reliable and valid instruments for use in adults with clinically relevant symptoms of depression and anxiety" (Bohlmeijer et al., 2011, p. 308).

The questionnaire covered five facets of mindfulness, non-reactivity, observation, awareness of actions, description, and non-judgement. Each item had five possible responses and were scored on a 5-point Likert scales, ranging from never or very rarely true scored as 1 and very often or always true scored as 5. Facet scores were calculated through summing the scores from the individual items within each facet, with negatively phrased questions reverse scored. Potential scores ranged from a minimum of 8 to 40 (except for the non-reactivity facet, which ranged from 7 to 35), with higher scores indicating more mindfulness. The FFMQ measures five distinct but related aspects of mindfulness, which can also be considered facets of an overall mindfulness factor" (Bohlmeijer et al., 2011, p. 314). Therefore, a global mindfulness score was calculated by combining scores from each subset to provide a total score (Williams, Dalgleish, Karl, & Kuyken, 2014).

The Self Compassion Scale - Short Form (SCS-SF)

The SCS-SF (Raes, 2011) was used to provide a measure of self-reported self-compassion. While the SCS-SF has not been commonly used in economic evaluations it was important to consider wider benefits from a societal perspective. In addition, the SCS-SF was used to explore the collection of information on potentially important mechanisms for change in MBPs. The training and orientation of an eight week mindfulness programme deliberately cultivates compassion, and has been reported to be a mediator of the positive effects of MBCT (Kuyken, Watkins, et al., 2010). Compassion offers an alternative to aversion and fear, allowing people to turn towards distress and pain rather than fleeing from it. It enables a shift towards kindness and curiosity and away from shame or blame (Feldman & Kuyken, 2011).

The SCS-SF consisted of six compassion related subscales, each made up of two items. The scales were self-kindness, self-judgment, common humanity, isolation, mindfulness and over-identified. The mean of subscale items provided a score for each scale. A total self-compassion score was computed by reverse scoring the negative subscale items (self-judgment, isolation, and over-identification) before calculating a total mean.

Health care resource use: Range of costs and sources of unit costs

In addition to outcomes the economic evaluation cost component of this study employed a Service Utilisation Questionnaire (SUQ) to measure the frequency of health and social care services of cancer patients in both the intervention and control arms of the study. The service utilisation questionnaire is a type of client service receipt inventory (CSRI). The CSRI has been used in over 100 studies since it was first developed in the mid-1980s (Chisholm et al., 2002, 2000) and can be used alone or in conjunction with other data collection methods such as patient record data. The SUQ was developed specifically for this study based of examples of best practice from previous clinical trials conducted at the Centre for Health Economics and Medicines Evaluation (CHEME) and published resources on the DIRUM database. The SUQ used in this study was retrospective, and asked patients about their resource use over a 3-month period preceding the date of the assessment point. A period of three months was sufficient for a representative picture of service use to be gauged, yet recent enough for the patient to recall accurately the frequency and nature of contacts (Roberts, Bergstralh, Schmidt, & Jacobsen, 1996). The SUQ was administered as a face-to-face interview at baseline and as a postal questionnaire or telephone interview at follow-up. The SUQ aimed to explore any contacts in addition to their cancer specific care rather than including resources associated with any on-going cancer treatment alone.

GP service use rates were considered against classifications of 'frequent attenders' to identify any high utilisers of services. There was no commonly recognised rating of what constitutes a 'frequent attender', with significant variation in the number of visits classified across studies (Morriss et al., 2012). In one study attendance of one or more visits per month was classified as frequent attendance (Jiwa, 2000). In another study up to 22 visits in a two year period was considered normal attendance compared with 30 or more visits constituting 'regular' attendance (Morriss et al., 2012). For this study frequent GP attenders were classified as participants reporting 3 or more visits[6] over the SUQ 3 month recall period.

Assessment of trial methods

Embedded within this study a formal assessment of trial methods was undertaken. This involved information collected through trial records including referral records which were documented to

[6] Using Jiwa (2000)'s regular attender classification of one or more visits per month.

monitor levels of patient invitation. Other sources of trial records included researcher notes which were recorded during the study set up and conduct of the trial, alongside the recruitment, data collection and evaluation stages. Micro-costing diaries were collected to detail the resources to deliver MBCT-Ca. At the end of the study data was sought from MBCT-Ca therapists on course attendance.

Invitation and referral of potential participants was reviewed at regular trial review meetings and at the end of recruitment (June 2014). The number of invitation notifications received from health professionals referring into the study were recorded. The initial conversion rate from invitation to patient opt-in response slip returned was calculated and presented as a percentage of total invitations. The final conversion rate was considered as the proportion of responders that enrolled in the trial. This is presented as a percentage of the cumulative number of patients who responded to the invitation.

Loss to follow-up (attrition) was defined as participants who formally withdrew from the study, died during the trial between T0 and T2, or failed to respond to any follow up questionnaires. Loss to follow up and missing data was considered separately as some participants did not respond at T1 but did return T2 booklets.

Quantitative data analysis methods

Statistical software

All analysis was conducted in Microsoft Excel 365 and IBM SPSS Statistics 27.0.

General approach to randomised feasibility trial statistical analysis and choice of tests conducted

Considering the sample size and stage of this pilot research limited statistical analysis was reported with the majority of results reported descriptively and compared narratively. Where statistical analysis was conducted it was not intended to be definitive but aimed to help identify potential trends in the data that warrant further consideration in follow-up research. To explore potential effects of the intervention, parametric tests for differences were used to compare outcomes with a normal distribution or non-parametric tests alternatives were used to assess differences in the distribution of data, both between trial group and within groups over time. The choice of statistical test and analysis was data driven with any significant differences between groups at baseline considered for inclusion within analysis of outcomes over time, with adjustment for baseline values in the analysis. No covariates were included and no baseline adjustment conducted where no differences were observed at baseline. Individual tests were conducted to compare each outcome variables of interest as outlined in the description of analysis below, using repeated measures tests to compare outcomes over time and independent samples tests to compare between groups. A p value of less than .05 was applied as the

threshold for significance in all statistical analyses conducted.

Perspective of economic evaluation analysis

The study perspective adopted was a primary NHS health and social care service perspective with a secondary societal perspective to capture wider costs and benefits of interventions.

Analysis population and completeness of dataset

The data analysis was conducted on an Intention to Treat (ITT) basis. A secondary 'Per Protocol' analysis was planned which restricted data to where no major protocol violations were observed, for example, where a participant was randomised to receiving the intervention but did not attend any sessions. A secondary per protocol analysis considering intervention dose was defined as patients attending 4 or more classes as used in previous MBP clinical trials (Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Brejcha, et al., 2015; Shawyer et al., 2016). The planned per protocol analysis was not conducted due to incomplete records on participant attendance.

The likely impact of missing values was explored in terms of the conduct of both a complete case analysis and an available case analysis. The complete case analysis was conducted using listwise deletion where a case was dropped from the analysis if the primary outcome was missing. A secondary available case analysis was conducted using pairwise deletion where missing values were only dropped when comparing the outcome of interest. While pairwise deletion enables more of the data to be included in the analysis each computed statistic may be based on a different subset of cases limiting comparability.

Study time horizon and discount rate

As the time horizon was less than 12 months (in both the trial study and service evaluation sub-study) discounting of costs and benefits was not considered necessary.

Analysis of costs

Intervention costs

MBCT-Ca intervention costs were collected through micro-costing cost diaries developed as part of the study (described in detail in Chapter 3 of this thesis). The additional costs of MBCT-Ca was estimated to be £690 (inflated to 2019 from micro-costing estimates reported in Chapter 3) per participant based on an average of 8 participants per course. The costs of MBCT-Ca delivered after the completion of the study to participants allocated to the TAU alone condition were not included as they occurred outside of the study period.

Resource use

Resource use was grouped by community-based services or hospital based services, with the mean number of contacts for each consultation type calculated. Baseline differences between groups were compared descriptively, with mean number of contacts and distribution of frequent GP attenders compared between the MBCT-Ca group and the TAU groups in the trial. Excluding medication costs, health and social care resources were costed using national unit costs (Curtis & Burns, 2019) (NHS Improvement, 2019) presented in £GBPs cost year 2018/2019 (see Appendix 25). Mean costs per participant were calculated per category of services used and differences between group costs discussed narratively in relation to the drivers of cost differences and the most common reasons given for resources used. With such a small sample and limited incidences of resource use observed statistical comparisons to compare groups was not performed.

Analysis of outcomes: Descriptive data on relevant outcome measure to assess the potential impact of MBCT-Ca

Primary outcome for economic evaluation

EQ-5D-3L was the primary measure of effect for this study, in order to pilot the methods for a primary cost-utility analysis. The primary economic outcome was expressed as QALYs with utility values obtained for the EQ-5D-3L (as described above in outcome measures). EQ-5D utility values were combined at different timepoints using the AUC approach to calculate QALYs gained or lost over time by each group (methods for AUC calculation described in full below)

Assessment of data normality

The choice of questionnaires was scrutinised in terms of general features of the questionnaires used in this study population, including exploration of the potential impact of skewed values on future analysis. This was achieved through Kolmogorov–Smirnov statistical tests of data normality at baseline and consideration of floor and ceiling effects.

Assessment of baseline values

Descriptive data on participant demographics and resource use costs were compiled and compared narratively between groups at baseline to consider trial group equivalence. Descriptive statistics for all health-related outcomes were reported and baseline differences between groups were assessed statistically (following normality tests to indicate appropriate selection of parametric or non-parametric test for equivalence).

In addition, EQ-5D mean values at baseline were compared descriptively with age-adjusted population norms (Kind, Hardman, & Macran, 1999). In terms of population norms, the mean (SD) EQ-5D utility for people aged 55-64 was 0.80 (0.26) while the mean (SD) EQ-5D utility for people aged 45-54 was 0.85 (0.25).

Assessment of extreme values

Ceiling and floor effects were considered to be present if 15% or more of respondents report the extreme values as defined in each outcome measure (Stucki, Liang, Stucki, Katz, & Lew, 1999; Terwee et al., 2007).

Assessment of outcomes over time

Descriptive statistics are presented for all outcome measure including change over time between baseline (T0), post-intervention (T1) and follow-up (T2). These were grouped by treatment allocation and presented over time across the duration of the study. Mean values for composite outcomes were reported alongside any sub-scales (for example for the EORTC-QLQ-C30).

Comparison of differences in utility measures between groups and within groups over time

To explore differences between trial groups the mean difference and percentage change on utility values were reported over time by group. The minimally important difference (MID) on the EQ-5D-3L utility scores was considered as mean difference over 0.063 (McClure, Sayah, Xie, Luo, & Johnson, 2017). Mean difference was calculated by subtracting the first mean value from the follow up mean value exploring differences between baseline (T0) and post intervention (T1), then between T1 and follow up (T2), and finally between T2 and T0. Percentage change was calculated by subtracting the before timepoint mean value (T0 or T1) from the subsequent timepoint mean value (T1 or T2); divided by the before value. Finally, results were multiplied by 100 to report the percentage change between the two timepoints under consideration.

Mean QALYs were calculated using the Area Under the Curve method depicted in Box 2 using participants' individual utility scores at each timepoints (Hunter et al., 2015). A baseline utility value and at least the T2 follow-up timepoint was considered the minimum required to enable the AUC QALY calculation on a complete case basis.

Box 2: Formula for calculating AUC QALYs from patient-level data as reported in Hunter et al (2015) P.358.

The formula to calculate the AUC or QALYs using patient-level data is shown in Eq. 1:

$$q_{jti} = \frac{(u_{j(t-1)i} + u_{jti})}{2}\delta_t \quad (1)$$

where u is the utility score, i denotes an individual, and t is time so that at baseline $t = 0$. For each group j ($j = 0$ for control and $j = 1$ for treatment), the consecutive time measures are added, averaged and then re-scaled (δ) for the percentage of a year that t and $t-1$ cover, so 0.5 for 6 months or 0.25 for 3 months and so on.

For the total duration of the trial, the total QALYs (Q) for each individual are the summation of the QALY calculations for each follow-up timepoint starting at $t = 1$, the first follow-up point (Eq. 2)

$$Q_{ji} = \sum_{t=1}^{T} q_{jti} \quad (2)$$

The mean QALYs for each treatment group (Q_j) are then calculated from the individual-level data, dividing the sum of all QALYs for all patients ($\sum Q_{ji}$) by the number of patients (n) (Eq. 3).

$$Q_j = \frac{\sum_{i=1}^{n} Q_{ji}}{n} \quad (3)$$

Pilot statistical analysis between groups was conducted for QALYs, comparing mean QALYs at 9 months between the MBCT-Ca group and the TAU group. Non-parametric tests for differences between total QALY in each trial group were assessed using the Mann-Whitney U test.

Individual change in ICECAP-A index values were calculated, with the AUC approach used to estimate mean YFC per treatment group (during the trial duration). This analysis was repeated for YFC at 9 months to explore any indicators of differences between trial groups when using the ICECAP-A measure of capabilities. Non-parametric tests for differences between total YFC in each trial group were assessed using the Mann-Whitney U test.

Comparison of differences in psychological distress measures between groups and within groups over time

The HADS, WHO-5 and EQ-5D-3L anxiety and depression domain were all used as indicators of psychological distress. Levels of psychological distress across the range of included outcomes were

reported descriptively with mean values reported for all dependent variable outcomes. The percentage of groups meeting threshold criteria (as defined below by outcome measure) for psychological distress were calculated.

All outcomes were then plotted to allow for a visual comparison both over time and between groups.

HADS

Mean HADS sub score and totals were calculated at each timepoint and compared between groups. The difference between mean scores at each timepoint and the percentage change of scores over time were explored to capture any reduction or increase in depression or anxiety severity. Difference between groups were explored using parametric tests or non-parametric tests in cases where data was not normally distributed.

In addition, the percentage of participants by trial groups over time scoring above and below the defined thresholds for anxiety, depression, and psychological distress on the HADS were reported. The proportion of participants with sub-scores $\geqslant$11 (the optimal threshold for identifying cases of depression or anxiety), were compared over time. A threshold of scores between 8-10 was used to classify borderline case status. In addition, the proportion of total score cases above the cancer population lower threshold of $\geqslant$13 and the standard general population threshold of $\geqslant$16 was explored by group. Comparison of the different psychological distress thresholds on the HADS outcome were plotted by group and over time to explore differences between the thresholds and the impact on interpretation of the data further.

The proportion of the whole cohort of trial participants with normal levels of function on the HADS measures was used as an indicator of the extent of the opportunity for primary prevention of depression in this population of people who have had cancer. A significant clinical change on the HADS was considered to be score reduction to below the clinical cut-off at follow -up, while a moderate effect size was required to be considered to be a MID (Boersma & Postma, 2021).

WHO-5

Mean WHO-5 scores were calculated at each timepoint and compared between groups. For monitoring change a 10% or greater improvement was considered a significant clinical important difference on the WHO-5. For depression screening a cut-off score of ≤ 50 was applied for the WHO-5 (Topp et al., 2015).

EQ-5D-3L anxiety and depression domain

EQ-5D-3L patterns of severity within the anxiety and depression domain were explored in terms of descriptive statistics and a visual comparison of plots depicting the proportion of respondents reporting no problems or degrees of some problems, over time and across trial groups.

Analysis of subgroups

Demographic variables including type of cancer diagnosis and time since treatment were collected and were planned to be explored as potentially important covariates for future analysis, however, the sample of subgroups was too small for meaningful statistical analysis within this pilot study. No sub group analysis was conducted.

Service evaluation analysis

Within the service evaluation cohort differences between pre and post outcomes were reported descriptively. Dependent variable outcomes were the same between trial groups and the service evaluation cohort, while there was only two timepoints and no comparison group to explore between group differences. Therefore, only within group differences were considered within this pilot analysis. Mean values, mean difference and percentage change were calculated for all dependent variables, exploring the difference between pre and post values in this cohort. A single parametric analysis of differences pre and post (with time as the independent variable) was undertaken using a one-way analysis of variance across the full range of outcomes as dependent variables with bootstrapping of 10,000 replications conducted to provide 95% confidence intervals around mean difference estimates. Statistical adjustment for multiple comparisons was conducted using the Bonferroni method. Post hoc tests were only conducted if there were indicators of significant change and for outcomes where the assumption of normality was violated at baseline. Only when these criteria were met were planned post hoc tests conducted (using a related samples using non-parametric Wilcoxon Signed Rank Test). This was used to explore whether any differences observed remained when using non-parametric tests for differences, rather than bootstrapping methods alone.

The range of psychological distress outcomes were plotted to allow for a visual comparison of participants meeting the thresholds over time by outcome.

No statistical analysis was conducted to compare differences between the randomised feasibility trial groups and the MBCT-Ca service evaluation cohort. Mean values relating to demographics, resource use and outcome measures are instead compared narratively to explore similarities between the trial cohort and service evaluation cohort and to build a picture of the participants attending these pragmatically derived MBCT-Ca courses.

Qualitative methods

There have been many benefits of qualitative research put forward, they are thought to offer a useful method for evaluating treatment innovation and particularly in clinical settings where patient experience is important (Nelson, Magin, & Thompson, 2017; Rosenthal, 2016).

Qualitative methods have also been highlighted for use in health economics (Coast, 1999; Coast & De Allegri, 2018). Examples of health economics qualitative studies include research that aims to improve knowledge of health systems, exploring behavioural factors to accessing and consuming health services, or improving understanding of what resources are being consumed alongside health. Framework or thematic analysis have been highlighted as approaches that can be used to answer questions of economic theory (Coast & De Allegri, 2018). Content analysis, which has similarities to both framework and thematic analysis, has been proposed as a qualitative method that can be used to answer research questions and quantified (Vaismoradi, Turunen, & Bondas, 2013). Narrative research can be used to highlight individual experiences of people (Creswell, 2013).

MBCT-Ca experience feedback form

To evaluate patient experience of receiving MBCT-Ca and taking part of the research, a two-page feedback form was administered after the final follow-up along with an invitation to participate in a brief qualitative semi-structured interview (see Appendix 26).

Qualitative semi-structured interviews

This thesis research adopted to use semi-structured interviews rather than other qualitative designs such as focus groups as the aim was to elicit individual participant experiences (Nyumba, Wilson, Derrick, & Mukherjee, 2018).

A topic guide was developed to steer the semi-structured interviews (Appendix 27), however, the questions aimed to be open-ended, and responses led by the participant. The topic guide was informed by the study objectives (as outline at the end of the introduction in this chapter) and the overall chapter research questions (see Chapter 1). The content aimed to focus on key research processes such as randomisation and questionnaires alongside participants to share their experiences of receiving their usual treatment and the MBCT-Ca (if applicable).

The content analysis process has been described as consisting of three key stages (Elo & Kyngäs, 2008):

1. Preparation – this involved an immersion in the qualitative data, transcribing audio interviews, and determining the key content and categories for analysis. All sources of data were combined into a file, consisting of interview data, feedback form responses, and other trial process records.
2. Organisation – this involved coding content into categories and grouping with codes relating to the key content areas.
3. Reporting – this involved a description of results and where appropriate a quantification of data as a proxy for significance, for example whether all, several or some of the participants

identified a key content area. The final stage of reporting was linking the analysis to the study objectives and overall chapter research questions.

Qualitative results were recorded narratively. Triangulation of the different study methods was used to compare similarities and differences in the results (Jick, 1979). The synthesis of mixed methods elements of this study are presented at the end of the results and discussed further in the discussion.

Assessment of patient Willingness to Pay (WTP)

Brief patient Willingness to Pay (WTP) information was elicited through a direct approach (Ryen & Svensson, 2015), with asking patients about their WTP for MBCT-Ca weekly session over 8 weeks. The WTP estimates were considered as both total costs per course and as a proportion of patients' household income. The participant derived estimates of WTP were discussed in relation to the suitability as an indicator of patient WTP for QALY gains and considered against the NICE threshold of £20,000 - £30,000 per QALY. In addition, the WTP weekly costs were compared narratively against the cost of alternative private health care services such as counselling services.

Approach to reporting of study results

This feasibility study yielded extensive results related to both participant outcomes and trial feasibility. Firstly, the study population, and trial process information were presented in line with the CONSORT statement (Schulz, Altman, & Moher, 2010). Secondly, patterns of health and wellbeing, and resource use at baseline in terms of equivalence between randomised trial groups were presented. Thirdly, economic outcomes over time at follow-up and where appropriate comparisons across groups were presented. Fourthly, psychological distress outcomes were plotted with a narrative description of differences between groups and indicators of anxiety and/or depression over time. Results of the service evaluation sub-study were then presented separately with narrative comparisons made with participant outcomes from the randomised feasibility trial reported earlier in the section. Finally, results of the qualitative analysis are reported narratively including assessment of participants experiences and perceived value of MBCT-Ca to conclude the results of this mixed methods study.

Results

Study population

The total number of participants enrolled into the randomised feasibility trial was 39 (see Table 15). The patient response rate to invitations varied between 41% to 62.5%. The enrolment rate into the trial was between 68% and 82%, equating to 74% of responders at the end of the trial. The eligibility of patients referred was high, with less than 10% of responders not meeting the inclusion criteria for the study (see

trial CONSORT diagram presented in Figure 14). After randomisation 22 were allocated to the intervention group and 17 were allocated to the control group.

Table 15: Review of patient trial invitations, responses and enrolment into trial conversion rate

Date of review	Cumulative N of invitations	Cumulative N of responses (%)	Cumulative N enrolled into trial (%)
23rd January 2013	25	11 (44%)	9 (82%)
15th July 2013	40	25 (62.5%)	17 (68%)
15th October 2013	54	30 (55.5%)	23 (77%)
17th December 2013	84	44 (52%)	31 (70%)
25th March 2014	129	53 (41%)	36 (68%)
1st June 2014			39 (74%)

Loss to follow-up

Attrition was 23% at T1 of the whole sample of trial participants, with higher rates of attrition in TAU (35%) compared with MBCT-Ca (14%). Loss to follow up increased to 53% at T2 in the TAU group and remained the same in the MBCT-Ca group. Reasons for loss to follow up included participants who formally withdrew from the study (*N=1*), died during the trial between T0 and T2 (*N=1*), or failed to respond to any follow up questionnaires (*N=7* by T1; *N=10* cumulative at T2).

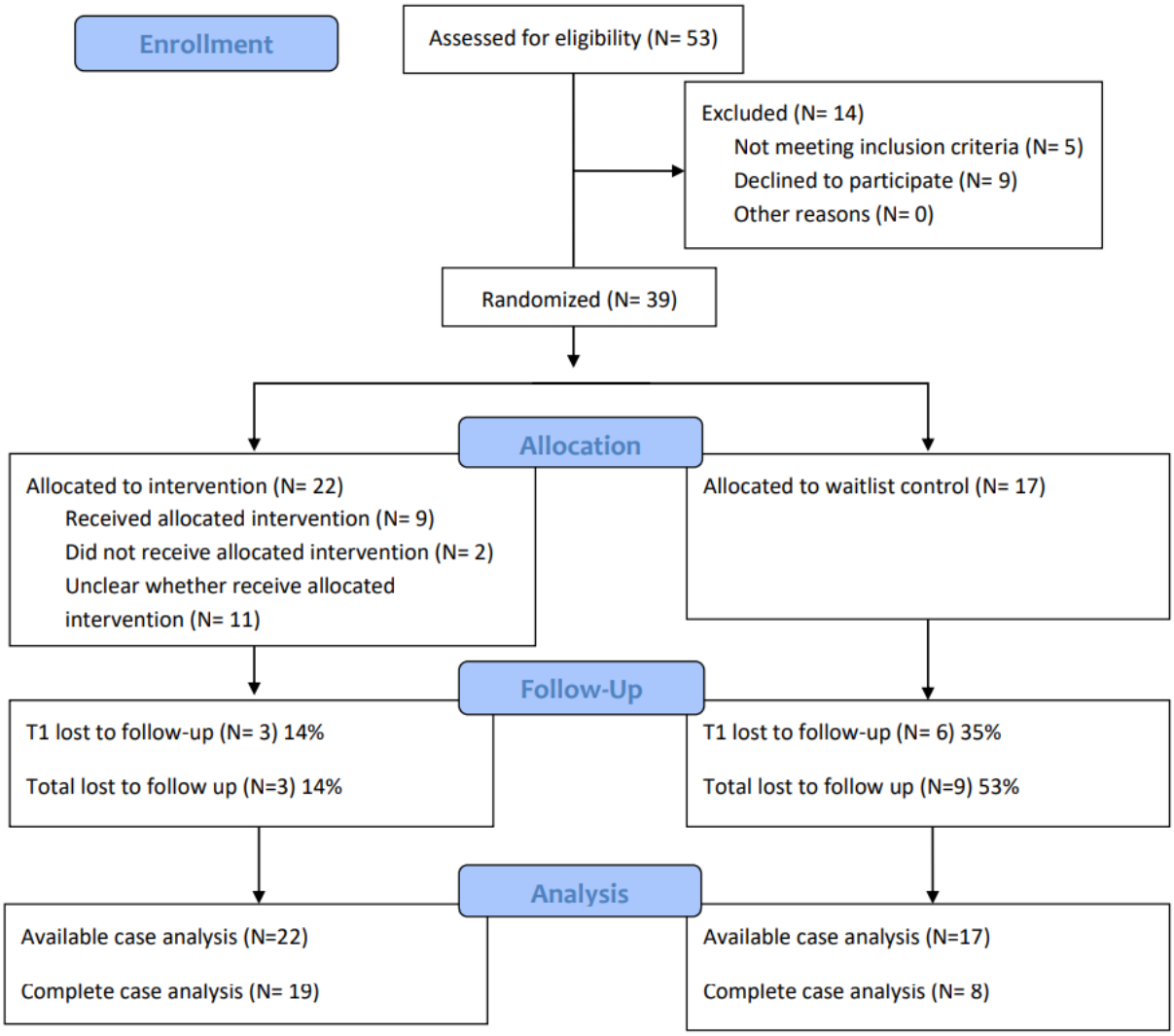


Figure 14: Consort diagram randomised feasibility trial of MBCT-Ca compared with TAU

Additional considerations in the feasibility study

Response rates and missing data

All 39 participants completed baseline visits and minimal missing data was present, with missingness representing participant skipping items they preferred not to answer. The return rate of T1 questionnaires was 69%, reducing to 59% of all completers by T2 (i.e., 23 participants completed T0, T1 and T2 assessments). When considering all follow up data, 77% of participants completed either T1 or T2. The number of participants who completed a T3 feedback form was 19 (49% response rate), and a smaller sub-set of participants opted-in to a qualitative interview (*N=7*, 18% of whole sample).

Adverse events and incidents

There were four adverse events recorded during the trial. One participant died during active participation three months after baseline was completed. Two participants died after T2 follow up and

we were notified when the end of study debrief forms were sent to participants. The sponsor was informed of the three serious adverse events which were not considered related to the trial. One further adverse incident was reported as a participant who experienced distress and became upset during the study. The incident was referred by the chief investigator to the DMEC for further investigation and any action if required. One additional incident was recorded during recruitment which related to a patient safety concern. The incident was deemed unrelated to the trial and occurred prior to enrolment in the study. It was reported to clinical contacts with the patient's consent for appropriate action.

Protocol violations

Unblinding of the chief investigator occurred during data entry of follow up questionnaire which occurred after all participants had concluded their T2 assessment.

Cohorts, clusters, and centres

There were four cohorts of recruitment into the randomised feasibility trial (see Table 16). Between December 2012 and May 2014 there were ten treatment clusters with each cluster linked to an MBCT-Ca course held across three hospital-based centres.

Table 16: Number of cohorts recruited, courses evaluated, and centres involved over time

Cohort number	Start of recruitment	End of recruitment	Number of MBCT-Ca course	Number of centres
Cohort 1	December 2012	January 2013	2	2
Cohort 2	February 2013	March 2013	1	2
Cohort 3	April 2013	September 2013	2	2
Cohort 4	October 2013	May 2014	5	3

Recruitment ranged from 2 to 6 participants per trial cluster with a small mean number of participants per trial cluster *(M=4.33)*. Recruitment was higher in one centre *(N=20)* where MBCT-Ca was more established. Roll out and recruitment into the third centre *(N=8)* was delayed until the final cohort which recruited from October 2013 until May 2014.

The service evaluation study ran concurrently with cohort 4 of the randomised feasibility trial: routine service participants attended two MBCT-Ca courses alongside trial participants, and one routine service course which was also attended by TAU control participants following completion of the active study period.

An additional 24 participants were enrolled into the study through the service evaluation route. Loss to follow up post intervention was 33% (*N=8*).

Baseline characteristics of study population

Clinical characteristics of study population and demographics

Of the study sample population over half had received treatment for breast cancer compared with other sites of disease (see Table 17). In terms of treatments received, surgery, chemotherapy and radiotherapy were the most common treatments, with some patients receiving more than one of each treatment. In addition, some patients were receiving ongoing treatments such as hormone therapy or Herceptin® medication. The average time since treatment (excluding maintenance treatment) was less than a year (8 months), and most recent cancer diagnosis was on average 1 year and 4 months before enrolment in the study. Less than 15% of the study population had a previous cancer diagnosis, with the average time since first cancer diagnosis being 9 years 3 months (for those with a previous experience of cancer).

Table 17: Baseline clinical characteristics of feasibility trial participants

	N	M(SD)
Primary site of disease diagnosis		
Breast cancer	22	
Gynaecological cancers	9	
Other cancers	8	
Secondary cancer diagnosis		
Breast, Ovarian, Vaginal, Liver, Lymph nodes	8	
Average time since most recent diagnosis		1 Year 4 Months
Previous cancer diagnosis		
Breast, Womb, Ovarian, Leukaemia	5	
Average time since previous cancer diagnosis		9 Years 3 months
Number of treatments received		3.03 (1.16)
Surgery procedures	40	
Chemotherapy courses	35	
Radiotherapy	25	
Herceptin® (Trastuzumab)	11	
Other	7	
Average time since treatment		8 Months

Most participants enrolled in the trial were white females of working age currently in employment or on long-term sick leave (see Table 18). The trial sample had a higher than average mean number of years in education (United Nations Development Programme, 2013). There was very little previous experience of meditation reported.

Table 18: Baseline socio-demographic characteristics of feasibility trial participants

	M(SD)	N
Sex		
Female		37
Male		2
Age (Years)	57.72(10.90)	
Average time in education (Years)	13(2.52)	
Employment status		
Employed part-time		5
Employed full-time		5
Long-term sick		10
Retired		14
Unemployed		5
Relationship status		
Married / Cohabiting		27
Single / Separated / Divorced / Widowed		12
Household		
Living with others		32
Living alone		7
Ethnicity		
White (British, Welsh, English, European, Other)		38
Mixed		1
Other		0
Meditation experience		
Previous experience		3
No previous experience		36
Medication use		
Antidepressants		26%
Pain medication		21%

To consider the baseline equivalence of groups demographics and clinical characteristics were reported by group allocation (see Table 19). The MBCT-Ca group had a higher proportion of participants who had been diagnosed with breast cancer, while the TAU group had a higher representation of other cancer patients. The time since diagnosis and the time since treatment was similar in both groups. The mean age was slightly higher in the MBCT-Ca group, however, when rounded to the nearest whole year both ages fell within the same age bracket of 55-64 years in terms of comparison with population norms (Kind et al., 1999).

Table 19: Baseline equivalence demographics and clinical characteristics by trial group

	MBCT-Ca	TAU
Primary site of disease diagnosis		
Breast cancer	64%	47%
Other cancers	36%	53%
Average time since treatment	9 Months	7 Months
Average time since most recent diagnosis	1 Year 6 Months	1 Year 2 Months
Mean age (Years)	59.95	54.82

Health and social care resource use

Table 20 shows the mean number of contacts per participant in each trial group, split between community-based care and hospital-based services. At baseline mean resource use costs were slightly higher in the MBCT-Ca group compared with TAU. This was the case for both community-based services and hospital-based services. Visits to the GP, district nurse visits at home, physiotherapy visits and talking therapy including counselling were the most used community services. The distribution of frequent attenders to GP was equivalent between groups at baseline. There were some occurrences of very high frequency contacts with physiotherapists and district nurse home visits at baseline for a small number of participants. In some cases visits were noted to be associated with cancer treatments, such as nurse visits to provide a blood sample taken prior to their chemotherapy appointment. In terms of hospital-based service resource use there were very few contacts involving overnight stays in hospital, and accident and emergency services. Outpatient appointments were reasonably high during this three-month recall period with the mean number of appointments in the MBCT-Ca group reported as 5.55 contacts and 4 appointments in the TAU group. Almost all outpatient visits related to cancer treatment or oncology follow up care. Total costs across community and hospital-based services were £529.59 higher per participant in the MBCT-Ca condition at baseline. This difference in cost was mostly driven by a small number of high-cost inpatient admissions, reported in the MBCT-Ca group compared with the TAU group who did not report any inpatient contacts at baseline. Two participants reported inpatient stays equating to a total of 13 nights in hospital, and were in both cases admissions following a surgery which was reported to be related to their cancer treatment e.g. osteoporosis following radiotherapy leading to a hip replacement.

Table 20: Mean (SD) contacts with primary and secondary care health services by trial group at baseline

	MBCT-Ca (*N=22*)	TAU (*N=17*)
Community-based care		
General practitioner (clinic)	1.09(1.02)	1.82(1.24)
General practitioner (home)	0(0)	0.06(0.24)
General practitioner (telephone)	0(0)	0.18(0.73)
Practice nurse	0.59(1.37)	0.71(1.57)
Phlebotomist	0(0)	0(0)
District nurse	1.82(4.17)	0.12(0.49)
Social worker	0.18(0.85)	0.06(0.24)
Mental health nurse or psychiatric nurse	0(0)	0(0)
Talking therapy / Counsellor	0.68(1.62)	2.5(2.12)
Dentist	0(0)	0(0)
Optician	0(0)	0(0)
Reflexology	0(0)	0(0)
Acupuncture	0(0)	0(0)
Chiropody / podiatrist	0(0)	0(0)
Physiotherapist	1(2.93)	0.06(0.24)
Exercise on referral	0.55(2.56)	0.47(1.94)
Occupational health therapist	0.23(1.07)	0(0)
Alternative therapist	0.05(0.21)	0(0)
Mediation services	0(0)	0.06(0.24)
Hospice	0(0)	0(0)
Mean community costs (SD) at baseline	£213.05(243.21)	£141.19(115.98)
Hospital based services		
Accident and emergency	0.18(0.50)	0.18(0.39)
Outpatient visits	5.55(7.31)	4(4.96)
Inpatient admission (short stay)	0(0)	0(0)
Inpatient admission (long stay)	0.09(0.29)	0(0)
Mean hospital costs (SD) at baseline	£951.36(1245.16)	£493.65(577.30)
Total mean costs per participant	£1164.42	£634.83

Medication data was only collected at baseline and incomplete information meant too many assumptions would need to be made regarding dose and duration to accurately cost medication use. One in four trial participants (26%) at baseline were receiving antidepressants and 21% taking regular pain medication at the start of the study. There was a mix of cancer related treatments recorded which will be influenced by cancer type, severity and treatments received, in addition to wider health and care services received. Participants were also asked to indicate if they were experiencing health problems including depression, and if so if they had sought support and received treatment. There was some evidence that some mental health support is sought through oncology services, some through primary

care and some through charities such as Tenovus. There were indicators that no consultation or treatment was sought by some participants.

Table 21 shows the mean number of community-based services and hospital-based resources used by trial participants at study follow-up point.

Table 21: Mean (SD) contacts with primary and secondary care health services by trial group at follow up

	MBCT-Ca		TAU	
	T1 (*N=18*)	T2 (*N=18*)	T1 (*N=9*)	T2 (*N=8*)
Community and home-based care				
General practitioner (clinic)	0.44(0.62)	0.89(1.60)	1.11(0.78)	2.00(0.93)
General practitioner (home)	0(0)	0(0)	0(0)	0(0)
General practitioner (telephone)	0(0)	0.33(1.41)	0(0)	0(0)
Practice nurse	0.56(1.46)	0.22(0.55)	0.67(0.71)	1.13(1.55)
Phlebotomist	0(0)	0.06(0.24)	0(0)	0(0)
District nurse	0.17(0.71)	0.11(0.47)	0(0)	0(0)
Social worker	0(0)	0(0)	0(0)	0(0)
Mental health nurse or psychiatric nurse	0(0)	0(0)	0(0)	0(0)
Talking therapy / Counsellor	0.39(1.42)	0(0)	0.67(1.66)	1.13(3.18)
Dentist	0.11(0.47)	0(0)	0(0)	0(0)
Other				
Optician	0.06(0.24)	0(0)	0(0)	0(0)
Reflexology	0(0)	0.11(0.47)	0(2.00)	0(0)
Acupuncture	0.06(0.24)	0.56(2.36)	0(0)	0(0)
Chiropody / podiatrist)	0(0)	0.17(0.51)	0(0)	0(0)
Physiotherapist	0(0)	0.06(0.24)	0(0)	0.25(0.71)
Exercise on referral	0(0)	0(0)	0.89(2.67)	0(0)
Occupational health therapist	0(0)	0(0)	0(0)	0(0)
Alternative therapist	0.11(0.32)	0(0)	0(0)	0(0)
Mediation services	0(0)	0(0)	0(0)	0(0)
Hospice	0(0)	0.06(0.24)	0(0)	0(0)
Mean community costs (SD)	£71.57 (113.44)	£120.61 (261.00)	£151.87 (143.25)	£152.88 (156.32)
Hospital based services				
Accident and emergency	0.06(0.24)	0(0)	0(0)	0(0)
Outpatient visits	1.5(2.57)	1.61(1.88)	0.67(0.87)	1.38(0.92)
Inpatient admission (short stay)	0(0)	0(0)	0(0)	0.13(0.35)
Inpatient admission (long stay)	0(0)	0(0)	0(0)	0(0)
Mean hospital costs (SD)	£183.33 (299.11)	£186.89 (218.43)	£77.33 (100.46)	£238.38 (230.70)
Intervention costs (MBCT-Ca allocation)	£690(0)	£0(0)	£0(0)	£0(0)
Total mean costs	£944.90	£307.50	£229.20	£391.25

Overall, mean resource use costs were similar between treatment groups during the trial follow-up period when excluding the MBCT-Ca intervention costs. For the 6 months recall period, total mean costs (excluding MBCT-Ca costs) were £562.40 in the MBCT-Ca group and £620.45 in the TAU group. If these costs were scaled up from 6 months to represent the full study duration of 9 months as outlined in the AUC QALY calculation, then total costs could be estimated to be £845.36 in the MBCT-Ca group and £936.08 in the control.

The total intervention cost on an intention to treat basis was £15,180 for the 22 participants allocated to receive MBCT-Ca. When including the costs of MBCT-Ca (*M=£690* per participant allocated to receive the course) the total mean cost of the MBCT-Ca group (£1252.40) rises to more than double the total costs of the TAU group.

Through the resource use information obtained, the most common community-based contacts were with the GP, practice nurse, district nurse and talking therapy services. There was some high frequency use by a small number of participants, for example, exercise on referral, by the nature of the scheme, involves attendance of between 8 and 12 sessions per person.

In both the MBCT-Ca and TAU group mean hospital outpatient attendance was lower during the trial follow-up period, than compared with baseline levels. The majority of outpatient visits were for oncology follow up appointments. There were minimal contacts with accident and emergency and overnight stays in hospital in both groups during the trial follow-up.

Health and wellbeing outcomes

Normality tests for outcome data: Kolmogorov–Smirnov test for normality indicated that EQ-5D-3L and ICECAP-A utility scores were skewed at baseline *EQ-5D D(39)=0.232, p=.000; ICECAP-A D(39)=0.226, p=.000,* while the other outcomes were normally distributed.

Group equivalence at baseline

Across all outcomes the distribution of data was considered equivalent between groups at baseline, as there was no statistically significant difference between independent samples Mann-Whitney U tests as displayed in Table 22.

Table 22: Non-parametric tests for difference between groups in the distribution of data by health outcome at baseline

	U	***df***	***p***
EQ-5D-3L	170.00	39	.644
EQ-5D VAS	186.50	37	.759
ICECAP-A	176.50	39	.769
EORTC-QLQ-C30 (Global health status/QoL)	151.00	39	.319
HADS (total)	185.50	39	.839
WHO (total)	164.50	39	.528

There were minimal differences between trial groups on HRQoL and wellbeing measure at baseline (see Table 23). The TAU group had a slightly higher mean EQ-5D-3L utility value than the MBCT-Ca group (0.02 utility mean difference), however, the MBCT-Ca group had higher values on the ICECAP-A, EORTC-QLQ-C30 summary scores and QoL, and the WHO-5 wellbeing scale when compared with TAU. Both groups scored lower than the population mean (SD) EQ-5D-3L utility health state index for 55-64 years age group of *M=0.80(SD=0.26)*.

Table 23: Descriptive statistics health related quality of life and wellbeing scores (available case)

	Baseline (T0)				Post-intervention (T1)				Follow up (T2)			
	MBCT-Ca		TAU		MBCT-Ca		TAU		MBCT-Ca		TAU	
Outcome and scale	N	M(SD)	N	M(SD)	N	M(SD)	N	M(SD)	N	M(SD)	N	M(SD)
EQ-5D-3L utility	22	0.68 (0.28)	17	0.70 (0.21)	16	0.72(0.27)	9	0.57(0.27)	18	0.70(0.31)	8	0.65 (0.29)
EQ-5D-VAS	22	69.86 (15.65)	16	68.94 (19.42)	18	77.39(16.32)	9	73.67(14.54)	18	73.39(20.62)	8	66.23(18.59)
ICECAP-A utility	22	0.84 (0.17)	17	0.84 (0.13)	18	0.81(0.18)	9	0.83(0.14)	18	0.81(0.19)	8	0.78(0.16)
EORTC-QLQ-C30 (Global health status/QoL)	22	68.94 (19.10)	17	64.71 (17.56)	18	70.83(19.10)	9	70.37(12.58)	18	67.13(20.10)	8	66.67(13.36)
EORTC-QLQ-C30 (Summary Score)	22	73.42 (16.10)	17	71.08 (12.83)	17	78.37(17.96)	8	79.31(11.07)	18	75.72(18.23)	8	71.65(14.58)
Function scales												
Physical functioning	22	76.67 (21.94)	17	73.73 (18.78)	18	77.04(24.97)	9	74.07(12.22)	18	77.41(24.54)	8	75.83(20.76)
Role functioning	22	63.64 (32.79)	17	62.75 (27.34)	18	79.63(30.55)	9	70.37(26.06)	18	66.67(36.16)	8	62.50(21.36)
Emotional functioning	22	65.91 (23.28)	17	58.82 (18.97)	18	65.28(22.19)	9	59.26(31.58)	18	65.28(25.76)	8	54.17(27.09)
Cognitive functioning	22	65.15 (24.07)	17	74.51 (21.24)	18	72.22(25.57)	9	64.81(24.22)	18	73.15(26.28)	8	62.50(30.54)
Social functioning	22	66.67 (29.99)	17	60.78 (30.15)	18	81.48(27.94)	9	74.07(29.00)	18	71.30(28.47)	8	64.58(22.60)
Symptom scales and items												
Fatigue	22	41.92 (23.99)	17	47.71 (22.49)	18	35.80(24.86)	9	40.74(16.67)	18	38.89(27.55)	8	48.61(22.17)
Nausea and vomiting	22	6.82 (9.84)	17	8.82 (11.96)	18	5.56(9.90)	9	0.00(0.00)	18	7.41(13.06)	8	6.25(8.63)
Pain	22	30.30 (28.47)	17	34.31 (26.66)	18	29.63(25.28)	9	37.04(20.03)	18	26.85(31.38)	8	33.33(23.57)
Dyspnoea	22	18.18 (24.62)	17	25.49 (25.08)	18	16.67(23.57)	9	22.22(23.57)	18	16.67(23.57)	8	20.83(24.80)
Insomnia	22	43.94 (31.52)	17	41.18 (32.34)	17	41.18(30.11)	8	20.83(30.54)	18	38.89(30.78)	8	33.33(35.63)
Appetite loss	22	16.67 (26.73)	17	17.65 (26.66)	18	12.96(23.26)	9	7.41(22.22)	18	20.37(30.55)	8	12.50(17.25)
Constipation	22	9.09 (18.35)	17	15.69 (26.66)	18	7.41(14.26)	9	11.11(16.67)	18	12.96(20.26)	8	16.67(17.82)
Diarrhoea	22	16.67 (24.67)	17	15.69 (29.15)	18	11.11(19.80)	9	7.41(14.70)	18	7.41(14.26)	8	16.67(25.20)
Financial difficulties	22	33.33 (38.49)	17	45.10 (47.05)	18	16.67(23.57)	9	37.04(38.89)	18	22.22(30.25)	8	41.67(42.72)
WHO-5 total score	22	52.91 (23.52)	17	48.94 (21.84)	18	55.78(26.83)	9	45.89(25.54)	18	48.89(26.66)	8	40.50(29.97)

Note. EQ-5D-3L higher scores indicate higher health related quality of life with a maximum value of 1. The ICECAP-A has a maximum value of 1 with higher mean scores indicated higher capability. A high score (out of 100) on global health status/QoL, summary score and functional scales represents a high level of health / functioning, while a high score on the symptom scales and items represents a high level of symptoms. WHO-5 scores are out of 100 with a higher mean score indicating higher wellbeing.

Table 24 shows the proportion of the study population at baseline where ceiling or floor effects were observed on HRQoL and wellbeing measures. Results are split by outcome measure and subscales. There were no ceiling effects present on the EQ-5D-3L descriptive system. There were no floor effects with less than 5% of participants reporting EQ-5D-3L values of zero (valued as equivalent to death) or worse. No floor or ceiling effects on other measures of HRQoL and wellbeing (ICECAP-A, EORTC-QLQ-C30 global health status scale and WHO-5) were observed. There were however high ceiling effects on the EORTC-QLQ-C30 function scales and some of the symptom scales and items. Full functioning was reported in 23% of participants on role functioning, and 21% of participants in cognitive functioning and social functioning scales respectively. Physical and emotional function scales were not limited by floor or ceiling effects. Except for the fatigue symptom scale, there were high ceiling effects (between 23% and 72%) observed across all symptom scales and items. In addition, the financial difficulties item also had a high floor effect (26% of participants reporting significant financial difficulties).

Table 24: Health related quality of life and wellbeing outcome measures floor and ceiling effects observed at baseline in a combine sample of trial participants (MBCT-Ca and TAU).

		Floor	Ceiling
	N	%	%
EQ-5D-3L utility	39	<15%	<15%
EQ-5D-VAS	38	<15%	<15%
ICECAP-A utility	39	<15%	<15%
EORTC-QLQ-C30 (Global health status/QoL)	39	<15%	<15%
Function scales			
Physical functioning	39	<15%	<15%
Role functioning	39	<15%	23%
Emotional functioning	39	<15%	<15%
Cognitive functioning	39	<15%	21%
Social functioning	39	<15%	21%
Symptoms			
Fatigue	39	<15%	<15%
Nausea and vomiting	39	<15%	62%
Pain	39	<15%	26%
Dyspnoea	39	<15%	51%
Insomnia	39	<15%	23%
Appetite loss	39	<15%	67%
Constipation	39	<15%	72%
Diarrhoea	39	<15%	67%
Financial difficulties	39	26%	46%
WHO-5	39	<15%	<15%

There were no floor or ceiling effects observed on either SCS-SF, FFMQ-SF or HADS outcome measures.

Mean scores on both HADS anxiety and depression sub-scales and total scores were similar between trial groups (see Table 25). The mean score for the anxiety subscale was above the threshold for borderline abnormal levels in both groups, while the mean score on the depression subscale was within the normal range in both groups. When considering the clinical cut-offs (indicating significantly abnormal levels of anxiety and depression), there was a higher proportion of normal levels on both subscales of depression and anxiety in the MBCT-Ca group (see Table 26). However, when considering total HADS scores, there was less difference between groups in terms of proportion of participants falling above the cancer threshold or general population threshold for problems. On the WHO-5, in parallel with the results presented in Table 23 (where the MBCT-Ca group had higher wellbeing index scores than the TAU group), the MBCT-Ca group had a lower proportion of participants compared the TAU group who scored below the depression threshold (≤50), indicating additional investigation psychological input may be required.

Table 25: Mean (SD) HADS scores at baseline, post intervention and follow up by trial treatment group (available case)

	Baseline (T0)				Post-intervention (T1)				Follow up (T2)			
		MBCT-Ca		TAU		MBCT-Ca		TAU		MBCT-Ca		TAU
	N	M(SD)	N	M(SD)	N	M(SD)	N	M(SD)	N	M(SD)	N	M(SD)
HADS (subscale anxiety)	21	9 (4.48)	17	9.29 (5.05)	17	8.24(4.89)	9	9.78(6.16)	18	8.17(5.19)	8	9.13(6.40)
HADS (subscale depression)	21	5.19 (4.11)	17	5.53 (4.20)	17	4.76(4.62)	9	4.44(3.68)	18	5.39(4.26)	8	5.63(3.70)
HADS Total	21	14.19 (7.82)	17	14.82 (8.71)	17	13.00(7.98)	9	14.22(9.58)	18	13.56(8.37)	8	14.75(9.63)

Note. higher mean scores indicate a higher severity of anxiety, depression, or psychological distress.

Table 26: Proportion (%) of trial participants reporting abnormal anxiety and depression levels at baseline

	Baseline (T0)				Post-intervention (T1)				Follow up (T2)			
		MBCT-Ca		TAU		MBCT-Ca		TAU		MBCT-Ca		TAU
	N	%	N	%	N	%	N	%	N	%	N	%
HADS (subscale anxiety)	21		17		17		9		18		8	
Normal (0-7)		42.86		35.29		47.06		33.33		55.56		50.00
Borderline abnormal (8-10)		23.81		29.41		23.53		22.22		16.67		0.00
Abnormal (≥11)		33.33		35.29		29.41		44.44		27.78		50.00
HADS (subscale depression)	21		17		17		9		18		8	
Normal (0-7)		76.19		64.71		76.47		66.67		83.33		62.50
Borderline abnormal (8-10)		9.52		23.53		17.65		33.33		5.56		37.50
Abnormal (≥11)		14.29		11.76		5.88		0.00		11.11		0.00
HADS Total	21		17		17		9		18		8	
Above cancer population threshold (≥13)		57.14		58.82		58.82		55.56		50.00		50.00
Above general population threshold (≥16)		42.86		41.18		29.41		44.44		33.33		50.00
WHO-5	22		18		18		9		18		8	
Below threshold (≤50)		45.45		52.94		33.33		55.56		44.44		62.50

Mean (SD) scores SCS-SF and FFMQ-SF baseline trial groups

There was baseline equivalence between trial groups on all secondary outcomes including the SCS-SF and FFMQ-SF.

Table 27: Mean (SD) SCS-SF and FFMQ scores at baseline by trial group

		MBCT-Ca		TAU
	N	M(SD)	N	M(SD)
SCS-SF summary score	22	3.05 (0.78)	17	3.17 (0.83)
FFMQ-SF global summary score	22	75.36 (13.14)	16	79.19 (11.90)
Non react	22	14.50 (3.50)	16	14.88 (3.38)
Observe	22	14.91 (3.05)	17	14.59 (3.24)
Act aware	22	16.14 (4.20)	17	16.18 (4.59)
Describe	22	15.73 (4.66)	17	17.18 (4.22)
Non judge	22	14.09 (4.62)	17	15.88 (4.12)

Note. SCS-SF higher mean scores indicate higher self-compassion with a highest value of 5. Global summary score is scored out of 195 with higher scores indicating higher mindfulness. Subscale scores are scored out of 40 except for 'Non react' which is scored out of 35.

Utility change over time, mean difference, and percentage change

In terms of HRQoL utility over time there was some variability in the data. Table 28 shows the percentage change and mean difference between timepoints by trial group. There was a small increase in utility for the MBCT-Ca group between baseline and final follow up compared with a small reduction in utility for the TAU group over the same period. Statistical analysis indicates that there were no significant differences between groups on EQ-5D-3L utility at any timepoint. The TAU group had a mean difference reduction in utility at T1 and an increase in utility at T2, both were above the UK MID threshold. However, between T0 and T2, there was only a borderline MID reduction in utility in the TAU group. The sample size was very small and there were no statistically significant differences within groups over time.

Table 28: Group level mean difference and percentage change on EQ-5D-3L utility over time

	MBCT-Ca		**TAU**	
Timepoints	**Mean difference**	**% change**	**Mean difference**	**% change**
T0-T1	0.04	5	-0.14	-19
T1-T2	-0.02	-3	0.08	14
T0-T2	0.02	2	-0.06	-8

In terms of capabilities, both trial groups had a small disutility over time, equating to a 4% reduction in capabilities in the MBCT-Ca group and a 6% reduction in the control group (see Table 29). There were no

significant differences between groups on ICECAP-A utility at any timepoint. There were no significant differences within groups over time.

Table 29: Mean difference and percentage change on ICECAP-A utility over time

	MBCT-Ca		TAU	
Timepoints	**Mean difference**	**% change**	**Mean difference**	**% change**
T0-T1	-0.02	-3	-0.01	-1
T1-T2	-0.01	-1	-0.05	-6
T0-T2	-0.03	-4	-0.06	-7

QALYs and YFC

When reviewing the complete case sample which included all primary and secondary outcomes the TAU sample size was reduced to 5 participants. Therefore, AUC QALYs and YFC were calculated on an available case basis with the availability of data on EQ-5D-3L and ICECAP-A at T0 and either T1 or T2 (see Table 30 and Table 31). There were no significant differences between trial groups in terms of total QALYs over the 9-month study duration as assessed by an independent samples Mann-Whitney U test: *U(26)=47.00, p =.177*. There were no significant differences between trial groups in terms of total YFCs over the 9-month study duration independent samples Mann-Whitney U test: *U(26) =57.50, p=.429*.

Table 30: Available case AUC QALYs at T1, T2 and total QALYs.

	Pre-post QALYs (T0-T1) *0.37 of a year i.e., 4.4 months*				Follow up QALYs (T1-T2) *0.38 of a year i.e., 4.6 months*				Total QALYs *0.75 of a year i.e., 9 months*		
	N	**Mean**	**Median**	**Std. Dev.**	**N**	**Mean**	**Median**	**Std. Dev.**	**Mean**	**Median**	**Std. Dev.**
MBCT-Ca	16	0.26	0.28	0.10	15	0.27	0.29	0.11	18	0.52	0.57	0.21
TAU	9	0.22	0.26	0.09	6	0.21	0.25	0.11	8	0.41	0.49	0.23

Table 31: Available case AUC YFCs at T1, T2 and total YFCs.

	Pre-post YFCs (T0-T1) *0.37 of a year i.e., 4.4 months*				Follow up YFCs (T1-T2) *0.38 of a year i.e., 4.6 months*				Total YFCs *0.75 of a year i.e., 9 months*		
	N	**Mean**	**Median**	**Std. Dev.**	**N**	**Mean**	**Median**	**Std. Dev.**	**Mean**	**Median**	**Std. Dev.**
MBCT-Ca	18	0.30	0.32	0.07	17	0.31	0.34	0.07	18	0.61	0.66	0.13
TAU	9	0.30	0.32	0.05	6	0.21	0.28	0.05	8	0.58	0.54	0.10

Mean scores and abnormal depression and anxiety indicators

Table 25 shows the available case mean HADS scores by trial group over time.

Table 26 shows the percentage of participants by group scoring above and below threshold for anxiety, depression, and psychological distress on the HADS and WHO-5.

Figure 15 shows the difference between groups over time in terms of percentage of sample considered as 'case' on HADS depression subscale, HADS anxiety subscale, HADS total score and WHO-5 total score.

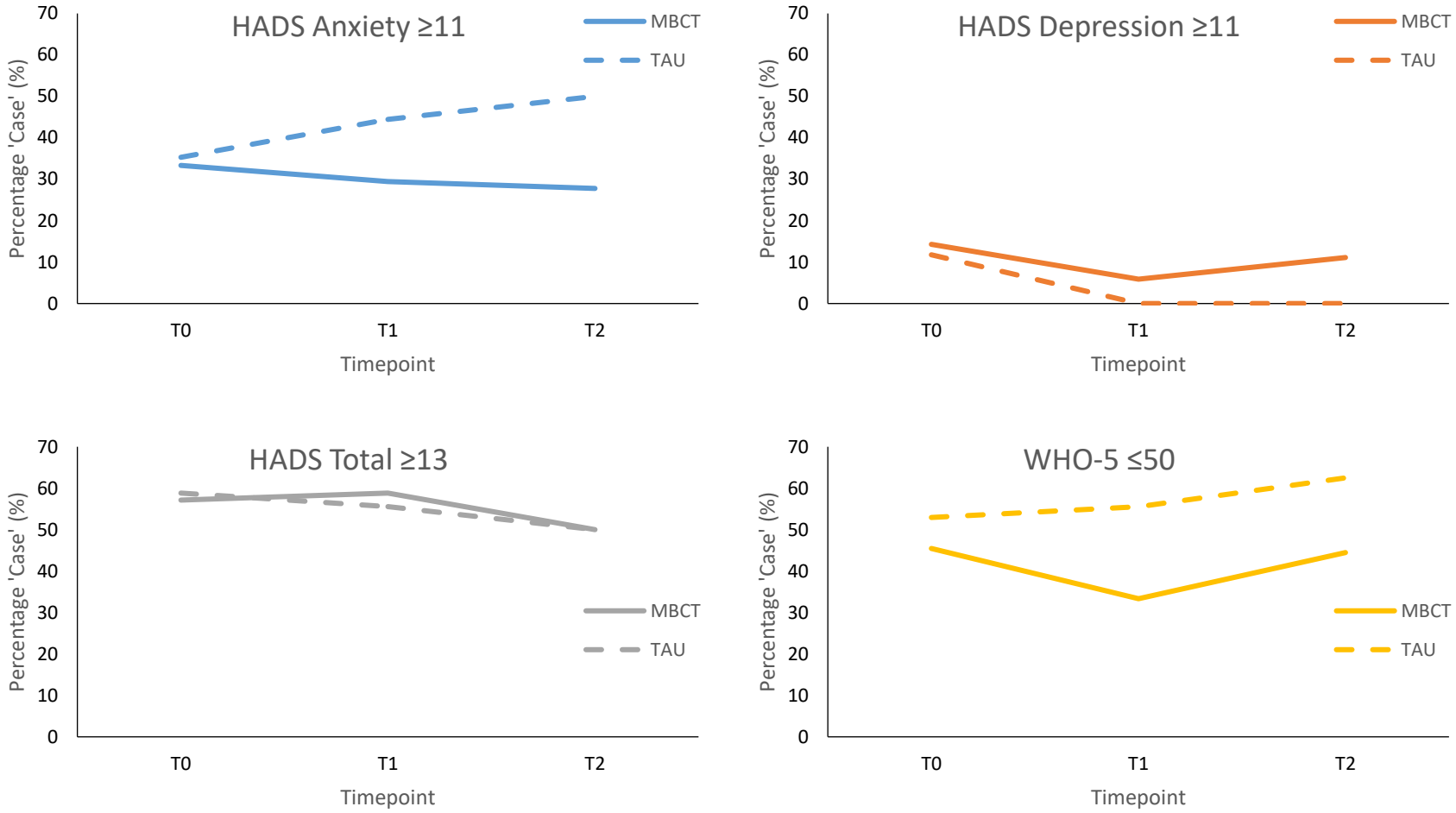


Figure 15: Percentage 'case' by outcome and by trial group over time

Figure 16 compares the percentage of trial groups experiencing psychological distress as classified by the two thresholds on the HADS total score (>13 as a cancer population threshold and >16 as a general population threshold). The trial groups were equivalent at baseline in terms of percentage of the group sample falling above the thresholds. The pattern of psychological distress over time was similar for both groups, however, when applying the higher general population threshold for distress there was a 15% difference between groups at T1 rising to 17% at T2.

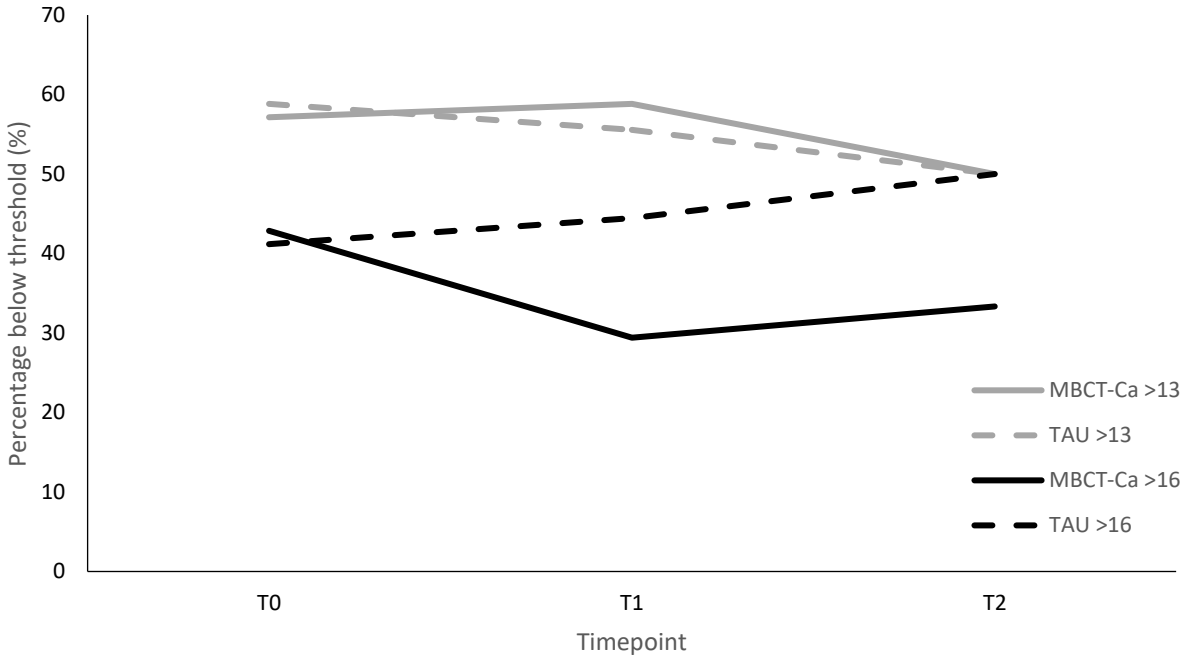


Figure 16: Percentage of group sample experiencing psychological distress by cancer and general population thresholds on HADS outcome

EQ-5D-3L anxiety and depression domain

Figure 17 displays the proportion of trial groups experiencing no problems compared with some problems on the depression and anxiety domain of the EQ-5D-3L over time. At baseline, 64% of the MBCT-Ca group and 65% of the TAU group reported some problems with anxiety and depression on the EQ-5D-3L. Both groups had an overall reduction in the proportion of participants reporting some problems with anxiety and depression on the EQ-5D-3L by T2, with 56% of the MBCT-Ca group and 63% of the TAU group. The percentage of the MBCT-Ca group reporting no problems rose slightly at each timepoint.

