MASTERS BY RESEARCH

Digital Health Solutions for Medication Adherence Support

Davies, Non

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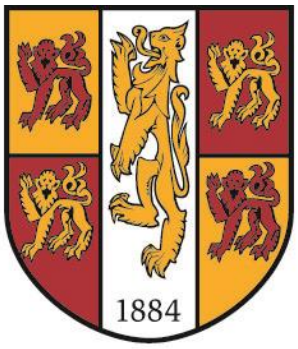
Digital Health Solutions for Medication Adherence Support.



PRIFYSGOL
BANGOR
UNIVERSITY

Non Wyn Davies

Student ID: 500545276

A thesis submitted for the degree of Master of Science by Research (MScRes)

[18/12/2023]

North Wales Medical School, Bangor University

Declarations

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

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

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Candidates contribution

Chapter 1 – Non Wyn Davies (NWD) (the candidate) drafted the initial version, with Professor Dyfrig Hughes (DH) (academic supervisor) providing comments for subsequent revision.

Chapter 2 – Under the supervision of DH, NWD wrote the protocol, designed the search strategy, ran the searches, screened publications for inclusion, extracted data, interpreted the results, and drafted the initial version, with DH providing comments for revision. Yasmin Noorani (academic support librarian) provided advice on the search strategy.

Chapter 3 – Under the supervision of DH, NWD designed and inputted the prompts, before screening and editing the messages for inclusion. NWD drafted the initial version, with DH providing comments for revision.

Chapter 4 – Ellen Lanham and Dr Adam Mackridge facilitated ND's collaboration on The Betsi Cadwaladr University Health board's service evaluation. Naeem Anjam (Moelwyn Pharmacy), Steffan John (Fferyllwyr Llŷn, Blaenau/D Powys Davies), and their colleagues recruited patients to use the app. Dr Elin Haf Davies (EHD) (company supervisor) provided expertise on Atom5™, with Dafydd Pierce-Evans (Aparito Ltd) configurating the app. EHD completed the first version of the secondary data analysis ethics form, with ND revising this and DH submitting the application for ethical approval. ND drafted the initial version of the protocol, patient information sheet, and write-up of Chapter 4, with DH providing comments for revision.

Chapter 5 – NWD drafted the initial version, with DH providing comments for subsequent revision.

Abstract

Background and aim

Medication non-adherence impacts patient health and wellbeing, whilst also influencing the safety, efficacy, and cost-effectiveness of medicines. The utilization of mobile health technologies, including text messages, telephone calls and smartphone-based apps, for improving medication adherence (initiation, implementation, persistence) is a growing field, but further research is warranted. This thesis aims to determine the feasibility of using a digital health intervention to support patients in adhering to their medications.

Methods

A systematic review of the literature was conducted to determine the effectiveness of mobile health interventions for improving adherence to oral anticoagulants. PubMed, Embase, Cochrane Central Register of Controlled Trials, and Web of Science were searched from 1/1/2000 to 11/11/2022, identifying 2,319 potentially relevant clinical trials. Of those, 16 studies were included in the final review, and assessed for risk of bias using a draft version of the risk of bias instrument for interventional adherence studies, and quality of reporting for adherence measurement and analysis. A narrative synthesis of the results was presented. Subsequently, a systematic methodological approach was undertaken to assess the feasibility of using artificial intelligence (ChatGPT-3.5) to develop health-promoting messages. Lastly, as part of an ongoing service evaluation by Betsi Cadwaladr University Health Board, the feasibility of a novel mobile health intervention (the Atom5™ app) for supporting poly-medicated patients recruited from community pharmacies in adhering to their medications was evaluated. The app provided medication intake reminders, combined with daily digital messages and gamification in the form of badges, in two languages (English/Welsh). Surveys created in Jisc were distributed to pharmacists across Betsi Cadwaladr University Health Board to gather their opinions of the messages before they were finalised for the app.

Results

Seven of the 16 studies included in the systematic review reported statistically significant improvements in oral anticoagulant adherence, of which four utilized telephone calls or text messages. However, most of the included studies were of poor methodological quality, with 15 studies being at either a high or serious overall risk of bias. Of the 300 initial adherence-related messages generated using ChatGPT-3.5, 108 duplicates were removed, with a further 47 messages removed after screening. This produced a final, refined list of 145 messages. Lastly, within the feasibility study, a total of 10 participants were onboarded onto the Atom5™ app, with 6 weekly adherence, and 3 patient experience questionnaires being completed. All responses to the participant experience questionnaire rated the reminders and digital messages as being useful, whilst also agreeing that they would recommend an app like Atom5™ in the future.

Conclusions

Together, these findings suggest that digital health interventions, including telephone calls, text messages, and smartphone-based apps, may be feasible options for supporting patients in adhering to their medication. Furthermore, our findings allude to the feasibility of using artificial intelligence to generate health-promoting messages.

Future directions

Future research should focus on optimizing mobile health support, such as by personalizing the intervention. These require testing in larger, longer-term trials, that include a more diverse pool of participants. Specific attention should be placed on improved methodological quality, particularly in the measurement, reporting and analysis of medication adherence. The potential use of artificial intelligence to generate health-messaging support, which might overcome some of the specific challenges involved with health message generation, warrants further investigation.

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List of abbreviations

WHO – World Health Organization

ABC – Ascertain Barriers to Compliance

MPR – Medication possession ratio

PDC – Proportion of days covered

MEMS – Medical events monitoring systems

BMQ – Beliefs about Medicines Questionnaire

NHS – National Health Service

CBT – Cognitive behavioural therapy

eHealth – electronic health

mHealth – Mobile health

COVID-19 – Coronavirus disease 19

OACs – Oral anticoagulants

DOACs – Direct oral anticoagulants

VKAs – Vitamin K antagonists

AI – Artificial intelligence

ChatGPT – Generative Pre-trained Transformer

CENTRAL – Cochrane Central Register of Controlled Trials

RTCs – Randomised controlled trials

RoBIAS – The risk of bias instrument for interventional adherence studies

ESPACOMP – The International Society for Patient Adherence

EMERGE – Medication Adherence Reporting Guideline

TEOS – Timelines–Events–Objectives–Sources

SWiM – Synthesis without meta-analysis

PROSPERO – The International Prospective Register of Systematic Reviews

KESS2 – Knowledge Economy Skills Scholarships 2

ESF – European Social Funds

BCUHB – Betsi Cadwaladr University Health board

PII – Personal identifiable information

SMS – Short-message service

BCTs – Behaviour chance techniques

CHAPTER 1 – INTRODUCTION

1.1 Defining medication adherence

Historically, the term medication adherence has often been used interchangeably with other, distinct, terms, including concordance, compliance, and persistence. Furthermore, several definitions of medication adherence have been proposed, used, and debated in the literature over the years, leading to confusion regarding the term's true meaning and significance (Blaschke *et al.,* 2012). For instance, an early definition of medication adherence proposed by Meichenbaum and Turk (1987) saw the term defined as *"the degree to which a patient follows the instructions, proscriptions, and prescriptions of his or her doctor."* More recently in 2003, The World Health Organization (WHO) (2003) proposed a more expansive definition of medication adherence as *"the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes – corresponds with agreed recommendations from a health care provider."* These different definitions of medication adherence exemplify the lack of uniformity in how the term is defined by different authors and organizations in the literature over the years.

In response to this, a panel of international experts developed a new taxonomy for defining adherence to medications under the Ascertain Barriers to Compliance (ABC) project (Vrijens *et al.,* 2012). The outcomes of this project saw Vrijens *et al.,* (2012) propose that adherence to medications should be defined as *"the process by which patients take their medications as prescribed, composed of initiation, implementation and discontinuation."* Within this definition, the initiation of a medication refers to when an individual takes the very first dose of a medication, whilst implementation refers to how well an individual takes their medication in relation to the prescribed regimen, from the first dose to the last. Discontinuation is the last step in the process and refers to when an individual ceases to take any more medication. These three phases describe different aspects of medication-taking behaviour, and together, form the basis of the now widely-adopted definition of adherence to medications, which is illustrated in Figure 1 (Vrijens *et al.,* 2012). Therefore, whilst a variety of definitions of medication adherence have been suggested in the literature over the years, for this paper, the definition proposed by Vrijens *et al.,* (2012) is the working definition.

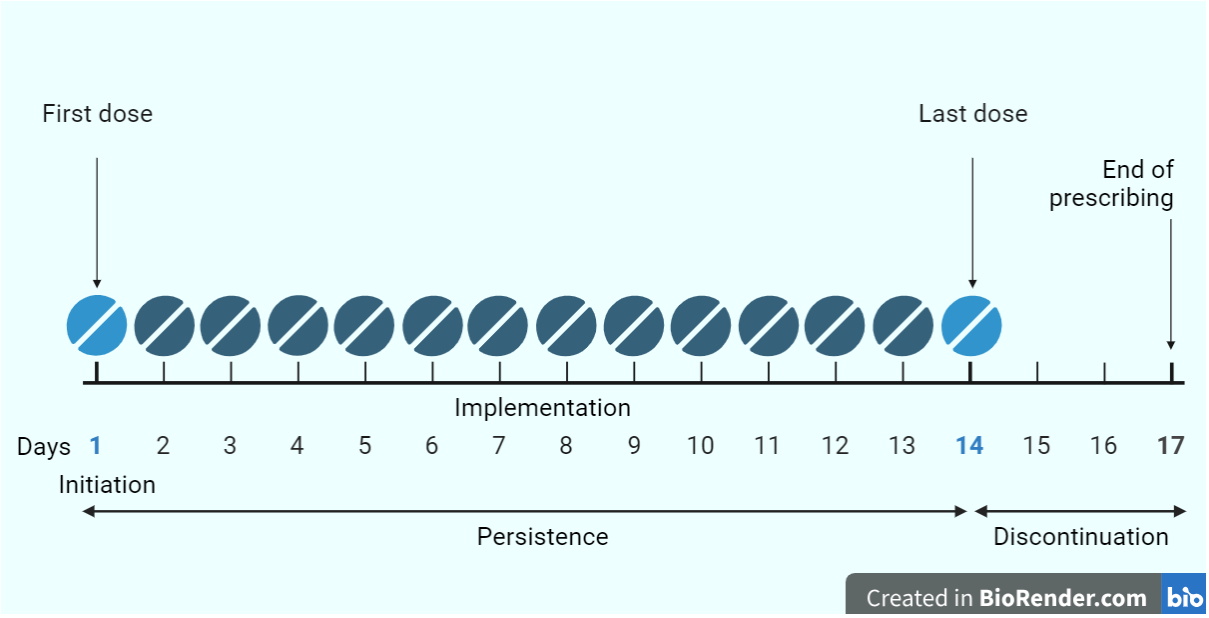

Figure 1 – A visualisation of medication adherence to a once-daily dosing regimen (Adapted from Vrijens *et al.,* 2012). Created in BioRender.com.

It is also important to define several other terms which are often wrongly used as synonyms to medication adherence, firstly compliance. Jimmy and Jose (2011) explain that the term compliance is distinct from adherence, defining compliance as *"the extent to which a patient's behavior matches the prescriber's advice."* They demonstrate that whilst compliance infers that a patient is to some degree obedient to the healthcare provider, adherence infers that more of a collaboration between both parties is taking place. In this way, the healthcare provider, and the patient work together to improve the health status of the patient. In achieving this, consideration of several factors, such as the lifestyle and values of the patient, against the professional opinion of the healthcare provider is important (Jimmy and Jose. 2011). Due to this lack of collaboration in the decision-making process between the patient and healthcare provider, compliance is often described negatively in the literature (Osterberg and Blaschke. 2005). For instance, compliance is often described as a phenomenon that negatively compromises the relationship between healthcare provider and patient. Compliance is also said to impact patient autonomy by inferring that the patient must accept the treatment advised by the healthcare professional (Chakrabarti. 2014; Vermeire *et al.,* 2001).

Whilst both adherence and compliance are said to refer to the behaviour of patients when taking their medication, concordance is distinct in its focus on the relationship between the healthcare provider and patient (Bell *et al.,* 2007). In this way, Chakrabarti (2014) defines concordance as *"a therapeutic relationship, which facilitates clinicians' and patients' views on treatment, and supports an informed choice of treatment by patients."* Concordance has now evolved to shared decision-making, in which the clinician and patient are both involved in the decision-making process, which is a relatively new field (Atal *et al.,* 2019).

