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It's Not a Linear Process: Psychological Wellbeing and Quality of Life in Multiple Sclerosis

Martin-Forbes, Pam

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IT'S NOT A LINEAR PROCESS:

PSYCHOLOGICAL WELLBEING AND QUALITY OF LIFE IN MULTIPLE SCLEROSIS

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North Wales Clinical Psychology Programme

MAY 2021

Submitted in partial fulfilment of the requirements for the degree of

Doctor of Clinical Psychology

Declarations

I hereby declare that this thesis is the result 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.

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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.

Pam Martin-Forbes

31/05/2022

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"It is good to have an end to journey toward; but it is the journey that matters, in the end"

The Left Hand of Darkness, Ursula K. Le Guin,

The title of this thesis - it's not a linear process – was said by a participant when describing their MS journey. In a much smaller way, it also encapsulates the experience of my thesis journey, as well as my trainee journey. It's been a bit like riding an old wooden rollercoaster: one minute, you're waving your hands in the air (like you just don't care), wearing an inane grin as your fillings threaten to rattle clean out of your cranium: all is well, because you've totally got this. The next, you've hurtled into a jarring dip, your outstretched hands have catapulted back down to smack you full in the face (true story), and you're borderline travel-sick. Fortunately, I've had the company of some wonderful people during these peaks and troughs, and discovered yet again that there's something of a buzz about a full-on journey with an endpoint. So strap yourselves in; here come the thank yous.

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Thesis Summary

This thesis broadly concerns quality of life (QoL) and wellbeing in people with a diagnosis of Multiple Sclerosis (MS). It begins with a systematic review into the effects of menopause on QoL in MS, followed by an empirical study exploring the experience of attending an online Acceptance and Commitment Therapy (ACT) group for people with MS, and its impact on QoL and wellbeing. The thesis concludes with a discussion relating to how findings might impact on future research and clinical practice.

Firstly, a systematic review investigated the potential dual-impact of menopause on MS. Hormone reduction during perimenopause can cause symptoms of depression and anxiety in the general population, sometimes triggering first-episode psychosis and major depression. Perimenopause in MS may lead to additional difficulties: reproductive hormones have anti-inflammatory properties, reductions of which can impact on MS severity and course, further impacting mental health. This review attempted to investigate this and assess how many studies approach the matter from a psychological perspective. Evidence of dual-impact of menopause was observed in the majority of the 13 papers included in this review. Only four of the 13 studies employed psychological measures; none approached the matter from a purely psychological perspective.

Secondly, people with MS were asked about their experience of attending an online ACT group. Reasons for engaging were explored, along with maintenance and attrition processes. Possible mechanisms behind changes in the way people experienced their diagnosis were discussed, and general feedback was summarised. Findings suggested that the group was generally well-accepted. ACT concepts appeared to facilitate psychological flexibility and bring about acceptance, which positively impacted wellbeing.

Lastly, both studies' findings and implications were brought together and discussed in the final chapter, followed by reflections on the research process.

List of Abbreviations

ACT: Acceptance and Commitment Ther.

AMH: Anti-Müllerian Hormone

ARR: Annualised Relapse Rate

BDI-II: Beck Depression Inventory-II

BPF: Brain Atrophy

CBT: Cognitive Behavioural Therapy

CES-D: Centre for Epidemiologic Studies Depression Scale

DASS-21: Depression, Anxiety and Stress Scale – 21 Items

DMTs: Disease Modifying Therapies

EDSS: Expanded Disability Scale

FSDS: Female Sexual Distress Scale

FSFI: Female Sexual Function Index

FSH: Follicle Stimulating Hormone

HC: Healthy Controls

HRT: Hormone Replacement Therapy

MFIS: Modified Fatigue Impact Scale

MRI: Magnetic Resonance Imaging

MS: Multiple Sclerosis

MSFC: Multiple Sclerosis Functional Composite

MSRS: Multiple Sclerosis Rating Scale

PCS: Physical Component Scale

PF10: 10-item Physical Functioning Scale

POMS: Profile of Mood State

PPMS: Primary Progressive MS

PwMS: People with MS

QoL: Quality of Life

RRMS: Relapsing-Remitting MS

SF-36: 36-Item Short Form

SPMS: Secondary Progressive MS

Chapter 1

Systematic Literature Review with Narrative Synthesis

The effect of menopause-related decrease in anti-inflammatory hormones on functioning and quality of life in people with Multiple Sclerosis: A review

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Abstract

Purpose: Perimenopause is associated with onset, or exacerbation of, mental health difficulties in the general population. In autoimmune conditions such as MS, the associated decline in reproductive hormones can lead to increased inflammation, negatively impacting symptom severity and course, thereby further exacerbating psychological difficulties. This systematic review synthesised literature relating to menopause and MS, to investigate this potential dual-impact. A secondary aim sought to assess how many studies investigated this from a psychological perspective.

Methods: Six electronic databases were systematically searched for literature pertaining to the effect of menopause (including perimenopause) on functioning, psychological wellbeing, and quality of life (QoL). A narrative synthesis of results was performed.

Results: Thirteen papers met inclusion criteria. Nine of these alluded to a 'dual-impact' of menopause in MS, thought to be due to anti-inflammatory hormone reduction, which led to negative impact on functioning, QoL and wellbeing. All included studies utilised measures of functioning, four studies employed psychological measures. No study investigated this from a purely psychological viewpoint.

Conclusion: There appears to be evidence for a 'dual-impact' of menopause on QoL in MS, but more robust prospective studies are needed in order to fully understand the mechanisms of this effect.

Keywords: Multiple Sclerosis; Psychological wellbeing; Menopause; Reproductive hormones; Inflammation; perimenopause

The effect of menopause-related decrease in anti-inflammatory hormones on functioning and quality of life in people with Multiple Sclerosis: A review

Menopause is thought to be unique to humans and some species of whale (Brent et al, 2015). Clinically, menopause is defined as a 12-month absence of menstruation, with no other explanation (Minkin, 2019), with post-menopause following the final menstrual period (Mulhall, Andel, & Anstey, 2018). Perimenopause (also known as menopause transition) precedes menopause, lasting between four and 14 years (Delamater & Santoro, 2018; McCarthy & Raval, 2020; Paramsothy et al., 2017). Perimenopause begins around age 40, with up to 10% experiencing perimenopause in their 30s (Nikolaou & Templeton, 2003). A smaller number do not show symptoms until their early 50s (Nicula & Costin, 2015).

Reproductive hormone levels - particularly oestrogen - decline during perimenopause (Gholizadeh, Sadatmahalleh & Ziaei, 2018). This decrease increases the likelihood of mental health difficulties such as anxiety (Bromberger et al., 2013) and depression (Campbell, Szoeke & Dennerstein, 2015), negatively affecting quality of life (QoL; Dotlic et al., 2021) and causing increased disability (Wariso et al., 2017). Perimenopause can be a catalyst for first psychotic episode (Musial et al., 2021; Soares & Warren, 2009), first major depressive episode (Bromberger et al., 2011), and a general increase in severity of schizoaffective symptoms (Perich, Ussher & Meade, 2017).

Physical symptoms as a result of perimenopause cause further impact on mental health and QoL (Avis et al., 2009), such as sexual dysfunction as a result of gynaecological changes (Delamater & Santoro, 2018), migraines (Hipolito Rodrigues et al., 2018), hot flushes, and night sweats (Worsley et al., 2014) which further exacerbate disrupted sleep (Geiger et al., 2019). Moreover, a rise in inflammation brought about by hormone changes can trigger an increase in joint pain (Fenton & Panay, 2016).

Symptoms may be alleviated by introduction of hormone replacement therapy (HRT), which can bring about improvements in sleep quality (Geiger et al., 2019), mood (Gleason et al., 2015), migraine frequency (Hipolito Rodrigues et al., 2018), and joint pain (Fenton & Panay, 2016). The mechanisms behind some of these improvements are thought to be oestrogen's anti-inflammatory and immunosuppressive properties (Watt, 2016).

Given the potentially pivotal role of inflammation, symptoms of autoimmune conditions can be exacerbated during the perimenopausal stage (Alpizar-Rodrigues et al, 2019; Karvonen-Gutierrez & Leis, 2021). This is thought to be due to menopausal reduction in oestrogen causing increases in inflammation, and not simply due to ageing (Mok, Wong & Lau, 1999).

Less is known about the psychological effects and impact on QoL of menopause on MS, compared to other autoimmune diseases (Bove, 2013). Recent research suggests that inflammation and neurodegeneration are present in all forms of MS (Hauser & Cree, 2020), therefore, it would be reasonable to speculate that perimenopause will exacerbate symptoms, thus further impacting on QoL, functioning, and psychological wellbeing, above and beyond that observed in those without autoimmune conditions.

Research question

The primary aim of this review was to interrogate the literature to assess the possible 'dual-impact' (or additive impact) of menopause on mental health and wellbeing in people with a diagnosis of MS, initially impacting on mental health due to menopausal processes (e.g. increased low mood, as would be the case for people without MS), subsequently impacting on mental health due to physical consequences of menopause on MS symptoms. This possible 'dual impact' occurs due to anti-inflammatory hormone reduction, which exacerbates symptom severity and disease progression, and causes additional psychological distress *above and beyond* that which would be experienced during perimenopause and

menopause without a diagnosis of MS. The secondary aim of this review was to ascertain how many studies – if any – investigate this from a psychological perspective.

Method

This study adhered to PRISMA recommendations (Page et al, 2021) and was pre-registered with PROSPERO: reference CRD42022319147.

Search Strategy

PICO framework was utilised (see Appendix A for PICO framework). Scoping searches were initially conducted, followed by a wide-ranging database search via Medline; PsycINFO; CINAHL; Web of Science; ASSIA, and ProQuest Dissertations and Theses Global. Search script consisted of the following criteria (example from PsycINFO search):

> ab("multiple sclerosis") AND (menopaus* OR perimenopaus* OR postmenopaus*) AND ("quality of life" OR wellbeing OR "psychological wellbeing" OR "mental health" OR "daily functioning" OR functioning)

No restrictions were set regarding language, research design and type of material, with the hope that this would provide further references of interest. Date of publication was broad - from January 1997 onwards - capturing 25 years of material. Initial database search was carried out on the 17th of January 2022, with articles published up to the 28th of February 2022 included. Materials gained from the first author's previous scoping searches were also included in the search.

Inclusion and exclusion criteria

The first author screened all titles and abstracts. Studies were assessed by way of inclusion criteria (See Table 1). Reliability checks were carried out using independent checks by the second author. Queries were to be agreed upon by consensus between both authors, but this was not needed, as both authors agreed on ratings, hence no queries were raised.

Quality assessment

Due to the heterogeneous nature of studies, specific critical appraisal tools from the Joanna Briggs Institute (2017) were utilised (See Appendix C-F). Higher number of affirmative categories was indicative of higher quality methodology.

Method of synthesis/analysis

Characteristics of included studies were noted and compared, and extracted into a bespoke spreadsheet. Narrative synthesis was performed where findings were tabulated and described. No studies were excluded based on quality assessment, but study quality was noted so as to enable a fuller understanding of available research.

Table 1

Inclusion and exclusion criteria

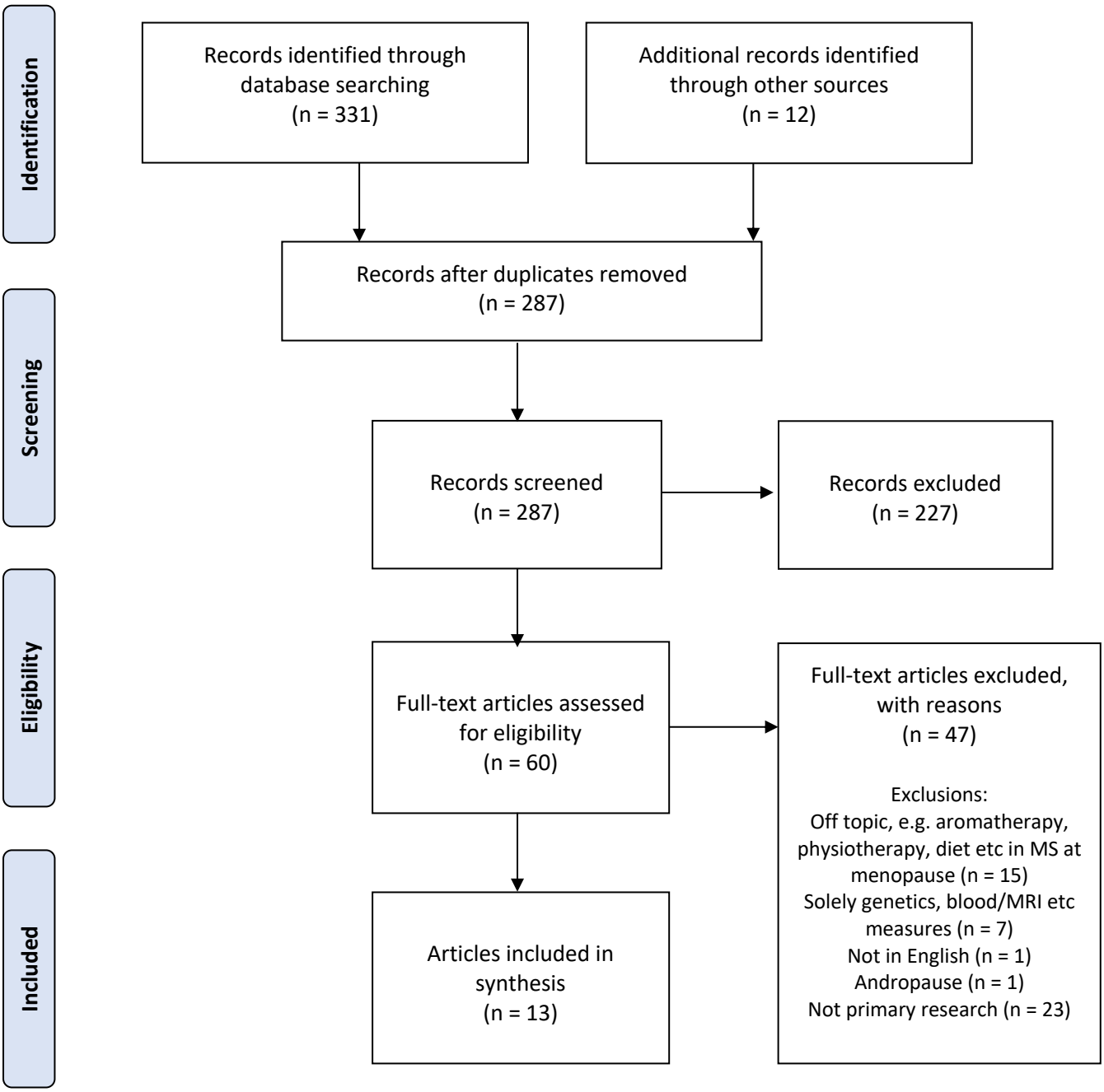
	Include	**Exclude**
Topic	MS and menopause (including peri- and post-) in abstract	MS without mention of menopause or vice versa
	Impact of menopause on MS symptom severity and/or course, quality of life (QoL), and wellbeing	MS and/or menopause as grouping variables but no focus on impact of menopause on MS symptom severity/course, QoL, and wellbeing
Population	Human	Animal, Genetics
Outcome measures	Health/functioning and/or psychological measures, e.g., mental health, QoL wellbeing, and daily functioning	Solely medical/physiological measures, e.g., blood, bone density, MRI scans
Type of publication	Primary research – articles or doctoral theses	Reviews, editorials etc

Results

Initial search produced 331 records (see Figure 1). Twelve were added from hand searches, mainly from citation chaining. Four of these are included in the final 13.