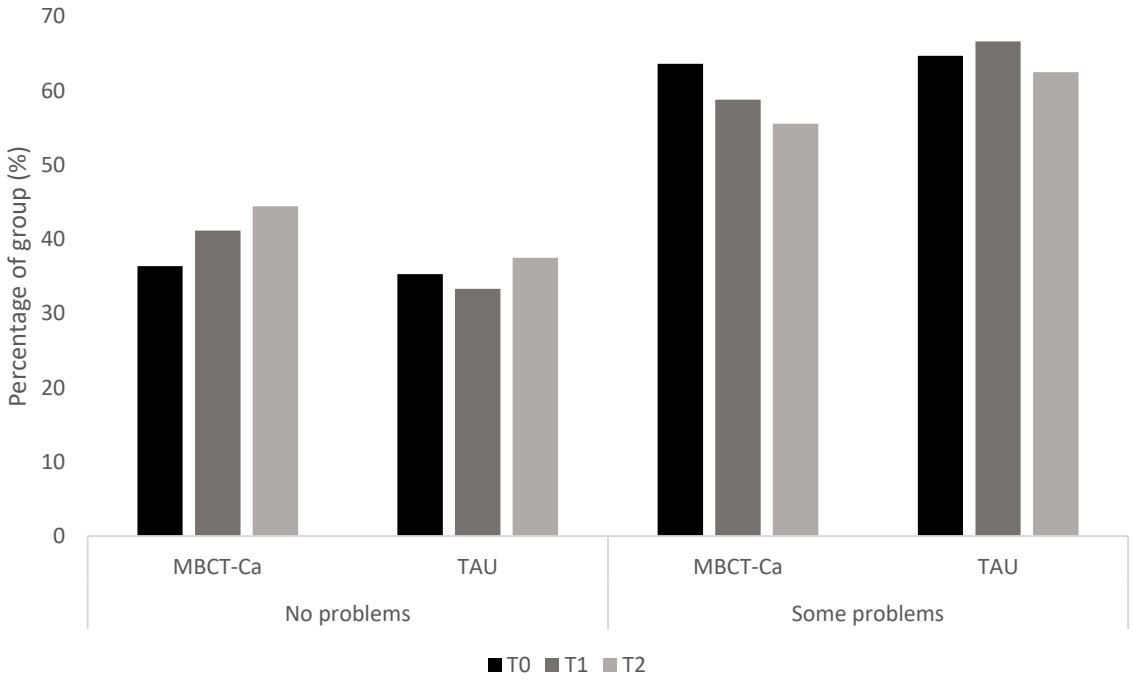


Figure 17: Percentage of trial group experiencing no problems or some problems on the EQ-5D-3L depression and anxiety domain

However, it is important to note that the sample size reduced over time with data considered on an available case basis. Most of the participants' anxiety and depression domain scores remained the same over time in both groups (See Table 32).

Table 32: Percentage of groups with no change on depression and anxiety EQ-5D-3L domain

	T0-T1	T1-T2	T0-T2
MBCT-Ca	82%	81%	83%
TAU	78%	50%	63%

Concurrent service evaluation results

In the concurrent service evaluation sample, 62.5% of participants had a primary diagnosis of breast cancer (see Table 33). In addition to cancer patients the service evaluation included one family member companion per patient. The average time since cancer diagnosis was 11 months more than the trial participants. The mean age of service evaluation participants was 3.5 years lower than the combined trial participant cohort and marginally falls into a lower age bracket of 45-54 for population norms.

The proportion of participants receiving antidepressants on enrolment to the study was no different between the trial cohort and service evaluation cohorts. However, a smaller percentage of the group reported taking pain medication at baseline in the service evaluation group compared with the control group.

Table 33: Baseline characteristics of MBCT-Ca service evaluation cohorts

	N	M(SD)
Primary site of disease diagnosis		
Breast cancer	15	
Other cancers	8	
Non-cancer patient	1	
Average time since most recent diagnosis		2 Year 3 Months (1983 days)
Previous cancer diagnosis	3	
Average time since previous cancer diagnosis		5 Years 11 month (1269 days)
Sex		
Female	22	
Male	2	
Age (Years)		54.26(8.19)
Medication use		
Antidepressants	25%	0.25(0.44)
Pain medication	13%	0.13(0.34)

Table 34 shows the mean number of health and social care service visits for the 3 months preceding MBCT-Ca attendance and the 2 months during attendance (excluding attendance relating to the MBCT-Ca course. GP attendance was the most common community-based resource used both before and during the study. When adjusting for difference in recall length, the mean costs at post intervention follow-up were £73.88 per month of recall, compared with £162.99 per month of recall at baseline. These slightly higher costs at baseline can be explained by small number of inpatient admissions and accident and emergency attendance associated with cancer treatment.

Table 34: Pre-post resource use of MBCT-Ca service evaluation cohorts

	Pre (3 months recall)	Post (2 months recall)
Community care		
General practitioner	1.71(1.63)	0.63(0.96)
Practice nurse	0.42(0.58)	0.125(0.34)
District nurse	0.04(0.20)	0(0)
Health visitor	0(0)	0(0)
Social worker	0(0)	0(0)
Mental health nurse or psychiatric nurse	0(0)	0(0)
Counsellor	0.67(0.96)	0.38(1.02)
Other		
Acupuncture	0.17(0.82)	0(0)
Chiropody / podiatrist	0.04(0.20)	0(0)
Physiotherapist	0.17(0.82)	0(0)
Mediation services	0(0)	0(0)
Mean community costs	£126.98	£43
Hospital based services		
Accident and emergency	0.13(0.61)	0.06(0.25)
Ambulance	0.13(0.61)	0(0)
Outpatient visits	2.13(3.62)	0.81(1.05)
Inpatient admission	0.13(0.61)	0(0)
Mean hospital costs	£362	£104.75
Total costs	£488.98	£147.75

Descriptive statistics for pre and post outcomes in the service evaluation cohort are presented in Table 35. The service evaluation sample had a higher baseline EQ-5D-3L mean utility score than both trial groups (Table 23). However, baseline scores were lower on the EQ-5D-VAS, ICECAP-A, EORTC-QLQ-C30 QoL in the service evaluation sample compared with both trial groups.

Table 35: Mean (SD) scores HRQoL and wellbeing pre and post MBCT-Ca service evaluation cohorts (available case)

		Pre (T0)		Post (T1)
Outcome and scale	N	M(SD)	N	M(SD)
EQ-5D-3L utility	23	0.74 (0.15)	16	0.83 (0.13)
EQ-5D-VAS	24	65.33 (15.69)	15	80.60 (9.95)
ICECAP-A utility	24	0.74 (0.17)	16	0.90 (0.06)
EORTC-QLQ-C30 (Global health status/QoL)	24	62.50(14.33)	16	76.04(12.12)
EORTC-QLQ-C30 (Summary Score)	24	72.48(12.31)	15	84.47(7.55)
Function scales				
Physical functioning	24	80.56(16.44)	16	90.42(7.69)
Role functioning	24	65.97(19.95)	16	85.42 (15.96)
Emotional functioning	24	51.04(22.70)	16	72.40(16.87)
Cognitive functioning	24	65.97(22.78)	16	84.38(12.87)
Social functioning	24	60.42(28.15)	16	83.33(21.08)
Symptom scales and items				
Fatigue	24	42.13(17.02)	15	28.89(12.46)
Nausea and vomiting	24	6.94(11.95)	15	3.33(6.90)
Pain	24	24.31(20.25)	15	17.78(18.33)
Dyspnoea	24	8.33(14.74)	15	4.44(11.73)
Insomnia	24	58.33(34.40)	15	35.56(32.04)
Appetite loss	24	16.67(24.08)	15	8.89(15.26)
Constipation	24	15.28(21.93)	15	13.33(21.08)
Diarrhoea	24	9.72(20.80)	15	4.44(11.73)
Financial difficulties	24	29.17(37.19)	16	14.58(17.08)
WHO-5 total score	24	38.33(21.55)	15	66.67(17.35)

At baseline the service evaluation sample data indicated high ceiling effects on all function scales excluding emotional functioning. Ceiling effects increased at post intervention as health improved and a higher proportion of the sample reported no problems on most function scales. There were high ceiling effects on most symptom scales and items both pre and post intervention (excluding fatigue symptoms which did not display any ceiling or floor effects). A baseline floor effect observed for insomnia symptoms was changed at post intervention into a ceiling effect. In addition, post intervention scores indicated 31% of the service evaluation sample reporting the highest possible score on the EQ-5D-3L. There were no baseline floor or ceiling effects on the HADS questionnaire. However, a ceiling effect on the HADS depression scale was observed at post intervention with 25% of participants experiencing no problems with depression.

Table 36: Floor and ceiling effects of HRQoL outcomes in service evaluation cohort at pre and post intervention

	Pre (T0)			Post (T1)		
	N	Floor %	Ceiling %	N	Floor %	Ceiling %
EQ-5D-3L utility	23	<15	<15	16	<15	31
EQ-5D-VAS	24	<15	<15	15	<15	<15
ICECAP-A utility	24	<15	<15	16	<15	<15
EORTC-QLQ-C30 (Global health status/QoL)	24	<15	<15	16	<15	<15
Function scales						
Physical functioning	24	<15	25	16	<15	25
Role functioning	24	<15	21	16	<15	50
Emotional functioning	24	<15	<15	16	<15	<15
Cognitive functioning	24	<15	21	16	<15	31
Social functioning	24	<15	25	16	<15	50
Symptoms						
Fatigue	24	<15	<15	15	<15	<15
Nausea and vomiting	24	<15	67	15	<15	80
Pain	24	<15	33	15	<15	40
Dyspnoea	24	<15	75	15	<15	87
Insomnia	24	29	<15	15	<15	27
Appetite loss	24	<15	58	15	<15	73
Constipation	24	<15	63	15	<15	67
Diarrhoea	24	<15	79	15	<15	87
Financial difficulties	24	<15	54	16	<15	56
WHO-5	24	<15	<15	15	<15	<15
HADS (subscale anxiety)	24	<15	<15	16	<15	<15
HADS (subscale depression)	24	<15	<15	16	<15	25
HADS Total	24	<15	<15	16	<15	<15
SCS-SF	23	<15	<15	16	<15	<15
FFMQ-SF	21	<15	<15	16	<15	<15

The service evaluation cohort had a higher mean score on depression subscale, anxiety subscale and total scores at baseline (see Table 37) compared with trial groups (see Table 25). At post intervention service evaluation participants HADS mean scores were lower than both MBCT-Ca and TAU groups at both T1 and T2.

Table 37: Mean (SD) HADS scores pre and post MBCT-Ca service evaluation cohorts (available case)

		Pre		Post
	N	M(SD)	N	M(SD)
HADS (subscale anxiety)	24	10.88(4.18)	16	6.63(4.40)
HADS (subscale depression)	24	6.46 (3.93)	16	2.81(2.37)
HADS Total	24	17.33(7.46)	16	9.44(5.85)

The proportion of service evaluation participants scores within the classifications of normal functioning, borderline, or abnormal levels of anxiety or depression are reported in Table 38. At baseline the majority (63%) of service evaluation participants reported low scores on the depression subscales (and were within the 'normal' classification) compared with three quarters of participants reporting borderline abnormal or abnormal levels of anxiety (on the HADS anxiety subscales). When considering combined scores on the HADS the scales indicated that 98% of service evaluation participants had levels above the threshold for cancer populations at baseline. Half of the service evaluation sample scored above the general population threshold for psychological distress on the HADS at baseline. On the WHO-5 wellbeing index scores below the threshold were observed in three quarters of the service evaluation sample at baseline.

This pattern of prominent anxiety prevalence compared with lower depression is comparable with the pattern of psychological distress reported in the trial groups. Across the whole trial sample (MBCT-Ca and TAU groups combined) HADS scores of 13 or higher as a cancer population clinical cut-off were observed in 58% of all trial participants at baseline, compared with 98% of the service evaluation cohort. When considering the higher general population threshold for abnormal anxiety and depression 42% of trial participants had scores of 16 or higher. This was largely equivalent to the rates observed in the service evaluation cohort, with 50% scoring above the general population threshold of 60 or above. The WHO-5 cut-off ≤50 indicated that 49% of all the trial participants could likely benefit from additional investigation and potentially support with their mental health. In addition, 75% of the service evaluation cohort had baseline scores below the WHO-5 threshold.

Table 38: Percentage of scores by anxiety and depression threshold pre and post MBCT-Ca service evaluation cohorts

		Pre		Post
	N	%	N	%
HADS (subscale anxiety)	24		16	
Normal (0-7)		25%		63%
Borderline abnormal (8-10)		25%		19%
Abnormal (11+)		50%		19%
HADS (subscale depression)	24		16	
Normal (0-7)		63%		100%
Borderline abnormal (8-10)		17%		0%
Abnormal (11+)		21%		0%
HADS Total	24		16	
Above cancer population threshold (≥13)		98%		38%
Above general population threshold (≥16)		50%		13%
WHO-5	24		15	
Below threshold (≤50)		75%		20%

Other secondary outcomes: Self-compassion and Mindfulness facets

Table 39 shows the mean (SD) scores for the SCS-SF and FFMQ-SF pre and post MBCT-Ca in the service evaluation study. On an available case group basis, there was an overall increase in self-compassion post-intervention mean scores and an improvement in all facets of mindfulness as reported by the FFMQ-SF.

Table 39: Mean (SD) scores SCS-SF and FFMQ-SF pre and post MBCT-Ca service evaluation cohorts

		Pre		Post
	N	M(SD)	N	M(SD)
SCS-SF summary score	23	2.67(0.64)	16	3.46(0.76)
FFMQ-SF global summary score*	21	70.86(9.84)	16	83.44(8.33)
Non react	22	13.64(2.63)	16	16.69(2.30)
Observe	23	13.22(3.07)	16	15.75(2.05)
Act aware	22	13.27(2.51)	16	17.06(2.32)
Describe	22	15.55(3.25)	16	18.25(3.42)
Non judge	22	14.36(3.47)	16	15.69(2.33)

*Global summary score is scored out of 195 with higher scores indicating higher mindfulness. Subscale scores are scored out of 40 except for 'Non react' which is scored out of 35.

Health related quality of life

Table 40 presents the pre and post health related quality of life mean scores when restricting the analysis to a complete case sample. There was an improvement on all general wellbeing, cancer specific measures, and psychological distress outcomes. The greatest percentage change observed was recorded on the WHO-5, with a 60% improvement in wellbeing scores at post intervention follow-up.

Table 40: Service evaluation pre and post descriptive statistics (complete case listwise N=13)

	Pre (T0)	Post (T1)	Mean difference	% change
Outcome and scale	M(SD)	M(SD)		
EQ-5D-3L utility	0.77(0.14)	0.83(0.13)	0.06	7%
EQ-5D-VAS	67.00(19.27)	81.62(10.05)	14.62	22%
ICECAP-A utility	0.77(0.21)	0.91 (0.06)	0.15	19%
EORTC-QLQ-C30 (Global health status/QoL)	64.10(16.80)	76.92(12.80)	12.82	20%
EORTC-QLQ-C30 (Summary Score)	76.44(11.41)	85.35(7.63)	8.91	12%
WHO-5 total score	41.85(25.44)	66.77(18.29)	24.92	60%
HADS total	16.00(7.76)	8.08(5.59)	-7.92	-50%
HADS anxiety	9.77(3.92)	5.31(3.47)	-4.46	-46%
HADS depression	6.23(4.09)	2.77(2.56)	-3.46	-56%

Table 41 shows the analysis of variance between pre and post outcomes recorded, controlling for multiple comparisons, and bootstrapped 95% confidence intervals around mean difference estimates. There was a significant difference observed across all measures.

Table 41: Service evaluation pre and post analysis of variance (complete case listwise N=13)

Measure	Mean Difference (Post-Pre)	Std. Error	Sig.[b]	95% Confidence Interval for Difference[b]	
				Lower Bound	Upper Bound
EQ-5D-3L utility	.057*	0.018	0.010	0.017	0.097
EQ-5D VAS	14.615*	4.113	0.004	5.654	23.577
ICECAP-A utility	.148*	0.054	0.018	0.030	0.266
EORTC-QLQ-C30 (Summary Score)	8.912*	2.459	0.003	3.554	14.269
EORTC-QLQ-C30 (Global health status/QoL)	12.821*	2.926	0.001	6.446	19.195
WHO-5 total score	24.923*	6.295	0.002	11.208	38.638
HADS total	-7.923*	2.132	0.003	-12.568	-3.278
HADS anxiety	-4.462*	1.072	0.001	-6.797	-2.126
HADS depression	-3.462*	1.107	0.009	-5.874	-1.049

**The mean difference is significant at the .05 level.*

[b]Adjustment for multiple comparisons: Bonferroni.

Post hoc related samples tests for difference (non-parametric)

Normality tests indicated that EQ-5D-3L and ICECAP-A data within the service evaluation cohort were not normally distributed. A post-hoc non-parametric test for differences was conducted to identify if the core analysis findings were sustained. The pre and post related-Samples Wilcoxon Signed Rank Test result for EQ-5D-3L *W(16)=45, p=.008*, indicated that the post-intervention utility was significantly different compared with baseline levels. The pre and post related-Samples Wilcoxon Signed Rank Test conducted on the ICECAP-A indicated that the findings were also upheld for capabilities, with a significant difference observed at follow-up compared with baseline levels: *W(16)=108, p=.006.*

Table 42 considers data completeness by outcome, the percentage change is reduced slightly compared with a complete case analysis, highlighting the potential impacts of dealing with missing data on research findings, particularly when sample size is small.

Table 42: Service evaluation pre and post analysis (complete by outcome)

		Pre (T0)	Post (T1)	Mean difference	% change
Outcome and scale	N	M(SD)	M(SD)		
EQ-5D-3L utility	16	0.78(0.13)	0.83 (0.13)	0.05	6
EQ-5D-VAS	15	67.73(17.97)	80.60 (9.95)	12.87	19
ICECAP-A utility	16	0.76(0.20)	0.90 (0.06)	0.14	18
EORTC-QLQ-C30 (Global health status/QoL)	16	65.10(15.88)	76.04(12.12)	10.94	17
EORTC-QLQ-C30 (Summary Score)	15	75.61(10.79)	84.47(7.55)	8.86	12
WHO-5 total score	15	42.13(23.99)	66.67(17.35)	24.54	58
HADS total	16	16.06(7.44)	9.44(5.85)	-6.63	-41
HADS anxiety	16	10.25(4.27)	6.63(4.40)	-3.63	-35
HADS depression	16	5.81(3.83)	2.81(2.37)	-4.00	-52

Mean QALYs and YFC

Mean QALY were calculated for the 8.84 week service evaluation period using AUC methods. Table 43 shows descriptive statistics for service evaluation QALYs. There was a mean QALY gain of 0.14 (95% CI 0.13 – 0.15).

Table 43: Service evaluation AUC QALYs

					Bootstrap sample (10,000 replications) 95% confidence intervals	
	Mean	**Median**	**Std. Deviation**	**Interquartile Range**	**Lower**	**Upper**
SE. MBCT-Ca (*N=16*)	0.14	0.13	0.02	0.04	0.13	0.15
**0.17 of a year i.e., 8.84 weeks*						

Mean YFC (using AUC) were calculated for the corresponding service evaluation period of 8.84 weeks. Results for YFC were the same as for QALYs, except for a slightly higher median score for YFC compared with QALYs.

Table 44: Service evaluation AUC YFCs

	Mean	Median	Std. Deviation	Interquartile Range	Bootstrap sample (10,000 replications) 95% confidence intervals	
					Lower	Upper
SE. MBCT-Ca (*N=16*)	0.14	0.15	0.02	0.03	0.13	0.15
**0.17 of a year i.e., 8.84 weeks*						

Comparison of psychological wellbeing outcomes over time

Figure 18 shows the percentage of service evaluation participants experiencing psychological distress on the HADS and WHO-5 outcomes directly before and after attending MBCT-Ca course. There is a downward trend across all outcomes with a reduction in proportion of participants scoring over the threshold for psychological distress on all outcomes.

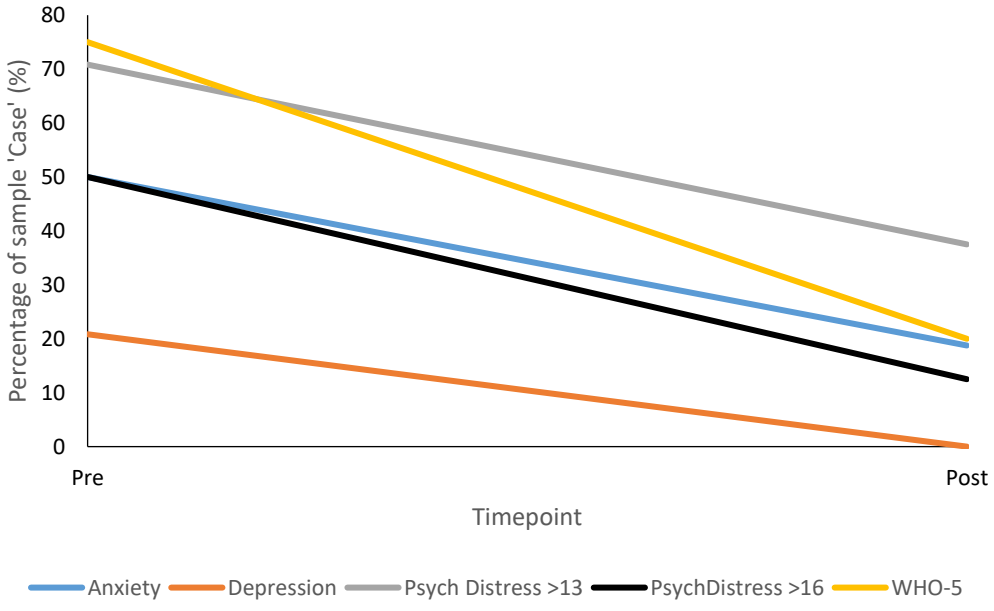


Figure 18: Percentage of service evaluation sample meeting 'case' status by outcome over time

Qualitative results and feedback forms

Results are presented as researcher reflections through the running of the trial, with additional analysis of content from both the qualitative interviews (*N=7* opted in and *N=6* interviews completed) and T3 feedback forms (*N=19*). Content analysis focused on the two major categories, firstly, research processes and secondly, patient experience of the intervention. Results are discussed in relation to the study objectives (see chapter introduction), chapter research questions (as outlined in Chapter 1) with opportunities for further research identified and discussed further in the discussion section.

Participant characteristics and trial group equivariance

Most participants who opted to participate in a telephone interview as a follow-up to the written feedback form had been allocated to the MBCT-Ca group on enrolment. Only one participant allocated to TAU opted in for a qualitative interview. Response rates at T3 were balanced between groups, however, due to a delay in sending out some of the T3 assessments, some participants allocated to TAU had since also attended an MBCT-Ca course once their waiting time had lapsed. The qualitative study participants may not be representative of all the trial study participants and some findings represent individual participant experiences. To appropriately represent data and the level of evidence underpinning the results, where there were multiple responses with similar findings these are reported as 'several' (3 or more) or 'some' (more than one) participants.

Category 1: Research processes

Research processes evidence is reported below from trial records including SAG and DMEC meeting minutes, recruitment forms, qualitative interview transcripts and participant feedback forms. Research processes outlined in the study objectives which shaped the semi-structured interview topic guide included recruitment, randomisation, intervention delivery and data collection.

1.1 Recruitment and participation

Recruitment challenges relating to forming a sufficient size intervention group are heightened when considering randomisation to a control group, and contextual factors such as more rural locations where potential participants are more spread out. With recruitment happening across a wide and diverse area, particularly in rural areas this meant long travelling time for research home visits. This in turn reduced the ability to spend time actively recruiting, relying on clinicians to drive forward recruitment. One researcher reflection recorded as part of research process notes collected throughout the trial process was that there was wide variability in clinicians' willingness to refer patients, with some clinicians making no referrals, and some making many.

There were some indicators from the trial records that clinicians likely took several factors into account when making the judgement to initiate a patient invitation. Factors included whether the course would be acceptable, appropriate, and accessible to patients; patient health status; potential future treatment requirements; and whether they felt that the patient would benefit from more immediate psychological support. For example, some patients were referred through the service evaluation route to receive MBCT-Ca rather than the randomised trial for patients who 'could not wait'. This would be worth exploring further if pursuing a pragmatic mixed service design in future research and wanting to understand clinician views further.

During this pragmatic trial the recruitment and intervention allocation methods were adapted to ensure the planned MBCT-Ca groups were viable to run with a sufficient minimum number of participants. In addition the delays to the intervention commencing in some cases resulted in a corresponding increase in the length of participation in the study. These changes to the randomisation strategy reduced the total number of participants allocated to TAU. This control cohort sample size reduction was further confounded by higher rates of attrition observed in TAU condition compared with MBCT-Ca group.

1.2 Randomisation

1.2.1 Randomisation acceptability: Participants were generally understanding of the randomisation process and accepted it was an important component of research designs. TAU was described as challenging due to insufficient psycho-social support and there was disappointment when allocated to control condition (see Extract 1). Several participants indicated a preference for being allocated to receive the MBCT-Ca course sooner rather than waiting in the TAU group (see Extract 2 and Extract 3).
Extract 1: "I was not particularly happy about being with the control group" (Participant A).
Extract 2: "I know that's the way RCT's work. It isn't easy waiting as there is limited psychological support available" (Participant B).
Extract 3: "That's the way it had to be done but I was crossing fingers hoping to go first!" (Participant C).

1.2.2. Researcher blinding to treatment allocation: Resource use recall which overlapped attendance on an MBCT-Ca courses or where monthly follow-up sessions are attended may result in unblinding of researchers to treatment allocation. Finally, the questionnaire booklets were commonly returned with notes to the research department highlighting factors such as change of address and at times providing details that resulted in un-blinding the researcher. These were screened by research admin to avoid early unblinding, however, at the point of data entry this information resulted in unblinding of the chief investigator who created the database. Due to researcher maternity leave data entry was conducted after the close of the study.

1.3. Pragmatic research design and intervention delivery

MBCT-Ca therapists were delivering the intervention as part of their usual practice and without any funding from the study. One course was cancelled due to unavailability of the therapist and resulted in a delay to intervention delivery while a substitute therapist was identified. The pragmatic nature of intervention delivery meant substantial variability in timing of follow-up with the average participation in the study being 9 months.

1.4 Questionnaires and data collection

In interviews and feedback forms several participants reported being pleased to help with research and were generally happy to complete questionnaires. Some participants highlighted that there was some overlap in the questionnaires. Some participants noted that the multiple choice and Likert nature of the questionnaire responses were difficult to precisely reflect their health, for example, wanting to be able to rate their health between two responses. This finding links to the development of the EQ-5D-5L which has come into common usage since this study was conducted, this may allow greater differentiation between response options and more accurately capture participants responses. One participant noted that they would likely respond differently on different days, highlighting the 'today' nature of some questionnaires such as the EQ-5D-3L.

One participant highlighted that questionnaires were easier to complete with some support from the researcher. At baseline the researcher (chief investigator / candidate) administered the questionnaires as a researcher led interview rather than an independent self-report participant completion of the questions. At follow-up some participants opted to complete the questionnaire booklets over the phone with research admin support staff. However, through the wider process evaluation trial records it was also highlighted that this raised challenges for both the interviewer (research admin support) and the participant, for example, with some of the more sensitive questions with symptoms relating to vomiting and diarrhoea on the EORTC-QLQ-C30.

Trial records and study data indicated that some follow-up questionnaires were not returned which contributed to missing data and attrition. Returning questionnaires in the post meant some delays to receiving them, and some questionnaires were considered lost in the mail based on correspondence with participants who noted they had already returned their booklet. In addition, there were a few incidences of questionnaire booklets mailed out without first logging the participant ID numbers. These booklets when returned were unable to be attributed to participants and replacement booklets were sent to participants. It is unknown whether this contributed to missing data and loss to follow-up. However, qualitative data indicated that this could contribute to participant burden (see Extract 4).

Extract 4: "I did fill one out that you didn't receive so the sub[stitute] one was very difficult" Participant C).

The delay in receiving follow-up questionnaires also resulted in some variation in the date of assessment recorded which impacts on the average study participation time.

The resource use questionnaire was broad enough to capture a wide range of community and hospital-based service use. However, the layout of questions contributed to some data collection errors and missing data. There were some indicators that participants found some questions unclear (see Extract 5), however, it was not possible to attribute participant experience to specific questions and this could equally apply to health and wellbeing questionnaires.

Extract 5: "Some questions were worded in a confusing way. However very happy to provide information" (Participants D).

For example, in some cases secondary care data was recorded under the 'Other section' of community services, however, data was left blank within the secondary care section. Partially complete entries, for example where services were listed but no number of visits were provided, were estimated to be one per service, however, it is acknowledged that this may underestimate the resources used by participants. While participants were instructed to mark 'No' when services were not used there were many incidences where data fields were left blank or 'none' was handwritten on the page. In these cases, service use (for the specific section) was estimated to be zero. Medication data was only recorded at baseline and contained insufficient information to establish whether there had been any recent dose changes to medications being received to manage mental health such as antidepressants.

1.5 Overall experience of participating in the research

Of the participants who provided feedback on participating in the trial, almost all indicated that they would be likely to recommend taking part in this research and that it was on the whole a positive experience.

Category 2: Intervention experiences

Intervention experiences evidence is reported from participant qualitative interviews and feedback forms. This category includes information about MBCT-Ca provided to participants, timing of the intervention, and barriers and facilitators to attending. In addition, group features relating to the participants, the location of course and the therapist delivering the course are presented. The perceived value of MBCT-Ca, unmet needs and wider access to psychological services are also discussed.

2.1 Information about MBCT-Ca and timing of course

In the interviews, feedback forms and trial records several participants highlighted that they wanted to know the dates of courses to help ensure that they could attend if allocated to the intervention. There were many indicators that participants were committed to attending the courses, but that they had other commitments that limited their availability to attend all sessions. Lifestyle factors including family, work and medical reasons were some of the barriers to attending.

Some participants highlighted that they felt there might be a window of time where help may be most helpful. One participant noted that one year post treatment was a good time as follow-up hospital care reduces, whilst concerns about cancer recurrence may be heightened. Another participant had a different opinion and felt that it may have been more beneficial for people who recently finished their treatment. There were indicators from the trial records and the patient interviews that MBCT-Ca groups may not be suitable in cases where patients were experiencing acute distress.

Some participants highlighted the need to travel to groups as a barrier to attending, particularly with the research being conducted in a rural area. There was some evidence of funding available within service provision to provide transport or reimbursement of travel costs. In relation to follow-up groups, the location was highlighted as a factor which would influence on-going attendance, with a closer location more acceptable to some participants.

2.2. Group features: barriers and facilitators to attending

A wide range of group factors were highlighted through the participant feedback and interviews. These included factors relating to the course participants, course therapist, course environment, length of the course and associated follow-up and the psycho-education focus.

Course participant factors

Each MBCT-Ca course contained participants from this thesis research and patients from routine access pathways through the community. The cancer diagnosis, stages of cancer and time since treatment had the potential to be broad amongst participants attending MBCT-Ca. However, the differences between trial and service evaluation participants were not apparent in the demographic data collected, with insufficient information collected on the stage and severity of cancer. Commonality within the group was highlighted by some participants as an important group factor. Meeting other people in similar circumstances and talking with likeminded people and in some cases making new friends were highlighted as positive benefits of group-based intervention (see Extract 6).

Extract 6: "Meeting others in the same situation helped me enormously" (Participant E).

In contrast, the clinical and demographic make up of cancer patient characteristics in the groups caused challenges where some group members were perceived as very unwell (see Extract 7).

Extract 7: "I understand the benefits of the mindfulness course, but have to say that I found some sessions distressing, especially I think because of the mix of the group, which included terminally ill people" (Participant F).

Course environment factors

The course environment was important. In addition to the location reported earlier in relation to travel to courses, the building and space that courses were held within was important to some participants. Some participants highlighted that attending the course, which was held in a hospice room and near to where people were receiving end of life care was challenging for patients in a recovery or recovered phase of cancer (see Extract 8). The location of the course links to results above around the demographic make up of the participants in a group, and the potential impacts on participant distress.

Extract 8: "I found it difficult that the course was set in a hospice – a place where people go when they are dying" (Participant B).

Course therapist factors

Therapist factors were highlighted as being important by some participants (see Extract 9). Given the sensitive nature of the course content and the characteristics of the participants, ensuring a therapist is suitable trained and sensitive to the group needs are likely to be important for successful delivery of MBCT-Ca.

Extract 9: "Excellent course, wonderful calming teachers. I was apprehensive to start but the experience changed my whole approach to dealing with cancer. Not only self-awareness but making new friends" (Participants G).

Duration of course and on-going support factors

The length of course and access to on-going sessions was highlighted by some participants (see Extract 10). Participants felt that on-going support was important but that follow-up drop-in sessions were not well attended. Follow-up sessions were not available routinely for all participants and no information about follow-up MBCT-Ca classes was collected as part of this study. Where follow-up sessions were held, there was variability in participant knowledge about sessions, with some participants indicating that they did not known about them but would like to know more.

Extract 10: "Great course – good for everyone not just cancer patients. Should be more follow-up. The course is too short for me – the abstract concepts take time to grasp and then follow through; let alone using the methods instinctively. I will request to attend again" (Participant H).

Psycho-education focus factors

Some participants highlighted that their reasons for wanting to attend the MBCT-Ca and the benefits they observed focused on anxiety rather than low mood or depression (see Extract 11). The MBCT-Ca course is tailored to focus on both depression and other psychological distress which may be prevalent following cancer treatment.

Extract 11: "I found it very helpful with controlling my stress and anxiety" (Participant E).

2.3. Perceived value of attending MBCT-Ca

There was some variation in whether participants perceived value of attending MBCT-Ca prior to attending. Some participants highlighted that they had anticipated some benefits from attending the MBCT-Ca course, while other participants indicated they did not expect it to help them. There were indicators that the perception of value may change and willingness to pay may increase after experiencing the course (see Extract 12).

Extract 12: "I would not have gone on the course if I had to pay as I didn't really think it would help me but now I would gladly pay" (Participant C).

There were some feelings of hope and anticipation of positive benefits reported by participants who had not yet attended MBCT-Ca (see Extract 13).

Extract 13: "I am hoping the course may help me" (Participant A).

These findings are also linked to evidence reported earlier relating to a preference to attend the intervention first, and clinicians' views on prioritising patients for earlier treatment, both of which were underpinned by an expectation that the course might help people.

Several participants reported positive outcomes from attending the MBCT-Ca (see Extract 14 and Extract 15). Benefit included improvements in mental health, quality of life and impacts on daily life in terms of useful skills (see Extract 16).

Extract 14: "The course leader was empathic and effective. The course has given me the tools to improve my mental health. It has given me some control over a difficult illness, and it addresses a neglected area" (Participant I).
Extract 15: "It made me take a step back from my life everyday (which is busy) and made me think and take notice of my feelings/emotions" (Participant J).
Extract 16: "I use some of the mindfulness skills taught every day and they help me cope" (Participant D).

In contrast to benefits reported by participants there were some indicators of participant distress, including issues highlighted above around mixed groups and the space that groups were held in for example when held in the hospice setting. In addition, there were indicators that participants had to experience turning towards difficulties to also experience some benefits (see Extract 17).
Extract 17: "I enjoyed the course but feel a bit self-conscious at times as I'm not used to showing my feelings but it was very helpful" (Participant K).

While it was not established what the overall levels of attendance were, there were indicators in the qualitative data that some participants attended a majority of sessions (see Extract 18) and others had missed sessions.
Extract 18: "I attended every session and the full day meditation, I have learnt to look after myself through making time to promote my own health, I can now also say no and not feel guilty!" (Participant D).

One researcher observation from trial records and participant interviews was that in one case where multiple MBCT-Ca sessions were missed that this might have introduce barriers to attending further sessions, and that this could lead to participant distress from not being able to complete the course.

In terms of general benefits from the MBCT-Ca course reported on the feedback forms, on a Likert scale from zero to ten (representing Not at all to Very much) the mean participant score was 8/10. Almost all participants who responded indicated that they would likely recommend the MBCT-Ca course to others. The majority of participants who had attended the MBCT-Ca course reported continuing to practice mindfulness between either once a week or several times a week after the course had finished.

2.4 Other issues relating to accessing psychosocial support in general

Some participants highlighted that there continue to be unmet needs for psycho-social support for cancer patients. In addition, from research data highlighting patterns in resource use, there was variation amongst patients in terms of whether they accessed support for health problems including depression. For those that did report accessing support, there was variation in where they went for it. For example, there was evidence that some participants went to their GP practice and were prescribed

antidepressants or pain medication while other participants sought support through routine secondary care services, for example, by mentioning depression to their oncology nurse. There was also a limited amount of evidence that participants gained support through social activities provided by charities.

Participant willingness to pay for MBCT-Ca

WTP information was elicited through a direct approach (Ryen & Svensson, 2015), and conducted as part of the end of study feedback form which asked participants whether they would have been willing to pay for the course and if so how much. Only twelve participants provided WTP information. The maximum WTP was between £0 and £249.99 per course. The mean WTP for an MBCT-Ca course was £95, while the median WTP was £49. This equated to between £5 and £11 per MBCT-Ca session (with the average course spanning 9 session). Excluding participants who reported being unwilling to pay, the mean WTP rose to £117 per MBCT-Ca course. Gross household income was collected in bands. The mean income of participants who responded in WTP assessment was between £18,000 - £30,000, while the median household income was £15,000 - £19,999.

The maximum WTP for an MBCT-Ca course elicited in this pilot study was lower than the mean cost of counselling services as an alternative private health care service[7]. There were limited indicators that income and perceived benefits from the course may be an influencing factor in participant WTP. However, further research with a larger sample size would be needed to explore predictors of WTP. The suitability of patient WTP as an alternative threshold for QALY gains and/or other benefits and comparison against the NICE threshold of £20,000 - £30,000 per QALY was not explored within this thesis research, however, may provide a useful alternative when considering a wider societal perspective for economic evaluations.

[7] The NHS reports the cost of private counselling in the UK as between £10 and £70 a session depending on where people live (see https://www.nhs.uk/mental-health/talking-therapies-medicine-treatments/talking-therapies-and-counselling/counselling/)

Discussion

Summary of principal findings

MBCT-Ca was developed to support participants to skilfully manage their heightened vulnerability to depression and other psychological challenges (such as anxiety) caused by the diagnosis and treatment for cancer. The period after cancer diagnosis and treatment is an opportunity for targeted interventions that prevent depression occurrence. This study assessed the methods and processes for patient recruitment including identification, referral, and enrolment into a randomised controlled trial. On enrolment 71% of all participants in the randomised feasibility trial had low scores on the depression subscales (within the 'normal' classification) at baseline, further highlighting that there is a large opportunity for primary prevention. In contrast, 61% of participants reported borderline or abnormal levels of anxiety at baseline.

The pilot health economics evaluation of this randomised feasibility study of MBCT-Ca (*N=39*) and concurrent service evaluation (*N=24*) indicated that MBCT-Ca and the research processes were overall acceptable to most patients who attended. Just under half the patients invited to participate opted to receive further information, and of those nearly three quarters enrolled into the trial. Barriers to recruitment included contextual factors such as the rural recruitment area and clinician views about referral. These are important factors which warrant further consideration. A total of ten MBCT-Ca course were held during the length of this thesis research, with recruitment across three hospital-based centres. Barriers to participant attendance highlighted by patients included the course location, travel to groups, timing, and availability of groups. In terms of determining the willingness for participants to remain in the study, total attrition from the research was 53% in the TAU group and 14% in the MBCT-Ca group.

It is important to capture a wide range of health and social care services as participants reported accessing mental health support from a range of sources, including their oncologist or oncology nurse in secondary care, their GP in primary care, and also some limited evidence of accessing charity services. There were indicators from the qualitative findings that there remains an unmet need for psycho-educational support, with participants highlighting a lack of specialist mental health support available to them.

It was feasible and acceptable to participants to collect a wide range of outcome measures and the study obtained descriptive data on relevant outcome measure to assess the potential impact of MBCT-Ca. The trial groups were equivalent at baseline in terms of percentage of the group sample falling above the thresholds for psychological distress. The pattern of psychological distress over time was

similar for both groups however, when applying the higher general population threshold for distress there was a 15% difference between groups at T1 rising to 17% at T2.

Of the randomised feasibility analyses conducted to explore potentially meaningful differences between group, there were no statistically significant differences between groups. In addition, there was no difference identified within groups over time between baseline and follow up assessments (at 9 months). The small sample size limited the validity of these analyses and appropriate caution is needed in interpreting the results, recognising the pilot and feasibility nature of this work.

For the service evaluation cohort, there were small significant changes in EQ-5D-3L scores over time observed however this was below the MID threshold. Without a valid control group for comparison, it is not possible to assess the level of changes to be expected naturally over time due to treatment as usual.

While clear progression criteria were not established prior to commencing the study to assess on what basis to recommend proceeding to a full trial, a pragmatic interpretation of the study findings was instead conducted, and results highlighted the need for further pilot work to establish effect size of benefits, capture more accurate resource use and to explore an active control condition to compare against. There are opportunities to learn from this feasibility study to improve the design and protocol for further research.

Lessons learnt from this study

Lessons learnt in relation to study research processes and methods

The embedded evaluation of research study methods yielded additional findings about the feasibility and acceptability of the research design, raising important points to be considered for future studies to increase recruitment, intervention adherence, and participant retention at follow-up.

There is a need for adequate funding of trial based research. Limited resources to conduct this study, with the source of funding limited to a studentship scholarship, impacted on the sample size through limiting rates of recruitment with one researcher and no research nurse provision through research infrastructure. This also raised challenges to conducting research to adhere to the protocol, for example, to remain blind to treatment allocation, collecting data on participants attendance and ensuring the availability of MBCT-Ca groups to attend at various timepoints in the study. Additional research funding would facilitate the inclusion of adequate staffing including a trial manager, researchers, clinical research nurses, administrative research support and the intervention therapists. Having several researchers would likely have helped with issues of blinding and the linked collection of data relating to participant attendance.

There is a need for further pilot testing and adaption of the service use measure, given some issues with the way the measures were completed. From the data collected in the SUQ it was not possible to cost all resources used by study participants and to compare across group condition, or to fully consider the cost of resource use over time. In terms of community care, there was insufficient information to ascertain whether all resources consumed were provided by the NHS, private or voluntary services, for example, alternative therapists such as chiropractors and homeopathy are more likely to be delivered outside of NHS services, and services such as reflexology may be provided in hospital or cancer centres or may be available through voluntary organisations. From the available resource use data, the costs of usual treatment were similar between the TAU group and the MBCT-Ca group, and the data was used to build up a picture of the typical resources used as part of usual care following cancer treatment. It is important to consider the timing of resource use data collection and whether the period of resource use recall overlaps with cancer treatment, as this will likely be different to participants who have a longer period since completed treatment. For example, at baseline participants reported a common reason for practice nurse appointments was for chemotherapy related blood tests, and hospital inpatient stays were linked to surgery recovery. In terms of data collection methods more generally, interview methods were used at baseline compared with postal self-complete measures at follow up timepoints. The completeness of data was substantially impacted at follow up and subject to available resources trial data may be improved through greater use of researcher collected outcome measures. Further qualitative work might help expand on whether the range of services accessed changes as participants move along from the point of cancer treatment.

The methods for the collection of complex medication data also need further pilot work as uncertainty around how to interpret incomplete questionnaires resulted in high levels of missing data and medication data not being costed as part of the resource use analysis. Specifically, medication use was only collected at baseline and there was limited information available regarding factors which could influence the costs such as the frequency and dose of medication. Consideration of the alternative methods of collecting and costing medication data is needed to ensure that information on dose, frequency and duration are collected across the duration of the study. Given the nature of MBCT-Ca delivered as a psychological therapy, and previous research exploring the use of medication during MBP trials (Kuyken et al., 2008; Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Morant, et al., 2015), medications impacting on symptoms of pain or psychological distress may be of particular importance to collect. Data collected direct from medical records may be an option to facilitate both a complete and accurate record of medication use over time.

There was some variation in the timing of assessments completed by participants and future research needs to establish a clearly defined window for completion of assessments. If outcomes are collected

significantly out of window then the outcomes may not be comparable to the rest of the sample. A period of up to 1 month would be reasonable to allow for small variations in outcome data timing without impacting on the comparability of data. The health economist working on future studies should ensure that date of assessment is included with economic data and that within window ranges are pre-defined along with details of any acceptable adjustment to provide a full range of cost data for the study period.

Without reducing attrition rates observed in this study a longer term follow up of outcomes is not likely to yield meaningful data on the long-term impact of MBCT-Ca. More generally for MBP research, longer term extrapolation using economic modelling methods may help enable estimates beyond the length of the trial follow-up period, however more data is needed to establish benefits from MBPs and whether these benefits are sustained over time.

The study employed a control group which received no active treatment, compared with the MBCT-Ca course delivered to the intervention group. With more than half of the TAU group lost to follow-up with 53% attrition in the control group, it raises an important feasibility question of whether an active control group could provide a better comparison for future studies, both in terms of reducing attrition and to prove a more equivalent intervention cost comparison. Other researchers have highlighted the need to move beyond a waitlist control in mindfulness in cancer research (Bower, 2016). Having no active control condition in economic evaluations may introduce a bias in the costings with the additional costs of MBCT-Ca delivery compared against no additional intervention treatment costs in the control group. The intervention group used more than twice the amount of resources than the control condition when including the cost of MBCT-Ca.

Lessons learnt in relation to choice of relevant outcomes

EQ-5D versus EORTC-QLQ-C30

Clinical and economic outcome measures were piloted including the EQ-5D-3L as a preference-based health related quality of life measure. This thesis research has shown that a generic utility measurement tool like the EQ-5D can be applied to the economic evaluation of MBCT-Ca, enabling a cost-utility analysis and comparison across different interventions delivered within a UK health service context. The EQ-5D-3L utility measure is commonly considered to be a key outcome in economic evaluations, however, the measure had the smallest percentage change in the service evaluation cohort, compared with change observed on other outcomes. The EQ-5D- 5L was not in common usage during this thesis research, however, future studies may benefit from the additional levels of responses which may capture more detail when there are some problems on a domain. There may be important benefits to quality of life that are missed if studies rely on EQ-5D utility alone. As an alternative to a generic

measure of HRQoL the EORTC-QLQ-C30 was considered, however, of particular concern was that there were high ceiling effects on EORTC-QLQ-C30 function and symptoms sub scales. A cancer specific HRQoL may be more appropriate in studies conducted in closer time proximity to cancer treatment than studies conducted within later survivorship stages of cancer recovery. It is important to consider whether the EORTC-QLQ-C30 is a useful outcome for economic evaluation, given that it is not preference based and that it cannot be used to calculate QALYs. Consideration of economic theory underpinning economic evaluation and the aim to maximise societal 'utility' rather than to improve disease-specific outcomes the relevance of cancer specific outcome measure may be less useful for economic evaluation of MBCT-Ca.

EQ-5D in addition to ICECAP-A

This thesis research has taken a wider view on wellbeing by going beyond health and quality of life indicators to consider capabilities. The ICECAP-A as a capabilities questionnaire was successfully used to provide an alternative viewpoint on the potential benefits from MBCT-Ca relevant from a broader societal perspective. Total ICECAP-A capabilities YFC were comparable with total QALYs in the service evaluation cohort. However, there was some small variation in the trial, with a higher YFC over the trial duration when compared with QALYs for the same period. While further methodological work is needed, this thesis research provides further support for health economics research to be feasibly explored within these different evaluative paradigms.

Assessment of psychological distress and wider relevant outcomes

In terms of useful clinical outcomes this thesis research has indicated that a broad wellbeing questionnaire like the WHO-5 is able to provide a useful indicator of levels of psychological distress, while benefiting from brevity due to its short format. The HADS subscales has enabled a distinction to be drawn in this thesis research between cases of depression and anxiety and raised the question of whether health economists should focus on clinical cases or heightened levels of psychological distress.

It is necessary to balance the number of questionnaires to yield sufficient information to address the economic questions with demands on participants. There are benefits to using shorter measures of psychological distress such as the WHO-5 which may be deemed sufficient for a secondary cost-consequence analysis.

Secondary outcomes such as the FFMQ-SF and the SCS-SF were not explored further in this health economics analysis other than to establish baseline equivalence and ceiling and floor effects of outcomes in this population. While they have not been used before as part of an economic evaluation, they may be relevant for future studies wanting to consider mechanisms for change and as a proxy for

engagement in the programme. Change on mindfulness facets may help validate a secondary per-protocol economic evaluation which includes patients attending four or more sessions and perhaps also those that complete the home practice elements. Secondary outcomes such as measures of self-compassion and mindfulness facets may provide valuable information for a theory of change which highlights which inputs and outputs warrant measurement. These wider outcomes are less likely to be directly useful for a narrow economic evaluation of MBCT-Ca, however, as health economics research is rarely conducted in isolation and a multi-disciplinary team approach to conducting trials is recommended, collecting these outcomes may help enable a full process evaluation of MBCT-Ca as a complex intervention to be included.

In view of MBCT-Ca as a clinically delivered intervention in the UK, a NHS perspective is likely to be considered the most appropriate primary approach, however, additional complementary analyses with the inclusion of secondary economic outcomes can capture the wider costs and benefits which remain important to capture from a societal perspective. Considering MBCT-Ca as a complex interventions, within complex systems, further supports the notion of adopting multiple perspectives of analysis and multiple forms of evaluation (Byford & Raftery, 1998; Zimmerman et al., 2011).

Lessons learnt from this feasibility study can now be used to develop a robust HEAP for future research evaluating MBCT-Ca.

Strengths and limitations of the study

The low overall recruitment indicates significant feasibility issues for a larger RCT if set within the same context. The embedded assessment of trial methods and qualitative study highlighted that there are important barriers to recruitment and per protocol running of the trial in this format.

This limitation was further confounded by high attrition rates in the TAU group, and the group sample size was therefore severely impacted. It is arguably the case that with modifications to stratification of randomisation, as a means to maximise exchangeability, some of the evident imbalances in the sample may have been avoided.

A further limitation was that there was only partial data collected on the attendance of participants allocated to receive MBCT-Ca, and that some participants were unable to attend the course due to the recruitment delays. As a result, it was considered that the MBCT-Ca group would be unlikely to represent a fully per-protocol cohort. A secondary service evaluation enabled the collection of information about the outcomes for patients referred through this non-randomised direct route to MBCT-Ca. Attendance in this context was higher because participants were recruited and then able to commence their course immediately. While it is acknowledged that these cohorts represent sufficiently

different groups and that there is no control group for the service evaluation cohort, the aim was to provide some pilot information about whether there is change over time following attendance on an MBCT-Ca course. When the trial and service evaluation cohorts were compared there was no clear differences between populations on most demographic items including age, gender, and cancer type. However, the service evaluation cohort were eligible to take part if their treatment was more than 12 months ago or ongoing, and on average more time had passed between participation and diagnosis compared with the trial cohorts. There may be important differences not captured by this study in terms of cancer prognosis and severity.

How patients want to access mental health support may be an important factor for considering access and future recruitment to MBCT-Ca research studies. While some participants highlighted seeking support through their oncologist, others accessed psychological support through primary care, or through voluntary and charity services. There were also some instances of talking therapy reported including counselling. While these were coded and costed equivalent to an hour of counselling in the community (Band 6 counsellor) it is important to consider that the cost of psychological therapy can vary considerably, future resource use tools that provide greater details about the types of psychological services accessed and where they were obtained would facilitate a more accurate costing of the mental health resource use.

The formalised assessment of trial methods embedded within this thesis research highlighted that perceived value by patients and clinicians may be an important factor in participation and attendance. There was a bias towards referring patients who need support through the service evaluation route rather than into a clinical trial where patients may be subject to a delay in attending MBCT-Ca.

It is a strength of this research that the resource use component was able to build a picture of usual care for patients recovering from cancer, and also to capture indicators from patient experience that there are unmet needs for psychological services. It is however a limitation of this thesis research that there was no active control group.

It was both a strength and a limitation of the study that participants from a mixed-cancer diagnoss population were recruited to participate within a pragmatic trial design. Most participants enrolled in the trial and service evaluation had previously received a diagnosis of breast cancer, however, a smaller number of participants with other cancers took part. There was a wide range both in time since treatment, differing stages of recovery, and to a lesser extent differing severities of illness that were represented. This provides useful indicators about the feasibility of recruiting mixed-cancer patient studies and increases the population pool from which to recruit from. The potential heterogeneity of the sample also highlighted challenges in interpretation of results with many potential covariates or

subgroups being considered for further analysis. In addition, the pragmatic pilot RCT and a service evaluation design caused some acceptability issues for some participants; with potentially significant differences in patient populations in terms of levels of illness and prognosis, and pragmatic locations of the course including some hospice locations. There was too small a sample to say anything meaningful about the attendance at MBCT-Ca of a support person alongside the person with cancer. Further research should consider the costs and benefits. Programme adaptations have considered MBCT for caregivers of people with cancer, delivered separate to courses tailored for cancer patients (Wood, Gonzalez, & Barden, 2015), however, no economic evaluation has been conducted to explore value of mixed or separate groups. While there was some diversity in the population sample in terms of cancer, almost all the patients were of white ethnicity, female and higher than population average education levels. There may be barriers to access and acceptability by minority groups that this study does not explore but warrants attention as part of the wider MBP research agenda.

It is a strength of this study that it employs mixed methods to explore acceptability of trial design and views relating to MBPs. The assessment of trial methods and patient views, combining qualitative interview and quantitative survey has enabled greater interpretation of the potential effects of MBPs, the barriers to implementation and important considerations for intervention delivery. The feedback form included open ended interview questions with written responses to supplement the telephone interview data, and to provide a broader assessment of the study methods. This yielded valuable information about the research processes and the intervention acceptability. However, the qualitative component of this study was just one element and as a result represents a high-level analysis with a small sample of participants views included with a self-selecting sample (18% of the pilot RCT population participated in semi-structured interventions). A purposive and diverse sample would likely increase the comprehensiveness of this research (Cheng & Metcalfe, 2018). For example, views may not be representative of participants who dropped out or who stopped completing questionnaires, therefore the transferability of these findings may be limited. There was 28% attrition overall, however, 53% loss to follow-up in TAU group resulting in very limited qualitative evidence from control participants. Future research should consider worst case scenario sensitivity analysis to assess whether loss to follow-up could change results in larger study (Dettpri, 2011).

The pragmatic study design with a mix of randomised feasibility study and service evaluation cohort raises challenges for the analysis of the data in terms of synthesis of results for potentially heterogeneous groups, and triangulation of the mixed methods into a clear set of findings and recommendations.

It is a limitation of this thesis research that there were incomplete records on participant attendance at MBCT-Ca sessions, this limited the ability to interpret levels of acceptability of the intervention and the

suitability of the research protocol. Evidence from qualitative interviews and trial records indicated that some participants missed some or all of the sessions and that randomisation to the intervention didn't always translate into attending the course. The availability of the participants to attend the intervention changed over time however delays to the delivery of MBCT-Ca course meant some participants were no-longer able to attend. Barriers to attendance and the timing of courses remain important feasibility items to assess in order to guide the methods for a future definitive trial.

It is a strength of this thesis research that a range of outcomes including capabilities and subjective wellbeing were considered, further consideration about the appropriate perspective and evaluative framework in which to assess MBCT-Ca is needed. Chapter 6 discusses considerations for the use of wider wellbeing outcomes as compared with health outcomes alone.

It is important to consider reflexivity (i.e., awareness of researcher role and potential bias) in the interpretation of this thesis research. It is acknowledged that ideally the lessons learnt from this study and interpretation of the various sources of data would be conducted by a team of people with greater PPI input into the final interpretation of the results. To reduce bias two independent coders who had not been involved in the study could have provided an independent analysis of the qualitative study, however, the immersion in the data across multiple sources was needed to combine results in the full assessment to address the study objectives and research questions. No interpretation of participant phenomenon is presented, rather the analysis is on the content shaped by the topic guide to address trial processes focused issues of acceptability, facilitators, and barriers to successful research. It would have been good practice to present these findings to the trial steering group including the patient and public representative members, however, due to the five year delay in finalising the trial data, analysis and write up this was not deemed possible. It is also acknowledged that there could have been further relevant information gained from the MBCT-Ca therapists and clinicians involved in referral. Ensuring future research considers formally collecting information from a wide range of stakeholders as part of the study protocol would likely improve the outcomes from methods assessment evaluations embedded within trial-based economic evaluations.

Comparison with other literature

In Chapter 2 of this thesis, a comprehensive systematic review highlighted three economic evaluations of MBPs delivered within cancer care. All the studies identified were published after the completion of the randomised feasibility trial reported within this thesis chapter.

1. *A Cost-Effective Mindfulness Stress Reduction Program: A Randomized Control Trial for Breast Cancer Survivors (Lengacher et al. 2015).*

In the first study, Lengacher et al (2015) evaluated a 6-week MBSR(BC) programme which was an adapted MBSR programme for breast cancer patient, while this thesis research piloted MBCT-Ca, an adapted MBCT programme for cancer patients (with any site of cancer eligible to participate). Both Lengacher et al (2015) and this thesis research compared an MBP with TAU. The Lengacher et al (2015) study population was breast cancer patients which was also the most common cancer site in this thesis research. Lengacher et al (2015) reports greater details on the stage of cancer, with most participants in stage I or II of cancer. In addition, the stage of cancer and type of treatment received was used as a stratification variable for randomisation into their RCT.

Lengacher et al (2015) had a larger sample size (*N=104* available case and *N=96* complete case) and a shorter trial duration, with the longest follow-up point at 12 weeks and a discounted extrapolated over a longer time horizon. Lengacher et al 2015) report low levels of attrition (less than 10% loss to follow-up at 6 and 12 weeks) despite a UC control group.

Lengacher et al (2015) conducted a primary cost-utility analysis using the SF-12 as a source of HRQoL over time for the calculation of QALYs gained, while this thesis research used the EQ-5D-3L. Only QALYs are reported rather than mean HRQoL so no comparisons with populations can be made between my study and theirs.

Patient opportunity cost was considered in terms of participants time, lost wages, travel, accommodation costs and childcare. Patient opportunity costs were averaged $592 (SD=$494) or $100 per session (total 6 sessions) with biggest factors being time lost to employment, childcare, and travel costs. No resource use costs were considered and no cost of UC. The average cost per participant in the intervention was $666.

Lengacher et al (2015) highlighted a range of post-treatment benefits for those who attended the MBSR(BC) course including a reduction in post-treatment fatigue, depression and anxiety and fear of recurrence as well as improving HRQOL, physical functioning and energy levels. The authors conclude that “assuming relatively lengthy post- treatment survival (e.g., 15 years or more) and sustained results, [MBSR-BC] appears to provide for significantly improved HRQOL at a comparatively low cost” (Lengacher et al., 2015, p. 217). The study reported a cost per QALY (at 12 weeks) equivalent to £17,918 or £4,167 per QALY if gains were extrapolated over 1 year (when converted to pounds and inflated to 2019 costs). While these results provided a positive indication of the potential cost-effectiveness of MBSR for breast cancer patients the authors acknowledge the modest sample size as a limitation of the study and note that there was some improvement in the UC condition over time.

2. *Mindfulness-based cognitive therapy (MBCT) is cost-effective compared to a wait-list control for persistent pain in women treated for primary breast cancer—Results from a randomized controlled trial* (Johannsen et al., 2017).

The second study identified in the systematic review reported on a RCT of MBCT tailored for breast cancer patients experiencing persistent pain (Johannsen et al., 2017). This study had a moderate sample size with a complete case sample of 84 participants making cost-effectiveness analysis feasible. The cost-effectiveness analysis conducted from a health care provider perspective indicated that MBCT was the dominant intervention with lower costs and better outcomes on average and had a high probability of being more cost-effective (between 70 – 85%) treatment compared with a waitlist control group in reducing pain intensity (MCID>2points on the pain outcome). In Johannsen et al (2017) the tailored MBCT programme had lower overall costs and better outcomes compare with TAU.

Unlike Lengacher et al (2015), health care utilisation was considered by Johannsen et al. (2017), however, the study did not include any utility measure and therefore no cost per QALY was presented. The authors highlight that future research should consider adopting a societal perspective, including indirect costs (productivity losses) and utility. Johannsen et al. (2017) reported higher drop off in the intervention than the waitlist, however, there was balanced attrition between groups on outcome measures. In my study, TAU had higher attrition levels compared with the intervention group, however, no comparison of drop off from intervention attendance could be assessed due to incomplete attendance records.

3. *Face-to-Face and Internet-Based Mindfulness-Based Cognitive Therapy Compared With Treatment as Usual in Reducing Psychological Distress in Patients With Cancer: A Multicenter Randomized Controlled Trial* (Compen, Bisseling, Donders, et al., 2017).