Table 1 – Summary of definitions relating to medication adherence.

Term	Reference	Definition
Medication adherence	(Vrijens *et al.,* 2012)	*"The process by which patients take their medications as prescribed, composed of initiation, implementation and discontinuation."*
Compliance	(Jimmy and Jose. 2011)	*"The extent to which a patient's behavior matches the prescriber's advice."*
Concordance	(Chakrabarti. 2014)	*"A therapeutic relationship, which facilitates clinicians' and patients' views on treatment, and supports an informed choice of treatment by patients."*
Primary non-adherence	(Adams and Stolpe. 2016).	*"When a new medication is prescribed for a patient, but the patient does not obtain the medication or an appropriate alternative within an acceptable period of time after it was prescribed."*

1.2 The impact of medication non-adherence

Non-adherence to medication is a significant concern, exemplified by The WHO (2003) declaring that *"increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment."* Most often, good medication adherence is outlined by an individual taking at least 80% of the medication that is prescribed to them (Ruff *et al.,* 2019), however, the appropriateness of using this threshold is questioned (Gellad *et al.,* 2017). Primary non-adherence is defined by Adam and Stolpe (2016) as *"when a new medication is prescribed for a patient, but the patient does not obtain the medication or an appropriate alternative within an acceptable period of time after it was prescribed."* This is distinct to initiation, which describes a patient taking their very first dose of a medication (Vrijens *et al.,* 2012). All the while, secondary non-adherence refers to when a patient does not collect subsequent prescription refills, despite collecting the first prescription (Adams and Stolpe. 2016). Whilst primary and secondary non-adherence are useful definitions, the ABC taxonomy provides a more detailed approach to defining medication adherence (Vrijens *et al.,* 2012).

Non-adherence negatively impacts several aspects of patient care, such as by reducing both the safety and effectiveness of treatment, increasing the cost of healthcare, and contributing to antibiotic resistance (Pagès-Puigdemont *et al.,* 2016; Shiovitz *et al.,* 2016). Non-adherence may also contribute to the progression of disease and a decline in health status (Aznar-Lou *et al.,* 2017). Furthermore, adherence to medications in clinical trials is often low, which compromises the results obtained (Valgimigli *et al.,*

2019). In the United States, medication non-adherence is responsible for around 50% of treatments not being successful, approximately 125,000 deaths, and 25% of hospital admissions annually (Kim *et al.,* 2018-a).

The impact of medication non-adherence on the cost-effectiveness of treatment has been researched in the literature for some time (Hughes *et al.,* 2001). Iuga and McGuire (2014) explain that medication non-adherence impacts healthcare costs by first worsening the health outcomes of a patient. In turn, patients with worsening health outcomes are increasingly dependent on the use of the healthcare system. In this way, the overall healthcare costs involved become increased. In the US, these increased costs are said to be passed onto the patient, such as through increased co-payments (Iuga and McGuire. 2014). Cutler *et al.,* (2018) also report this relationship between lower adherence rates and higher associated healthcare costs, whilst also stressing the lack of good quality research into the economic implications of non-adherence in the literature.

Due to people living longer, medications are now being increasingly used for the management of chronic diseases (Alosaimi *et al.,* 2022). Approximately 15 million individuals are said to be living with a chronic disease in the United Kingdom, with this number anticipated to rise to around 18 million by 2025 (Stewart *et al.,* 2022). Worryingly, evidence suggests that adherence rates to medications are lower in individuals living with chronic diseases than in those with acute conditions (Alosaimi *et al.,* 2022). It is estimated that approximately 50% of individuals living with chronic diseases do not take their medication as prescribed (Pagès-Puigdemont *et al.,* 2016), with the odds of medication non-adherence said to be highest in individuals with hypertension, depression, and diabetes mellitus (Alosaimi *et al.,* 2022). Considering that 41 million deaths annually are a result of a chronic disease, representing a total of 74% of all deaths across the globe (WHO. 2022), medication non-adherence in individuals living with chronic diseases is of great concern.

1.3 Measures of medication adherence

There are several different ways in which medication adherence can be measured, with each method having its advantages and limitations. These measures can be split into different categories, such as subjective and objective (Langendoen-Gort *et al.,* 2023), or direct and indirect methods (Ernawati *et al.,* 2022). Whilst subjective methods involve the medication-taking behaviour of patients being evaluated, objective methods involve the collection of more accurate data (Langendoen-Gort *et al.,* 2023). In this way, whilst direct measures involve directly observing a patient taking their medication or the measurement of a drug or metabolite concentration in the blood, indirect measures involve using self-report questionnaires, analysis of secondary databases or monitoring medication-taking behaviour through pill counts and electronic medication packaging (Lam and fresco. 2015; McRae-Clark *et al.,* 2015). Despite direct measures being often considered the most reliable method for measuring

medication adherence, they also have limitations. They are often expensive, invasive, and difficult to execute, and do not always consider the possible effect of individual differences on medications (Vermeire *et al.,* 2001). Furthermore, directly observing a patient taking their medication is not always a practical option, with some patients also able to falsify ingestion (Farmer. 1999).

Indirect measures, such as through the analysis of secondary databases, are useful and practical options for measuring adherence. Secondary database analysis is largely carried out by evaluating data collected by pharmacies, such as prescription refilling activity, which is often translated into the medication possession ratio (MPR) or proportion of days covered (PDC). This is an inexpensive method of measuring adherence but assumes that prescription refilling activity directly relates to how well a patient is taking their medication, which might not always be the case. Despite allowing many people on several different medications to be analysed over an extensive period, by solely analysing data from secondary databases, potential reasons why patients are nonadherent are difficult to determine (Anghel *et al.,* 2019).

Self-reports are a practical, inexpensive, and non-invasive method of measuring medication adherence (Stirratt *et al.,* 2015). Most frequently, self-reports require participants to subjectively answer a series of questions about their medication-taking behaviour. For instance, the 8-item Morisky scale is said to have a completion time of around five minutes and can capture unintentional non-adherence, such as due to forgetfulness or lack of understanding, as well as intentional non-adherence, in which patients make the conscious decision to omit medication doses (Tesfaye and Peterson. 2021). An advantage of using self-report measures of adherence is their ability to provide information surrounding the medication-taking behaviours. This might include the reasoning for medication non-adherence, as well as the personal beliefs of patients. Disadvantages of using self-reports include the potential for overreporting, which may be a conscious choice by the patient or due to other problems, such as memory. Furthermore, self-reports often lack the ability to generate data regarding the timing of dose intakes, with differences in the wording of phrases across different self-report scales also problematic (Stirratt *et al.,* 2015). Social desirability bias may also come into play, in which patients report behaviours that are perceived to be more desirable (Latkin *et al.,* 2017).

Pill Counts involve the counting of a patient's medication and subsequently comparing this number with the number that was prescribed. Advantages of this indirect method of measuring medication adherence include it being inexpensive and easy to perform. Disadvantages include that pill counts are not inclusive to all forms of medication (Lam and Fresco. 2015), such as liquids and creams, which would require other measures, such as being weighed, or assessing the liquid level remaining in a bottle (Storm *et al.,* 2008; Williams *et al.,* 2013). Further limitations include the inability to provide reasons for the observed adherence pattern, and the risk of overestimating the true rate of adherence (Lam and Fresco. 2015). Aiming to address some of the logistical issues surrounding both clinic and home-based pill counts, as well as to minimise the risk of patients dumping their pills prior to visits, known as pill dumping, unannounced telephone pill counts are now growing in popularity (Frederiksen *et al.,* 2014).

Electronic medication packaging is defined by Checchi *et al.,* (2014) as *"electronic adherence-promoting devices integrated into the packaging of a prescription medication."* This is often considered the gold standard for measuring medication adherence rates (McRae-Clark *et al.,* 2015), with several of the previously discussed methods, including pharmacy data, self-reports, and pill counts, described as unreliable (van Onzenoort *et al.,* 2010). Medical events monitoring systems (MEMS) are one form of electronic medication packaging and are pill bottles fixed with electronic caps. These caps monitor the medication-taking behaviour of patients by tracking the date and time at which the cap is opened and, theoretically when medication is ingested (Hartman *et al.,* 2019). Interestingly, there is evidence to suggest that electronic medication packaging is associated with improved medication adherence rates (Checchi *et al.,* 2014). In this way, this may present a degree of psychological bias due to patients being aware that their medication-taking behaviour is being monitored (Shiomi *et al.,* 2021).

Consequently, despite there being several different methods for measuring medication adherence, a reasonable approach to take, which is often the recommended approach, is to use a combination of several different methods in combination. In this way, the limitations of one method might be minimised by the advantages of another to improve the reliability of the results generated (Lam and Fresco. 2015).

Table 2 – Measures of medication adherence

<table>
<tr><td></td><td colspan="2">Objective</td></tr>
<tr><td>Direct</td><td colspan="2">Example: Measurement of a drug or metabolite concentration in blood
Pros: Accurate and reliable
Cons: Invasive, expensive, difficult to execute, does not always account for the effect of individual differences on medications
Example: Observing a patient ingesting medication
Pros: Reliable
Cons: Not always practical, patients may falsify ingestion</td></tr>
<tr><td></td><td>Objective</td><td>Subjective</td></tr>
<tr><td>Indirect</td><td>Example: Pill counts
Pros: Inexpensive and easy to perform, can be performed over the telephone
Cons: Not inclusive to all medication forms, do not provide reasons for the behaviours, risk of overestimation
Example: Analysis of secondary databases
Pros: Practical and inexpensive, can assess many people on several different medications over an extensive period</td><td>Example: Self-reports
Pros: Practical, inexpensive, and non-invasive, can capture intentional and unintentional non-adherence, provide reasons for behaviours.
Cons: Risk of overreporting (including due to social desirability), no standard wordings across different self-report scales.</td></tr>
</table>

	Cons: Do not provide reasons for the behaviours, assumes that refill activity directly correlates with medication-taking **Example: Electronic medication packaging** *Pros:* Gold-standard, precise and easily quantifiable *Cons*: Expensive, requires data download	

Information taken from (Anghel *et al.,* 2019; Farmer. 1999; Frederiksen *et al.,* 2014; Lam and fresco. 2015; Latkin *et al.,* 2017; McRae-Clark *et al.,* 2015; Osterberg and Blaschke. 2005; Stirratt *et al.,* 2015; Tesfaye and Peterson. 2021; Vermeire *et al.,* 2001).

1.4 Barriers to medication adherence

Medication non-adherence often results from the interplay of different factors, with The WHO (2003) stating that these factors can be grouped into five categories, which are those related to the patient, socioeconomic circumstance, healthcare system, condition, or treatment. A systematic review by Easthall *et al.,* (2019), aiming to understand medication adherence barriers in patients prescribed cardiovascular disease prevention medicines, mapped the identified barriers to the Theoretical Domains Framework. Whilst reporting that most domains were well-represented in the literature, including knowledge, beliefs about capabilities, and social influences, barriers including social/professional role, as well as identity and behaviour regulation lacked representation (Easthall *et al.,* 2019).

It is also important to note that the validity of using participant and disease characteristics to predict adherence rates remains debatable, with the importance of age, sex, and race on medication adherence therefore being of limited importance (Holmes *et al.,* 2014; Steiner. 2010). For instance, the impact of patient age has been much debated in the literature over the years, with it often being assumed that older individuals are worse at adhering to their medications, for example, due to defects in cognitive ability (Burnier *et al.,* 2020). Despite this, the relationship between age and medication adherence is not as clear-cut. For instance, Kim *et al.,* (2019) report that as the age of participants increased up to 69 years, the rate of adherence to antihypertensive medication also increased, but after this, the rate of adherence began decreasing. All the while, Leven *et al.,* (2017) report that adults aged 65 years or older were better at adhering to their post-liver transplant medication than those under 65 years of age.

Similarly, whilst some authors suggest that males are better at adhering to their medications (Chen *et al.,* 2014; Manteuffel *et al.,* 2014), others suggest that females are superior at this (Boucquemont *et al.,* 2019; Li *et al.,* 2008). Boucquemont *et al.,* 2019 further linked the observed gender differences with age, stating that gender variations were only observed between the young men and women in the study and not observed between the younger adolescents. Whilst Chen *et al.,* (2014) propose reasons including gender differences in perceptions about medication adherence and illness to explain the observed

differences, Manteuffel *et al.,* (2014) linked this to the reduced likelihood that the women in the study received the recommended medication treatment and monitoring. Furthermore, according to Vervloet *et al.,* (2020), women often have negative perceptions about medication, which may also be linked to women experiencing more severe and frequent side effects.