Figure 1

PRISMA Flow Diagram



Analysis

Screening and selection

Database and hand search produced 343 records (see Figure 1). Duplicates were removed, and titles and abstracts assessed according to inclusion/exclusion criteria. Study details were entered into a spreadsheet. Sixty studies were found to be suitable for further assessment of eligibility, which involved full-text screening. At this stage, one study applied qualitative methodology, and 59 utilised health-related outcome measures, i.e., physical functioning, disability rating etc. Twelve of the 60 studies employed psychological measures. No study investigated psychological impact alone. Studies that did not investigate the effect of menopause on MS were excluded, and reasons listed in the spreadsheet. This process resulted in 13 studies.

Characteristics of included studies

Publication dates of the final 13 studies ranged from 2006 to 2020. Data collection dates ranged from 1976 to June 2018, the wide range mainly due to use of large longitudinal cohort study data.

Five of the 13 studies focussed on impact of menopause on the course of MS (see Table 2 for study titles and design). Of the remaining eight, six studies investigated the link between oestrogen and MS progression and/or symptoms: one assessed impact of HRT on MS physical symptoms; one explored whether women declined quicker than men after age 50, and four explored the effect of reproductive hormones on MS course and severity. The remaining two studies investigated prevalence of – and factors associated with - sexual dysfunction (SD) in women with MS, with secondary investigation into the role of menopause in SD.

Table 2

Summary of studies included in this review

Study	Publication Title	Design	Country	Outcome measures	Sample size	Psychological measure?
1. Baroncini et al (2019)	Impact of natural menopause on multiple sclerosis: a multicentre study	Cohort	Italy	EDSS, annualised relapse rate (ARR)	n=148	Health only
2. Bove, Healy, Musallam et al (2016)	Exploration of changes in disability after menopause in a longitudinal multiple sclerosis cohort	Cohort	USA	EDSS main measure; SF-36, MFIS, CES-D utilised as secondary measures	n=724	Yes: Health, QoL, and Psych (mainly health)
3. Bove, White et al (2016)	Hormone therapy use and physical quality of life in postmenopausal women with multiple sclerosis	Cohort	USA	10-Item Physical Functioning Scale (PF10) and PCS	n=95	Health QoL only
4. Bove, Musallam et al (2013)	No sex-specific difference in disease trajectory in multiple sclerosis patients before and after age 50	Cohort	USA	EDSS, BPF, SF-36, relapse rate, MFIS, CES-D	n=551	Yes: Health, biochemical, QoL, and Psych
5. Bove, Healy, Secor et al (2015)	Patients report worse MS symptoms after menopause: findings from an online cohort	X-Sec	USA	Multiple Sclerosis Rating Scale (MSRS)	n=513	Health and self-report cognition only
6. Bove, Vaughan et al (2016)	Women's experiences of menopause in an online MS cohort: A case series	Qual	USA	Qualitative	n=212	Health only

Study	Publication Title	Design	Country	Outcome measures	Sample size	Psychological measure?
7. Gava et al (2019)	Prevalence and psychopathological determinants of sexual dysfunction and related distress in women with and without Multiple Sclerosis	X-Sec	Italy	EDSS, Female Sexual Function Index (FSFI), FSDS, Profile of Mood State (POMS), BDI-II	n=306	Yes: Health and Psych
8. Graves et al (2018)	Ovarian aging is associated with grey matter volume and disability in women with MS	Cohort	USA	EDSS, Multiple Sclerosis Functional Composite (MSFC), AMH in blood	n=415	Health and biochemical only
9. Holmqvist et al (2006)	Symptoms of multiple sclerosis in women in relation to sex steroid exposure	X-Sec	Sweden	Survey questionnaire	n=128	Health only
10. Konstantinidis et al (2019)	Female sexual dysfunction among Greek women with multiple sclerosis: correlations with organic and psychological factors	X-Sec	Greece	EDSS, Depression, Anxiety and Stress Scale (DASS-21), FSFI	n=248	Yes: Health and Psych
11. Ladeira et al (2018)	The influence of menopause in multiple sclerosis course: a longitudinal cohort study	Cohort	Portugal	Expanded Disability Status Scale (EDSS), MRI	n=37	Health & physiological
12. Triantafyllou et al (2016)	Association of sex hormones and glucose metabolism with the severity of multiple sclerosis	X-Sec	Greece	EDSS, Follicle Stimulating Hormone (FSH) levels	n=133	Health and biochemical only
13. Zeydan et al (2020)	Reproductive history and progressive multiple sclerosis risk in women	X-Sec & Case control	USA	EDSS	n=223 n=533	Health only

Seven studies utilised existing research databases (see Table 3): the Mayo Clinic Cohort Study of Oophorectomy and Aging-2 (Rocca et al, 2017); the CLIMB cohort, part of the larger SUMMIT cohort (Bove, Chitnis et al, 2018); the Nurses' Health Study (NHS cohort; n.d.), and the PatientsLikeMe (PLM) research platform (Brownstein et al, 2009).

Study design

Six studies employed a cohort design, six were cross-sectional studies, one case-control (along with a cross-sectional study in the same paper), and the remaining study adopted qualitative methodology.

Study measures

To assess severity and course of MS, most studies (9/13) utilised the Expanded Disability Status Scale (EDSS; Kurtzke, 1983). The EDSS was the sole validated measure in one study, while three utilised biochemical and/or physiological measures alongside the EDSS. Five studies administered physical health; QoL, or psychological measures alongside the EDSS.

Studies investigating physical functioning and/or health-related QoL used the following measures: the 10-item Physical Functioning Scale (PF10; Pugliatti et al, 2008) – a subscale of the Medical Outcomes Study (MOS) 36-Item Short-Form Health Survey (SF-36; Ware & Sherburne, 1992); the Multiple Sclerosis Functional Composite (MSFC; Fischer et al, 1999); the Modified Fatigue Impact Scale (MFIS) a modified form of the Fatigue Impact Scale (Fisk et al, 1994), and the Multiple Sclerosis Rating Scale (MSRS; Wicks, Vaughan & Massagli, 2012) – primarily a measure of physical functioning with a small number of questions on mood. One study utilised the Female Sexual Function Index (FSFI; Rosen et al, 2000) to assess physical elements of sexual function.

Only four of the 13 studies employed psychological measures. Some focussed on depression: Beck's Depression Inventory-II (BDI-II Beck, Steer & Brown, 1996), and Centre

Table 3

Additional study characteristics (Abbreviations: see page 20)

Study	Sample characteristics	Study aims	Outcome
1. Baroncini et al (2019)	Women from Lombardia (Italy) n=148; recruited from 16 MS centres, with Relapsing-Remitting MS (RRMS) or Secondary Progressive MS (SPMS) Mean age = 50.3 92% received Disease Modifying Therapies (DMTs) during study Observed before (mean = 3.7 years) and after (mean = 3.5 years) menopause Outcome measures: annualised relapse rate (ARR) and level of disability according to EDSS rating	To understand impact of menopause on MS, taking inflammation and progressive form into account Observational prospective multi-centre cohort study	AAR rate stable in perimenopause, decreased after menopause EDSS score comparisons performed on n=108 with 3 years of data, suggested increasing disability during study period, especially after menopause Natural menopause appeared to usher in progressive form of MS, probably due to loss of oestrogen (with its neuroprotective and anti-inflammatory properties). Natural ageing also a factor
2. Bove, Healy, Musallam et al (2016)	Women with MS or Clinically Isolated Syndrome (CIS: first episode of symptoms that are often precursors to MS) n=724 Median age at natural menopause = 51.5 50.8% Postmenopausal Longitudinal data from Comprehensive Longitudinal Investigation of MS (CLIMB) cohort Followed for mean 10.4 years through menopausal transition; premenopause mean = 5.4 years; post = 5.1 Outcome measures: EDSS rating, timed walk, and Patient Reported Outcomes (PROs) re QoL	To examine impact of menopause on MS course, severity, and progression Observational prospective longitudinal cohort study	EDSS rating higher after menopause indicating more rapid change in disability after natural and surgical menopause (surgical being younger age-group) Change thought to be partly due to ageing, but also driven by reduction in oestrogen. No statistical change re PROs from perimenopause to menopause

Study	Sample Characteristics	Study aims	Outcome
3. Bove, White et al (2016)	Women with definite or probable MS (n=95) recruited from Nurses' Health Study (NHS) Data from 1976 to 2004 Health behaviour and medical history questionnaire completed every 2 years, PF10 every 4 years 61 participants taking hormone replacement therapy (HRT); 34 not taking HRT Comparison group of 31,935 postmenopausal women without MS from NHS cohort for secondary outcome Outcome measure: physical functioning (PF10)	Assess whether HRT affects physical QoL in women with MS who are postmenopausal. Secondary aim: compare MS with non-MS Observational prospective longitudinal cohort study	HRT associated with higher health QoL in postmenopausal women with MS when compared to pre- and perimenopausal women with MS HRT associated with lower health QoL in women without MS Difference thought to be due to anti-inflammatory effect of oestrogen, and its effect on MS course
4. Bove, Musallam et al (2013)	Men and Women with MS in two age cohorts representing before (38-46 years of age) and after (52-62 years of age) age 50 <50yoa: mean age of 42 (n=169) >50yoa: mean age 57 (n=97) Total number of men = 60 Total number of women = 206 Longitudinal data from Comprehensive Longitudinal Investigation of MS (CLIMB) cohort started in 2000 Followed-up for average of 2.6 years Neurological exam every 6 months, MRI annually Record of ARR PROs re QoL data collected	Investigate whether women have a steeper decline after age 50 (post-menopause) in comparison to men the same age Observational prospective longitudinal cohort study	No differences in objective acceleration of decline post-50 for women compared to men, according to EDSS and MRI Increased disability and decline in ARR in both women and men post-50 No sig. MRI change pre- and post-50 (all) <50 women higher disability than <50 men Women scored lower on subjective physical symptom summary score and lower physical functioning (PROs) than men over 50 years of age Suggests changes not driven primarily by change in female sex hormones

Study	Sample Characteristics	Study aims	Outcome
5. Bove, Healy, Secor et al (2015)	n=513 Premenopausal and Postmenopausal women with MS, 53.4% of sample postmenopausal Premenopausal = 202 (mean age = 40.3) Natural menopause = 103 (mean age = 57.4) Surgical menopause = 110 (mean age 53.0) Chemotherapy-induced menopause = 17 (mean age = 51.7) Data gathered from a large-scale research platform: PatientsLikeMe (PLM) Outcome measure: Online reproductive questionnaire including MS Rating Score (MSRS) and HRT use	Assess subjective impact of menopause on MS disease severity Cross-sectional observational descriptive study	Worse MS disease severity in postmenopausal women. Additionally, earlier age at menopause = worse disease severity No protective effects of HRT use (in past and/or present) on MSRS score In general, results suggestive of neuroprotective function of oestrogen in MS
6. Bove, Vaughan et al (2016)	Free text responses from 127 postmenopausal women with MS Study data gathered from participants on online research platform PatientsLikeMe (PLM) 212 responses to question: “We are interested in learning about how women’s MS symptoms change at menopause. From the literature, there is no clear information on whether symptoms get better, worse, or are unchanged” 127 responses relating to menopause or HRT. Other responses related to e.g., pregnancy, summations re cause etc, and not included in final analysis	To gain an understanding of themes around whether and how menopause affects MS Qualitative study utilising grounded theory approach	Five themes: Perimenopausal onset of MS symptoms Overlap of MS and menopause symptoms MS exacerbated by hot flashes Acceleration of disease after menopause, including fatigue and cognitive symptoms HRT and its effect on MS symptoms Some women who experienced MS onset a considerable time before or after menopause, reported no effect of menopause on MS, for example: “I cannot tell you changes when periods stopped because I hadn’t been diagnosed with MS way back then”

Study	Sample Characteristics	Study aims	Outcome
7. Gava et al (2019)	153 white women with MS (mean age = 47.3), 153 healthy controls (HC; mean age = 48.5), attending a gynaecology clinic in Bologna Inclusion criteria: no hormone intake at study commencement nor previous 6 months, BMI <36, no history of hysterectomy, MS >1 year Only women with MS completed POMS and BDI-II Measures re menopausal status on subset of women who were sexually active in last month: MS premenopausal = 79; MS postmenopausal = 40; HC premenopausal = 74; HC postmenopausal = 57	To investigate prevalence of sexual dysfunction (SD) in women with MS and compare to HC Secondary aim: to understand any demographic, psychological, and MS-related factors in SD Cross-sectional prevalence study	SD rates similar in pre-and post-menopausal women with MS but greater than pre- and post-menopausal HC Distress and low mood more prevalent in women with MS Increasing disability (EDSS), age and presence of low mood associated with SD (FSFI) in women with MS Higher rates of low mood in women with MS and SD than MS without SD
8. Graves et al (2018)	Cohort longitudinal analyses incl. only women with MS (n=415, mean age = 42.6) recruited from EPIC study 269 women contributed to at least 2 timepoints 149 women contributed to all 4 timepoints EPIC: longitudinal study investigating MS phenotype and genotype, based at University of California, San Francisco Baseline cross-sectional analyses also included for HC (n=180, mean age = 44) to allow comparison of anti-Müllerian hormone (AMH) levels. AMH levels measured at baseline, 3, 5, 8-10 years	To investigate pattern of MS progression in women according to levels of AMH, associated with ovarian ageing and menopause Observational prospective longitudinal cohort study data Baseline cross-sectional case-control analysis	Lower AMH associated with higher levels of disability (EDSS) and loss of grey matter (MRI) in women with MS, irrespective of disease duration and age. AMH levels at baseline similar in MS and HCs Ovarian ageing signalled worsening disease course, possibly due to neuroprotective role of sex steroid hormones HRT seemed to improve progression and alleviate symptoms Similar pattern to rheumatoid arthritis, another autoimmune disease

Study	Sample Characteristics	Study aims	Outcome
9. Holmqvist et al (2006)	Premenopausal and postmenopausal women with MS recruited from Linköping (n=94) and Sundsvall (n=46) in Sweden. Mean age = 51 Type of MS: RR (n=69), PPMS (n=11), SPMS (n=48) Postmenopausal = 72 of which HRT users = 35 All participants received questionnaire re demographics, reproductive history, contraception/HRT use, MS activity ratings at pregnancy and menopause Sundsvall participants also gave feedback re postpartum and menstrual changes, and oral contraceptives	Assess MS symptom change due to pregnancy, postpartum, menopause, oral contraception (OC) and/or postmenopausal HRT Retrospective cross-sectional study	56% reported no oestrogen-related change at menopause, 40% felt menopause caused worsening of MS symptoms 55% (n=16) of those who had received HRT after menopause reported no change in MS symptoms, 41% (n=12) reported worsening symptoms The remainder showed associations with high-oestrogen and improvements or lack of adverse MS symptoms; low-oestrogen associated with worsening of MS symptoms No differences according to type of MS
10. Konstantinidis et al (2019)	248 Greek women with MS Mean age = 45.84 Patients recruited from urology/neuro-urology clinics Divided into three age-groups: 18-34 (n=28); 35-50 (n=146), and 50+ (n=74) with 96 being menopausal Disability rating (EDSS) Psychological measure (DASS-21) Sexual dysfunction (FSFI)	To ascertain prevalence of SD in Greek women with MS and factors that correlate with this Prospective cross-sectional prevalence study	64.5% of sample demonstrated clinical levels of SD Increasing age and disability associated with high levels of depression and stress (DASS-21) and SD (FSFI rating) in women with MS Increasing age associated with high levels of anxiety Menopause found to be risk factor for SD in women with MS, but not main factor