The third study compared health care utilisation (with no costs reported) in a population of patients with cancer and psychological distress as part of a three arm RCT (*N=245*) comparing group-based face-to-face delivered MBCT and internet e-MBCT, both tailored for the target population with a treatment as usual (TAU) control group (Compen, Bisseling, Donders, et al., 2017). There was no difference during the study period in health care resources used except for a higher rate of hospital outpatient visits (such as chemotherapy) observed in the TAU group. The authors highlight that the intervention costs of e-MBCT are likely to be lower than traditional face-to-face MBCT (for example due to no travel costs and overheads) and hypothesize that it could be a more cost-effective mode of delivery. MBCT and e-MBCT had promising clinical outcomes compared with TAU with a significant reduction in psychological distress, fear of cancer recurrence and health related quality of life (on mental health domains alone).

In parallel with this thesis, Compen et al (2017) conducted research on MBCT for patients with any site of cancer. However, one notable difference it that in Compen's study, their population sample also included patients currently in active treatment, rather than after treatment had concluded. Compen et al (2017) included patients with baseline scores on the HADS of ≥11 to indicate psychological distress. Results indicated that, similar to the findings from this thesis, that anxiety is an important aspect of psychological distress for patients recovering from cancer.

e-MBCT may have lower costs and may be especially relevant when considering new ways of supporting patients through remote health care following the pandemic. In addition to the RCT, Compen and colleagues report on a linked qualitative study exploring the barriers and facilitators to participation and delivery of e-MBCT (Compen, Bisseling, Schellekens, et al., 2017). The treatment setting, format of the programme and factors relating to the therapist and patients were highlighted as important themes. These findings echo results reported in this thesis particularly highlighting the location of the course as an important factor in acceptability and facilitator to participation.

Areas for future research

Specifically, in relation to this thesis research, further pilot work is needed to improve on the methods trialled in this chapter for the collection of health and social care resource use. Future studies should record medication at follow-up to see if there is any change in medication e.g., antidepressants or pain medication over time. Given the focus of other MBP research on maintenance antidepressant use it may be relevant to also consider whether there has been a recent change in psychotropic medication (recent changes were considered to be an exclusion criteria in Compen et al., 2017).

Wider costs and benefits from a societal perspective are needed to fully consider whether psychological wellbeing contributes to a person's ability to maintain employment (as a contribution to both personal finances and the wider economy), and opportunities to enjoy leisure time (as an important indicator of social value). Further research to explore the capabilities approach as an alternative economic paradigm is needed to build on the early stage research presented in this thesis and other methodological research published in the literature (Mitchell et al., 2017).

A further pilot RCT in a more populated area, focused on one course location may help recruit sufficient sample to gain more TAU data. Finally, a multicentre RCT that is powered to evaluate the effectiveness and cost-effectiveness of MBCT-Ca is still needed. Further pilot research is needed to estimate the effect of the intervention compared with alternative care, and a power calculation to determine a sample size is needed for a full definitive RCT. Comparisons against an active control group may be helpful to retain a sufficient sample for future analysis and assess the likely cost-effectiveness of MBCT-Ca.

There remain gaps in evidence around who may benefit and what the mechanisms of change are in MBPs for cancer survivors and further research is needed (Haydon, Boyle, & Bower, 2018). Most of the evidence evaluating MBPs in cancer care to date focuses on breast cancer recovery, with less evidence relating to other sites of cancer diagnosis. For whom the intervention is most valuable from a health economics perspective warrants further evaluation in considering a precision public health approach. One recent study has highlighted both psychological and physical benefits from MBPs. For example promising psycho-immune outcomes of MBSR in patients newly diagnosed with breast cancer (Witek Janusek, Tell, & Mathews, 2019). Further research which considered the most cost-effective timing of intervention delivery following cancer diagnosis is also needed.

The COVID-19 pandemic will have had many impacts on cancer care, much of which is yet to be realised. Recent studies have considered the effectiveness and acceptability of MBPs for cancer patients delivered through the internet (Compen, Bisseling, Donders, et al., 2017; Compen, Bisseling, Schellekens, et al., 2017; Messer, 2017). Remote delivery of MBPs may be an accessible option that can help overcome some of the barriers to attending MBCT-Ca that were highlighted by participants (for example, travel to groups or course location being unpleasant) and may have lower delivery costs. Blended delivery of MBPs are also increasingly being considered in research particularly in workplace settings (Vonderlin, Biermann, Bohus, & Lyssenko, 2020), however, there remains little assessment of cost-effectiveness in these formats.

Conclusions

This mixed methods study brought together qualitative findings on patient experiences and a full range of quantitative outcomes relating self-reported health and wellbeing and use of public sector services following cancer treatment. In consideration of targeting specific vulnerability to psychological distress in this population of people recovering for cancer treatment, early feasibility findings from the research in this thesis indicated that there were high levels of anxiety in the study population and that there were indictors of an unmet need for psychosocial support. These findings are in support of the case for greater investment in effective and cost-effective psycho-social support more generally. Further research is needed to establish whether MBCT-Ca can be a cost-effective intervention to support this population.

In considering a proportionate universalist approach (Marmot, 2010), where health actions are required at a universal level to address public health problems and inequalities, this thesis turns next to the application of MBPs in schools (Chapter 5).

Chapter 5: Working towards universal prevention – a non-randomised matched cohort feasibility study of a mindfulness-based school curriculum.

Chapter preface

Chapter 5 reports on a concurrent economic evaluation, alongside a pragmatic non-randomised study with a matched control group, of a school-based mindfulness curriculum for Sixth Form students (aged 16-18 years), delivered by trained in-house classroom teachers or assistants. This chapter addresses the fifth principal thesis research question of "What are the appropriate methods for measuring and valuing costs and benefits of embedding mindfulness in secondary school curriculum?" The health economics feasibility study (embedded within an empirical study conducted in 2015 by Sanger and colleagues) piloted methods for a primary cost-utility analysis using the EQ-5D-5L mapped to EQ-5D-3L, as a source of utility weights for the calculation of Quality Adjusted Life Years (QALYs). Methods for a secondary cost-effectiveness analysis using GHQ-12 as a screening tool to identify cases of depression are discussed. As the assigned research officer for the health economics analysis, I refined the analysis plan, cleaned, and scored the economic data and completed the pilot analysis written up as presented in this thesis (Chapter 5). This chapter offers a universalist approach (Marmot, 2010) to overcoming public health challenges and preventing depression through early universal intervention with MBP delivered in schools to adolescents. This is not intended to replace a targeted approach to interventions delivered to populations at greatest risk of depression as presented in Chapter 4, however, this thesis goes on to discuss how as part of a precision public health approach, both universal and targeted interventions are needed to address depression prevention.

Chapter 5 Abstract

Background

There is an economic case for early universal intervention and prevention of mental health problems. However, there is little evidence of economic evaluations considering mindfulness programmes delivered in schools.

Methods

A non-randomised matched cohort feasibility study aimed to pilot elements of the design of an economic evaluation for a MBP delivered in Sixth Forms to adolescents. This study included a feasibility assessment of outcome measures such as the EQ-5D-5L as a primary economic outcome for calculating QALYs for cost-utility analysis and the GHQ-12 as a screening tool for early signs of mental health

problems and outcome for cost-effectiveness analysis. A checklist for feasibility studies is presented as a framework for evaluating early-stage health economics studies in MBP.

Results

A complete case analysis of 38 participants (*N=23* in the MBP group) is reported with key differences to results from an available case analysis of 98 participants (*N=40* in the MBP group) is discussed. Ceiling effects of trial-based economic outcome measures such as the EQ-5D-5L in healthy populations are discussed. Mean QALYs were *M=0.560, 95% CI [0.53, 0.58]* for the MBP group and *M=0.558, 95% CI [0.52, 0.59]* for the control group over the 8-month trial duration. GHQ-12 scores above 12 as a clinical cut-off was observed in 66% of all participants at baseline. Feasibility of collecting brief resource use information from student participants on GP attendances and rates of absenteeism was confirmed as feasible. There were small, non-significant changes in health-related quality of life and depression over time, and no difference between groups detected in this pilot analysis. Total mean costs (including intervention costs, GP resource use and indirect productively losses costs) were £1,234.42 in the MBP group and £1,106.77 in the control group. When valuing forgone education in terms of estimates of life time lost earning the total mean costs were £3,462.04 in the MBP group and £3,099.90 in the teaching as usual group.

Discussion

Wider reaching resource use data is needed for a full societal perspective analysis. Valuation of forgone education, as measured by school absenteeism is discussed for inclusion as a relevant societal cost in future school based economic evaluation. A threshold analysis on cost is proposed to explore the sensitivity of results to variation in costs.

Conclusions

This chapter concludes with a set of recommendations relevant to MBP feasibility trials and future research in MBPs in schools. This study provides further pilot evidence in support of the case for earlier intervention capable of primary depression prevention and highlights that greater mental health support for adolescents and young people may be needed.

Introduction

Mental health problems in adolescence and childhood

Adolescence is a time of significant brain development and change for young people, with high stress and academic demands, social pressures and approaching a transition time into adulthood (Backes & Bonnie, 2019). It is a 'sensitive point' for depression onset and important stage in development of emotional regulation (Thapar, Collishaw, Pine, & Thapar, 2012). The World Health Organisation indicates that during adolescence depression is a leading cause of years lost to illness and disability (World Health Organization, 2020).

Depression prevalence in children and young people has been rising (Pitchforth et al., 2018). An estimate of 10% of children in secondary schools require some mental health support (Rethink Mental Illness, 2020). Half of all mental health problems begin by age 15, rising to three quarters by early adulthood (Kessler et al., 2005). Depression in adolescence often goes undetected (and untreated) until adulthood with symptoms often attributed to more normal teenage emotions and behaviours (Thapar et al., 2012). In adults with depression the age of onset of symptoms and highest frequency of first episode of depression was reported to be between age 13-15 years (Williams et al., 2012).

Prevention and early intervention

The Department of Health highlights the importance of preventing mental illness and mitigate its effects when it does occur through mental health promotion and early intervention in childhood (Department of Health, 2011).

The life trajectory of children who experience poor mental health is similar to that of children raised in poverty, with a higher likelihood of poor outcomes into adulthood, with lower academic attainment, reduced rates of employment and poorer career progression opportunities, in addition to higher likelihood of contacts with social justice and welfare systems (Khan, 2016). All of these consequences have high economic and social costs.

It is commonly reported that there are high rates of returns from investment in the earliest years of life, with a diminishing rate of returns through the life course (Heckman, 2008). While there remains a large economic and prevention argument for investment in this early period more recent evaluations comparing rates of returns of a large number of programmes has highlighted evidence of some of the highest benefit-cost ratios from programmes delivered in late adolescence (Rea & Burton, 2020).

Spending on health promotion, mental health literacy and wellbeing

According to McCrone et al (2008) "very little NHS money is currently devoted to mental health promotion (around one-tenth of one per cent of NHS mental health spend for adults of working age)" (McCrone et al., 2008, p. 123). However, other sectors have taken action to try to improve emotional wellbeing including initiatives in schools such as the 'Social and emotional aspects of learning (SEAL) programme' (Department for Education, 2010a) and 'Personal, social, health and economic (PSHE) education' (UK Government, 2013) which includes an emotional health and wellbeing strand (McCrone et al., 2008).

National curriculum and how schools have changed – policy direction (wellbeing)

While there is "no duty on schools to have a separate mental health policy" (Brown, 2018, p. 71) schools have a duty of care to protect the wellbeing of children and staff. In Wales, where education is a devolved matter, there is evidence of greater focus on wellbeing in the New Curriculum for Wales 2022 (Welsh Government, 2020) which aims to work towards the goals set out in the Well-being of Future Generations (Wales) Act 2015 (UK Government, 2015).

Societal changes have also resulted in education policy that addressed changing needs of society, for example breakfasts for all children and tackling childhood obesity as result of poor diet and inactivity, addressing areas that might historically have been met at home by parents and support from wider community.

There is an equity argument for an education system that helps support children growing up in poverty and helps mitigate for a poor start in life.

Schools as universal prevention opportunities

Current NICE guidance highlights the important role of schools in the early identification of depression symptoms (NICE, 2019a). Schools are an ideal setting to reach a high number of children, including those at heightened risk of early onset depression. They offer a universal delivery opportunity where every child can access an intervention. This can help reduce stigma around targeting particular groups of people, encourage health promotion for all and potentially help normalise talking about mental health amongst peers (Department of Health and Department of Education, 2017).

McDaid et al (2015) make the case that embedding programmes into a whole school approach, such as changes to the curriculum with emphasis on teaching skills and positive mental health can be more effective than short stand-alone interventions with a narrow focus, however, they require implementation and delivery with fidelity to achieve benefits (McDaid et al 2015). Some have argued

that “multilevel, systems-based interventions as an alternative to … downstream interventions” may be more effective and now require greater research attention (Caldwell et al., 2019).

“Schools and colleges are an important site for mental health promotion and mental ill health prevention” (Marshall, Wishart, Dunatchik, & Smith, 2017, p. 66). The majority of schools (90%) provide some mental health and wellbeing training to at least some staff to help support pupils, however, whether health promotion initiatives are effective requires further evaluation (Marshall et al., 2017).

Economic evaluations in education

High emphasis is placed on evaluation in the form of teacher performance assessment and pupil outcomes in terms of attainment particularly in relation to ‘core’ subjects such as Maths and English (Hutchings, 2015). The Education Reform Act (DES 1988) led to the introduction of Ofsted [Office for Standards in Education, Children’s Services and Skills], national testing and published league tables. These accountability structures gave the government greater control over the curriculum of education to be taught. In addition, the introduction of competition through published league tables about pupil attainment created an educational market with opportunities for parents to make an informed choice in the selection of school for their children (Hutchings, 2015).

These accountability measures are reported to have increased pressures on both teacher and pupils. (Hutchings, 2015). With teachers focusing on preparing children for tests and on children to reach their targets. This focus on testing and performance is argued to have resulted in teachers and schools spending less time on ‘foundational subjects’ such as music and geography (Hutchings, 2015). In addition, the impacts on children caused by increased pressure from tests and exams were reported to be substantial with “increasingly high levels of school-related anxiety and stress, disaffection and mental health problems” (Hutchings, 2015, p. 5).

In 2010 the UK coalition government emphasised the importance of research evidence in education to improve teaching and learning (Department for Education, 2010b). With the exception of focus on the cost-effective use of capital budgets to build and maintain school building (Department for Education, 2010b) and in more general terms the impact of educational attainment on the economy, there has been little focus on economic evaluations informing school practice. There are many reasons for a lack of focus on the evaluation of cost-effectiveness of interventions or changes to systems in part because benefits are often delayed while budgets are short-term usually within political time frames (World Health Organization - WHO, 2002). In addition, schools are complex systems where many methodological considerations are needed to determine research that is appropriate for example more pragmatic evaluations than RCTs, ethical considerations on any negative outcomes, and working with vulnerable populations i.e., children with challenges relating to research consent.

In the same way that health effects are not the only benefit of health interventions (Brouwer, 2019), education programmes can have wide reaching benefits that extend to other people and other sectors. The perspective of analysis for economic evaluations within the education system is important, as while budgets are rarely directly shared across the public sector the benefits of education intervention are likely to spill over into almost all sectors.

There are methodological considerations of the appropriate range of costs and benefits to include for example inclusion of forgone education, the opportunity cost of unplanned absence from school, and how to measure and value the costs. For example there is an argument that the value of days off school could be equivalent to a caregivers lost wages (actual or mean national daily wage) or linked to educational attainment and loss of potential future earning, consistent with human capital approach (Andronis, Maredza, & Petrou, 2019).

Effectiveness of psycho-social prevention interventions in schools

There is existing evidence on prevention of depression in schools (see McDaid et al. 2015 for a review) with some evidence of cost-effectiveness (McDaid et al., 2015).

Recent systematic review and meta-analysis exploring evidence of anxiety and depression prevention in schools found that "in universal secondary settings, mindfulness and relaxation-based interventions showed a reduction in anxiety symptoms relative to usual curriculum" (Caldwell et al., 2019). In another systematic review and meta-analysis they found evidence that "school-based programs aimed at decreasing anxiety and depression were effective, [however] these effects are not long-lasting" (Feiss et al., 2019, p. 1668). In both reviews effect sizes were small to moderate and there was a lack of evidence supporting prevention of depression on both a universal or targeted basis (Caldwell et al., 2019; Feiss et al., 2019).

A systematic review considering depression, anxiety and stress prevention programmes for university student populations highlighted on average moderate effects regardless of prevention level (universal or targeted) (Rith-Najarian, Boustani, & Chorpita, 2019).

Internationally, economic modelling of the cost-effectiveness of after-school screening and psychological intervention to 11-17 year olds showing elevated signs of depression was considered likely to be cost-effective compared with teaching as usual of the normal health curriculum in Australia (Mihalopoulos, Vos, Pirkis, & Carter, 2012). The screening and subsequent intervention programme had an ICER of AUD$5,400 per DALY averted (2003 cost year), well below a value for money threshold of AUD$50,000 per DALY. In addition, a targeted intervention in the USA for at risk teenagers (13-18 year olds) with depressed parents indicated that 15 sessions of CBT resulted in a cost per QALY of $9,275 in

2000 (Lynch et al., 2005). This targeted intervention delivered in addition to usual care was reported to be cost-effective compared with the control condition who received usual care alone. Evidence from other countries requires consideration of generalisability to UK education system (National Institute for Health and Clinical Excellence, 2008) and particular assessment of the likely acceptability by schools, health professionals, parents and children.

Mindfulness in schools

Children learn through experience and are naturally curious as they experience things for the first time (National Research Council, 2000). By adolescence opportunities for play and exploration are commonly replaced with learning that focuses on following teachers instructions without the curiosity and energy that filled the classroom in earlier year groups (National Research Council, 2000). Mindfulness involves practicing 'beginners mind', approaching experience with awareness and without judgement. Personality traits such as openness to experience and trait curiosity have been linked to Mindfulness practice and are thought to be potentially important factors in the effectiveness of MBPs (Ivtzan, Gardner, & Smailova, 2011). Childhood and adolescence may be an important intervention timepoint for learning about awareness and sustaining innate childhood curiosity, particularly if these skills can be protective against future ill-health and help improve long term wellbeing. There are large number of publications on the effects on MBPs for children and adolescents, many with interventions delivered in schools settings (McKeering & Hwang, 2019; Zenner, Herrnleben-Kurz, & Walach, 2014).

Early research has indicated that MBPs can improve outcomes for adolescents on wellbeing, educational attainment, attention and sociability, alongside a reduction in stress (Bögels, Hoogstad, van Dun, De Schutter, & Restifo, 2008; Meiklejohn et al., 2012). One small study reported some small cognitive and socio-emotional improved outcomes, but no significant effect on behavioural and academic outcomes (Maynard, Solis, Miller, & Brendel, 2017). Supported by systematic review and meta-analysis which reported benefits to cognitive performance (Zenner et al., 2014).

Evidence of MBPs for adolescents and young people regarding the effects on stress, anxiety and depression treatment and prevention are somewhat mixed (Chi, Bo, Liu, Zhang, & Chi, 2018; Johnson, Burke, Brinkman, & Wade, 2016; Kallapiran, Koo, Kirubakaran, & Hancock, 2015; Klingbeil et al., 2017; Raes, Griffith, Van der Gucht, & Williams, 2014), and what influences whether MBPs are effective is not fully understood and still warrants further investigation. Much of the evidence is criticised for having small sample sizes, small outcome effects, and concerns over quality and risk of bias (Kallapiran et al., 2015; Zenner et al., 2014). There is variation of MBPs delivered in schools (Semple, Droutman, & Reid, 2017).

According to a recent meta-analysis MBPs delivered during late adolescence (15–18 years) (compared with middle childhood and early adolescents periods) may provide a key window for intervention (Carsley, Khoury, & Heath, 2018). Although on the whole effect sizes were small MBPs that "consisted of combinations of various mindfulness activities had the largest effects on mental health and well-being outcomes" (Carsley et al., 2018, p. 693).

The focus of MBPs delivered in schools is not always on mental health prevention alone. Evidence from a small pilot RCT of a MBP for adolescent girls at risk of type 2 diabetes with mild to moderate depression *(N=33*) provided early evidence of a benefit to metal health symptoms but also a "greater decreases in insulin resistance and fasting insulin at post-treatment" compared with students receiving a CBT control condition (Shomaker et al., 2017, p. 66).

A non-randomised controlled feasibility study of Mindfulness in Schools Programme for children aged 12-16 (*N=522*) in UK secondary schools reported that children experienced fewer depression symptoms post MBP relative to control cohorts (Kuyken et al., 2013b). Benefits were sustained at follow-up (3 months) along with lower stress and improved wellbeing (Kuyken et al., 2013b). Limitations of the study were largely a feature of its feasibility nature, with acknowledgement of selection bias of interested schools and non-randomisation of sites (although schools were matched on a number of key variables) and a small number of outcome measures (Kuyken et al., 2013b). The study did not include an economic evaluation or pilot economic outcome measures. A large cluster randomised controlled trial is now underway with 5700 students (12-14 years), followed up for a longer period of 2 years (Kuyken et al., 2017). The planned trial-based economic evaluation includes a primary cost-utility analysis, using the EQ-5D-Y (Wille et al., 2010) to generate utility scores for the calculation of QALYs (Kuyken et al., 2017). A secondary series of cost-effectiveness analysis is planned with effectiveness expressed in terms of the study primary outcomes: 1) depression risk, 2) wellbeing and 3) socioemotional and behavioural functioning (Kuyken et al., 2017). The economic analysis will be conducted from a health and social care perspective plus the addition of educational based services (Kuyken et al., 2017). In addition this study highlights the need to consider longer-term outcomes and employs decision analytic modelling to extrapolate beyond the trial period (Kuyken et al., 2017).

According to Erwin and Robinson (2016) "in the USA, articles about mindfulness practices in education as cost-effective classroom tools with the potential to increase positive student outcomes have been published in The New York Times (Bornstein, 2014), Wall Street Journal (Glazer, 2011), and Los Angeles Times (MacVean, 2014)" (Erwin & Robinson, 2016, p. 270). The opinion pieces cited by Erwin & Robinson (2016) mention the high costs of alternative therapy, alongside the negative economic impacts of school expulsion and some benefits of school performance and attention, however, none point to any economic evaluations that support the statement on cost-effectiveness.

Given the challenges of conducting large scale evaluations in childhood and adolescence, particularly in the context of a wealth of existing interventions delivered within schools it is important to learn from early stage evaluations and consider mechanisms of change evidence (Saunders & Kober, 2020). The theory underpinning MBPs potential to prevent mental health problems is logical, and is well supported by neuroscience studies (Sanger & Dorjee, 2015; Tang & Leve, 2016). Pilot study evaluations have indicated that mindfulness can improve self-regulation of emotion in late childhood (Deplus, Billieux, Scharff, & Philippot, 2016) and improve self-reported wellbeing (Sanger & Dorjee, 2016).

Rationale for a feasibility study

This research study was conducted in 2014 and at the time there was little attention on the economic evidence for Mindfulness in Schools programmes, however, there was a growing interest in introducing mindfulness practice into schools in practice. The introduction above has been updated to represent current understanding on the effectiveness and cost-effectiveness of MBPs in schools. There remains no published economic evaluations of Mindfulness in Schools to our knowledge although as discussed in Chapter 2 evidence is forthcoming (Kuyken et al., 2017).

In addition, at the time of this study it was common for early-stage evaluation studies to not include economic costs and outcomes and little guidance was available to researchers on the appropriate methods for conducting health economics feasibility research. Since this point more articles and guidance have been published including a commentary on the considerations for health economics feasibility studies by Gannon (2017).

Embedding economic outcomes into early-stage evaluations can provide an opportunity to test the outcome in terms of completeness and acceptability to participants. This is necessary for the development of good quality future RCTs. In addition, the higher likelihood of ceiling effects in relatively healthy populations can be explored to establish if traditional health economics tools can appropriately be used to capture benefits of MBPs.

There may be important resource use considerations that can be explored from a health economics perspective in the evaluation of mindfulness in schools delivered as a tool for depression prevention on a universal basis. There is evidence that GP use can be high in certain groups of children where psychological distress is prevalent, for example, children with behaviour problems (Gardner et al., 2017).

This feasibility study reports on the pilot health economics evaluation of a school-based mindfulness training for adolescents aged 16-18 years. Full details of source study and neuroscience outcomes are reported elsewhere) (Sanger & Dorjee, 2015, 2016; Sanger, Thierry, & Dorjee, 2018).

Methods

Aims

The aims of this pilot health economics study were to assess the feasibility of collecting indicative costs and outcomes relevant to the chosen study perspective and review the perspective for future trials. Data was collected with the purpose of informing the development of a Health Economic Analysis Plan (HEAP) for full definitive trial to explore whether a Mindfulness in Schools curriculum was likely to be cost-effective compared with usual curriculum in students attending Sixth Form education?

Objectives

The objectives of the health economics component of the study were to:

1. Report on the methods for collecting service use information and information relating to time off school from the study population,
2. Describe the frequency of GP attendance in this population, report on the cost of GP resources used and compare GP visits descriptively with age-appropriate population norm information, and explore demographic factors which may influence GP attendance,
3. Report on rates of unplanned absence from school, estimate the value of forgone education and explore the approach to valuing time off school to inform future analysis,
4. Report on descriptive data on relevant outcome measures to assess the potential impact of mindfulness in schools considering both generic outcomes and depression specific outcome measures,
5. Conduct pilot assessments where appropriate to explore potentially meaningful differences between the mindfulness curriculum group and the teaching as usual group, and explore trend in outcomes over time.

Trial registration and source of data (candidate contribution statement)

This health economics component of a feasibility study forms part of a non-randomised matched cohort trial (Registration: ISRCTN89407829 - http://www.controlled-trials.com/ISRCTN89407829)

The source study was designed by KS, DD and RTE (candidate supervisor), the study team developed the study protocol and selected the health economics outcomes for inclusion in the pilot economic evaluation sub-study. LB (candidate) was assigned as the health economics research officer to conduct the feasibility assessment. LB wrote the health economics analysis plan as outlined below and wrote up the study presented in this chapter. Bangor University research ethics and governance approvals were obtained for the study and specifically amended to permit inclusion of analysis as a case study as part of

this thesis. Data was provided to LB as electronic data files, which collated to a partial data set of the full study data i.e., limited to key outcome measures considered likely to be relevant to the economic analysis by the study team (detailed below).

Ethics

The study was approved by the Bangor University School of Psychology ethics committee and amended (see Appendix 28) to provide permission for the candidate to analyse the health economics data (Reference 11284-A13520). Participants were given full information about the study and completed an informed consent form. All participants were given the right to withdraw from the study at any time and could choose to refuse to answer any questionnaire items without reason. Reported results present aggregated data, to ensure that no individual was identifiable.

Design

The full study design was outlined in full elsewhere (Sanger & Dorjee, 2016; Sanger et al., 2018). Four schools in the North Wales region were invited to participate in a longitudinal matched cluster teaching as usual control non-randomised study. Schools were matched based on socioeconomic status and academic attainment. The first two schools that agreed to participate were assigned to the intervention and the second two schools to the control condition. The study design consisted of two groups (intervention and control conditions), with repeated measures dependent variables (GP attendance, time of school, health related quality of life, depression), measured across three timepoints (T0, T1 and T2).

Participants

Sixth Form students aged between 16 and 18 years attending either intervention training group or matched control schools were invited to participate on an opt-in basis. Baseline differences between groups in terms of age and previous mindfulness experience participants were assessed and are discussed elsewhere (Sanger & Dorjee, 2016). The final assessment was conducted in the September following the completion of Year 13, therefore all Year 13 participants were lost to follow up at the final assessment.

Intervention and control conditions

The Mindfulness in Schools .b Foundations programme

"An age appropriate mindfulness-based school curriculum (.b Foundations), designed for adults and educators was delivered. This course was chosen instead of the standard '.b' curriculum intended for

secondary school pupils to reflect the maturity of the age group targeted for this intervention. The .b Foundations pro- gramme was created by the Mindfulness in Schools Project (MiSP; http://mindfulnessinschools.org/) team and draws strongly from Mark Williams and Daniel Penman's 'Mindfulness: Finding Peace in a Frantic World' [42]. The course was delivered over eight 50- min. weekly sessions plus an initial orientation session, taught by students' regular teachers within the PSHE curriculum slot. This is a relatively new model of delivering mindfulness-based courses in schools, which have typically been taught by external mindfulness trainers. The implementation model involved a long-term commitment from teachers, who first completed a prolonged period of mindfulness instruction themselves. This consisted of the .b Foundations course taught over six weeks, three months of individual practice to establish comprehension, and then 14-h training in how to deliver the .b Foundations course to sixth form students. Teachers only proceeded to this last training phase if they wished to continue, and showed a sufficient personal mind- fulness practice as assessed by an experienced mindfulness trainer. Supervision from the trainer was also given during the student course period" (Sanger & Dorjee, 2016, pp. 3–4).

The programme was delivered within school hours as part of the school curriculum. Hereafter, this group is referred to at the intervention group or the MBP group.

Control group

The control condition consisted of teaching as usual, this included PSHE modules which provided some elements of an active control condition (Sanger et al., 2018). Control schools were offered the same mindfulness training after data collection was completed. Hereafter, this group is referred to at the control group or teaching as usual.

Measures

Timepoints for assessment of measures

Students self-reported outcome measures were completed at three timepoints *(T)* for both control and intervention schools. These were *T0* baseline (January 2014), *T1* post-intervention (April 2014), and at *T2* a final follow-up (September 2014).

Demographics

Limited demographic information was provided for the health economics component of the feasibility study consisting of age (in years at baseline), gender, and previous experience of mindfulness.

Health care resource use

Brief resource use in the form of levels of GP service use was collected to assess the feasibility of obtaining health care resource use information from student populations (see Appendix 31: Resource use questions extract from socio-demographic form).

A period of three months was thought to be sufficient for a representative picture of service use to be gauged, yet recent enough for the participant to recall accurately the frequency and nature of contacts (Roberts et al., 1996). In a recent study "over half of Year 10 pupils (aged 14-15) reported that they visited within the previous three months (52% boys, 57% girls)" (Hagell & Shah, 2019, p. 140). Longer periods of resource use recall have been associated with greater recall errors (Clarke, Fiebig, & Gerdtham, 2008). The six month recall data collected at follow up timepoints were extrapolated (assuming linearity) providing an estimated full cost of GP use for the duration of the trial (8 months).

Baseline resource use was assessed in terms of equivalence between groups. Levels of GP service use were compared against national average attendance rate for this age cohort and time period.

Relevant background and methods to assess national average GP attendance

After an initial peak in attendance in age 0-4 years (attributed to common infant illness) there is a trend towards rising rates of primary care attendance through the age groups into adulthood. "Statistical information for this age group is limited in the UK since national data are usually collected in the age bands '5–14', and '15–24 years"(Walker & Townsend, 1999, p. 165). "Young people access their GPs regularly for a wide range of health issues. Generally, it is estimated that young people visit the GP several times a year. In their teens this averages out at approximately twice a year for young men and more than four times for young women (HSCIC, 2009)" (Hagell & Shah, 2019, p. 140).

Table 45 shows the consultation rates per year with a general practitioner or nurse, by sex, and year. Using figures from 2013-14 (age group 15-24 years) the mean attendance in primary care (GP and nurse consultations) was *M=1.97* (Males) and *M=4.55* (Females) per year, a slight rise on rates from the previous year (Hobbs et al., 2016).

Table 45: Consultation rates per year with a general practitioner or nurse, by sex, and year

		2012-13		2013-14	
Age group	**Consultations**	**Male**	**Female**	**Male**	**Female**
15-24	total (n) per 10,000	19621.55	45443.95	19736.37	45520.48
	mean (m) per person	1.962	4.544	1.974	4.552

GP service use was considered by sub-group of gender (subject to sub-groups containing a minimum number of each gender[8]) with national data indicating that males are significantly less likely to access general practice than females. Gender was therefore considered to be a potentially important covariate in analysis involving resource use.

Forgone childhood education (unplanned absence from school)

School attendance and lost schooling time were valued and discussed in relation to inclusion in future economic evaluations. Absenteeism can impact on children's educational attainment; however, it can be difficult to measure and value in economic evaluations, and outside the scope for studies with a narrower perspective of analysis. There are various method for measuring, valuing and including forgone childhood education and leisure time costs in economic evaluation (Andronis et al., 2019).

Monthly school unplanned absence data was planned to be collected direct from schools for the academic year proceeding baseline (Sept 2012 – July 2013) and the following year i.e., during and after the intervention (Sept 2013 – July 2014), for all pupils participating in the study. Unplanned absence data was instead provided at each timepoint and reported by Sanger et al (2018) to be self-reported by participants. Unplanned leave was provided in days at baseline (for the previous academic year 2012/13). From the information available the duration of the recall period at T1 and T2 was not clear from the data and questionnaire booklets were not available for validation due to the delay in the health economics analysis being conducted. It was estimated that the recall period was for the time between assessments, 3 months at T1 and 5 months at T2 (including the summer holiday break equating to 3.5 months adjusted).

When considering rates of school absenteeism and changes over time it is was important to note that there has been long-term downward trend in levels of absenteeism in Wales (Davies, Huxley, & Taylor, 2017). In addition there has been variation of absenteeism observed across Wales, with the schools in this study (based in Gwynedd and Conwy, in North Wales) reporting absence rates well below the average for Wales (StatsWales, 2019; Welsh Government, 2019). Across Wales the percentage of all half-day school sessions missed by compulsory school age students in 2013/14 was 6.4% reducing to 6.2% in 2014/15. In Gwynedd, during 2013/14 5.8% of sessions were missed due to absence, compared with 6.1% of sessions missed in Conwy for the same period. The following academic year (2014/15), percentage rates of sessions missed reduced to 5.4% in Gwynedd and 5.8% in Conwy.

[8] Data was supressed where numbers are lower than N=7 to ensure data is not attributable to individuals.

Persistent absentees which were defined as 20% or more of school sessions missed may be higher in Year 11 at the end of compulsory education than in Sixth Form year groups (Davies et al., 2017). During 2012/13 academic year 8.8% of Year 11 students were classed as persistent absentees. The percentage of persistent absentees decreased the following academic year (2013/14) in Year 12 to 3.5% and reduced again in Year 13 (2014/15) to 1.4%. In the proceeding cohort of students this downward trend for decreasing rates of persistent absenteeism was also observed. When considering less persistent absence, in Year 12 (in 2013/14) 43% of students missed more than 5% of school sessions, the following year (in 2014/15) in Year 13 this reduced to 35.9%.

Valuation and associated costs of forgone education from unplanned school absences

There are a number of suggested approaches for valuing forgone education for inclusion in economic evaluation. Positive returns to an individual from attending formal education often involve consideration of increased academic attainment (qualifications) and future earning potential. The highest marginal rate of return from education comes from university education (Bhutoria, 2016).

The consensus on the impact of education on human capital has changed considerably over time, taking in to account factors such as prevalence of education by age and gender and the substantial change in industry through history (de Pleijt, 2018). Economists continues to be discuss the link between human capital and economic growth (de Pleijt, 2018), noting that investments in human capital are associated with higher Gross Domestic Product (GDP) and lower inequality (Bhutoria, 2016). Each additional year of education has been estimated to equate to between 18 per cent and 35 per cent higher GDP per capita.

The rate of return to education can also be expressed in annual per capita income (Andronis et al., 2019, p. 3)**.** In a UK context there are not published rates of return for Sixth Form attendance in 2012-2014 that were identified as part of this chapter and further literature and data would be needed to estimate the impact of school absence observed in this study in terms of human capital and per capita income.

Using the recent high-level estimate of £40,000 lost lifetime earnings per person from missing half a year of schooling during the covid-19 pandemic (Institute For Fiscal Studies, 2021) and a school year equating to a total 190 days per academic year (Long, 2021), a missed day of school could be valued at an estimated £421.05 of lost earnings over a lifetime. This estimate assumed that each day was valued equally and there was no compound value of missing culminative days of schooling all together.

One further approach that has been proposed is for school absence to be valued as equal to a day of lost wages (Andronis et al., 2019, p. 3), this is likely to be important when considering spill-over effects of time off school from study participants to parents who may need to take time off work to look after their children or for Sixth Form students holding part time jobs (with days off school which may also be

linked to missed work days). In 2019 the mean equivalised household disposable income of individuals was £35,900 (while the median income was £29,600). Based on the number of working days in 2019 this equates to a mean loss of income of £141.90 per day (median loss of income £117).The cost of a day of unplanned absence from school was valued in two ways, firstly, a cost of £421.05 per day from estimates of lost lifetime earnings, secondly, a cost of £141.90 per day was used relating to lost earnings from an estimate of one day of missed work associated with school absence.

Intervention costs

Full intervention costs as established in Chapter 3 for a range of MBPs were reviewed for relevance to the .b Foundations course delivered within schools as a programme embedded within the school curriculum. The programme was taught by the usual class teacher or teaching assistant within school hours. The staff costs for delivery were not deemed to be appropriate for inclusion in the intervention costs without also costing the staff time delivering the usual curriculum in the control condition. However, there were initial set up costs that warranted consideration with the MBP teachers required to undertake two levels of training, first an 8-week training to develop a personal mindfulness practice and then a teacher training to be able to deliver the MBP to others in the school. Teacher salary costs were estimated from NASUWT, the Teachers' Union, Teachers' Pay Scales 2018-20 for with a mid-spine point M3 classroom teacher gross annual salary of £27,652.55 (£34863.55 including on-costs) in 2019 (NASUWT, 2020) used in the base case costing and total working hours of 1,265 hours per year, resulting in an hourly rate of £27.56 (including on-costs). Course fees for mindfulness in schools teacher training were obtained from the Mindfulness in Schools website ("Mindfulness in Schools Project (MiSP)," 2020). Total set up costs were annuitised and discounted at a rate of 3.5% over a 5-year period (see Equation 3 and annuitisation methods reported in Chapter 4). Total ongoing costs consisted of teacher mindfulness supervision costs. Supervision costs were based on one hour per month of supervision costed as £50 per session by telephone or Skype, with cost estimates provided by a UK Centre for Mindfulness.

Patient Reported outcome measures and forms of economic evaluation to be piloted

This feasibility evaluation was used to assess the suitability of outcome measures including the EQ-5D-5L (described below) as a source of HRQoL utility values for the calculation of QALYs and the GHQ-12 (described below) as a screening tool for depression.

EuroQol-5 Dimensions – 5 level version (EQ-5D-5L)

The EQ-5D-5L (see Appendix 29) is a generic HRQoL questionnaire suitable for use with adult populations (Herdman et al., 2011; The EuroQol Group, 1990). This study includes a population of sixth form adolescents aged 16-17 and thus consideration of age-appropriate outcomes for this population

are important. With the age of study population close in years to adulthood and the absence of a suitable value set, the EQ-5D-Y (Youth Version) aimed at measuring HRQoL in children and adolescents (Wille et al., 2010) was not considered appropriate for use. Therefore, the EQ-5D-5L was used in this study. The appropriateness of the EQ-5D-5L and EQ-5D-Y in economic evaluations is considered in more depth in the discussion section of this chapter and in Chapter 6.

As with the EQ-5D-3L described in Chapter 4 the EQ-5D-5L questionnaire was formed of two distinct parts a descriptive system and visual analogue scale. The descriptive system questionnaire consisted of five questions, covering five health domains (mobility, self-care, usual activities, pain-discomfort, and anxiety-depression), each with five levels of severity responses (ranging from no problems to very severe problems). The responses provided a five-digit HRQoL profile score, or health state, for example 1-1-1-2-3 (there are 3125 different possible health states) which was then converted to a single index utility value through application of societal preference weights. In the UK societal preference weights have been developed for the EQ-5D-3L using representative population surveys using a time-trade off techniques to establish a vale for each health state (Dolan, 1997).

While societal preference weights have been developed for the EQ-5D-5L (Devlin, Shah, Feng, Mulhern, & van Hout, 2018; Devlin & van Hout, 2014), they have not been successfully validated. In line with the NICE position statement (NICE, 2019b) EQ-5D-5L profiles were mapped to the EQ-5D-3L through cross-walking methodology (van Hout et al., 2012) to result in 243 possible health states. UK adult population valuations for the EQ-5D-3L were then applied to provide utility values. The EQ-5D-5L questionnaire produced a possible range of scores between -0.59 and 1, with 1 meaning full HRQoL.

The EQ-VAS (visual analogue scale) was used as a thermometer style question with health today indicated on the chart and results scored between 0 (worst possible health) and 100 (best possible health).

The Short General Health Questionnaire (GHQ-12)

The GHQ-12 (see Appendix 30) consists of 12 questions (Goldberg & Williams, 1988). As a brief outcome measure with generic health questions it has been a popular tool for detecting psychological distress in non-clinical samples (Hankins, 2008). It has been validated for detecting depression in the general population (Lundin, Hallgren, Theobald, Hellgren, & Torgén, 2016). It has also been successfully used as a screening tool in adolescent populations (Baksheev, Robinson, Cosgrave, Baker, & Yung, 2011).

Various scoring methods have been validated for the GHQ-12 including the “Standard method (all items coded 0-0-1-1), Likert method (all items coded 0-1-2-3), and the Corrected method (positively phrased items coded 0-0-1-1 and negatively phrased items coded 0-1-1-1)” (Lundin et al., 2016, pp. 68–69).

Items were converted to index values using the Likert scoring method with possible ranges of 0-36. A clinical cut-off score of ≥12 Likert points was used to indicate clinical levels of depression. Alternative cut-off levels have been proposed for the standard and corrected scoring method (NICE, 2009b). However, the threshold of ≥12 Likert points is thought to have sufficient sensitivity and specificity "for separating those with depressive disorders from those without a depressive disorder" (Lundin et al., 2016, p. 72).

Data cleaning and validity checks for analysis

Validity of electronic data was assessed against key process criteria to identify out of range values against questionnaire scoring algorithms. For example, EQ-VAS scores above 100 or below 0 would need to be clarified and a high number of out-of-range values could provide valuable evaluations of both participant and researcher processes.

GHQ-12 question data ranged from values of 1 (as the lowest score) to 4 (as the highest score score). For the health economics study individual question values were transposed to fit with the 0-3 Likert scoring method with 1 converted to 0, 2 converted to 1 and so on.

In addition, there was one incidence of a half value recorded for GP attendances e.g., 4.5 GP visits for the preceding 3 months at baseline. To apply unit costs based on the average appointment length in the UK, all GP visits should be rounded up to the nearest whole number i.e., 4.5 becomes 5 visits. There was some evidence that EQ-5D-VAS had been scored with half values recorded e.g., 76.5.

Other trial process measures considered the inclusion of all participant ID numbers and timepoint information recorded against each row of data. For example, timepoint information was supplied as part of electronic data in the form of baseline (T0), post intervention (T1) and follow-up (T3), however, the specific dates of assessment were not available with the economic electronic data and were not requested at the point of data transfer. The study protocol indicated that data was planned for collection in January 2014, April 2014, and final assessment in September 2014, however, it was not possible to validate whether data was collected within these windows (e.g., within 1 month of assessment point) or whether any outcomes were delayed.

The timing of data collection is relevant for a future trial including whether a full period of resource use data can be captured or whether patterns of service use can be extrapolated from short recall periods to a longer time horizon. Timing of outcomes can be important with contextual factors having a potential impact of health over time and on expected patterns of resource use, for example understanding what relevant events are happening at the same time as data collection may be important e.g., students facing imminent exams may experience higher levels of stress than post exam period, if outcomes are

collected significantly out of window, then the outcomes may not be comparable to the rest of the sample. The health economist working on future studies should ensure that date of assessment is included with economic data and that within window ranges are pre-defined along with details of any acceptable adjustment to provide a full range of cost data for the study period.

In addition, the recall period of the unplanned absences provided by schools which was specified at the study design stage was not represented in the health economics data, with unplanned leave (days) provided at each timepoint rather than for the academic year proceeding baseline (Sept 2012 – July 2013) and the following year i.e., during and after the intervention (Sept 2013 – July 2014).

MBP intervention attendance data was not available in the electronic economic dataset. The source study protocol outlined that school teachers collected information on intervention attendance. Future trials should ensure that protocol adherence measures are built into studies and available to the health economist to enable both per protocol and intention to treat analysis. Major protocol violations such as participants attending the non-allocated intervention or not attending any sessions can provide valuable information about the feasibility of a future trial and the acceptability to participants of the intervention itself or any research processes such as randomisation if included. Barriers to attending the intervention could be further explored through qualitative or survey methods to identify any changed to the protocol and patient facing information that may be needed to ensure a successful future trial. Health economics data was provided by intervention group but school level information within groups (*N=2* schools per group) was not obtained as part of the economic data. Information at a school or site level may be important to assess whether there is an impact of clustering on analysis i.e., whether each school provide comparable result or whether there is important difference which may explain variation in results. Given consideration of factors which influence successful implementation of MBPs and the potential for a whole school approach to delivery, variation in schools depending on approach to implementation may warrant further consideration in future economic analysis.

Assessment of missing data

Outcome data completeness was assessed providing information about the feasibility of collecting outcomes and the completeness of the sample for data analysis. Missingness was considered in terms of levels of 1) completely missing, with participants having no data at all after being assigned an ID number, 2) partially missing, with participants having data at A) one or more timepoint or B) one or measure available. Data that was completely missing was considered as the participant having been withdrawn from the study and was not included in the sample size for analysis. Data that was partially missing was included where possible with pairwise deletion of outcomes used to provide an available case sample (where missing values were only dropped when comparing the outcome of interest) and

listwise deletion providing a complete case sample where a case was dropped from the analysis if the primary outcome was missing. While pairwise deletion enabled more of the data to be included in the analysis each computed statistic may be based on a different subset of cases limiting comparability.

Little's MCAR test was used to assess whether data was considered missing completely at random. Imputation of missing data was not performed in this feasibility study to minimise the introduction of bias, listwise deletion of missing values was conducted where missingness was considered to be completely at random to provide a complete case sample.

The complete case sample excluded Year 13 pupils as all participants aged 18 were lost to the final follow-up which was conducted in the September after they had left Sixth Form.

Analysis sample

For the purpose of exploring the feasibility assessment results were explored both in terms of available case (pairwise deletion) and repeated on a complete case basis (listwise deletion) with complete outcomes of EQ-5D-5L [excluding VAS], GHQ-12 and GP resource use at T0, T1 and T2.

Perspectives

The health economics component of the feasibility study was conducted from a primary NHS health care and education sector perspective with a secondary societal perspective including the addition of forgone education impacts.

Methods of analysis

Statistical software

All analysis was conducted in Microsoft Excel 365 and IBM SPSS Statistics 27.0.

General approach to pilot health economics analysis

While no full economic evaluation was conducted as part of this pilot, methods for a primary cost-utility analysis and a secondary cost-effectiveness analysis were explored. The approach in the health economics component of the feasibility study was largely descriptive to plot and explore patterns and trends in data.

All statistical analysis was conducted not with the purpose of being considered definitive but to pilot methods and to identify trends in the data that warrant further consideration in follow-up research. For

example, Age and Gender were explored as potentially important covariates for future analysis, however, the sample of subgroups was too small for meaningful inclusion within the pilot analysis.

While groups were matched (but not randomised) it was important to assess whether groups had equivalence at baseline. Baseline differences for cost outcomes and effectiveness outcomes were compared to indicate potential interpretation considerations of the analysis.

Descriptive statistical methods: Costs

GP resource use

Descriptive statistics for GP visits were calculated for each group at each timepoint on an available case and complete case basis. The total [sum of means i.e., $=(M^{T0}+M^{T1}+M^{T2})$] for the 9-month recall period included within the three timepoints was calculated. Eligible GP costs for the purpose of the health economics assessment were GP resource use reported at T1 and T0. Mean GP visits were extrapolated to a year (assuming linearity of GP visits over time) and were compared with national averages.

GP service use frequencies were descriptively compared against classifications of 'frequent attenders' to identify any high utilisers of services. There was no commonly recognised rating of what constituted a 'frequent attender', with significant variation in the number of visits classified across previous studies. For this study GP resource use attendance over a period of 3 months was classified as either 1) frequent use (≥3 visits[9]) 2) normal use (1-2 visits)[10] or 3) no use (0 visits). Resource use that exceeded the population mean number of GP visits per year (identified in a recent previous study as six and a half visits per year) (Gerich, Moosbrugger, & Heigl, 2020) was considered to be very frequent attendance. Data was suppressed to whole sample when the sample was less than 7.

GP attendance descriptive statistics were explored by gender on both an available and complete case.

GP visits were costed using national unit costs (Curtis & Burns, 2019) and all costs expressed in 2019 Pounds Sterling (£). A unit cost of £39 per GP visit was applied. While the data was collected in 2014, due to delays in data entry and access to data the database was not finalised and locked until 2020. All costs were reported in the cost year 2018/19 to better reflect current decision-making contexts. Resource use costs were not discounted as the study period was less than 12 months.

Forgone education

[9] Using Jiwa (2000)'s regular attender classification of one or more visits per month.

[10] Based on Morris et al (2021)'s normal attender classification with visits less than once a month.

Forgone education was calculated as the mean number of unplanned leave days from school reported. Descriptive statistics were produced on an available case basis and on a complete case basis.

Total costs

Total costs were calculated as the mean cost of GP resources used during the study time horizon (T1 and T2), eligible intervention costs represented as a cost per pupil, along with estimates of forgone education costs. The total costs were varied based on the differential value of forgone education applied (see forgone education valuation methods described above).

Descriptive statistics methods: Outcomes

EQ-5D-5L

Ceiling and floor effects of the EQ-5D-5L measure were explored on an available case and repeated on a complete case basis. Ceiling effects were defined as ≥15% of responders at each timepoint recording no problems in each domain, scoring the highest possible utility value. Floor effects were defined as ≥15% of responders at each timepoint as the lowest possible scores, of states valued as zero or as negative values.

Mean values, mean difference and percentage change were calculated on an available case and repeated on a complete case basis. EQ-5D utility mean values were compared descriptively with age-adjusted population norms (Janssen et al., 2019; Kind et al., 1999). Mean difference was calculated by subtracting the first mean value from the follow up mean value exploring differences between baseline (T0) and post intervention (T1), then between T1 and follow up (T2), and finally between T2 and T0. Percentage change was calculated by subtracting the before timepoint mean value (T0 or T1) from the subsequent timepoint mean value (T1 or T2); divided by the before value. Finally, results were multiplied by 100 to report the percentage change between the two timepoints under consideration. When considering change over time for utility the minimally important difference (MID) was considered as a mean difference over 0.063 (McClure et al., 2017).

On a complete case basis, changes in EQ-5D health profiles and any direction of change over time was explored using the pareto principle, with the percentage of each group meeting the classification of their health profile either remaining the same, worsening, improving or incurring a mixed change across the domains observed. The percentage difference between groups meeting these classifications was compared between T1 and T0, T1 and T2 and T2 and T0.

On a complete case basis mean QALYs were calculated using the AUC method using participants' utility scores at each timepoints (using the same method outlined in Chapter 4 by Hunter et al., 2015). Mean

QALYS were calculated on a complete case basis, bootstrapping 10,000 replications for 95% confidence intervals. These were compared between groups with incremental QALYs calculated as the difference between means at 8 months.

EQ-5D profiles domains were explored on a whole sample basis, plotting those that reported no problems compared with some problems, expanding out to explore levels of severity within the problems as a feature of the five level EQ-5D descriptive system. The proportion of the whole sample reporting problems on each domain was compared over time. Group level responses to the anxiety/depression health domain were compared descriptively with rates as indicated by the GHQ-12 screening threshold for depression (scores of ≥12).

The 'Pareto classification of health change' (Devlin, Parkin, & Browne, 2010; EuroQol Research Foundation, 2019) was applied and explored in terms of whether there was 1) an improvement on one or more domain scores (classified as 'Improve'), 2) a worsening of one or more domain scores (classified as 'Worse'), 3) no change to domain scores (classified as 'Same') or 4) a mixed response where there is both improvement and reduction across the health profile (classified as 'Mixed'). Descriptive statistics were presented on the proportion of health change using the Pareto classification system, with a descriptive comparison over time and by group.

Depression screening

Ceiling and floor effects were assessed for the GHQ-12. Mean GHQ-12 scores were calculated at each timepoint and compared descriptively between groups. GHQ-12 descriptive statistics (mean difference percentage change and percentage above clinical cut-off) were calculated on an available case basis and repeated on a complete case basis. Change of scores over time were explored to capture any improvement or worsening of health over time.

On a complete case basis GHQ-12 scores were plotted against threshold for depression and patterns of depression case status over time were explored on a complete case basis. With a descriptive comparison between groups across the mapped classifications.

Incidences of participants reporting scores of 12 or more, classified as the clinical cut-off indicating depression, were compared across timepoints as a whole cohort, treatment group, and individual level. Cohort levels of depression at baseline were reviewed to assess opportunities for depression onset prevention. Treatment group depression levels were compared at baseline for equivalence and for difference between groups at each timepoint. Individual levels of depression were mapped over time to explore the patterns of depression occurring through the duration of the study (Jan – Sept 2014), in terms of depression level at T0, first episode if depression was not present at baseline, remission from a

previous episode, and relapse into a new episode. Figure 19 shows the depiction of progression of depression stages over time used for reference in this research.

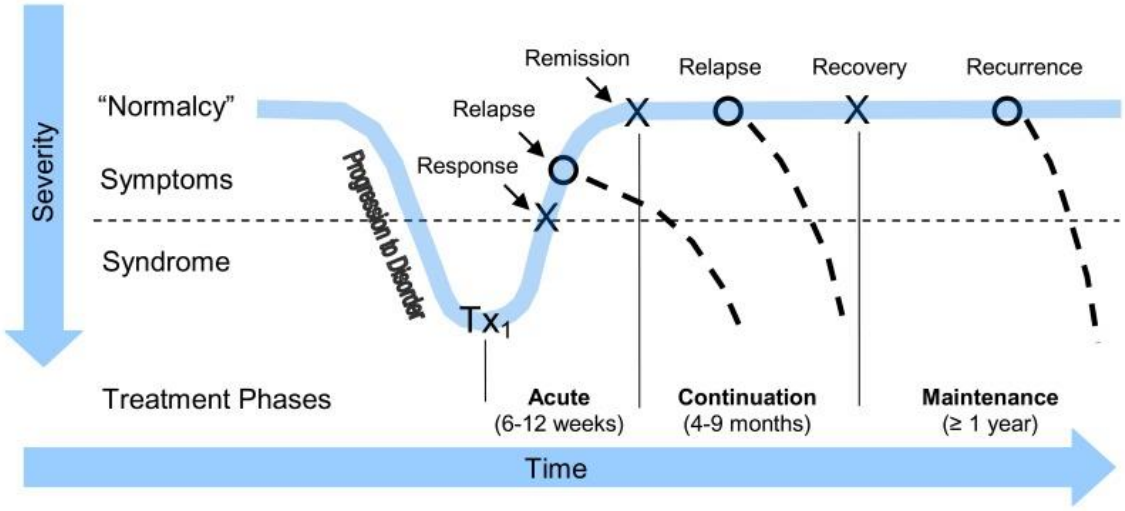


Figure 19: Progression of depression severity and stages over time.

"Source: Recreated based on Kupfer, 1991. Tx_1=treatment attempt 1; dashed lines indicate hypothetical worsening of depressive severity. Remission, the goal of for treatment, refers to the resolution of depressive symptoms and return to premorbid functioning; response refers to substantial clinical improvement which may or may not reach remission" (Gartlehner et al., 2015)

Depression case status over time was considered using patient-level data against a case matrix of patterns of depression status over time (Table 46). These eight profiles of patterns of depression are shown in Figures 20 to 27 below, adapted from diagrams by Lalor et al (2015). Outcomes were presented as dichotomous with depression case (GHQ-12 scores ≥12) depicted by 1 on the plots and no depression case (GHQ-12 scores <12) depicted by 2. The percentage of each group allocation meeting the classified pattern was assessed, banded in intervals of 5% (with 0-15% category suppressed due to the small sample size). The diagrams and patterns reported did not contain any details on severity or trends towards improving or worsening within the case and no case categories.

Table 46: Case matrix of patterns of depression cases over time

	Matrix Key: **X** *≥12 (GHQ-12)* ☐ <12 (GHQ-12)	**Case Matrix**		
		T0	**T1**	**T2**
1.	Constant Low - Persistent case depression at all timepoints	**X**	**X**	**X**
2.	Resolving (delayed) - Baseline depression and T1 case, 'remission' at T2	**X**	**X**	☐
3.	Spike - Baseline depression, 'remission' at T1 mid-point improvement, and relapse to depression at T2	**X**	☐	**X**
4.	Resolving (early) - Baseline depression, 'remission' at T1, and sustained 'recovery' at T2	**X**	☐	☐
5.	Worsening (early) – Mid-point onset with constant low - T1 depression onset, with no remission / recovery by T2	☐	**X**	**X**
6.	Trough - Mid-point T1 depression onset, with remission / recovery T2	☐	**X**	☐
7.	Worsening (delayed) - Late onset depression at T2, no prior depression at T0 or T1	☐	☐	**X**
8.	Constant High - No depression at any timepoint	☐	☐	☐

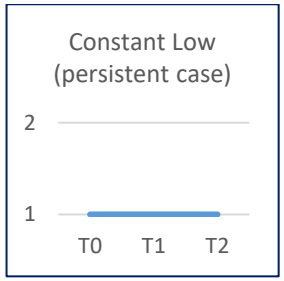


Figure 20: Constant Low (persistent case)

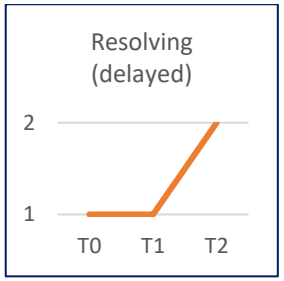


Figure 21: Resolving (delayed)

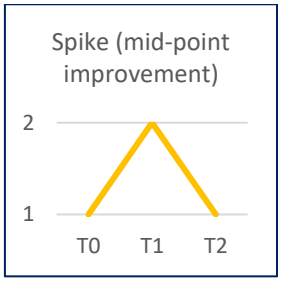


Figure 22: Spike (mid-point improvement)

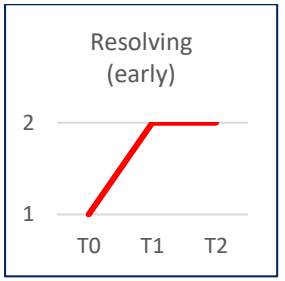


Figure 23: Resolving (early)

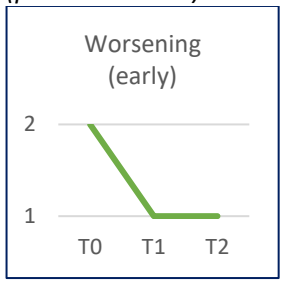


Figure 24: Worsening (early)

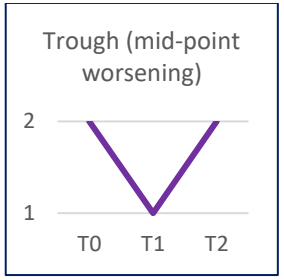


Figure 25: Trough (mid-point worsening)

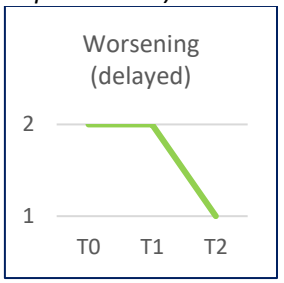


Figure 26: Worsening (delayed)

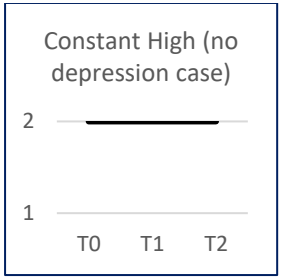


Figure 27: Constant High (no depression case)

Inferential statistical analysis: Outcome and Costs

Normality tests at baseline

Baseline costs (GP resource use), EQ-5D-5L and GHQ-12 were assessed with for Kolmogorov-Smirnov Normality Test's for normality within the sample (either available case or complete case). This was used to assess the distribution of data and informed the statistical tests used for establishing differences (described in full below).

Inferential statistics for considering baseline equivalence for costs and outcomes

On an available case basis independent sample parametric tests (T-Test) or non-parametric tests (Mann Whitney U) assessed differences at baseline for GP attendance, EQ-5D and GHQ-12. In a complete case basis difference between groups were repeated for GP attendance, EQ-5D and GHQ-12.

Inferential statistics to consider gender as a potential covariate for GP resource use comparisons

Repeated measures of GP resource use at each timepoint were ranked and compared using non-parametric Friedman's test, including gender (Male or Female) as a categorical variable to split the output. Exploring gender as a categorical was applied across the whole sample of participants on a complete case basis to maximise the sample size.

Inferential statistics for considering utility and depression differences between group and over time

To compare both utility and depression between groups and over time, a complete case assessment was conducted using a repeated measures general linear model multivariate analysis of variance test, with 95% confidence intervals produced around mean estimates. The independent variable of group allocation (2 groups) was used to compare dependent variables (EQ-5D and GHQ) with the factor of time (3 levels) considered for within group effects. No covariates were included in the analysis, the Bonferroni method was applied to control for multiple comparison testing. Results from the MANOVA from both a multivariate and univariate analyses were reported. Where multivariate analysis indicated significant differences between groups or by factor of time, results of the embedded univariate analysis were available to assess any impact of by outcome measure. Where significant results were identified in cases where outcome data was not considered to be normally distributed in baseline assessments, the embedded homogeneity test results were reviewed to establish if assumptions of equal distribution were violated (as indicated by a significant Levene's Test of Equality of Error Variance). Where homogeneity was not established alternative non-parametric tests for differences between data distributions were available for post hoc analysis.

Results

First this section reports on findings in relation to study sample size, missing data, demographics, and descriptive statistics; and then reports on the pilot inferential statistical analysis relating to study costs and outcome as outlined in the methods.