Other barriers to medication adherence include socioeconomic circumstance and race, with individuals from lower socioeconomic backgrounds or ethnic minority groups often shown to have lower medication adherence rates (McQuaid and Landier. 2018). For instance, a study investigating racial differences in the adherence rates to medications for hypertension, hyperlipidaemia, and type 2 diabetes mellitus, reported that Blacks and Hispanics had adherence rates that were 7.5 percentage points fewer than Whites. Moreover, after controlling for socioeconomic measures, these racial differences were still observed (Xie *et al.,* 2019). Similarly, a study investigating adherence rates to antidepressant medication reported that medication adherence was more probable in individuals receiving a higher income than in those on lower incomes (Ji and Hong. 2020).

Several beliefs may influence medication adherence, which might include an individual's beliefs about their medication-taking ability, the degree of trust they hold in the healthcare provider's expertise, opinions regarding natural or home therapies, and understanding of the illness (Chia *et al.,* 2006). In a systematic review by Holmes *et al.,* (2014), which aimed to predict medication adherence using health psychology theories, the determinants of medication adherence deemed as being significant included self-efficacy, perceived barriers, perceived susceptibility, necessity beliefs, and medication concerns. To capture the beliefs of participants regarding medicines, The Beliefs about Medicines Questionnaire (BMQ) was developed by Professor Robert Horne and colleagues. It assesses belief across two divisions, comprised of four subsets. Whilst the BMQ-general assess necessity and concerns (5-item scales), the BMQ-specific assess harm and overuse (4-item scales) (Horne *et al.,* 1999).

Beliefs influencing medication adherence rates may also be cultural or religious. For instance, a study by Batarfi *et al.,* (2021) report that the act of fasting during Ramadan results in 53.1% of individuals modifying their medication-taking schedules during this period (changing dosing times, skipping doses altogether or taking double the number of doses). This modification of mediation-taking behaviour was more prevalent in individuals taking twice-a-day doses, with modifying medication-taking schedules during Ramadan also associated with an increased likelihood of hospitalisation by around 3-fold (Batarfi *et al.,* 2021).

Language barriers may also come into play, with language barriers in healthcare said to contribute to miscommunication, as well as heightened levels of anxiety (Meuter *et al.,* 2015). When looking at the impact of language barriers on medication adherence, a study by Wilson *et al.,* (2005) that focused on patients who did not speak the local language, reported that 34.7% of patients did not understand how to use their medication and that 41.8% struggled to understand the label on the medication packaging. Furthermore, 15.8% of participants experienced adverse reactions to the medication, which resulted from a lack of understanding of the instructions provided by the healthcare professional (Wilson *et al.,*

2005). In this way, Kahler and LeMaster (2022) conclude that the medication adherence outcomes of patients with limited English proficiency could be enhanced through the integration of healthcare professionals who are able to communicate in their language, or by alternatively providing interpreters who can do this in their place (Kahler and LeMaster. 2022).

Health literacy is defined by Liu *et al.,* (2020) as *"the ability of an individual to obtain and translate knowledge and information in order to maintain and improve health in a way that is appropriate to the individual and system contexts."* Thus, having good health literacy means that individuals have the tools needed to take control of their health and well-being. Importantly, poor health literacy can be directly linked with several negative connotations, including an increased risk of hospitalization and mortality, substandard health status, decreased capacity to comprehend labels on medication packaging, and increased health-related costs (Coughlin *et al.,* 2020). Evidence in the literature suggests that good health literacy can be positively associated with medication adherence (Miller. 2016). A systematic review conducted by Schönfeld *et al.,* (2021) describes a significant positive association between health literacy and medication adherence in six of the included publications, which were from five different studies, with a further two studies reporting positive associations that were not significant (Schönfeld *et al.,* 2021).

Psychological illness may also be a barrier to adherence, with Grenard *et al.,* (2011) reporting that the odds of non-adherence in patients diagnosed with depression was 1.76 times greater than the odds of non-adherence in patients without depression. They proposed several risk factors thought to contribute to these observed differences, including reduced energy and motivation, absence from social settings, and differences in expectations regarding treatment (Grenard *et al.,* 2011). Similarly, Sundbom and Bingefors (2013) report that depression and anxiety, acting either alone or in combination, were correlated with both unintentional and intentional medication non-adherence, but more so with intentional non-adherence. This was due to a fear of adverse drug reactions in the individuals who had anxiety alone, or both anxiety and depression, whilst this was due to individuals with depression alone, or both depression and anxiety, actually experiencing adverse drug reactions (Sundbom and Bingefors. 2013).

In terms of the treatment itself, the complexity of the medication-taking regimen may be an important consideration, with patients said to only understand and remember around 50% of what is said by their healthcare provider (Schillinger *et al.,* 2003). Treatment complexity is defined by Muir *et al.,* (2001) as *'the number of medications (polypharmacy) and the number of times per day or "doses" that the patient takes a medication (multiple dosing schedules)."* For instance, in a study investigating the influence of regimen complexity on medication adherence in individuals with type 2 diabetes mellitus, Ayele *et al.,* (2019) reported that the patients deemed to have a high medication complicity index were less adherent than those with either a low- or moderate-level medication complicity index (Ayele *et al.,* 2019). Moreover, evidence in the literature exhibits that individuals are less adherent to twice-daily medications than to once-daily medications (Smits *et al.,* 2022; Coleman *et al.,* 2012).

Other barriers related to the treatment itself might include side effects, drug formulations and palatability, with a study by DiBonaventura *et al.,* (2012) that focused on patients with schizophrenia concluding that medication side effects could be significantly correlated with medication non-adherence. In terms of drug formulations, in certain populations, such as the elderly, oral drug formulations may be challenging, for example, due to difficulties swallowing (Taylor and Glass. 2018). Whilst common drug formulations for children include oral liquids and mini or chewable tablets, individual differences, as well as age and developmental phase, might affect their acceptability (Khan *et al.,* 2022). Due to children being more sensitive to bitter tastes than adults, this is often problematic in terms of adherence, with most medications having a bitter taste (Mennella *et al.,* 2013). In paediatric medicine, the palatability of a medication has been shown to influence how well children adhere to medications, including antibiotics (Baguley *et al.,* 2012).

Cost may also be an influential factor, with adults in England required to pay a fee of £9.65 per item that is prescribed or opt for a prepayment certificate that would result in some savings (NHS. 2023-a). Whilst exemptions allow certain individuals to receive free National Health Service (NHS) prescriptions in England (NHS. 2023-b), in Wales, Scotland and Northern Ireland, all patients receive NHS prescriptions for free (Welsh Government. 2017). Cost-related medication non-adherence is said to entail behaviours including not filling prescriptions on time or at all, omitting medication doses altogether, or taking a reduced number of doses (Nekui *et al.,* 2021). A study by Dillon *et al.,* (2018) reported that financial burden due to medication co-payment significantly decreased self-reported adherence. All the while, a recent study by Dusetzina *et al.,* (2023) reports that 1 in 5 adults are estimated to experience medication non-adherence which is related to the cost of medication (Dusetzina *et al.,* 2023).

The relationship between the patient and healthcare provider is defined by Deniz *et al.,* (2021) as *"a process in which information about the patient and the disease is collected, a diagnosis is made, a treatment plan is made, the patient is cured, and support is offered to the patient."* By having a good patient-healthcare provider relationship, several aspects of patient care can become improved, such as trust, communication, sense of satisfaction and treatment adherence. Furthermore, by having a good relationship, the risk of miscommunication between the patient and the healthcare provider can become reduced (Biyazin *et al.,* 2022). Good communication between patient and healthcare provider, as well as implementing shared decision-making, can be correlated with good medication adherence (Chang *et al.,* 2021). According to Zolnierek and DiMatteo (2009), when comparing the risk of non-adherence between physicians who communicate well, with those who do not, the risk of patients being nonadherent to their medications is 19% higher. Furthermore, by providing physicians with communication training, patients are 1.62 times more likely to be adherent to their medications, than if the physician providing the care did not receive any communication training (Zolnierek and DiMatteo. 2009).

1.5 Interventions to support patients in adhering to their medications

Interventions to support individuals in adhering to their medications can be categorised in different ways. For instance, in a review by Kini and Ho (2018), interventions were categorized into six groups, which were patient education, medication regimen management, consultation with a pharmacist for the management of chronic diseases, cognitive behavioural therapies (CBTs), including motivational interviewing, reminders, and incentives. All the while, a paper by Osterberg and Blaschke (2005) categorised interventions into four groups, which were patient education, dosing schedule improvement, increased clinic opening hours, and improved communication between patients and healthcare professionals.

When educating patients, good communication between the healthcare provider and patient is essential for its success (Marcus. 2014). In doing this, the healthcare professional should ensure that the transfer of knowledge between themselves and the patient is energetic and exciting, as well as be tailored to the demands of the individual (Paterick *et al.,* 2017). When promoting medication adherence through patient education, healthcare professionals should also ensure that they sufficiently explain how a medication should be taken, whilst addressing any hesitancies patients might have. Furthermore, healthcare professionals should explore the potential influence of any established knowledge or beliefs patients may possess (Costa *et al.,* 2015).

The positive impact of patient education on medication adherence is evident in the literature. For instance, a study by Taibanguay *et al.,* (2019) concluded that an educational pamphlet on rheumatoid arthritis, both alone and in combination with a 30-minute counselling session, significantly improved medication adherence. Similarly, a more recent study by Contreras-Vergara *et al.,* (2022) reported that a pharmaceutical educational intervention, which included a one-on-one educational session with a pharmacist, significantly improved medication adherence rates in individuals with type 2 diabetes mellitus and systemic arterial hypertension.

The implementation of behavioural strategies has also proven beneficial in supporting medication adherence. Motivational interviewing is defined by Bischof *et al.,* (2021) as *"a technique that has been specifically developed to help motivate ambivalent patients to change their behavior."* Motivational interviewing is comprised of several key elements, which include open-ended questions, active listening, affirmation, and praise, and the incitement of statements which are self-motivational (Bischof *et al.,* 2021). Despite being originally used to promote behavioural changes in individuals with addiction problems, motivational interviewing is now widely used in several different conditions and contexts. Described as a style of communication, it is essential that those practising motivational interviewing find an appropriate balance between being empathetic with the individual, whilst also being assertive enough to invigorate behavioural changes (Resnicow and McMaster. 2012). A systematic review by Palacio *et al.,* (2016) reported that motivational interviewing positively impacted medication adherence rates, with

this effect remaining across different exposure times and across counsellors of differing educational levels.

CBT is another behavioural strategy used to support medication adherence, defined by Nakao *et al.,* (2021) as *"a type of psychotherapeutic treatment that helps people to identify and change destructive or disturbing thought patterns that have a negative influence on their behavior and emotions."* Described as a form of talking therapy, CBT has been implemented in a range of mental health conditions, including anxiety, depression, schizophrenia, and post-traumatic stress disorder, but can also be implemented in physical health conditions. CBT is formed around the concept that your feelings and thoughts influence how you behave. In this way, combating negative thoughts and feelings through CBT can invigorate positive behavioural changes (Mind. 2021). CBT and motivational interviewing are often employed together (El-Mallakh and Findlay. 2015), with evidence in the literature alluding to the potential benefit of implementing CBT and motivational interviewing simultaneously to promote medication adherence (Easthall *et al.,* 2013; Inwanna *et al.,* 2022).

The management of medication regimens may also be useful in supporting medication adherence, with complex medication regimens negatively influencing medication adherence (Ayele *et al.,* 2019). One way in which this can be combated is through simplifying medication regimens, for example, by implementing fixed-dose combinations to reduce the number of different medications needing to be taken. Alternatively, complex medication regimens could be simplified by reducing the dosing frequency of a medication, if this is possible (Elnaem *et al.,* 2020). As part of this, switching from short-acting to long-acting medications might be important. Other medication regimen simplification strategies might include ensuring that all medications are administered at the same time, via the same administration route, again, if this is possible (Bell *et al.,* 2021). Such medication regimen simplification interventions have already been shown as effective in the literature, with a systematic review by Baumgartner *et al.,* (2020) reporting that polypills, which are also called fixed-dose combinations, can be correlated with improved medication adherence rates. A more recent systematic review by Wei *et al.,* (2023) concluded similar results, favouring fixed-dose combinations for supporting medication adherence.