Study	Sample Characteristics	Study aims	Outcome
11. Ladeira et al (2018)	37 postmenopausal women with MS; MS diagnosed at least 1 year prior to menopause Mean age at time of menopause = 49.8 Comparison of clinical and radiological outcomes 5 years pre- and post-menopause ARR and EDSS data collected routinely during neurology clinic visits in Lisbon, Portugal 19 of 37 had MRI data, as well as EDSS and ARR. Menopause data gathered via interview Pre-menopausal EDSS (first evaluation), EDSS at menopause (final menstrual period) and post-menopausal EDSS (last evaluation of post-menopausal period)	To establish impact of menopause on MS course Mix of retrospective (menopause data) and prospective (EDSS and ARR) longitudinal cohort design	Participants with MRI results differed to others as they appeared to have significantly less active form of MS compared to those without MRI data Decrease in ARR 5 years post-menopause for all of sample, regardless of MS duration Most of the sample switched to DMTs during study period, which might contribute to lower relapse rate Post-menopausal rating of disability (EDSS) remained stable and continued at a similar rate to pre-menopause
12. Traintafyllou et al (2016)	Men with RRMS (n=52, mean age = 39.06) Women with RRMS: premenopausal (n=66, mean age = 36.22) and postmenopausal (n=15, mean age = 51.93) attending outpatient clinic Venous blood samples to assess levels of sex-hormones such as FSH, testosterone, and estradiol (oestrogen) EDSS score to evaluate MS severity/disability Socio-demographic data Clinical history Treatment history of MS	To assess relationship between MS severity and levels of reproductive hormones Cross-sectional observational study	Low levels of FSH associated with higher disability in premenopausal group but not postmenopausal group Lower oestrogen levels associated with higher disability in postmenopausal women Lower levels of free androgen associated with higher disability in men No sex-specific difference in disease trajectory

Study	Sample Characteristics	Study aims	Outcome
13. Zeydan et al (2020)	Two studies investigating the same aim: Cross-sectional study: Men (n=70, median age = 66.3) and postmenopausal women (n=163, median age = 62.6) with MS. Recruited from large multiple clinic-based progressive MS cohort Case control study: Postmenopausal healthy controls (n=396) birth-matched to postmenopausal women with MS (n=137 of above 163 women) HC data from the Mayo Clinic Cohort Study of Oophorectomy and Aging-2 (population-based cohort study) Survey of reproductive history, lifestyle and environmental information, personal, medical, and genetic history	Investigation of onset of RRMS, progressive disease, and severe disability, including effect of menopause Cross-sectional study of reproductive history in MS Case control study of onset of periods, pregnancy, and menopause in MS with matched controls	Early menopause and nulliparity (not having borne children) associated with earlier onset of progressive form of MS Pregnancy (even if early termination) associated with reduced MS risk and delayed onset of MS (dose effect). Relapse rate reduced during pregnancy, with a short period of increase in relapses immediately after giving birth 36% of women experienced menopause before a progressive form of MS. In this group, age at menopause was associated with age at progressive MS onset, and more severe disability Earlier menopause associated with worse MS prognosis by impacting on disease progression Age at first period and menopause did not differ between MS group and HCs Findings suggest oestrogen is beneficial for MS symptoms and onset

Abbreviations: **AMH** = Anti-Müllerian Hormone; **BDI-II** = Beck Depression Inventory-II; **BPF** = Brain atrophy; **CES-D** = Centre for Epidemiologic Studies Depression Scale; **DASS-21** = Depression, Anxiety and Stress Scale – 21 Items; **EDSS** = Expanded Disability Scale; **FSDS** = Female Sexual Distress Scale; **FSFI** = Female Sexual Function Index; **FSH** = Follicle Stimulating Hormone; **MFIS** = Modified Fatigue Impact Scale; **MRI** = Magnetic Resonance Imaging; **MSFC** = Multiple Sclerosis Functional Composite; **MSRS** = Multiple Sclerosis Rating Scale; **PF10** = 10-item Physical Functioning Scale; **POMS** = Profile of Mood State; **SF-36** = 36-Item Short Form

for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). One utilised the Depression, Anxiety and Stress Scale – 21 Items (DASS-21; Lovibond & Lovibond, 1995), another administered the Profile of Mood State (POMS; McNair, Lorr, & Droppleman, 1971), a measure of overall mood, combining tension, anger, fatigue, depression, confusion, and vigour. Other wellbeing measures included the Short Form-36 (SF-36; Ware & Sherburne, 1992) - primary focus being on physical functioning with questions on emotional wellbeing, providing an overall mental health component summary scale – and the Female Sexual Distress Scale (FSDS; Derogatis et al, 2002), which measures psychological distress as a result of sexual dysfunction.

Study quality

The first and second authors assessed study quality (See Appendix B for quality ratings), utilising the Joanna Briggs Institute (2017) critical appraisal tools (See Appendix C-F). Both authors agreed on 126 quality ratings, with queries pertaining to six of these ratings (4.5% of ratings). These six ratings involved whether exposures were measured similarly in one study, for example, or whether some of the quality rating questions were applicable to a specific study. These were discussed with the third author present, and agreement reached by consensus.

Main findings

Sex-specific effects on disease course

Studies 4 and 12 found no objective measure of sex-specific difference in MS disease trajectory (see Table 3) according to EDSS ratings and biochemical readings, suggesting no effect of menopause. In the case of Study 4, subjective measures indicated significantly lower QoL, and higher rates of disability and low mood, in female participants, compared to male.

Study 12 demonstrated an association between lower oestrogen levels and higher levels of disability in postmenopausal women with MS. Likewise, this study found an

association between lower free androgen levels and higher levels of disability in men with MS, androgens having similar anti-inflammatory properties to oestrogen (Cutolo et al, 2006).

Effects of reduced oestrogen on MS

Study 11 found no difference in disability status from pre- to post-menopause in a cohort of women with MS. Most participants switched to Disease Modifying Therapies (DMTs), which were thought to have contributed to these findings. Studies 2 and 12 found lower levels of oestrogen were associated with higher levels of disability in postmenopausal women. Study 2 also reported more rapid deterioration and progression, post-menopause. While partly due to ageing, deterioration was also seen in younger participants who underwent surgical menopause, suggesting that oestrogen was the driver of this change.

Study 1 also reported that while ageing was partly responsible for deterioration, menopause - reduction of oestrogen in particular - appeared to usher in a progressive form of MS. Study 11 described similar outcomes: relapse rates reduced five years post-menopause, signalling a more progressive (neurodegenerative) form of the disease (therefore higher levels of physical disability). Study 13 also concluded that the earlier the onset of menopause, the earlier the transition to a progressive form of MS, and the worse the prognosis and course of progression.

Effects of other reproductive hormone decrease on MS

Other reproductive hormones seemed to have a role in increased disability and progression. Study 12 found low levels of Follicle Stimulating Hormone (FSH) were associated with deterioration and increased disability in premenopausal women with MS. This was contrary to expectations (low levels indicate healthy ovaries and younger age) and was not observed in postmenopausal women. When included in a multivariate model it did not predict stage of MS. Study 8 found low levels of anti-Müllerian hormone (AMH), indicating ovarian ageing, were related to higher levels of disability in women with MS. Low

levels of AMH also correlated with higher levels of grey matter atrophy, independent of duration of MS, and age.

Effect of hormone replacement therapy on MS symptoms

Study 8 described improved functioning, reduced disability, slowed/paused progression, and alleviated symptoms of MS, with introduction of HRT. Study 3 also observed improved health-related QoL in postmenopausal women with MS taking HRT, but HRT was associated with lower health-related QoL in women without MS. This was thought to be due to the anti-inflammatory effect of oestrogen producing more benefit for those with MS. Conversely, Study 5 did not observe protective effects of HRT according to MSRS score, but disease severity ratings were deemed to suggest a neuroprotective role of oestrogen in MS.

Study 9 is the earliest in our review, and retrospective. Just over half of their sample reported no differences in MS symptoms due to menopause, 5% reported improvement, with the remainder reporting worsening symptoms. Similarly, just over half of those who had used HRT reported no change in MS activity at menopause, rated on a questionnaire created by the study team.

Qualitative findings

Study 6 was the only qualitative study in the sample. Five themes were identified (see table 3). Some women reported no effect of menopause on MS symptoms. Authors commented that these were primarily women whose menopause significantly pre- or post-dated MS onset. Others reported that menopause hastened change and/or exacerbated MS symptoms.

Impact of sexual dysfunction on quality of life

Studies 7 and 10 focussed on sexual dysfunction (SD) in women with MS, arguably an important factor for QoL. Study 7 found pre- and postmenopausal women with MS

displayed similar rates of SD, but higher rates, lower functioning, and higher distress than healthy controls (HC). Menopause was noted as a risk factor for SD in both studies. Study 10 also observed high rates of SD in pre- and postmenopausal women with MS. Menopause was also a risk factor for higher stress, depression, and anxiety in postmenopausal women with MS in comparison to premenopause.

Discussion

Thirteen studies are included in this systematic literature search. Included studies investigated effects of menopause-related hormone decrease on the course of MS and whether this impacts on functioning, QoL, and/or psychological wellbeing *in excess* of that anticipated as a result of menopause in people without MS. Additionally, this review examined how many of those studies employed psychological measures.

Study quality

There is much heterogeneity of study design, and studies are generally rated as moderate quality. Study 6 – a qualitative paper - has the poorest quality rating; results being solely derived from one free-text question in an otherwise quantitative study whose results are published elsewhere. Study 9 is the earliest and sole retrospective study in this sample, rated as poor quality. No validated measures were administered in this study, and no details given regarding time since menopause for postmenopausal women in the sample. Additionally, a sub-sample received a longer questionnaire.

Studies 12 and both studies in paper 13 scored full points in their respective checklist items, and studies 2 and 3, scored full points in all applicable items.

EDSS findings

Nine studies utilised the EDSS as primary measure of disease trajectory and functioning. The EDSS is widely used. This is partly due to the fact that it is the only measure of clinical ability in MS, approved by the Food and Drug Administration in the US (Uitdehaag, 2014). However, it has been criticised for its variability due to its subjective nature (Marzullo et al, 2019); bimodal scoring system (Kalincik et al, 2015); over-reliability on physical ability (Weinstock-Guttman, Sormani & Repovic, 2019), and lack of sensitivity in detecting change, especially in lower levels of disability (Rabadi & Vincent, 2013;

Uitdehaag, 2014). Therefore, findings which rely on EDSS ratings should be interpreted with caution, particularly if EDSS is the sole measure of disability and functioning.

Comparisons of men and women

Investigating sex-specific differences can help assess potential impact of menopause on MS. Studies focussing on this did not observe significant differences in objective measures. Objective measures were based solely on EDSS, alongside biochemical and/or radiological measures, and did not take daily functioning into account. In contrast, subjective measures utilised in one of these studies did show higher levels of distress and lower levels of functioning in women when compared to men, with higher levels of disability noted in postmenopausal women with lower oestrogen levels. Likewise, men with lower levels of free androgen experienced higher levels of disability (androgens being anti-inflammatory and reducing with age). A recent review (Ysrraelit & Correale, 2021) investigating the role of androgens and MS symptoms reported similar findings. Given the anti-inflammatory role of both oestrogen and androgens, differences post-50 may not be significantly different between the sexes, as similar mechanisms (involving loss of anti-inflammatory hormones) may be involved.

Impact of HRT on symptoms

Recent reviews describe HRT as beneficial for peri- to post-menopausal women with MS (Ali, Mangold, & Peiris, 2017; Bove et al, 2021; Christianson, Mensah & Shen, 2015). In contrast, two of the present review studies did not report any benefit of HRT. One study's authors pointed out that their research was not specifically designed nor powered to detect this, and that they had classified women undergoing hysterectomy with ovaries preserved, as post-menopausal, which may have diluted the effect of menopause. Similarly, a retrospective study concluded that just over half of the women who used HRT in their sample did not experience benefits as a result of HRT, but time since menopause was not clear. Similar to

the aforementioned recent reviews, the prospective studies in the present sample did find evidence for HRT and symptom improvement, as well as evidence of HRT pausing/slowing disease progression.

Effect of menopause-induced hormone loss on MS

Recent reviews evidence ovarian ageing and menopause-induced hormone reduction as triggering progression and exacerbating severity in MS (Krysko et al, 2020). Eight of the 13 review studies find evidence for this, with an additional study observing this effect in just under half of its participants. While ageing is the largest predictor of worsening progression in MS (Zeydan & Kantarci, 2020), there is compelling evidence for the pivotal effect of oestrogen reduction, above and beyond the effects of age (Sparaco & Bonavita, 2021). Evidence for this is often seen in younger women having undergone surgical menopause, such as that observed in three of the present review studies, all of which reported worsening of symptoms and impact on disease course, in this population.

Psychological measures of impact of menopause on MS symptoms and progression

In order to assess a potential dual-impact of menopause on QoL and mood in people with MS, over and above that observed in people without MS, measures of psychological wellbeing are needed, such as those utilised in Studies 2, 4, 7 and 10. One study found no change in psychological measures from perimenopause to menopause, which was in contrast to a recent review carried out by the same lead author, who noted higher levels of psychological difficulties in menopausal women with MS (Bove, Okai et al, 2021). The other three studies did find evidence for decline in psychological wellbeing from perimenopause to menopause.

Review studies investigating SD reported lower mood in women with MS with SD when compared to women with MS without SD, highlighting the impact of SD on QoL. They

also found menopause to be a risk factor for SD, but not the main factor as younger pre-menopausal women with MS also had higher rates of SD than healthy controls.

Limitations

While the overall results seem to support a 'dual impact' of menopause in MS, this review was a first attempt at understanding this process, and as such, has several limitations. Many included studies utilise cross-sectional design, therefore no indications of long-term effects are given. Additionally, a number of review studies seemingly discount the perimenopause stage, when oestrogen levels are in the process of reducing.

Included papers varied in terms of focus, sample, and methodology. This made it somewhat challenging to draw definitive conclusions in relation to the review question. One study, for example, included people diagnosed with Clinically Isolated Syndrome (CIS) in their group of people with MS. CIS is often a precursor of MS (Antonelou et al, 2015), but is a one-time event where symptoms akin to MS are recorded in a single episode, and as such might differ in some fundamental aspects. This is similarly the case for studies that included women with partial hysterectomy (with functioning ovaries) in their 'hysterectomy' group, for example. Moreover, RRMS, SPMS and PPMS differ in terms of presentation, although many studies include all three in their study population, therefore conclusions are sometimes unclear in terms of gaining a full understanding of the mechanisms at play with regard the review question.