Sample size

A total of ninety-nine Sixth Form students participated in the study, after allocation of schools and consent, the sample size per group was *N=40* in the MBP intervention training group and *N=59* in the teaching as usual matched control schools. One participant did not provide any data at any timepoint and was withdrawn from the study resulting in a revised sample size of *N=58* in the control group.

Missing data

Complete economic outcome data consisting of EQ-5D-5L, EQ-5D VAS and GHQ-12 at every timepoint was available for 48% of the MBP group (*N=19*) and 21% of the control group (*N=12*). Complete EQ-5D-5L and GHQ-12 inclusion was increased when excluding the EQ-5D VAS from the completeness criteria, with 58% of the MBP group (*N=23*) and at 28% of the control group (*N=16*). There was the least amount of missingness for the GHQ-12 alone with 63% complete in the MBP group (*N=25*) and 31% complete in the control group (*N=18*).

The complete case sample size was slightly reduced when including complete GP resource use data at both T1 and T2 timepoints with 63% complete for the MBP group (*N=25*) and 28% complete in the control group (*N=16*). Complete school attendance data at T1 and T2 timepoints was available for 63% of the MBP group (*N=25*) and 26% of the control group (*N=15*).

Across the whole sample there was substantially more missing data at T2 with 58% missing entirely (*N=57* missing) than at T1 where 18% were missing (*N=18* missing) which can be largely explained by attrition of Year 13 cohort who were no longer at the school at the T2 final follow-up timepoint (September 2014).

When considering completeness across both outcome and cost combined (i.e., GP resource use data at both T1 and T2, EQ-5D-5L [excluding VAS] and GHQ-12 at all timepoints) there was a complete case sample size of 58% (*N=23*) in the MBP group and 26% (*N=15*) in the control group. When also including school absence at T1 and T2 58% (*N=23*) of MBP group had complete data compared with 24% of the control group (*N=14*). The sample size was not increased through excluding secondary GHQ-12 outcomes for a complete case cost-utility analysis.

Patterns of missingness and missing value analysis of all economic outcomes and resource use indicated that missing data was missing completely at random as assessed using Little's MCAR test, *χ2(147)=144.61, p=.540*.

Demographics

The sample of students that opted in to the research were reported to be representative of a sixth form population cohort (Sanger et al., 2018).

Age

Age was reported in whole years, ranging from 16 years to 18 years old, with the median age 17 years old across the sample. Of the total sample there was a higher proportion of Year 13 participants in the control group, resulting in a higher mean age in the control group (*M=17.10*) compared with the MBP group (*M=16.58*). The control group consisted of 83% aged 17 or 18 years compared with the MBP group where 53% were aged 17 or 18 years.

The complete case sample excluded Year 13 pupils as all participants aged 18 were lost to final follow-up. On a complete case basis 48% were aged 17 in the MBP group compared with 33% in the control group, with the rest of the groups aged 16 years old.

Gender

The sample included more female (*N=58*) participants than male (*N=38*) participants[11]. In the total sample size, the control group had a higher percentage of females (64%) compared with the MBP group (55%). On a complete-case basis females represented 67% of the control group compared with 61% of the MBP group.

GP Resource use results (available case)

On an available case basis (pairwise deletion), GP resource use data was not normally distributed. Results were significant on Kolmogorov-Smirnov Normality Test for GP resource use *D(96)=0.362, p=.000.* There were no significant differences between GP use of groups on the independent samples Mann Whitney U test GP *U(96)=1038.50, p=.570*.

Table 47 shows the mean number of GP visits at each timepoint, by group allocation. The total number of GP visits reported from all time points was 2.163 for the MBP group and 2.61 for the control group.

[11] Demographic data was missing for *N=2* participants.

Extrapolated to a year the average consultations would be 2.884 in the MBP group and 3.48 in the control group, which is within the expected range of national averages for this age group and period (2012-2014).

Table 47: Descriptive statistics of GP visits by timepoint and group (available case)

Intervention	Timepoint	N	Minimum	Maximum	Mean	Std. Deviation
MBP group	T0	38	0	10	0.87	1.95
	T1	34	0	10	0.74	1.76
	T2	25	0	5	0.56	1.29
Control	T0	58	0	6	0.80	1.38
	T1	46	0	5	0.87	1.36
	T2	16	0	11	0.94	2.74

Frequent attenders (available case)

At each timepoint there were very low incidences of very frequent attenders with the highest number of GP visits during a single timepoint recorded as 11 visits (Table 47).

GP service use on an available case sample (*N=96*) at baseline indicated 13% of the sample reporting frequent GP use, 21% reporting normal to occasional attendance and the majority 67% reporting no visits to GP services in the 3 months before the assessment. At T1 (*N=80*) there was an increase in participants visiting the GP at least once with 41% reporting normal use or more frequent use. At T2 (*N=41*) the proportion of participants reporting no visits to the GP increased to 76%, slightly above rates at baseline.

GP resource use results (complete case)

On a complete case basis there was no difference between costs and GP resource use identified at baseline on a complete case basis as indicated by the results of the Mann Whitney U test, *U(38)=162.500, p=.768.*

Figure 28 depicts the mean number of GP visits over time by group (on a complete case basis). For the economic study period (data collected at T1 and T2) the mean number of GP visits for the 3-month recall period between T0 and T1 were low in both groups with less than 1 visit to the GP on average (*M=0.91*) in the MBP group and the control group (*M=0.80*). Mean GP visits in the MBP group were lower at T2 for the 3-month period preceding the assessment (*M=0.35*). GP visits rose slightly in the control *(M=1.00)* as reported at T2. Mean GP visits for the 6-month recall period were lower in the MBP group (*M=1.26*) compared with the control group (*M=1.8*).

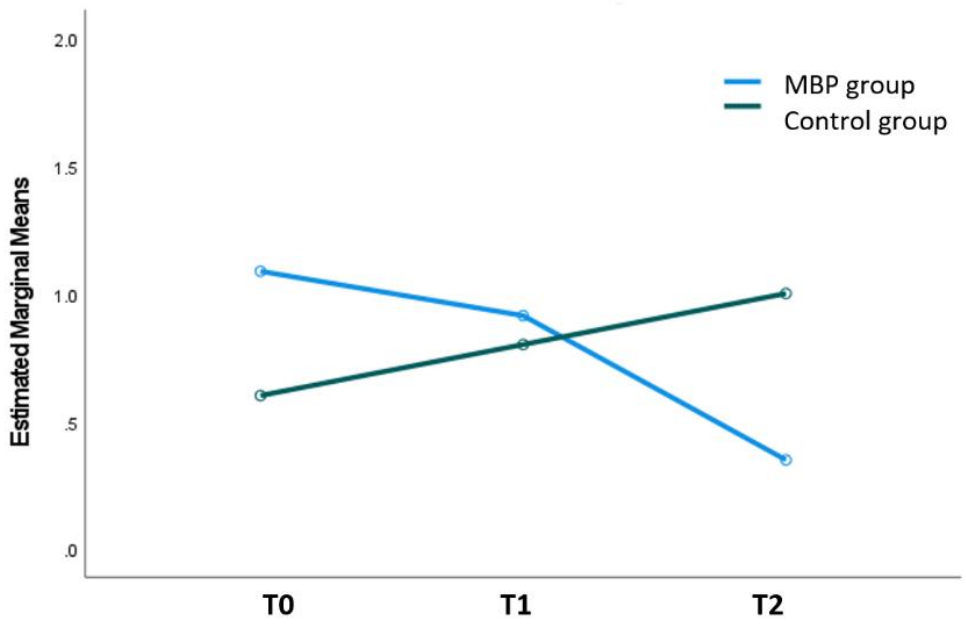


Figure 28: Estimated marginal means of GP attendance over time (complete case) by treatment group

GP resource use frequent attenders (complete case)

On a complete case basis data on frequent attenders of GP services is reported as a whole sample (*N=38*) and condensed further without treatment groups to protect confidentiality. There was a small number of regular attenders (frequent use) at baseline (13% of the whole study sample) with normal to no resource use representing the majority of the sample in both groups (Table 48).

Table 48: Frequency of GP attendance by group at baseline (complete case).

Intervention	Frequent use (3 or more)	Normal use (1-2)	No use (0)
MBP (*N=23*)	13%	16%	71%
Control (*N=15*)			

GP visits by participant gender (available case)

On an available case basis, the mean number of GP visits was higher for females than males at all timepoints (Table 49).

Table 49: Descriptive statistics of GP attendance by timepoint and gender of participant (available case)

Time	Gender	N	M	SD	95% confidence intervals Lower Bound	Upper Bound
TO	Female	58	0.97	1.48	0.58	1.36
	Male	28	0.61	1.81	0.11	1.20
T1	Female	47	0.98	1.84	0.44	1.52
	Male	31	0.61	0.95	0.26	0.96
T2	Female	26	1.04	2.41	0.07	2.01
	Male	15	0.13	0.35	-0.06	0.33

GP visits by participant gender (complete case)

On a complete case basis considering GP attendance by groups and gender, data is only partially reported with information suppressed where the sample reduced to N<7 (see Table 50).

A non-parametric Friedman's test of difference among repeated measure indicated that gender may be an important covariate for future analysis with a significant difference in GP attendance over time for males, $X^2_F(2)=7.913, p=.019$, but not females $X^2_F(2)=0.558, p>.05$.

Table 50: Descriptive statistics of GP attendance by timepoint, group and gender of participant (complete case)

Time	Group	Gender	M	SD	95% confidence intervals Lower Bound	Upper Bound
TO	MBP	Female	0.929	1.592	0.010	1.847
		Male	1.333	3.279	-1.187	3.854
	Control	Female	0.900	1.595	-0.241	2.041
		Male	*	*	*	*
T1	MBP	Female	0.929	2.645	-0.598	2.456
		Male	0.889	0.782	0.288	1.490
	Control	Female	1.100	1.524	0.010	2.190
		Male	*	*	*	*
T2	MBP	Female	0.500	1.160	-0.170	1.170
		Male	0.111	0.333	-0.145	0.367
	Control	Female	1.500	3.408	-0.938	3.938
		Male	*	*	*	*

* data is supressed when N<7

GP resource use costs

The results of the complete case costing of GP resource use indicated the mean cost of GP visits in the MBP group was £35.61, compared with £31.20 for the control group at T1. Mean GP costs in the MBP group reduced at T2 for the 3-month period preceding the assessment with a mean cost of £13.57 per

participant. Mean GP costs rose slightly in the control to at T2 with a mean cost of £39. Mean GP visits for the 6-month recall period costed £49.18 in the MBP group compared with the control group where mean costs were £70.20 in the control group. If GP resource use was extrapolated to the full duration of the trial i.e., from 6 months to 8 months mean costs would be £65.57 in the MBP group and £93.60 in the control.

Forgone education (unplanned leave) results

Across the whole cohort (on a complete case basis), there was a combined sample average of *M=3.72* (*Mdn=0.5*) number of days absent from school in the preceding academic year (2012/13) at baseline. By group there was a higher number of days of school in the MBP group (*M=4.48*; *Mdn=3*) compared with the control group (*M=2.75; Mdn=0*).

Reported unplanned absence at baseline was generally low with 79% missing less than 5% of school sessions[12], 18% missing between 5-10% of sessions, 3% reported missing between 10-20% of sessions and no student reporting an absence equivalent to persistent absentees for the previous academic year. At baseline mean absence was higher for students aged 17 (in either Year 12 or 13) (*M=4.59 SD=4.971 Mdn=3*) than for students aged 16 (Year 12) (*M=3.09, SD=5.415, Mdn=0*). There were no participants aged 18 (in Year 13 2013/14) in the complete case sample.

On a complete case basis, at post intervention unplanned absent days were similar between the MBP group (*M=4.87, SD=5.29, Mdn=3*) and the control group (*M=4.14, SD=5.26, Mdn=2*). At follow-up unplanned absent days were lower in both the MBP group (*M=3.11, SD=2.75, Mdn=3*) and control group (*M=3.00, SD=4.74, Mdn=2*).

[12] Number of school sessions estimated to be 155 days (310 half day sessions), with 20% absence equating to 31 days (62 half days) missed.

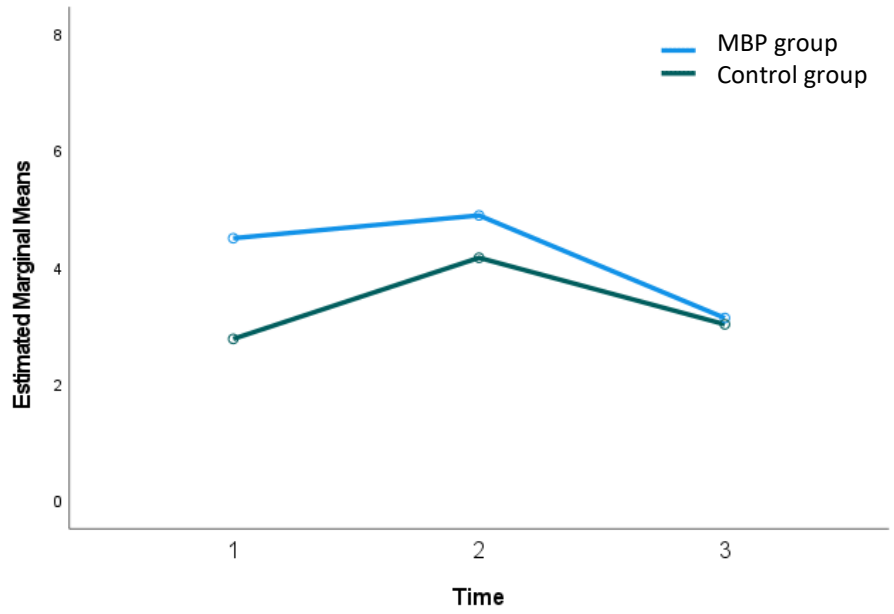


Figure 29: Estimated marginal means of unplanned school absence over time (complete case) by treatment group

Available case descriptive statistics for self-reported unplanned leave is presented by group and timepoint (see Table 51). The mean days absent for 2012/13 year was higher in the control group compared to the MBP (*Mean difference=1.625 days*). For both groups the number of unplanned days absent reported was lower at T1 than T2, however, as the period of recall for post intervention and follow-up data is uncertain it is not possible to determine whether these points are comparable.

Table 51: Descriptive statistics for self-reported unplanned leave (Days) by group and timepoint (available case analysis)

Intervention	Outcome	N	Min.	Max.	Mean	Std. Deviation
MBP group	T0	36	0.0	23.0	3.63	4.93
	T1	34	0.0	20.0	4.21	5.03
	T2	25	0.0	10.0	3.26	3.05
Control	T0	58	0.0	30.0	5.25	5.54
	T1	45	0.0	30.0	4.71	5.97
	T2	16	0.0	17.0	2.81	4.64

To consider absence of participants in all age groups (including those not included at T1 and T2), data was aggregated for both treatment groups and considered on an available case basis at baseline. Mean absence days (for academic year 2012/13) were highest for students aged 18 (*M=5.92, SD=4.486, Mdn=5, N=18*). Mean absence days were also higher for students aged 17 (*M=5.05, SD=5.627, Mdn=4, N=49*) compared with those aged 16 (*M=3.00, SD=5.144, Mdn=0, N=27*).

Time off school and financial value of forgone education

On a complete case basis, the mean number of unplanned absent days during the study period (reported at T1 and T2) were slightly higher in the MBP group (*M=7.98*) compared with the control group (*M=7.14*).

When valued as lost lifetime earnings for the student this equated to mean costs of £3,359.98 in the MBP group and £3,006.30 in the teaching as usual group.

When valued as equivalent to a day of lost disposable income this equated to mean costs of £1,132.36 in the MBP group and £1,013.17 in the teaching as usual group.

MBP Intervention Costs

Total set up costs discounted and annuitized over a 5-year period equated to £494.84 per year. Total annual costs for delivering .b Foundations in schools were estimated to be £1094.84 per year (for 5 years) with costs reducing to £600 per year thereafter. The costs per student was estimated to be £36.49 based on a class cohort of *N=30* pupils and only one course delivered per year.

Table 52: Top-down intervention costs for MBP set up and on-going teacher supervision

	Number of units	Unit cost	Total cost
Estimated set-up costs			
Staff salary training (hours)	49.5	£27.56	£1,364.22
Course fees initial .begin training	1	£150	£150
Course fees Teach .b training	1	£720	£720
Total set-up costs			£2,234.22
Total annual set up costs (annuitized over 5 years)			£494.84
Estimated ongoing costs			
Supervision costs	12	£50	£600
Total annual on-going costs			£600

Total costs

Combining average MBP intervention costs per pupil with average GP resource use costs would increase total per pupil costs to £102.06 in the MBP group. With no additional intervention costs applied to the teaching as usual control cohort, costs remained at an average £93.60 per pupil.

Including forgone education cost estimates with a day of unplanned absence valued as lost lifetime earnings, would increase total mean costs to £3,462.04 in the MBP group and £3,099.90 in the teaching

as usual group. While including forgone education cost estimates with a day of unplanned absence equivalent to an average day's wages in the UK, would result in total mean costs of £1,234.42 in the MBP group and £1,106.77 in the control group.**Descriptive statistics: outcomes**

Normality tests

On an available case basis (pairwise deletion), data was not normally distributed. Results were significant on Kolmogorov-Smirnov Normality Test for EQ-5D *D(95)=0.192, p=.000*; and GHQ-12 *D(96)=0.145, p =.000*. This was evidenced with a high proportion of participants having full health (in the EQ-5D).

Normality tests were repeated for complete case baseline outcomes and cost, data was considered normal by dependent variable grouping for GHQ-12 data with Kolmogorov-Smirnov Normality Test result non-significant, *D(39)=0.109, p=.200*. EQ-5D was not normally distributed with Kolmogorov-Smirnov Normality Test results significant, *D(38)=0.180, p=.003,* on a complete case basis. Data was normal or trending towards normal when grouping by condition factor with non-significant results for the MBP group, *D(23)=0.153, p=.171*; and contrasting results for the control group, *D(15)=0.224, p=.042*.

Health Related Quality of Life and utility (EQ-5D-5L)

Baseline equivalence

An independent samples Mann Whitney U non-parametric test was performed to assess differences at baseline. There were no significant differences between groups on EQ-5D-5L on either an available case basis *U(95)=907.00, p=.175,* or on a complete case basis *U(38)=162.500, p=.768.*

Review ceiling and floor effects

The EQ-5D-5L displayed high levels of ceiling effects (28% to 48%). On a complete case basis ceiling effects for the EQ-5D-5L were observed in 21% to 29% of all participants. The EQ-5D VAS had no observed ceiling effect (on both available case and complete case basis). There was no evidence of floor effects observed for the EQ-5D-5L or the EQ-5D VAS.

EQ-5D utility values (descriptive statistics)

Available case (pairwise deletion) sample

Table 53 shows the mean EQ-5D scores by group and timepoint, on an available case basis. There was a small increase in mean scores in both groups on the EQ-5D-5L at T1 before a reduction at T2. Mean scores at T2 were below mean levels at T0 in both groups.

Table 53: Available case (pairwise deletion) descriptive statistics for EQ-5D-5L and EQ-5D VAS by treatment group and timepoint

Group	Outcome (timepoint)	N	Min.	Max.	Mean	Std. Dev.	Median
MBP group	EQ-5D-5L (T0)	38	0.635	1	0.85	0.11	0.84
	EQ-5D VAS (T0)	34	40	100	80.57	14.14	85
	EQ-5D-5L (T1)	30	0.570	1	0.87	0.13	0.88
	EQ-5D VAS (T1)	29	70	98	88.09	7.40	90
	EQ-5D-5L (T2)	25	0.617	1	0.84	0.12	0.84
	EQ-5D VAS (T2)	25	56	100	80.04	13.00	80
Control	EQ-5D-5L (T0)	57	0.635	1	0.88	0.10	0.85
	EQ-5D VAS (T0)	53	32	100	79.70	11.02	80
	EQ-5D-5L (T1)	43	0.380	1	0.90	0.14	1
	EQ-5D VAS (T1)	43	50	100	81.98	11.73	85
	EQ-5D-5L (T2)	17	0.218	1	0.81	0.20	0.84
	EQ-5D VAS (T2)	17	35	99	75.41	15.49	80

Table 54 shows the mean difference and percentage change over time in mean utility by group. There was a disutility in both groups with a negative mean difference reported at both T1 and T2. The disutility was larger in the control group than the MBP group, with a 7% reduction in utility in the control group compared with a 1% reduction in utility in the MBP group. There was no MID change observed for the MBP group, however, the mean scores for the control cohort reduced by more than the MID.

Table 54: EQ-5D-5L mean difference between timepoints and percentage change over time by condition (available case)

	MBP		Control	
Timepoints	Mean difference	% change	Mean difference	% change
T0-T1	0.02	3%	0.02	2%
T1-T2	-0.03	-4%	-0.08	-9%
T0-T2	-0.01	-1%	-0.07	-7%

Note negative mean and percent change values denotes an improvement in GHQ-12 scores.

**Means and standard deviations rounded up to 2 decimal places and percentages to nearest whole percent.*

In Figure 30 mean EQ-5D-5L utility values are plotted by group against timepoint to observe changes over time.

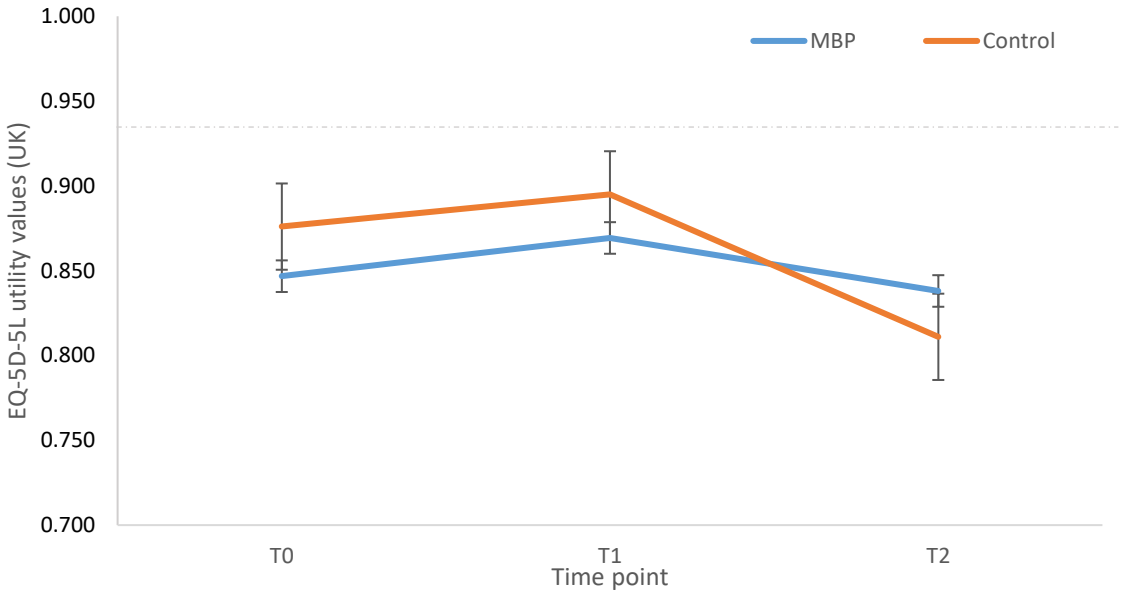


Figure 30: EQ-5D-5L mean index values for MBP and control conditions, at baseline (T0), post intervention (T1) and follow up (T2): Available Case (pairwise deletion)

EQ-5D population norms

On an available case basis baseline (T0) EQ-5D-5L values for both the MBP group (*M=0.847*) and control group (*M=0.876*) are below the UK population norm for 18-24 year old index value of 0.934 (Janssen et al., 2019). EQ-5D-5L mean index values do not reach population norm levels at any timepoint (see dashed line on Figure 30). While EQ-5D-5L index values increase slightly at T1, they decline at T2 to below baseline levels, in both intervention and control group.

Complete case (listwise deletion) sample

Table 55 reports on descriptive statistics for EQ-5D-5L on a complete case basis with mean values reported by group. On a complete case basis mean EQ-5D-5L utility values at baseline were *M=0.84, SD=0.10* (MBP) and *M=0.88, SD=0.09* (control). At T1 post intervention *M=0.84, SD=0.13* (MBP), *M=0.84, SD=0.10* (control). The mean difference between groups was -0.04 with MBP group mean lower than the control group at baseline. There was no difference between group means at T1. At T2 the mean difference between groups was 0.04 with the MBP group mean higher than the control group.

Table 55: Complete case (listwise deletion) descriptive statistics for EQ-5D-5L by treatment group and timepoint

Group	Outcome (timepoint)	Min.	Max.	Mean	Std. Dev.	Median
MBP group (*N=23*)	EQ-5D-5L (T0)	0.68	1	0.84	0.10	0.84
	EQ-5D-5L (T1)	0.57	1	0.84	0.13	0.81
	EQ-5D-5L (T2)	0.62	1	0.84	0.13	0.84
Control (*N=15*)	EQ-5D-5L (T0)	0.72	1	0.88	0.09	0.85
	EQ-5D-5L (T1)	0.38	1	0.84	0.10	0.84
	EQ-5D-5L (T2)	0.22	1	0.80	0.20	0.84

Table 56 shows the mean difference in utility values over time and by group on a complete case basis. Over time the mean utility values in the MBP group did not change from baseline values[13] while the control group change in means was negative (-0.03) with a -4% change indicating a reduction in utility at postintervention. When comparing mean EQ-5D-5L utility values at T2 to baseline there was no difference in the MBP group and an overall 9% reduction in utility in the control (mean difference T2-T0=-0.07). This reduction in utility in the control group is considered above the MID for change on the EQ-5D-5L. At T2 follow-up mean EQ-5D-5L utility values did not change (from T1) for the intervention, *M=0.84, SD=0.13* (MBP), and reduced by 5% in the control, *M=0.80, SD=0.20* (control).

Table 56: EQ-5D-5L mean difference and percentage change over time (complete case)

	MBP		Control	
Timepoints	**Mean difference**	**% change**	**Mean difference**	**% change**
T0-T1	0.00	0%	-0.03	-4%
T1-T2	0.00	0%	-0.04	-5%
T0-T2	0.00	0%	-0.07	-9%

[13] When reported to more than 2 decimal points there is a very slight increase in mean values by 0.001522 (T1-T0), 0.001086957 (T2-T1) and 0.002608696 (T2-T0). The difference between group mean utility scores at T1 was -0.00422.

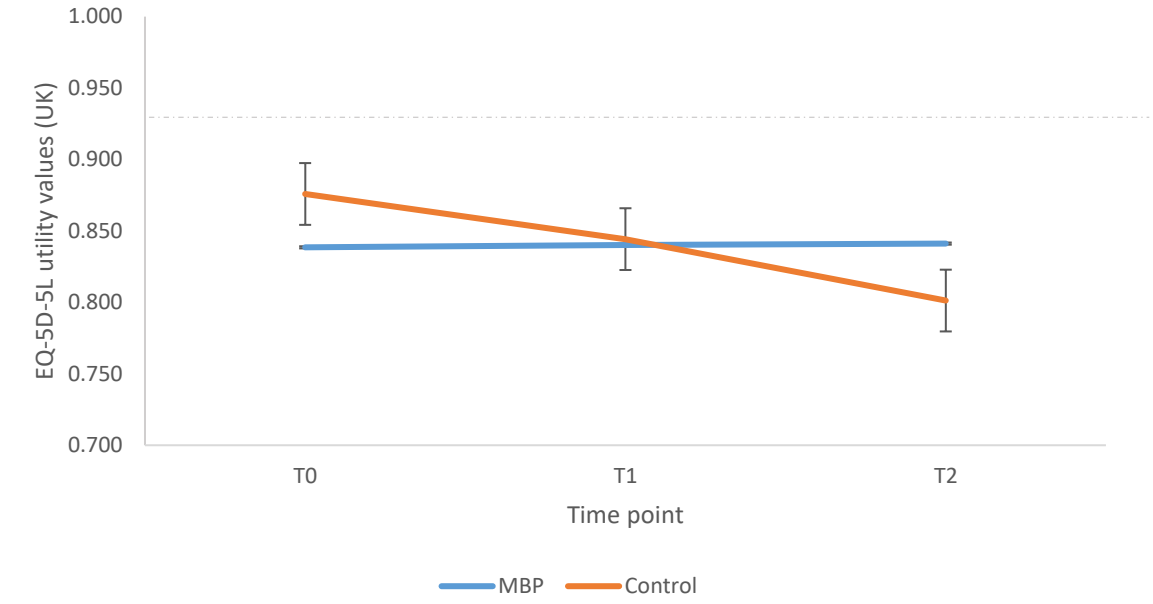


Figure 31: EQ-5D-5L mean index values for MBP and control conditions, at baseline (T0), post intervention (T1) and follow up (T2): Complete Case (listwise deletion).

EQ-5D-5L profiles

Data was condensed into combined whole sample of participants to explore the spread of responses on EQ-5D-5L domains. At baseline most participants reported having no problems on any EQ-5D-5L domain (see Figure 32). Nearly half (48%) of respondents across the sample reported some problems with anxiety and depression at baseline.

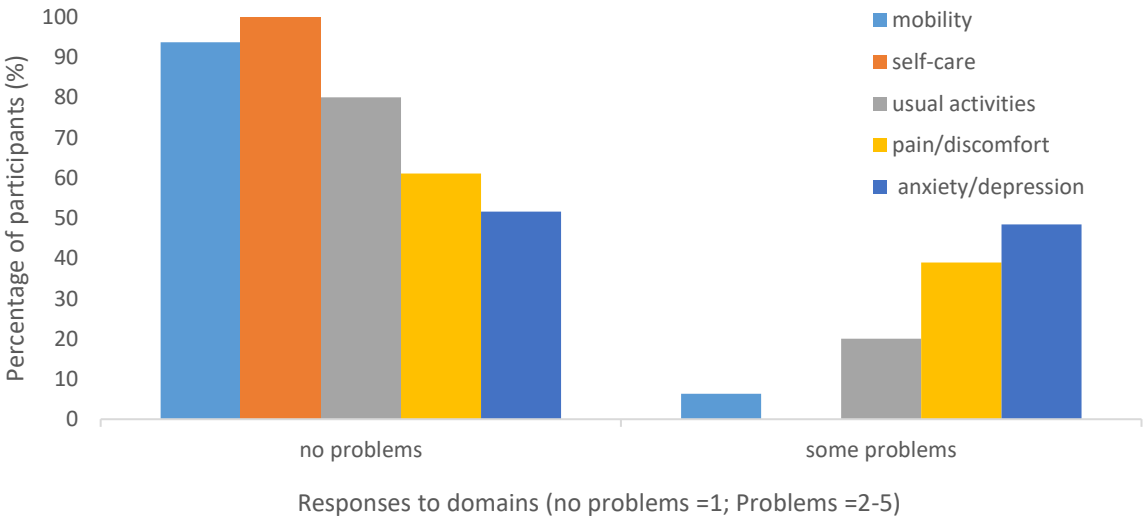


Figure 32: Baseline EQ-5D-5L proportion of participants responding no problems compared with some problems by domain (available Case)

Where participants reported problems on domains, these were generally reported to be slight problems with very few moderate, severe, and extreme problems (see Figure 33).

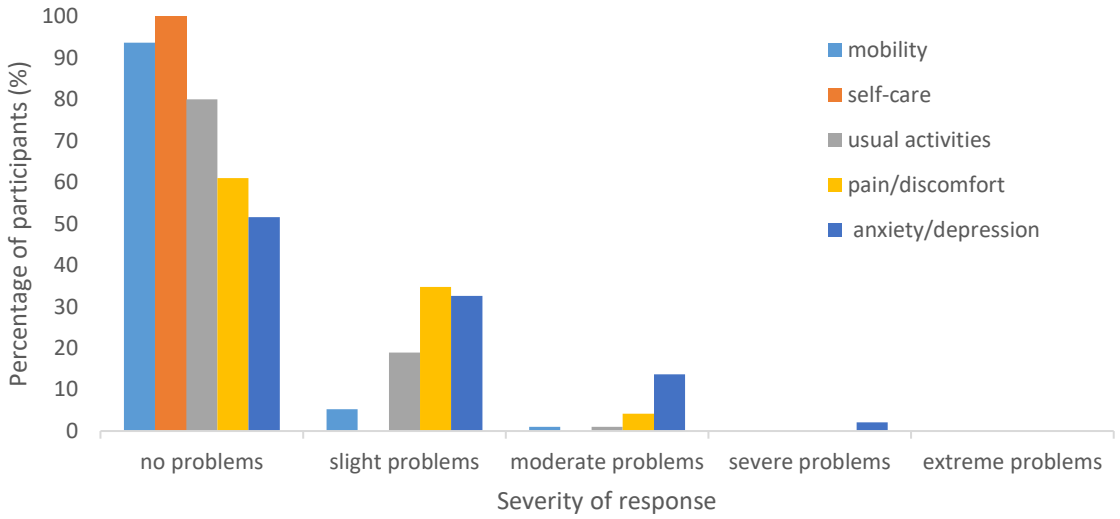


Figure 33: Baseline EQ-5D-5L proportion of participants responding levels of severity by domain (available case)

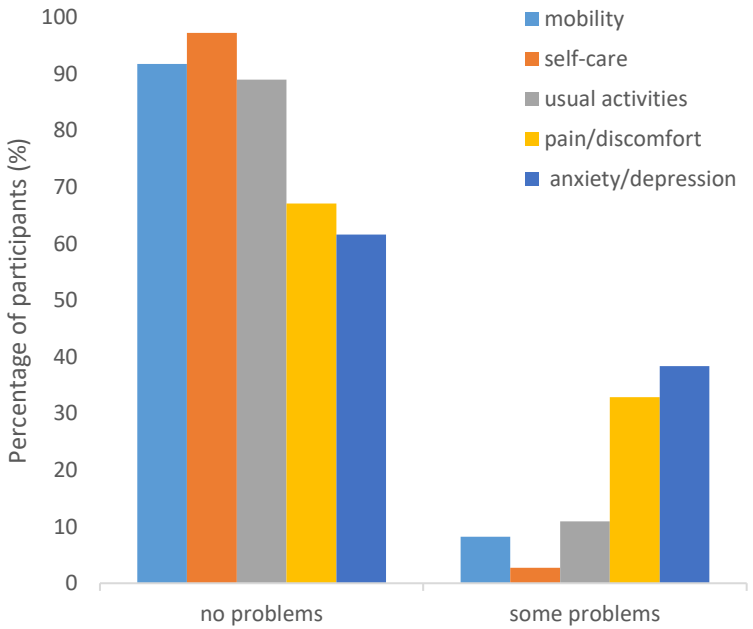


Figure 34: Post-intervention (T1) problems on EQ-5D-5L by domain (available case)

At post intervention there is a slight reduction in problems reported across domains compared with T0. The depression and anxiety domain had the highest level of problems, with 38% reporting some level of problems (see Figure 34) (of which the majority were again reported to be slight).

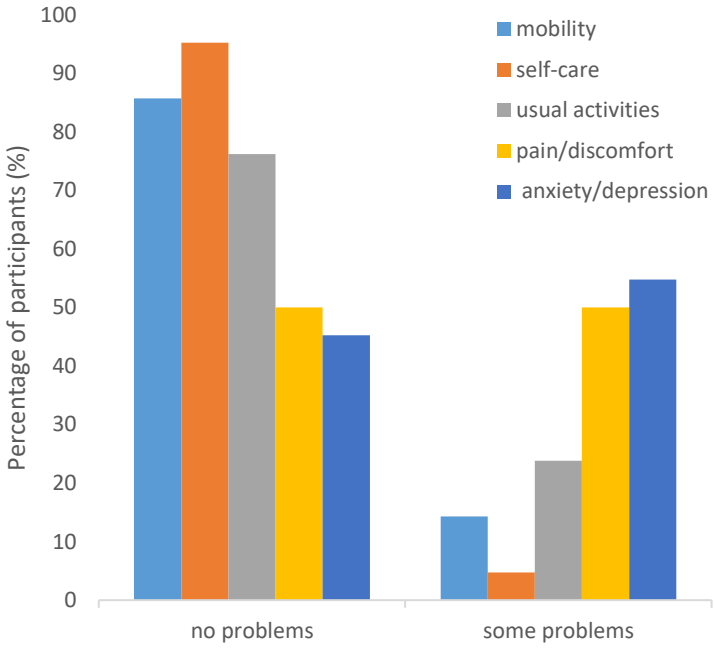


Figure 35: Follow up (T2) problems on EQ-5D-5L by domain (available case)

Figure 35 indicates a rise in problems reported at T2 across all domains compared with both T1 and T0. Half of all respondents reported some levels of pain and discomfort at T2. Similarly, 55% reported some problems on the anxiety and depression domain at T2.

Pareto principle health change

Using the Pareto classification of health change (Devlin et al., 2010; EuroQol Research Foundation, 2019) there was a greater percentage of improvement in health observed in the MBP group than in the control group with 43% (compared with 27% in the control) of participants improving in one or more domains between baseline and post intervention (T1) without any reduction in other health domains (see Table 57).

Table 57: Pareto classification of health change between baseline and post intervention (T1) number of participants, percent of group and percentage difference between groups.

		%	%difference
MBP (*N=23*)	Same	22%	-4.928
	Worse	22%	-11.59
	Improve	43%	16.812
	Mixed	13%	-0.29
Control (*N=15*)	Same	27%	4.9275
	Worse	33%	11.594
	Improve	27%	-16.81
	Mixed	13%	0.2899

Table 58: Pareto classification of health change between post intervention (T1) and follow up (T2) number of participants, percent of group and percentage difference between groups.

		%	%difference
MBP (*N=23*)	Same	30%	10.435
	Worse	35%	-5.217
	Improve	30%	3.7681
	Mixed	4%	-8.986
Control (*N=15*)	Same	20%	-10.43
	Worse	40%	5.2174
	Improve	27%	-3.768
	Mixed	13%	8.9855

Table 59: Pareto classification of health change between baseline and follow up (T2) number of participants, percent of group and percentage difference between groups.

		%	%difference
MBP (*N=23*)	Same	17%	-22.61
	Worse	39%	-7.536
	Improve	26%	12.754
	Mixed	17%	17.391
Control (*N=15*)	Same	40%	22.609
	Worse	47%	7.5362
	Improve	13%	-12.75
	Mixed	0%	-17.39

At follow-up (T2), both groups had the highest percentage of worse health classification with 35% (MBP) and 40% (control) with one or more domain in a worse status than at post intervention (T1) (see Table 58). The same was observed at T2 when compared with baseline, with both groups reporting the highest percentage of worse health classifications (39% MBP) and (47% control) (see Table 59).

Mean and incremental QALYs

Table 60: QALY descriptive statistics by group with bootstrapping

					Bootstrap sample (10,000 replications) 95% confidence intervals	
	Mean	**Median**	**Std. Deviation**	**Interquartile Range**	**Lower**	**Upper**
MBP (*N=23*)	0.56	0.56	0.07	0.12	0.53	0.59
Control (*N=15*)	0.56	0.57	0.07	0.11	0.52	0.59

Mean QALYs were the same for both groups over the 8-month trial duration (see Table 60). There was no incremental mean QALY gain (over 8-months) observed at two decimal places, with only minimal differences observed when values were reported to more than two decimal places, with mean QALYs *M=0.560 (SD 0.068)* for the MBP group and *M=0.558 (SD 0.067)* for the control group indicating an exact value mean QALY gain of *M=0.002229106* in favour of the MBP group.

Inferential statistical analysis results: EQ-5D

Descriptive statistics indicated that differences were very small both within groups and between groups. There were no differences in mean QALYs between groups. However, in the control group a reduction in mean utility exceeded the threshold for MID.

Therefore, further statistical analysis was deemed appropriate to consider differences between groups and over time. Results of the repeated measures GLM MANOVA indicated no differences between

groups, *F(2,35)=0.39, p=.962; Wilk's Λ=.998, partial η^2 =.002*. In addition, there were no differences over time (within subjects effects) *F(4,33)=1.35, p=.272; Wilk's Λ=.859, partial η^2 =.141*. Levene's test indicated equal variances at all timepoints for EQ-5D at T0, *F(1,36)=0.007, p =.933*; T1, *F(1,36)=3.57, p=.067*; T2, *F(1,36)=0.727, p=.399*. There were no differences on univariate tests by outcome and no further post-hoc tests were conducted.

ICERs were not calculated as there was no meaningful difference in utility between groups in the pilot analysis.

Depression screening results (GHQ-12)

There were no differences between groups at baseline scores on GHQ-12 on an available case basis, *T(94)=.497, p=.621,* or on a complete case basis, *T(36)=-.064, p=.949.*

Review ceiling and floor effects

Ceiling effects were classified as more than 15% of participants scoring the maximum of 36 while floor effects were defined as 0, when using the Likert scoring method. There was no evidence of floor or ceiling effects observed at any timepoint for the GHQ-12 (on both an available case and complete case basis).

Available case descriptive: GHQ-12 mean scores and clinical cut-off cases

Table 61 shows descriptive statistics for the GHQ-12 by group and timepoint on an available case basis.

Table 62 shows the mean difference and percentage change in GHQ-12 scores by group and over time. Mean scores in both groups improved between baseline and T1 with a 5% improvement in scores the control group and an 18% improvement in scores for the MBP group (see Table 62). Mean score fell below clinical cut-off (≥12) at T1 in the MBP group (M=11.55) (see Table 61). The difference by group in mean GHQ-12 scores between timepoints and the percentage change is shown in Table 62.

Table 61: GHQ-12 descriptive scores (available case) by group and timepoint

Group	Timepoint	N	Min.	Max.	Mean	Std. Dev	Median	% Depression (≥12)
MBP group	T0	38	0	30	14.053	6.217	13	63%
	T1	33	4	28	11.545	5.449	12	52%
	T2	25	6	26	13.200	5.172	12	68%
Control	T0	58	2	28	13.414	6.127	13	57%
	T1	43	3	25	12.721	5.105	12	58%
	T2	18	5	31	13.278	6.201	14	67%

Table 62: GHQ-12 mean difference between timepoints and percentage change over time by group (available case)

	MBP		Control	
Timepoints	**Mean difference**	**% change**	**Mean difference**	**% change**
T0-T1	-2.507	-18%	-0.693	-5%
T1-T2	1.655	14%	0.557	4%
T0-T2	-0.853	-6%	-0.136	-1%

Note negative values denotes an improvement in scores.

Figure 36 depicts a line chart showing the mean scores for groups over time on an available case basis. The dashed line represents the clinical cut off for depression cases applied (>12).

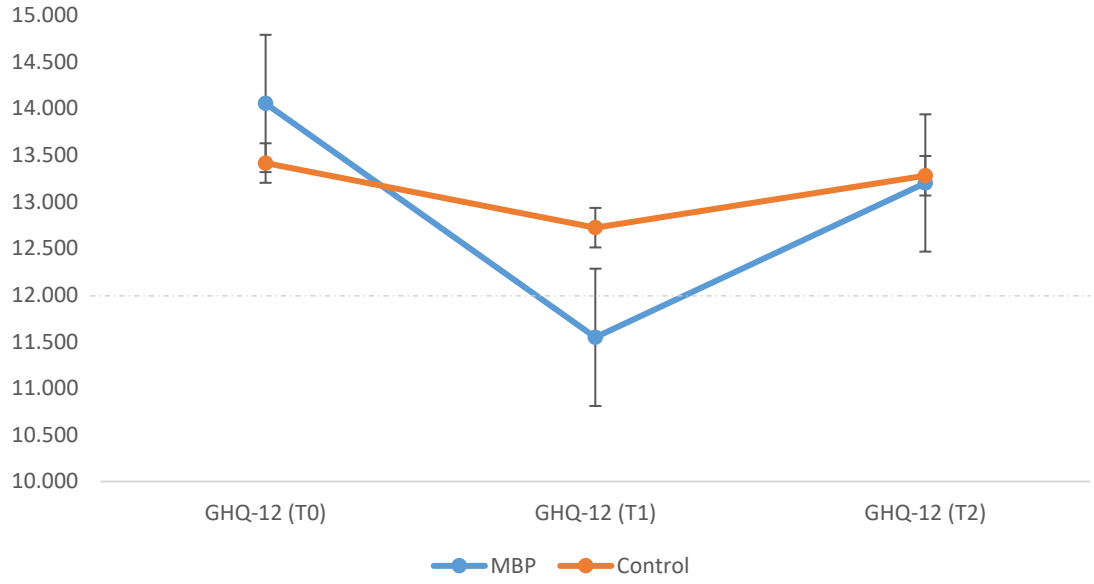


Figure 36: GHQ-12 mean scores for MBP and control conditions, at baseline (T0), post intervention (T1) and follow up (T2): Available case (pairwise deletion)

Complete case descriptive: GHQ-12 mean scores and clinical cut-off cases

Table 63 shows descriptive statistics for the GHQ-12 on a complete case basis presented by group and timepoint. On a complete case basis mean GHQ-12 scores at baseline were *M=14(SD=6.07)* in the MBP group and, *M=14.13(SD=6.53)* in the control group. Across the whole sample at baseline 66% of participants had GHQ-12 scores equal or greater than the clinical cut-off for depression of 12 (Likert scoring). In the MBP group 70% had clinical levels of depression according to the GHQ-12, compared to 60% of the control group.

Table 63: GHQ-12 descriptive scores (complete case) by group and timepoint

Group	Timepoint	N	Min.	Max.	Mean	Std. Dev.	Median	% Depression (≥12)
MBP group	T0	23	0	30	14	6.07	13	70%
	T1	23	6	28	13.13	5.45	12	65%
	T2	23	6	26	13.65	5.14	13	74%
Control	T0	15	4	25	14.13	6.53	14	60%
	T1	15	3	22	11.87	5.18	11	47%
	T2	15	5	31	13.67	6.49	14	67%

GHQ-12 scores over time indicated that scores reduced at post-intervention to *M*=13.13*(SD=5.45)* in the MBP group and *M*=11.87*(SD=5.18)* in the control group. In parallel with the reduction in mean scores (between T0 and T1), the proportion of clinical depression reduced in both groups at post intervention (65% in the MBP group and 47% in the control group). At final follow-up (T2) the proportion of participants above the clinical cut-off for depression rose in both groups, to the highest levels (74% in the MBP group and 67% in the control scored 12 or greater on the GHQ-12). Mean scores for both groups rose at final follow-up to *M=13.65(SD=5.14)* in the MBP group and *M=13.67(SD=6.49)* in the control. However, mean scores remained lower than baseline levels in both groups with a mean difference of -0.35 in the MBP group and -0.47 in the control group (see Table 64).

Table 64: GHQ-12 mean difference and percentage change over time (complete case)

	MBP		Control	
Timepoints	**Mean difference**	**% change**	**Mean difference**	**% change**
T0-T1	-0.87	-6%	-2.27	-16%
T1-T2	0.52	4%	1.80	15%
T0-T2	-0.35	-2%	-0.47	-3%

Note negative values denotes an improvement in scores.

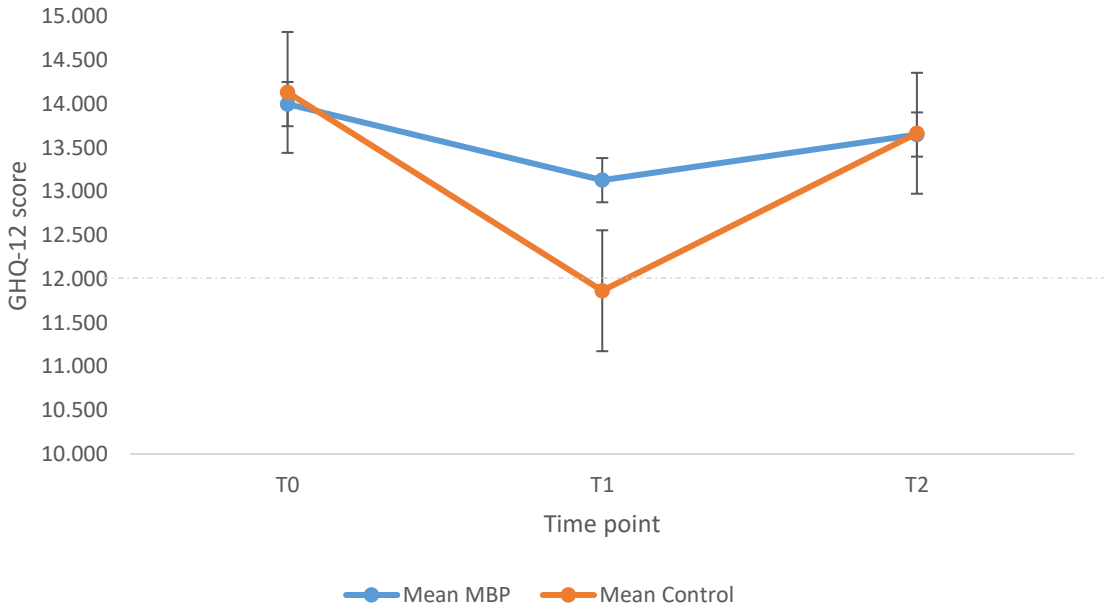


Figure 37: GHQ-12 mean scores for MBP and control conditions, at baseline (T0), post intervention (T1) and follow up (T2): Complete Case (listwise deletion)

Figure 37 shows the complete case mean GHQ-12 scores by groups and over time. The pattern of scores over time visually appears similar between groups with scores improving slightly between T0 and T1 in both groups, before reducing at T2. For the control group the mean scores at T1 are below the threshold for depression.

Patterns of depression case status over time (complete case)

Prevalence of patterns of depression cases over time using patient-level data are depicted in Table 65, with grouping by treatment condition. Categorisation banding is condensed in the lower range to ensure data is aggregated sufficiently.

MBP had higher percentage rates of 'persistent cases of depression', with 39% of participants recording GHQ12 scores higher than the clinical cut-off for depression at every timepoint (compared with 27% of the control group). However, the MBP had 10% higher proportion of participants meeting case definitions at base line compared with the control. Considering the high rates of clinical cut-off depression at baseline and the potential for baseline differences between groups, inclusion of clinical outcomes at baseline as a covariate in a future regression analysis is likely to be appropriate. The next most common pattern observed was a spike improvement where baseline depression case, improved to non-case levels at T1 before returning to depression levels at T2. There were very small incidences of other patterns of depression (described in Table 65 with classification details and diagrams depicted in the study methods) with less than 15% of each group matching the patterns of depression.

Table 65: Patterns of depression cases using patient-level data depicted by timepoint and by group allocation (% banded in intervals)

Matrix Key: **X** *≥12 (GHQ-12)* ☐ <12 (GHQ-12)	**Case Matrix**			**MBP**	**Control**
	T0	**T1**	**T2**		
1. Constant Low	**X**	**X**	**X**	35-40%	25-30%
2. Resolving (delayed)	**X**	**X**	☐	0-15%	0-15%
3. Spike	**X**	☐	**X**	15-20%	20-25%
4. Resolving (early)	**X**	☐	☐	0-15%	0-15%
5. Worsening (early)	☐	**X**	**X**	0-15%	0-15%
6. Trough	☐	**X**	☐	0-15%	0-15%
7. Worsening (delayed)	☐	☐	**X**	0-15%	0-15%
8. Constant High	☐	☐	☐	0-15%	0-15%

Inferential statistical analysis results: GHQ-12

Based on the descriptive statistics reported there were some small differences between groups observed. Further statistical analysis was deemed appropriate to consider differences between groups and over time. Results of the repeated measures GLM MANOVA indicated no differences between groups, *F (2, 35)=0.39, p =.962; Wilk's Λ =0.998, partial* η^2 *=.002*. In addition, there were no differences over time (within subjects effects) *F (4, 33)=1.35, p=.272; Wilk's Λ=0.859, partial* η^2 *=.141*. Univariate analysis for GHQ-12 did not indicate any differences by outcome.

Discussion

Summary of principal findings

This study has demonstrated the feasibility of collecting brief cost and outcome data relevant to a public sector perspective, including self-reported GP attendance and unplanned absence information, from Sixth Form students. Despite high ceiling effects recorded on the EQ-5D-5L, mean utility levels indicated that this adolescent cohort started and ended the study with lower-than-average HRQoL compared to the general population. In addition, the GHQ-12 has indicated that levels of depression amongst this population cohort may be high with between 47% and 74% reporting levels over the selected threshold indicating clinical case levels during this study. Overall, there was an increase in depression cases but a small reduction in depression scores over time. These findings have implications for future cost-effectiveness analysis e.g., aiming to explore cost per case of depression prevented. A 'shifting the curve' costing approach which considers depression severity may be helpful in considering the cost of more secondary prevention, where depression may be prevalent in the population.

In comparison of mindfulness teaching curriculum compared with teaching as usual there were no differences observed between groups. In addition, there were no significant differences on outcomes observed within groups over time. Total costs of GP resource use and MBP intervention costs were £102.06 in the MBP group compared with teaching as usual costs of GP attendance costs alone at £93.60 per pupil in the control group. From this feasibility study there is no definitive answer to the question of whether mindfulness in schools is likely to be cost-effective if integrated into the Sixth Form curriculum compared with delivery of the traditional curriculum alone. However, this was not the aim or expectation from this early-stage health economics study.

Methodological considerations for future economic evaluations of MBPs in schools – including strengths and limitations of the study

This study has helped explore the economic case for intervention in a school setting and considered the appropriate perspective of analysis in education setting with potential benefits falling across public and private sectors. There have been many lessons learnt from this study, which now provide an opportunity to discuss some important methodological considerations for future economic evaluations of mindfulness in schools. These relate to the trial design, the conduct of health economics research alongside clinical trials, the target population for depression prevention in schools, methods for assessment of depression, the statistical methods appropriate for future research, measuring resources, measuring, valuing forgone education, costing the curriculum, and consideration for the appropriate control comparator for an MBP school curriculum.

Conducting health economics alongside clinical trials

It is a limitation of this study that the health economics component of the feasibility study was conducted retrospectively and that it was not possible to control the approach taken in relation to the outcomes measured and the range of costs including, for example, only GP contacts were included rather than a wider range of resource use which could be considered appropriate to a public sector perspective of analysis. In addition, this delay in conducting the economic assessment led to issues with greater uncertainty over the data (e.g. the period over which absences were recorded) which could have been resolved had the main study and health economics study been finalised concurrently. The delay in conducting the health economics analysis compared with the source trial means that things have moved on in terms of best practice in methods, plus it is more difficult to resolve discrepancies without direct consultation with the source study team. Ideally, health economics study and main outcomes work should happen simultaneously with joint recommendations for future research considering both cost and effectiveness findings.

This thesis research presented in this chapter contained limited evaluation of wider factors. The source study included a wide range of factors including a neuroscience and task performance study evaluation which is reported elsewhere (Sanger & Dorjee, 2016; Sanger et al., 2018). In addition, other source study outcomes included 1) the Perceived Stress Scale (PSS) (Cohen, 1994), 2) Five-Facet Mindfulness Questionnaire (FFMQ) (Baer et al., 2006), 3) a Meta-Cognitions Questionnaire- Adolescent Version (MCQ-A) (Cartwright-Hatton et al., 2004), 4) the World Health Organization, Well- Being Index 5- item version (WHO- 5) (World Health Organisation, 1998) 5) the Toronto Empathy Questionnaire (TEQ) (Spreng, McKinnon, Mar, & Levine, 2009), 6) acceptability of the intervention questionnaire form assessed as part of the source study outcome measures (Sanger & Dorjee, 2016; Sanger et al., 2018).

Previous experience of mindfulness may be a relevant covariate which was not explored in this health economics component of the feasibility study. However, the source study collected detailed information on mindfulness practice (both formal and informal practice) in the period after the intervention. More feasibility work with secondary outcomes included and available to the health economist is needed to enable an embedded process evaluation within a definitive trial. Inclusion of dose considerations and a secondary per protocol analysis for attending a minimum number of mindfulness sessions should be included within future economic analysis plans for MBPs in schools.

This was a small feasibility study and the analyses conducted aimed to be appropriate to this early evaluation stage of research. The approach taken aimed to explore potentially impactful variables that need consideration in future analysis, for example, adjustments for baseline differences and inclusion of relevant covariates is likely to be appropriate for analysis within a definitive RCT, with the health

economist working together with trial statisticians to develop a suitably stable model to allow for more complex analysis of costs and outcomes.

In general terms it is a limitation that there is a high risk of bias due to the non-randomised design, and that there is likely to be a selection bias in that the schools receiving the intervention were the most interested in receiving the intervention. A cluster randomised RCT design would help prove a more robust control group to compare the effects of MBP with.

The target population for primary depression prevention in a universal context

This study highlighted the high levels of indicated depression in adolescents and offered some considerations for health economic research evaluating the prevention of depression.

For older pupils there is a strong case for intervention, due to the timing of high consequence exams and upcoming life transitions. It is however a limitation that all participants aged 18 were lost to final follow-up (which was conducted in the September after they had completed Year 13). An alternative baseline and pre-summer holiday analysis with earlier collection of follow-up assessment may help capture any sustained impacts for this cohort.

With this chapter aiming to explore more generally the case for universal depression prevention, at an early stage in the life course through schools, the findings in this study may point towards the need to consider earlier intervention for primary prevention of depression in adolescents. MBPs embedded within compulsory education years may offer access to all children. Further research considering the appropriate timing of MBP interventions for effective primary prevention in a universal application is needed. There are utility measurement considerations for economic evaluations for younger children (see research recommendation 1 below) which this study has not been able to address, with the age of population more appropriate for adult questionnaires and value sets.

Consideration of the assessment of depression and appropriate threshold for a clinical case

This study had a small sample size with a short follow-up period, particularly when considering a complete case sample. It does not provide details on what happens to the pattern of depression i.e., whether cases of depression relapse or recover beyond the duration of the trial and into adulthood.

One limitation of the study it that there is some uncertainty around the appropriate threshold for depression on the GHQ-12 in adolescent populations and whether a gender variation is needed. One study has suggested a lower threshold score of "9/10 for males and 10/11 for females was [considered] optimal" to detect depression and anxiety amongst high school students aged 15 – 18 years in Australia (Baksheev et al., 2011). An earlier published threshold indicated that a threshold of 13/14 for males and

18/19 for females aged 11-15 years in Australia was an appropriate threshold (Tait, French, & Hulse, 2003). In this study with adolescents aged 16-18 years, I applied the threshold of ≥12 (Likert scored) which has been previously validated in a general population sample against a structured psychiatric interview (Lundin et al., 2016). However, the Lundin et al. (2016) study was conducted in a Swedish population and although the diagnostic approach to psychological disorder is comparable to the UK (with the DSM-IV-TR system used), the results may not be generalisable to a UK population. One recent UK study published in the Lancet used GHQ-12 scores to consider the impact of the COVID-19 pandemic on mental health in the population (Pierce et al., 2020). This study converted the Likert scores into a binary 0 (representing 'not at all' and 'no more than usual' responses) and 1 (for 'rather more than usual' and 'much more than usual' responses), in line with the 'standard scoring' method described by Lundin et al. (2016). Pierce et al. (2020) suggest using a "score of 4 or more, as used on the Health Survey for England Official Statistics indicator" (Pierce et al., 2020, p. 885).

When conducting a post-hoc rescoring of complete case GHQ-12 baseline values in this thesis feasibility study and applying the threshold of 4 or more, the proportion of cases in each group reduced to 39% in the MBP treatment group and 47% in the control group (compared with 70% MBP and 60% control). Further investigation is needed to explore the optimal threshold for adolescents in the UK and the extent to which varying the threshold for depression may influence economic evaluations aiming to consider costs per depression cases avoided.

The mapping of depression case status over time did not contain any details relating to depression severity or trends towards improving or worsening within the case and no case categories. Plotting GHQ-12 scores and depression case status over time would help capture greater level of detail to indicate whether additional patterns of resolving and worsening are present.

Limitations in the methods for inferential statistics and uncertainty

This study presents a wealth of descriptive statistics on a range of outcomes relevant for the economic evaluation of MBPs in schools, providing descriptive data and important lessons learnt to inform the design of future trials. Indicators of potential trends over time and potential differences between groups were explored as indicators of what might be most appropriate in further studies.

The statistical analysis conducted in this study was of a pilot nature and was sensitive to a small sample size. A comprehensive analysis which adequately controls for multiple comparisons, both within and between groups, is needed with a larger sample size to determine whether any observations in this feasibility research are statistically significant. While it is acknowledged that economic evaluations are often underpowered (Briggs, Claxton, & Sculpher, 2006) a larger sample size study would be needed to

reduce levels of uncertainty around estimates and explore whether MBP delivered in schools can be cost-effective compared with traditional curriculum.

In this study the majority of descriptive statistics reported focus on mean value estimates, while the inferential statistical analysis to explore difference in outcomes between groups and over time conducted largely used parametric tests. There were however potentially important variations in the economic data on normality tests and while homogeneity tests indicated that the distribution of data was likely to be equal between groups, there is uncertainty about the appropriate choice of statistical tests to compare difference between variables. Caution is needed in the interpretation of the parametric analysis reported in this chapter, with consideration of the relatively small sample size and the evidence relating to the distribution of the data included. Alternative tests would need to be conducted to establish whether the pilot results in this chapter are upheld or whether they are sensitive to the type of tests for differences used, for example, if analysis was repeated with non-parametric tests. Parametric tests to compare differences between mean values may still be used when data is not normally distributed particularly when bootstrapping methods are used as these do not require assumptions of normality to be met (Knief & Forstmeier, 2021). It is the convention to use parametric tests with bootstrapping in economic evaluation despite cost data commonly being truncated and positively skewed due to typical patterns of resource use (Elliot & Payne, 2005). In this small sample size feasibility assessment, the analysis was not intended to be definitive but instead explore these methods for future research.

Measuring resource use

This study had a narrow resource use range which was not sufficient for a wide perspective. Resource use collection in younger cohorts would likely add significant challenge to an already challenging process, with high rates of missing data common within resource use collection tools, and the need to collect data from a proxy for children's populations. This study has shown that adolescents are able to recall GP attendance over a three-month period and recall the main reason for attendance. There are however important ethical considerations with asking children about medical attendance which may be a sensitive topic. Although data was successfully reported there was no way of validating the accuracy of recall from this study.