Multi-compartment compliance aids may also prove useful, with evidence in the literature alluding to the benefit of their implementation in supporting medication adherence (Gutierrez *et al.,* 2017; Shah *et al.,* 2021). According to The Care Quality Commission (2022), multi-compartment compliance aid *"is a general term for a device designed to contain individual doses of medicines in separate compartments or blisters."* To achieve this, medication is usually taken from its original packaging, and organized into a device, with the goal of supporting patient medication adherence to subsequently enhance treatment outcomes (Counter *et al.,* 2017). Medication is usually split by day of the week, as well as by dosing time if this is relevant for the patient. Whilst sometimes being described as pill boxes or blister packs, multi-compartment compliance aids aim to prevent unintentional non-adherence, which might include taking too many doses or missing doses altogether (Shenoy *et al.,* 2020).

Limitations of using multi-compartment compliance aids include the time-consuming nature of their assembly, with the need for an individual to sort medication into individual compartments increasing the chance of errors occurring. Furthermore, if the multi-compartment compliance aids are reusable, an individual may replace a dropped medication dose into the incorrect compartment, which would contribute to unintentional non-adherence (Lecouturier *et al.,* 2011). Further limitations include that multi-compartment compliance aids are not inclusive to all medication types, might be difficult for those with eyesight problems to use, and are associated with increased costs. Multi-compartment compliance aids are also said to potentially impact patient autonomy, as well as reduce the knowledge they possess about their medications (Elliot. 2014). Moreover, the design of a multi-compartment compliance aid is an important consideration, with certain groups of individuals, such as the elderly, more prone to experiencing difficulties in handling multi-compartment compliance aids, and thus, accessing their medications (Sadamoto *et al.,* 2022).

1.6 Digital health interventions - definitions

Various definitions of digital health exist in the literature, with no one definition having been identified as the agreed standard, drawing parallels with the term medication adherence, as previously discussed. Nonetheless, frequently used words contained in the various definitions of digital health are said to be health, technology, and electronic health (eHealth), to name a few (Fatehi *et al.,* 2020). According to The United States Food and Drug Administration (2020), digital health is defined as *"The broad scope of digital health includes categories such as mobile health (mHealth), health information technology (IT), wearable devices, telehealth and telemedicine, and personalized medicine."* The term is comprised of two main groups, which are mHealth and eHealth (Chan. 2021). Chan (2021) defines eHealth as *"the use of information and communication technologies for health,"* and mHealth as *"medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices."* Table 3 provides a summary of the discussed definitions relating to digital health.

Categories of digital health devices include those that are wearable, implantable, ingestible, and portable. Wearable devices, such as patches that are applied to the skin, are often used to measure vital signs, including heart rate and temperature. Implantable devices include cardiac pacemakers that can be externally configured, whilst ingestible devices are often in the form of smart pills, which can be used for internal body monitoring. Portable devices, for instance, smart watches, allow for continuous, real-time monitoring (Mukherjee *et al.,* 2022).

Advantages of implementing digital health technologies in healthcare settings include the ability to monitor patients in real-time, in a way that can be tailored to the individual. Furthermore, the utilization of digital health technologies can lead to improvements in the way in which healthcare is conveyed to patients, whilst also warranting patients to have increased control over their health and care through

informed decision-making (Awad *et al.,* 2021). Following the recent coronavirus-19 (COVID-19) pandemic, the use of digital health technologies in healthcare became advanced. It is said that 97% of adults living in the United Kingdom have either communicated or received care from the NHS using technology following the onset of the pandemic (Flott *et al.,* 2021). Furthermore, the implementation of digital health technologies was central to the management of the virus, which included aiding in its diagnosis and managing its dissemination (Tilahun *et al.,* 2021). Moreover, the implementation of digital health also proved useful in managing those exposed to the virus, including their self-isolation, as well as in the reporting of information (Gentili *et al.,* 2022).

Despite this, important considerations when implementing digital health solutions in healthcare settings might include ethical issues such as user consent, as well as data control considerations, namely data privacy (Manteghinejad and Javanmard. 2021). Moreover, by implementing digital health technologies, there are concerns that healthcare might become automated, in which patients will experience increasingly restricted healthcare professional contact. Training is also crucial for the correct implementation and execution of digital health technologies, in which individuals will need to consider how digitally literate they are in relation to the technology in question (Utukuri *et al.,* 2022). Furthermore, discussions regarding the overuse of smartphones are evident in the literature, which is said to negatively impact both physical and mental health (Adamczewska-Chmiel *et al.,* 2022). This research also extends to the implications of smartphone overuse in healthcare professionals and the impact this has on the quality of care that they provide (King *et al.,* 2020).

Table 3 – Summary of definitions relating to digital health.

Term	Reference	Definition
Digital Health	(The United States Food and Drug Administration. 2020)	*"The broad scope of digital health includes categories such as mobile health (mHealth), health information technology (IT), wearable devices, telehealth and telemedicine, and personalized medicine."*
➢ Electronic health (eHealth)	(Chan. 2021)	*"The use of information and communication technologies for health."*
➢ Mobile health (mHealth)	(Chan. 2021)	*"Medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices."*
Smartphone	(Bakker *et al.,* 2016)	*"An advanced mobile phone that functions as a handheld computer capable of running software apps."*

Applications (apps)	(Higgins 2016)	*"Self-contained programs for smartphones designed to fulfill a particular purpose."*
Wearable technology/device	(Smuck *et al.,* 2021)	*"Any miniaturized electronic device that can be easily donned on and off the body, or incorporated into clothing or other body-worn accessories."*

1.7 Digital health interventions to support medication adherence

Apps are useful aspects of mHealth, with evidence in the literature alluding to the benefit of implementing apps to support medication adherence (Armitage *et al.,* 2020, Li *et al.,* 2021). Apps have various potential functions, which might include conveying health information to patients and collecting health-related data (Backes *et al.,* 2020). These apps can also be linked to wearable devices, with companies such as Fitbit, using wearable devices to collect data related to an individual's activity level (Tran S *et al.,* 2022). In terms of patient education, an app can provide a single interface for a patient to access all the required information about their medication, which makes for a very efficient process. In this way, apps are particularly useful for those who are on several different medications (Dayer *et al.,* 2013). When educating patients via digital health technologies, the digitization of existing health-related educational resources could occur. For example, this might include the conversion of book-based information into a digital PDF document (Car *et al.,* 2022).

Apps are often combined with electronic reminders for patients to take their medication, which are commonly in the form of telephone calls or text messages (Pérez-Jover *et al.,* 2019). Text messages can be scheduled to arrive at specific time points, with it being approximated that of all text messages sent, 99% are opened by users. Moreover, it is estimated that 90% of text messages are opened within three minutes of being received (Kuwabara *et al.,* 2020). Electronic reminders can also be delivered via the app itself or through wearable devices (McBride *et al.,* 2020; Marengo and Barberato-Filho. 2023). Reminders delivered via wearable devices can be released directly through the device, or by alternatively directing alerts to mobile devices. These alerts might incorporate elements such as vibrations or lights, which would usually originate from the wearable device itself (Marengo and Barberato-Filho. 2023).

When aiming to promote medication adherence, apps might incorporate gamification or incentives into their design (Berglund *et al.,* 2022). Gamification is defined by Berglund *et al.,* (2022) as *" the use of game design elements in contexts other than gaming to increase user engagement and experience,"* which may include the ability to progress to different levels, scoring systems, prize earning, and storytelling (Cheng *et al.,* 2019). Financial incentives may also be employed, with a study investigating the impact of app-based financial incentives, as well as app-based financial penalties, on medication adherence in individuals with severe mental illness reporting positive results (Guinart *et al.,* 2022).

Telephone follow-up calls can also be standalone interventions for promoting medication adherence, described as an affordable and uncomplicated intervention to arrange (van Loon-van Gaalen *et al.,* 2021). The purpose and content of these calls might be to educate patients about their disease or treatment, discuss how their symptoms might be best managed, as well as to provide a degree of reassurance (Mistiaen and Poot. 2006). For instance, in a study by Huang *et al.,* (2013), that investigated the impact of telephone follow-up calls on the adherence rates to ART, a positive impact on participant medication adherence was reported.

It could be suggested that electronic medication packaging can be considered a method for measuring medication adherence, whilst also being an intervention to promote adherence. This is due to its positive effects on medication adherence, likely owing to individuals being increasingly aware that their medication-taking behaviour is being evaluated (Shiomi *et al.,* 2021). This is supported by a systematic review conducted by Chan *et al.,* (2022), aiming to investigate whether electronic adherence monitoring would impact medication adherence and other outcomes in individuals living with chronic conditions. They concluded that adherence in the electronic adherence monitoring subgroup was significantly higher than in the subgroup without electronic adherence monitoring. Moreover, electronic medication packaging may also incorporate financial incentives or reminders into their design. For instance, in two pilot studies conducted by Volpp *et al.,* (2008), entering participants into a daily lottery draw significantly improved medication adherence rates.

1.8 Thesis outline

Acknowledging the growing body of literature that recognises the importance of digital health technologies in supporting adherence to a range of different therapies, the main aim of this paper is to determine the feasibility of using a digital health intervention to support patients in adhering to their medications. This will be achieved through the course of five chapters, each with their aims. This first introductory chapter has provided an overview of the subject, focusing on key topics and definitions related to medication adherence and digital health.

In the second chapter, a systematic review of the literature will be presented, in which existing literature was explored and collated. The review aimed to determine the effectiveness of mHealth interventions in supporting patients to adhere to oral anticoagulants (OACs), which included both direct OACs (DOACs) and vitamin K antagonists (VKAs). DOACs, including rivaroxaban, apixaban, dabigatran, and edoxaban, provide benefits over warfarin (a VKA), which includes requiring less frequent monitoring (Khouja *et al.,* 2022). In this way, mHealth offers a potential substitute for the historical interaction between clinician and patient that occurred in clinics for the management of warfarin, but further research into this is warranted.

The third chapter aimed to determine the feasibility of using artificial intelligence (AI) to generate health-promoting messages using Open AI's Generative Pre-trained Transformed-3.5 (CHatGPT-3.5). AI has

the potential to leverage some of the specific challenges involved with health message development, including its resource-intensive nature (Dergaa. 2023), and limited diversity, including in message phrasing, content, and number. Additionally, according to Bartlett *et al.,* (2020), studies that describe using AI platforms, such as ChatGPT, to develop messaging support often lack descriptions of the methods used, presenting a gap needing to be addressed within the field.

The fourth chapter aimed to determine the feasibility of a novel mHealth intervention (The Atom5™ app) for supporting participants, recruited from community pharmacies, in adhering to their medications. The Atom5™ app combines alerts in the form of reminders and daily messaging with gamification (bronze, silver, and gold badges). The implementation of smartphone-based apps for supporting participants in adhering to their medications are growing in popularity (Armitage *et al.,* 2020), but the useful components for supporting the adherence of patients recruited from community pharmacies remain unknown, and further research is required.

The fifth chapter discusses the results, and includes a summary of the overall thesis findings, with reference to other literature. This chapter also includes a discussion of the strengths and limitations of the research, as well as recommendations for future research, and implications for wider clinical practice.

CHAPTER 2 – SYSTEMATIC REVIEW

Mobile health interventions to improve adherence to oral anticoagulant treatment: A systematic review

2.1 Abstract

Background and aim

Non-adherence to oral anticoagulants is responsible for significant morbidity and mortality worldwide, with non-adherence to direct oral anticoagulants of particular concern due to their shorter half-lives compared to warfarin, and less forgiveness to dose omissions. Mobile health interventions have been used as a potential method for improving medication adherence. This review aims to investigate the effectiveness of mHealth interventions in improving oral anticoagulant adherence.

Methods

PubMed, Embase, Cochrane Central Register of Controlled Trials and Web of Science were searched from 1/1/2000 to 11/11/2022 using terms based on mobile health, oral anticoagulants, medication adherence and randomised controlled trials. The risk of bias for interventional adherence studies tool was used to assess the risk of bias. A meta-analysis was not performed due to the heterogeneity of the studies and, instead, a narrative synthesis was undertaken.

Results

A total of 2,319 studies were screened from which 16 studies met the criteria for inclusion. Four of the 7 studies associated with significant improvements in adherence tested telephone calls or text messages for participant follow-up support or as medication intake reminders. However, study quality was generally poor, with many not reporting critical information, or deemed to have a *'high'* risk of bias.