Furthermore, review search terms were broad: while all investigate the role of menopause on severity and progression of MS symptoms, their focus does vary. Additionally, not all women will experience psychological difficulties during perimenopause and menopause, which will also be the case for women with MS. Resilience (Süss & Ehlert, 2020), past history of depression, perceived levels of stress, relationship with body image, and self-esteem (Willi et al, 2021), as well as sleep quality, social support, and symptoms of

anxiety (Li et al, 2022), are some of the factors that predict psychological difficulties in menopause in the general population, which will be as relevant in MS as they are to those without MS. As such, there may be women who do not experience any psychological difficulties due to menopause in itself, but may experience those difficulties in connection with reduced functioning and physical impact of reduction of anti-inflammatory hormones in MS; these women will not experience a dual-impact in terms of their psychological wellbeing, as their psychological wellbeing was not initially affected by menopause.

Suggestions for further research

More high-quality trials are needed to better understand the impact of menopause on MS progression and severity. Bove, Anderson and colleagues (2022) have recently carried out a short feasibility trial investigating the effects of HRT on peri- and postmenopausal women with a diagnosis of MS, in real time. While no significant differences were seen between intervention and control groups (possibly due to the short timeframe), beneficial changes in psychological and physical QoL, menopausal symptoms, and physical disability, were in the direction of the treatment arm. Furthermore, the study demonstrates that such trials are feasible.

With regard to a measure of psychological effect of menopause on MS symptoms and progression, complicated processes are at play. For example, perimenopause and menopause often overlap with MS diagnosis (Angum et al, 2020); likewise the transition to a more progressive form of MS (Krysko et al, 2020). There are arguably also significant personal and social changes at this time, such as children leaving the family home, or demands of caring for elderly parents (Wister & Mitchell, 2022). Reduction in mood and psychological wellbeing would be understandable (due to processing the diagnosis, and coping with physical and social/personal changes), and arguably might not solely be due to the effect of menopause. Robust methodologies are needed in order to unpick the various components.

Furthermore, given that hormonal changes occur over a prolonged period and begin many years prior to menopause (Krysko et al, 2020), more robust longitudinal studies are needed in order to gain a better understanding of the complex processes at play.

Given the paucity of psychologically-focussed studies, and that most MS studies appear to have a biomedical focus (evidenced by the number of included studies that were published in biomedical journals), studies into the psychological aspects of perimenopause and menopause in MS (and other autoimmune, neurodegenerative, and long-term conditions) are needed. Longitudinal studies in particular, investigating the psychological impact of perimenopause and menopause, would arguably begin to shed some light on the processes at play, and possibly identify factors that influence positive outcomes and coping styles.

Conclusion

Despite its limitations, this systematic review has brought together studies investigating the effect of menopause on MS symptoms and its impact on QoL and psychological wellbeing; impact above and beyond that which may be experienced by people without MS due to the role of anti-inflammatory hormone reduction. Findings provide some support for a 'dual impact', thereby contributing to a growing body of evidence pertaining to menopause in autoimmune conditions in general, and MS specifically. It is hoped that further research into this subject will help add to our understanding of the impact of menopause on mental health and wellbeing in MS. It is also hoped that more research will potentially uncover strategies to reduce this impact in order to not only pause or stabilise disease trajectory at this time, but support quality of life and psychological wellbeing.

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Appendices

Appendix A

PICO framework

PICO	
P: Population	People with Multiple Sclerosis
I: Intervention or Exposure	Perimenopause or menopause
C: Comparison or Control	People without Multiple Sclerosis
O: Outcome	Psychological wellbeing and quality of life

PICO specific to the review question:

P – Do people with **Multiple Sclerosis**

I – going through **perimenopause/menopause**

C – experience this differently to **people without Multiple Sclerosis**

O – in terms of **psychological wellbeing and quality of life**?

Appendix B

Quality assessment ratings

Study	Checklist	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11
1	Cohort	N/A	N/A	N/A	√	√	X	√	√	√	N/A	√
2	Cohort	N/A	N/A	N/A	√	√	√	√	√	√	N/A	√
3	Cohort	N/A	N/A	√	√	√	√	√	N/A	N/A	N/A	√
4	Cohort	√	√	√	√	U	N/A	√	√	N	N/A	√
5	X-Sec	X	√	N/A	√	√	√	√	√	-	-	-
6	Qual	X	√	U	X	X	X	X	X	√	X	-
7	X-Sec	√	√	√	√	√	X	√	X	-	-	-
8	Cohort	√	√	√	√	√	U	√	√	-	-	-
9	X-Sec	√	√	√	X	N/A	N/A	X	√	-	-	-

Study No.	Checklist	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11
10	X-Sec	√	√	N/A	√	X	X	√	√	-	-	-
11	Cohort	X	√	√	√	√	N/A	√	√	√	N/A	√
12	X-Sec	√	√	√	√	√	√	√	√	-	-	-
13	X-Sec	√	√	√	√	√	√	√	√	-	-	-
	Case Control	√	√	√	√	√	√	√	√	√	√	√

Note: Cohort design quality assessment tool includes 11 items, Qualitative contains 10, Cross-Sectional contains 8 items, and Case Control contains 10 items
KEY: √ = yes; X = no; U = unclear; N/A = not applicable

Appendix C

JBI CRITICAL APPRAISAL CHECKLIST FOR COHORT STUDIES

	Yes	No	Unclear	Not applicable
1. Were the two groups similar and recruited from the same population?	☐	☐	☐	☐
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were confounding factors identified?	☐	☐	☐	☐
5. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐
8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☐	☐	☐	☐
9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☐	☐	☐	☐
10. Were strategies to address incomplete follow up utilized?	☐	☐	☐	☐
11. Was appropriate statistical analysis used?	☐	☐	☐	☐

Appendix D

JBI CRITICAL APPRAISAL CHECKLIST FOR ANALYTICAL CROSS SECTIONAL STUDIES

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	☐	☐	☐	☐
2. Were the study subjects and the setting described in detail?	☐	☐	☐	☐
3. Was the exposure measured in a valid and reliable way?	☐	☐	☐	☐
4. Were objective, standard criteria used for measurement of the condition?	☐	☐	☐	☐
5. Were confounding factors identified?	☐	☐	☐	☐
6. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
7. Were the outcomes measured in a valid and reliable way?	☐	☐	☐	☐
8. Was appropriate statistical analysis used?	☐	☐	☐	☐

Appendix E

JBI CRITICAL APPRAISAL CHECKLIST FOR QUALITATIVE RESEARCH

		Yes	No	Unclear	Not applicable
1.	Is there congruity between the stated philosophical perspective and the research methodology?	☐	☐	☐	☐
2.	Is there congruity between the research methodology and the research question or objectives?	☐	☐	☐	☐
3.	Is there congruity between the research methodology and the methods used to collect data?	☐	☐	☐	☐
4.	Is there congruity between the research methodology and the representation and analysis of data?	☐	☐	☐	☐
5.	Is there congruity between the research methodology and the interpretation of results?	☐	☐	☐	☐
6.	Is there a statement locating the researcher culturally or theoretically?	☐	☐	☐	☐
7.	Is the influence of the researcher on the research, and vice- versa, addressed?	☐	☐	☐	☐
8.	Are participants, and their voices, adequately represented?	☐	☐	☐	☐
9.	Is the research ethical according to current criteria or, for recent studies, and is there evidence of ethical approval by an appropriate body?	☐	☐	☐	☐
10.	Do the conclusions drawn in the research report flow from the analysis, or interpretation, of the data?	☐	☐	☐	☐

Appendix F

JBI CRITICAL APPRAISAL CHECKLIST FOR CASE CONTROL STUDIES

	Yes	No	Unclear	Not applicable
1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	☐	☐	☐	☐
2. Were cases and controls matched appropriately?	☐	☐	☐	☐
3. Were the same criteria used for identification of cases and controls?	☐	☐	☐	☐
4. Was exposure measured in a standard, valid and reliable way?	☐	☐	☐	☐
5. Was exposure measured in the same way for cases and controls?	☐	☐	☐	☐
6. Were confounding factors identified?	☐	☐	☐	☐
7. Were strategies to deal with confounding factors stated?	☐	☐	☐	☐
8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?	☐	☐	☐	☐
9. Was the exposure period of interest long enough to be meaningful?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐

Chapter 2

Empirical Study

Attending an online ACT group for people diagnosed with Multiple Sclerosis: Participant experiences of engagement, maintenance, and utility

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Abstract

This qualitative study explores the experience of people with Multiple Sclerosis (MS) who attended an online Acceptance and Commitment Therapy (ACT) group. Nine participants with a diagnosis of MS were included in this study. The study was open to all attendees, irrespective of number of sessions attended, in order to gain a breadth of experience and further understanding of mechanisms behind maintenance and attrition. Eight participants attended six or more of the eight group sessions, with one attending one session.

A thematic analysis was performed, resulting in four themes, each with two/three sub-themes. The first theme 'Where do I sign? And do I want to…?' related to the process of making the decision to attend the group. The second theme 'Finding my place' involved factors contributing to group engagement and maintenance, along with feelings around group connection and the online experience. The third theme 'Course-related change (or not)' concerned implementing course strategies, and how these impacted on participants' daily life. The final theme was 'General course feedback' where opinions on content and facilitation, as well as suggestions for improvement, were summarised.

The course was viewed positively, with the majority of participants adopting elements of the ACT approach in their daily life. This consequently brought about positive changes, some of which were felt to be life-changing. While most participants gained some benefit from attending the group, they also stressed the importance of systems to support maintenance of benefits in the long-term.

Keywords: Multiple Sclerosis, Acceptance and Commitment Therapy, Psychological intervention, group intervention, online intervention

Attending an online ACT group for people diagnosed with Multiple Sclerosis: Participant experiences of engagement, maintenance, and utility

Multiple sclerosis (MS) is the most common disabling non-traumatic condition that affects younger people (Kobelt et al., 2017). Depression affects up to 50% of people with MS, while anxiety affects up to 42% (Boeschoten et al., 2017; Kalb et al., 2019; Wallis et al., 2019); more than 20% experience both depression and anxiety (Leavitt et al., 2020). MS symptoms have a detrimental effect on quality of life (Visser et al., 2021, Wilski et al, 2019) causing feelings of stigma (Broersma et al., 2018); factors that might partly account for higher levels of suicidal ideation and intent (Foley, 2015).

Psychological intervention in MS

Group-based peer support is recommended for chronic conditions such as MS (NICE, 2009 & 2020), as well as mindfulness-based training and CBT (NICE, 2014). British Psychological Society (2021) guidelines particularly recommend group-based Acceptance and Commitment Therapy (ACT) for MS.

Kangas & McDonald (2011) argue that cognitive restructuring (a central factor in CBT, for example) is not particularly effective for people coming to terms with significant life changes such as those experienced in long-term conditions; significant changes which are grounded in reality. Having its roots in behaviour therapy and utilising mindfulness practice (Hayes et al., 2006), ACT focuses not on controlling or eliminating cognitions but on facilitating people to live well, irrespective of cognitions and illness-related limitations (Kangas & McDonald, 2011). ACT fosters psychological flexibility, which can reduce anxiety, low mood, and stress, and improve quality of life (QoL; Pearlman & Thorsteinsson, 2019), thus making ACT a natural therapeutic ‘contender’ to assist people in living well with long-term conditions. Furthermore, relaxation techniques such as mindfulness (practiced in ACT) can reduce cortisol and increase dopamine levels (Newberg & Yaden, 2018), both of

which have positive effects on inflammation (Pacheco, Contreras & Zouali, 2014); crucial in the management of autoimmune conditions such as MS.

ACT and MS

ACT is one of the most studied third wave therapies (Micallef-Trigona, 2016), with a sizeable evidence-base (Hacker, Stone & MacBeth, 2016). ACT has been successfully utilised for chronic conditions in general (Brassington et al., 2016; Graham et al, 2016) including Parkinson's Disease (Ghielen et al., 2017), brain injury (Kangas & McDonald, 2011), and Motor Neurone Disease (Pearlman & Thorsteinsson, 2019).

There is a growing body of evidence for ACT in MS, with positive outcomes such as increased resilience, improved QoL, and reduction in low mood, disease severity, and stress levels (e.g., Giovannetti et al., 2020; Masjedi-Araani & Khanalilou, 2018; Packenham et al., 2018; Potter et al., 2021; Proctor et al., 2018).

Online groups

People with chronic conditions may have barriers to participating in face-to-face groups, many of which can be overcome with online attendance (Synnot et al, 2014). Online groups for people living with chronic conditions have delivered mixed results. Self-guided online programmes have been effective (Pöttgen et al, 2018), in some cases more effective than interactive online group programmes (Ghahari et al, 2010). With regard to online (interactive) interventions, White and colleagues' meta-analysis (2022) found evidence for reduction in depression, anxiety, and general psychological distress in chronic conditions. Similarly, Fischer and colleagues (2015) observed reductions in depression.

A recent review of qualitative research exploring the experience of online versus face-to-face ACT groups for people with chronic conditions concluded that an online forum was acceptable and effective (Herbert et al, 2022). Similarly, Vugts and colleagues (2018) found quantitative evidence for efficacy of online ACT groups in chronic conditions.

Qualitative research involving online ACT groups and people with MS

Synnot and colleagues (2014) compared online with in-person groups for MS, utilising thematic analysis methodology. Online groups yielded more on-topic feedback and more thoughtful and articulate responses, while face-to-face methods tended to be more interactive. Both approaches yielded rich data and were perceived as valuable and helpful.

A number of qualitative studies explore experiences of people with MS (Desborough et al, 2020). Similarly, qualitative studies explore experiences of engaging in ACT for people with chronic conditions (Herbert et al, 2022). However, a search of the literature did not locate qualitative studies exploring the experience of engaging in ACT groups for people with MS.

Rationale for current study

The present study sought to provide qualitative insight into the experience of attending an online ACT group for people with MS. It assessed the utility and acceptability of the intervention. Processes involved in engagement, maintenance, and course-related change were explored, and mechanisms behind this change considered. Lastly, suggestions for improvements and general feedback, were summarised.

Method

Methodology

Thematic Analysis (TA) according to Braun and Clarke's methodology (2022), was the most appropriate method due to its flexibility. A semi-structured interview schedule was utilised (Appendix A). Questions were open-ended, and topics involved participants' motivations to join the group, experience of participating, and practical feedback about the group. The interview encouraged reflection around change (or expectation of change) regarding participant relationship with MS, and exploration of means of change.

Recruitment

Participants were recruited from a pool of 24 people who attended one of two online ACT groups running on the same day. This was in order to facilitate attendance for those that worked (who might not be able to attend in the daytime) and therefore give an opportunity for a range of people to attend. The late morning daytime group made allowances for early-morning fatigue, which the group organiser was alerted to via anecdotal experience of past group participation. Groups were organised and funded by MS Society in Wales (MS Cymru). They ran for eight weeks from mid-October to mid-December 2021 and were facilitated by the third author. After groups ended (and ethical approval given), the first author liaised with the Director of MS Cymru. The latter passed on information (see Appendix B) and gained consent for the first author to contact attendees to discuss the research. After a brief discussion via Zoom or telephone, participants gave written or electronic informed consent (see Appendix C) for the full interview. Consent was also recorded verbally at commencement of interviews. Recruitment and recordings were carried out from early January to mid-February 2022.

Participant characteristics

Nine participants' responses (five female, four male) are included in this study. This number aligns with Braun & Clarke's (2013) recommendations for a small to moderate sized study. Six participants attended the evening group; the remaining three, the daytime group. Group attendance ranged from one to all eight sessions, with eight participants attending six sessions or more. The study was purposefully open to all attendees regardless of number of sessions attended, to secure a breadth of experience and further understanding of maintenance and attrition.