Measuring and v*aluing forgone education*

In this study school absenteeism information was collected through recall from participants. However, collection direct from education providers who are required to record attendance records for all pupils could reduce missing data or be used to validate participant recall (see research recommendation 2 below).

While there is not a consensus on the best practice for methods to value forgone education, it is a limitation of this study that the value of forgone education is based on high-level estimates of the cost of missed work and the cost of missed days schooling on lifetime earnings. Estimates are illustrative of various proposed methods rather than precise estimates of the cost of missed schooling. In this study there were no differences between groups, and no difference to population norms in terms of missed schooling and caution is needed in interpretation of the estimated value of forgone education in this feasibly study. Regarding the calculation of the value of a day off school it is important to note that due to the age of the study population costing parents time off work may not be appropriate. Further methodological work on measuring and valuing forgone education is highlighted as a recommendation for further research (see research recommendation 2 below).

Estimation of programme costs and consideration of appropriate control condition

For MBPs delivered in school, usual teaching already provides a reasonable active control condition. This is on the basis that the mindfulness teaching is embedded within the curriculum to achieve the same learning objectives. Usual teaching already provides elements of socialisation within school classes and the differences between resources to deliver the teaching is unlikely to be large beyond initial costs of training. A fully costed estimate of the additional resources to implement MBPs within schools and whether they are embedded rather than additional in practice warrants further exploration.

Programme costs were estimated based on the Mindfulness in Schools project course for adults called '.b Foundations'. There was limited micro-level data available on the resources involved in training and delivery of the intervention and many assumptions were made. More research is needed to explore the micro and meso level factors which may impact on the study costs and benefits (see research recommendation 3 below). In addition, consideration for the resource implications for delivering an MBP curriculum for younger children would be needed to consider intervention in education more widely. Further mixed methods research could help evaluate the contextual factors for implementation within school systems and the wider impacts on a range of stakeholders in future economic evaluation of MBPs in schools.

Comparison with other literature

Results from the source study evaluating pre and post outcomes for all participants who completed a neuroimaging study component at both timepoints *N=40* students (*N=19* in the MBP training group) in relation to school absences and GP attendance were reported elsewhere as follows:

"ANOVAs revealed no change in absenteeism over time (F(1, 38) = .6, p = .45), between group (F(1, 38) = 1.3, p = .25) or an interaction (F(1, 38) = .9, p = .35). GP visits were also not affected by time (F(1, 38) = .6,

p = .44) or group differences (F(1, 38) = 1.2, p = .28), the time by group interaction was marginally significant (F(1, 38) = 3.0, p = .09, η2 = .07). To investigate the possibility of differential effects for vis its due to physical and mental health reasons, GP visits were further broken down accordingly (e.g., asthma and stress, respectively). For mental health- related visits only, the ANOVA showed no change over time (F(1, 38) = .3, p = .58) or group (F(1, 38) = .7, p = .42), but there was a significant time by group interaction (F(1, 38) = 5.0, p = .03, η2 = .12). However, follow- up paired samples t tests revealed only trends towards significance, with some reduction in the training group (t(18) = 1.7, p = .11, d = .39) and a non- significant increase in GP visits over time in the control group (t(20) = −1.5, p = .16, d = .32). Nevertheless, the effect sizes suggest a small but meaningful association between mindfulness practice and health, and, given the short time- scale this was measured over (8 weeks), it merits consideration. On visual inspection there appeared to be pre- test group differences on GP visits (. . .). However, independent t- tests confirmed that these were only marginally significant at pre- test for general and specifically mental health visits (ps > .05). This was most likely due to the non- randomized nature of participant recruitment." (Sanger et al., 2018, p. 6).

Pre and post outcomes were not compared within the health economics study without inclusion of the follow-up timepoint, so no direct comparison can be made. This study further highlights the potential impact of decisions about sample analysis and time horizon of analysis. There are important implications for dealing with missing data and attrition. These two studies highlight that the patterns of service use can change over time, with a trend towards significance between groups over time on GP attendance that may not be maintained at the five-month follow-up assessment identified by Sanger et al. (2018).

"The inclusion of health-related data adds to insights from previous school-based interventions, suggesting that mindfulness training may reduce adolescents' needs to seek mental health advice. Marginal decreases in GP visits for psychological reasons (e.g., stress, trouble sleeping) were found in the training group, as control participants reported slight in- creases. This divergent pattern of GP visits was supported by a small to moderate effect size, which is important to examine given the limited sample size and timeframe. The timing of data collection may be relevant here, as students were preparing for summer exams and the potential for stress and anxiety would have been high. Thus, mindfulness practice may have had a buffering effect on psychological well- being, manifesting in less need to seek help during a challenging period" (Sanger et al., 2018, p. 8).

The source study highlights the importance of considering time and context in data collection (Sanger et al., 2018), this is also particularly relevant to health economics research where health care resource use and health outcomes may be influences by seasons with higher attendance in winter months than in summer for example.

The MYRIAD trial protocol identified in the systematic review presented in Chapter 2 of this thesis (Kuyken et al., 2017) highlights an important study which has the opportunity to add to the limited economic evidence base on MBPs in schools. While the results of this study are forthcoming it is not possible to compare findings from this thesis feasibility research. The MYRIAD trial offers a considerable sample size to facilitate greater analysis of outcomes and provides a later stage of study in a translational research context. The use of economic modelling methods in the MYRIAD study could help provide a useful benchmark to other researchers wanting to evaluate both short and long-term benefits of MBP prevention initiatives in public sectors.

Wider implications

With the high frequency of depression onset thought to occur during adolescence as early as 13 years old, interventions to prevention depression may need to occur earlier, building resilience through pre-school, primary and early secondary school years. Mindfulness practices in early childhood education may have positive benefits, however the research is at an earlier stage than for older children (Erwin & Robinson, 2016), especially in relation to economic evidence.

Screening for depression during school years including sixth from could be a useful tool to help identify early onset depression that requires treatment or interventions which can help mitigate the impacts. NICE research recommendation identifies the need for evaluations of group mindfulness for young people 12-18 with mild depression (NICE, 2019a).

Areas for further research

Recommendation 1: Research focusing on utility measurement in child populations is still needed for MBP in schools' research

The challenges of conducting cost-utility analysis in children populations have been discussed (van IJzendoorn & Bakermans-Kranenburg, 2020). People value health states differently for children (Kreimeier et al., 2019). The EQ-5D-Y (Wille et al., 2010) has been adapted for adolescents but there is no value set to make it useful for use in cost-utility analysis. In addition, the EQ-5D-Y 5L questionnaire has been in development but without value sets its use in cost-utility analysis is limited (Kreimeier et al., 2019).

While researchers have recommended that health economists should continue to use EQ-5D in children population studies, greater methodological work to develop methods that better take account of children in decision making is still needed (Noyes & Edwards, 2011).

Recommendation 2: Further guidance and methodological work is needed for researchers conducting economic evaluations of MBPs in schools (including forgone education)

There is little methodological guidance about including forgone education or other productivity losses in economic evaluations of health focused educational interventions. Future research should look to compare unplanned absence with trends in national and local school attendance data or control group to establish whether MBPs have an impact on the amount of forgone education. There are different options to valuing school attendance, and appropriate methods will likely depend on study perspective and age of school age children regarding where there are anticipated spill over effects to parents' employment. The period of recall is an important consideration in terms of how accurate recall is for children over varying lengths of time. Increasing the validity of data through opportunities to cross-reference self-reported study data against school records should be explored.

Recommendation 3: Close collaboration is needed to obtain more accurate estimates of resources, integration, and impact of the MBP within the school, and costs of programme delivery

Costing the MBP has some challenges as while there is an opportunity cost of a teacher's time to deliver mindfulness in the curriculum (i.e., they could be delivering something else during this time), costing a teacher's time in the MBP group but not in the control condition would disadvantage the new intervention. There are micro level considerations about whether factors such as mindfulness supervision, admin and student support had any impact on teacher's workload. Working closely with the school provider could help capture information on the time spent by teachers during the full implementation process including the initial mindfulness teacher training and then time spent teaching during programme delivery. There are also meso level considerations around implementation decisions. For example, delivering a MBP within a whole school approach versus a single year group has clear resource implications. Further feasibility research could explore whether there are wider resource allocation impacts when a school embeds mindfulness in the curriculum at varying extents. Obtaining this additional information may provide important details for further economic evaluations.

MBPs vary and programme features need to be considered in developing both intervention cost estimates and subsequent economic evaluations. For example, the costs of delivering MBPs to younger children cohorts will vary depending on the staff resources, whether the interventions are embedded into existing curriculum or delivered in addition to usual teaching, and whether the course are led by 'bought in' trained teachers external to the school. In general terms (not specific to MBP) there is some previous evidence that externally delivered school based programmes were superior to internally deliver programmes by school staff (Werner-Seidler, Perry, Calear, Newby, & Christensen, 2017). MBP research has also noted that "outcomes differed according to whether the intervention was delivered by

an outside facilitator compared to trained educators/teachers" (Carsley et al., 2018, p. 693). In this thesis pilot study, the MBP teachers had 9 months experience and were supported by experienced mindfulness practitioners. Future survival analysis considering staff turnover may be relevant in the development of on-going programme costs.

Delivering evidence-based programmes with fidelity with suitably trained staff remains an important factor in ensuring effectiveness and cost-effectiveness. MBP implementation research and practice recommendations are relevant here (BAMBA – British Association of Mindfulness-Based Approaches, 2015; Rycroft-Malone et al., 2014). More research is needed to explore the drivers for these findings and impacts of programme costs.

Conclusions

There are methodological challenges for evidencing the economic case for depression prevention when at baseline depression levels are high. Further trials with larger sample size and cluster randomised RCT design are needed. In addition, longer term follow-up data and modelling of lifetime effects would help demonstrate whether there is a public health prevention economic case for investment in mindfulness in schools. Economic evaluations of mindfulness in schools' programmes for younger children warrant attention to help establish the best use of limited resources. There is a strong case for considering earlier intervention capable of primary prevention of depression, in both the life course and depression pathway, but also the need for greater mental health support for adolescents and young people. For MBPs embedded within schools, bringing together education economics and health economics is needed, and a wider perspective of analysis is likely to be appropriate. In line with findings reported in Chapter 4 recognising the complex nature of both the intervention and the system in which it is implemented highlights that multiple perspectives of analysis may be appropriate.

The world has changed rapidly for the current generation of children and advances in new technologies offer new benefits but also potential risk (Anderson, Rainie, & Luchsinger, 2018). These contextual issues are important as we learn more about the impact of childhood environments and experiences on mental health, child behaviours and cognitions that are formed during this time. The COVID-19 pandemic which occurred after the completion of this thesis research will likely have impacted the wellbeing of children. Considerations about how best to support the mental wellbeing of children are even more important now in recovering from the pandemic and education will play a predominant role in this process (Bozkurt et al., 2020; Farmer et al., 2020; Singh et al., 2020).

Chapter 6: Setting MBP health economics feasibility work in the continuum of translational research

Chapter preface

The implementation of innovations in health care is known to be a slow process, in addition there are barriers and challenges to translating research into practice (Price & St John, 2019). "Translational research as a concept has been widely used and applied in scientific literature for more than a decade. It is most broadly and simply defined as research steps to take discoveries from the bench to the bedside and back again" (Fort et al., 2017, p. 60). Within the context of a translational research framework, there are lessons to be learnt from early-stage trials to develop robust methodologies to evaluate MBPs. Feasibility studies are particularly important where there may be significant uncertainty around the appropriate design of an economic evaluation, which is characteristic of MBPs delivered as complex interventions within complex settings. This chapter returns to MBPs within the context of the translational research continuum and offers a checklist for health economics within the feasibility stage and insights about where public health practitioners might intervene to promote better mental health at a population level. This methodological discussion chapter addresses the sixth and seventh principal thesis research questions of "How well does the health economic toolkit work for MBPs?" and "What lessons can be learnt from pilot and feasibility MBP research and the challenges of evaluating complex interventions?" This chapter is followed by a general discussion chapter (Chapter 7) which offers a synthesis of findings across the whole thesis.

What we already know

In 2015, I co-authored a paper published in the journal Mindfulness which for the first time posed a range of questions about what elements should be included in an economic evaluation of mindfulness-based interventions. This paper highlighted the particular challenge of how best to capture the ways that MBPs help people adjust to or build resilience to difficult life circumstances, and to disseminate effectively to enable policy makers to judge the value of the contribution that MBIs can make within the context of the limited resourcing of public services. Since then, my PhD research has brought me to the conclusion that the best way to do this is to:

1. Set economic evaluation of MBPs within a translational research framework for complex intervention evaluation.
2. Emphasise how key the feasibility stage is in this process and that there is a need to explore how economic evaluation can best be undertaken and build this into the health economics analysis plan (HEAP) of a full RCT or other study design.

The importance of the translational research context

The translational research arena is relatively new and arose out of concerns that rapid developments in basic science faced blocks to reaching direct patient benefit in a research to practice context (Fort et al., 2017). The conclusion of this early debate about translational research was the need for a common language of the various stages of research. Informed by translational research literature and guidance, this chapter highlights the importance of embedding health economics at each stage of the evaluation process, and in particular the lessons to be learnt from early evaluations. Figure 38 displays the continuum of evidence cumulation and synthesis required for translational research of complex interventions as adapted from the framework presented by (Campbell et al., 2000). This process considers four distinct stages of trials-based evaluations of complex interventions, first informed by underpinning basic science (depicted as a stage 0) and followed by a final stage of policy change (stage 5). While this process is depicted as a continuum where each stage informs the next, it is important to consider the argument that this process is not completely linear, but involves feedback loops (Campbell et al., 2000), and both evidence-based practice and practice-based evidence are important to fully understand complex interventions (see right side of Figure 38). This complete process, from "bench to the bedside and back again" (Fort et al., 2017, p. 60) where practice-based evidence is utilised can improve the successful implementation of interventions (Cook & Cook, 2016).

With respect to MBPs, the topic of this thesis, this framework can be used to describe the stages from the conception of MBP programmes through to the economic evaluation or the value for money of the programmes in the public sector context, either as targeted prevention programmes as in the case of MBPs for cancer patients (presented in Chapter 4), or as a universal schools-based programme (presented in Chapter 5).

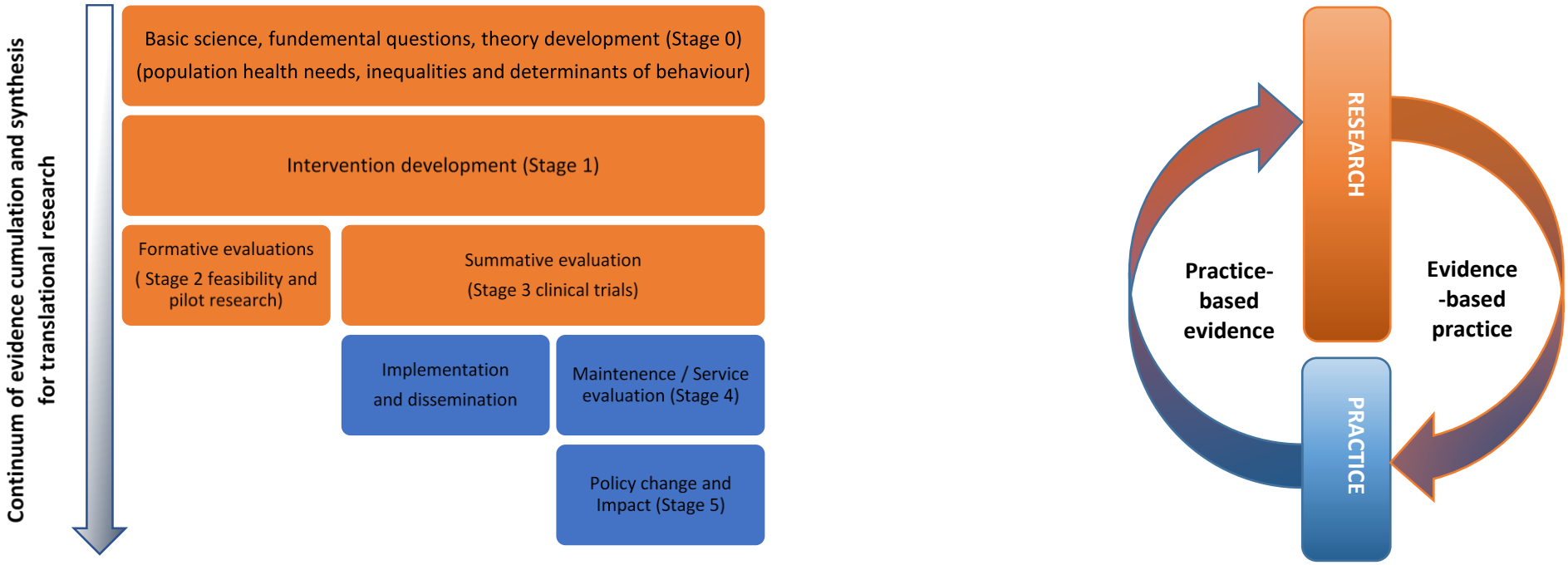


Figure 38: Evaluating MBPs as complex interventions within a translational research framework adapted from Campbell et al (2000).

Trial methodologies and MBPs as complex prevention interventions

To guide methodological decisions, it is helpful to consider MBPs as both complex interventions and as public health prevention initiatives. The challenge to the health economist is how best to capture the ways that MBPs may help prevent future mental health problems, and to disseminate effectively to enable policy makers to judge the value of the contribution that MBPs can make within the context of the limited resourcing of public services.

While it is commonly recognised that RCTs are considered to be the gold standard within which to assess effectiveness and cost-effectiveness (Kendall, 2003), it is necessary to consider first whether an economic evaluation is appropriate and second whether a RCT is appropriate for integration of economic evaluation (Coyle et al., 1998).

"There are many different designs of trials and not all studies of MBPs will be in trial settings. However, in order for evidence of the effectiveness of an MBP to be considered on an equal plane by the medical and clinical professions, RCTs are necessary, with opportunities to build a concurrent economic evaluation within such a trial (Ramsey, McIntosh, & Sullivan, 2001)"(Edwards et al., 2015).

In many settings, MBPs are available in practice however despite the growing economic evidence base (see Chapter 2) many are yet to have routine rigorous evaluation to justify public resources investment (Bishop, 2002). In these cases where programmes have been informally implemented before being recommended by NICE or other public bodies, research to evaluate their effectiveness and cost-effectiveness may need to adopt a more pragmatic approach that embraces the real-world nature of the delivery and current uptake of MBPs (Edwards et al., 2008). Pragmatic trials are conducted in the community, in full knowledge that the setting and the real-world is likely to impact on trial outcomes, but that with an appropriate sample size and randomisation will be able to demonstrate a difference in effect between the intervention being studied and the control condition (Gamerman, Cai, & Elsäßer, 2019).

What lessons can be learnt from pilot and feasibility research on MBPs?

Where trial based economic evaluations are appropriate, early-stage evaluation work is valuable to improve the design of studies. In general external pilot trials can help evaluate the processes of a main trial, ensuring recruitment, randomization and treatment all work as planned before commencing large RCTs (Arain et al., 2010; Gannon, 2017), and provide useful information about the necessary sample size for a main trial (Whitehead et al., 2015).

From a health economics perspective prior testing of the methods to collect costs and benefits for the purpose of economic evaluation can help reduce missing data, improve reliability of evidence, and help ensure all relevant outcomes to the perspective of analysis are obtained.

Historically, there is a publications bias against reporting small studies often with a high risk of bias (for example when conducted without random allocation or a control group). In addition, there is bias towards publication of positive results with null findings rarely published. While journals such as BMC Pilot and Feasibility Studies launched in 2015 have improved this considerably there remains limited published information about the early-stage research conducted to evaluate MBPs. Reflections on the feasibility studies depicted in Chapter 4 and Chapter 5 of this thesis are presented through this methodological discussion chapter in the context of key considerations for future research evaluating MBPs from a health economics perspective.

What tools are available to MBP researchers conducting health economics studies?

There are a range of tools available to health economists evaluating complex public health interventions, many already highlighted through this thesis including:

- NICE guidance relating to both clinical guidance, technology appraisal and public health evaluation.
- Checklists for the design, conduct and reporting of economic evaluations, and MBP fidelity checklists and good practice guidance.
- Outcome measures including generic preference-based measures and clinical outcomes to demonstrate potential benefits of MBPs.
- Resource use tools to measure consumption of health and social care resources.
- Costing resources to measure the costs of delivery and guidance on considering the budget impact of implementation of MBPs to varying extents.

More recently, there has been a focus on providing greater guidance on the importance of developing Health Economic Analysis Plans (HEAPs) to guide the economic evaluation of complex interventions. Historically, there have been less use of HEAPs (Dritsaki, Gray, Petrou, & al., 2018) compared with statistical analysis plans (SAPs) however currently best practice is that HEAPs need to be prepared alongside wider trial plans and study protocols (Thorn et al., 2020). HEAPs provide a checklist for items to be considered during trial based economic evaluations, many items of which can be piloted and refined through inclusion of health economics in early-stage trials. A standardised HEAP can contribute to greater consistency across economic evaluations (Thorn et al., 2020). However, little guidance exists

for health economics feasibility research (Gannon, 2017) and wide variation in the scope of early studies exists in the case of MBP research (see Chapter 2).

Methodological design questions

This chapter focuses on the specific considerations for health economists to consider when developing methods for economic evaluation of MBPs as complex interventions. This chapter aims to present an update to the recommendations described by Edwards, Bryning and Crane (2015) to review key methodological design questions to guide researchers of MBPs and highlight the existing toolkit of resources available to health economists. Methodological considerations at different stages of translational research framework are discussed, with lessons learnt from two foundational pilot and feasibility studies presented as case studies in Chapter 4 (MBP in cancer recover) and Chapter 5 (MBP in school curriculum).

This chapter has been informed by recently published guidance on HEAPs (Thorn et al., 2020) for trial based economic evaluations and publications relating to health economics feasibility trials (Gannon, 2017). This chapter offers an adapted framework specific to the design, conduct and reporting of health economics feasibility studies evaluating MBPs. The chapter discussed four key stages:

- Section 1: Feasibility study overview and pilot economic methods
- Section 2: Feasibility trial processes including economic data collection & management
- Section 3: Economic data summary and factors for future economic analysis
- Section 4: Health economics reporting and implications

The methodological questions attached to each of these stages are presented in Table 66 in the form of an adapted checklist for the design and conduct of a health economics feasibility HEAP and explored further below with worked examples from empirical studies presented in Chapter 4 and Chapter 5 and wider relevant literature discussed. Based on the work presented in Chapters 4 and 5 of this thesis, the following checklist was developed and its application through this chapter is illustrated.

Table 66: A template pilot checklist for researchers conducting feasibility trials of MBPs

	Yes	Page number	No	N/A
Section 1: Feasibility study overview and pilot economic approach				
1. The aims and the objective(s) are described				
2. The pilot economic approach is described including perspective of analysis, jurisdiction, study population				
3. The time horizon for the research is justified and discount rate considered				
4. The intervention(s) are described, and delivery costs considered				
5. The benefits to be measured are identified, methods for the measurement and valuation are described with any existing thresholds for meaningful change specified				
6. The range of costs to be considered is described, methods for the measurement and valuation are outlined				
Section 2: Trial processes including economic data collection & management				
7. A study protocol is developed				
8. Delegation log for health economics data processes is established				
9. Outcomes are registered				
10. Scoring algorithms are defined and data entry is checked for accuracy				
11. Storage of data both short and long term is considered				
12. Data is checked for validity with out of range defined and data cleaning conducted				
13. Missing data is considered, and analysis sample defined				
Section 3: Economic data summary and factors for future economic analysis				
14. A summary of the data and any analysis is outlined and is appropriate for the feasibility stage of study				
15. Equivalence between groups is considered				
16. Benefits are assessed for indicative pilot results and effect size established (where appropriate)				
17. Patterns of resource use are considered				
18. Uncertainty is considered through sensitivity analysis				
Section 4: Health economics reporting				
19. Reporting is informed by best practice guidelines and checklists				
20. Summary of principal findings are consistent with data summary and appropriate for a feasibility study				
21. Strengths and limitations are clearly reported				
22. Results are compared with other published literature				
23. Recommendations for future research are reported				
Appendices				
A1: Study documentation are included in the appendices				

Section 1: Feasibility study overview and pilot economic approach

Figure 38 shows stage 2 of the translational research process to be about the feasibility study stage. To reiterate, the purpose of a feasibility study is to find out "whether something can be done, should we proceed with it, and if so, how. A pilot study asks the same questions but also has a specific design feature: in a pilot study a future study, or part of a future study, is conducted on a smaller scale" (NIHR, 2021).

***What are the aims and objectives of the health economic component of feasibility studies*?**

In a trial based economic evaluation typically the research question would be formalised in terms of "How cost-effective is the MBP, for people with 'x' condition, in the setting 'y', as compared with 'z' as usual practice" (Edwards et al., 2015). The research question should define the intervention, the population, and the setting for the purpose of evaluating cost-effectiveness before introducing the alternative with which it will be compared. When considering the whole continuum of translational research that contributes to the evaluation of MBPs as complex interventions, then a range of research questions can be identified, occurring both prior to a definitive trial based economic evaluation question, for example through feasibility research and afterwards, for example, through implementation research. Table 67 depicts examples of some research questions appropriate for different stages of MBP complex intervention economic evaluation.

In translational research, where each study stages sequentially inform the next, early pilot and feasibility studies require appropriate research objectives to first test the parameters that could be used in a future economic evaluation. The aims of a feasibility study may be to establish levels of acceptability, accuracy and explore uncertainty about the most appropriate ways to address future research questions. Rather than focusing on outcome alone, research questions in pilot trials should ideally consider processes such as recruitment, randomisation, data collection, and consider the extent to which progression criteria are met. Many of these factors are relevant to feasibility trials in general not just health economics studies, however it is rare that health economics would be the sole focus of a study.

Evaluation of the trial protocol to assess data collection methods and potentially linked completeness of data can help provide useful information to improve the design of future studies. For example, there could be order effects of questionnaires that influence completeness of data, if the health economics measures are included at the very back of the large questionnaire booklet then the likelihood of participants completing all core questions may be low.

There may be multiple objectives of a feasibility study a primary objective is likely to focus on the methods for assessing costs and benefits however secondary objectives may consider reviewing the data obtained to better understand the study population in terms of health state and disease burden, and to build up a picture of the types of services routinely used that may be relevant to capture in economic evaluations that follow.

Table 67: Examples of research questions appropriate for continuum of stages of MBP complex intervention economic evaluation

Stage of research	Examples of research focus	Examples of health economics research question
Stage 0	Cost of illness, Population health needs, drivers of health market behaviours, behavioural economics, population preferences, inequalities	What is the preventable cost of mental health conditions?
Stage 1	Intervention development, mechanisms of intervention, proof of concept, formative assessment of costs and benefits	What are the range of costs and benefits relevant to the perspective of analysis?
Stage 2	Pilot testing outcomes and re-testing	What are the appropriate outcome measures for evaluating benefits of a mindfulness-based curriculum in secondary schools?
Stage 3	Cost-effectiveness	Is MBCT cost effective compared with maintenance antidepressants for the management of recurrent depression in primary care?
Stage 4	Implementation, service evaluation, budget impact, survival analysis, social return on investment	What is the budget impact of implementing MBCT-Ca within secondary care at local and national levels?
Stage 5	Policy change, population health, population need/cost of illness, programme budget and marginal analysis	What is the economic case for mental health prevention?

Note: the research questions presented here are not a comprehensive list and are for illustrative purposes only.

What is the pilot economic approach including planned perspective(s) of analysis, and which form of economic analysis method is most appropriate?

As discussed in Chapter 1, traditionally, health economists have distinguished between several methods of analysis. Drummond and colleagues (2015) outlines these as cost–benefit (which measures costs and benefits in monetary terms), cost-effectiveness (which measures outcomes in some appropriate natural unit), cost-utility (which measures outcomes in some universal measure of health gain, e.g. the quality-adjusted life year QALY) and cost-consequence analysis (that compares costs with a full range of disaggregated outcomes) (Drummond et al., 2015).

To determine the method of economic evaluation that is most appropriate and the range of benefits and costs to be collected, it is necessary to identify from whose perspective costs and benefits are being evaluated. While the perspective of analysis can be varied irrespective of the method of economic evaluation, the perspective helps indicate which costs and benefits are relevant. The choice of outcomes may influence what economic evaluation methods would be most appropriate to use. Not including an outcome of importance may limit the methods of economic evaluation possible, for example, without a source of utility outcomes it is not possible to conduct cost-utility analysis. The context of the research is important with a need to consider the jurisdiction and country of research, and population and setting in which the MBP is designed to be delivered. Consideration of the relevant inputs and outputs of an intervention are important for helping to determine the perspective of analysis, for example, this may involve identifying the range of stakeholders who incur costs relevant to the intervention or who benefit from the effects of the intervention.

The expansion of MBPs applied to non-clinical settings such as schools and workplaces, has further highlighted the drive to move away from the medical model of health. Analysis within this paradigm would traditionally be conducted from a NHS perspective of analysis in the UK. This would commonly involve a narrow set of costs and benefits directly relevant to the NHS. There has been increasing imperative to move towards a broader public sector multi-agency perspective or whole society perspective of analysis (Edwards et al., 2008; Edwards & McIntosh, 2019; S. Walker et al., 2019). This broader approach recognises the need to collect a diverse range of costs and benefits across different sectors that may incur costs or benefit from the intervention being evaluated (Edwards et al., 2015). This may include considering third sector organisations including non-government bodies, charities and voluntary services alongside other public sector bodies such as local authorities, education providers and private businesses.

In 2015 cost-benefit was proposed as a potential way of “capturing the benefits of MBPs in non-health care settings such as schools and workplaces. In the case of researchers interested in measuring the

costs and benefits of mindfulness training in education or in the workplace, capturing the financial impact of improving educational standards or reducing absenteeism may be an effective way of measuring benefits. In addition to cost–benefit analysis, cost-consequence analysis has been recommended by those tackling the methodological challenges of public health interventions, as a way of capturing a full range of benefits, to the individual, family, setting, school or workplace and wider society (Kelly et al., 2005; Weatherly et al., 2009)" (Edwards et al., 2015, pp. 493–494). However, to date the majority of MBP trials with concurrent economic evaluations have adopted a cost-utility or cost-effectiveness approach, the majority of which were conducted in a clinical setting (see Chapter 2 for systematic review). For MBPs that focus on mental health treatment or prevention it is appropriate that a health care perspective of analysis is given due consideration in the UK, with the NHS incurring high costs of depression and mental health highlighted as a priority concern for the NHS (McCrone et al., 2008).

Particularly in the case of impacts on different sectors where different evaluative contexts and decision rules exist then it may be appropriate to adopt more than one perspective (Byford & Raftery, 1998; Garrison, Pauly, Willke, & Neumann, 2018) and more than one form of economic evaluation may be appropriate to offer a comprehensive picture of value for money in different contexts.

It is important to consider that the potential benefits and costs associated with MBPs may not be confined to the individual receiving the intervention and the sector in which is delivered and there is a need to consider spill over effects, referred to by economists as 'externalities' (Weatherly et al., 2009). When considering MBPs as preventative public health interventions delivered by the health sector there may have benefits to social care, education sector, justice service and the wider economy, considering the impacts of mental health on these areas. It is in considering this that well-being becomes the concern of all government sectors and supports this shift from the medical model paradigm of health to a more integrated 'whole systems' perspective alongside a 'whole person' model considering physical, mental, emotional and psychosocial wellbeing (Ijaz, Rioux, Elder, & Weeks, 2019).

It may be that cost-consequence analysis is also the most appropriate design for an economic evaluation of an MBP. However, it is important to note that cost-consequence analysis does not allow for a simple comparison with other health interventions as is possible with cost per-QALY estimates and may not be appropriate when a clear decision rule is required (e.g., in health care). In principle, a trial of MBP in a setting or patient group where generic measures have been shown to be sensitive, e.g. depression treatment (Sapin, Fantino, Nowicki, & Kind, 2004; Sobocki et al., 2007), and where a threshold is relevant for a funding decision as in the case of NICE in the UK (NICE, 2013a), a cost-utility approach may be more appropriate. A cost-utility analysis or cost-effectiveness analysis embedded in a wider cost-

consequence analysis may meet commissioners need to inform a decision rule, whilst acknowledging the wider range of outcomes from a MBP (Edwards et al., 2015).

Outside of trial based economic evaluations, SROI, a form of cost-benefit analysis is becoming more popular to show social value generated from interventions to a range of stakeholders (Fujiwara, 2015). While less commonly used in health care evaluation SROI is popular in economic evaluations in private sectors with industry and employer looking to demonstrate impact of their services (Banke-Thomas et al., 2015).

Given that all resources with an opportunity costs should be captured, where benefits and costs span multiple sectors a broad societal perspective is necessary (Walker et al., 2019). A broad perspective of analysis, or multiple perspectives of analysis have been highlighted as useful in Chapter 4 and Chapter 5 of this thesis, when considering the complex nature of MBPs and the complex systems in which they are implemented.

***What is the appropriate time horizon for the research? Is economic modelling likely to be useful in MBP research*?**

The contrast of the two MBP applications presented in this thesis aimed to explore the economic evaluation of MBPs targeting different stages of depression prevention. This work raises important considerations about how to capture benefits of MBPs, particularly when benefits may occur into the future beyond the short duration of many trial-based economic evaluations. Many previous MBP economic evaluations have focused on depression relapse rather than primary prevention of depression, however MBPs as part of a school curriculum aim to adopts a much earlier intervention point. With the episodic nature of depression relapse changes in depression may be expected to be observed within the trial window. In contrast, earlier intervention (primary prevention) approaches delivered as a public health promotion and resilience building programme benefits and costs may fall well outside the trial time horizon. It can be challenging to quantify and observe prevention benefits as part of time limited clinical trials. If economic evaluations of MBPs have a short follow-up period, then any future benefits won't be valued, and this will likely reduce the potential probability of cost-effectiveness results in a trial. A pragmatic approach that considers the results from a range of sources may provide a more complete picture of societal value of an MBP to inform policymakers across sectors on investment decisions. More research is needed to establish whether MBPs can be effective as public health interventions and whether they offer value for money if implemented at varying extents.

Economic evaluations that contain future costs and benefits (that occur more than 12 months in the future) should be discounted. This is necessary to weight costs and benefits appropriately reflecting the time in which they occur, and the value people place on them. In the case of many public health

interventions benefits may be observed along a longer time horizon compared to medicines or other treatments. NICE have argued that discounting methods could result in a substantial undervaluation of preventative interventions (NICE Citizens Council, 2011) and highlighted that sensitivity analysis that considers a differential discount rate of 1.5% may be useful to be compared with the reference case analysis, typically at a rate of 3.5% (Brouwer et al., 2005; NICE, 2014a). careful methodological considerations are needed as the conclusions drawn from cost-effectiveness estimates may be influenced by the discount rate selected, (NICE, 2014a; O'Mahony et al., 2011, 2015). To date the majority of the MBP economic evaluation studies have adopted a short time horizon of under one year and neither costs nor benefits were discounted. Where studies had a longer time horizon costs and benefits were discounted at a rate between 2% and 3.5%.

Depending on the payer perspective and context of research with narrow budgets within short political time frames there may by systemic limits on the value placed on benefits which occur in the future, much like time preference by individuals. What is needed now is methodological research exploring how to measure and value future benefits from prevention initiatives. "Economic modelling is used by health economists, particularly in the pharmacological industry, as an alternative to economic evaluation alongside a clinical trial using patient level data, particularly where there is a need to extrapolate beyond the length of follow-up (Briggs et al., 2006). Modelling allows consideration of uncertainty, particularly probabilistic decision analytic modelling. It involves drawing estimates of costs and estimates of effectiveness and the probabilities of patients/individuals moving from one health state to another, e.g. from episodes of wellness to relapse in depression, in a Markov model (Briggs & Sculpher, 1998). However, to construct meaningful models, sufficient data is required. There are at present very few trials of MBPs that include an economic evaluation component and, even when those underway now are published, there will still be relatively few. There is a need to consider that cost and outcome findings from an MBP in one setting, e.g., cancer care, cannot necessarily be extrapolated to a completely different setting, e.g., workplace well-being. More trials and economic evaluations are needed in a range of settings" (Edwards et al., 2015, p. 496).

The World Health Organization highlights that we are often required to balance what is considered gold standard methodological rigour with pragmatic considerations for what is feasible, ethical, and timely to inform rapid decision making that adopts greater prevention of cure:

"Although the generation of cost-effectiveness evidence is often best approached through long term prospective studies (e.g., a randomized control group, long-term follow-up, etc.), the time and costs of undertaking this type of research limits the availability of such type of data. Indeed, experimental controlled trials may not always be feasible because of ethical considerations or sample size requirements. In such circumstances, modelling studies, which attempt to simulate a clinical trial using

publicly available data sources, provide a useful alternative approach to generating evidence on the costs and consequences of preventive interventions. Although subject to a number of concerns relating to the over-simplification of (public health) reality, diversity of data sources, and the need for multiple assumptions relating to key parameters, modelling studies do not require recruitment and follow-up of subjects and can therefore be undertaken much more quickly. Such models can provide decision-makers with an overall estimation of the expected health gains of an intervention strategy (e.g., reduced incidence of a mental health condition, or averted disability) as well as the costs associated with obtaining this health gain (e.g., administrative costs, training, early identification). There are currently very few reliable data on the costs or cost-effectiveness of alternative mental health preventive strategies in different WHO regions. By conducting a range of appropriate experimental and modelling studies, however, such an evidence base can be constructed in a way that will offer policy-makers and health care managers important population-level information on the short- and longer-term costs and effects of different intervention options" (World Health Organization - WHO, 2002, p. 24).

This emphasis of pragmatism requires efforts in real-world settings, outside of trial-based economic evaluations, to collect data on population health with longitudinal follow-up up particularly as interventions are rolled out into to routine practice are important. For example, as MBPs are implemented within schools through education policy and national curriculum evaluation is needed so that benefits in the future can be measured over time to justify continued inclusion or potentially disinvestment and reinvestment into more effective and cost-effective interventions. The forthcoming results from the MYRIAD trial (Kuyken et al., 2017) may add to the limited evidence base on MBP economic modelling research and could help provide guidance to other researchers wanting to evaluate both short and long-term benefits of prevention initiatives in schools. Lessons to be learnt from each study should be assessed and future research built on this learning. Greater strides in open access data allowing for secondary data analysis where appropriate across studies and across populations and where possible building a longer-term follow-up to validate estimates of economic models.

There are some small evaluation studies that have indicated small to moderate effect sizes for mindfulness in schools, and while the evidence on cost-effectiveness has not kept pace, the interventions are often implemented anyway. According to MISP mindfulness in schools is growing at a higher rate in Wales than other areas of the UK (MISP, 2020). It has been argued that there is a clear opportunity to embed mindfulness into the new 2022 national curriculum in Wales ("Mindfulness in Schools Project (MiSP)," 2020; MISP, 2020). This may offer an opportunity for monitoring population level outcomes, however, consideration of what would be appropriate comparison data is needed. Longer term outcomes from MBP implementation in schools should be collected alongside modelling work to enable increasingly confident estimates over time.

Looking to the far end of the translational research framework population-based service planning for implementation of MBCT has highlighted the value of modelling to assess population needs and facilitate implementation by determining the number of therapists needed to treat the population (Patten & Meadows, 2009)**.** However, there remains a sparsity of simulation modelling in mental health and barriers to publishing modelling studies (Long & Meadows, 2018).

***What is the intervention, and with what alternative intervention or situation is the MBP to be compared*?**

The control condition needs to be a clinically relevant alternative or, as is conventional, reflect 'usual practice', which sometimes can mean no active treatment. In a trial of the management of relapse of depression (Kuyken et al., 2008), compared MBCT plus maintenance antidepressants (mADM) with mADM alone. This trial was designed to reflect widespread 'usual care' and acknowledged MBCT as a component of care rather than a straightforward alternative to pharmacological management. This thesis research has highlighted some of the challenges with comparison conditions, from a TAU control condition in the MBCT-Ca randomised feasibility study which experience high attrition to a matched school cohort in the evaluation of mindfulness embedded into the school curriculum compared with teaching as usual of the traditional curriculum. In both studies the costs of MBP need to be balanced against the cost of delivering usual care, which in some cases may involve very little resource use. It is as important to compare the resources required in the intervention arm of a trial but also costs of the control arm, to allow for calculation of an ICER.

In the evaluation of psychosocial interventions, especially group-based interventions, which contain an element of 'socialisation', there may be some beneficial effect of just meeting (Webber & Fendt-Newlin, 2017), and factors such as this should be considered in documenting, describing and standardising the control condition in a trial of a MBP. A number of studies have used active control groups within the trial design of MBP evaluation (Grossman, Tiefenthaler-Gilmer, Raysz, & Kesper, 2007; Zautra et al., 2008). One such trial that aimed to dismantle the various components of MBP to explain the mechanism of an effect, the active control condition, Cognitive Psycho Education was described and was designed to include all components of MBCT except the mindfulness meditation practice (Williams et al., 2010). This trial aimed to establish whether MBCT was effective in preventing relapse into depression for people who become suicidal when depressed.

The appropriate type of control intervention for MBPs are not likely to be the same across MBPs delivered in different settings for example MBCT for cancer patients compared with an mindfulness embedded within teaching curriculum as a universal intervention in schools. For MBCT-Ca an active control condition, with group-based socialisation elements and psycho-education would be highly

superior to a comparison with no treatment. This would provide a more equal comparison for intervention costings and provide a mechanism for reducing attrition for the research through increasing contact and improving communication with participants. For MBPs delivered in school, usual teaching already provides a reasonable active control condition. This is on the basis that the mindfulness teaching is embedded within the curriculum to achieve the same learning objectives. Usual teaching already provides elements of socialisation within school classes and the differences between resources to deliver the teaching is unlikely to be large beyond initial costs of training. A fully costed estimate of the additional resources to implement MBPs within schools and whether they are embedded rather than additional in practice warrants further exploration.

How are the economic benefits to be measured, and what is an important change on such measures?

Clinical outcomes and measures of effectiveness

As with the evaluation of many clinical interventions a primary outcome of analysis needs to be defined before starting an evaluation. When considering the appropriate benefits to be evaluated in MBP research, particularly in clinical research, it is important to note that there is commonly a distinction between the primary effectiveness outcome and the economic benefits. Cost-effectiveness analysis will commonly share the same measure of effect as the primary study evaluation to develop a cost per unit of clinical effect, for example, cost per depression free day (Kuyken et al., 2008). In addition to selecting the main outcome for measurement, there needs to be consideration of what constitutes a clinically important change or minimally important difference on the measures of effect. The outcome measure needs to reflect the area of expected change from the MBP. In Chapter 4 the focus of MBCT-Ca rather than aiming to change the prognosis of a disease such as cancer, instead provides psychological support for patients dealing with diagnosis, treatment and the overall experience of cancer (Shennan, Payne, & Fenlon, 2011).

The area of greatest evidence for expected change from MBPs remains focused on the management of recurrent depression. There is evidence for reduction in rates of depression relapse (Piet & Hougaard, 2011). The mechanism by which MBCT achieves this preventative effect through changing the participants' relationship to the experience of depression (Kuyken, Watkins, et al., 2010). Rather than fighting to prevent a depression relapse, participants develop a compassionate and interested relationship with the negative thoughts and emotions that can precipitate a depression episode. This radical shift in attitude and approach creates a range of other well-being-enhancing effects beyond protection from depression. Researchers are increasingly working to capture the diversity of effects both through process evaluation integrated within RCTs (Williams et al., 2010) and through qualitative evaluations which can capture the subtleties of an approach (Allen, Bromley, Kuyken, & Sonnenberg,

2009). In the last six years there has been greater attention on the mechanisms of change and mediation analysis of MBPs (Alsubaie et al., 2017; Gu, Strauss, Bond, & Cavanagh, 2015; Mackenzie & Kocovski, 2016; van der Velden et al., 2015). However there remains uncertainty around the important mechanisms leading to change through MBP and further mediation studies with methodological rigour are called for (Alsubaie et al., 2017; Gu et al., 2015; van der Velden et al., 2015).

There is rarely only a single available tool for measuring benefits such as depression. For comparison across studies, it is useful to choose commonly used questionnaires such as the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983). This is with the aim of supporting service commissioners reviewing evidence to interpret the relative benefit of achieving an improvement on the chosen outcome measure. While using the same measures as those used in other studies aids comparability, it also has the disadvantage of narrowing the range of outcomes that are being evaluated and valued. There is little consensus around the most appropriate outcome tools and research teams will often have a different preference to others, important factors may involve the cost of outcomes, the length of questionnaires, the training requirements to administer the chosen tool and the mode of delivery. Even within a specific outcome measure there are decisions to be made about what is a significant change or what the appropriate cut-off or threshold is for determining abnormal levels of psychological distress. For example, in Chapter 4 a range of thresholds were explored for suitability within a population of patients recovering from cancer treatment, these included a general population threshold of $\geqslant$16 on the HADS compared with a lower threshold of $\geqslant$13 considered suitable for cancer populations (Singer et al., 2009). In addition, in Chapter 5 the appropriate GHQ-12 threshold score indicating symptoms comparable with clinical cases of depression was discussed in for an adolescent population in schools setting. This methodological decision was further compounded by variations in scoring methodologies available to researchers working with these outcomes. A feasibility trial provides a valuable opportunity to investigate some of these factors, particularly where uncertainty remains, so that information from early stage of research can be used to inform the development of a definitive trial HEAP.

Secondary outcomes relevant to mechanisms of change or wider cost-consequence analysis

Considering secondary outcomes researchers may need to also include measures which capture the particular shift in relationship to experience that is the core focus of mindfulness-based training (Baer, 2011). These are increasingly being included in large trials (Kuyken, Hayes, Barrett, Byng, Dalgleish, Kessler, Lewis, Watkins, Morant, et al., 2015; Williams et al., 2010) using measures of mindfulness such as the Five Factor Mindfulness Questionnaire (Baer et al., 2006), self-compassion such as the Self-Compassion Scale (Neff, 2003), rumination (Ruminative Responses Subscale of the Response Styles Questionnaire; (Treynor, Gonzalez, & Nolen-Hoeksema, 2003), dysfunctional attitudes (Dysfunctional

Attitudes Scale; (Oliver & Baumgart, 1985)) and acceptance (Acceptance and Action Questionnaire; (Hayes et al., 2004).

Utility measurement for economic evaluations

For the health economist clinical benefits rarely enable suitable comparisons for decisions makers and a cost-utility approach is commonly recommended for use in the evaluation of health care interventions. The requires use of a generic preference-based utility measure which considers both impact on life expectancy and health-related quality of life. With respect to MBPs, the challenge facing health economists relates, firstly, to capturing the benefits of helping people accept or adjust to difficult life circumstances and promote resilience and, secondly, to relating these benefits to limited resources in health and other public services. MBPs used to help people with severe depression and suicidal thoughts may contribute to improving life expectancy across a trial population (Williams, Duggan, Crane, & Fennell, 2006). MBPs may improve health-related quality of life across existing life expectancy in many different settings and for a range of health conditions or life circumstances.

In the UK, the National Institute of Health and Care Excellence supports the use of the EQ-5D (The EuroQol Group, 1990) in health economic evaluations of interventions and health technologies (NICE, 2013a). EQ-5D is a validated generic, health-related, preference-based measure comprising five domains: mobility, self-care, usual activities, pain and discomfort, anxiety, and depression. Each domain has three levels (no problems, some/moderate problems, and extreme problems). The EQ-5D scoring system defines 243 (3^5) possible health states with two additional states (dead and unconscious), where death has a value of 0 and best imaginable health has a value of 1. The questions are complemented by a thermometer style, visual analogue scale, with 0 representing worst imaginable health and 100 representing best imaginable health, on which respondents are asked to indicate their current health state. EQ-5D has the benefit of being short, clear, and quick to complete. The more recent introduction of a five-level version of the EQ-5D which includes the addition of slight and severe problems to each domain (EQ-5D-5L; (Herdman et al., 2011)) may deliver improved performance while still retaining the benefit of brevity, consisting of just five questions (Scalone et al., 2013).While a value set for the EQ-5D-5L continues to be developed, NICE recommends use of an interim scoring method which maps health states to the EQ-5D-3L profiles (NICE, 2019b; van Hout et al., 2012).

Critics of the EQ-5D have highlighted a bias towards physical pain compared to mental health (van IJzendoorn & Bakermans-Kranenburg, 2020). The EQ-5D has been successfully used in trials of major depression more generally (Sapin et al., 2004; Sobocki et al., 2007) and in MBP economic evaluations [see Chapter 2 for an overview of outcomes used in MBP studies]. For example, the question 'I can undertake my usual activities' may at first appear to be directed purely at the physical functioning of the

individual and does not discern how the individual is relating to their functioning; however, it is important to note that our psychological functioning may also influence our ability to undertake these usual activities. While mindfulness-based training may not directly influence functional capacity to undertake usual activities, it is likely to affect the level of ease with which the individual lives within their current capacities (Kuyken, Byford, et al., 2010). An individual who is at ease is more likely to be able to seek and accept appropriate levels of support and less likely to suffer from psychological distress in relation to their functional capacity (Kuyken, Byford, et al., 2010) (Edwards et al., 2015).

In considering whether conventional research instruments such as EQ-5D and SF-6D are sufficiently sensitive to reflect benefits of MBPs there are contrasting results from clinical trials to date. In a trial of MBCT for medically unexplained symptoms conducted in the Netherlands, the resultant QALY gains were very small leading to an ICER of €57,000 per QALY (van Ravesteijn et al., 2013a). This is significantly above the threshold of what society feels is an appropriate investment to gain a QALY, as operationalised by decision making bodies such as NICE in the UK (NICE, 2013a). In contrast, Janssen et al (2019) calculated a cost per QALY of €21,963 from a societal perspective for a MBP delivered in an adult population with ADHD. Lengacher et al (2015) reported a cost per QALY of $22,200, reducing to $5,163 per QALY if treatment effects were maintained from three months to a full year. While there are challenges with generalisability from international studies to implementation within the UK, if replicated within the UK these results would likely fall below the NICE threshold for investment.

Further methodological research is needed to consider what choice of generic outcome are most sensitive to disease-specific changes and most appropriate for use with the population and clinical context in which the MBP is being delivered (Brazier, Yang, Tsuchiya, & Rowen, 2010). When studies wish to consider QALY gains, there is more than one option of generic outcomes, with measures including the EQ-5D or SF-6D. The SF-6D is reported to suffer less with ceiling effects with worst best health anchored on a different scale to the EQ-5D and have been argued to be more appropriate for populations with higher overall health (Kontodimopoulos, Argiriou, Theakos, & Niakas, 2011). Although both measure may be interchangeable in their ability to produce a single index measure of utility for the calculation of QALYs, the choice of outcome measure remains important as evidence highlights choice of EQ-5D or SF-6D in mental health populations can produce different results (Lamers, Bouwmans, Straten, Donker, & Hakkaart, 2006).

The appropriate economic outcome may depend on the population of study. For example, the feasibility research in this thesis highlighted variation in ceiling effects on generic outcomes such as the EQ-5D in generally healthy populations such as in children in schools compared with clinical populations such as adults following cancer treatment. The findings from this thesis research have implicated that these variations in generic outcomes may not be mirrored in clinical outcomes. For example, despite high

rates of depression indicated in the adolescent population (reported in Chapter 5) there were high ceiling effects of the EQ-5D-5L with between 28% and 48% of the samples reporting full health on the outcome. The MBCT-Ca feasibility study with adults (reported on in Chapter 4) was less susceptible to ceiling effects in generic outcomes, with ceiling and floor effects instead observed on specific cancer function and symptom scales perhaps indicative of the time since cancer diagnosis and treatment in this study sample. The challenges of conducting cost-utility analysis in children populations have been discussed in previous literature (van IJzendoorn & Bakermans-Kranenburg, 2020) and in Chapter 5 of this thesis. The EQ-5D-Y (Wille et al., 2010) has been adapted for adolescents but there is no value set to make it useful for use in cost-utility analysis. In addition, the EQ-5D-Y 5L questionnaire has been in development however without value sets their use in cost-utility analysis is limited (Kreimeier et al., 2019).

Alternative child specific utility measures such as the CHU-9D (Furber & Segal, 2015; Stevens, 2010) have gained traction in economic evaluations in adolescent populations (Stevens & Ratcliffe, 2012). The CHU-9D has the benefit of enabling a cost-utility analysis while offering different options for value sets for example with the adolescent-specific value set developed in Australia (Ratcliffe et al., 2012) as a comparison with the adult-specific scoring algorithm (Stevens, 2010).

While researchers have recommended that health economists should continue to use EQ-5D in children population studies, greater methodological work to develop methods that better take account of children in decision making is still needed (Noyes & Edwards, 2011). It is commonly acknowledged that people value health states differently for children (Kreimeier et al., 2019) and whether existing population value sets appropriately capture societal views remains an important point for economic evaluations and decision making in this field.

Considering economic outcomes as complementary to or as an alternative to the QALY approach

Alternatives to an extra-welfarism societal utility maximisation paradigm with the QALY approach at the centre, include the capabilities framework (Lorgelly, Lorimer, Fenwick, Briggs, & Anand, 2015; Sen, 1999). While related to extra-welfarism and correlated with health related quality of life, the capabilities approach adopts a broader construct of wellbeing compared with utility (Coast, 2004), focusing on what people feel able to achieve. This is much more in line with an asset approach to public health than traditional deficit models of health (Morgan & Ziglio, 2007). As discussed in Chapter 4 the ICECAP measure offers an outcome for evaluation within a capabilities framework (Al-Janabi et al., 2012, 2013; Grewal et al., 2006). The original ICECAP-O, developed for older adults has five domains: attachment, security, role, enjoyment and independence and four levels of capability (ranging from a lot to none; (Grewal et al., 2006). The development of the ICECAP-A is suitable for use with younger adult

populations (Al-Janabi et al., 2012). The ICECAP-A aims to measure factors relevant to an adult population rather than older adults and identifies five domains: stability, attachment, autonomy, achievement, and enjoyment and four levels of capability (Al-Janabi et al., 2012).

Advocates for a capabilities approach in economic evaluation have highlighted contrasting desired of maximizing population health or sufficient capability in economic evaluation. In terms of valuing the ICECAP there are alternative approaches even within this paradigm, these focus of assessing years of sufficient capability or years of full capability. Proud et al (2019) highlight that "sufficiency represents an alternative normative approach to maximisation (as adopted in cost-utility analysis) and hence adoption of sufficiency would represent a further, significant, shift towards the ICECAP-O being used as a tool within a distinct conceptual framework. A significant programme of future research would be needed to identify a sufficient state of well-being, as defined by ICECAP-O. The issue of an appropriate monetary threshold would also potentially need to be addressed" (Proud et al., 2019, p. 1437).

Closer to QALYs in maximisation is consideration of assessing years of full capabilities (YFC) as piloted in Chapter 4 of this thesis. This later approach more comparable with QALYs in terms of a maximisation societal goal, it is important to note that YFC and QALY approaches are distinctively different, particularly in terms of decision making where more work is needed to identify willingness to pay thresholds for a year of full capability (Proud et al., 2019). Choices around appropriate method for valuing the questionnaires adopted require acknowledgment of the evaluative framework and implications for decision makers with Goranitis et al (2016) highlighting that these "different evaluative spaces and decision-making rules have the potential to offer opposing treatment recommendations" (Goranitis et al., 2016, p. 500).

In fact, most recent guidance suggests that adopting a capabilities approach may be complementary to more tradition methods of economic evaluation however further conceptual and methodological work is needed before ICECAP may be suitable as an alternative to utility measures such as the EQ-5D: "Positive evidence of the measure's content and construct validity is beginning to accumulate, but further conceptual and policy debate is needed regarding the equity implications of switching between evaluative spaces" (Afentou & Kinghorn, 2020, p. 515).

Capabilities across the life course research has focused in reverse chronological order, with older populations at the conception, to adult populations and clinical groups in recency. However the approach is yet to be substantially extended to children, although methodological work to consider the application of capabilities to childhood is underway (Health Economics Bristol, n.d.; Mitchell et al., 2021).

Summary of outcome options for a comprehensive but practical evaluation

Compromises must be made between desires for comprehensiveness in data collection and concerns over data burden. Decisions relating to which data should be collected alongside a trial and the length of follow-up are dependent both on the need to measure all relevant resource use and consideration of the opportunity costs of data collection. In consideration of the stage of economic evaluation of MBPs and the continued need for methodological enquiry, the inclusion of generic preference based outcomes, condition specific and intervention-specific outcome measures should continue to be included where possible (Edwards et al., 2015).

***What is the range of costs to be considered*? *How are costs of a MBP to be measured*? How will they be valued?**

Costs include costs of intervention and wider resources consumed through the study period. MBPs are unlikely to come with an off the shelf market price like medical devices and pharmaceuticals to inform the costs for an economic evaluation. Some public health programmes may have a licence fee that provides programme materials such as workbooks, however MBPs still require someone trained to deliver the intervention.

Costing the delivery of an MBP may involve the initial costs of training of the mindfulness teacher (and these costs can be annuitised over an appropriate period, e.g., 3–5 years, when the teacher might be expected to continue teaching); running costs, including ongoing supervision of teachers and attendance on continuing professional development training; room hire; overheads; materials such as books and CDs for home practice; and administrative support. Consideration of who will likely deliver the programme if implemented requires consideration, if existing employees then training costs would need to be factored in, alongside longer-term supervision and on-going training requirements to meet good practice recommendations.

If an external organisation or consultant is to deliver the programme then these training costs are more likely to have occurred historically and are unlikely to be part of the programme cost however should be reflected in the rate of pay or total fee payable, i.e., appropriate for level of qualifications. With teacher training experience often argued to be essential this model may be more feasible and sustainable as investment in current staff can fail without on-going budgets to enable ongoing training or retraining because of staff turnover.

Even with internal staff delivery, many teachers may subsidise the cost of delivering an MBP through personally incurring the costs of ongoing training and supervision, which may be viewed as personal development and deepening of their personal mindfulness practice (Bryning et al., 2015). On the basis that teachers' time does have an alternative use, these costs should be calculated and included in the

economic evaluation. This principle applies to such things as room hire, which may appear to be 'free' (for example a bookable room in a hospital, school, or workplace).

It is necessary that their market costs are included either in the base case analysis or in sensitivity analysis to illustrate how costs of running an MBP vary under different assumptions, for example, about rates paid to teachers or the number of teachers in each group.

As discussed in Chapter 3 of this thesis there are different methods for costing. A recent costing framework paper some of the most comment costing methodologies (Špacírová et al., 2020).

Micro-costing is the bottom-up construction of the costs of a programme, treatment, or intervention. Micro-costing can involve careful specification of training costs, staffing costs, venue overheads, materials, and staff travel, where appropriate. Micro-costing techniques have been used effectively in similar group-based interventions such as group parenting programmes (Charles et al., 2013) and are appropriate in an MBP context. Micro-costing has been used to determine the full costs of delivering MBPs in different settings as presented in Chapter 3 of this thesis.

Alternative modes of delivery and implementation raise methodological considerations for the resources to be costed. Costing a whole school approach is even more challenging when complex interventions are delivered within complex systems, for example when MBPs are embedded into the national curriculum and further methodological work is needed to consider appropriate methods for costing integrated MBPs.

According to the principles of economic evaluation, all resources with alternative uses within the chosen perspective need to be measured and valued. Where MBPs are being delivered within a health and/or social care setting as well as identifying the costs of delivery, it is necessary to capture the impact of service use by individuals following an intervention. It is important to assess whether MBPs lead to any increase in appropriate service use (through information and contact gained or recognition and acceptance of problems), substitution or reduction of service use, or a reduction in reliance on services (such as the family doctor).

The DIRUM database (www.dirum.org) provides a repository of resource or service use instruments appropriate for different clinical and non-clinical settings (Ridyard & Hughes, 2012). Capturing resource use and associated costs enables health economists to draw conclusions about the impact of MBPs on demands on traditional health and social care services. These broader societal findings could be important to those wanting to make a case for the funding of MBPs in future and potential integration into primary care, school, or workplace.

Piloting CSRI questionnaires can identify whether they will be completed accurately, containing units, user friendly, with a suitable recall period at each timepoint for example or as a diary kept. There has been little research in MBP evaluations to compare other methods of resource use data collection for example through health data repositories or from employers or schools e.g., on sickness absence.

Building on the feasibility research presented in this thesis a greater range of resource use relevant to a societal perspective cost-effectiveness analysis of MBP are needed in future research. Chapter 5 thesis research successfully collected brief health care resource use information from young people however recall was limited to 3 months and to GP service use alone. Patterns of service use and details from resources to identify any missing resources that may be relevant e.g., reason for GP attendance indicates some other services that might be attended in this population. Other health and social care resource use may be relevant outcomes for a societal perspective analysis for example in one recent study results indicated that high anxiety predicted GP attendance while high depression predicted emergency department attendance (Saini et al., 2020).

Section 2: Trial processes including economic data collection & management

Developing a feasibility study protocol can be used to map out all important trial processes including the economic data collection and management. Assessment measures built into feasibility studies to consider trial processes are needed to provide more information on the acceptability and feasibility of novel applications of MBPs. In addition, internal evaluation of trial methods can provide a framework for recording the important lessons learnt from feasibility studies on the recruitment, measurement and valuation of outcome measures and other factors which may influence findings of future cost-effectiveness research.