Conclusions

Our review suggests that mHealth interventions involving telephone and text messages may be effective in improving oral anticoagulant adherence in adults. Future research should focus on identifying how these can be optimized with respect to the frequency of delivery, content of calls or messages and potential for automation. Research should focus on larger, longer-term trials with emphasis placed on trial design, conduct and reporting.

2.2 Introduction

Worldwide, VKAs have been considered the mainstay OACs for stroke prevention and treatment of venous thrombosis for the last 60 years. More recently, however, there has been a shift towards the use of DOACs, to the extent that they are now often the preferred choice – mainly due to the reduced need

for monitoring and the associated improved convenience to patients, lower incidence of major bleeding and fewer food- and drug-drug interactions (Banerjee *et al.,* 2020; Ozaki *et al.,* 2020).

Despite their several advantages, adherence to DOACs is a major problem, with real-world evidence indicating that around 20% of patients discontinue treatment prematurely and that around 40% of patients do not take their doses as prescribed (Mitrovic *et al.,* 2020; Tarn *et al.,* 2023). Missed and delayed dosing, is potentially more hazardous with DOACs than with warfarin due to their shorter durations of action (Ozaki *et al.,* 2020). This represents the implementation phase of adherence; one of three defined by Vrijens *et al.,* (2012), along with initiation and persistence.

Non-adherence to medication is a complex phenomenon, with several determinants often contributing. These have been categorised by The WHO according to whether they are factors related to the patient, their socioeconomic circumstances, healthcare systems, condition or treatment (The World Health Organization. 2003). Barriers related to the patient may include inadequate motivation, a low educational level, and cultural issues. Barriers related to the treatment itself may include its complexity, cost, and the adverse effects experienced (Kleinsinger. 2018). In the case of DOACs, less frequent contact with clinicians due to the reduced need for monitoring, may represent missed opportunities for providing adherence support (Bartoli-Abdou *et al.,* 2018).

One potential method for improving medication adherence involves mHealth technologies (Gandapur *et al.,* 2016). MHealth is defined by The WHO as *"medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices"* (Bradway *et al.,* 2017). Most mHealth interventions are based on smartphones due to their popularity (Gandapur *et al.,* 2016). The recent COVID-19 pandemic has been a prominent driver for mHealth development, with technologies that allow patients to be monitored in real-time, in remote settings, proving invaluable in times when patient contact was scarce (Dauletbaev *et al.,* 2021).

There have been numerous studies of the effectiveness of mHealth adherence-enhancing interventions for chronic disease management. A review by Xu and Long (2020) indicated that app-based interventions may be useful in hypertension management, for instance, by promoting medication adherence; and more recently, mHealth interventions were shown to have the potential to be both well-accepted and effective in diabetes management (Zamanillo-Campos *et al.,* 2022; Olomu *et al.,* 2022). In the context of DOACs, mHealth offers a potential substitute for the patient/clinician interaction that has historically occurred via anticoagulation clinics for the management of warfarin. The aim of this systematic review is to determine the effectiveness of mHealth interventions that promote adherence to OACs.

2.3 Methods

2.3.1 Eligibility criteria

Population: The review included studies whose participants were ≥18 years of age. Participants were required to be self-responsible for taking oral anticoagulants, which could be either vitamin k antagonists or DOACs.

Intervention: The review focused on mHealth interventions aimed at promoting medication adherence.

Comparator: The comparator could be any suitable control group.

Outcome: Included studies were required to include a measure of medication adherence as an outcome.

Study type: The review focused on randomized controlled trial evidence, published in the English language

2.3.2 Information sources

The databases PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science were searched from 1/1/2000 to 11/11/2022.

2.3.3 Search strategy

Search terms were based on the concepts of (i) mobile health (mHealth), (ii) oral anticoagulants (OACs), (iii) medication adherence and (iv) randomised controlled trials (RCTs). These terms were combined using Boolean 'AND' and 'OR' operators, but no restrictive field tags were used to increase the search sensitivity, as detailed in Appendix A.

2.3.4 Selection process

The results were exported into the reference managing software, Zotero, and duplicate results were removed. The screening and selection of studies against the eligibility criteria was performed by one reviewer. This was initially done by the titles and abstracts, then by the articles' full-texts.

2.3.5 Data collection process

Data extraction was performed by one reviewer.

2.3.6 Data items

The following data were extracted: the author, publication year, country, duration, sample size, demographics, study methodology, characteristics of the intervention and control groups, details of the outcomes assessed and their measures, study results, and the authors' interpretation of the results.

2.3.7 Methodological quality (risk of bias assessment)

To assess the methodological quality of the studies included in the review, the risk of bias instrument for interventional adherence studies (RoBIAS) was employed (Sinnappah *et al.,* 2023). This tool was in development at the time of writing, and is subject to further validation, however, it includes the main

points from the International Society for Patient Adherence (ESPACOMP) Medication Adherence Reporting Guideline (EMERGE) (De Geest *et al.,* 2018) and the Timelines–Events–Objectives–Sources (TEOS) framework for medication adherence research (Dima *et al.,* 2021; Dima *et al.,* 2022). Studies were scored on four domains (**bias related to; study design and implementation of study procedures, randomisation and blinding procedures, adherence outcome measurement and reporting, data analysis and interpretation**) across a scale of whether items were *fully present* (a score of 5) or *fully absent* (a score of 1). Items considered *not relevant* were given a score of 0. This produced an overall score for each domain, corresponding to a bias judgement, ranging from *very low* to *critical*, and *unsure* if all items across all domains were scored zero.

2.3.8 Synthesis methods

A meta-analysis will not be performed due to differences across the RCTs, which included diversity in the methodology, intervention characteristics and reported outcomes of studies. Alternatively, a narrative synthesis of the data was undertaken in which studies were grouped by frequencies – such as of the mHealth intervention employed, the adherence methods used, and the outcomes assessed. In summarising the findings, emphasis was placed on studies that were highest in methodological quality (risk of bias) or largest in cohort size. Data are displayed in tabular format, organized according to OAC and then by date. Reporting aimed to align with the synthesis without meta-analysis (SWiM) guideline (Campbell et *al.,* 2020).

2.4 Results

A total of 2,319 studies were identified. The removal of 557 duplicates resulted in 1,762 results that were potentially relevant. A total of 1,673 results were excluded by title and abstract screening, resulting in 89 full-text articles being sought for retrieval. A total of 88 full-text articles were retrieved. Of these, 73 articles were excluded for reasons detailed in Figure 2, leaving 16 studies included in the final review.

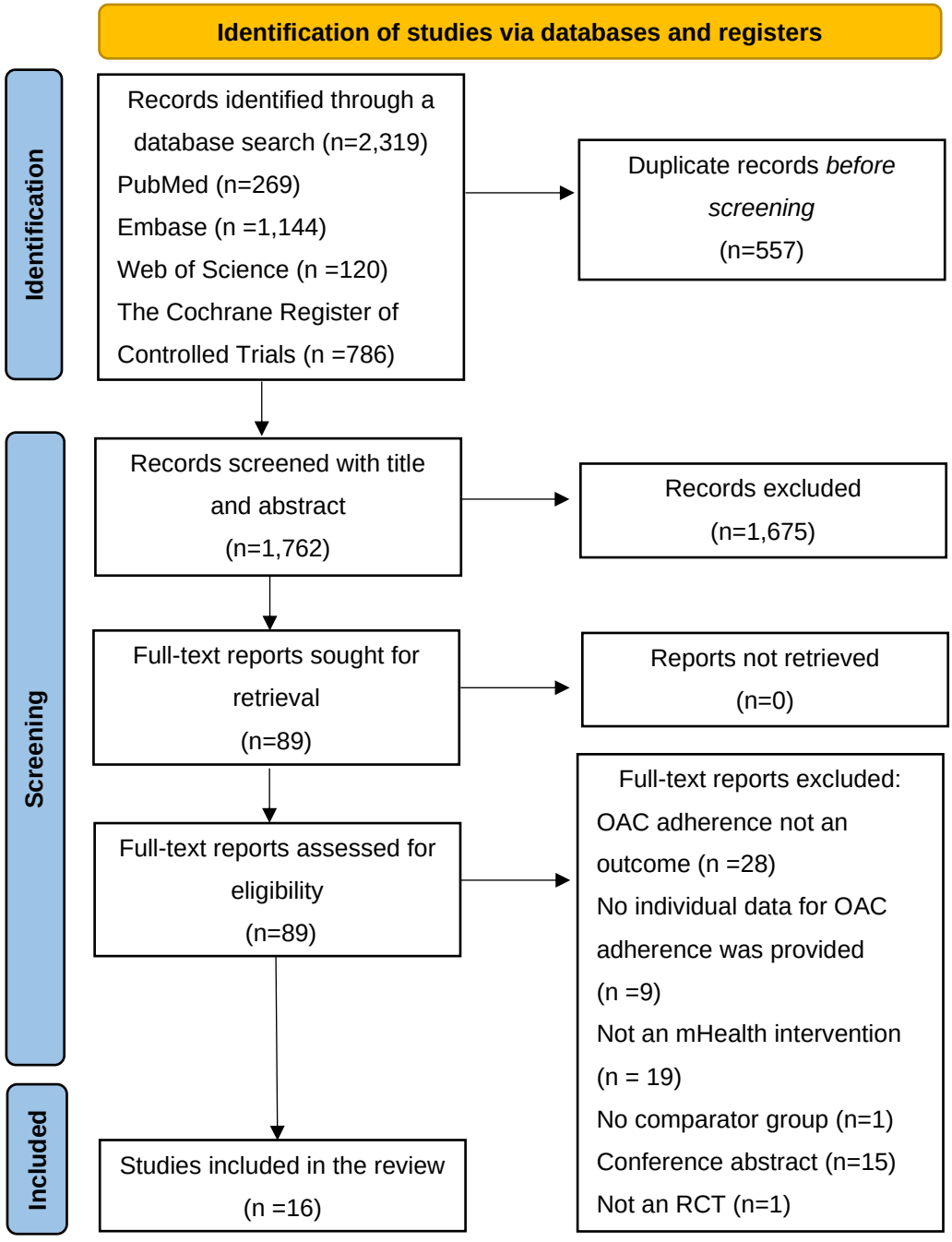

Figure 2 – Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram. Adapted from Page *et al.,* 2020. OAC; Oral anticoagulant, mHealth; Mobile health, RCT; Randomised controlled trial.

2.4.1 Study characteristics

Study characteristics are summarized in Table 4. A total of 8,492 participants were randomised across the 16 studies, recruited from 12 different countries. Most (nine studies) were conducted in the United States of America. Study sample sizes ranged from 28 to 3,821, and follow-up periods ranged from 30 days to one year. All studies were based in settings of ambulatory care, with no mean or median age falling below 57 (SD 13.2) years of age. Overall, 43.1% of participants were female.

Details of the experimental methods are summarized in Table 5. The studies assessed both clinical, and non-clinical outcomes. Medication adherence was the primary outcome in seven studies (studies 1,4,10,11,13,14,16) and reported as a secondary outcome in the other nine studies (studies 2,3,5-9,12,15). Four studies (studies 2,3,6,15) stated a primary outcome other than medication adherence, with two based on health-related quality of life (studies 6,15) and two based on anticoagulation control according to the international normalised ratio range (studies 2,3). Four studies (studies 5,8,9,12) did not state the primary outcome explicitly, whilst the primary outcome results of one study (study 7) were reported in a separate publication. Five studies (studies 4-8) considered adherence to both warfarin and at least one DOAC, three studies (studies 1,2,3) assessed adherence to warfarin alone, six (studies 9-14) to DOACs, while it was not specified in two further studies (studies number 15,16). Most RCTs used a parallel design, with just one (study 9) using a crossover design. The reporting of the blinding processes used was generally poor, with four studies (studies 1,4,11,13) not reporting their blinding process explicitly and just two studies (studies 8,10) reporting double-blind allocation. The sample size calculation was not reported in 5 studies (studies 4,8,9,12,13).