Participants were aged early-30s to mid-60s, average age being 51.4 years. Time since diagnosis ranged from one year to 18, with an average of 7.3 years. Participants identified as

White British/Welsh and resided in Wales. Participants chose a pseudonym (with no requirement that it be gender-concordant), and identifiable details removed from transcripts to protect anonymity. The majority of participants had a diagnosis of Secondary Progressive MS (SPMS), with a smaller number diagnosed with Primary Progressive MS (PPMS), and fewer again diagnosed with Relapsing-Remitting MS (RRMS).

ACT group format

Both ACT groups ran for 1.5 hours with a 5-minute break in the middle, over eight weeks (see Appendix D for flyer and Appendix E for group content). Sessions followed a similar format: check-in, followed by a PowerPoint-based theoretical component introducing an ACT strategy, with a goal-setting exercise to finish. Groups placed emphasis on coping with transitions and losses, holding in mind experiences of this client group. Normal reactions to loss were covered, and acceptance in terms of continuing to do things that matter (valued actions), while also finding alternative ways to express these. The more typical meaning of acceptance was also discussed, focussing more on difficult internal experiences in the moment. Check-in was timetabled at the beginning of groups in order to facilitate group discussion regarding MS and when it first became part of each participant's life. Impromptu dialogues around other MS-related issues and how the ACT was relevant to these, also featured as part of the groups.

Data generation

Interviews were carried out by the first author over a one-month period from end of January to end of February 2022, between four and six-weeks since group completion. Interviews were held on Zoom, recorded, live-transcribed, and uploaded onto an encrypted drive. Interviews ranged from 40-120 minutes, averaging 85 minutes. The interviewer was not part of the team delivering the training. The third author (the group facilitator) did not have access to full transcripts, nor were they aware of participant identity. Potential

participants were informed of this and that responses would be anonymised, in order to foster a safe space in which to discuss their experiences.

Participants were very open with their responses. Despite not being part of the interview schedule, most participants linked their MS journey (from diagnosis) to questions about their ACT group experience.

Data analysis

Transcription and analysis were carried out by the first author, following Braun & Clarke's (2006) recommendations. This involved checking the live-transcript while re-listening to the session, correcting errors, and noting initial impressions; some being codes, others theme-like in quality. After re-reading the transcript, more impressions were generated and noted. After further readings, some themes remained, while others became redundant. Sections of transcript were highlighted according to codes and resultant themes. Core components became evident, which strengthened the impression that they were indeed, themes. Themes were re-investigated in light of examples. The narrative developed organically, leading naturally to the story within the experience. This was written up into a report, utilising appropriate extracts (See Appendix G-I for examples), in order to link back to the study rationale.

Ethical considerations

Ethical approval was granted by Bangor University School of Psychology Research Ethics Committee (Ref: 16999; see Appendix G). The third author facilitated the ACT group and therefore was not involved in consent and transcription.

Quality assurance

The first author kept a detailed memo which helped foster an awareness of perspectives, and encouraged fuller understanding of implicit processes. The second author audited themes and verbalisations/transcripts.

Epistemological approach

The first author approached interviews and analysis from a pragmatic contextualist perspective, with a recognition that context affects expression as well as interpretation. Participant reports were considered accounts of real events, framed within the context of their situation and perspective. Where possible, analysis attempted to take this into account.

Reflexive statement

The first author is a white, Welsh female, training to be a clinical psychologist. Neither she nor members of her immediate family have a diagnosis of MS, but a close family member has an autoimmune condition. She has a friend who was diagnosed with MS some years ago.

The first author applies ACT in a clinical environment and feels this is the model which resonates most for her. She generally believes in its efficacy, which could have affected her reading of transcripts and introduce a degree of bias. The third author has extensive experience as a clinician and is an accredited ACT trainer. The second author is an experienced clinician in a separate clinical area, and therefore holds a more neutral position, which facilitated recognition of potential bias, flagged up during online meetings.

Findings

The data generated four themes, some of which had two, others three, subthemes (Table 1). Themes encapsulated the experience of participating in the ACT group, with a loose narrative form. Other themes emerged regarding people's MS 'journey'. These were not included in this analysis, but supplied richer contextual global data, which influenced some of the analysis and discussion.

Transcript notations are as follows:

Italics	Participant quotes
...	Material omitted
[text]	Note added by author for explanatory purposes

Table 1.

Themes and subthemes

Themes	Subthemes
1. Where do I sign? And do I want to…? The thought process around making the decision to attend and to keep attending	**1.1. I'll give it a shot:** motivation for taking a chance on the course
	1.2. Holding up the mirror: discomfort/expectations around meeting other group members with MS; seeing my future
2. Finding my place: Participants' experience of being part of the group. Relationship with other group members, connection to the facilitator, and role of virtual meetings in this.	**2.1. Comparisons** with the rest of the group: gaining a sense of place in terms of who I am in light of my MS diagnosis
	2.2. Group connection/support/dynamics: the role of the group in the experience of participating; commonalities in difference
	2.3. The online experience: the good, the bad, and the 'comfortable in my PJs'
3. Course-related change (or not): Thinking differently about MS (or not) and the desire for change to be maintained.	**3.1. Adopting good habits:** change of practice; small adjustments = big impact
	3.2. In it for the journey: need for continuation; short term solutions = short term gains
4. General course feedback Feedback to MS Cymru and facilitator for future ACT for MS groups.	**4.1. Course content:** what resonated and why? What fell on stony ground, and why?
	4.2. Course facilitation: walking the tightrope between leader and participant
	4.3. Focused benefits: additional/alternative group ideas

1. Where do I sign? And do I want to…?

1.1. I'll give it a shot

Most group members had attended other courses and were trying to find something that resonated with them, to assist them to live well with their MS. There was an element of trying everything available:

"*I'm just trying to pick up as much information as I can really...*" (Gary).

Some were looking to further their knowledge of - and for help with - the condition. Mim described this as a process of research:

"*I am exploring, and I'm analysing and seeing what works, what doesn't work…* [to try] *to sort of manage my illness or come to terms with it*".

There was a suggestion that people were looking for answers, ways to resolve particular difficulties, such as Macsen:

"*...I started thinking, well, I need some help maybe, with my way of thinking and the way I'm interpreting things*".

Generally, people were looking for whatever might be useful, and the fact that the group involved Acceptance and Commitment Therapy was not particularly important. Exceptions were Felicity and Katherine: Felicity had read about ACT previously and bought an ACT self-help book, while Katherine stated:

"*…the one thing that stood out to me was the word acceptance. It was because that was something that I was personally troubled with*".

There was a general feeling of 'testing the waters' and that people would move on relatively quickly if the group wasn't addressing their needs.

1.2. Holding up the mirror

Group members voiced some fears and doubts about joining the group. These tended to be around whether the course would suit them, and a slight feeling of nervousness at

meeting a group of people they didn't know. For some, fears were due to discomfort around being in the company of others with a diagnosis of MS, and in particular, those further along in their journey or with more obvious disability:

> "*I wasn't worried about meeting strangers, if you like, for the first time, or being in a group* [but] *I am a little bit uncomfortable in being with my own kind…Is this my future?*" (Mim).

There was a degree of 'othering', of not wanting to identify with the condition, along with resistance around - and fears to do with - associating with MS. Five of the nine participants voiced some concerns relating to fear of seeing their future self, reflecting the understandable experience of resistance to probable change, and suggesting a layer of ambivalence in approaching the group.

2. Finding my place

2.1 Comparisons with the rest of the group

While some recognised others' challenges as different, they also recognised proactiveness, resolve and determination of others, in this. There appeared to be something about the group experience which facilitated an understanding of the person beneath the condition, no matter how far they were in their personal MS journey. Katherine spoke about the positive element of this:

> "…*people who were older and less physical than me, they were adjusting and getting about… I think that reversed my previous experiences* [of being part of an MS group] *and I thought, well, you know, if someone who is more severely restricted than I am, can overcome challenges and do things…if they're making that effort and succeeding, then it should be easier for me, it's achievable*."

This was echoed by most participants, and some stated their surprise that this was their experience.

Another shared realisation was that despite many commonalities, everyone's MS was different, as Millie reflected:

> "*I thought it would be a group of people like me, looking for the same things I was looking for; they were all different. But the ones I remember most are the ones who were not like me*".

Differences weren't seen as negative, more like unexpected. Gaining an understanding of the nuances of the diagnosis appeared to be enlightening and helpful.

2.2. Group connection/support/dynamics

While every participant alluded to the individual nature of everybody's MS experience, they also recognised a common goal amongst difference, and a feeling that 'out in the real world' they might not have had the opportunity, or possibly the motivation, to form a bond:

> "*You know, in one sense we're a real odd bod group of people, you wouldn't put us together, d'you know what I mean?...But we met and bonded over some real commonality, and interestingly in a way, I don't think the commonality was MS actually, I think it was, I think it was deeper than that*" (Becky).

There appeared to be a shared understanding of grief, enforced change, and an impact created by something outside of themselves, that transcended day-to-day differences, and fostered a sense of closeness.

Participants in one group stated that some of this closeness was borne out of a sense of equality; a sense of mutual respect for each member's contribution. This may not have been experienced as strongly in the other group, and appeared to affect their experience of connection. Macsen, for example:

> "... [the dynamic] ...*was something that I struggled with a little bit*".

Mim similarly stated:

> "*...like any diverse group there might be a few people that you click with and others you can't stand, I mean, it's, that's just life really isn't it, MS or not…I had no connection with anyone else in that group to know how they found it, you know, even to ask them*".

Jill, on the other hand, who was a member of the same group, did benefit from connection:

> "*I think* [attending the group has] *helped me*…[with] *coming to terms with what we have... everything about the course actually, made me accept that I've got MS.* [The facilitator] *and the group, they made me sit back and think, well it's not just you Jill, there's other people going through this as well, that have difficulties and whatever, you know*".

There appeared to be powerful mechanisms underlying this theme, mechanisms that may have partly been due to the ACT strategies themselves, and to the process of acceptance in particular, which might have facilitated a bond, and a shared emotional processing of grief.

2.3. The online experience: the good, the bad, and the 'comfortable in my PJs'

Overall, there appeared to be more benefits to being online, than drawbacks. While Mim felt online working didn't facilitate connections, she acknowledged some benefits:

> "…*it doesn't drain my energies in the same way* [as face-to-face] *...it didn't feel quite as intimate as being with the people in the room* [but] *it felt more manageable* [because of that]".

The intimacy in this sense may have alluded to resistance around identifying with others with MS. Others spoke of the freeing sense of not being physically on show, suggesting that their physical condition – despite it being invisible in many cases – felt prominent to them.

Group members spoke about the levelling effect of being online, and how this window into people's worlds fostered connections:

> "*...it gives you a person in context…and there is something about that where you can possibly find something, you know, even if it's a book on my shelf where you think, oh yeah, you know, that you might sort of find something that kind of starts those links, I suppose, even from the first day*" (Becky).

Additionally, there were practical benefits:

> "*It's actually easier because I've just got to listen to the screen, you know; when you're in a circle say* [in person], *I might not be able to hear the person that's further away, so for me…I did prefer* [being online]" (Millie).

3. Course-related change (or not)

3.1. Adopting good habits

Gary felt the group built on strategies he was already utilising:

> "[the course] *got me thinking about things in a more structured way shall we say, what I should be doing and how to do things, whereas in the past I was just trying to do it*".

When it came to reflecting on course-related change, Macsen felt the group opened up possibilities:

> "*…I'm more living in the present as opposed to the past or the future, and it's made me more positive*".

Katherine talked about small changes making a big difference:

> "*I think I'd be in a much worse place now if it wasn't for the course, and simply because I think perhaps I would have shied away from trying things, I would have perhaps conceded unwittingly that things were beyond me, written off chunks of my life that I enjoy…this course helped me to come to terms with the fact that just little practical changes, made doing even significantly big things possible, without ruining*

them…you don't notice the bits that have had to change because you're still enjoying the bigger picture".

Katherine had been surprised at how practical the course was, and how this had impacted on her psychological wellbeing. Her reflections suggested a level of emotional processing, facilitated by attending the group. Felicity also spoke about the positive impact of adopting ACT strategies and how this affected her wellbeing:

"*I am a lot better at being present and realizing what's going on around me and not worry about the past, not worry about the future, which were those things that really made my life difficult in the past.* [The course] *made me less sad about the things that I can't do anymore and focus more on the really positive things... so that's, that's made a big difference, because they're not, well, I'm not so sad am I, so, it's all good*".

These experiences seemed to speak to the benefit of ACT skills learned as a result of attending the group, and of the benefit of being part of a group experience in general; the interactional group process seeming to support emotional processing, while the ACT strategies and course content encouraged a certain way of perceiving each individual's situation which helped them make sense of that processing.

3.2. In it for the journey

While there was a general feeling of benefitting from the course, there was also a feeling that benefits need 'topping up' in order to be maintained. John (who only engaged in one session of the ACT group, but had attended previous courses) stated:

"*So, having a course around here that helps for such-and-such a time is great, but it's not great that if after* [eight] *weeks you've got better, you've reached a level where you think 'oh great, fantastic, now you can go off and do it yourself'. But nobody ever does*".

John talked about the extra strength and motivation that maintaining benefits – without any additional help – required; the sense being that these were difficult to muster for someone with MS. Similarly, Felicity felt benefits were hard-fought and sometimes didn't last:

> "*...quite often I do courses more than once. Just to remind myself of them, and to build upon the memory*".

Everyone bar one participant talked about a desire for more time, in terms of the group. Some suggested that weekly sessions ran for longer, others that one subject was discussed over two or more weeks, while others suggested top-up sessions. While the experience of group connection was valuable for most participants and might have formed the desire for more time/sessions, participants observed that even without this they would have continued to attend the group, as the ACT strategies benefitted them.

4. Course feedback

4.1. Course content

Check-ins at the beginning of the session, would often over-run. Despite this, all bar one participant found them valuable, enjoyable, and inspiring. Check-ins frequently built on strategies from the previous session; participants would hear someone talk about doing something, and would consequently feel less stigma around doing it themselves: using a motorised scooter, for example.

With regards to values work, while Mim did not particularly enjoy check-ins and felt the course itself did not resonate with her, she too benefited from the realisation that:

> "*…the things I value as a person, that hasn't changed. You know, that is unchanged by illness and that was quite liberating and important, to find something that actually was unchanged*".

This was especially significant, as many of Mim's statements seemed to express a raw and visceral grief. In her realisation regarding the unchanged nature of values, she had some

respite from this, and a recognition that MS had not taken everything away from her. Values work appeared to have been useful to all participants:

> "*I'd never ever, ever thought about* [values], *like ever…but when you start thinking about it...you can see how important it is, and how many times* [in the past], *the things that you do that haven't worked* [were when I went] *against what those values were in the first place*" (Felicity).

In terms of feedback relating to course wording, Mim observed:

> "[practices talked] *about standing on your own two feet and walking, and I know that they are metaphorically meant, but…how that language and the imagery...grated with me...I'm acknowledging there are nerves in me that it's touching on, that I'm sort of reacting to, that maybe somebody else in the group was just, they're just metaphors aren't they, you know*...[but] *the able-bodied or the abled person's use of the imagery and the terminology, that, I found quite jarring*".

This was a valuable insight, and one again that seemed to contain much grief and a sense of being 'othered', which were felt keenly by Mim.