The data collection tools can first be piloted in early stage research, ideally with a sample of participants similar to the intended population for future research (Coyle et al., 1998). According to Coyle et al (1998) the testing of outcome measures "applies to all data collection methods, from the simplest checklist to the most complex patient diaries or interviews. The pilot study should test the validity, consistency, reliability, and response rate of the forms to be used. If one or more of these criteria are not satisfied, the relevant forms should be redesigned and repiloted. In particular, if the pilot study indicates that there may be large amounts of missing data due to incomplete responses or nonresponse, consideration should be given to alternative designs and methods of data collection. A high percentage of missing data may result in biases in the data recorded, which may not be random between the study groups. This could lead to invalid results" (Coyle et al., 1998, pp. 141–142).

Consideration of the source of data for health economics is important. Data may be available from previous studies, with open access data storage considered increasingly important. Longer term storage

of data (subject to ethical approvals and regulations relating to data management) may provide useful opportunities for secondary data analysis or economic modelling. If health economic evaluation is conducted alongside a new clinical trial then clear delegation of data collection, storage (both short and long term) and trial processes are needed. Training in the collection and entering of data with clear code books are needed to avoid errors on transfer of data to health economics team or researcher. For certain commonly used health economic outcomes such as the EQ-5D and ICECAP-A there is a registration process for use of the measures, and for outcomes used in certain contexts such as commercial settings there are license fees that are payable for there use. The health economist should make sure that the relevant outcomes are available for use in the study and that relevant permissions are in place to ensure that the data can be collected and used for to achieve the outcomes of the feasibility study. Once outcome have been selected decisions need to be made about the methods for scoring and thresholds relevant for the analysis, for example, the methods for scoring GHQ-12 reported in Chapter 5 of this thesis and the choice of cut off for psychological distress classification used for the HADS measure used in Chapter 4. Exploring these options for scoring and thresholds for relevant economic outcomes can be a useful component of feasibility studies, to inform the analysis of future trials.

Important lessons from the feasibility research presented in this thesis highlight that the health economists should work closely alongside other researchers during the development of study design, data collection and conduct data monitoring checks during a clinical trial. In line with good practice guidelines for the conduct of clinical trials and economic evaluations more generally detailed methods should be agreed apriori and included in a HEAP for example defining methods for scoring outcomes. Developing data codebooks to accompany economic datasets could improve data validity when there are multiple members of a team involved in research. There are steps that can be taken to improve the validity of data and subsequent certainty of results such as conducting data checks against original questionnaires with transparency processes ensuring data cleaning and any revisions to scoring and valuing the data are clearly recorded. Ensuring access to the questionnaire data is important to conducting full data checks and cleaning economic data, particularly when conducted by a researcher separate to the conduct of the core study (as presented in Chapter 5 of this thesis). Ideally, economic analysis should be conducted as close to the completion of the study as possible to facilitate these process measures suggested and to ensure the timely publication of research findings alongside main study outcomes.

Wider trial progression criteria may focus on factors such as recruitment and acceptability. While health economics progression criteria may be appropriately restricted to the completion of outcome measures and levels of missing data.

Section 3: Economic data summary and future economic analysis

***What is the planned analysis? Are the study results sensitive to changes to our assumptions*?**

Data analysis for any health economics study should be planned and clearly outlined. The approach to data synthesis and analysis within feasibility studies should be appropriate for the stage of the study. Where groups are compared, consideration of equivalence between groups would be important to explore, alongside pilot assessments of benefits subject to adequate power. "The early trials of MBPs were very small (Grossman, Niemann, Schmidt, & Walach, 2004) and underpowered (Baer, 2003). The power of a trial is the extent to which we are able to detect a 'real' difference between the intervention and control condition, and not just a difference that might come about as a result of random difference in the population (Altman, 1991). Powering is also important to trials of MBP because trials will often by their nature be what are called 'cluster randomised trials' with each group of participants constituting a cluster as randomisation takes place at group level rather than individual level, perhaps with a waiting list control (Williams, Russell, & Russell, 2008). The dynamics of delivering an intervention in a group context need to be acknowledged when planning powering. The researcher must consider whether one MBP group is the same as another, with a different teacher, a different room and held at a different time of day. This will determine the number of study participants necessary to detect a true difference in outcomes of interest between arms of the trial. Powering is important to economic evaluation in that we are concerned with joint distributions of costs and effects for each participant in a trial. It is well accepted in health economics that cost data is skewed to the right (Briggs & Gray, 1998). This is because in any sample of patients or individuals most observations are likely to be low in cost; however, characteristically there will be a few individuals who are very high consumers of health and social care. Ideally, a robust economic evaluation needs to be based on an even larger sample size than that needed to show clinical power (Briggs & Gray, 1998). This rarely ever happens in clinical trials of any intervention. Sample size is in practise determined by clinical outcomes and limitations to the research design due to ethical considerations and research funding opportunities. It is the task of the health economist within a multi-disciplinary trial team, to simultaneously bring attention to the accurate measurement of costs *and* to the appropriate measurement of outcomes or benefit" (Edwards et al., 2015, p. 493).

Levels of effect in terms of cost-effectiveness alone would not normally restrict a pilot study progressing to full trial, studies are almost all likely to be small and underpowered to show differences between groups, however pilot focus on trends particularly around whether there are substantial cost differences which may be the case when comparing an MBP with a waitlist condition. A pilot study can provide sufficient information to inform the design of a larger definitive trial including the appropriate sample size. Coyle et al (1998) further highlights that "a study protocol should include consideration of sample

size and the power to detect differences in economic variables. No consensus exists on appropriate methods for calculating the necessary sample size for economic evaluation alongside clinical trials. Also, a priori sample size calculations require a level of information on resource use and costs that may not exist before the commencement of the study. However, the design of an economic evaluation should contain, where possible, an estimate of the differences in costs and effects that could be detected by the sample size used for the clinical endpoints" (Coyle et al., 1998, p. 143).

Future cost-effectiveness analysis of MBPs should control for group equivalence, normality of data, account for clustering and consider key covariates in the statistical analysis. Sensitivity analysis is used in economic evaluation to allow the researcher to vary the base case analysis to explore how sensitive results are to changes in key parameters, e.g. in a health care setting: length of hospital stay, grade of staff or dose of a drug (Drummond et al., 2015). A key issue in economic evaluation of group-based psychological therapies is dose. If people do not attend all classes or a defined number of classes (as outlined in the trial protocol), they do not get a 'sufficient dose', and this may affect both the average cost of an intervention, and potentially outcomes. The challenge for the health economist is to define the 'base case' for analysis. In the case of MBPs, these are the assumptions underpinning the main analysis, for example, the number of individuals attending a class and the number of classes constituting a MBP programme. Research plans should consider whether analysis will be conducted on an ITT basis or whether per protocol adherence will be a requirement for inclusion in the analysis sample. Approach to dealing with missing data and what constitutes a complete case should be clearly defined in a HEAP. Feasibility research can be useful to explore these factors, to ascertain to what extent results are sensitive to change when excluding study data. If a per protocol analysis is adopted as a base case then it remains important to establish whether results are sustained on an intention to treat basis, with adherence to protocols as much an issue in practice as it is in clinical trials, and the aim for study findings to be robust when implemented in real-life contexts. Concerns about generalisability from a trial setting led us to consider whether the setting and context of a trial determine its findings and extent to which those findings may be replicated more widely in practice. This is very much the case when considering societal or health equity considerations.

As discussed earlier the range of resources used by participants should be reported and valued in the economic evaluation. Collection of resource use in feasibility stage studies can provide useful data summaries and help explore factors which are relevant for future economic evaluations. In very small studies it may not be possible to identify clear patterns of resource use however reporting on service use data can build up a picture of typical health care, social care, and voluntary service use by the study population. In Chapter 5 of this thesis brief resource use data was collected and explore in relation to GP attendance over time and by groups. Considerations for whether resource use can be extrapolated from

one timepoint to another warrants further investigation in terms of dealing with missing resource use data and in terms of extrapolating over a partial trial period. Where all timepoints were complete a visual assessment was made to compare whether resource use varied over time at an individual level. There was little variation for low users of resource use (either no use or normal use). However, 'very frequent attenders' were not consistent over time, i.e., when 10 (or more) GP visits were recorded in the 3-month period this was only the case at a single timepoint, with the two other timepoints recording visits within the normal range. Given the potential impacts of time on resource use in this cohort extrapolation and missing data imputation warrants careful consideration.

Health economists have developed a range of more sophisticated probabilistic sensitivity analysis techniques which aim to further address uncertainty, going beyond using mean values for key parameters such as costs, clinical outcomes and utility values, and instead use the full distribution of these parameters to estimate uncertainty (Andronis, Barton, & Bryan, 2009). It is a benefit of feasibility trials that they can be used to identify areas of uncertainty for helping to define the base case analysis and sensitivity analysis for future trials.

Section 4: health economics reporting

***How should results be reported and compared with the findings of other studies, and used to advise service commissioners and policy makers*?**

Reporting is informed by best practice guidelines and checklists such as 'The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement' (Husereau et al., 2013). While pilot studies should report a clear summary of principal findings this should be consistent with data summary and appropriate for the feasibility stage of the study. Strengths and limitations should be clearly reported, acknowledging areas of bias and uncertainty for transparency. As with all studies results should be compared with other published literature, highlighting where there are comparable and contrasting findings which warrant further consideration. There are likely to be many recommendations for future research by the nature of the feasibility study.

Finally, study documentation from feasibility research can provide valuable knowledge transfer in research particularly by sharing examples of what worked well and what requires further pilot work. Where possible relevant study documents can be registered on databases such as DIRUM for resource use tools or included as appendices if reports or journal articles published.

Discussion

Summary of main points

There is extensive health economics toolkit available to researchers conducting economic evaluations of MBPs as a public health and prevention programme. Tools for the health economist evaluating MBPs include checklists for appraising, conducting, and reporting research; outcome measures for valuing benefits such as EQ-5D for the calculation of QALYs; NICE guidance for public health evaluation and technology appraisal; repositories of resource use tools including DIRUM and PSSRU annual unit costs reports. Consistent with the evaluation of other public health interventions consideration of the appropriate research design to make best use of health economics tools is needed, such as embedding economic evaluations alongside RCTs and economic modelling beyond trial durations.

This chapter highlights specific considerations relevant for the economic evaluation of MBPs using a translational research framework for the evaluation of complex intervention evaluations. The appropriate use of pilot and feasibility research can help provide the foundations for testing study designs, outcome measures and their ability to capture the full range of costs and benefits. This chapter offers a meta perspective on lessons learnt from two feasibility studies (presented in Chapter 4 and Chapter 5), while the earlier chapters give the specific study results. Questions specific to the design of economic evaluations and early-stage health economics work are updated and discussed to help inform future research evaluating MBPs. The Health Economics Analysis Plans (HEAPs) framework discussed as part of the health economics toolkit is an important resource for economic evaluation alongside RCTs however there is little guidance for the conduct of pilot and feasibility studies including health economics. A checklist for feasibility health economics research is presented considering the economic approach to be piloted, the trial processes, the appropriate summary and analysis of data, and the reporting of studies to inform future research. A reflective critical analysis of the suitability of outcome measures and methods for establishing costs of MBPs and resources consumed during study timelines is presented, with recommendations to include preference based generic outcome measures alongside clinical specific patient reported outcomes.

Wider implications for practice: A precision public health approach to depression prevention

The World Health Organization has stated the economic case for prevention highlighting that "preventive interventions that can be implemented and sustained at a reasonable cost whilst generating clear health gains in the population can be expected to represent a cost-effective use of resources relative to more resource-intensive, treatment-based approaches" (World Health Organization - WHO, 2002, p. 24). This thesis highlights opportunities for prevention of depression on many levels: 1) at different stages of depression (onset, recovery, relapse prevention) 2) at different points in the life course trajectory and 3) at various stages in the public health prevention spectrum.

Figure 39 shows a multilevel approach to the prevention of depression (Mclaughlin, Mclaughlin, & Sci, 2011), adapted from a public-health approach to diabetes (McKinlay & Marceau, 2000). This model of prevention highlights potential intervention points , starting with upstream public policy changes that help address the root causes of ill-health including poverty and inequalities; and ending with downstream treatment of mental health problems, often delivered as high-cost tertiary programmes to slow down the progression of ill health (as discussed in Chapter 1, see Figure 1). In between these two ends of the spectrum (where the largest distribution of programmes appear) come midstream intervention points. This model provides a whole system multi-agency approach, including private sector settings (i.e., workplaces) and a public sector setting (i.e., education settings, health, and social services), to deliver both universal and targeted programmes, and systems level change. This model of care is underpinned by proponents of proportionate universalism where both targeted and universal approaches are balanced to address health inequity (Carey, Crammond, & De Leeuw, 2015; Marmot, 2010). Knowing when to invest, for whom, and how to achieve the greatest benefits, is increasingly being recognised as requiring a precision public health approach. A precision public health approach requires a move away from a focus on medicine to treat illness and a move toward prevention. "Precision public health interventions might therefore be most usefully enacted within a reframed proportionate universalist approach whereby some interventions are universally provided, while others are targeted or precisely tailored to meet the needs of, and offset barriers to health encountered by vulnerable subgroups" (Olstad & McIntyre, 2019, p. 7) .

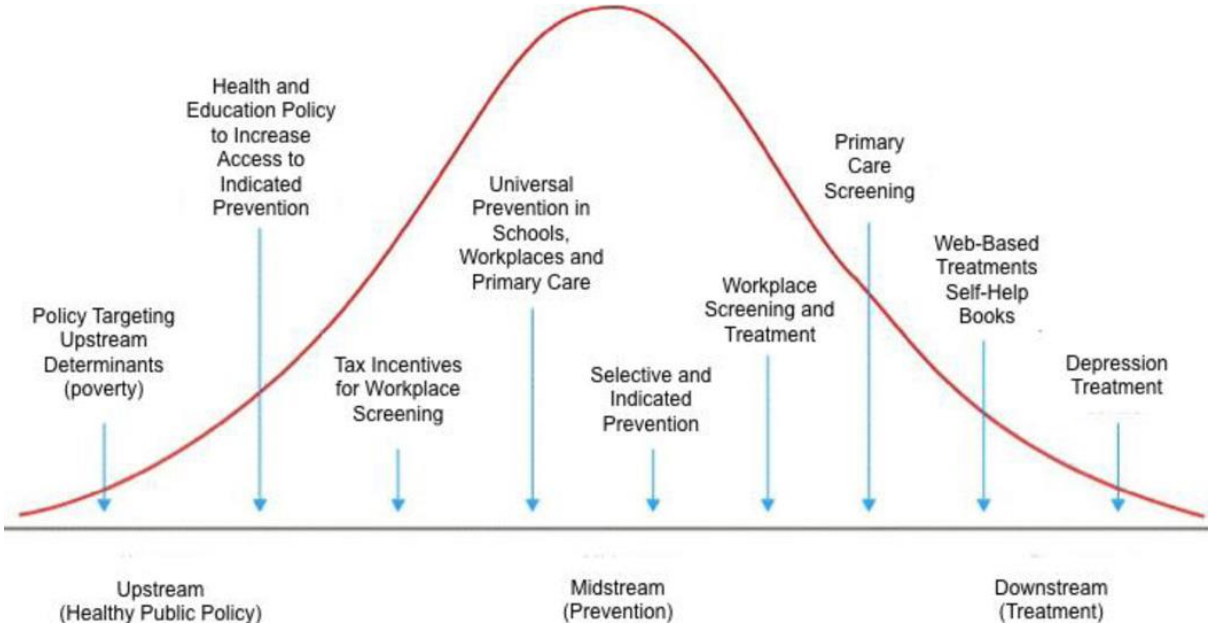


Figure 39: Multilevel approach to the prevention of depression (Mclaughlin et al., 2011) *adapted from a public-health approach to diabetes* (McKinlay & Marceau, 2000).

A recent systematic review and meta-analysis of depression and anxiety prevention interventions (in general rather than specific to MBPs) compared universal and targeted delivery (Werner-Seidler et al.,

2017). They identified small effect sizes across all studies. They did however highlight that targeted programmes had a greater depression prevention effect than universal programmes. To my knowledge there has been no direct comparison of universal verses targeted delivery of MBPs.

An MBP embedded within the school curriculum provides both a good opportunity for universal access to mindfulness, and an example of early intervention in the life course and (hopefully) before onset of depression. While aiming to explore a primary prevention opportunity on a universal basis, the evidence from the mindfulness in school' feasibility study (presented in Chapter 5) indicated that MBPs delivered in adolescence may occur too late for effective primary prevention. With increasing evidence pointing towards the age of onset of first symptoms of depression occurring in adolescence (Williams et al., 2012), it is necessary to consider the precision public health question of when best to intervene. What is not known is whether MBPs delivered at this point may still have prevention benefits and a shifting the curve approach to the economic assessment of depression cases in adolescents is warranted. The upcoming results of the Myriad trial and planned longer term follow-up aims to help answer these questions (Kuyken et al., 2017).

This thesis research largely focuses on midstream prevention. MBPs delivered as midstream prevention, with interventions offered both early in the life course on a universal basis and as targeted interventions at a later stage may be helpful alongside more upstream prevention in health policy. To reduce downstream costs and health problems, a precision public health approach that focuses on tackling social determinants of health and root cause of health inequalities is needed for earlier upstream prevention of depression, coupled with both universal and targeted prevention in midstream intervention points are needed. This approach considers factors on both an individual level and a systemic societal level, considering the root causes and vulnerabilities to depression and an opportunity to tackle them at the source.

Conclusions

Taking a more precision public health approach to depression prevention requires earlier upstream intervention on both a life course and disease pathway basis (Mclaughlin et al., 2011; Olstad & McIntyre, 2019). There is a public health case for a whole system multi-agency approach involving system level change, universal interventions, and targeted programmes to prevent depression.

There is an economic case for a broader societal perspective and important considerations around the ability for comparison and measurement across sectors. The challenges of capturing longer-term economic benefits of prevention in clinical trials are discussed and warrants the development of further methodological guidance. Robust extrapolation beyond clinical trials and economic modelling are needed and anticipated from studies in progress (Kuyken et al., 2017). Health economists should

consider the value of patient and public experience with greater use of PPI and qualitative methodologies informing the design of economic evaluations (Al-Janabi et al., 2020; Coast, 1999; Coast & De Allegri, 2018). These diverse methodologies should be considered part of the health economists toolkit for evaluating complex preventative interventions such as MBPs.

Embedding health economics into the entire translational process of complex intervention evaluation can help bridge the gaps in evidence to improve evidence-based practice. Further guidance on economic evaluations within complex systems in warranted (Rutter et al., 2017; Shiell et al., 2008). These suggestions for well-designed economic evaluations of MBPs in health and other settings, mirror current thinking on the challenges and opportunities of public health economics.

Chapter 7: General discussion

Summary of principal findings

This thesis outlines the background context of a growing public health challenge of mental health problems through the life course, and the unaffordable financial demands on multiple sector budgets. Drawing on economic theory and methodological guidance for evaluating complex interventions in the UK, this thesis explores whether MBPs may be one part of a multi-faceted approach to this challenge, by offering a cost-effective option for preventing and addressing mental health problems.

This thesis highlights the need for the systematic development and evaluation of MBPs as complex interventions; integrating the best available previous research to inform future research and implementation, and so maximising impact. Embedding health economics into the entire translational framework of MBP evaluation can help bridge current empirical gaps which in turn to facilitates evidence-informed implementation. The outcome data on MBPs in a range of areas is now highly convincing and lays the ground for implementation. However, there are key information gaps in the evidence jigsaw that are needed before policy makers and budget holders can make evidence informed decisions about which intervention to prioritise within their service delivery. Health economics research adds this critical dimension by providing information about value for money which informs resource prioritisation decisions.

This thesis addresses the methodological challenge of developing the economic evidence for MBP implementation by conducting two feasibility studies, and by examining the implications of this for research development going forward. Feasibility studies can be used to test and refine the methods of economic evaluation of MBPs, and explore cost drivers and patterns of health care resource use alongside trends of effectiveness. Lessons to be learnt from two feasibility stage health economics studies are presented, exploring the application of MBPs in a targeted health care context (Chapter 4) and a more universal schools-based context (Chapter 5). This contrast is in line with best practice thinking on precision public health, considering where and when to invest to prevent ill health.

This thesis also highlights the existing economic evidence for MBPs, and where current good practice guidelines on economic evaluations can be applied to the evaluation of MBPs. The largest body of economic evidence relates to MBPs for depression management. However, the findings of cost-effectiveness are mixed and warrant further well-designed evaluation and longer-term extrapolation of results related to long term prevention. I offer a new adapted checklist for researchers integrating health economics into feasibility stage research, and methodological guidance for researchers conducting economic evaluations of MBPs as complex interventions (Chapter 6).

Future research which considers a precision public health approach across a continuum of prevention should explore whether MBPs may be of most value when applied at a universal level or at a targeted level. Larger definitive trials with robust methodology and longer-term economic modelling of MBPs as potentially preventative interventions are needed and in some areas e.g., schools, are forthcoming (Kuyken et al., 2017) to fully explore whether they can be implemented as cost-effective uses of scarce public sector resources.

Review of research questions answered in each chapter

Research question 1: What existing literature is there on the cost-effectiveness of MBPs?

Chapter 2 explores the existing economic evidence base for MBPs to date, using systematic review methods (PROSPERO 2017 CRD42017074848). This systematic review highlights the number of MBP economic evaluations (which has significantly grown in the last 10 years and more studies are in progress), indicated by inclusion within the review of 19 study protocols and 28 trial registrations. The review highlights that the methods used in economic evaluations vary considerably which considerably limits the scope for comparison across studies, interventions, populations, and sectors. Furthermore, while many of the studies had small numbers of participants, there were few studies that focused directly on pilot objectives for economic evaluations. There can be important lessons from pilot and feasibility trials which warrant reporting to steer future studies, such as levels of missing data, completion rate of economic outcomes and methods use to cost the MBP. MBPs often focus on prevention, with benefits observed in the future. This means that few studies capture the complete potential benefit of the intervention. Longer-term follow-up or extrapolation beyond the length of clinical trial is needed. Further research is also needed on the economics of depression prevention and the potential cost-effectiveness of MBPs at different stages of the life course. My review in this thesis provides the first substantive review of all published economic evaluations of MBPs delivered in any public or private sector (health care, social care, education, employment) to any population (i.e., not exclusive to mental health).

Research question 2: What is the cost (and drivers of cost) in the delivery of MBPs?

Chapter 3 considers approaches to costing MBPs and provides base case micro-costings for a range of MBPs delivered to different populations and in different settings, with the costs considered from a provider perspective. The biggest driver of cost per participant was the number of participants per group and the programme context, with clinical courses within the NHS having the highest overall cost. Knowing more about the life cycle of MBPs, considering factors such as staff turnover and the need for ongoing investment in training, and whether MBPs delivery is sustained over time, will help provide information to develop more accurate estimates of budget impact over time. There may be lessons to

be learnt from survival analysis that has been conducted evaluating the implementation of other psycho-social interventions in the UK to establish the lifecycle of programmes (Swales, Taylor, & Hibbs, 2012). The costing of MBPs was considered on a closed group basis where there was a limited number of spaces within each group and that once allocated to attend the cost was incurred in an intention to treat model of analysis. The cost of MBPs requires detailed micro information on the resources required to deliver and implement the programme. In addition, meso considerations of context, organisations, and environments are needed, to reflect the complex settings that MBPs are often delivered within.

Research question 3: What are the appropriate methods for measuring and valuing costs and benefits of MBCT-Ca?

Chapter 4 of this thesis presents an early evaluation of MBCT-Ca delivered as a targeted prevention programme to support people in recovery following cancer treatment when they are particularly vulnerable and at heightened risk of depression and anxiety. My randomised feasibility trial (ISRCTN23380065) explored the methods for a future definitive RCT. Careful consideration around the pragmatic nature of the research process was needed with the context of existing provision of mindfulness services for patients locally. This required trade-offs between methodological best practice and practical requirements for balancing patient and clinician preferences and programme logistics. There were issues of willingness to recruit and refer patients into a RCT of MBCT-Ca where patients may have been allocated to a TAU condition before being offered access the intervention. These indicators warrant further consideration as to whether recruitment was dependant on clinician assessment of patient need and characteristics. This was a feasibility trial, so the sample size was too small to enable generalisability of the findings. There were high rates of attrition in the control condition, and in line with recommendations from the literature, an active control condition may be a more appropriate comparator to a usual care or waitlist control for future research.

The feasibility analysis led to findings about the suitability of a range of outcome measures for future MBCT-Ca research. A broad range of clinical and economic outcome measures were piloted including the EQ-5D-3L (The EuroQol Group, 1990) as a preference-based health-related quality of life measure. The EQ-5D-5L was developed following the design of this PhD thesis study (Herdman et al., 2011). Now that there is an interim scoring method (van Hout et al., 2012) to map five level values to the three level value sets, this might be more suitable for future studies of MBCT-Ca to provide greater sensitivity to differences in levels of problems on health domains. The EORTC-QLQ-C30 (Fayers et al., 2001) as a cancer condition specific outcome measure was considered as an alternative to the generic preference-based measure. However, there were high ceiling and floor effects limiting the use of this outcome to measure changes in HRQoL over time. The HADS (Zigmond & Snaith, 1983) and WHO-5 (World Health Organisation, 1998) provided useful information about levels of psychological distress on the whole and

more specific indicators of anxiety and depression. There are benefits (i.e., reducing participant burden and levels of missing data) to the brevity of some of the outcomes such as the EQ-5D (compared with the EORTC-QLQ-C30) and the WHO-5 (compared with the HADS). Based on this small study, both quantitative and qualitative evidence indicated that short-term anxiety may be more important to measure than depression in this population. Secondary outcomes such as measures of mindfulness facets and self-compassion may be useful for studies wishing to demonstrate important covariates of cost-effectiveness estimates such as engagement with the MBP and individual resilience. These may be important to capture information about the mechanisms of change and be relevant for the development of a logic model. However, they are unlikely to be directly useful outcomes for health economic evaluation from a narrow perspective.

The findings of the study point towards the need for further feasibility research. However, overall, the economic methods piloted in this thesis are already suitable for future studies. As this MBP delivery was embedded within the NHS, a cost-utility analysis from a NHS and personal social services perspective would be appropriate for a primary economic analysis in a future trial. This feasibility study highlighted that it is possible to collect an appropriate range of cost and outcome information in this population. A secondary cost-effectiveness analysis from a societal perspective should include wider cost considerations such as productivity losses and assess the cost of any improvements in psychological distress. A cost-consequence analysis may also be useful to consider the costs of a wider range of outcomes such as any cases of depression prevented.

The follow-up period of this study was short, with ethical considerations in the context of a feasibility trial making longer-term follow-up unfeasible. The challenges of capturing the benefits of prevention in economic evaluations embedded into clinical trials are discussed. Pragmatic trials of complex interventions are inherently challenging. A longer-term modelling of MBCT-Ca on a lifetime time horizon could help assess the likely cost-effectiveness of MBCT-Ca in the primary prevention of depression.

Research question 4: What is the perceived value of MBCT-Ca and how much would cancer patients be willing to pay for it?

Using a mixed-methods research design, Chapter 4 also includes qualitative analysis of the experience of the feasibility trial participants. There was a mix of patient experiences in terms of the perceived value of MBCT-Ca. On the whole patients anticipated or hoped that it would help them deal with psychological distress, and there was a preference to attending the course sooner rather than waiting to attend. In addition, there was a preference from some professionals to refer directly into the treatment, and for some patients to attend through a service evaluation route indicating that overall, the perceived value of MBCT-Ca was higher than usual care. There was limited information collected on willingness to

pay for MBCT-Ca. However, initial results from this pilot evaluation indicate that patients may be willing to share some of the cost of services. Overall, they are unlikely to be willing to bear the full cost of programmes delivered within clinical settings, particularly where the costs may be higher with small groups of patients (see Chapter 3 for a discussion). Some patients incurred travel costs, and location of courses and follow-up sessions were highlighted as barriers to accessing care. Qualitative findings indicated that WTP and perceived value could change after experiencing the MBCT-Ca and reporting positive benefits. This qualitative feedback highlighted that pre-course perceptions may be a potential barrier to enrolment in courses. Further research is needed to consider the costs of MBCT-Ca programmes with varying approaches to implementation, different group sizes and different people trained to deliver the intervention (e.g., internally running the course compared with external contractors brought in to deliver).

Research question 5: What are the appropriate methods for measuring and valuing costs and benefits of embedding mindfulness in secondary school curriculum?

Chapter 5 considers the economic case for early intervention and prevention of offering mindfulness training in a school context, as a programme to support positive mental well-being at a time of transition in adolescence. Interventions delivered within a school setting provide a unique opportunity to enable access to everyone within the setting rather than just for those who are at heightened vulnerability. A non-randomised matched cohort feasibility study (ISRCTN89407829) explores methods for the design of a future economic evaluation. Data for the health economics feasibility study was provided from the source trial, which was conducted external to this PhD research (Sanger & Dorjee, 2015, 2016; Sanger et al., 2018). Working concurrently as the health economist retrospectively assigned to evaluate this programme, I refined the methods for evaluation from a health economics perspective, cleaned and scored the health economics data, conducted the analysis, and wrote up the findings as reported within this thesis. Findings included the suitability of a range of outcome measures for future mindfulness in schools research, including assessment of appropriate outcome measures such as the EQ-5D-5L (Herdman et al., 2011) as a primary economic outcome and the General Health Questionnaire (Goldberg & Williams, 1988) as a screening tool for early signs of mental health problems in this age group. Ceiling effects of trial-based outcome measures in healthy populations are discussed. The feasibility of collecting resource use information from participants including school absenteeism and GP attendance were assessed. This pilot study has highlighted that in a future definitive trial of mindfulness in schools it is feasible to collect utility outcomes from 16–18-year-olds. However, this is not generalisable to younger populations where additional utility measurement and valuation considerations are needed. This pilot study has also demonstrated that it is achievable to collect some relevant outcomes and costs for a cost-utility analysis or a cost-effectiveness analysis from a health care

and education perspective. Further feasibility research is needed to explore whether outcomes relevant to a wider societal or public sector perspective can be collected and valued appropriately in economic evaluations of MBPs delivered within schools. A cost-consequence analysis from a societal perspective may be an appropriate method to help capture the potential cross-sectoral impacts of MBPs embedded into education, considering costs and benefits to local authorities, the health sector, personal social services and including wider benefits of productivity losses and forgone education as an outcome relevant to the wider economy. This pilot study supports the case for earlier intervention (Kuyken et al., 2017), with the age of depression symptoms onset highlighted in previous research first occurring in adolescence (Williams et al., 2012; World Health Organization, 2020). This thesis study indicated higher than anticipated levels of depression, with a high proportion of participants scoring above the clinical threshold for depression used in this study. However, there is uncertainty in the methods used to score the GHQ-12 to indicate depression. Clearer guidance on the most appropriate clinical cut-off on the GHQ-12 within this study population would aid future cost-effectiveness evaluations which aim to demonstrate cases of depression prevented over time. Economic evaluations of MBPs as a primary depression prevention intervention may need to be explored earlier in the life course. This small feasibility study highlights the need for greater mental health support for adolescents and young people, and recommends an exploration of opportunities for secondary depression prevention interventions.

Research question 6: How well does the health economic toolkit work for MBPs?

Chapter 6 draws on the extensive health economics toolkit available to researchers conducting economic evaluations of MBPs as public health and prevention programmes. Tools for the health economist evaluating MBPs include checklists for appraising, conducting, and reporting research; outcome measures for valuing benefits such as EQ-5D for the calculation of QALYs; NICE guidance for public health evaluation and technology appraisal; and repositories of resource use tools including DIRUM and PSSRU annual unit costs reports. It is increasingly recognised that health economists should consider the value of patient and public experience with greater use of PPI and qualitative methodologies informing the design of economic evaluations, particularly when evaluating complex interventions (Al-Janabi et al., 2020; Coast & De Allegri, 2018; Moore et al., 2015). This thesis research has highlighted the value of both PPI and qualitative methods to enrich health economics research (Chapter 4). Consistent with the evaluation of other public health interventions, consideration of the appropriate research design to make best use of health economics tools is needed, such as embedding economic evaluations alongside RCTs and economic modelling beyond trial durations. These diverse methodologies should be a part of the health economist's toolkit for evaluating complex preventative interventions such as MBPs. Questions specific to the design of economic evaluations and early-stage

health economics work are updated from the paper I co-authored in 2015, and discussed further to help inform future research evaluating MBPs (Edwards et al., 2015).

Research question 7: What lessons can be learnt from pilot and feasibility MBP research and the challenges of evaluating complex interventions?

Chapter 6 highlights specific considerations relevant for the economic evaluation of MBPs using a translational research framework for the evaluation of complex intervention evaluations. The appropriate use of pilot and feasibility research can help provide the foundations for testing study designs, outcome measures and their ability to capture the full range of costs and benefits. Chapter 6 offers a meta perspective on lessons learnt from the two feasibility studies (presented in Chapter 4 and Chapter 5). The Health Economics Analysis Plans (HEAPs) framework (Thorn et al., 2020; Thorn, Ridyard, Hughes, & Al., 2016) discussed as part of the health economics toolkit is an important resource for economic evaluation alongside RCTs. However, there is currently little guidance for the conduct of pilot and feasibility studies including health economics. I present a checklist for feasibility health economics research which considers the economic approach to be piloted, the trial processes, the appropriate summary and analysis of data, and the reporting of feasibility studies to inform future research. A reflective critical analysis of the suitability of outcome measures and methods for establishing costs of MBPs and resources consumed during study timelines is presented, with recommendation to include preference based generic outcome measures alongside clinical specific patient reported outcomes. There is an economic case for a broader societal perspective and important considerations around the ability for comparison and measurement across sectors. There remain opportunities for longer-term benefits to be explored through economic modelling. Through this thesis research I have made the case for adopting multiple perspectives of analysis for the evaluation of MBPs, considering the complex nature of the intervention and complex systems of health care and education sectors in which they have been implemented. This wider perspective aims to enable a full range of inputs and outputs relevant to decision makers and stakeholders to be considered in the economic evaluation of MBPs.

Strengths and limitations of this thesis

Strengths

This thesis benefits from drawing on the diverse disciplines of psychology and health economics, and used multiple methodologies to explore the large topic of the economic evaluation of MBPs. Multidisciplinary research is particularly important in the domain of public health as it allows researchers to draw on different disciplines in a complementary fashion to bring forward understanding across both psychology and health economics fields (van Teijlingen, Regmi, Adhikary, Aryal, & Simkhada, 2019). The diverse tools and methods across psychology and health economics enrich research into

mental health, and are thus able to influence policy makers looking to invest in effective and cost-effective prevention programmes (Hanoch & Gummerum, 2008). The application of health economics to the evaluation of MBPs has increased over the last decade. This thesis brings together elements of economic evaluation including methods for the costing of MBPs, measuring and valuing wider costs and outcomes, to add to the evidence base for the implementation of MBPs.

This thesis adopted a life course approach to considering precision public health, in terms of beginning to explore where MBPs may be most beneficial in preventing depression. A novel contribution of this work was the conduct of feasibility health economics research applied to evaluate both a targeted depression prevention intervention in cancer recovery and a more universal delivery of mindfulness embedded into the school curriculum for adolescents. An important strength of utilising feasibility research was to be able to establish whether the methods adopted are suitable for future research. For example, the missing data evidence from the research use questionnaire in this thesis can be used to inform the revision of the tool, or suitable alternatives available from repositories that could be used to improve data collection in future MBP research. A significant implication of this thesis is that it highlights the importance of health economics tools to help guide and inform researchers when conducting economic evaluations of MBPs.

To explore targeted application to people at heightened risk of depression following cancer treatment, a randomised feasibility trial was conducted, using methods considered to be best practice in the evaluation of complex interventions. This thesis study involved piloting methods for a RCT design including randomisation and researcher blinding. The study was conducted with ethical approval and in a transparent manner, the research process was guided by a panel including patient representatives to ensure participants were well informed and were able to share their experience of engaging in the research. This study included an extensive assessment of both the intervention acceptability and methods employed. It is a strength of this research that it used both quantitative and qualitative methods to consider the impacts of MBCT-Ca on people with cancer. This work is in line with recommendations for greater use of qualitative research in health economics (Coast & De Allegri, 2018). This research included a broad range of outcomes, including comparison of different evaluative paradigms considering the applicability of QALYs and capabilities in the evaluation of MBPs.

The non-randomised matched cohort mindfulness in schools study conducted as part of this thesis is the first to report on health economics of mindfulness delivery in a sixth form population. This study indicated potentially high levels of depression in adolescents and raises some important considerations for health economic research evaluating the prevention of depression. It has helped explore the economic case for intervention in a school setting and considered the appropriate perspective of analysis in this setting with potential benefits falling across public and private sectors. There are utility

measurement considerations for economic evaluations for younger children. While it is a limitation that the school programme was not truly universal as piloted in one age cohort within a secondary school, the results provide valuable information about opportunities for intervention in depression prevention in adolescents where depression onset is known to be prevalent.

Limitations

This thesis had several limitations which warrant consideration. Firstly, while acceptability of patients approached to enrolling in the MBCT-Ca research was high, there was limited recruitment and a high loss to follow-up particularly in participants allocated to the TAU control condition. It is a limitation of this research that the sample size was too small to conduct further analysis to explore the effect size of MBCT-Ca.

It is a limitation of this study that the health economics component of the mindfulness in Sixth Form feasibility study was conducted retrospectively and that it was not possible to control the approach taken in relation to the outcomes measured and the range of costs. This meant that there was very limited resource use data collected, restricted to GP contacts, and there were issues with uncertainty over the data (e.g. period over which absences were recorded).

This thesis aimed to explore depression prevention on a universal targeted basis, using a life course model of intervention. Earlier intervention in the life course, in childhood, in a universal school setting has been used to demonstrate a universal prevention opportunity for depression prevention in this thesis. Intervention at a later stage in the life course, coupled with known risk factors for depression following cancer has been used to demonstrate a targeted application of depression prevention. However, on reflection both examples of intervention may be more appropriately considered to be targeted than universal, as depression may already be highly prevalent in adolescence and in this age cohort, school is not universal in the UK. The findings are not generalisable to earlier age groups and there are important methodological considerations relevant to MBPs in compulsory education. As a universal intervention point earlier application of MBP is needed, with the curriculum embedded within compulsory education years offering access to all children. Further research considering the appropriate timing of interventions for effective universal application is needed.

A pilot health economics feasibility study checklist is presented to guide future feasibility research in health economics; however, further methodological work is needed to validate the items included. While it is acknowledged that the work within this thesis is at a pilot stage, this is the first stage in the process of translating evidence into practice and may help guide service commissioners wishing to appraise the level of existing evidence supporting investment into MBP delivery.

This thesis offers considerable breadth of research; however, it is a limitation that the depth limits the interpretation and generalisability of some of the findings. As discussed in Chapter 2, the initial stage of this thesis comprised of a systematic review of the literature whereby searches were updated prior to completion of the thesis; however, there was a considerable increase in publications during this time resulting in a large body of evidence to synthesise, and consequently requiring high-level comparisons across various populations, interventions, and settings. In parallel the micro-costing research conducted across nine varied MBPs provides a framework for costing; however, due to important contextual factors which have been shown to impact on resources, these costs may not be generalisable to other settings and warrant an update to reflect changes in practices around training pathways and models of implementation, for example online delivery of programmes and MBPs embedded into existing systems rather than external organisation delivery of MBPs as a standard.

Future research

This thesis highlights transparently throughout where unanswered questions remain, and further research is needed. There are many recommendations made for future research throughout. Typically, health economics research is underrepresented in publications evaluating MBPs. This thesis presents the case that health economics should be embedded into each stage of the translational research process for evaluating MBPs as complex interventions. The methods for early feasibility stage MBP research are discussed with knowledge generated to inform subsequent stages such as definitive RCTs and implementation of MBP. There remain gaps in the methodological guidance for the conduct of health economics feasibility work. In addition, the methods for the evaluation of MBPs in different sectors warrants clearer guidance, for example, utility measurement and valuing forgone education in mindfulness in schools' research.

MBPs are not all the same and the costs of programmes can vary depending on their size, location and the variations made to the core MBSR and MBCT programmes to adapt to the population. Questions remain about the necessary dose of intervention attendance and whether inclusion of features such as the all-day practice session delivered within the MBCT and MBSR programmes, impacts on cost-effectiveness estimates. In addition, there remains uncertainty about the costs of alternative modes of delivery such as MBPs delivered online. A budget impact assessment (Mauskopf et al., 2007; Sullivan et al., 2014) may be useful to explore what the likely costs of implementation would be if MBPs were embedded into universal school curriculum to varying extents. There is a case for starting with Wales where there is a precedent for considering well-being in the new curriculum and a strong policy agenda for supporting future generations (Davies, 2016).

MBPs as preventative interventions are argued to build resilience and avoid mental ill health through training people to respond skilfully to stressors and notice early signals of poor mental health. Health promotion interventions in general can change behaviour at an individual level, a broader community or societal level, or impact on public policy to improve health (Liu et al., 2012; Stead, Hastings, & Eadie, 2002). Despite this emphasis this thesis research has highlighted that in many cases, MBPs are evaluated with short time horizons and with short-term health improving outcomes, rather than focusing on prevention benefits as health promotion interventions. Future research which considers longer follow-up, economic modelling and population level modelling in the UK is needed to assess the impact of preventing mental health problems, whether that is through MBPs or alternative interventions. Research to develop an MBP logic model and theory of change from an economics perspective may help depict the full range of inputs and outputs relevant to a range of stakeholders.

This thesis research has explored a societal perspective for the evaluation of MBPs, an approach which can capture wider costs and benefits. These wider impacts are particularly relevant to MBP research where psychological wellbeing may contribute to a person's ability to maintain employment (as a contribution to both personal finances and the wider economy), and opportunities to enjoy leisure time (as an important indicator of social value). Further research to explore the capabilities approach as an alternative economic paradigm is needed, to build on the early stage research presented in this thesis and other methodological research published in the literature (Mitchell et al., 2017).

This thesis research has shown that a generic utility measurement tool like the EQ-5D can be applied to the economic evaluation of both an MBP in cancer care and an MBP embedded into the school curriculum. This would enable a cost-utility analysis and comparison across different interventions delivered within a UK health service context. Consideration of whether a QALY approach is as appropriate in education-based settings warrants further exploration. Through this thesis I have adopted a wider view on wellbeing moving beyond health and quality of life indicators to consider capabilities in MBP research. The ICECAP-A as a capabilities questionnaire was successfully used to provide an alternative viewpoint on the potential benefits from MBCT-Ca relevant to a broader societal perspective. This thesis research provides further support for health economics research to be conducted within these different evaluative paradigms. To my knowledge capabilities approach has not been applied to research within a child population, and questions of whether this is feasible remain. In parallel there remain challenges for utility measurement in child populations and the development of value sets for common child-specific utility questionnaires. When considering the education sector priorities and that a core aim of education is to help children fulfil their potential, then it is understandable that economic evaluations in education may include a focus on academic attainment and future earning potential alongside health outcomes. A cost-consequence analysis from a societal

perspective may provide a useful framework to explore these potential broad outcomes in both education and clinical settings. Finally, social return on investment application to MBPs warrants further attention, the methodological framework has the advantage of developing a theory of change and identification of inputs and outputs from a societal perspective which may be relevant to MBP economic evaluation.

There are many tools available for measuring depression and other forms of psychological distress. This thesis research has indicated that a broad wellbeing questionnaire like the WHO-5 is able to provide a useful indicator of levels of psychological distress, while benefiting from brevity due to its short format. The HADS subscales enabled a useful distinction to be drawn between cases of depression and anxiety in cancer populations, and raised the question of whether health economists should focus on clinical cases or heightened levels of psychological distress. The GHQ-12 provided a short and valid measure to assess psychological distress in an adolescent population; however, there remains uncertainty about the appropriate clinical cut-off to accurately measure and value shifts in depression status. Selection of the appropriate psychological distress outcome for future research needs to consider the population and timeframe for analysis.

It is necessary to balance the number of questionnaires to yield sufficient information to address the economic questions with demands on participants. Feasibility research can be particularly useful to consider levels of ceiling and floor effects, acceptability of questions and levels of missing data and pilot thresholds for clinical cut-offs, where there is uncertainty about what is appropriate. There are benefits to using a range of short measures to be included within a cost-consequence analysis.

Considering MBPs as complex interventions (delivered within complex systems), further supports the view that it is appropriate to adopt multiple perspectives of analysis and conduct multiple forms of economic evaluation. For health focused interventions delivered in the UK, a NHS perspective is likely to be considered the most appropriate primary approach. However, considering the potential spill over effects to other sectors, particularly when adopting a longer-term prevention view, additional complementary analyses with the inclusion of secondary economic outcomes can capture the wider costs and benefits which remain important to capture from a societal perspective. Lessons learnt from the feasibility research presented in this thesis can now be used to develop a robust HEAP for future research evaluating MBCT-Ca and MBPs embedded within a school setting. Further research to develop the theory of change and a logic model from a health economics perspective would be useful to ensure a full range of inputs and outputs are included within future MBP economic evaluation. While there has been an increase in research exploring mechanisms of change of MBPs (Alsubaie et al., 2017; Gu et al., 2015; Mackenzie & Kocovski, 2016; van der Velden et al., 2015), further consideration from a health

economics perspective is warranted to fully inform a precision public health approach to MBP implementation.

This thesis research was conducted prior to COVID-19; however, future MBP research may need to consider the long-term impacts of the pandemic. The side effects of national and local measures to help manage the pandemic will have had significant implications for the population with many adults experiencing social isolation and impacts on employment. These factors are all likely to contribute to a higher need for mental health intervention and there will be high demands on limited health care resources. In general, there are funding barriers to investment in prevention as short political time horizons rarely facilitate a longer-term funding perspective. It may be increasingly difficult to prioritise prevention in this upcoming post-pandemic period with high demands for treatments on the NHS. However, there remains a strong economic case for scaling up of ROI evidence from prevention. There are opportunities for evaluating MBP as part of the COVID-19 recovery, to explore more novel modes of delivery such as distance learning of mindfulness and whether these modes of delivery can be cost-effective as part of a wider mental health prevention agenda.

Wider implications

Exploring the economic case for MBPs has highlighted considerations of how people access non-pharmaceutical mental health treatment. The MBCT-Ca pilot research presented in this thesis highlighted that many people did not access support for health problems including depression, and those that sought support did so from a range of services including their GP or practice nurse or more specialist services relevant to their cancer recovery. Evaluating health interventions is often set within the context of a 'medical model' of health (Laing, 1971), where psychological disorders are a product of physical illness that can be treated with medication (Deacon, 2013). While the medical model of health emphasises medical interventions as treatments, it faces criticism for focusing on disability and ill health alone rather than peoples abilities (Swaine, 2011). More holistic models of mental health are needed that include factors such as socio-economic circumstances or psychosocial influences on health-related quality of life (Engel, 1977; Farre & Rapley, 2017). Health economists have highlighted the importance of combining both quantity in terms of life years gained with quality of life, within QALYs providing a "paradigmatic indicator" of the biopsychosocial model of health (Prieto & Sacristán, 2003, p. 2).

According the Royal College of Psychiatrists in the UK a greater emphasis on social aspects of the biopsychosocial approach are needed and social prescribing "provide a legitimate option for those without a mental illness but with psychosocial stressors, thus avoiding potential over-pathologising and inappropriate management of these issues within a medical model" (Royal College of Psychiatrists,

2019). In addition, “social prescribing has the potential to significantly improve the sustainability of mental health care” and may reduce the burden on the NHS (Royal College of Psychiatrists, 2019).

The social prescribing model evaluated through SROI which included an embedded MBP indicated that there was £10 of social value generated from every £1 invested (Fox Advising CIC, 2012). While there were concerns about the methodological rigour of this research it warrants further evaluation, particularly considering that MBPs are increasingly available in the community and social prescribing is becoming more prevalent. There has been expanding provision of IAPT services in England with MBCT considered to be a core component to increase access to psychological therapy (NHS England, 2017, 2018; NHS Health Education England, 2019). There remains variability in the availability of MBP services in the UK, good quality health economics evaluations may help support the case for increasing the access to MBPs in the community through social prescribing or IAPT services (or equivalent) (Rycroft-Malone et al., 2017).

In 1990 Jon Kabat-Zinn highlighted in his book Full Catastrophe Living his vision for MBSR which he had introduced into a public hospital setting to improve outcomes for people with chronic pain. Coupled with achieving personal benefits for patients Kabat-Zinn aimed to influence the system of how health care was understood and delivered. His vision was an integrative health care paradigm involving participatory medicine, where patients actively collaborate in their health care, and which acknowledges the multiple influences on an individual’s health (Kabat-Zinn, 1990). It is increasingly acknowledged that systems level change is needed to tackle challenges facing public health, this likely involves co-production of health services across public sectors and other stakeholders, and takes into account the wider environment that health and wellbeing exist within (Local Government Association, 2021). Health outcomes are influenced by factors relating to the individual, communities and organisations, and the wider society and environment (Braveman & Gottlieb, 2014). Translational research is needed to assess the impacts of complex interventions, whole system-level change, and the wider policy context to work towards a precision public health agenda that both addresses upstream causes (at all levels) at source, and addresses the downstream consequences for individuals when health is not optimal (McLaughlin, 2011; Raine et al., 2016). While there are methodological challenges for the economic evaluation of systems-level change particularly how it incorporate health equity impacts (Love-Koh, Mirelman, & Suhrcke, 2020), there are a wealth of economic tools and methods available to evaluate impact of a proposed multi-level public health approach to depression prevention (McLaughlin, 2011).

Original contributions

This thesis consolidates the growing economic evidence for investment decisions in MBPs. To date there has been insufficient focus on the economic case for or against MBPs to establish whether they provide value for money, in the context of limited public resources. This thesis provides the first substantive review of MBP economic evaluations across public and private sectors, and highlights lessons that can be learnt from early economic evaluations of MBPs as complex interventions delivered within complex systems. A health economics analysis checklist for feasibility studies is presented to help guide researchers on important methodological design considerations. This thesis builds on the developing interest in precision public health, exploring targeted and universal delivery of MBPs. There remains a need to collect further evidence on the cost-effectiveness of MBPs as preventative interventions. This thesis offers guidance and recommendation to improve the development of robust pragmatic methodologies that can establish what provides value for money in the context of limited public health resources.

Conclusions

Embedding health economics into the entire translational framework of MBP evaluation can help bridge the gaps in evidence to improve evidence-based practice and successful implementation. Translational health economics may benefit from greater inclusion of stakeholder perspectives and co-production of research to aid implementation of evidence into practice (Price & St John, 2019). MBPs can be thought of as a public health preventative intervention, a psycho-social intervention and as a complex intervention, often delivered within complex systems. This thesis highlights the importance of embedding health economics into each stage of the translational process to evaluate complex interventions and improve the transferability of research evidence into practice. There are a range of methods and tools available to health economists to evaluate MBPs, however there remains challenges in measuring and valuing mental health prevention. Further research is needed on the economics of depression prevention and the potential cost-effectiveness of MBPs at different stages of the life course. Effective evaluations of complex interventions may require uncertainty to be explored and multiple perspectives to be considered (Zimmerman et al., 2011). Feasibility research can inform future trials of MBPs with concurrent economic evaluations, and lessons learnt in early-stage research can identify areas of uncertainty and improve the design of a HEAP to produce meaningful results to inform policy makers. Further real-world research going beyond short trial designs is needed to capture whether MBPs in practice help prevent future mental health problems. Future research which considers a precision public health approach should justify why either a targeted or a universal approach has been taken. These suggestions for well-designed economic evaluations of MBPs in health and other settings, mirror current thinking on the challenges and opportunities of public health economics.

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Appendices

Appendix 1: PRISMA self-assessment checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	51
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	51
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	54
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	57
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	55
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	59
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	57
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	58

Section/topic	#	Checklist item	Reported on page #
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	56
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	64
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	64
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	61
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	64
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	64
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	62
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	66
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	75
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	358
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	67
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	n/a
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	358

Section/topic	#	Checklist item	Reported on page #
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	101
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	109
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	110
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	19

Appendix 2: Critical quality appraisal of full economic evaluations

	Aikens et al. (2014)	Bogosian et al. (2015)	Herman et al. (2017)	Janssen et al. (2019)	Johannsen et al. (2017)	Kuyken et al. (2008)	Kuyken et al. (2015a&b)	Lengacher et al. (2015)	Rakel et al. (2013)	Shawyer et al. (2016)	van Dongen et al. (2016)	van Ravesteijn et al. (2013)
1. Is the study population clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
2. Are competing alternatives clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
3. The rationale for choosing alternatives is stated?	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes
4. Is a well-defined research question posed in answerable form?	No	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
5. Is the form of economic evaluation used stated?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
6. Is the economic study design appropriate to the stated objective?	N/A	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Details of any model used are given and justified?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
8. Is the actual perspective(s) chosen stated clearly and justified as appropriate?	No	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes
9. Is the primary outcome measure(s) for the economic evaluation clearly stated?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	Aikens et al. (2014)	Bogosian et al. (2015)	Herman et al. (2017)	Janssen et al. (2019)	Johannsen et al. (2017)	Kuyken et al. (2008)	Kuyken et al. (2015a&b)	Lengacher et al. (2015)	Rakel et al. (2013)	Shawyer et al. (2016)	van Dongen et al. (2016)	van Ravesteijn et al. (2013)
10. Are all important and relevant outcomes for each alternative identified?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11. Are all outcomes measured appropriately?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12. Are methods to value benefits stated and appropriate?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
13. Are all important and relevant costs for each alternative identified?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14. Are all costs measured appropriately in physical units?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
15. Are costs valued appropriately?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
16. The currency and price date are recorded (with any adjustment via conversion or inflation appropriate)?	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
17. Is the chosen time horizon appropriate in order to include relevant costs and consequences?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	Aikens et al. (2014)	Bogosian et al. (2015)	Herman et al. (2017)	Janssen et al. (2019)	Johannsen et al. (2017)	Kuyken et al. (2008)	Kuyken et al. (2015a&b)	Lengacher et al. (2015)	Rakel et al. (2013)	Shawyer et al. (2016)	van Dongen et al. (2016)	van Ravesteijn et al. (2013)
18. Are all future costs and outcomes discounted appropriately and the rate justified?	No	N/A	N/A	N/A	Unclear	No	Yes	Yes	N/A	Yes	N/A	N/A
19. An explanation is given if costs and benefits are not discounted?	No	No	Yes	No	No	No	N/A	N/A	No	N/A	Yes	No
20. Does the paper provide appropriate evidence that the programme would be effective?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
21. Is an incremental analysis of costs and outcomes performed?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
22. Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No
23. The answer to the economic study question is given?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
24. Do the conclusions follow from the data reported?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

	Aikens et al. (2014)	Bogosian et al. (2015)	Herman et al. (2017)	Janssen et al. (2019)	Johannsen et al. (2017)	Kuyken et al. (2008)	Kuyken et al. (2015a&b)	Lengacher et al. (2015)	Rakel et al. (2013)	Shawyer et al. (2016)	van Dongen et al. (2016)	van Ravesteijn et al. (2013)
25. Conclusions are accompanied by the appropriate caveats?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
26. Does the study discuss the generalizability of the results to other settings and patient/client groups?	No	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
27. Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes
28. Are ethical and distributional issues discussed appropriately?	No	No	No	Yes	No	No	No	No	No	No	No	No
29. Risk of bias assessment rating (including randomisation, blinding, incomplete data and selective reporting)	Low	High / moderate	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Unclear	Unclear	High / moderate
30. Consideration of MBP fidelity / reporting assessment.	High / moderate	High / moderate	Low / Unclear	High / moderate	High / moderate	High / moderate	High / moderate	Low / Unclear	Low / Unclear	High / moderate	Low / Unclear	High / moderate

Note: N/A = Not applicable

Appendix 3: Critical quality appraisal partial economic evaluations

	(Bota et al., 2016))	(Compen, Bisseling, Donders, et al., 2017)	(Ferszt et al., 2015)	(Fjorback et al., 2013)	(Klatt et al., 2016)	(Knight et al., 2015)	(Rohricht et al., 2018)	(Roth & Stanley, 2002)	(Tulloh et al., 2018)	(Zgierska et al., 2017)
1. Is the study population clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Are competing alternatives clearly described?	Yes	Yes	N/A	Yes	Yes	Yes	N/A	N/A	Yes	Yes
3. The rationale for choosing alternatives is stated?	Yes	Yes	N/A	Yes	Yes	Yes	N/A	N/A	Yes	No
4. Is a well-defined research question posed in answerable form?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Is the form of economic evaluation used stated?	No	No	No	No	No	No	No	No	No	No
6. Is the economic study design appropriate to the stated objective?	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Details of any model used are given and justified?	N/A	Yes	N/A	Yes	N/A	N/A	N/A	N/A	N/A	N/A
8. Is the actual perspective(s) chosen stated clearly and justified as appropriate?	No	No	No	No	No	No	No	No	No	No
9. Is the primary outcome measure(s) for the economic evaluation clearly stated?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
10. Are all important and relevant outcomes for each alternative identified?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
11. Are all outcomes measured appropriately?	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

	(Bota et al., 2016))	(Compen, Bisseling, Donders, et al., 2017)	(Ferszt et al., 2015)	(Fjorback et al., 2013)	(Klatt et al., 2016)	(Knight et al., 2015)	(Rohricht et al., 2018)	(Roth & Stanley, 2002)	(Tulloh et al., 2018)	(Zgierska et al., 2017)
12. Are methods to value benefits stated and appropriate?	N/A	N/A	N/A	N/A	Unclear	N/A	NA	N/A	N/A	N/A
13. Are all important and relevant costs for each alternative identified?	Unclear	N/A	N/A	N/A	Unclear	Unclear	Unclear	No	N/A	Unclear
14. Are all costs measured appropriately in physical units?	Unclear	N/A	N/A	N/A	Unclear	Unclear	Yes	No	Yes	Yes
15. Are costs valued appropriately?	Unclear	N/A	N/A	N/A	Unclear	Unclear	Yes	No	Yes	Yes
16. The currency and price date are recorded (with any adjustment via conversion or inflation appropriate)?	No	N/A	N/A	N/A	No	Unclear	Yes	No	Yes	Yes
17. Is the chosen time horizon appropriate in order to include relevant costs and consequences?	Yes	N/A	N/A	N/A	Yes	Yes	Yes	Yes	Yes	Yes
18. Are all future costs and outcomes discounted appropriately and the rate justified?	No	N/A	N/A	N/A	No	No	No	No	No	Yes
19. An explanation is given if costs and benefits are not discounted?	No	N/A	N/A	N/A	No	No	No	No	No	No
20. Does the paper provide appropriate evidence that the programme would be effective?	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes

	(Bota et al., 2016))	(Compen, Bisseling, Donders, et al., 2017)	(Ferszt et al., 2015)	(Fjorback et al., 2013)	(Klatt et al., 2016)	(Knight et al., 2015)	(Rohricht et al., 2018)	(Roth & Stanley, 2002)	(Tulloh et al., 2018)	(Zgierska et al., 2017)
21. Is an incremental analysis of costs and outcomes performed?	No	N/A	N/A	N/A	No	No	No	No	No	No
22. Are all important variables, whose values are uncertain, appropriately subjected to sensitivity analysis?	No	No	No	No	No	No	Unclear	No	Unclear	No
23. The answer to the economic study question is given?	No	N/A	N/A	N/A	Yes	Yes	Yes	Yes	Yes	Yes
24. Do the conclusions follow from the data reported?	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
25. Conclusions are accompanied by the appropriate caveats?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
26. Does the study discuss the generalizability of the results to other settings and patient/client groups?	Yes	Yes	No	No	Yes	No	Yes	No	Yes	Yes
27. Does the article indicate that there is no potential conflict of interest of study researcher(s) and funder(s)?	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes
28. Are ethical and distributional issues discussed appropriately?	No	Yes	Yes	Yes	No	No	No	No	Yes	Yes
29. Risk of bias assessment rating (including randomisation, blinding, incomplete data and selective reporting)	High	Low	High	Moderate	High	High	High	High	High	Moderate

	(Bota et al., 2016))	(Compen, Bisseling, Donders, et al., 2017)	(Ferszt et al., 2015)	(Fjorback et al., 2013)	(Klatt et al., 2016)		(Knight et al., 2015)	(Rohricht et al., 2018)	(Roth & Stanley, 2002)	(Tulloh et al., 2018)	(Zgierska et al., 2017)
30. Consideration of MBP fidelity / reporting assessment.	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear

Note: N/A = Not applicable

Appendix 4: Critical quality appraisal of SROI economic evaluations

	Social Value Cymru (2016)	Fox Advising CIC (2016) *
Research question		
1. Was a well-defined question posed?	Yes	Unclear
Reason for use of SROI Method		
2. Were authors transparent about why SROI methodology was chosen? (e.g. strategic planning/funding requirements)	Yes	Yes
3. Did authors report relevant background literature/ justify the need for the study?	Yes	No
Scope		
4. Was the range of stakeholders included/excluded justified?	Yes	Unclear
5. Was the range of stakeholders wide enough to adequately answer the research question? (principle of understanding change)	Yes	Yes
6. Was it clear how stakeholders were involved and what data would be gathered from them?	Yes	Yes
7. Was ethics obtained/informed consent provided?	Unclear	Unclear
Theory of change/impact map		
8. Was the theory of change clear? i.e. the relationships between inputs, outputs and outcomes	Yes	Unclear
9. Were unintended outcomes (positive/negative) detailed?	Yes	Unclear
Study Design		
10. Was the study design appropriate for the study question? (Control group, pre-post)	Yes	Yes
11. Was the sample described in detail/was the sample justified?	Yes	No
Analysis		
12. Were inputs clear with non-monetized inputs valued appropriately?	Yes	Unclear
13. Were capital costs, as well as operating costs included?	Yes	Unclear
14. Were costs that occur in the future 'discounted' to their present values? Was justification given for the discount rate used?	Yes	Yes
15. Was dead-weight clearly described and calculated?	Yes	Yes
16. Were the indicators valid and comprehensive? (Were the sources of all values clearly identified?)	Yes	Unclear
17. Were the proxies valid and comprehensive? (Were the sources of all values clearly identified?)	Yes	Unclear
18. Was length of benefit established and justified? (Drop-off) (In capital projects, did authors establish and differentiate between length of benefit and life expectancy of the asset?)	Yes	Unclear

	Social Value Cymru (2016)	Fox Advising CIC (2016) *
19. Were limitations and biases reported?	Yes	Yes
20. Was the final SROI ratio interpreted?	Yes	Yes
21. Was sensitivity analysis performed? Was justification provided for the range of values (or for key study parameters) in the sensitivity analysis?	Yes	Yes
Other		
22. Risk of bias assessment rating (including randomisation, blinding, incomplete data and selective reporting)	n/a	n/a
23. Consideration of MBP fidelity / reporting assessment.	Low / Unclear	Low / Unclear

The Hutchingson et al (2019) quality appraisal framework for SROI assessment was used for Q.1-21
The Template for Intervention Description and Replication (TIDieR) checklist was screen for Q.23 MBP reporting (Crane & Hecht, 2018)
*Fox Advising CIC (2016) Impact map was requested but unavailable resulting in limited information for quality appraisal.