Table 4 – Characteristics of the included studies

Study number	Author Year Country	Study methodology	Sample size	Inclusion criteria	Sample demographics (Age in years)	Follow-up period	Measure of adherence
1	Peng *et al.,* 2014 China.	A multicentre, parallel, cluster-randomised, controlled trial of an interactive website for improving adherence to warfarin, statins, antiplatelets, antihypertensives, and antidiabetics (blinding process not explicitly reported).	Control=2,026 (24 clusters) Intervention=1,795 (23 clusters)	Aged ≥18, suffered a stroke due to cerebral infarction/transient ischemic attack, admitted to hospital within 30 days of occurrence, stable, was independent beforehand.	Mean age=60.36 (SD 11.66) (control), 61.48 (SD 11.47) (intervention) 31.94% female.	12 months.	Not explicitly reported.
2	Kimmel *et al.,* 2012 The USA.	A parallel, randomised, controlled trial of lottery-based incentives for improving warfarin anticoagulation control (only investigators and analysts blinded).	Control=48 Intervention=53	Aged ≥21 years, receiving care at the University of Pennsylvania Anticoagulation Management Centre, target INR between 2-3, have previously achieved stable anticoagulation with warfarin.	Median age=59.5 (control), 64.0 (intervention) 44% female.	6 months.	The Med-emonitor (a MEMS).
3	Kimmel *et al.,* 2016 The USA.	A four-arm, multi-centre, parallel, randomised, controlled trial of lottery-based incentives and reminders for improving out-of-range INR values (only coordinators, investigators and analysts blinded).	Control=68 Interventions=67 (lottery), 67 (reminder), 68 (lottery + reminder)	A functioning telephone line, expected to be on warfarin therapy for a minimum of 6 months, INR between 2.0-3.5, experienced a minimum of one out-of-range INR reading within 90 days before study enrolment/at study enrolment.	Overall median age=62 32% female.	6 months.	The Med-emonitor (a MEMS).
4	Labovitz *et al.,* 2017 The USA.	A parallel, randomised, controlled trial of an artificial intelligence platform for improving adherence to warfarin and DOACs (blinding process not explicitly reported).	Control=13 Intervention=15	Diagnosis of ischemic stroke (with/without preceding transient ischemic attack, with a NIHSS score between 1-20), prescribed OAC.	Mean age=57 (SD 13.2) 53.6% female.	12 weeks.	Pill counts, visual confirmation of drug being taken via artificial intelligence and plasma sampling.
5	Toscos *et al.,* 2020	A parallel, randomised, controlled trial of an online educational portal (primary outcome not explicitly	Control=80 Intervention=80	Adult cardiology outpatient at Midwestern United States hospital, nonvalvular AF diagnosis, OAC	Mean age=71.1 (SD 8.5) 37.50% female.	6 months.	Smart pill bottle.

	The USA.	reported, group allocation was unblinded).		prescription, internet/computer access, a MyChart account/ready to register.			
6	Gallagher *et al.,* 2020 Australia.	A multi-centre, prospective, parallel, randomised, controlled, feasibility study of an electronic OAC decision support tool for improving HRQL (researcher conducting final assessments blinded).	Control=36 Intervention=36	Aged ≥18 years, electrocardiogram displaying AF.	Mean age=65 (SD 11) 44% female.	3 months.	Morisky medication adherence scale.
7	Noseworthy *et al.,* 2022 The USA.	A single-blind, parallel, multicentre, encounter-randomised, controlled trial of an online OAC shared decision-making tool used during an in-person encounter.	Control=459 Intervention=463	Aged ≥18, have non-valvular AF, CHA_2DS_2-VASc score ≥1 (men)/ ≥2 (women), can read and comprehend the consent form.	Mean age=71 (SD 10) (control), 71 (SD 11) (intervention) 39.37% female.	10 months.	Pharmacy refill data.
8	Liu *et al.,* 2022 China.	A double-blind, parallel, randomised, controlled trial of follow-up telephone calls conducted by a clinical pharmacist (primary outcome not explicitly reported).	Control=64 Intervention=61	DVT diagnosis, discharged in the acute phase following treatment, received warfarin/rivaroxaban following discharge, voluntary participation.	Mean age=61.89 (SD 11.52) (control), 63.80 (SD 12.09) (intervention) 50.4% female.	6 months.	Standardized form.
9	Desteghe *et al.,* 2018 Belgium.	A single-blind, 3-phase crossover, controlled trial, in which patients on DOACs were randomised to daily telemonitoring or telemonitoring with immediate telephone feedback in case of intake errors, followed by an observation phase without daily transmissions.	24 participants randomised were to each group.	Have consecutive AF, currently taking/starting apixaban or rivaroxaban.	Mean age=72 (SD 9) 50% female.	9 months.	MEMS, pill count and MMAS-8.
10	Montalescot *et al.,* 2020 Belgium, France,	A double-blind, parallel, randomised, controlled trial of an educational programme for improving adherence to apixaban.	Control=583 Intervention=579	Non-valvular AF/atrial flutter diagnosis (new or existing), ≥ 1 $CHADS_2$ score.	Mean age=72.6 (SD 8.9) (control), 73.1 (SD 9.1) (intervention) 48.02% female.	48 weeks.	Electronic monitoring device (the Helping Hand).

	Germany, Italy, Spain, Switzerland, and the UK.						
11	Tran AT *et al.,* 2022 The USA.	A parallel, randomised, controlled trial of a smartphone-based application, paired with an online portal, for improving adherence to apixaban (blinding process not explicitly reported).	Control=50 Intervention=50	Have non-valvular AF, a CHA_2DS_2VASc score of 2/higher and can be treated with apixaban for 6 months.	Median age=70.8 50% female.	6 months.	Pill counts.
12	Chen *et al.,* 2017 The USA.	An open-label, parallel, randomised, controlled trial of using electronic personal health records for health-related education and management (primary outcome not explicitly reported).	Control=44 Intervention=46	Aged ≥18 years, diagnosed with AF, prescribed dabigatran for stroke prevention, can read, and comprehend English, have internet access.	Mean age=66 30% female.	30 days.	Pharmacy dispensing and refill data.
13	Merks *et al.,* 2022 Poland.	A cluster-randomised (stratified by pharmacy size), controlled trial of telephone follow-up calls paired with smartphone-based reminders to improve adherence to dabigatran (blinding process not explicitly reported).	Control=172 Intervention=153	Aged ≥18 years, diagnosed with venous thromboembolism/non-valvular AF, prescribed dabigatran for the first time, could be contacted by telephone, spoke Polish sufficiently for assessment.	Mean age=67.1 (SD 10.1) (control), 67.6 (SD 10.5) (intervention) 49.8% female.	90 days.	Questionnaire.
14	Turakhia *et al.,* 2021 The USA.	An open-label, randomised, controlled trial of a blended digital and human intervention to improve DOAC adherence.	Control=67 Intervention=72	Aged ≥18, recently (≤90 days) prescribed rivaroxaban for AF, nonadherence risk of at least 1 of 4, possess a smartphone.	Mean age=65 (SD 9.6) 30% female.	6 months.	Pill counts and pharmacy refill data.
15	Guhl *et al.,* 2020 The USA.	An open-label, parallel, randomised, controlled trial of a smartphone-based application to improve HRQL.	Control=59 Intervention=61	Aged ≥18 years, have chronic AF, prescribed OAC for stroke prevention,	Mean age=72.1 (SD 9.10) 51.7% female.	30 days.	Questionnaire.

				speak adequate English to use the intervention.			
16	Tzikas *et al.*, 2021 Greece.	A prospective, parallel, randomised, controlled trial of motivational interviewing to improve adherence to an unspecified OAC (participants and study personnel unblinded, but outcome and data analysist blinded).	Control=509 Intervention=500	Aged ≥18, AF diagnosis, OAC prescription at discharge.	Median age= 76.0 (control), 75.5 (intervention) 46.48% female.	1 year.	Claimed prescriptions.

INR; International normalized ratio, AF; Atrial fibrillation, MMAS-8; 8-part Morisky Medication Adherence Survey, NIHSS; NIH stroke scale, OAC; Oral anticoagulation, CHA_2DS_2-VASc; Congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack, thromboembolism, vascular disease, age 65–74 years, sex category, PDC; Proportion of days covered, DOAC; Direct oral anticoagulant, TTR; Time in therapeutic range, MEMS; Medical events monitoring system, USA: United States of America, UK; United Kingdom, HRQL; Health-Related Quality of Life.

Table 5 – Study methods.

Study number	Intervention	Other non-mhealth aspects of the study	Comparator	Primary outcome and measure(s)	Secondary outcome(s) and measure(s)
1	An interactive educational website that could only be accessed using a provided password. The website included content on stroke prevention, details on the risk factors involved, the role of medication in reducing the risk, and lifestyle modifications.	Medication intervention and neurologist care. Potential adaptations to lifestyle (specifically the effects of smoking, diet, and exercise) were discussed with participants.	Care as chosen by a neurologist. No access to the interactive/website education was provided.	1. Adherence to warfarin, statins, antiplatelets, antihypertensives, and antidiabetics for preventing stroke (measure not explicitly reported).	2. New onset of ischemic stroke, new onset of haemorrhagic stroke, acute coronary syndrome, and all-cause death.
2	A daily lottery, administered via the Med-emonitor. Upon opening the monitor and confirming warfarin intake, participants were in with a chance of winning $10 (one in five) or $100 (one in 100) daily. This data was transferred via a telephone line to research personnel.	Usual clinic visits at two weeks, three, and six months. Data was collected, but no additional interventions were given during these visits.	Usual clinic visits at two weeks, three and six months. No interventions were given during these visits.	1. Warfarin anticoagulation control (percentage of out-of-range INR).	2. Warfarin adherence (measured by the Med-emonitor). 3. Thromboembolism. 4. Bleeding events.
3	The Med-emonitor stored and dispensed warfarin, with encouraging/educational automated messages exhibited on its screen. The reminder group had additional reminders/alarms. The lottery group could win $10 (one in five) or $100 (one in 100) daily upon warfarin intake. The remaining group had a combination of reminders and a daily lottery.	Data collection occurred on a regular basis (in person/by telephone). No further details were explicitly reported.	Participants were provided with the Med-emonitor, which had the same functions as the ones provided for the intervention groups (but without the reminders/alarms/lottery incentives). Data collection occurred on a regular basis (in person/by telephone), but no further details are explicitly reported.	1. Percentage of time out of INR range.	2. Percentage of days with incorrect warfarin adherence (measured by the Med-emonitor). 3. Bleeding, stroke, and thrombotic events.

4	Medication adherence was determined by artificial intelligence software, which also provided dosing instructions and reminders (sent within an hour of a missed dose, or towards the end of the specified dosing time). Clinicians were alerted by intake errors in an automated manner via email/text.	No.	Participants were not monitored daily, but no further details are explicitly reported.	1. Adherence to warfarin, dabigatran, rivaroxaban, or apixaban (measured by pill counts, visual confirmation of drug being taken via artificial intelligence and plasma sampling).	2. Activated partial thromboplastin time. 3. Prothrombin time. 5. Artificial intelligence usability and feasibility (measured by questionnaire).
5	Medication was stored and dispensed using a smart pill bottle. The MyChart online portal allowed messages and reminders to be delivered to the participant upon an intake error. Educational material (such as risks and side effects) and video links could also be accessed in MyChart.	No.	Standard care. Medication was dispensed and stored using a smart pill bottle.	Do not state which outcome was the primary outcome.	1. Medication adherence for warfarin and DOACs (measured using a smart pill bottle). 2. Intervention uptake (measured by MyChart logins). 3. AF knowledge (measured by a series of questions).
6	An electronic OAC decision support tool was used to facilitate a cardiac nurse-led session, encouraging suitable OAC use. Three to four telephone follow-up calls were conducted by a cardiac nurse where progress was reviewed (three calls would be attempted). The length of the calls is not explicitly reported.	The cardiac nurse-led session assessed risk factors and discussed medication management. Motivational interviewing for goal setting was employed with resources printed/provided in a written format for the participants. The session duration was about one hour (but varied based on each participant).	Usual cardiologist/general practitioner follow-up care, who was responsible for determining the frequency of follow-up.	1. HRQL (measured by the SF-12 questionnaire).	2. Medication adherence for warfarin and DOACs (measured using the Morisky medication adherence scale). 3. Cardiovascular risk factors (BP, BMI, waist circumference, and physical activity) measured by conducting measurements and by using the global physical activity questionnaire. 4. Appropriate use of OAC (measured by the CHA_2DS_2-VASc where a score of ≥2 is indicative of OAC use unless a contradiction is present, 0 is indicative of OAC not being

					necessary expect in certain scenarios, and 1 indicating that OAC use is appropriate unless being female was an isolated risk factor).
7	An online OAC shared decision-making tool used during an in-person encounter. Information is provided by the tool such as the risks involved, the cost of the medication and possible interactions. The tool can be viewed and accessed online without any restrictions (no further details are explicitly reported).	The encounter was in-person.	Usual care (no further details are explicitly reported).	Primary outcomes (participant-perceived quality of the shared decision-making tool, measured by a survey) have been previously published (Kunneman *et al.,* 2017).	1. Primary (measured by pharmacy refill data) and secondary (expressed as PDC for DOACs and TTR for warfarin) adherence. 2. Clinical safety outcomes.
8	Follow-up telephone calls by a clinical pharmacist were made post-discharge every week for the six-month duration of the study (no further details regarding the content/duration of the calls are explicitly reported).	Usual care that mirrored that of the control group.	The usual guidance on medication, routine monitoring, and education was provided by a clinical pharmacist. Telephone follow-up calls made at three- and six-months post-discharge by a clinical pharmacist.	Do not state which outcome was the primary outcome.	1. TTR. 2. Warfarin and rivaroxaban medication adherence (measured using a standardized form). 3. Adverse events. 4. Patient satisfaction (measured by questionnaire).
9	A MEMS cap was used to monitor medication adherence. During the feedback phase, clinicians conducted telephone calls if an 'unprotected day' occurred, defined as ≥3 (apixaban) or ≥1 (rivaroxaban) missed doses or excess doses during the previous 24 hours.	No.	A MEMS cap was used to monitor participant medication adherence. Participants were required to position the MEMS onto a wireless reader following each dose intake for data to be transferred.	Do not state which outcome was the primary outcome.	1. Apixaban and rivaroxaban adherence (measured by a MEMS, pill count and MMAS-8). 2. Cost-effectiveness. 3. Patient experience (measured by questionnaire).