Felicity commented about the simplicity and utility of ACT strategies:

> "[the skills taught on the course] *all make complete sense* [laughs]…*when they're written down on paper you're like God, this stuff is just so simple, but we all know, in reality, it never actually is simple to do any of those things, otherwise we wouldn't have a problem*".

This echoed some of the comments around the energy and motivation required to maintain benefits.

4.2. Course facilitation

Becky stated, "*One of the*... [positives] *was just the excellent way in which the group was held and kept safe and given space*".

The facilitator would join in with check-ins, but Mim felt this was inappropriate:

> "*What I find difficult is the kind of, almost I'm one of you, stance by the facilitator. That is quite difficult, because actually, you're not one of us in that when they do a... check in, I noticed that the facilitator would answer the questions and sort of be part of the group like I'm one of you, but you're not one of us in this*".

Conversely, others commented about their appreciation of the facilitator joining in with check-ins; Katherine, for example:

> "*...it's not top-heavy, it's not someone preaching down to you, and you just sit there and listen and answer the odd question. It seemed to be more circular...more communicative...more participatory…I think it puts everyone at ease*…[it] *seemed more fluid and it encourages more discussion*".

This was an interesting insight into how the same process could cause such differing experiences.

4.3. Focused benefits

John attended one group: the second session. He felt that the course was more suitable to newly-diagnosed people, although not all newly-diagnosed people:

> "*...it wouldn't have been right for me when I got my diagnosis*".

He felt it did not suit someone who had been diagnosed for many years and had made their peace with their diagnosis. During a previous course, John felt that he, and others like him, had something to offer:

> "*I felt I could have been useful as a tutor, not actually running the course, but suggesting things, talking about my experience...".*

John reflected on his ability to give something back; rather than feeling 'othered' due to length of diagnosis, he felt his experience could help others with MS.

Participants suggested family-member groups, and structuring groups according to stage/length of diagnosis, in particular for newly-diagnosed people. But Becky cautioned:

> "*I think people who've just been diagnosed... are especially different…newly diagnosed people are a special case; I think they need treating very carefully and tenderly".*

Finally, Katherine echoed many of the other participants when she talked about what the course meant to her:

> "*Everyone's circumstances are different. Everyone's challenges are different and* [some are] *bigger than others. And everybody's inclination to tackle the challenges are different. But the benefits, the, the difference that can be made, the difference can benefit everyone…I don't want to sound melodramatic and say that it's life changing, but* [the course] *can, it can improve your life, improve the way you tackle the diagnosis, and move you in the right direction*".

It appeared that in general, the course was well received, felt to be useful in both a practical and psychological sense, and for most participants this translated to significant beneficial changes. Feedback relating to able-bodied language, and the differing experiences of group bonding and preference of facilitation style, was additionally valuable in light of future ACT groups, and were gratefully appreciated.

Discussion

This research added to evidence regarding feasibility and suitability of online ACT groups for people with MS, and attempted to capture the experience of participating in such a group, run by MS Cymru. The process involved in making the decision to participate, in forming a bond (or not) with the group, and in course-related change was explored. General feedback regarding course content and structure was also summarised, while processes involved in change and positive impact were considered.

Interviews, coding, and theme generation

Interviews were engaged and rich in terms of material. Participants were open and generous in their responses, reflecting on their MS journey from diagnosis to present day. Some tended to focus more directly on what was asked, digressing very little, but they too linked their diagnosis journey to their experience of the group.

Themes were relatively clear and coherent. Four themes were generated, each with two or three subthemes. The first encapsulated the process of making the decision to attend, and to keep attending. Within this were motivations for engaging (or not), as well as fears and discomforts around joining the group. The second theme involved 'finding my place'. This included subthemes relating to comparisons with other group members, becoming part of the group, and the experience of engaging virtually in said group. The third theme concerned course-related change and expectation of change. This concerned potential big impacts of small changes, and the need for ongoing support. The final theme summarised feedback on course content, facilitation, and ideas about alternative formats.

Group acceptability

Comments relating to acceptability tended to be focussed on the first two themes: 'Where do I sign? And do I want to...?' and 'Finding my place'. Contextual factors – some of which were evident from wider conversations around diagnosis - may have influenced the

way the group was experienced. The more negative responses were reported by one individual who felt themselves to be further advanced than the rest of the group, and another who expressed high levels of grief in her life; a common theme in chronic conditions such as MS (Sesel et al, 2021).

Perceiving ‘acceptance’ as having negative connotations such as giving up, or weakness, were associated with a less positive experience, in our sample. Previous research suggests that people who view acceptance as positive are more likely to gain more from ACT groups, and that their conversation will tend to be more positively focussed (Ford et al, 2018). The majority of participants talked about a positive change in focus as a result of attending the group and adopting ACT philosophies. These in turn, impacted on general wellbeing and QoL.

The subtheme ‘The online experience’, revolved around the acceptability of attending the group in an online forum. All study participants agreed that the online nature of the group facilitated attendance. Although ‘breaktime chats’ were not a feature, most participants felt they had formed a bond with other group members. Future groups might encourage group members to come back online while they have their break, to foster those informal conversations.

Participants also spoke of the benefit of not having to travel to a venue, and the added benefit of not being physically on-show. Body image difficulties connected to the diagnosis, are recognised in people with MS (Di Cara et al, 2019), which can further impact on QoL and readiness to engage in social activities. The apparent safety of the online forum appears to have reduced this discomfort for a number of group members, while practical concerns such as being able to hear all group members equally (which would be more difficult in person) were also appreciated.

Engagement and maintenance

Engagement and maintenance factors were concentrated in the first two themes. The subthemes ‘Comparisons’ and ‘Group connection/support/dynamics’ highlight the positive role of identifying with others within the group and of sharing a common goal (Borek et al, 2019). Moreover, bonding as a group has positive effects when group members feel a shared understanding of their condition (Cameron et al, 2018). This sense of identifying with other group members and of having a shared understanding, enabled the majority of group members to form a close connection; one which gave them a sense of belonging, despite their differences. The experience, for these people in particular, was enhanced by this connection, which may have facilitated their engagement, but their connection may have also been facilitated by the ACT components of the course. More research would be needed to clearly understand the interplay of these components, but it seems reasonable that both had a part to play in participants’ favourable view of the group, and their ability to translate this into practical and psychological benefits.

Early non-attendance is strongly associated with dropout (Hawker, 2007). The participant who disengaged after one session (the second overall session), had not been able to join the group for the first session. Introductory session attendance may have been pivotal in creating the bonds that most of the group had begun to forge, therefore he may not have felt the same level of investment in the group.

Two people described not experiencing a bond with other group members, to varying degrees, one of whom did not identify with the condition, and therefore did not appear to share a common goal. The other person did identify with the condition – difficulties around group connection were due to other factors - and discussions held during check-ins resonated with them, and were perceived as useful. This person, therefore, was able to gain some benefit in terms of practical help and a change in perspective. Additionally, group members

made suggestions in the final subtheme ‘Focused benefits’, regarding ACT groups according to stage of MS, and for family members, which would promote a stronger sense of shared identity and engagement.

Course-related change

The third theme and its subthemes – ‘Adopting good habits’ and ‘In it for the journey’ – explored the concept of course-related change. While there was an exception, most of the sample engaged with elements of the ACT philosophy, and this seemed to facilitate some degree of positive change. The catalyst for this may stem from ACT’s focus on promoting psychological flexibility (Harris, 2019), the degree of which predicts change in therapy (Brandon, Pallotti, & Jog, 2021). Psychological flexibility is closely related to resilience (Gentili et al, 2019) and appears to mediate positive change (Trompetter et al, 2015; Lin et al, 2018; Puolakanaho et al, 2020), partly by reducing avoidance (Younesi et al, 2020).

Mindfulness practices were viewed favourably by all bar one of our sample, and continued to be practiced after the group had come to an end. Mindfulness- and acceptance-based interventions have been successful in improving quality of life in MS (Han, 2021), and this appears to have been the experience of the ACT group, in general, who utilised ‘being in the moment’ strategies to improve everything from eating habits to being around family, to going for a walk.

A surprising element for some was the level of practical help gained from the group. This fed into emotional processing, and was felt to further enhance change. It was difficult to unpick whether this was due to a group effect, or facets of the ACT philosophy, but the sense was that it involved a mix of both.

General feedback and suggestions

The final theme contained feedback pertaining to the course, with subthemes divided into content, facilitation, and further suggestions. Service-users have successfully co-

facilitated ACT groups previously (Butler et al, 2016; O'Dell et al, 2020), which John suggested in his feedback. Co-production with people with MS, would enable group developers to focus on and develop the group further, which would also assist in developing appropriate metaphors.

Group members also spoke about the need for ongoing support to maintain positive change. Previous studies have reported benefits from booster sessions (Pakenham et al, 2018). Ongoing support often depends on funding, but participants felt that, given how much they appeared to have gained from the course, continued support was an important consideration.

Check-ins were seen as useful and valuable. This is consistent with Synnot and colleagues' (2014) research, which illustrated the importance of sharing experiences and knowledge about the condition, and how helpful this could be. While check-ins were almost universally seen as helpful, a number of participants alluded to them being time-consuming.

Limitations.

Although the present study seems to attest to the utility and acceptability of the ACT course for people with MS, there are several limitations. Arguably the most important is potential bias within interpretation and reporting of the research. While the second author supplied insights, and both the first and third authors were mindful of their investment in the methodology, underlying bias may remain.

One of the aims of the study was to understand whether ACT concepts, or the experience of being part of the group, was key to subjective change. Asking participants what they felt was at the root of this change was limited, as many of them did not necessarily know the answer. While group members alluded to both being instrumental in varying degrees, it has not been possible to clearly define underlying mechanisms. Some of this might become

clearer if comparisons are made between ACT-based groups, and groups utilising different methodologies, for example CBT, mindfulness-based, compassion-focussed, etc.

While this was a small to medium sized study according to Braun and Clarke's (2022) thematic analysis guidelines, gaining a wider breadth of experience in terms of engagement, would have been beneficial. The present study was grateful for the involvement of a participant who disengaged from the group, and from someone who did not engage with the methodology, albeit that they attended every session. These were lone voices, and hearing more alternative viewpoints would have enriched this study further.

Furthermore, data analysis was carried out between four and six-weeks after the last group session had taken place. This may have impacted on ability to recall specific factors, but was also required in order to assess whether participants were utilising ACT techniques after the group had ended.

Despite its limitations, it is hoped that the present study will contribute to qualitative research into online groups for people with MS.

Conclusion

The present study contributes to a growing body of evidence into feasibility and efficacy of ACT for MS. It suggests that ACT in an online format, is acceptable to participants, and is seen as effective in the main. ACT strategies appear to be important, as well as group connection, but which has most influence, is less clear. This study illustrated the possibility of life-changing adjustments as a result of a combination of adopting an ACT perspective and attending a group with people facing similar fundamental challenges. In conclusion, the general experience of attending the group appears to have been a positive one, and feedback was valuable and insightful.

Funding

The third author was employed to develop and facilitate the ACT course. Neither author received payment for the research and write-up of this study.

Declaration of conflicting interests

Attempts to address the third author's involvement in developing and facilitating the ACT course are illustrated in the method section. Additionally, the second author has no affiliation with ACT, and neither he nor the first author had any involvement in the development and facilitation of the course.

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Appendices

Appendix A

Semi-structured interview schedule

Opener: What made you join the group? What thought process did you go through to make the decision to attend? What were your expectations (if any) about the group? How did they compare with the reality?

What was the best part of attending the group? What helped you to keep going to them?
AND/OR what was it about the experience that made you feel less inclined to attend?
Was there anything about being part of an online group rather than face to face? Do you think that was helpful to you? Why?
OR why not?

Were there any practical elements of the group that you used day to day? What were they (if there were)? How were they useful to you? Do you still use them now? What do you think could have been useful (if there weren't any elements)?
Did you feel a change in the way you approached daily life due to taking part in the group? If yes, how? And what do you think caused it?

What would you have done a little differently? Is there anything you felt should have been included but wasn't? Or something that was that shouldn't? How would it have been helpful? How was it not so helpful?

At the end of the group, did you think any differently about your MS? In what way?
AND/OR do you think that attending the group should have changed the way you thought about it?
Was there a 'message' you took from the things that you talked about in the group? If not, what did you take from the group, if anything?

Closing: so that's pretty much all I have to ask. Is there anything else you'd like to say that I haven't asked? Or any questions you'd like to ask of me?

Appendix B

PARTICIPANT INFORMATION SHEET

Rhaglen Seicoleg Glinigol Gogledd Cymru
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Study title: Experiences of attending an MS Cymru online ACT group.

Invitation to participate in a research study

We are inviting you to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve. We would like you to take the time to read the following information carefully and to discuss it with others if you wish. Please ask us if there is anything that is not clear or if you would like more information. You can take as long as you like to decide whether or not you want to take part.

What is the purpose of the study?

In this study, we want to hear about your experiences of attending the Acceptance and Commitment Therapy (ACT) group, run by MS Cymru. The study will explore which components, if any, of the group were the most useful. We will ask you about your experience of attending the group, including whether you found anything helpful and/or unhelpful and the reasons for these. Your views will help the facilitators and MS Cymru, develop the group further.

Why have I been asked to take part?

We are inviting you to take part because you have attended a group run by MS Cymru. Even if you only attended a very small number of sessions, we're interested to hear about your experiences.

Do I have to take part?

It is up to you whether or not you want to take part. If you decide to, we will give you this information sheet to keep, and we will ask you to sign a consent form. After agreeing to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time - or not to take part - will not affect your relationship with the MS Society, nor will it affect your rights in any way.

What will I be asked to do?

If you decide to take part, the researcher, Dr Pam Martin-Forbes, will make arrangements to meet with you; this could be in person or via an online platform such as Teams or Zoom. This meeting will last approximately one and a half hours, and – with your permission – will be

recorded. Pam will type up your conversation together. This is called transcribing, and the full typed up interview is a transcription.

All identifiers will be anonymised (we won't use your name or any other details which give clues about who you are). The recording will be deleted as soon as research is complete, by the end of August 2022. The appointment can be spread over two visits. If you get tired during the interview, please tell the researcher you would like to stop, and they can arrange to see you again, to finish the interview. You can also choose whether the researcher talks to you in English or Welsh. If you are a Welsh speaker, the researcher can carry out the interview in Welsh if you prefer.

Who are the research team?
The researcher who will be meeting with you to carry out the interview is Dr Pam Martin-Forbes. She is a Trainee Clinical Psychologist, in her final (third) year of training. Pam will be Supervised by Dr Mike Jackson, (Research Director) and Dr Elizabeth Burnside, (Academic Director) from the North Wales Clinical Psychology Programme, Bangor University. Since Elizabeth has also been the group facilitator, she will ***not*** be informed about whether you take part in the research and will not read any interview transcripts nor listen to recordings. We hope that this will enable you to speak freely about your experiences of the group. Dr Jackson will read some of the interview transcripts to assist with the analysis. Both supervisors will be involved with the final report.

What are the possible disadvantages and risks of taking part?

We do not think that taking part will involve any disadvantages or any specific risks to you. Some of the questions might lead to you talking about your health and well-being; in some circumstances, this may mean that you think about things that might be upsetting. If this happens, the researcher will try to make sure that you are not left feeling upset. You will be able to contact the researcher afterwards if you need to.

What are the possible benefits of taking part?

You may find it interesting and enjoyable to talk with the researcher. Additionally, the information you give us will help us understand more about the experience of being part of the group.