Appendix 5: Items included in the Template for Intervention Description and Replication (TIDieR) checklist: information to include when describing an intervention, with additional guidance (in italics) on applications to MBP research

Item number	Item
Brief name	
1.	Provide the name or a phrase that describes the intervention and *reference to the most recent curriculum guide*—i.e., *MBSR* (Santorelli et al. 2017*)*
Why	
2.	Describe any rationale, theory, or goal of the elements essential to the intervention. *In addition to referencing published literature on this issue, theoretical rationales are needed for any adaptations, or tailoring to a particular population or context.*
What	
3.	Materials: Describe any physical or informational materials used in the intervention, including those provided to participants or used in intervention delivery or in training of intervention providers. Provide information on where the materials can be accessed (such as online appendix, URL). *For example, written course materials and guided mindfulness meditation practices.*
4.	Procedures: Describe each of the procedures, activities, and/or processes used in the intervention. *If using a published MBP curriculum guide this is not needed—only include descriptions of adaptations. Detail in full if delivering a new MBP.*
Whom provided	
5.	For each category of intervention provider, describe their expertise, background, and any specific training given. *Describe (1) what MBP teacher training has been undertaken by trial teachers, (2) how they adhere to ongoing MBP Good Practice Guidelines such as on-going practice, and (3) measures of teacher competence that were used to select trial teachers*
How	
6.	Describe the modes of delivery (such as face to face or by some other mechanism, such as internet or telephone) of the intervention and whether it was provided individually or in a group. *If following a standard MBP curriculum guide this is not required—only detail deviations/adaptations from standard protocols, or if a new curriculum, detail in full, including delivery method* (i.e., *in person teacher-led group sessions; digital delivery, etc.*).
Where	
7.	Describe the type(s) of location(s) where the intervention occurred, including any necessary infrastructure or relevant features.
When and How Much	
8.	Describe the number of times the intervention was delivered and over what period of time including the number of sessions, their schedule, and their duration, intensity, or dose. *If following a standard MBP curriculum guide this is not required—only detail deviations/adaptations from standard protocols, or give full details of new MBPs.*
Tailoring	
9.	If the intervention was planned to be personalized, titrated, or adapted, then describe what, why, when, and how. *Describe how individual needs/vulnerabilities of MBP group participants were handled by the trial teacher(s), and whether any steps such as individualized additional meetings with the teacher were used to address issues that varied by participant.*
Modifications	
10.	If the intervention was modified during the course of the study, describe the changes (what, why, when, and how).
How well	
11.	Planned: If intervention adherence or fidelity was assessed, describe how and by whom, and if any strategies were used to maintain or improve fidelity, describe them. *Describe whether an MBP fidelity tool was used to assess intervention delivery* via *reviews of recorded sessions were employed, by whom and how. Describe the rationales for the choices made.*
12.	Actual: If intervention adherence or fidelity was assessed, describe the extent to which the intervention was delivered as planned. *Detail the assessed level of MBP teaching competence, adherence and differentiation in the results section of the paper.*

Source: (Crane & Hecht, 2018) adapted from (Hoffmann et al., 2014)

Appendix 6: Trial registration records and summary of economic evaluation methods

#	Record ID	Title	Year	Registration site:	MBP (e.g., adaptation of MBSR or MBCT)	Population / condition	Economic approach	Related publications
1	ACTRN12611001184965	'Mindfulness, cognitive processes and coping in chronic illness: insights from a study of joint replacement surgery'	2011	https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12611001184965	MBSR	'Musculoskeletal'	Cost-effectiveness (Decision-analytic modelling)	Protocol (Dowsey et al., 2014b) Main outcomes (Dowsey et al., 2019) Health economics: None identified
2	ACTRN12612000306819	'Living Well with Prostate Cancer: a randomised controlled trial of a mindfulness intervention for men with advanced prostate cancer'	2012	https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=362214	MBCT	Prostate Cancer	Unclear: 'Implementation expenses'	Protocol (Chambers et al., 2013) Main Outcomes (Chambers et al., 2017) Health economics: None identified
3	ACTRN12617001284358	'Can an allied health and nursing expanded scope Treatment Access Pathway (TAP) improve health outcomes for people with persistent pain? A pragmatic randomised controlled trial'	2017	https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=373328	MBSR	Pain	Cost-utility	Health economics: None identified
4	EUCTR2013-003888-59-NL	'My child has ADHD: Medication or Meditation?	2014	https://www.clinicaltrialsregister.eu/ctr-search/trial/2013-003888-59/NL	Other: MYmind protocol (Mindfulnesstraining for Youngsters	ADHD	Cost-effectiveness and cost-utility analysis	Protocol (Meppelink et al., 2016)

#	Record ID	Title	Year	Registration site:	MBP (e.g., adaptation of MBSR or MBCT)	Population / condition	Economic approach	Related publications
		Mindfulness training versus medication in the treatment of childhood ADHD'			with ADHD and their parents).			Health economics: none identified
5	IRCT20160103025817N4	'The Study Effectiveness of Mindfulness integrated Cognitive Behavior Group Therapy on patients with Multiple Sclerosis'	2018	https://en.irct.ir/trial/29957	MiCBT (Mindfulness integrated Cognitive Behavior Group Therapy)	MS	Cost of treatment	Main outcomes (Bahrani, Zargar, Yousefipour, & Akbari, 2017) Health economics: none identified
6	ISRCTN86619085	MYRIAD: My Resilience in Adolescence, a study examining the effectiveness and cost-effectiveness of a mindfulness training programme in schools compared with normal school provision	2017	http://www.isrctn.com/ISRCTN86619085	MBCT embedded into school curriculum	Adolescents (secondary schools)	Cost-utility, cost-effectiveness, decision analytic modelling	Protocol (Kuyken et al., 2017) Health economics: none identified
7	ISRCTN03386834	'MIndfulness-based Training in the Workplace - evaluating the cost effectiveness and impact on emotional wellbeing'	2013	https://www.isrctn.com/ISRCTN03386834	Mindfulness-based programme adapted for workplace delivery	NHS staff	Cost-effectiveness	Health economics: none identified
8	ISRCTN11723441	'Randomised controlled trials of interventions to improve NHS staff stress and wellbeing'	2017	https://www.isrctn.com/ISRCTN11723441	MBCT	NHS staff	Productivity costs	Health economics: none identified
9	ISRCTN13495752	'LIGHTMind 2: low-intensity guided help through mindfulness'	2017	https://www.isrctn.com/ISRCTN13495752	MBCT workbook self-healp	Adults with depression or anxiety	Cost-effectiveness	Health economics: none identified

#	Record ID	Title	Year	Registration site:	MBP (e.g., adaptation of MBSR or MBCT)	Population / condition	Economic approach	Related publications
10	ISRCTN23380065	'Exploring the cost effectiveness of Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca)'	2012	https://www.isrctn.com/ISRCTN23380065	MBCT-Ca	Cancer	Cost-utility and cost-effectiveness	Reported on in Chapter 4
11	JPRN-UMIN000016142	'Mindfulness-based cognitive therapy for patients with cancer'	2015	https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000018741	MBCT	Cancer	Cost-utility	Main outcomes: (Park et al., 2020) Health economics: none identified
12	JPRN-UMIN000031885	'Effectiveness and cost-effectiveness of mindfulness-based programs for improving the subjective well-being of healthy individuals: a randomized wait-list controlled trial'	2018	https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000036376	MBCT	General population	Cost-effectiveness and cost-utility	Protocol:(Sado et al., 2020)
13	NCT006946668	'The (Cost-) Effectiveness of Mindfulness-training and Cognitive Behavioural Therapy in Adolescents and Young Adults With Deliberate Self Harm'	2008	https://clinicaltrials.gov/ct2/show/NCT00694668	MBCT	Deliberate self-harm (young people aged 15+ and adults <35 years)	Cost-effectiveness and cost-utility	Health economics: none identified
14	NCT01654289	'University of Wisconsin Meditation & Exercise Cold Study'	2012	https://clinicaltrials.gov/ct2/show/NCT01654289	MBSR	Acute respiratory infection (ARI)	Productivity losses and resource use economic costs	Main outcomes and partial economic evaluation (Barrett et al., 2018)
15	NCT01775995	'Meditation-CBT for Opioid-treated Chronic Low Back Pain'	2013	https://clinicaltrials.gov/ct2/show/NCT01775995	MBCT	Pain	Productivity losses and resource use economic costs	Reported in systematic review (Zgierska et al., 2017)

#	Record ID	Title	Year	Registration site:	MBP (e.g., adaptation of MBSR or MBCT)	Population / condition	Economic approach	Related publications
16	NCT01864707	'Acupuncture or MBSR for Patients With Fatigue and MS'	2013	https://clinicaltrials.gov/ct2/show/NCT01864707	MBSR	MS	Cost-utility analysis	Protocol (Bellmann-Strobl et al., 2018)
17	NCT02190968	'Reducing Residual Depressive Symptoms With Web-based Mindful Mood Balance'	2014	https://clinicaltrials.gov/ct2/show/NCT02190968	Mindful Mood Balance (web-based programme adapted from MBCT)	Depression	Cost-effectiveness	Main outcomes (Dimidjian et al., 2014). Outcomes including intervention costs (Segal et al., 2020)
18	NCT02275559	'Asthma Symptom Management Through Mindfulness Training'	2014	https://clinicaltrials.gov/ct2/show/NCT02275559	MBSR	Asthma	Cost-effectiveness (resource use)	None identified
19	NCT02786797	'Efficacy of MBSR Treatment of Cognitive Impairment Among Breast Cancer Survivors'	2016	https://clinicaltrials.gov/ct2/show/NCT02786797	MBSR	Cancer	Health care utilisation and costs	Editorial piece (Bulen Love, 2018)
20	NCT03100981	'Online Mindfulness for Women Treated for Breast Cancer and Men Treated for Prostate Cancer'	2017	https://clinicaltrials.gov/ct2/show/NCT03100981	Internet-delivered MBCT	Cancer	Cost-effectiveness (SF-12+)	Main outcomes (Nissen et al., 2019) Predictors of treatment response (Nissen et al., 2021) Health economics: none identified

#	Record ID	Title	Year	Registration site:	MBP (e.g., adaptation of MBSR or MBCT)	Population / condition	Economic approach	Related publications
21	NCT03361514	'Discontinuation of Antidepressant Medication in Primary Care'	2017	https://clinicaltrials.gov/ct2/show/NCT03361514	MBCT	Depression	Cost-utility	Protocol (Wentink et al., 2019)
22	NCT03406052	'Smartphone-enabled Health Coaching Intervention for Youth Diagnosed With Major Depressive Disorders'	2018	https://clinicaltrials.gov/ct2/show/NCT03406052	online mindfulness-based cognitive behavioural therapy (MB-CBT)	Depression - Youth	intervention costs	Main outcome (Ritvo et al., 2021) Health economics: none identified
23	NCT03425487	'Mindfulness-based and Compassion-based Interventions in Anxious-Depressive Symptomatology in Mental Health Services'	2018	https://clinicaltrials.gov/ct2/show/NCT03425487	MBSR	Mental health	Cost-utility	Protocol (Montero-Marin et al., 2019)
24	NCT03671681	'Mindfulness Therapy for Chronic Migraine'	2018	https://clinicaltrials.gov/ct2/show/NCT03671681	Mindfulness-based therapy	Migraine	Productivity losses and resource use economic costs	None identified
25	NCT03826836	'Mind Our Heart Study'	2019	https://clinicaltrials.gov/ct2/show/NCT03826836	MBSR	atherosclerotic cardiovascular disease	Cost-utility	None identified
26	NTR2222 (old) NL2105 (new)	'Mindful Body Trial: mindfulness training for medically unexplained symptoms'	2010	https://www.trialregister.nl/trial/2105	MBCT	medically unexplained symptoms	Cost-utility	Reported in systematic review (van Ravesteijn et al., 2013b)
27	NTR3453 (old)	'Mindfulness training for patients with structural heart disease'	2012	https://www.trialregister.nl/trial/3306	Online Mindfulness Training	Heart disease	Cost-utility	Main outcomes (Gotink et al., 2017)

#	Record ID	Title	Year	Registration site:	MBP (e.g., adaptation of MBSR or MBCT)	Population / condition	Economic approach	Related publications
	NL3306 (new)							Health economics: none identified
28	NTR3483 (old) NL3351 (new)	'Investigating two home-based interventions for people suffering from chronic fatigue after cancer'	2012	https://www.trialregister.nl/trial/3351	MBCT	Cancer	Productivity losses	Main outcomes (Bruggeman-Everts, Wolvers, van de Schoot, Vollenbroek-Hutten, & van der Lee, 2017) Health economics: none identified

Appendix 7: Referrals letter to clinicians

Centre for Health Economics and Medicines Evaluation
IMSCaR
Arduwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

PRIFYSGOL BANGOR UNIVERSITY

Canolfan Economeg Iechyd a Gwerthuso Moddion
SYMaCh
Arduwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

13th January 2014

RE: Referrals For Mindfulness Research

Dear Colleague,

We are still recruiting for the Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) research project. Courses throughout 2014 will be held across North Wales at Alaw ward (Bangor), St Kentigern Hospice (St Asaph) and Nightingale House (Wrexham).

The following patients are eligible to participate:

- Patients who completed active cancer treatment including surgery, chemotherapy, radiotherapy, hormone therapy (or a combination of these). There is no maximum time since treatment.
- Patients receiving on-going medication who are considered clinically stable by the recruiting clinician and patients receiving on-going hormone therapy are also able to participate.

Please find enclosed invitation leaflets for patients:

- ✓ Please give all patients that meet these inclusion criteria an invitation letter
- X You do not need to give the patient detailed information about the study or go through consent procedures
- ✓ Please attach one yellow 'patient notes' sticker to the notes to help ensure each patient is only asked once
- ✓ Please notify us by email each time a patient is invited so that we can record the number of patients that are eligible to participate in this research and how many referrals are made throughout the research.

If you have any questions about the study please contact us on 01248 388550 or by emailing l.bryning@bangor.ac.uk

Thank you for your on-going support with this study.

Sincerely,

Professor Nick Stuart
Consultant Oncologist

Lucy Bryning
Tenovus PhD Student

ISRCTN23380065

Background to the study for your information:

What is Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca)?

Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) is an 8-week group-based intervention developed at Ysbyty Gwynedd for cancer patients over the last twelve years. Each class (approx. two and a half hours) is led by a trained teacher and includes between 7 and 12 people. During the classes participants are taught how to do mindfulness meditation. This includes learning how to pay attention to their breath and body, and exercises to help people become more aware of the moment-to-moment changes in our mind and body.

What is this research about?

This is the first research project to evaluate MBCT-Ca. This pilot trial is being conducted across BCUHB in collaboration with local cancer consultants to assess the feasibility of conducting a large multi-site randomised control trial, which would be able to investigate the efficacy of mindfulness for cancer patients and inform future practice. As part of this pilot trial we aim to explore whether MBCT-Ca is cost-effective and identify any changes in patient wellbeing, self-compassion, quality of life, depression, and anxiety.

What will happen to patients who decide to take part?

Patients who return the response slip attached to their invitation leaflet will be contacted by the research team directly and sent more information about the study. The process of receiving consent will then take place during a home visit appointment. Patients who consent to the research will be randomly allocated to receiving mindfulness now or mindfulness after a wait period of approximately five months. Patients will be asked to continue with any existing treatment they are receiving as MBCT-Ca will be delivered in addition to treatment as usual.

For more information please contact us on 01248 388550 or by emailing l.bryning@bangor.ac.uk

ISRCTN23380065

Appendix 8: Patient invitation letter and self-referral response slip

Centre for Health Economics and Medicines Evaluation

IMSCaR
Arduduwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
Arduduwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Invitation to Take Part in a Research Project

This leaflet is to tell you about a research project that we think may be of interest to you. The aim of the research is to find ways to help people cope with the anxiety and stress that can come from having had cancer.

The project will be using an approach called Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca). This technique has been developed over the past 10 years specifically for people who have had cancer. We think the technique may be able to help people who have had cancer. The research will help us to learn more about this.

To learn MBCT-Ca patients attend a group meeting each week for 8 weeks. The groups are led by a trained teacher and consist of between 7 and 12 people. Each class lasts about two and a half hours during which participants will learn about MBCT-Ca. This includes meditation, gentle movement and exercises to help become more aware of the moment-by-moment changes in the mind and body.

The course also includes education about the psychological effects of living after cancer and about the links between thinking and feeling. There is also advice on how best to look after yourself when your emotions and moods threaten to overwhelm you.

If you take part in the research we would want to monitor carefully how you were feeling and how you were coping. We would do this by asking you to complete a set of short questionnaires on three occasions over a period of about 7 months.

You would be invited to attend one of our MBCT courses either soon after you agree to take part or after a waiting period of about 6-8 months. Whether you are offered MBCT-Ca now or after a wait will be chosen at random by a computer program.

If you would be interesting in hearing more about this project please complete the slip on the following page and return in the freepost envelope provided by April 7th 2014. This does not mean you would be obliged to take part.

You can also contact the research team directly on 01248 388550 or e-mail l.bryning@bangor.ac.uk. If we don't hear from you we will assume you are not interested in taking part.

The trial is being carried out by researchers at Bangor University working with the Cancer Consultants in North Wales. This research has been funded by Tenovus, Wales' leading cancer charity.

Thank you for taking the time to read about this research.

ISRCTN23380065
Invitation Leaflet. V3 01/08/2013

Centre for Health Economics and Medicines Evaluation

IMSCaR
Arduduwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
Arduduwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Gwahoddiad i gymryd rhan mewn project ymchwil

Bwriad y daflen hon yw rhoi gwybod i chi am broject ymchwil yr ydym yn meddwl y gall fod o ddiddordeb i chi. Nod yr ymchwil yw cael hyd i ffyrdd o helpu pobl i ymdopi gyda'r pryder a'r straen a all godi ar ôl cael canser.

Bydd y project yn defnyddio dull gweithredu o'r enw Therapi Gwybyddol drwy Ymwybyddiaeth Ofalgar ar gyfer Canser (MBCT-Ca). Datblygwyd y dechneg hon dros y 10 mlynedd ddiwethaf yn benodol i bobl sydd wedi cael canser. Credwn y gall y dechneg hon helpu pobl sydd wedi cael canser. Bydd yr ymchwil yn ein helpu i ddysgu mwy am hyn.

I ddysgu am MBCT-Ca, bydd cleifion yn mynd i gyfarfodydd grŵp bob wythnos am 8 wythnos. Arweinir y grwpiau gan athro/athrawes hyfforddedig, a byddant yn cynnwys rhwng 7 a 12 o bobl. Mae pob dosbarth yn para tua dwy awr a hanner lle bydd y rhai sy'n cymryd rhan yn dysgu am MBCT-Ca. Bydd yn cynnwys myfyrdod, ychydig o symudiadau ac ymarferion ysgafn i helpu i ddod yn fwy ymwybodol o'r newidiadau eiliad-wrth-eiliad yn y meddwl a'r corff.

Mae'r cwrs hefyd yn cynnwys dysgu am effeithiau seicolegol bywyd ar ôl cael canser ac am y cysylltiadau rhwng meddwl a theimlo. Ceir cyngor hefyd am y ffordd orau i ofalu am eich hun pan fydd eich emosiynau a'ch hwyliau'n bygwth mynd yn drech na chi.

Os byddwch yn cymryd rhan yn yr ymchwil, byddwn yn monitro'n ofalus sut yr ydych yn teimlo a sut yr ydych yn ymdopi. Byddwn yn gwneud hyn drwy ofyn i chi lenwi set o holiaduron byrion dair gwaith yn ystod y cyfnod o oddeutu 7 mis.

Cewch eich gwahodd i ddod i un o'n cyrsiau MBCT naill ai'n fuan ar ôl i chi gytuno i gymryd rhan, neu ar ôl cyfnod aros o 6-8 mis. Rhaglen gyfrifiadurol fydd yn dewis ar hap os cewch gynnig le ar y cwrs MBCT-Ca yn awr neu ymhen rhai misoedd.

Os oes gennych ddiddordeb mewn clywed mwy am y project hwn, llenwch y bonyn ar y dudalen ganlynol a'i ddychwelyd yn yr amlen radbost cyn 7 Ebrill 2014. Ni fydd hyn yn golygu y bydd rhaid i chi gymryd rhan.

Gellwch hefyd gysylltu â'r tîm ymchwil yn uniongyrchol ar 01248 388550, neu anfon e-bost at l.bryning@bangor.ac.uk. Os na chawn ateb, byddwn yn cymryd nad oes gennych ddiddordeb mewn cymryd rhan.

Cynhelir yr arbrawf gan ymchwilwyr ym Mhrifysgol Bangor yn gweithio gyda'r Ymgynghorwyr Canser yng ngogledd Cymru. Cyllidir yr ymchwil hwn gan Tenovus, yr elusen canser flaenllaw yng Nghymru.

Diolch am eich amser yn darllen am yr ymchwil hwn.

ISRCTN23380065
Invitation Leaflet. V3 01/08/2013

Centre for Health Economics
and Medicines Evaluation

IMSCaR
Ardudwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

Canolfan Economeg Iechyd
a Gwerthuso Moddion

SYMaCh
Ardudwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Invitation to Take Part in a Research Project

Yes, please contact me more with information about the Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) trial.

Name……

Address……

……Postcode ……..……..

Email Address……

Telephone: ……

MAY WE LEAVE MESSAGES ON THIS PHONE? (Please tick one)

Do not leave a message ☐
Leave name and number only ☐
Leave full message ☐

Please return to:

Lucy Bryning
CHEME,
FREEPOST BG35
IMSCaR,
ARDUDWY
Bangor University,
Gwynedd,
LL57 2PZ

Contacting us does not mean you have to take part. All information will be kept strictly confidential.

ISRCTN23380065
Invitation Leaflet. V3 01/08/2013

Centre for Health Economics
and Medicines Evaluation

IMSCaR
Ardudwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

Canolfan Economeg Iechyd
a Gwerthuso Moddion

SYMaCh
Ardudwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Gwahoddiad i gymryd rhan mewn project ymchwil

Hoffwn gael rhagor o wybodaeth am y treial Therapi Gwybyddol drwy Ymwybyddiaeth Ofalgar ar gyfer Canser (MBCT-Ca).

Enw…..……..……

Cyfeiriad ……

…… Cod Post ……..……..

Cyfeiriad E-bost ……

Ffôn: ……

A GAWN NI ADAEL NEGESEUON AR Y RHIF HWN? (ticiwch un)

Peidiwch â gadael neges ☐
Gadewch enw a rhif yn unig ☐
Gadewch neges lawn ☐

Anfonwch y ffurflen at:

Lucy Bryning
CHEME,
RHADBOST BG35
IMSCaR,
ARDUDWY
Prifysgol Bangor,
Gwynedd,
LL57 2PZ

Nid yw cysylltu â ni'n golygu bod rhaid i chi gymryd rhan. Bydd yr holl wybodaeth yn cael ei chadw'n hollol gyfrinachol.

ISRCTN23380065
Invitation Leaflet. V3 01/08/2013

Appendix 9: Clinical referral notification form

Cost effectiveness of MBCT-Ca: A pilot pragmatic randomised trial

I have invited 1 patient

Date: ……..

Name of referrer: ……..

Signature of referrer: ……

Please return to:

Lucy Bryning

CHEME,

FREEPOST BG35

IMSCaR,

Dean Street

Bangor University,

Gwynedd,

LL57 1UT

Alternatively, please email l.bryning@bangor.ac.uk with the following subject line

Subject: 1 patient invited to MBCT-Ca pilot trial

Appendix 10: Postal recruitment invitation cover-letter

Annwyl

Ysgrifennaf atoch yn dilyn eich ymweliad diweddar â'r ysbyty i glinig Alaw. Hoffwn eich gwahodd i gymryd rhan mewn project ymchwil rydym yn meddwl y gall fod o ddiddordeb i chi. Bwriad yr ymchwil yw ceisio helpu pobl sydd wedi cael canser.

Bydd y project yn dilyn dull Therapi Gwybyddol drwy Ymwybyddiaeth Ofalgar ar gyfer Canser (MBCT-Ca) a ddatblygwyd yng ngogledd Cymru yn ystod y 10 mlynedd ddiwethaf. Amgaeaf daflen gyda rhagor o wybodaeth a manylion cyswllt os hoffech gael rhagor o wybodaeth am y project. Os oes gennych ddiddordeb mewn gwybod mwy am y project, llenwch y ffurflen amgaeedig a'i dychwelyd yn yr amlen radbost.

Yn gywir

Yr Athro Stuart

Oncolegydd Ymgynghorol

Ysbyty Gwynedd

ISRCTN23380065
Invitation Leaflet. V3 28/08/2013

Dear

I am writing to you following you recent hospital visit to the Alaw clinic. I would like to invite you to take part in a research project that we think may be of interest to you. The resarch is to try and help people who have had cancer.

The project will be using an approach called Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) which has been developed in North Wales over the past 10 years. I have enclosed a leaflet that gives a bit more information and contact details should you wish to discuss the project in greater detail. If you would be interesting in hearing more about this project please complete the slip enclosed and return in the freepost envelope provided.

Kind regards,

Professor Stuart

Consultant Oncologist

Ysbyty Gwynedd

ISRCTN23380065
Invitation Leaflet. V3 28/08/2013

Appendix 11: Randomisation specification

Randomisation Specification Document for MBCT-Ca Pilot

Status	Version	Date
Agreed	1	07/01/13

North Wales Organisation for Randomised Trials in Health (NWORTH)
Bangor University, College of Health & Behavioural Sciences,
Institute of Medical & Social Care Research, Y Wern, Normal Site, Holyhead Road, Bangor, Gwynedd LL57 2PZ
Telephone: 01248 388095
Email nworth@bangor.ac.uk
http://www.bangor.ac.uk/imscar/nworth

Randomisation brief: Primary objective of the study is to explore cost-effectiveness of MBCT-Ca delivered in addition to treatment as usual, as compared to treatment as usual alone.

Agreed by:	Lucy Bryning and Dr. Zoë Hoare on protocol version 1 26.03.12
Setting:	Hospital – Oncology
Participants:	120
Allocation ratio:	1:1
Intervention:	Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) vs Treatment as Usual
Type:	Sequential. A separate system for each cohort will be implemented
Stratification variables:	Centre (Bangor /St Asaph)
Method:	Email and web. NWORTH will receive randomisation details from Lucy Bryning and perform the randomisation. The outcome will be recorded by Katherine Betteridge (CRMP) who will generate the outcome letter for the participant. The mindfulness teacher will be informed of the participants in the intervention group by Katherine Betteridge (CMRP).
Blinding:	Lucy Bryning will be blind to treatment allocation. Katherine Betteridge (CMRP) will be informing the mindfulness teacher of the intervention participants. The participants will be informed of randomisation result by letter produced in CRMP
Confirmation:	s.smith@bangor.ac.uk, sps001@bangor.ac.uk, michelle.williams@bangor.ac.uk, huw.roberts@bangor.ac.uk, d.s.hunnisett@bangor.ac.uk, k.betteridge@bangor.ac.uk
Group constraints:	Minimum capacity of 8 per group; Maximum capacity of 12 per group. This will be implemented by a manual count. Once either intervention or control group has reached 12 in a centre, the cohort in the centre will be closed. Randomisation will then continue in the next cohort. Randomisation can continue in the other centre in the cohort until the maximum of 12 is reached. There will be a separate system for each cohort.

Emergency randomisation procedures: Randomisation is not time critical and can therefore be done at a later date. A period of approximately 2-3 weeks will be available for randomisation.

North Wales Organisation for Randomised Trials in Health (NWORTH)
Bangor University, College of Health & Behavioural Sciences,
Institute of Medical & Social Care Research, Y Wern, Normal Site, Holyhead Road, Bangor, Gwynedd LL57 2PZ
Telephone: 01248 388095
Email nworth@bangor.ac.uk
http://www.bangor.ac.uk/imscar/nworth

Timescale: Start : Jan 2013 End: July 2014

Other information: Participant ID - 5 digit number – First two numbers indicating centre (10 YG; 20 YGC/St Asaph) – Last three numbers will be sequential (001, 002)
Participant Initials – Min 2 letters/Max 3 letters
Participant DOB - DD/MM/YYYY
Consent (yes=proceed) – YES / NO
Inclusion criteria met (yes=proceed) – YES / NO

Trial contact: Lucy Bryning 01248 388550 Email: *l.bryning@bangor.ac.uk*

	Name	Position	Signed	Date
Prepared By:	Zoë Hoare	NWORTH Statistician	ZHoare	7/1/13
Reviewed By:	Yvonne Sylvestre	NWORTH Statistician	Sylvestre	7/1/13
Approved By:	Lucy Bryning	CHEME PhD STUDENT	LBryning	7/1/13

WEB Based randomisation Centre information

DELETE SECTION IF EMAIL RANDOMISATION

A list of centre names associated with the trial.

1. Ysbyty Gwynedd
2. Ysbyty Glan Clwyd/St Asaph

User account information

A log of who needs access to the trial, which centres and whether they are blinded or not.

These users will be created on account to allow them to randomise participants. If they are blinded to result their confirmation screen will inform them that the randomisation has been successful and results have been emailed to the appropriate person. If they are not blind then the result will appear on screen as well as being emailed to the stipulated addresses.

FIRST NAME	SURNAME	JOB TITLE	TELEPHONE	EMAIL ADDRESS	BLINDED TO RESULT	To which centres access is needed
Lucy	Bryning	PhD student	01248 388550	l.bryning@bangor.ac.uk	YES	YG, YGC
Sioned	Smith	CHEME Administrator	01248 388314	s.smith@bangor.ac.uk	NO	YG, YGC
Katherine	Betteridge	Research Assistant	01248 382923	k.betteridge@bangor.ac.uk	NO	YG, YGC

North Wales Organisation for Randomised Trials in Health (NWORTH)
Bangor University, College of Health & Behavioural Sciences,
Institute of Medical & Social Care Research, Y Wern, Normal Site, Holyhead Road, Bangor, Gwynedd LL57 2PZ
Telephone: 01248 388095
Email nworth@bangor.ac.uk
http://www.bangor.ac.uk/imscar/nworth

Questionnaire information

Outline of the questionnaire required for randomisation

This is a stipulation of how the questions will appear on the web system and any associated validation that is required This is what the IS team should use to populate the new system.

Question Name	Question Type	Validation	Is this a Stratification variable?
Question text to be displayed on screen ***Participant ID***	*Text/drop down/radio* ***Text***	*Acceptable numerical range, valid DOB* ***5 digit number – First two numbers indicating centre (10 = YG; 20 = YGC) – Last three numbers will be sequential (001, 002)***	*YES/NO* ***NO***
Participant Initials	***Text***	***Letters (Min 2, Max 3)***	***NO***
Participant Date of Birth	***Text***	***DD/MM/YYYY***	***NO***
Centre	***Drop down***	***St Asaph, Bangor***	***YES***
Participant CONSENT	***Drop down***	***YES / NO*** ***Must be Yes to proceed***	***NO***
Participant inclusion criteria met?	Drop down	Must be yes to proceed	NO

North Wales Organisation for Randomised Trials in Health (NWORTH)
Bangor University, College of Health & Behavioural Sciences,
Institute of Medical & Social Care Research, Y Wern, Normal Site, Holyhead Road, Bangor, Gwynedd LL57 2PZ
Telephone: 01248 388095
Email nworth@bangor.ac.uk
http://www.bangor.ac.uk/imscar/nworth

Appendix 12: NHS REC-West confirmation of favourable ethical approval

Part of the research infrastructure for Wales funded by the National Institute for Social Care and Health Research, Welsh Government.
Yn rhan o seilwaith ymchwil Cymru a ariannir gan y Sefydliad Cenedlaethol ar gyfer Ymchwil Gofal Cymdeithasol ac Iechyd, Llywodraeth Cymru

NISCHR
Gwasanaeth Moeseg Ymchwil | RES | Research Ethics Service

Pwyllgor Moeseg Ymchwil Gogledd Cymru - Y Orllewin
North Wales Research Ethics Committee – West

Betsi Cadwaladr University Health Board
Ysbyty Gwynedd
Clinical Academic Office
Bangor, Gwynedd
LL57 2PW

Telephone/ Facsimile: 01248 - 384.877
Email: Rossela.Roberts@wales.nhs.uk
Website : www.nres.nhs.uk

Miss Lucy Bryning
Centre for Health Economics and Medicines Evaluations
IMSCaR, Dean Street Building
Bangor, Gwynedd
LL57 1UT l.bryning@bangor.ac.uk

20 August 2012

Dear Miss Bryning,

Study title: **Exploring the Cost Effectiveness of Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) delivered in addition to treatment as usual (TAU) as compared with TAU alone: A pilot pragmatic randomised controlled Trial.**
REC reference: **12/WA/0095**
IRAS reference: **94524**

Thank you for your letter of 06 July 2012, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chairman.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter		30 March 2012
REC application submission 94524/309793/1/736		30 March 2012
Protocol	1	26 March 2012
Protocol Summary/Synopsis	1	26 March 2012
Summary/Synopsis Flowchart	1	26 March 2012
Other: Protocol time-line	1	26 March 2012
Letter from Sponsor School of Psychology Research Ethics and Governance Committee		29 March 2012
Letter from Statistician		27 March 2012
Letter of invitation to participant	2.2	28 May 2012
Participant Information Sheet	2.2	28 May 2012
Participant Consent Form	2.1	28 May 2012
GP/Consultant Information Sheets	1	26 March 2012
Interview Schedules/Topic Guides	1	26 March 2012
Other: Debrief Form	1	26 March 2012
Other: GP End of Trial Letter	1	26 March 2012
Other: Oncology End of Trial Letter	1	26 March 2012
Questionnaire: EQ-5D		
Questionnaire: ICE-CAP-A		
Questionnaire: EORTC QOL C30		
Questionnaire: SCS-SF		
Questionnaire: HADS		
Questionnaire: FFMQ-SF		
Questionnaire: WHO-5		
Questionnaire: Demographics	1	26 March 2012
Questionnaire: SUQ	1	26 March 2012
Investigator CV (Miss Lucy Bryning)		26 March 2012
Other: Academic Supervisor CV (Dr Rebecca Crane)		
Other: Academic Supervisor CV (Prof Rhiannnon Tudor Edwards)		
Evidence of insurance or indemnity	UMAL	01 August 2011
Response to Request for Further Information		06 July 2012

[Pages 3 and 4 redacted]

Appendix 13: Randomised feasibility trial study information sheet

Centre for Health Economics and Medicines Evaluation

IMSCaR
Ardudwy Hall
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

PRIFYSGOL BANGOR UNIVERSITY

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
Neuadd Ardudwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Mindfulness for people who have had cancer: a pilot research trial

Study Information Sheet

We would like to invite you to take part in a research study. This information is to help you understand what the research will involve and why we are doing it. Please take time to read it and feel free to discuss it with others if you wish. If you do not understand anything or you would like more information, please contact us. You can take time to decide whether or not you wish to take part.

What is Mindfulness-Based Cognitive Therapy for Cancer (MBCT-Ca)?

MBCT-Ca is a group-based treatment that has been developed for people who have had cancer. It involves attending one class a week for 8 weeks. Each class is led by a trained teacher, includes between 7 and 12 people, and lasts about two and a half hours.

During the classes you would learn how to do mindfulness meditation. This would include learning how to pay attention to your breathing and body, and exercises to help you become more aware of the moment-to-moment changes in your mind and body. You would also be shown how thinking and feeling are linked and how best to look after yourself when your emotions or moods may start to overwhelm you.

You will receive information about depression and the psychological effects of cancer. You would be encouraged to practice the meditation at home on a regular basis with the help of CDs.

What is the purpose of the study?

We want to learn more about MBCT-Ca and about how it might help people who have had cancer. This study will help us to find out if we need to do more research and will also help with planning local cancer care.

Why have I been chosen?

We are interested in whether MBCT-Ca can help people like you who have completed treatment for cancer (such as surgery, chemotherapy, radiotherapy or hormone therapy). If you are receiving on-going hormone therapy or other on-going medicines you may also be able to participate.

What will happen to me if I take part?

If you decide to take part in the study we will arrange to meet you at a time convenient for you. This interview will last about 1 hour and will take place at your home or another place if you would prefer. We will talk to you about the study and you will be able to ask questions if you are unsure of anything. We will also check that this is a suitable study for you to take part in.

ISRCTN23380065
Information Sheet. V4. 28/08/13

To see whether MBCT-Ca is helpful we need to compare people who attend the courses now with another group of people who are have usual care but don't attend the MBCT-Ca course. Therefore, if you participate in the study, you will be chosen to either take MBCT-Ca straight away or after a wait of 6-8 months.

If you consent to taking part we will ask you to complete a booklet of questionnaires and a short interview with the researcher.

After the first meeting you will be allocated to one of the two groups, either 'MBCT-Ca now' or 'MBCT-Ca later' (after a wait of 6-8 months). Whether you are offered MBCT-Ca now or after a wait will be chosen at random by a computer program

If you are in the 'MBCT-Ca now' group you will meet the MBCT-Ca teacher to discuss the classes in more detail and discuss how this course will fit in with your current lifestyle. This will be followed by the eight weekly sessions, each of about two and a half hours. The classes will be held at Ysbyty Gwynedd (Bangor), St Kentigern Hospice (St Asaph), or at Nightingale House (Wrexham). You will be invited to travel to the classes closest to your home address unless you tell us you would prefer to attend a different class.

In addition to weekly sessions, you will be asked to spend about an hour each day practising at home. This includes regular mindfulness practice (with the use of an audio CD) and shorter exercises that help people to become mindful in everyday life. It can be difficult to make time for this, so please think carefully about whether you are able to make this commitment, before agreeing to take part.

If you are in the MBCT-Ca later group you will be able to take part in the courses in about 6-8 months.

During the course of the study, everyone will be asked to complete questionnaires (by post or telephone) and short interviews (by telephone or at your home); this will be before and immediately after the MBCT-Ca course and again after 3 months. These questionnaires will ask about your health and wellbeing, including brief details of your cancer diagnosis. We will also ask about the types of services you have contacted recently. All of the questions are optional and you can choose to miss any questions that you don't feel comfortable answering. You are also able to choose to end the interview or assessment early if you would like to. These questionnaires will take no more than 30 minutes to complete.

During the group sessions the mindfulness teacher may be video recorded. This is done so that the quality of the teaching can be checked and so that we can research how conversations take place between teacher and participants during mindfulness classes. This helps us understand how the teaching process supports participants learning. We hope that this will influence future training of teachers and so will be of benefit to participants in future classes. The camera will be positioned so that it only captures the image of the teacher, but it will also record the voices of the people in the group. The recordings will be used for research, supervision and training purposes only and the confidentiality of the people in the group will be protected at all times.

At the end of the study you will be invited to take part in an extra interview with the researcher and asked questions about your experience of taking part in the research. These

individual interviews will be audio recorded. If you would prefer not to be recorded then you may ask the researcher not to do this.

Everyone in the study will be able to receive other treatments or to seek other help (e.g. from their GPs/specialist teams) in the usual way.

Your participation in the study will be approximately 7 months. It is important that you think carefully about whether or not you are willing to make the commitment of time needed.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. If you have concerns about staying in the study then you can discuss this with us. You are still free to withdraw at any time without giving a reason. Withdrawal will not affect the care you receive outside of this research.

Who will be informed of my involvement in the study?

If you decide to take part then we will let your GP know this. This means that your GP can take it into account when planning other treatments.

What will happen to my data?

If you join the study, people given permission from Bangor University or the NHS Trust to check that the study is being carried out correctly may look at the data collected.

All data collected will be kept strictly confidential within the limits of the law (Data Protection Act, 1998). You will not be named or identifiable in any report or publication that comes from this study. We may use direct quotes from interviews and from the class recordings but these would also be kept anonymous.

All data would be kept on password-protected computers or in locked filling cabinets at Bangor University. Data will be stored for 15 years and will be destroyed after this time.

You may choose to withdraw from the study at any time and you would have the right to request that your data is not used.

What happens if I change my mind?

You are free to withdraw from the study at any time. You do not have to give a reason. If you withdraw from the study, we would still like to use any information we collected before your withdrawal.

If you begin the MBCT-Ca classes but then decide to stop attending we would still like you to complete the remaining research questionnaires if possible. This is because it will give us a balanced understanding of how people feel about the courses. However you do not have to do so if you do not want to.

Who do I contact about the study?

This research is being conducted by the Centre for Health Economics and Medicines Evaluation (CHEME) in collaboration with the Centre for Mindfulness Research and Practice (CMRP), at Bangor University.

If you have any further questions about this study please contact Lucy Bryning on 01248 388550 or email l.bryning@bangor.ac.uk.

Who do I contact with any concerns or complaints about this study?

While we do not think that taking part in this study will cause any harm, if you have any concerns or complaints about any aspects of this study then please contact Professor Robert T. Woods, Acting Director of the Institute of Medical and Social Care Research, Bangor University, Bangor, Gwynedd, LL57 2DG or e-mail b.woods@bangor.ac.uk.

In addition, participants may contact Hefin Francis, School Manager, School of Psychology, Adeilad Brigantia, Penrallt Road, Bangor, Gwynedd, LL57 2AS, or email h.francis@bangor.ac.uk

The normal NHS complaints procedure is also available. If you are harmed due to someone's negligence then you may have grounds for legal action for compensation against Bangor University (in respect of any harm arising out of the participation in the trial) or the NHS (in respect of any harm which has resulted from the clinical procedure being undertaken).

Who is funding this research?

This research is funded by Tenovus, a leading Wales cancer charity.

Who has reviewed this research?

This research has been reviewed and approved by the School of Psychology Ethics Committee and the NHS North Wales (West) Research Ethics Committee.

Centre for Health Economics and Medicines Evaluation

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Bangor University
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Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
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Ymwybyddiaeth ofalgar i bobl sydd wedi cael canser: peilot ymchwil

Taflen Wybodaeth ynglŷn â'r Astudiaeth

Hoffem eich gwahodd i gymryd rhan mewn astudiaeth ymchwil. Bydd y wybodaeth hon yn eich helpu i ddeall beth fydd yn digwydd yn yr ymchwil, a pham yr ydym yn ei gwneud. Cymerwch amser i ddarllen y wybodaeth, a thrafodwch ei chynnwys gydag eraill os dymunwch. Os oes yna rywbeth nad ydych yn ei ddeall neu os hoffech ragor o wybodaeth, croeso i chi gysylltu â ni: Cymerwch eich amser cyn penderfynu a ydych yn dymuno cymryd rhan neu beidio.

Beth yw Therapi Gwybyddol drwy Ymwybyddiaeth Ofalgar ar gyfer Canser (MBCT-Ca)?

Triniaeth mewn grŵp yw MBCT-Ca a ddatblygwyd ar gyfer pobl sydd wedi cael canser. Mae'n golygu mynd i un dosbarth yr wythnos am 8 wythnos. Caiff pob dosbarth ei arwain gan athro/athrawes hyfforddedig, cynnwys rhwng 7 a 12 o bobl, ac sy'n para tua dwy awr a hanner.

Yn ystod y dosbarthiadau byddech yn dysgu sut i wneud myfyrdod ymwybyddiaeth ofalgar. Byddai hyn yn cynnwys dysgu sut i dalu sylw i'ch anadlu a'ch corff, ac ymarferion i'ch helpu i ddod yn fwy ymwybodol o'r newidiadau moment-i-foment yn eich meddwl a'ch corff. Byddech chi'n dysgu hefyd sut mae meddwl a theimlo'n gysylltiedig, a sut orau i edrych ar ôl eich hun pan fydd eich emosiynau neu eich hwyliau'n dechrau mynd yn drech na chi.

Byddwch yn derbyn gwybodaeth am iselder, ac effeithiau seicolegol canser. Cewch eich annog i ymarfer y myfyrdod gartref yn rheolaidd a chyda chymorth cryno-ddisgiau.

Beth yw diben yr astudiaeth?

Rydym am ddysgu mwy am MBCT-Ca a sut y gallai helpu pobl sydd wedi cael canser. Bydd yr astudiaeth hon yn ein helpu i wybod a oes arnom angen gwneud rhagor o ymchwil, a bydd hefyd yn helpu i gynllunio gofal canser lleol.

Pam rydw i wedi cael fy newis?

Hoffem wybod a all MBCT-Ca helpu pobl fel chi sydd wedi cwblhau triniaeth ar gyfer canser (fel llawdriniaeth, cemotherapi, radiotherapi neu therapi hormonau). Os ydych yn derbyn therapi hormonau neu feddyginiaethau eraill ar hyn o bryd mae'n bosib y byddwch yn gallu cymryd rhan hefyd.

Beth fydd yn digwydd i mi os byddaf yn cymryd rhan?

Os ydych yn penderfynu cymryd rhan yn yr astudiaeth byddwn yn trefnu eich cyfarfod ar adeg sy'n gyfleus i chi. Bydd y cyfweliad yn para tua awr, ac yn cael ei gynnal yn eich cartref, neu yn rhywle arall os ydyw'n well gennych. Byddwn yn siarad gyda chi am yr

astudiaeth, a byddwch yn gallu gofyn cwestiynau os ydych chi'n ansicr ynghylch unrhyw beth. Mi fyddwn ni hefyd yn gwneud yn siŵr bod hon yn astudiaeth addas i chi gymryd rhan ynddi.

Er mwyn gweld a yw MBCT-Ca o fudd, rhaid i ni gymharu pobl sy'n mynd ar gyrsiau yn awr gyda grŵp arall o bobl sy'n cael gofal arferol, ond nad ydynt yn mynychu'r cwrs MBCT-Ca. Felly, os byddwch yn cymryd rhan yn yr astudiaeth, cewch eich dewis naill ai i ddilyn MBCT-Ca yn syth bin, neu ar ôl aros 6-8 mis.

Os byddwch yn cytuno i gymryd rhan, byddwn yn gofyn i chi lenwi llyfryn o holiaduron, a chael cyfweliad byr gyda'r ymchwilydd.

Ar ôl y cyfarfod dechreuol, cewch eich gosod yn un o'r ddau grŵp, naill ai 'MBCT-Ca yn awr' neu 'MBCT-Ca yn ddiweddarach' (ar ôl aros 6-8 mis). Rhaglen gyfrifiadurol fydd yn dewis ar hap a fyddwch yn cael cynnig MBCT-Ca i chi yn awr neu ar ôl aros.

Os ydych chi yn y grŵp 'MBCT-Ca yn awr', byddwch yn cwrdd â'r athro/athrawes MBCT-Ca i drafod y dosbarthiadau'n fanylach, a thrafod sut bydd y cwrs hwn yn ffitio i mewn gyda'ch ffordd o fyw ar hyn o bryd. Yn dilyn hyn ceir yr wyth sesiwn wythnosol, a phob un yn para tua dwy awr a hanner. Cynhelir y dosbarthiadau yn Ysbyty Gwynedd (Bangor), Hosbis St Kentigern (Llanelwy) neu Dŷ'r Eos (Wrecsam). Cewch eich gwahodd i deithio i'r dosbarthiadau agosaf i'ch cyfeiriad cartref oni bai eich bod yn dweud wrthym y byddai'n well gennych fynd i ddosbarth gwahanol.

Yn ogystal â'r sesiynau wythnosol, gofynnir i chi dreulio tua awr bob diwrnod yn gwneud eich ymarfer adref. Mae hyn yn cynnwys ymarfer ymwybyddiaeth ofalgar rheolaidd (gan ddefnyddio CD sain) ac ymarferion byrrach sy'n helpu pobl i ddod yn ymwybodol o bethau mewn bywyd bob dydd. Gall fod yn anodd neilltuo amser i wneud hyn, felly os gwelwch yn dda, meddyliwch yn ofalus a allwch chi wneud yr ymrwymiad yma, cyn cytuno i gymryd rhan.

Os ydych chi yn y grŵp 'MBCT-Ca yn ddiweddarach', byddwch yn gallu cymryd rhan yn y cyrsiau ymhen tua 6- 8 mis.

Yn ystod yr astudiaeth, gofynnir i bawb lenwi holiaduron (drwy'r post neu ffôn) a chael chyfweliadau byrion (dros y ffôn neu yn eich cartref); bydd hyn yn digwydd cyn y cwrs MBCT-Ca, ac yn syth ar ei ôl, ac eto ar ôl 3 mis. Bydd yr holiaduron hyn yn gofyn i chi am eich iechyd a'ch lles, yn cynnwys manylion byr am eich diagnosis canser. Byddwn yn gofyn i chi hefyd am y mathau o wasanaethau yr ydych wedi cysylltu â nhw'n ddiweddar. Dewisol yw'r holl gwestiynau, a gellwch ddewis peidio ag ateb unrhyw gwestiynau nad ydych yn teimlo'n gyffyrddus yn eu hateb. Gallwch hefyd orffen y cyfweliad neu'r asesiad yn gynnar os hoffech wneud hynny. Ni fydd yr holiaduron hyn yn cymryd mwy na 30 munud i'w llenwi.

Yn ystod y sesiynau grŵp, efallai y bydd yr athro / athrawes ymwybyddiaeth ofalgar yn cael ei recordio ar dâp fideo. Gwneir hyn fel gellir gwirio ansawdd yr addysgu ac fel y gallwch ymchwilio i sut mae sgyrsiau'n digwydd rhwng yr athro ac aelodau'r dosbarth yn ystod dosbarthiadau ymwybyddiaeth ofalgar. Mae hyn yn ein helpu ni i ddeall sut mae'r broses addysgu yn cefnogi dysgu'r rhai sy'n cymryd rhan yn yr ymchwil. Rydym yn gobeithio y bydd hyn yn dylanwadu ar y ffordd mae athrawon yn cael eu hyfforddi yn y dyfodol ac felly y bydd o fudd i rai sy'n mynychu dosbarthiadau yn y dyfodol. Gosodir y camera fel ei fod

yn ffilmio'r athro /athrawes yn unig, ond bydd hefyd yn recordio lleisiau'r bobl yn y grŵp. Defnyddir y recordiadau at ddibenion ymchwil a hyfforddiant yn unig, a gwarchodir cyfrinachedd y bobl yn y grŵp bob amser.

Ar ddiwedd yr astudiaeth,cewch eich gwahodd i gymryd rhan mewn cyfweliad ychwanegol gyda'r ymchwilydd, a gofynnir cwestiynau i chi ynghylch eich profiad o gymryd rhan yn yr ymchwil. Caiff y cyfweliadau unigol hyn eu recordio. Os byddai'n well gennych beidio â chael eich recordio, yna gellwch ofyn i'r ymchwilydd beidio â gwneud hyn.

Bydd pawb yn yr astudiaeth yn gallu derbyn triniaethau eraill neu ofyn am gymorth arall (e.e. gan eu meddygon teulu/timau arbenigol) yn y ffordd arferol.

Byddwch yn cymryd rhan yn yr astudiaeth am tua 7 mis. Mae'n bwysig eich bod yn meddwl yn ofalus a ydych yn fodlon ymrwymo i'r amser sydd ei angen.

A oes rhaid imi gymryd rhan?

Chi sydd i benderfynu a ydych am gymryd rhan ai peidio. Os byddwch yn penderfynu cymryd rhan, rhoddir y daflen wybodaeth hon i chi i'w chadw a gofynnir i chi arwyddo ffurflen gydsynio. Os oes gennych unrhyw bryderon ynghylch aros yn yr astudiaeth, yna gellwch drafod hyn gyda ni. Mae gennych hawl o hyd i dynnu'n ôl unrhyw bryd heb roi rheswm. Ni fydd hyn yn effeithio ar y gofal yr ydych chi'n ei dderbyn y tu allan i'r ymchwil hon.

Pwy fydd yn cael gwybod fy mod yn cymryd rhan yn yr astudiaeth?

Os penderfynwch gymryd rhan, byddwn yn rhoi gwybod i'ch meddyg teulu. Golyga hyn y gall eich meddyg teulu ei ystyried wrth gynllunio triniaethau eraill.

Beth fydd yn digwydd i'm data?

Os byddwch yn ymuno â'r astudiaeth, gall pobl sydd wedi cael caniatâd gan Brifysgol Bangor neu'r Ymddiriedolaeth GIG edrych ar y data a gasglwyd er mwyn gwirio bod yr astudiaeth yn cael ei chynnal yn gywir, .

Bydd yr holl ddata a gesglir yn cael eu cadw'n hollol gyfrinachol o fewn cyfyngiadau'r gyfraith (Deddf Gwarchod Data, 1998). Ni fyddwn yn eich enwi na rhoi manylion personol amdanoch mewn unrhyw adroddiad na chyhoeddiad sy'n deillio o'r astudiaeth hon. Gallwn ddefnyddio dyfyniadau uniongyrchol o gyfweliadau ac o'r recordiadau o'r dosbarth, ond bydd y rhain yn cael eu cadw'n ddienw hefyd.

Bydd yr holl ddata'n cael eu cadw ar gyfrifiaduron y gellir eu defnyddio drwy gyfrinair yn unig, neu'n cael eu cloi mewn cwpwrdd ffeilio ym Mhrifysgol Bangor. Caiff y data eu cadw am 15 mlynedd a'u dinistrio ar ôl hynny.

Gellwch ddewis gadael yr astudiaeth unrhyw bryd, a bydd gennych hawl i ofyn i ni beidio â defnyddio eich data.

Beth fydd yn digwydd os byddaf yn newid fy meddwl?

Gellwch dynnu'n ôl o'r astudiaeth unrhyw bryd. Nid oes raid i chi roi rheswm. Os byddwch yn tynnu'n ôl o'r astudiaeth, byddwn ni'n dal yn awyddus i ddefnyddio unrhyw wybodaeth a gasglwyd gennym cyn i chi dynnu'n ôl.

Os byddwch yn dechrau'r dosbarthiadau MBCT-Ca, ond yna'n penderfynu rhoi'r gorau i fynd, byddwn ni'n dal yn awyddus i chi lenwi'r holiaduron ymchwil sydd ar ôl os gellwch. Y mae hyn oherwydd y bydd yn rhoi dealltwriaeth gytbwys i ni o sut mae pobl yn teimlo am y cyrsiau. Fodd bynnag, nid oes raid i chi wneud hynny os nad ydych chi'n dymuno.

Gyda phwy y dylwn gysylltu ynglŷn â'r astudiaeth?

Cynhelir yr ymchwil hon gan y Ganolfan Economeg Iechyd a Gwerthuso Moddion (CHEME) ar y cyd â'r Ganolfan Ymchwil ac Ymarfer Ymwybyddiaeth Ofalgar (CMRP), ym Mhrifysgol Bangor.

Os oes gennych ragor o gwestiynau am yr astudiaeth, mae croeso i chi gysylltu â Lucy Bryning ar 01248 388550, neu e-bost: l.bryning@bangor.ac.uk.

Â phwy dylwn i gysylltu os oes gennyf bryderon neu gwynion ynghylch yr astudiaeth hon?

Er nad ydym yn meddwl y bydd cymryd rhan yn yr astudiaeth hon yn achosi unrhyw niwed, os oes gennych chi unrhyw bryderon neu gwynion ynghylch unrhyw agwedd ar yr astudiaeth hon, cysylltwch â'r Athro Robert T. Woods, Cyfarwyddwr Gweithredol y Ganolfan Ymchwil Gofal Meddygol a Chymdeithasol, Prifysgol Bangor, Bangor, Gwynedd, LL57 2DG neu e-bostiwch b.woods@bangor.ac.uk.

Gall y rhai sy'n cymryd rhan gysylltu hefyd â Hefin Francis, Rheolwr yr Ysgol, yr Ysgol Seicoleg, Adeilad Brigantia, Ffordd Penrallt, Gwynedd, LL57 2AS, neu e-bostiwch h.francis@bangor.ac.uk

Mae trefn cwynion arferol y GIG ar gael i chi hefyd. Os cewch eich niweidio o ganlyniad i esgeulustod rhywun, yna efallai y bydd gennych sail dros gymryd camau cyfreithiol i gael iawndal yn erbyn Prifysgol Bangor (mewn cysylltiad ag unrhyw niwed sy'n codi o gymryd rhan yn yr arbrawf) neu'r GIG (mewn cysylltiad ag unrhyw niwed sydd wedi deillio o'r drefn glinigol a ddilynwyd).

Pwy sy'n ariannu'r ymchwil hon?

Cyllidir yr ymchwil gan Tenovus, elusen canser flaenllaw yng Nghymru.

Pwy sydd wedi adolygu'r ymchwil?

Adolygwyd a chymeradwywyd yr ymchwil hon gan Bwyllgor Moeseg yr Ysgol Seicoleg a Phwyllgor Moeseg Ymchwil GIG Gogledd Orllewin Cymru.

Appendix 14: Randomised feasibility trial informed consent form

Centre for Health Economics and Medicines Evaluation

IMSCaR
Ardudwy Hall
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

PRIFYSGOL BANGOR UNIVERSITY

Canolfan Economeg Iechyd a Gwerthuso Meddion

SYMaCh
Neuadd Ardudwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Mindfulness for people who have had cancer: A pilot research trial

Consent Form

Please initial box

I confirm that I have read and understand the information sheet dated ..... (version .....) for the above study. I have had the opportunity to consider the information, ask questions and have had any questions I asked answered satisfactorily. ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, and without my medical care or legal rights being affected. ☐

I agree to the interview sessions being audiotaped. ☐

I agree to the use of direct quotes from research data and understand that these will be kept anonymous. ☐

I agree to the treatment sessions being videotaped for supervision, research and training purposes. I understand that no participant will be visible on the tapes, and no identifying information about participants will be given when using the tapes. I understand that class recordings will be destroyed after a period of 15 years. ☐

I understand that relevant data collected during the study may be looked at by individuals from the research team, as well as from responsible members of Bangor University and the NHS Trust for the purpose of audit and monitoring, and where it is relevant to my taking part in this research, I give permission for these individuals to have access to my record. I understand that personal data will be identified using only a number code and will be destroyed after a period of 15 years. ☐

I understand that all information will be kept strictly confidential within the limits of the law. ☐

I agree to my GP being informed of my participation in the study. ☐

I agree to be randomly allocated to MBCT-Ca plus Treatment As Usual [TAU] or TAU alone. ☐

I agree to take part in the above study. ☐

_____	_____	_____
Name of Patient	**Date**	**Signature**
_____	_____	_____
Researcher	**Date**	**Signature**

2 COPIES TO BE COMPLETED: One for the participant to keep; one to be held at research site

Appendix 15: Adverse event report form

MBCT-Ca Pilot Trial: Adverse Event Report Form

Patient ID		**Start date**	**End date/ Duration**
Initials	**Participant ID number:**		

Description of event:

……

……

Intensity of event: □ **mild** □ **moderate** □ **severe**

Status/Outcome: □ **resolved** □ **ongoing**

……

……

Expectedness of event:

□ **expected** □ **unexpected** …….

Causality (relationship to MBCT-Ca):

□ **not related** □ **unlikely to be related** □ **possibly related**

□ **probably related** □ **definitely related**

Seriousness: □ **Not serious** □ **Results in death *** □ **Life-threatening***

□ **Requires hospitalization*** □ **Prolongation of existing hospitalization***

□ **Results in persistent or significant disability or incapacity***

□ **Congenital anomaly*** □ **Birth defect***

□ **Other (specify)*** …….

*** Event is considered serious. Within 24 hrs report to the R & D dept.**

Name of Investigator (Please print):

Investigator Signature:

Appendix 16: Participant enrolment letter to GP

Centre for Health Economics and Medicines Evaluation

IMSCaR
Ardudwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
Ardudwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

ADDRESS
ADDRESS
ADDRESS
ADDRESS
ADDRESS

DATE

Cost effectiveness of MBCT-Ca: A pilot pragmatic randomised trial V.1

Dear **DR NAME**

This letter is to let you know that Bangor University is currently conducting a research trial that your patient **PATIENT (DOB)** has enrolled in. The trial is being carried out by researchers at the Centre for Health Economics and Medicines Evaluation (CHEME) in collaboration with the Centre for Mindfulness Research and Practice (CMRP) to investigate the cost effectiveness of Mindfulness Based Cognitive Therapy for cancer (MBCT-Ca) for people who have received active cancer treatment (including surgery, chemotherapy, radiotherapy, hormone therapy or a combination of these). Patients receiving ongoing cancer medication who are considered clinically stable by the recruiting clinician and patients receiving ongoing hormone therapy are also able to participate.

The treatment will be compared against a waitlist condition in which people will be asked to continue with any other treatments they are already receiving. The mindfulness condition is also delivered in addition to treatment as usual and participants are advised therefore to continue with any care they are currently receiving. Participants in the trial will be involved for a period of approximately 7 months. At the end of the trial everyone involved will have the opportunity to choose to receive the treatment.

Mindfulness is the awareness that emerges through actively paying attention to the present moment without judgement. Mindfulness Based Cognitive Therapy for Cancer patients (MBCT-Ca) is a form of group-based treatment combining mindful meditation and cognitive therapy techniques, specifically tailored towards cancer patients.