10	Each participant chose a reminder tool. Access was provided to a virtual clinic, including telephone follow-up within a week of group allocation to check understanding. Between 10-20 days later, another call was made. Calls were then conducted monthly to offer advice and stress the value of adhering to medication.	Information about Apixaban was provided by the investigator, which included both an information sheet and a card. Intervention participants received an educational booklet.	Information about Apixaban was provided by the investigator, which included both an information sheet and a card.	1. Apixaban dosing regimen implementation adherence (measured using the Helping Hand).	2. Apixaban persistence. 3. Clinical events.
11	The AliveCor Kardia is a smartphone-compatible ECG monitor to measure heart rhythm. For five days a week, participants took a reading every day. An online portal was used to assess participant monitoring adherence, with portal-based reminders sent by a nurse if participant nonadherence was evident.	Participants were instructed on the application by a nurse. Participants received a prefilled pill organizer.	Standard AF treatment and monthly nurse visits, where the smartphone ECG was used to measure heart rhythm.	1. Apixaban adherence (measured by pill count).	2. Composite of deaths, stroke, and hospitalization for congestive heart failure/AF.
12	Patient training on an individual basis (and refresher training at week eight of the study) to access the online PHR (MyChart) via a mobile/computer device. MyChart allows participants to access educational material, communicate with clinicians, review results of tests, arrange/review appointments, and manage prescriptions.	No.	Access to the PHR (MyChart) without any training or personalization.	Did not state which outcome was the primary outcome.	1. Dabigatran adherence (measured using pharmacy refill data). 2. Dabigatran knowledge (measured by questionnaire, with higher scores indicative of better knowledge). 3. Patient engagement (measured by the PAM survey, range 0-100 with higher scores indicative of better engagement).
13	Telephone follow-up at seven, 21 and 90 days by a pharmacist that integrated the NMS programme.	A pharmacist educated the participants on the medication during dispensing. A dabigatran	Usual pharmacy care, with follow-up telephone calls made by a pharmacist at	1. Dabigatran adherence (measured by questionnaire).	No other outcomes were assessed.

	Participants were given the opportunity to ask questions during these calls. Reminders were sent via a smartphone-based application, but it is not explicitly reported whether these reminders were automated or triggered by nonadherence.	information sheet with pictures was provided.	seven, 21 and 90 days. The group could use any smartphone-based application/reminder system if they wished to do so.		
14	The Care4Today smartphone-based application tracked adherence and refill activity whilst sending reminders. Text messages were sent ('semi-automated'), and telephone calls were made if medication ingestion was as low as zero, one or two days a week. If calls went unanswered, information was transferred to the participant via voicemail and text.	No.	Usual AF care was provided by the participant's primary AF clinician (who was the prescriber and responsible for medication refills).	1. Rivaroxaban adherence (measured by pill counts/refill data).	2. Proportion of participants with PDC ≥ 80%. 3. Change in the MMAS-8 scores. 4. Medication persistence (measured by the proportion of participants with active prescription at 6 months).
15	The smartphone-based Kardia application measures HR and rhythm. The smartphone-based animated counsellor interacts with the participant, with conversations focused on education, symptoms, and adherence. Dialogue is personalized based on previous conversations, using the participant's real name and details. Participants used both applications every day.	No.	Sole access to the application.	1. HRQL (measured by the AFEQT instrument, 0-100 range with higher scores indicative of better HRQL).	2. Self-reported adherence to anticoagulation. OAC N/S. (measured by questionnaire with lower values indicative of better adherence). 3. Intervention acceptability (qualitative).

16	Telephone calls were made at week 1, months two, and six, to reiterate the in-person education that was provided upon discharge.	A discussion (between 15 to 20 minutes) regarding OAC treatment with a study team member upon discharge and a leaflet summarizing all the information provided. Motivational interviewing was a key aspect, aiming to motivate participants to adhere to their medications.	Standard AF care.	1. OAC (N/S) adherence (measured by claimed prescriptions).	2. OAC persistence. 3. Treatment gaps (continuous OAC use=no gaps/gaps <7 days, transient treatment gaps=7-89 days, and major treatment gaps=3 months/more). 4. Clinical events (cardiovascular and thrombotic death, major bleeding, and myocardial infarction).

INR; International normalized ratio, MMAS-8; 8-part Morisky Medication Adherence Survey, AF; Atrial fibrillation, OAC; Oral anticoagulation, HRQL; Health-related quality of life, DOAC; Direct oral anticoagulant, TTR; Time in therapeutic range, BP; Blood pressure, BMI; Body max index, OAC; Oral anticoagulation, CHA_2DS_2-VASc; Congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack, thromboembolism, vascular disease, age 65–74 years, sex category, PDC; Proportion of days covered, PHR; Personal health record, PAM; Patient activation measure, AFEQT; Atrial fibrillation effect on quality of life, MEMS; Medical events monitoring system, SF; Short form 12 survey.

2.4.2 mHealth interventions

Seven different mHealth interventions were described within the included studies, with eight studies (studies 4-7,9,11,12,15) including an element of personalization and nine (studies 3-6,9,10,11,13,14) using a multi-component mHealth intervention. The mHealth interventions most frequently employed were telephone calls and text messages (studies 4,6,8,9,10,12,14,16). Patients were called by telephone to review their progress, provide information, or answer queries. In three studies, (studies 4,9,14) telephone calls and text messages were conducted or sent in response to episodes of non-adherence, acting as reminders for participants to take their medication. Other methods of electronic reminders included alerts and notifications via smartphone-based applications and online portals (studies 3,4,5,10,11,13,14). Web-based platforms were used to promote patient education and healthcare management in four studies (studies 1,5,11,12). RCTs that assessed smartphone-based applications and electronic medication dispensers or caps included two which additionally incorporated lottery-based incentives into the technical design of the electronic dispenser (studies 2,3). Other trials assessed shared decision-making OAC support tools (studies 6,7) and an artificial intelligence platform (study 4).

Most studies reported usual or standard care as the comparator group.

2.4.3 Definition and measurement of adherence

Just one study (study 10) reported explicitly the adherence phase studied (implementation). A range of methods for measuring adherence were used across the studies (Table 6). Electronic measures, such as smart pill bottles and medication events monitoring systems, were the most frequently employed. Other methods included self-reported measures of adherence (questionnaires and standardized forms), pharmacy data (dispensing and refill data), artificial intelligence determination of dose-taking, plasma sampling and pill counts. One study did not specify the adherence measure used (study 1), four studies (studies 1,6,8,11) did not report the metric used to quantify adherence, and five studies (studies 2,5,9,12,13) did not report the method of data aggregation used to summarize the adherence data collected.

Table 6 – Adherence characteristics.

Study number	Phase	Measurement	Metric	Data aggregation
1	Not explicitly reported.	Not explicitly reported.	Not explicitly reported.	The number of adherent participants, as determined by the SMART program (details unspecified), expressed as a percentage of the total number of participants in the group, for each group.
2	Not explicitly reported.	The Med-emonitor (a MEMS).	Percentage of days incorrect.	Not explicitly reported.
3	Not explicitly reported.	The Med-emonitor (a MEMS).	Percentage of days that adherence was incorrect.	Median (IQR) for each group.
4	Not explicitly reported.	Pill counts, visual confirmation of drug being taken via artificial intelligence and plasma sampling.	The pill count metric is not explicitly reported. Plasma samples were described as 'adherent' if the minimum therapeutic range (which is not explicitly reported) was reached.	Mean cumulative adherence per patient (pill count, artificial intelligence). The mean number of 'adherent' samples, expressed as a percentage of the total number of samples (plasma sampling).
5	Not explicitly reported.	Smart pill bottle.	The number of doses taken as a proportion of the number of prescribed doses.	Not explicitly reported.
6	Not explicitly reported.	Morisky medication adherence scale.	Not explicitly reported.	The number of participants with 'low, 'medium,' and 'high' scores, expressed as a percentage of the total number of participants in the group, for each group.
7	Not explicitly reported.	Pharmacy refill data.	The number of prescriptions filled (primary adherence), the proportion of days covered for DOACs and time spent in the therapeutic range for warfarin (secondary adherence).	The number of participants who filled their first prescription, expressed as a percentage of the total number of participants in the group, for each group (primary adherence).

				Mean for each group (secondary adherence).
8	Not explicitly reported.	Standardized form.	Not explicitly reported.	The number of cases in the same period, self-reduction of medication frequency, and missed and low doses, expressed as a percentage of the total number of participants in the group, for each group
9	Not explicitly reported.	MEMS, pill count and MMAS-8.	The proportion of prescribed doses taken (taking adherence) and the proportion of days with the correct number of doses taken (regimen adherence) are established by MEMS data. MMAS-8 scoring system nor pill count metric explicitly reported.	Not explicitly reported.
10	Implementation.	Electronic monitoring device (the Helping Hand).	The proportion of days adhering to the prescribed regimen.	Mean (SD) for each group.
11	Not explicitly reported.	Pill counts.	Not explicitly reported.	Median (IQR) for each group.
12	Not explicitly reported.	Pharmacy dispensing and refill data.	Medication Possession ratio.	Not explicitly reported.
13	Not explicitly reported.	Questionnaire.	The questions are outlined.	Not explicitly reported.
14	Not explicitly reported.	Pill counts and pharmacy refill data.	The proportion of days covered.	Mean (SD) and median (IQR) for each group.
15	Not explicitly reported.	Questionnaire.	The questions are outlined.	The number of participants answering ‘yes,’ expressed as a percentage of the total number of participants in each group, for each question.

16	Not explicitly reported.	Claimed prescriptions.	The proportion of days covered ('good adherence' defined as PDC >80%).	The number of 'good adherence' events, expressed as a percentage of the total number of participants in each group, for each group.

PDC; Proportion of days covered. IQR; Inter quartile range, SD; Standard Deviation, DOACs; Direct oral anticoagulants, MEMS; Medical events monitoring system, MMAS-8; 8-part Morisky Medication Adherence Survey.

2.4.4 Summary of findings

Seven studies reported a significant improvement in medication adherence (Table 7). Telephone calls or text messages were most frequently associated with statistically significant improvements in medication adherence (studies 8,9,13,16). For instance, the least biased study included in this review conducted by Tzikas *et al.,* (2021), (study 16) reported mean (SD) OAC adherence (based on percentage of days covered >80% derived from 1-year of prescriptions claims data), as 0.85 (± 0.26) in the intervention group, compared with 0.75 (± 0.31) in the control group ($p<0.001$). Three studies (studies 3,9,13) reporting a significant improvement used an intervention that was comprised of multiple components of mHealth. In the largest of these studies, Merks *et al.,* (2022) (study 13) described self-reported adherence to the prescribed dose at 90-days as 78.4% in the intervention group, compared with 39.7% in the control group; a difference of 38.7% (OR 5.51,95% CI 3.08–9.85, p=0.0001). Electronic medication dispensers or smart pill bottles were used in two studies that indicated statistical significance (studies 3,9). Kimmel *et al.,* (2016) (study 3) additionally incorporated lottery incentives into the technical design of the dispenser, and reported a 11.6% (95% CI −14%, −0.3%) difference in the percentage of days with incorrect warfarin adherence between lottery (12.1%) and control (23.7%).