Will I be paid for taking part in the study?

We will give you £30, as a token of appreciation for your time and contribution.

What if something goes wrong?
If you are unhappy or dissatisfied about any aspect of the study, we would like you to tell the researcher in the first instance, so that they can try to address your concerns and find a solution. You can also talk to the researcher's supervisor, Dr Mike Jackson, Research Director, North Wales Clinical Psychology Programme, Bangor University, Bangor, Gwynedd LL57 2AS. Tel: 01248 388746, email mike.jackson@bangor.ac.uk

If you prefer, you can talk to Dr Elizabeth Burnside, who facilitated the group you attended. She is also Pam's supervisor, and Academic Director at the North Wales Clinical Psychology Programme. Tel: 01248 382204, email e.burnside@bangor.ac.uk

If you are not satisfied with our response, you can make a complaint to Dr Huw Roberts, School Manager, School of Human and Behavioural Sciences, Bangor University, Bangor, Gwynedd, LL57 2AS. Email: huw.roberts@bangor.ac.uk

How will you use information about me?

The data you supply us will be processed in accordance with data protection policies and will comply with the General Data Protection Regulation (GDPR) 2016. We will keep information that you give us - such as your name, contact details, and date of birth – securely and carefully. Your personal information will always be kept separately from your recordings and interview transcripts, so that that you cannot be recognised from what you have told us.

Your information will only be used to carry out the research or to ensure that the research is being done correctly. We will change your name and any other identifying information when we transcribe (type out) your interview, to protect your identity. We will keep all information about you safe and secure.

Once we have finished the study, we will delete your recording. We will keep your interview transcript so we can check it if necessary. This will be stored securely for a maximum of 5 years. We will write our reports so that no-one could recognise you as someone who took part in the study.

What are my choices about how my information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep the information you have given us up to that point.
- If you agree to participate in this study, you will have the option to participate in future research using your data saved from this study.

Where can I find out more about how my information is used?

You can find out more about how we use your information by:

- Asking the researcher or contacting us 01248 388719
- Contacting Bangor University's Data Protection Officer, Gwenan Hine, Head of Governance and Compliance, on 01248 382413 or gwenan.hine@bangor.ac.uk
- Looking up our data protection policy online at https://www.bangor.ac.uk/governance-and-compliance/dataprotection/documents/Data%20Protection%20Policy%20approved%20v7.1%20July%202021.pdf

Will my taking part in the study be kept confidential?

All information that we collect about you during the course of the study will, in normal circumstances, be kept strictly confidential. The only situation in which we might need to share information about you with other professionals is if the researcher observes or hears anything that causes grave concern about your safety or well-being, or someone else's. If this happens, the researcher has a duty to inform an appropriate professional. We would make every effort to explain to you why we need to share this information before doing so.

What will happen if I don't want to carry on with the study?

You can withdraw from the study at any time without giving a reason. If you withdraw from the study, it will not affect your relationship with the MS Society and will not affect your rights in any way. We will continue to use the information we collected before you decided to withdraw, as what you tell us will have been anonymised (anything that identifies you as you will have been taken out).

What will happen to the results of the research study?

We will present the results at scientific conferences and publish them in scientific journals when the study is complete. We will send you a report of the results if you would like to know about them.

Who is organising the research?

The research project is led and funded by the North Wales Clinical Psychology Programme (NWCPP). Funding covers the running costs of the research project. The researcher does not receive any personal financial benefits as a result of the study, but it will form part of their thesis for the qualification of Doctor of Clinical Psychology (D.Clin.Psy).

Who has reviewed the study?

All research carried out by Clinical Psychology trainees is reviewed by an independent group of people, called a Research Ethics Committee, to protect participant safety, rights, well-being and dignity. This study has been reviewed by the School of Psychology Ethics Committee, Bangor University.

Who can I contact for further information?

For more information, please contact:
Dr Pam Martin-Forbes, North Wales Clinical Psychology Programme, Bangor University, Gwynedd LL57 2AS.
Telephone: 01248 388719
E-mail: p.martin-forbes@bangor.ac.uk

Thank you for considering taking part in this research study.

Appendix C

Consent form

Rhaglen Seicoleg Glinigol Gogledd Cymru
Ysgol Gwyddorau Dynol ac Ymddygiad
Adeilad Brigantia, Ffordd Penrallt
Bangor, Gwynedd, LL57 2AS

Ymchwilydd: Dr Pam Martin-Forbes
e-bost: p.martin-forbes@bangor.ac.uk

PRIFYSGOL BANGOR UNIVERSITY

North Wales Clinical Psychology Programme
School of Human and Behavioural Sciences
Brigantia Building, Penrallt Road
Bangor, Gwynedd, LL57 2AS

Researcher: Dr Pam Martin-Forbes
e-mail: p.martin-forbes@bangor.ac.uk

CONSENT FORM

Title of Project: Experiences of attending an MS Cymru online ACT group.
Ethics System Reference Number: 2021-16999

I confirm that I have read and understood Participation Information Sheet dated 25/10/2021 version 1.0 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason. I understand that if I withdraw, this will not affect my relationship with the MS Society nor my legal rights in any way.	☐
I understand that if the researcher hears or observes anything that causes serious concern about my safety or well-being, they have a duty to inform other professionals about this.	☐
I consent for voice recordings to be taken during the study for use by the study team only (my recording will be deleted after the interview has been transcribed).	☐
I consent to verbatim quotes being used in publications; I will not be named, and details that might identify me will be removed.	☐
I agree to take part in the above study.	☐
OPTIONAL: I give permission for the information collected about me to be used to support other research in the future and understand that it may be shared anonymously with other researchers.	☐

Name of Participant	Date	Signature
_____	_____	_____
Researcher taking consent	Date	Signature
_____	_____	_____

Appendix D

ACT group flyer and intervention description

Acceptance and Commitment Therapy – ACT- Online 8 week group

What is ACT?
Acceptance and Commitment Therapy is usually pronounced as a single word – 'ACT'. The aim of ACT is to help people to find more meaning and fulfilment in everyday life, whilst managing inner experiences such as difficult thoughts, emotions and physical struggles more effectively. ACT is an evidence-based intervention which has been shown to be helpful for people living with long term health conditions, people with a wide range of emotional health concerns and as an approach to general wellbeing. In short, most human beings might find ACT helpful!

The core elements of ACT can be distilled to three main areas:

Opening up: Learning to drop the struggles with difficult thoughts and feelings that can sometimes hold us back.

Being aware: Learning to pay attention to the moment more often, to learn from the wisdom of your own experience and to appreciate life more fully.

Take action: Getting a better idea of what really matters to you and challenging yourself to do more of that, more often.

What the group involves
The 8 week ACT group offered by the MS society involves attendance at 8 weekly online sessions using zoom, each one lasting an hour and a half. You'll join a group of around 10 - 12 other individuals, which is a great way to learn. Sharing experiences, ideas and weekly tasks makes for a richer experience and people often comment on how helpful it is to connect with others in similar circumstances when learning new skills.

Each week a new topic will be introduced and discussed, with in-session activities to bring ideas to life. You'll be encouraged to set yourself a new small challenge each week to do between sessions, with group members and the facilitator providing encouragement and support to each other.

When it will happen?
The group will start on Thursday October 7th with the option of attending either a morning or evening stream (both will be running at the same time). You're asked to choose one stream, morning or evening, and stick with that one throughout the 8 weeks.

Who is the facilitator?
The group will be facilitated by Dr Elizabeth Burnside. Elizabeth is a Clinical Psychologist and peer reviewed ACT trainer, with over 12 years' experience of delivering ACT training and therapy. As well as working in private practice, Elizabeth works for the North Wales Clinical Psychology Training Programme at Bangor University.

Appendix E

ACT group protocol MS Cymru

Session one

- Icebreaker and introductions
- Main ACT topic: Introduction to the choice point model and values.
- Values Exercise
- Choice point model
- Weekly challenge – each participant to choose one action to engage in over the next week that is important to them, but something they know they can do.

Session two

- Recap of values
- Check in on weekly challenges
- Acceptance version one
- Common elements of grief and change
- Acceptance through values
- Values exercise
- New weekly challenge

Session three

- Recap
- Check in on weekly challenges
- New topic – being present/mindfulness
- Choice point
- Exercise
- New weekly challenge

Session four

- Recap
- Check in on weekly challenges
- Mindful breathing
- New topic – acceptance II willingness
- Exercises and metaphors
- Choice point
- New weekly challenge

Session five

- Recap
- Check in on weekly challenges
- Noticing/Mindfulness
- New topic – Thinking and defusion
- Metaphor
- Exercise
- Choice point
- New weekly challenge

Session six

- Recap
- Check in on weekly challenges
- Mindfulness
- Topic: Defusion continued
- Exercises
- Review of ACT so far
- New weekly challenge

Session seven

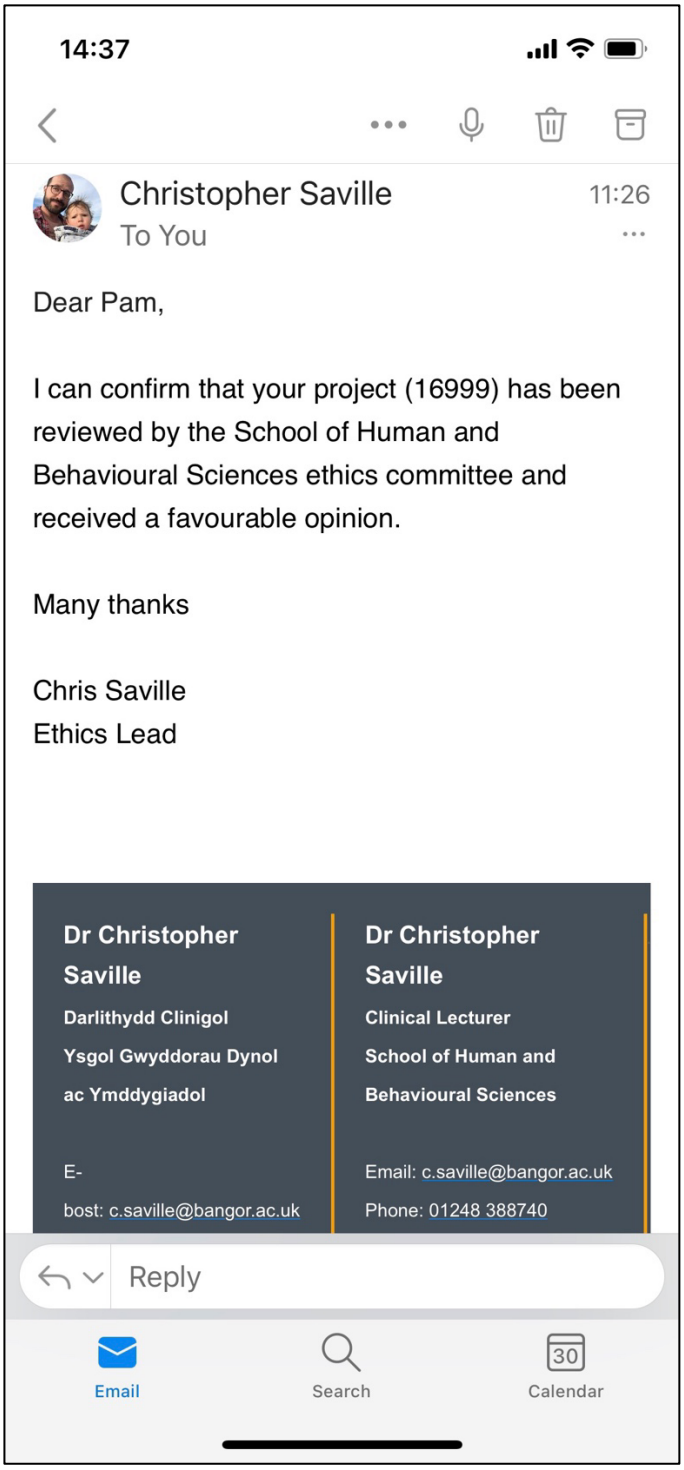
- Recap
- Check in on completion of review sheets and actions
- New topic. ACT and the self
- Exercise
- Metaphor
- Choice point
- New weekly challenge

Session eight

- Recap
- Check in on weekly challenges
- More on self as context and observer self.
- Metaphor
- Exercise
- Celebrate ending
- Facilitate any suggestions that group members keep in touch

Appendix F

School Ethics Permission Screenshot



Appendix G

Excerpt from participant transcript

Transcription	Codes	Themes
10:42:42 But the, this this course helped me to come to terms with the fact that just little practical changes made doing even significantly big things possible without ruining them without, without me thinking that you know that the the event that I'm attending	Small changes big benefits Possibility	Small adjustments I'm still me Positives of the course
10:43:01 or the tasks that I'm doing that it's now so hard to overcome that it can't be done or is ruined by the condition.	Circumnavigating the condition	Adopting good habits
10:43:19 It was just coming to terms with the fact that it only takes little changes. And then you can enjoy everything that you used to do.	Coming to terms Continuation of life	Acceptance as necessity Small adjustments
10:43:24 But in such a slightly different way that it didn't detract from doing it, it didn't make you think that the, the adjustments were too much of an effort to still do things.	Doing things differently	Small adjustments
10:43:35 It was just some sort of, you know, just, just a little change, and you don't notice the bits that have had to change because you're still enjoying the bigger picture. So, it starts off as a practical assistance, and really came at the right time for me, to be a great weight off my mind it was, sort of a great	Small changes, but benefit of maintaining life	I'm still me Small adjustments
10:44:04 psychological boost		
10:44:09 I think I'd have been intolerable had I not had that you know, I mean, it would have changed my personality to a much more miserable and much more.	Without course things would be different	Grief of change I didn't choose this
10:44:22 erm, I don't want to say depressive, but it would have been.		
10:44:28 I would be noticeably different I'd have been noticeably more miserable I'd have been noticeably, but when it came along at just the right time to help, so it really has helped.	Life without the course Came along at the right time Course helpful	Course feedback Change of practice
10:44:40 It sounds like there would have been a lot of frustration there		
10:44:44 Definitely.		
10:44:47 Erm, I just wrote down now, because I just remembered that you were saying that in the short term that you found it helpful. Erm, Do you think that there's anything about it that you'll use kind of from this point forward that, that's just going to be part of your everyday life?		
10:45:05 I think it's changed my.		
10:45:13 It's changed my expectations of living with the condition, from being, I said, I think I, from the early days, the medical help I got from, from the chap that gave me the diagnosis.	Changed expectations of living with MS	Positives of the course Change of practice?