A range of coping skills may be developed on the MBCT-Ca course, which can be used on an informal everyday basis for managing uncertainty, existential concerns, and fear of recurrence. Many participants who experience low mood, helplessness and hopelessness have also found ways of using their mindfulness practice to relate with kindness and compassion to whatever is difficult for them.

If you have any concerns about **PATIENT NAME** participation in this trial or there are significant changes to **PATIENT NAME** health during the study period that you think we should be aware of please contact the research team directly on 01248 388550; or Email: l.bryning@bangor.ac.uk

If you would like to receive more information about this project or you would like to speak to us further about the study please contact us.

Kind regards,

Lucy Bryning
Tenovus PhD Student

Centre for Health Economics and Medicines Evaluation

IMSCaR
Ardudwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
Ardudwy
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Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

ADDRESS
ADDRESS
ADDRESS
ADDRESS
ADDRESS

DATE

Cost-effeithiolrwydd MBCT-Ca: Hap-arbrawf pragmatig peilot V.1

Annwyl **INSERT DR NAME**,

Bwriad y llythyr hwn yw rhoi gwybod i chi bod Prifysgol Bangor ar hyn o bryd yn cynnal arbrawf ymchwil y mae eich claf, **PATIENT (DOB)** wedi cofrestru arno. Gwneir yr arbrawf gan ymchwilwyr yn y Ganolfan Economeg Iechyd a Gwerthuso Moddion (CHEME) ar y cyd gyda'r Ganolfan Ymchwil ac Ymarfer Ymwybyddiaeth Ofalgar (CMRP) i ymchwilio i gost-effeithiolrwydd Therapi Wybyddol drwy Ymwybyddiaeth Ofalgar ar gyfer canser (MBCT-Ca) i bobl sydd wedi derbyn triniaeth at gancr actif (gan gynnwys llawdriniaeth, cemotherapi, radiotherapi, therapi hormonau neu gyfuniad o'r rhain). Gall cleifion sy'n derbyn meddyginiaethau canser cyfredol, ac sy'n cael eu hystyried yn glinigol abl gan y clinigwr recriwtio, a chleifion sy'n derbyn therapi hormonau cyfredol, gymryd rhan.

Caiff y driniaeth ei chymharu gyda chyflwr rhestr aros, lle gofynnir i bobl barhau gydag unrhyw driniaethau eraill y maent eisoes yn eu derbyn. Caiff y cyflwr ymwybyddiaeth ofalgar ei gyflwyno hefyd ar ben y driniaeth arferol, a chynghorir y rhai sy'n cymryd rhan felly i barhau gydag unrhyw ofal maent yn ei dderbyn ar hyn o bryd. Bydd y rhai sy'n cymryd rhan yn yr arbrawf yn gwneud hynny am gyfnod o tua 7 mis. Ar ddiwedd yr arbrawf bydd pawb sy'n cymryd rhan yn cael cyfle i ddewis derbyn y driniaeth.

Ymwybyddiaeth ofalgar yw'r ymwybyddiaeth sy'n dod i'r amlwg drwy dalu sylw gweithredol i'r foment bresennol heb farn. Mae Therapi Wybyddol drwy Ymwybyddiaeth Ofalgar i gleifion Canser (MBCT-Ca) yn fath o driniaeth mewn grŵp sy'n cyfuno myfyrdod ystyriol a thechnegau therapi wybyddol, wedi eu haddasu'n benodol ar gyfer cleifion canser.

Gellir datblygu amrywiaeth o sgiliau ymdopi ar y cwrs MBCT-Ca, y gellir eu defnyddio ar sail anffurfiol bob dydd er mwyn rheoli ansicrwydd, pryderon ynghylch bodolaeth, a phryder cael pwl arall o hynny. Mae llawer o'r rhai sydd wedi cymryd rhan a oedd yn dioddef o iselder, diymadferthedd ac anobaith, hefyd wedi canfod ffyrdd o ddefnyddio'u hymarfer ymwybyddiaeth ofalgar i ystyried beth bynnag sy'n anodd iddynt gyda charedigrwydd a thrugaredd.

Os oes gennych unrhyw bryderon ynghylch rhan **PATIENT** yn yr arbrawf hwn, neu bod newidiadau sylweddol yn iechyd **PATIENT** yn ystod y cyfnod astudio y credwch y dylem fod yn ymwybodol ohonynt, cysylltwch â'r tîm ymchwil yn uniongyrchol ar 01248 388550; neu e-bostiwch: l.bryning@bangor.ac.uk

Os hoffech dderbyn mwy o wybodaeth am y project hwn, neu os hoffech siarad gyda ni ymhellach am yr astudiaeth, mae pob croeso i chi gysylltu â ni.

Dymuniadau gorau,

Lucy Bryning
Tenovus PhD Student

Appendix 17: NHS REC-West sub-committee favourable ethical approval amendment

Part of the research infrastructure for Wales funded by the National Institute for Social Care and Health Research, Welsh Government.
Yn rhan o seilwaith ymchwil Cymru a ariannir gan y Sefydliad Cenedlaethol ar gyfer Ymchwil Gofal Cymdeithasol ac Iechyd, Llywodraeth Cymru

NISCHR RES Gwasanaeth Moeseg Ymchwil | Research Ethics Service

Pwyllgor Moeseg Ymchwil Gogledd Cymru - Y Orllewin
North Wales Research Ethics Committee - West

Betsi Cadwaladr University Health Board
Ysbyty Gwynedd
Clinical Academic Office
Bangor, Gwynedd
LL57 2PW

Telephone/ Facsimile: 01248 - 384.877
Email: Rossela.Roberts@wales.nhs.uk
Website : www.nres.nhs.uk

Miss Lucy Bryning
Centre for Health Economics and Medicines Evaluations
IMSCaR, Dean Street Building
Bangor, Gwynedd
LL57 1UT l.bryning@bangor.ac.uk

20 September 2013

Dear Miss Bryning,

Study title:	**Exploring the Cost Effectiveness of Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) delivered in addition to treatment as usual (TAU) as compared with TAU alone: a pilot pragmatic RCT**
REC reference:	**12/WA/0095**
IRAS reference:	**94524**
Amendment number:	**AM01**
Amendment date:	**05 September 2013**

The above amendment was reviewed at the meeting of the Sub-Committee held on 19 September 2013.

Ethical opinion

The Sub-Committee reviewed the amendment and noted that the proposed amendment consists of 5 components:
1. Amendment to the inclusion criteria (as recruitment for the trial has been lower than anticipated) to include: patients who completed treatment more than 12 months ago as well as patients receiving on-going medication and considered clinically stable by the recruiting clinician.
2. Amendment to invite MBCT-Ca patients not participating it the trial (e.g. patients who do not meet the inclusion criteria or who are currently part of an existing psychological pathway) into a service evaluation arm of this project and use for research routinely collected outcomes.
3. Amendment to the qualitative interview assessment time point (T3) to include a two-page feedback form to evaluate patient experience and satisfaction of attending the MBCT-Ca course or waiting to receive the intervention.
4. Amendment to include a secondary recruitment strategy to target surgical patients who currently on follow up in hospital clinics. Eligible patients will be identified in a number of ways including accessing records held on CANISC (National Health database of cancer patients in Wales) and surgical clinic
These proposed changes have been reviewed by the trial advisory committee, which includes representation from independent clinical staff, patient and carers, and academic researchers.

On the basis of the submitted documentation the Sub-Committee decided that this amendment raises no ethical issues.
The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Covering Letter		05 September 2013
Notice of Substantial Amendment (non-CTIMPs) (submission 94524/498168/13/324/22607)	AM01	05 September 2013
Protocol	2	28 August 2013
Letter of invitation to participant	3	28 August 2013
Participant Information Sheet	4	28 August 2013
Participant Consent Form	3	04 December 2013
Participant Information Sheet: Service Evaluation	1	28 August 2013
Participant Consent Form: Service Evaluation	1	28 August 2013
Feed-back form	1	28 August 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/WA/0095	**Please quote this number on all correspondence**

Yours sincerely

Rossela Roberts

Mr Derek James Crawford, MBChB, FRCS
Chair
E-mail: rossela.roberts@wales.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

[Pages 3 and 4 redacted]

Appendix 18: End of study participant letter (debrief form)

Centre for Health Economics and Medicines Evaluation

Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

Canolfan Economeg Iechyd a Gwerthuso Meddion

Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Cost effectiveness of MBCT-Ca: A pilot pragmatic randomised trial V.1

End of Study Letter

Thank you for participating in this research study. This study aimed to evaluate the benefits and costs of an intervention developed for people with cancer. Mindfulness Based Cognitive Therapy for Cancer patients (MBCT-Ca) is a form of group based treatment combining mindful meditation and cognitive therapy techniques, specifically tailored towards cancer patients. We are interested in whether MBCT-Ca can help people who have had cancer and have had active cancer treatment (including surgery, chemotherapy, radiotherapy, hormone therapy or a combination of these). This study will offer valuable preliminary evidence for seeking funding for a larger study looking at the costs and benefits of MBCT-Ca and will help inform the planning of local service delivery.

To see whether MBCT-Ca is helpful we needed to compare people in the mindfulness group with a group of people who are not receiving mindfulness at the moment. This group was called treatment-as-usual (TAU) and continued with usual care. At the end of the study period this group should have been invited to attend an upcoming MBCT-Ca course.

What happens next?

If you were in the MBCT-Ca group you will now be invited to attend any optional mindfulness days run by the mindfulness teacher. If you were in the TAU group you will should have been invited to receive a MBCT-Ca course. If you haven't been able to attend a course and would like to, please contact the Centre for Mindfulness Research and Practice (CMRP) on 01248 382498 or find upcoming courses on their website (www.bangor.ac.uk/mindfulness/). Once you have completed the 8-week programme you will also be able to attend optional all day meditation practice sessions for course graduates.

Who can I contact about the study?

Please contact Lucy Bryning on 01248 388550 or email l.bryning@bangor.ac.uk should you have any further questions about this study. If you would like us to send you a report with a summary of the study findings when available please contact us. This research was conducted by the Centre for Health Economics and Medicines Evaluation (CHEME) in collaboration with the Centre for Mindfulness Research and Practice (CMRP), School of Psychology under the supervision of Rebecca Crane who can be contacted on r.crane@bangor.ac.uk and Professor Rhiannon Tudor-Edwards who can be contacted on r.t.edwards@bangor.ac.uk.

Who funded this research?

This research was funded by Tenovus, a leading Wales

Who reviewed this research?

This research has received a favourable review from the School of Psychology Ethics Committee and the NHS North Wales West Research Ethics Committee.

Who do I contact with any concerns or complaints about this study?

If you have any concerns or complaints about any aspects of the way in which you have been approached or treated during the course of this study, or the conduct of individuals conducting this study, then please contact Professor Robert T. Woods, Acting Director of the Institute of Medical and Social Care Research, Bangor University, Bangor, Gwynedd, LL57 2DG or e-mail b.woods@bangor.ac.uk

In addition, participants may contact Hefin Francis, School Manager, School of Psychology, Adeilad Brigantia, Penrallt Road, Gwynedd, LL57 2AS, or email h.francis@bangor.ac.uk

As well as this the normal NHS complaints mechanism is available. If you are harmed due to someone's negligence then you may have grounds for legal action for compensation against Bangor University (in respect of any harm arising out of the participation in the clinical trial) or the NHS (in respect of any harm which has resulted from the clinical procedure being undertaken).

Thank you for participating in this research study.

Appendix 19: BCUHB honorary research contract record for research passport

GIG CYMRU NHS WALES
Bwrdd Iechyd Prifysgol Betsi Cadwaladr University Health Board

Adran Gweithlu & Datblygiad Sefydliadol
Ysbyty Bryn y Neuadd, Llanfairfechan,
Sir Conwy, LL33 0HH

Workforce & Organisational Development Department
Bryn y Neuadd Hospital, Llanfairfechan,
County of Conwy LL33 0HH

Private & Confidential

Miss Lucy Bryning
2 Mason Street
Bangor
Gwynedd
LL57 1DE

Ein cyf / Our ref:
Eich cyf / Your ref:
☎: 01248 682854
Gofynnwch am / Ask for: Emma Thomas
E-bost / Email:
emma.thomas9@wales.nhs.uk
Dyddiad / Date: 19 July 2012

Received 23/7/12

Two signed copies returned on 23/7/12

Dear Miss Bryning

Honorary Research Contract – Betsi Cadwaladr University Local Health Board

I am pleased to offer you an honorary research contract with the Betsi Cadwaladr University Local Health Board.

I enclose three copies of your honorary research contract and would be grateful if you could sign all three copies. Please return two signed copies to Emma Thomas, Workforce Development Officer, in the envelope provided. You should retain the other copy for your records. We will send a copy of the signed contract to your substantive employer/place of study.

The contract, if accepted by you, begins on 23.07.2012 and ends on 01.06.2014, unless terminated earlier in accordance with the clauses in the contract.

We will not reimburse any expenses you incur in the course of your research unless we have agreed to do so by prior arrangement. Similarly, we accept no responsibility for damage to or loss of personal property.

Your Research Passport may be subject to random checks carried out by us within the lifetime of the project. The information contained in your research passport must therefore remain up to date and accurate at all times.

If your circumstances change in relation to your health, criminal record, professional registration or any other aspect that may impact on your suitability to conduct research, or your role in research changes, you must inform your employer through its normal procedures. You must also inform your nominated manager within the Betsi Cadwaladr University Health Board.

Cyfeiriad Gohebiaeth ar gyfer y Cadeirydd a'r Prif Weithredwr / Correspondence address for Chairman and Chief Executive:
Swyddfa'r Gweithredwyr / Executives' Office
Ysbyty Gwynedd, Penrhosgarnedd
Bangor, Gwynedd LL57 2PW
Gwefan: www.pbc.cymru.nhs.uk / **Web:** www.bcu.wales.nhs.uk

Finally, once you have signed and returned two copies of the contract, you should contact the Research & Development Department of the Betsi Cadwaladr University Health Board, who will arrange for you to be issued with an ID badge.

Yours sincerely

EJ Thomas.

Emma J Thomas
Workforce Development Officer

cc: R&D office – Ysbyty Gwynedd, Betsi Cadwaladr University Health Board
HR department – substantive employer/place of study

Appendix 20: Incident report form

Incident Report Form

Type of Report: SAE-related ☐ Risk-related ☐ Uninitiated contact ☐

(with research team, not therapist)

Name of staff involved:

Participant name:

Details of incident: (e.g. type of contact / cause for concern)

Action Taken: (e.g. none taken, discussed with colleague, etc)

Signed: **Date:**

Risk Procedures

Email sent to…… Yes / No

(always 'yes' for risk procedures)

Patient's General Practitioner Contacted: Yes / No (By participant? Yes / No)

Additional procedures for SAEs **(in addition to risk procedures)**

SAE form completed and faxed Yes / No

Appendix 21: Service evaluation project information sheet

Centre for Health Economics and Medicines Evaluation

IMSCaR
Ardudwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

PRIFYSGOL BANGOR UNIVERSITY

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
Ardudwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca): a service evaluation project

Project Information Sheet

We would like to invite you to take part in a project to help us assess one aspect of your care. This information is to help you understand what the project will involve and why we are doing it. Please take time to read it and discuss it with others if you wish. If anything is not clear or you would like more information, please ask. You can take time to decide whether or not you wish to take part.

What is the purpose of the project?

We want to learn more about Mindfulness-Based Cognitive Therapy for Cancer (MBCT-Ca) and about how it might help people with cancer and the people who support them. We are interested in whether MBCT-Ca can help people like you who have had treatment or who have been supporting someone with cancer. We'd also like to know what you thought of the course so that we can improve if for future participants. This project will also help us know if we need to do more research and will help with planning local cancer care.

What will happen to me if I take part?

If you decide to take part in the project we will first talk to you about the project and you will be able to ask questions if you are unsure of anything. If you consent to taking part we will ask you to complete a set of questionnaires both before your first mindfulness class and again after the course has finished. These questionnaires will ask about your health and wellbeing, including brief details of your cancer diagnosis. We will also ask about the types of services you have accessed recently. All of the questions are optional and you can choose to miss any questions that you don't feel comfortable answering. These questionnaires will take no more than 30 minutes to complete.

During the group sessions the mindfulness teacher may be video recorded. This is done so that the quality of the teaching can be checked and so that we can research how conversations take place between teacher and participants during mindfulness classes. We aim to better understand how the teaching process supports participants' learning. We hope that this will influence future training of teachers and so will be of benefit to participants in future classes. The camera will be positioned so that it only captures the image of the teacher, but it will also record the voices of the people in the group. The recordings will be used for research, supervision and training purposes only and the confidentiality of the people in the group will be protected.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. If you have concerns about staying in the project then you can discuss this with us. You are still free to withdraw at any time without giving a reason. Withdrawal will not affect the care you receive outside of this research.

If you decide not to take part then it is important you understand that the group sessions may still be video recorded for the reasons mentioned above.

What will happen to my data?

If you join the project, people from Bangor University or the NHS Trust, with appropriate permission, may look at the data collected to check that the project is being carried out correctly. All data collected will be kept strictly confidential within the limits of the law (Data Protection Act, 1998). You will not be identifiable in any report or publication that comes from this project. We may use direct quotes from the class recordings but these would also be kept anonymous. All data would be kept on password-protected computers or in locked filling cabinets at Bangor University. Data will be stored for 15 years and will be destroyed after this time.

What happens if I change my mind?

You are free to withdraw from the project at any time. You do not have to give a reason. If you withdraw from the project, we would still like to use any information we collected before your withdrawal.

If you begin the MBCT-Ca classes but then decide to stop attending we would still like you to complete the remaining project questionnaires if you can. This is because it will give us a balanced understanding of how people feel about the courses. However you do not have to do so if you do not want to.

You may choose to withdraw from the project at any time and you would have the right to request that your data is not used. All data will be treated in accordance of the Data Protection Act (1998).

Who do I contact about the project?

This project is being conducted by the Centre for Health Economics and Medicines Evaluation (CHEME) in collaboration with the Centre for Mindfulness Research and Practice (CMRP), at the Bangor University. If you have any further questions about this project please contact Lucy Bryning on 01248 388550 or email l.bryning@bangor.ac.uk.

Who do I contact with any concerns or complaints about this project?

While we do not think that taking part in this project will cause any harm, if you have any concerns or complaints about any aspects of this project then please contact Professor Robert T. Woods, Acting Director of the Institute of Medical and Social Care Research, Bangor University, Bangor, Gwynedd, LL57 2DG or e-mail b.woods@bangor.ac.uk. In addition, participants may contact Hefin Francis, School Manager, School of Psychology, Adeilad Brigantia, Penrallt Road, Gwynedd, LL57 2AS, or email h.francis@bangor.ac.uk

The normal NHS complaints procedure is also available. If you are harmed due to someone's negligence then you may have grounds for legal action for compensation against Bangor University (in respect of any harm arising out of the participation in the trial) or the NHS (in respect of any harm which has resulted from the clinical procedure being undertaken).

Who is funding this research?

This research is funded by Tenovus, a leading Wales cancer charity.

tenovus your cancer charity eich elusen canser

Who has reviewed this research?

This research has been reviewed and approved by the School of Psychology Ethics Committee and the NHS North Wales (West) Research Ethics Committee.

Service Evaluation Participant Information Sheet. V1. 28/08/2013

Appendix 22: Service evaluation project informed consent form

Centre for Health Economics and Medicines Evaluation

IMSCaR
Ardudwy
Bangor University
Gwynedd, LL57 2PZ
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

PRIFYSGOL BANGOR UNIVERSITY

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
Ardudwy
Prifysgol Bangor
Gwynedd, LL57 2PZ
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Mindfulness for people who have had cancer: A service evaluation project

Consent Form

Please initial box

I confirm that I have read and understand the information sheet dated 28.08.13 (version 1) for the above study. I have had the opportunity to consider the information, ask questions and have had any questions I asked answered satisfactorily. ☐

I understand that my participation is voluntary and that I am free to withdraw at anytime, without giving any reason, and without my medical care or legal rights being affected. ☐

I agree to the treatment sessions being videotaped for supervision, research and training purposes. I understand that no participant will be visible on the tapes, and no identifying information about participants will be given when using the tapes. I understand that class recordings will be destroyed after a period of 15 years. ☐

I understand that relevant data collected during the study may be looked at by individuals from the research team, as well as from responsible members of Bangor University and the NHS Trust for the purpose of audit and monitoring, and where it is relevant to my taking part in this research, I give permission for these individuals to have access to my record. I understand that personal data will be identified using only a number code and will be destroyed after a period of 15 years. ☐

I understand that all information will be kept strictly confidential within the limits of the law. ☐

I agree to take part in the above study. ☐

Name of Patient	Date	Signature
Researcher	**Date**	**Signature**

ISRCTN23380065
Service Evaluation Consent Form. V1.1 10/01/14

Background Information
About You

Name……

Address……

……Postcode ……..……..

Email Address……

Telephone: ……..

Preferred day/time to be contacted by phone: ……

MAY WE LEAVE MESSAGES ON THIS PHONE? (Please tick one)

Do not leave a message ☐
Leave name and number only ☐
Leave full message ☐

Gender: Female ☐ Male ☐ **Date of Birth:** ___/___/_____

When did you receive your cancer diagnosis? *Approximate date:* ___/___/_____

What was your diagnosis? ……

……

What treatment did you receive following your diagnosis?

Surgery ☐

Approximate date treatment finished: ___/___/_____

Chemotherapy ☐

Approximate date treatment finished: ___/___/_____

Radiotherapy ☐

Approximate date treatment finished: ___/___/_____

Hormone Therapy ☐

Approximate date treatment finished: ___/___/_____ or On-going ☐

Other (please state) ……

……

Approximate date treatment finished: ___/___/_____ *or On-going* ☐

ISRCTN23380065
T0. V1. 10.01.14

Are you currently receiving any other treatment, medication or taking part in any other interventions? **Yes / No**

If Yes, please provide details of any medications you are currently receiving (both prescription and non-prescription) or any other on-going treatments/interventions.

Do you currently do any **meditation** other than the MBCT-Ca course? **Yes / No**

Do you have any qualifications? **Yes / No**

If Yes please could you tell us what your highest qualification is?

PhD, Dr, Dphil	☐	MA, MSc, Mhil, MBA	☐
BA, BSc, Bed	☐	A levels or equivalent	☐
GCSE, O levels, GNVQ	☐	Professional qualification	☐

Other (Please specify) .....

Current employment status:

Full-time	☐	Part-time	☐
Self-employed	☐	Sick leave	☐
Disability	☐	Retired	☐
Unemployed	☐	Other (Please specify).....	

If you are currently working, what is your job title? .....

If you are on sick leave, retired or unemployed, is this because of:

Physical health	☐
Mental health	☐
Both physical and mental health	☐

Other reason (Please specify) .....

If you are not working, please could you tell us how are you supporting yourself now?.....

Are you?

Single	☐	Cohabiting	☐
Married	☐	Separated	☐
Divorced	☐	Widowed	☐

Do you have any children? Yes / No

If Yes how many? .....

Who do you live with? .....

Please indicate your current **household income** from the following options:

< £15,000	☐	£15,000 - £19,999	☐
£20,000 - £29,999	☐	£30,000 - £39,999	☐
£40,000 - £49,999	☐	£50,000 - £59,999	☐
£60,000 - £69,999	☐	£70,000 - £99,999	☐
£100,000 +	☐	Prefer not to say	☐

What is your ethnic background? .....

What is your first language? .....

Questionnaire 1

By placing a tick in **one** box in **each** group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

Self-Care

I have no problems with self-care ☐

I have some problems washing or dressing myself ☐

I am unable to wash or dress myself ☐

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ☐

I have some problems with performing my usual activities ☐

I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety/Depression

I am not anxious or depressed ☐

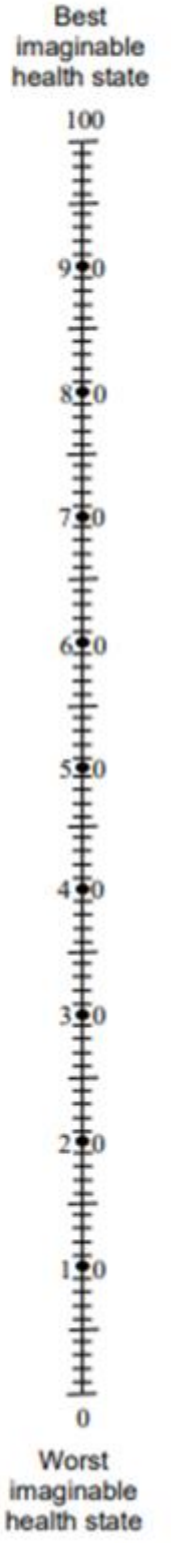
I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



For office use only

ISRCTN23380065
EQ-5D

Questionnaire 2

By placing a tick (✓) in ONE box in EACH group below, please indicate which statement best describes your quality of life at the moment.

	Tick one box only in each section
1. Feeling settled and secure	
I am able to feel settled and secure in **all** areas of my life	☐
I am able to feel settled and secure in **many** areas of my life	☐
I am able to feel settled and secure in **a few** areas of my life	☐
I am **unable** to feel settled and secure in **any** areas of my life	☐
2. Love, friendship and support	
I can have **a lot** of love, friendship and support	☐
I can have **quite a lot** of love, friendship and support	☐
I can have **a little** love, friendship and support	☐
I **cannot** have **any** love, friendship and support	☐
3. Being independent	
I am able to be **completely** independent	☐
I am able to be independent in **many** things	☐
I am able to be independent in a **few** things	☐
I am **unable** to be at all independent	☐
4. Achievement and progress	
I can achieve and progress in **all** aspects of my life	☐
I can achieve and progress in **many** aspects of my life	☐
I can achieve and progress in **a few** aspects of my life	☐
I **cannot** achieve and progress in **any** aspects of my life	☐
5. Enjoyment and pleasure	
I can have **a lot** of the enjoyment and pleasure	☐
I can have **quite a lot** of the enjoyment and pleasure	☐
I can have **a little** enjoyment and pleasure	☐
I **cannot** have **any** enjoyment and pleasure	☐

ISRCTN23380065
ICECAP- A

Questionnaire 3

Please think about how often/how much each of the statements below applies to you.
Please tick **one** *box in* **each** *row.*

1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or suitcase?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

2. Do you have any trouble taking a long walk?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

3. Do you have any trouble taking a short walk outside the house?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

4. Do you need to stay in bed or a chair during the day?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

5. Do you need help with eating, dressing, washing yourself or using the toilet?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

During the past week:

6. Were you limited in doing either your work or other daily activities?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

During the past week:

7. Were you limited in pursuing your hobbies or other leisure time activities?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

8. Were you short of breath?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

9. Have you had pain?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

10. Did you need to rest?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

11. Have you have trouble sleeping?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

12. Have you felt weak?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

13. Have you lacked appetite?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

14. Have you felt nauseated?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

During the past week:

15. Have you vomited?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

16. Have you been constipated?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

17. Have you had diarrhea?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

18. Were you tired?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

19. Did pain interfere with your daily activities?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television??

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

21. Did you feel tense?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

22. Did you worry?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

During the past week:

23. Did you feel irritable?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

24. Did you feel depressed?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

25. Have you had difficulty remembering things?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

26. Has your physical condition or medical treatment interfered with your family life?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

27. Has your physical condition or medical treatment interfered with your social

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

28. Has your physical condition or medical treatment caused you financial difficulties?

Not at all	A little	Quite a bit	Very Much
☐	☐	☐	☐

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1 2 3 4 5 6 7

Very poor Excellent

30. How would you rate your overall quality of life during the past week?

1 2 3 4 5 6 7

Very poor Excellent

Questionnaire 4

Please read each item and tick the box for the reply which comes closest to how you have been feeling in the past week. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than long thought-out responses. *Please tick* **one** *box for* **each** *item.*

I feel tense or 'wound up':

- Most of the time ☐
- A lot of the time ☐
- From time to time, occasionally ☐
- Not at all ☐

I still enjoy the things I used to enjoy:

- Definitely as much ☐
- Not quite as much ☐
- Only a little ☐
- Hardly at all ☐

I get a sort of frightened feeling as if something awful is about to happen:

- Very definitely and quite badly ☐
- Yes, but not too bad ☐
- A little, but it doesn't worry me ☐
- Not at all ☐

I can laugh and see the funny side of things:

- As much as I always could ☐
- Not quite as much now ☐
- Definitely not so much now ☐
- Not at all ☐

Worrying thoughts go through my mind:

- A great deal of the time ☐
- A lot of the time ☐
- From time to time, but not too often ☐
- Only occasionally ☐

I feel cheerful:

- Not at all ☐
- Not often ☐
- Sometimes ☐
- Most of the time ☐

I can sit at ease and feel relaxed:

- Definitely ☐
- Usually ☐
- Not often ☐
- Not at all ☐

I feel as if I am slowed down:

- Nearly all the time ☐
- Very often ☐
- Sometimes ☐
- Not at all ☐

I get a sort of frightened feeling like 'butterflies' in the stomach:

- Not at all ☐
- Occasionally ☐
- Quite often ☐
- Very often ☐

ISRCTN23380065
Hospital & Anxiety Depression Scale (HADS)

I have lost interest in my appearance:

- Definitely ☐
- I don't take as much care as I should ☐
- I may not take quite as much care ☐
- I take just as much care as ever ☐

I feel restless as if I have to be on the move:

- Very much indeed ☐
- Quite a lot ☐
- Not very much ☐
- Not at all ☐

I look forward with enjoyment to things:

- As much as I ever did ☐
- Rather less than I used to ☐
- Definitely less than I used to ☐
- Hardly at all ☐

I get sudden feelings of panic:

- Very often indeed ☐
- Quite often ☐
- Not very often ☐
- Not at all ☐

I can enjoy a good book or radio or TV programme:

- Often ☐
- Sometimes ☐
- Not often ☐
- Very seldom ☐

Questionnaire 5

Please read each statement carefully before answering. For each question please circle the number between 1 and 5 that best indicates how often you behave in the stated manner

1. When I fail at something important to me I become consumed by feelings of inadequacy.

1 2 3 4 5

Almost never Almost always

2. I try to be understanding and patient towards those aspects of my personality I don't like.

1 2 3 4 5

Almost never Almost always

3. When something painful happens I try to take a balanced view of the situation.

1 2 3 4 5

Almost never Almost always

4. When I'm feeling down, I tend to feel like most other people are probably happier than I am.

1 2 3 4 5

Almost never Almost always

5. I try to see my failings as part of the human condition.

1 2 3 4 5

Almost never Almost always

6. When I'm going through a very hard time, I give myself the caring and tenderness I need.

1 2 3 4 5

Almost never Almost always

7. When something upsets me I try to keep my emotions in balance.

1 2 3 4 5

Almost never Almost always

8. When I fail at something that's important to me, I tend to feel alone in my failure.

1 2 3 4 5

Almost never Almost always

9. When I'm feeling down I tend to obsess and fixate on everything that's wrong.

1 2 3 4 5

Almost never Almost always

10. When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people.

1 2 3 4 5

Almost never Almost always

11. I'm disapproving and judgmental about my own flaws and inadequacies.

1 2 3 4 5

Almost never Almost always

12. I'm intolerant and impatient towards those aspects of my personality I don't like.

1 2 3 4 5

Almost never Almost always

ISRCTN23380065
Self compassion scale – Short Form (SCS-SF)

Questionnaire 6

Below is a collection of statements about your everyday experience. Please tick **one** box in **each** row to indicate how frequently or infrequently you have had each experience in the last month (or other agreed time period). Please answer according to what really reflects your experience rather than what you think your experience should be.

1. I'm good at finding the words to describe my feelings.

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

2. I can easily put my beliefs, opinions, and expectations into words

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

3. I watch my feelings without getting carried away by them

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

4. I tell myself that I shouldn't be feeling the way I'm feeling

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

5. it's hard for me to find the words to describe what I'm thinking

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

6. I pay attention to physical experiences, such as the wind in my hair or sun on my face

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

7. I make judgments about whether my thoughts are good or bad.

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

8. I find it difficult to stay focused on what's happening in the present moment

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

9. when I have distressing thoughts or images, I don't let myself be carried away by them

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

10. generally, I pay attention to sounds, such as clocks ticking, birds chirping, or cars passing

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

11. when I feel something in my body, it's hard for me to find the right words to describe it

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

12. it seems I am "running on automatic" without much awareness of what I'm doing

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

ISRCTN23380065
5 Facet Questionnaire: short form (FFMQ-SF)

13. when I have distressing thoughts or images, I feel calm soon after.

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

14. I tell myself I shouldn't be thinking the way I'm thinking

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

15. I notice the smells and aromas of things

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

16. Even when I'm feeling terribly upset, I can find a way to put it into words

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

17. I rush through activities without being really attentive to them

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

18. Usually when I have distressing thoughts or images I can just notice them without reacting

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

19. I think some of my emotions are bad or inappropriate and I shouldn't feel them

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

20. I notice visual elements in art or nature, such as colours, shapes, textures, or patterns of light and shadow

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

21. when I have distressing thoughts or images, I just notice them and let them go

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

22. I do jobs or tasks automatically without being aware of what I'm doing

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

23. I find myself doing things without paying attention

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

24. I disapprove of myself when I have illogical ideas

Never or very rarely true	Not often true	Sometimes true Sometimes not true	Often true	Very often or always true
☐	☐	☐	☐	☐

ISRCTN23380065
5 Facet Questionnaire: short form (FFMQ-SF)

Questionnaire 7

Please read each statement and tick the box for the reply which comes closest to how you have been feeling in the last two weeks. *Please tick* **one** *box for* **each** *item.*

During the last two weeks:

1. I have felt cheerful and in good spirits

All of the time	Most of the time	More than half the time	Less than half of the time	Some of the time	At no time
☐	☐	☐	☐	☐	☐

2. I have felt calm and relaxed

All of the time	Most of the time	More than half the time	Less than half of the time	Some of the time	At no time
☐	☐	☐	☐	☐	☐

3. I have felt active and vigorous

All of the time	Most of the time	More than half the time	Less than half of the time	Some of the time	At no time
☐	☐	☐	☐	☐	☐

4. I woke up feeling fresh and rested

All of the time	Most of the time	More than half the time	Less than half of the time	Some of the time	At no time
☐	☐	☐	☐	☐	☐

5. My daily life has been filled with things that interest me

All of the time	Most of the time	More than half the time	Less than half of the time	Some of the time	At no time
☐	☐	☐	☐	☐	☐

Service Utilisation Questionnaire

Mindfulness study

We would like to improve the services available to you. It would be helpful if you could tell us how many times **in the last three months** you have had contact with the following list of health, social and voluntary service professionals. We are also interested in *where* the service was provided: at home, at the GP surgery, at hospital, at the health clinic or at another place.

Community health and social services

1. In the last 3 months have you used any of the following services?

Note: please tick the 'no' box if you have not used the service

Service	No	Yes	No. of home visits	No. clinic or office visits	Average duration of contact (minutes)
GP	☐	☐	☐☐	☐☐	☐☐☐
Practice nurse (at GP surgery)	☐	☐	☐☐	☐☐	☐☐☐
Community/District Nurse	☐	☐	☐☐	☐☐	☐☐☐
Community psychiatric / Community Mental Health Nurse	☐	☐	☐☐	☐☐	☐☐☐
Health Visitor	☐	☐	☐☐	☐☐	☐☐☐
Social worker or care manager	☐	☐	☐☐	☐☐	☐☐☐
Mediation service (e.g. Relate)	☐	☐	☐☐	☐☐	☐☐☐
Counsellor	☐	☐	☐☐	☐☐	☐☐☐
Other - *please describe in box*	☐	☐	☐☐	☐☐	☐☐☐

Service Utilisation Questionnaire
Mindfulness study

Hospital services

2. In the last 3 months have you used any of the following hospital services?

Note: please tick the 'no' box if you have not used the service

Service	No	Yes	Number of visits	Reason for using service (condition, specialty)	
Accident & Emergency Department (A&E)	☐	☐	☐☐		
Did you travel by ambulance?	☐	☐	☐☐		Type of consultant/ department visited
Outpatient Department Attendance	☐	☐	☐☐		
Inpatient admission	☐	☐	☐☐		Number of Inpatient nights ☐☐
Other - *please describe in box*	☐	☐			

Voluntary services

3. In the last 3 months have you used any voluntary services?

Please describe in the box

ISRCTN23380065
T0. V1. 10.01.14

Service Utilisation Questionnaire

Mindfulness study

4. In the last **three months** have you experienced any health problems including depression?

YES ☐ NO ☐

If yes, did you see a healthcare professional about your health problem? YES ☐ NO ☐

If yes, who did you see? .....

Did you receive treatment such as medication/therapy? YES ☐ NO ☐

If yes, what was the treatment? .....

5. Have you given up or cut down on work in the last three months?

Yes, given up work ☐

Yes, take time off ☐

Yes, cut down ☐

No ☐

If yes, please estimate how much income you have lost over the last three months as a result of this? **£**..... Gross ☐ Net ☐

Thank you for completing these questionnaires.

Your help is very much appreciated

Box for Admin Use Only

Participant Identity Number: ☐☐☐☐☐☐☐☐☐☐☐☐

Which assessment is this? *Please tick* **one** *box only.*

Baseline Assessment [X]

1st Follow-up ☐

2nd Follow-up ☐

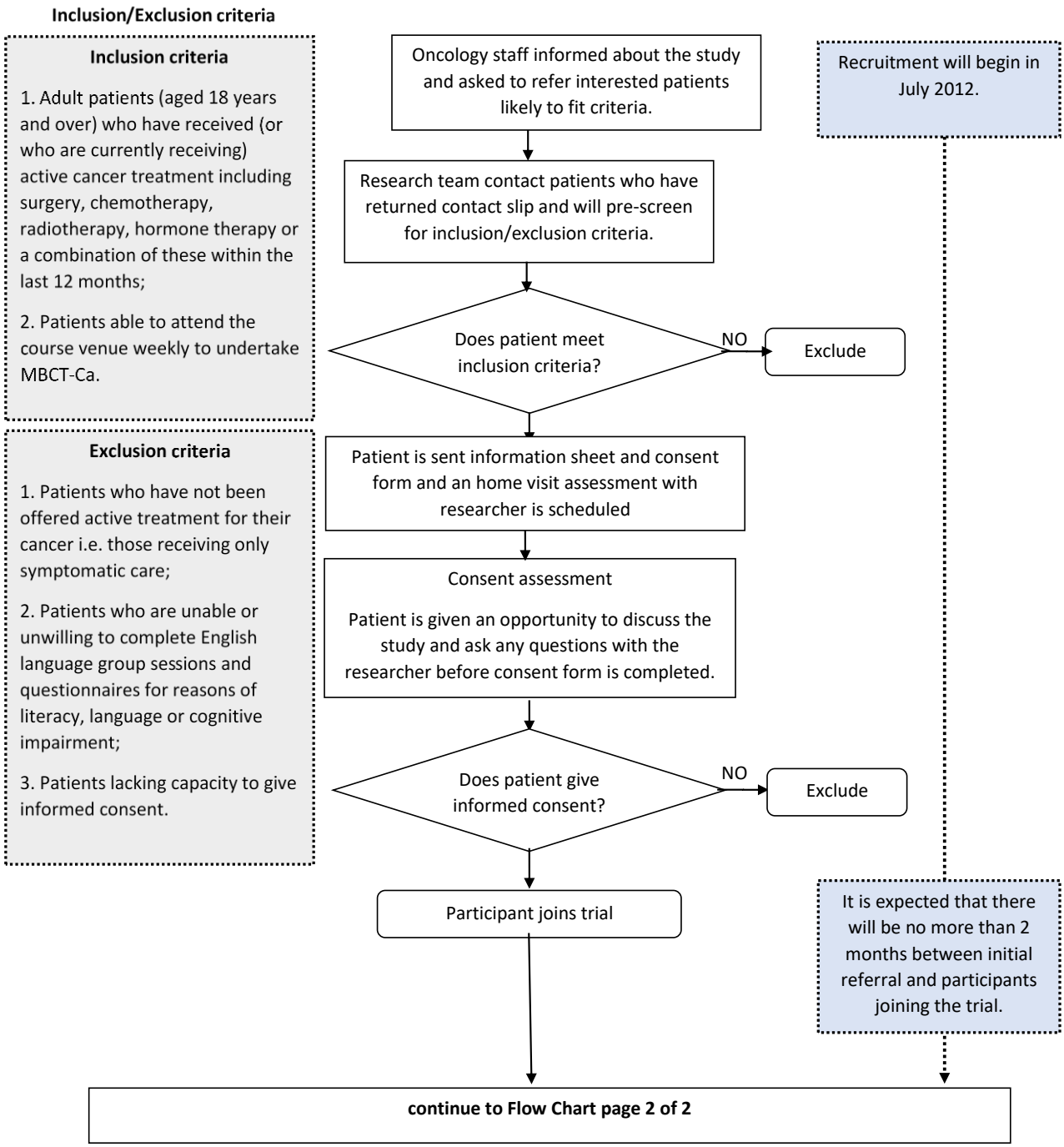
Researcher _____

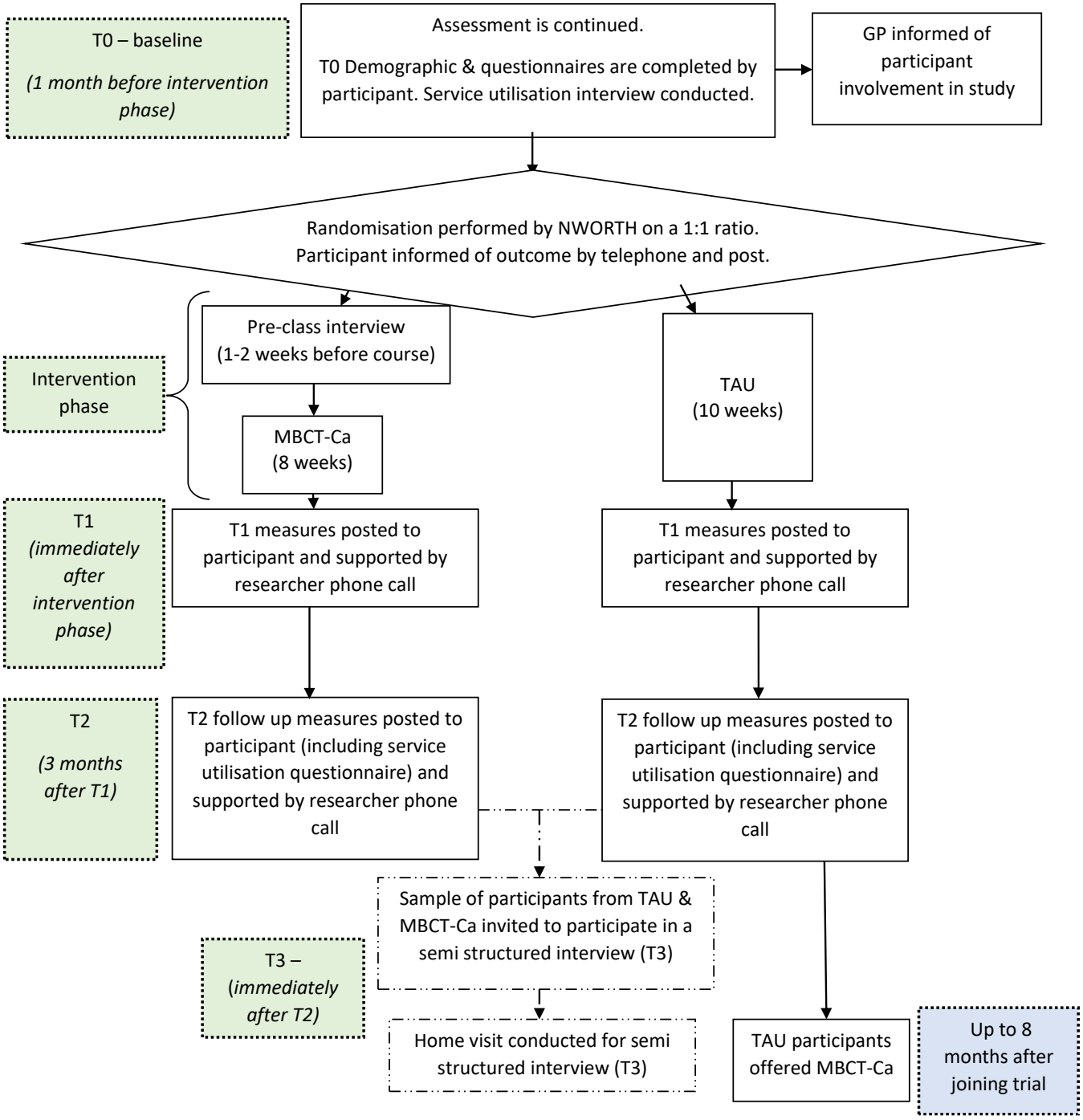
Date sent: ☐☐/☐☐/☐☐☐☐ (d d / m m / y y y y)

Received by:

ISRCTN23380065
T0. V1. 10.01.14

Appendix 24: Randomised Feasibility Trial Flow Chart




T0 – baseline
(1 month before intervention phase)
Assessment is continued.
T0 Demographic & questionnaires are completed by participant. Service utilisation interview conducted.
GP informed of participant involvement in study
Randomisation performed by NWORTH on a 1:1 ratio.
Participant informed of outcome by telephone and post.
Intervention phase
Pre-class interview
(1-2 weeks before course)
MBCT-Ca
(8 weeks)
TAU
(10 weeks)
T1
(immediately after intervention phase)
T1 measures posted to participant and supported by researcher phone call
T1 measures posted to participant and supported by researcher phone call
T2
(3 months after T1)
T2 follow up measures posted to participant (including service utilisation questionnaire) and supported by researcher phone call
T2 follow up measures posted to participant (including service utilisation questionnaire) and supported by researcher phone call
Sample of participants from TAU & MBCT-Ca invited to participate in a semi structured interview (T3)
T3 – (immediately after T2)
Home visit conducted for semi structured interview (T3)
TAU participants offered MBCT-Ca
Up to 8 months after joining trial

Appendix 25: Unit costs table

All costs reported in 2018/19 cost year, £GBP Pounds Sterling

	Community based service use	Cost	Unit	Additional notes	Source	Page	Section
1.	Chiropody / Podiatrist (Band 5)	£34	Per working hour	Costed as 30-minute home visit	(Curtis & Burns, 2019)	111-113	9
2.	Counsellor (Band 6)	£45	Per working hour	Costed as one hour clinic visits	(Curtis & Burns, 2019)	111-113	9
3.	Dentist	£133	Per hour of patient contact	Costed as 30-minute appointments	(Curtis & Burns, 2019)	124	10.6
4.	Dietician	£90	Per visit		(NHS England, 2019)	AHP (service code)	A03 (currency code)
5.	District nurse	£67	Per hour of patient related work	Costed as 30-minute home visit	Inflated from 2015 to 2019 (Curtis & Burns, 2015)	169	
6.	Exercise on referral scheme	£29.10	Per session		Inflated from 2008 to 2019 (Edwards, Linck, et al., 2013)	P8	Table 4
7.	GP	£39	Per appointment (9.22 minutes)		(Curtis & Burns, 2019)	120	10.3b
8.	GP e-consultation	£37.60	Per consultation		(Curtis & Burns, 2019)	122	10.4
9.	GP home visit / GP out of hours	£73.09	Per visit		Inflated from 2014 to 2019 (Goodman et al., 2017)	171	Table 35
10.	Occupational health therapist (Band 5)	£34	Per working hour	Costed as one hour home visit	(Curtis & Burns, 2019)	111-113	9
11.	Occupational therapy (one-to-one)	£97	Per visit		(Curtis & Burns, 2019)	P.82	7.1

12.	Optician	£30.71	Per appointment		(Department of Health & Social Care, 2020; Department of Health, 2015)	2	N/A
13.	Phlebotomist (at GP surgery) (Band 2)	£3.42	Per appointment		Inflated from 2014 to 2019 (National Institute for Health and Care Excellence (NICE), 2015)	P.8	Table 4
14.	Physiotherapist (Band 5)	£34	Per working hour	Costed as one hour home visit	(Curtis & Burns, 2019)	111-113	9
15.	Physiotherapist (one-to-one)	£54	Per visit		(Curtis & Burns, 2019)	P.82	7.1
16.	Practice nurse	£42	Per hour	Costed as 20 minute clinic appointment	(Curtis & Burns, 2019)	118	10.2
17.	Social worker	£51	Per hour	Costed as one hour appointment	(Curtis & Burns, 2019)	130	11.1
18.	Reflexology	£65	Per hour	Costed as one hour visit	(Cancer Research UK, 2019)	N/A	N/A
19.	Acupuncturist	£91	Per procedure		National tariff payment system (2018 /19) (NHS Improvement, 2019)		AB23Z
	Hospital resource use	Cost	Unit		Source	Service code	Currency code
20.	Accident and Emergency	£168	Per visit		National tariff payment system (2018 /19) (NHS Improvement, 2019)	180	
21.	Ambulance services	£125	Per average unit		(Curtis & Burns, 2019)	P.82	7.1
22.	Non-elective inpatient stays (short stays)	£631	Per episode		(Curtis & Burns, 2019)	P.82	7.1
23.	Non-elective inpatient stays (long stays)	£3,053	Per episode		(Curtis & Burns, 2019)	P.82	7.1

24.	Medical oncology follow-up outpatient attendance (multi-professional)	£116	Per average unit		National tariff payment system (2018 /19) (NHS Improvement, 2019)	370	WF02A
25.	General surgery (Multi professional - First attendance including 30% uplift)	£206	Per appointment		National tariff payment system (2018 /19) (NHS Improvement, 2019)	100	N/A
	Other services	Cost	Unit	Notes	Source		
26.	Mediation services	£910	Per mediation case	Average mediation time 12 months, unit cost to be prorata for time period.	Inflated from 2007 to 2019 (National Audit Office, 2007)	P.10	Table 2
27.	Chiropractor (Other Therapist, Adult, One to One)	£83	Per average unit		National tariff payment system (2018 /19) (NHS Improvement, 2019)		A01A1
28.	Homeopathy(Other Therapist, Adult, One to One)	£83	Per average unit		National tariff payment system (2018 /19) (NHS Improvement, 2019)		A01A1
29.	Hospice day attendance	£70	Per session	Costed as session lasting 4.8 hours.	(Curtis & Burns, 2019)	P.66	5.3

Appendix 26: End of study participant letter (feedback form)

Centre for Health Economics and Medicines Evaluation

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PRIFYSGOL BANGOR UNIVERSITY

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
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April 2014

Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca) study.

Thank you for your participation in this study.

We would like to ask you about your experience of taking part in this research and attending the Mindfulness course if you have done so. I have enclosed is a feedback form for you to complete and return in the freepost envelope provided. If you would like to take part in an optional telephone interview to tell us more about your experience you can indicate this on the form or contact us on 01248 388550.

End of Study Information

This study aimed to evaluate the benefits and costs of an intervention developed for people with cancer. Mindfulness Based Cognitive Therapy for Cancer patients (MBCT-Ca) is a form of group based treatment combining mindful meditation and cognitive therapy techniques, specifically tailored towards cancer patients. We are interested in whether MBCT-Ca can help people who have cancer and have had active cancer treatment (including surgery, chemotherapy, radiotherapy, hormone therapy or a combination of these). This study will offer valuable preliminary evidence for seeking funding for a larger study looking at the costs and benefits of MBCT-Ca and will help inform the planning of local service delivery.

To see whether MBCT-Ca is helpful we needed to compare people in the mindfulness group with a group of people who are not receiving mindfulness at the moment. This group was called treatment-as-usual (TAU) and continued with usual care and will now have the opportunity to receive MBCT-Ca during the next course.

What happens next?

If you were in the MBCT-Ca group you will now be invited to attend optional mindfulness days by the mindfulness teacher. If you were in the TAU group you will now be invited to receive the MBCT-Ca course and will also be able to attend additional optional mindfulness days after completing the 8-week programme.

Who can I contact about the study?

Please contact Lucy Bryning on 01248 388550 or email l.bryning@bangor.ac.uk should you have any further questions about this study. This research is being conducted by the Centre for Health Economics and Medicines Evaluation (CHEME) in collaboration with the Centre for Mindfulness Research and Practice (CMRP), School of Psychology under the supervision of Rebecca Crane who can be contacted on r.crane@bangor.ac.uk and Professor Rhiannon Tudor Edwards who can be contacted on r.t.edwards@bangor.ac.uk.

Who funded this research?

tenovus your cancer charity

This research was funded by Tenovus, a leading Wales cancer charity.

Who reviewed this research?

This research has received a favourable review from the School of Psychology Ethics Committee and the NHS North Wales West Research Ethics Committee.

Who do I contact with any concerns or complaints about this study?

If you have any concerns or complaints about any aspects of the way in which you have been approached or treated during the course of this study, or the conduct of individuals conducting this study, then please contact Professor Robert T. Woods, Acting Director of the Institute of Medical and Social Care Research, Bangor University, Bangor, Gwynedd, LL57 2DG or e-mail b.woods@bangor.ac.uk - In addition, participants may contact Hefin Francis, School Manager, School of Psychology, Adeilad Brigantia, Penrallt Road, Gwynedd, LL57 2AS, or email h.francis@bangor.ac.uk

As well as this the normal NHS complaints mechanism is available. If you are harmed due to someone's negligence then you may have grounds for legal action for compensation against Bangor University (in respect of any harm arising out of the participation in the clinical trial) or the NHS (in respect of any harm which has resulted from the clinical procedure being undertaken).

Thank you again for taking part in this research study, your help is greatly appreciated.

MBCT - Ca Evaluation Questionnaire. V1. 18/03/13

Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca)
Research Evaluation

Instructions: For questions 1 – 3, **please circle your response or tick the box** that best indicates how you feel about participating in this research project.

1. **Overall, did you find taking part in this research a positive experience?** Yes ☐ No ☐

2. **Would you recommend taking part in this research to future participants?**

Definitely not	Unlikely	Possibly	Probably	Definitely
☐	☐	☐	☐	☐

3. **Do you want the opportunity to feedback your experience by taking part in a short telephone interview** Yes ☐ No ☐

   If yes, please provide details in the box below telling us when you would like us to contact you and the best telephone number.

   Time/Day: **Telephone no:**

4. **Please tell us what you thought of *filling in the questionnaires* during the research?**

5. **Please tell us what you thought of *being randomly assigned* to either receive the mindfulness course or the control group (where you had to wait to receive the mindfulness course)?**

6. **Do you have any other comments? If so please detail below.**

If you have now attended the mindfulness course

please complete the course evaluation overleaf.

Mindfulness Based Cognitive Therapy for Cancer (MBCT-Ca)
Course Evaluation

Instructions: For questions 7 – 11, **please circle the number or tick the box** that best indicates how you feel about the MBCT-Ca course.

7. **How much did you benefit from the mindfulness classes?**

0	1	2	3	4	5	6	7	8	9	10
Not at all										Very much

8. **Would you recommend this MBCT-Ca course to future participants?**

Definitely not	Unlikely	Possibly	Probably	Definitely
☐	☐	☐	☐	☐

9. **To what extent do you intend to continue practicing mindfulness?**

Never	Occasionally	Once a month	Once a week	Several times a week	Daily
☐	☐	☐	☐	☐	☐

10. **Although you did not pay for the mindfulness classes during this research study, would you have been willing to pay for this 8 week MBCT-Ca course (i.e. classes, workbook, CDs)? If so, how much would you be willing to pay for the whole course?**

Not at all ☐	£50 - £99.99 ☐	£150 – £199.99 ☐	£250 - £299.99 ☐	£350 - £499.99 ☐
£0 - £49.99 ☐	£100 - £149.99 ☐	£200 – £249.99 ☐	£300 - £349.99 ☐	£500 + ☐

11. **Please indicate your current household income (gross) from the following options:**

Less than £15,000 ☐	£30,000 - £39,999 ☐	£60,000 - £69,999 ☐
£15,000 - £19,999 ☐	£40,000 - £49,999 ☐	£70,000 - £99,999 ☐
£20,000 - £29,999 ☐	£50,000 - £59,999 ☐	More than £100,000 ☐
		Prefer not to say ☐

12. **Did you have to pay any extra costs e.g. travel, caring for a family member and childcare due to your participation in the mindfulness classes? If so, please tell us how much per week?**

13. **Please write any additional comments about your experience of the MBCT-Ca course.**

Appendix 27: Topic guide and semi-structured interview schedule

Centre for Health Economics and Medicines Evaluation

IMSCaR
Dean Street
Bangor University
Gwynedd, LL57 1UT
Tel: 01248 388550
Contact: l.bryning@bangor.ac.uk

PRIFYSGOL BANGOR UNIVERSITY

Canolfan Economeg Iechyd a Gwerthuso Moddion

SYMaCh
Stryd y Deon
Prifysgol Bangor
Gwynedd, LL57 1UT
Ffôn: 01248 388550
Cyswllt: l.bryning@bangor.ac.uk

Cost effectiveness of MBCT-Ca: A pilot pragmatic randomised trial V.1

Semi-Structure Interview Schedule

- Introduction to researcher
- Recap on research study
- Explanation of interview procedures including audio recording
- Confirm consent to continue and remind participants of their right to withdrawn and to omit to answer any questions
- Participant given the opportunity to ask any questions

Interview questions

- Tell me about your experience of participating in this research study (e.g. completing questionnaires)?
- How did you feel about being randomised to receive the _____ condition?
- Tell me about your experience of receiving the _____ condition?
- Has there been any change to your quality of life since joining this study?

Participants ID ☐ 1

Interview Schedule. V1. 26/3/12

Appendix 28: Non-randomised matched cohort study Bangor University Schools Ethical amendment approval confirmation

Wednesday, 14 October 2015 22:24:55 British Summer Time

Subject: Ethics application 11284-A13520
Date: Thursday, 8 October 2015 11:08:20 British Summer Time
From: Ethics Shared Mailbox
To: Kevanne Louise Sanger
CC: Dusana Dorjee, Lucy Bryning, Rhiannon Tudor Edwards, Guillaume Thierry, Rebekah Jane Kaunhoven

Hi Kevanne,

I am writing to let you know that I have now granted approval to the amendments to your Ethics application.

Kind regards,

Becky

Rebecca Ryan
Administrative Assistant

Coleg Gwyddorau Iechyd a Ymddygiad
Prifysgol Bangor, Bangor, Gwynedd, LL57 2UW
Ffôn: 01248 388423

College of Health and Behavioural Sciences
Bangor University, Bangor, Gwynedd, LL57 2UW
Tel: 01248 388423

Appendix 29: EQ-5D-5L

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

- I have no problems in walking about ❑
- I have slight problems in walking about ❑
- I have moderate problems in walking about ❑
- I have severe problems in walking about ❑
- I am unable to walk about ❑

SELF-CARE

- I have no problems washing or dressing myself ❑
- I have slight problems washing or dressing myself ❑
- I have moderate problems washing or dressing myself ❑
- I have severe problems washing or dressing myself ❑
- I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

- I have no problems doing my usual activities ❑
- I have slight problems doing my usual activities ❑
- I have moderate problems doing my usual activities ❑
- I have severe problems doing my usual activities ❑
- I am unable to do my usual activities ❑

PAIN / DISCOMFORT

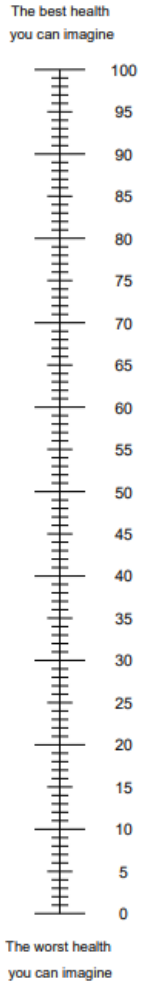
- I have no pain or discomfort ❑
- I have slight pain or discomfort ❑
- I have moderate pain or discomfort ❑
- I have severe pain or discomfort ❑
- I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

- I am not anxious or depressed ❑
- I am slightly anxious or depressed ❑
- I am moderately anxious or depressed ❑
- I am severely anxious or depressed ❑
- I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



Appendix 30: General Health Questionnaire (GHQ-12)

Have you recently…?

1. Been able to concentrate on whatever you are doing	Better than usual	Same as usual	Less than usual	Much less than usual
2. Lost much sleep over worry	Not at all	No more than usual	Rather more than usual	Much more than usual
3. Felt that you are playing a useful part in things	More so than usual	Same as usual	Less than usual	Much less than usual
4. Felt capable of making decisions about things	More so than usual	Same as usual	Less than usual	Much less than usual
5. Felt constantly under strain	Not at all	No more than usual	Rather more than usual	Much more than usual
6. Felt you couldn't overcome your difficulties	Not at all	No more than usual	Rather more than usual	Much more than usual
7. Been able to enjoy your normal day to day activities	More so than usual	Same as usual	Less than usual	Much less than usual
8. Been able to face up to your problems	More so than usual	Same as usual	Less able than usual	Much less able than usual
9. Been feeling unhappy and depressed	Not at all	No more than usual	Rather more than usual	Much more than usual
10. Been losing confidence in yourself	Not at all	No more than usual	Rather more than usual	Much more than usual
11. Been thinking of yourself as a worthless person	Not at all	No more than usual	Rather more than usual	Much more than usual
12. Been feeling reasonably happy, all things considered	More so than usual	About same as usual	Less able than usual	Much less able than usual

Appendix 31: Resource use questions extract from socio-demographic form

Socio-demographics Form for Participants

Project Title: *Neuro-cognitive effects of mindfulness training in secondary school pupils*

Participant ID:	

Question 1: Age _____ **Question 2: Gender (circle one)** Male Female

[Questions 3 – 6 retracted]

Question 7: In the last academic year (Sept 2013 – July 2014), please state the number of days unplanned absences from school that have you had e.g. absence due to sickness? ☐

Question 8: How many visits to your GP have you made in the last 3-months? ☐

Question 8b: Of the GP visits mentioned above, please state the number that related to:

Stress	
Sleep	
Anxiety	
Other	
If you mentioned any GP visits due to other reasons, please provide details below:	