Appendix H

Excerpt from (another) participant transcript

Transcript	Codes	Themes
10:43:33 And maybe because it was on an online platform. It didn't feel quite as intimate as being with the people in the room, it felt more manageable I know that's.	Benefit of lack of intimacy	Dynamics of a virtual group The online experience
10:43:46 I find that interesting because we talk about the disinhibiting effect actually of being online you would think would encourage people to overshare because they're in their own environments and they feel comfortable, but actually it didn't seem to work	Unexpected result of online interaction	Dynamics of a virtual group The online experience
10:43:58 that way.		
10:44:03 That was a positive thing?		
10:44:06 Yes, it was just basically another group of people.	Just like any group of people	Comparisons
10:44:10 Yeah, yeah.		
10:44:12 How about your expectations in terms of the material.		
10:44:18 So, you'd said about how jarring the title was, how did the actual content...		
10:44:27 How did you find that in terms of the reality of the course? *Okay.*		
10:44:32 I did wince a bit as soon as the mindful word came up.	Resistance to mindfulness	
10:44:37 Mindfulness is not the panacea of all ills. For some people it works really well and they benefit from it. Not everybody. I don't find passive mindfulness, at all helpful so that grated, and I felt right.	View that everyone sees mindfulness as the answer	Course feedback
10:44:52 Okay, I just need to grit my teeth and get on with this, and I've found this before, with other groups that I've been in using mindfulness, and if I can give you a comparison really, if you live with tinnitus.		
10:45:07 They say you manage it by actually hearing through the tinnitus so you don't focus on the tinnitus now living in a damaged body, I have a lot of neural tinnitus.	Mindfulness turning the spotlight on damaged body	My damaged body
10:45:18 I get a lot of buzzing and crackling. If I start doing a body scan.	Ditto	
10:45:25 I'm tuning into all that neural tinnitus. And it can be really quite overwhelming and the feeling is of grief, because my body is shouting at me, I'm damaged I'm damaged, I'm damaged, and you're focusing in when I do a body scan, I'm actually, in turn, going	Mindfulness turning the spotlight on damaged body Grief	My damaged body Need for external focus
10:45:43 and listening to my internal narrative which is always buzzing and crackling and damage and what doesn't work.	Ditto	My damaged body
10:45:49 And I really don't like that.		

Appendix I

Excerpt from (a third) participant transcript

Transcript	Codes	Themes
16:04:10 So there are problems swallowing, partly because I don't, I'm not actually thinking about what I'm doing when I'm eating, and I'm just shoving it in watching telly or something [unclear] properly then I swallow too much then I start choking but because now I have to be more present, and you know	Practical improvement Being present Health benefit	My damaged body
16:04:30 present when I'm eating, which has therefore reduced my choking, because it has happened many times, it does happen sometimes, you know, but not necessarily because of anything.	Positive change	Group encouraging new habits
16:04:43 whereas before it was mainly because I wasn't slow enough and wasn't present enough to realize what I was doing.	Being present	
16:04:50 Yeah,		
so that's really helpful, actually.	Helpful	Positive feedback
16:04:56 Yeah.		
16:05:04 So I suppose I'm getting the impression that it's helped sort of emotionally, and, and, quality of life kind of things, and maybe physically?		
16:05:13 Definitely, because I think we, we don't always realize how intertwined the two things are. So, for example, you feel, one of your values is, one of my values, is to be fit and more healthy and going for a walk is encompassing that, is one of the things that I can do.	Values practice	Values work
16:05:34 But quite often, we'd go for a walk, with me, we will go for a walk.		
16:05:39 And we'll be... even if I was on my own I'd be thinking about stuff in my head. Not really concentrating and I couldn't tell you what was on my walk, but I'd be more present now.		Course-related change
16:05:50 I spend more time looking at actually where I'm going. And really looking, just looking, so looking at plants, or looking at buildings, and it's amazing the things you've never seen before in the neighbourhood.	Change of practice More present Positive impact	Group encouraging new habits
16:06:02 You know, I was surprised at actually the things that I did realize once you just, once you just stopped your brain a little bit. Just keep focusing on stuff, not even everything, just rummage around in there, but my head's very much like that just lots of stuff going on. So being present definitely has more of a focus on helping me physically.	Surprise at positive impact Being present	Course-related change

Chapter 3

Contributions to Theory and Clinical Practice,

Followed by reflective commentary

Contributions to Theory and Clinical Practice

This final chapter will discuss implications of both the systematic review findings and empirical study results, in terms of research and clinical practice. It will conclude with reflections around the experience of carrying out these studies.

The literature review explored a process with possible wide-ranging implications for quality of life (QoL) and wellbeing in people with MS, while the empirical study sought to understand processes around engaging in a programme that could also impact on QoL and living well with the condition, from a psychological perspective.

Systematic review

Menopause – a process of ageing - was described in one early publication as "an inevitable living decay" (Wilson, 1966, as cited in Atkinson, Carmichael & Duberley, 2021, p.660). While menopause is no longer talked about in quite such unhelpful terms, it arguably remains a negatively perceived and medicalised issue in Western culture (Namazi et al, 2019). While it appears to be generally viewed with some ambivalence in South Asian (Singh & Sivakami, 2020) and African cultures (Ande et al, 2011; Hall et al, 2007) this is in contrast to East Asian (Shea, 2020) and Arabian cultures (Alharthi et al, 2020), where menopause is viewed with acceptance. In the UK specifically, menopause remains somewhat of a taboo subject (Beck, Brewis & Davies, 2018). Recently, matters of menopause gained much needed recent attention with the televising of Davina McCall's Channel 4 documentary: Sex, Myths, and the Menopause (Sands, 2021), normalising a subject that has often been the butt of mother-in-law jokes and subject of shame.

While there appears to be a slight rise in interest in, and education around, menopause in general, less is known about the effects of menopause on autoimmune conditions such as Multiple Sclerosis (MS; Christianson, Mensah & Shen, 2015). Our review sought to add to the evidence-base regarding menopause, and specifically, the potentially additive impact of

menopause on quality of life and wellbeing for people with MS, while drawing attention to how few studies appear to investigate this from a psychological perspective.

Implications for future research

Previous reviews of MS and menopause tend to focus on medical and/or physiological impact (e.g., Karageorgiou, Lambrinoudaki & Goulis, 2020, and Midaglia et al, 2022). Our review appears to be the first investigating this in terms of a dual-impact of menopause for people with MS: general effects of menopause on psychological wellbeing, along with added detrimental effects of reduction in oestrogen causing physical impact and deterioration, which further impacts psychological wellbeing. The review therefore adds to those voices requesting more research be done into this potentially impactful matter.

The review also aimed to highlight the paucity of research into psychological aspects of menopause in MS and other autoimmune conditions. Autoimmune conditions are largely researched from a biomedical perspective, with significantly less emphasis on psychological impact. Indeed, none of the papers included in the final review explored effects of menopause and inflammation on MS from a solely psychological perspective. Furthermore, papers in the initial screening process, including those that were included in the final review, were published in journals with a primarily medical focus. The review hoped to correct this in a small way, by approaching the subject from a psychological perspective.

Implications for clinical practice

Highlighting specific difficulties around menopause for people with MS, will hopefully emphasise the importance of not only recognising these difficulties, but also treating them if appropriate. Routinely offering physical/medical treatment, in the form of hormone replacement therapy (HRT), might alleviate potential additional psychological burden brought on by increased severity of physical symptoms. This could protect against decline in functioning, and added negative impact on wellbeing and QoL. It is also hoped that

review findings will highlight the potential additional need for psychological therapy for people with MS who are approaching menopause, as well as those who are post-menopausal.

Alerting clinicians to the need to be vigilant with regards to identifying possible menopause-induced difficulties for people with MS, is particularly important, especially in the face of diagnostic overshadowing: the assumption that all symptoms are attributed to one health condition (Iezzoni, 2019). In this case, clinicians may overlook potential additive effects of menopause, and accredit all difficulties to MS itself, and therefore see them as untreatable. These considerations are also pertinent to other autoimmune conditions, such as Lupus, rheumatoid arthritis, type 1 diabetes, myasthenia gravis, coeliac disease, pernicious anaemia, and psoriasis (Marrack, Kappler, & Kotzin, 2001).

Empirical study

The empirical study explored the experience of nine people with MS, who attended an online ACT group run by MS Cymru. The study utilised qualitative methodology, namely thematic analysis. Main aims of the study were to investigate whether the group was acceptable and ultimately useful to those that attended, and to try and understand some of the mechanisms around making the decision to attend and keep attending (or not), the experience of being part of the group, and how this impacted on QoL and wellbeing.

ACT strategies were perceived as useful, enabling positive change in many cases. The online format facilitated attendance, and brought other practical benefits such as removing the need to travel, as well as other factors such as illness-induced lack of confidence, possible mobility issues, and reducing self-consciousness around physical factors. While components such as in-person break-time conversations and catchups had not been possible, most attendees formed a close bond with the rest of their group regardless. Participants commented about practical elements of the course, and how these, in turn, helped psychologically. Small

changes were seen to have a big (positive) impact for many, and ACT philosophy was embraced by most.

In order to investigate issues of engagement and attrition, the invitation to participate was extended to all who attended the course, irrespective of number of sessions. One participant attended one session of eight, and gave valuable insights into factors around engagement, suggestions around groups for people in a particular stage of MS, and co-facilitating/co-producing similar groups in future. The ACT philosophy did not resonate with one member of the group, and they too gave enlightening and insightful feedback about their experience.

Implications for future research

This study contributed to the qualitative evidence-base around acceptability of online ACT groups for people with chronic conditions, autoimmune conditions, and neurological conditions; specifically MS. It also investigated the utility of ACT for people with MS, which in turn might aid understanding regarding other long-term and neurodegenerative conditions. It will hopefully inform future research pertaining to the mechanisms behind successful group engagement, in a virtual forum in particular.

The empirical study also attempted to understand some of the emotional processing involved in acceptance of a chronic and degenerative condition such as MS, and factors associated with QoL. The study may shed light on whether ACT components may have encouraged psychological flexibility in particular, this being a core component of the philosophy (Jenaabadi & Hosseini, 2020). While it was not possible to pick apart which features – the content, or the group experience - were the most salient in terms of this process, the empirical study has attempted to add to some of the understanding around this.

Implications for clinical practice

In terms of clinical practice, the empirical study attempted to raise awareness around online group dynamics, and their role not only in engagement, but in maintaining that engagement. This will hopefully be beneficial to the creation and development of effective group interventions, which might utilise some of these mechanisms in order to foster positive experiences for those undertaking such groups.

Additionally, the empirical study sought to understand what participants require from online ACT groups, and how best to serve people with MS – and other autoimmune, chronic and/or neurodegenerative conditions - to utilise strategies embedded in the course. Features such as appropriate language – metaphors and practices which take into account disability, which are not phrased from an able-bodied perspective – may help tailor ACT group interventions further.

Reflective commentary

"I may not have gone where I intended to go,

but I think I have ended up where I needed to be"

The Long Dark Tea-Time of the Soul, Douglas Adams

Just into the second year of training, I became aware of a chronic sense of tiredness, which became omnipresent exhaustion, affecting me physically and cognitively as the months went by. I was desperate for bed by 7pm, and wiped-out at the weekend. Eventually, blood tests confirmed low ferritin levels. By this point, my research – the planned empirical paper as well as the systematic review - was not only *not* coming along but was too late to commence. A couple of potential studies looked possible, and at what felt like the eleventh

hour, I was contacted about the aforementioned research. It fitted my interests, and I grabbed it gratefully with both hands. At that point, it looked like I might need extra time added to the course due to how behind I was. A temporary prescription of ferrous fumarate and some bloody-mindedness allowed me to forge ahead; I was too busy *trying* to do rather than questioning whether I *could* do it or not. Once I'd built a head of steam, a couple of issues raised their head and the research and the empirical study in turn, looked like they might fall through; I was facing the daunting prospect of starting again, which would put me back even further in terms of the academic component of the course. Luckily, things quietly and quickly fell into place in both cases, and I was able to navigate each roadblock with a mixture of detours and assistance.

Writing up has been a heady mix of enjoyment and frustration, and firsts: my first systematic review, and my first qualitative piece of research. The systematic review initially felt overwhelming, but with the help of a good textbook, and interest in the subject, it's been taxing but enjoyable. My previous research idea (that didn't get off the ground due to all the tiredness) revolved around perimenopause/menopause. This possibly primed me to spot that there appeared to be unique difficulties relating to these, in people with autoimmune disorders such as MS. I had discovered this while researching MS generally, and saw my opportunity to explore it from a more psychological perspective than most of the papers I had read while researching.

Regarding the empirical paper, I have always held a curiosity and a readiness to engage in qualitative methodology - I have carried out several qualitative interviews for various studies - but I never had the opportunity to use this methodology for my own research. While I felt it would be a good fit for me, I feared it might be a bit highbrow, overly-philosophical, and complex. And as so often happens, previous supervisors adhered to quantitative methodology, therefore, so did I. While it is true that I have, indeed, grappled

with understanding epistemology and ontology (despite having studied philosophy for two years of my undergrad psychology degree!), the experience of meeting participants, carrying out interviews, and (surprisingly) of coding and working with the ensuing transcripts has been enjoyable, humbling, and enlightening.

The people that participated in the study were open and generous with their responses; they often gave me more than I asked for. Most if not all, told me something about the process of diagnosis, some of their daily trials and tribulations, as well as their experience of attending the ACT group. It led to a rich and full experience for me, and despite my own non-MS diagnosis status, I felt it was easy to connect with each and every participant. There were common themes, some of which were instantly evident, even at the interview phase. Others were more subtle, and came from re-visiting the transcripts, getting a sense of the person, and putting all their experiences together. I found this 'piecing together' a surprisingly natural process in that I enjoyed the detective work, which in my novice state felt akin to a series of formulations, in some senses. I was surprised also at how easily the narrative flowed, and how I enjoyed reflecting on my own 'place' in that narrative.

As is evident in the empirical paper, there was a general feeling that the ACT group had been beneficial, for all bar one person. I was pleased that this person felt they were in a safe enough space to be honest and open, and although I sometimes noticed my own resistance at some of their comments, I also felt I understood facets of the underlying narrative and therefore empathised with them.

Given the overall positive response, I was also aware of my own sense of relief that my favoured therapeutic approach seemed to have been not only received well in the main, but also that it was helping people to change aspects of their life; it was making a real difference. I noticed some 'need' to report this in my analysis, so I ensured that I regularly

brought myself back to the requirement of allowing the data to do the talking in order to address my bias; this was their story, I was merely the storyteller.

I also noticed a sense of wanting to show respect to everyone who gave their time by allowing as much of their own words to be heard, as possible; if people were willing to help me with the research, then the least I could do was include their comments in my work. Given the restrictions of word count, I found myself struggling with balancing this with the inclusion of my own reflections, initially favouring participant voices. My supervisors redirected me to the need to also include my reflections, and made me aware that this was still paying that respect I felt was essential; it was still using people's generously given information; their 'message' would be reflected in the study as a whole.

I have also felt that uncomfortable feeling that Braun & Clarke write about in their Thematic Analysis book, of not quite knowing when coding and themes are 'complete'. I think I will always feel that the thematic analysis is an unfinished piece of work; the feeling that everything I could say wasn't fully said, that word counts get in the way, and that there may not be an actual limit to what we can pick up from people's stories.

I have been lucky to have been able to express my values in this research. After my own original study ideas didn't come to fruition, to be approached about an ACT-based study was in line with my preferred therapeutic model, one which reflects my world view in many ways. Additionally, my doctoral research as a whole has given me a platform (in the systematic review) to draw attention to a particular issue that I feel is not only not given enough attention, but one that is consistently misunderstood and talked about with hushed voices: menopause. So while I might have started the journey with other ideas in terms of which direction I was heading, it appears that "I have ended up where I needed to be".

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Word Count

Thesis section	Excluding references, tables, appendices etc	Inclusive
Thesis summary	285	287
Systematic review	4345	11004
Empirical study	6856	13204
Contributions chapter with Reflective commentary	2497	2948
Title pages, acknowledgements, abbreviations, contents, word count	N/A	766
Total word count	**19983**	**28209**

"Mischief Managed"

Fred Weasley, Prisoner of Azkaban