2.4.5 Methodological quality (risk of bias assessment)

Overall, the studies included in this review were of poor methodological quality (Table 8), with 15 studies deemed to be either at a '*serious*' or *'high'* overall risk of bias. Generally, studies scored best with respect to study design and implementation of procedures, data analysis and interpretation. Studies scored worst in relation to adherence outcome measurement and reporting.

Table 7 – Summary of findings.

Study number	Primary outcome results and significance (Intervention vs. comparator)	Secondary outcome(s) results and significance (Intervention vs. comparator)	Author's conclusion
1	1. Adherence at 12-months: Statins 56% vs. 33% (P=0.006). Antiplatelet 81% vs. 75% (P=0.088). Antihypertensive 67% vs. 69% (P=0.661). Antidiabetic 73% vs. 67% (P=0.297). No percentages or significance values were reported for warfarin due to the small number of participants.	2. Composite secondary endpoints at 12-months: 3.50% vs. 3.59% (P=0.921).	The website-based educational intervention program was proven to be feasible but failed to significantly improve adherence rates and outcomes.
2	1. Overall warfarin anticoagulation control: 23.0% vs. 25.9% (unadjusted OR 0.81, 95% CI 0.53-1.22, P=0.3051).	2. Overall warfarin adherence (percentages interpreted from Figure 2B of the study): 18% vs. 23% (unadjusted OR 0.78, 95% CI 0.49-1.25, P=0.3038). 3. No thromboembolism. 4. No bleeding that required hospitalization but 3 ED visits in the intervention group and 17 minor bleedings in the intervention group vs. 10 minor bleedings in the control group (P=0.36).	Overall anticoagulation control was not significantly impacted by the Med-emonitor's lottery intervention. A significant impact was only seen in a small subgroup of 'high risk for poor adherence' participants during *post-hoc* analysis.
3	1. Percentage of time out of INR range: 30.1% (lottery) vs. 23.8% (reminder) vs. 23.9% (lottery + reminder) vs. 31.6% (control) (P=0.29).	2. Percentage of days with incorrect warfarin adherence: 12.1% (lottery) vs. 21.8% (reminder) vs. 17.6% (lottery + reminder) vs. 23.7% (control) (P=0.03). Significance was only observed between lottery and control groups (95% CI −14%, −0.3%, but no P value explicitly reported). 3. Bleeding events: 6.2% (lottery) vs. 6.3% (reminder) vs. 7.6% (lottery + reminder) vs. 6.2% (control) (P= 1.00). One stroke (P=0.76) and two thrombotic events (non-CNS) in the lottery group (P=0.18).	Reminders, but not lottery incentives alone or in combination with reminders, proved beneficial in improving warfarin control. Despite this, improved warfarin adherence was only observed in the lottery incentives group.
4	1. Pill count mean cumulative adherence: 97.2% (SD 4.4%) vs. 90.6% (SD 5.8%). Plasma sample adherence: 100% vs. 50%. Artificial intelligence mean cumulative adherence: 90.5% (SD 7.5%).	2. Activated partial thromboplastin time: 41.7 vs. 48.4. 3. Prothrombin time: 35.1 vs. 32.9. 4. INR: 3.4 vs. 3.1. 5. Artificial intelligence usability and feasibility: 73.3% (pre-study) and 83.3% (post-study) rated the intervention 'extremely good.'	Medication adherence was increased by the intervention. This highlights the potential benefit of real-time monitoring for promoting DOAC treatment behavioural changes.

	Significance level not reported.	Significance level not reported.	
5	Do not state which outcome was the primary outcome.	1. Overall warfarin and DOAC adherence: 93.1% vs. 89.5% (95% CI -0.04-0.002, P=0.08). 2. Intervention uptake during the study: 42.7 ± 37.0 vs. 15.9 ± 16.0 (χ^2 = 62.04, P< 0.0001). 3. AF knowledge at follow-up was higher in the intervention than in the control group (χ^2=6.66, P=0.0099, controlled for AF knowledge at baseline), but no percentages were explicitly reported.	Both Medication adherence and AF knowledge were increased by the intervention. This illustrates the feasibility of using health-promoting technologies in mature adults.
6	1. HRQL at 3-months: Physical component summary 51 vs. 45 (P=0.03). Mental component summary 53 vs. 52 (P=0.42). Physical functioning 75 vs. 50 (P=0.04). Role Physical 75 vs. 50 (P=0.01). Bodily pain 75 vs. 50 (P=0.12). General Health 60 vs. 60 (P=0.17). Vitality 50 vs. 38 (P=0.19). Social functioning 75 vs. 75 (P=0.44). Role emotional 88 vs. 75 (P=0.16). Mental Health 75 vs 63 (P=0.19).	2. Warfarin and DOAC adherence at 3-months: No significant differences between intervention and control groups (P=0.81), but no overall percentages were explicitly reported. 3. Cardiovascular risk factors at 3-months: Systolic BP 125 ± 21 vs. 124 ± 15 mm Hg (P=0.80). Diastolic BP 71 ± 11 vs 73 ± 11mm Hg (P=0.39). BMI 30.0 ± 6.7 vs. 30.2 ± 5.9 kg/m^2 (P=0.90). Waist circumference 104 ± 13 vs. 104 ± 16cm (P=0.97). Physical activity levels 8.5 ± 1.1 vs 8.4 ± 1.2 (P=0.60). Smoking status 6.1% vs. 3.0% (P=1.0). 4. Appropriate OAC use at 3-months: 93.9% vs. 97.0% (P=1.0).	No significant impacts were seen at follow-up succeeding intervention implementation. This suggests that greater intervention intensity is needed when moving forward.
7	Primary outcomes have been previously published.	1. Primary adherence: 78% vs. 81% (95% CI 0.57-1.19). DOAC mean secondary adherence: 74.1 vs. 71.6 (95% CI -3.5-8.3). Warfarin mean secondary adherence: 66.6% (95% CI 61.9-71.4) vs. 64.4% (95% CI 42.8-54.1). 2. Combined major bleeding, cerebrovascular event, and any cause of death: 13% vs. 14%.	Primary and secondary adherence were not significantly impacted, nor were the clinical safety outcomes following the implementation of a shared decision-making tool.
8	Do not state which outcome was the primary outcome.	1. TTR and proportion of patients with a TTR ≥65%: 73.22% ± 11.32, 77.5% vs. 60.15% ± 14.75, 44,9% (P<0.05). 2. Medication adherence: Warfarin and rivaroxaban adherence was higher in the intervention group (P<0.05) but no overall percentages were explicitly reported. 3. Adverse events:	The risk of haemorrhage and thrombosis became decreased, whilst the safety, effectiveness, and adherence to warfarin and rivaroxaban became increased

		Haemorrhagic stroke 1.64% vs 12.5% (P=0.019). Minor haemorrhage events 11.8% vs. 31.3% (P=0.007). Thrombosis events 0 vs. 7.8% (P=0.033). 4. Patient satisfaction: General satisfaction 4.1 ± 0.81 vs. 3.6 ± 0.91 (P=0.041). Follow-up technical quality 4.1 ± 0.68 vs. 3.6 ± 0.91 (P=0.282). Follow-up impersonal manner 4.1 ± 0.74 vs. 3.6 ± 0.69 (P=0.019). Pharmacist patient communication 4.2 ± 0.72 vs. 3.5 ± 0.73 (P=0.003). Follow-up financial aspects 3.9 ± 0.73 vs. 3.6 ± 0.94 (P=0.391). Follow-up timeliness 4.1 ± 0.85 vs. 3.5 ± 1.02 (P=0.048). Follow-up accessibility and convenience 4.3 ± 0.67 vs. 3.7 ± 1.01 (P=0.017).	following a pharmacist-led intervention.
9	Do not state which outcome was the primary outcome.	1. Active phase adherence: Taking adherence 99.0% vs. 97.4% (P<0.001). Regimen adherence 96.8% vs. 93.8% (P=0.002). Pill count adherence 99.0% vs. 97.9% (P=0.002). Observational phase adherence: Significant decreases were only observed in taking adherence (99.1% to 94.3%, P=0.049) and pill count adherence (99.1% to 96.7%, P=0.013). MMAS-8 scores: 7.8 ± 0.4 (telemonitoring with feedback) vs. 7.4 ± 0.9 (telemonitoring) vs. 7.6 ± 0.5 (observational phase). No between-group significance values were explicitly reported. 2. Cost-effectiveness: Incremental cost of the feedback to prevent one stroke €344,289, but estimates suggest that this could be reduced to €15, 488 by focusing on patients classed as high risk, that have low adherence, and by using technology that is optimized. 3. Patient-reported experience: 87.2% said that the MEMS was practical. 97.6% said that feedback was useful. 63.8% said that they had an increased awareness of adherence.	High rates of adherence were observed by implementing a telemonitoring intervention, with this effect being escalated upon adding the element of feedback. Focusing on high-risk/low-adherence cohorts could make the intervention more cost-effective.
	1. Apixaban dosing regimen implementation adherence at 48-weeks: 90.4% ± 18.0 (continued intervention),	2. Apixaban persistence at 48-weeks: 86.1% (continued intervention, 95% CI 81.3–89.7) vs. 85.2% (control, 95% CI 81.5–88.2) vs. 87.8% (secondary control, 95% CI 83.4–91.1) (P>0.5).	Implementation of the intervention did not result in any additional significant benefit being observed,

10	90.1% ± 18.6 (control), 89.3% ± 18.1 (secondary control) (P>0.7).	3. Clinical events at 48-weeks: 4.8% (4.5% vs. 5.1%) of participants experienced at least one event which led to permanent discontinuation, but no P values were explicitly reported.	with adherence and persistence rates being high regardless of the intervention.
11	1. Apixaban adherence at 6-months: 100% vs. 99.7% (P=0.247).	2. Composite secondary endpoints: 8 (SD 17.8) vs.10 (SD 20.4) (P=0.067).	The intervention did not result in a significant improvement in medication adherence between groups (all participants had a higher than anticipated adherence rate).
12	Did not state which outcome was the primary outcome.	1. Dabigatran adherence: 97.47% ± 3.72 vs. 87.67% ± 14.48 (P=0.012*). 2. Knowledge score from baseline to 3-months: 3.75*± 0.892 to 4.23 ± 0.912 (P=0.005) vs. 3.70 ± 0.966 to 3.95 ± 0.846 (P=0.124*). 3. PAM score from baseline to 3-months: 63.03* ± 13.77 to 65.78* ± 13.92 (P=0.078) vs. 63.08* ± 14.73 to 63.56* ± 11.25 (P=0.814).	The study supports the use of the MyChart PHR for AF patient medication adherence, as well as for dabigatran knowledge improvement.
13	1. Adherence to prescribed dose at 90-days: 78.4% vs. 39.7% at (OR 5.51,95% CI 3.08–9. 85, P=0.0001). Adherence to daily usage at 90-days: 5.5 ± 1.3 vs. 4.4 ± 2.0 (P< 0.0001). Fully adherent patients at 90-days: 26.1% vs. 13.2% (OR = 2.32, 95% CI 1.18 – 4.56, P=0.0145).	No other outcomes were assessed.	Polish community pharmacy interventions (using smartphones and pictograms) can lead to improved medication adherence.
14	1. Rivaroxaban adherence at 6-months: 0.86±0.25 vs. 0.88±0.25 (P=0.62).	2. PDC ≥ 80% at 6-months: 91.9% vs. 85.1% (P=0.62). 3. Change in MMAS-8 from baseline to 6-months: 0.60 vs 0.70 (P=0.76). 4. Medication persistence: 70.8% vs. 82.1% (P=0.12).	The intervention proved feasible, with no major differences observed between trial arms (with high adherence in both).
15	1. HRQL score from baseline to 30-days: 81.5 (SD 14.2) to 85.2 (SD 14.1) vs. 76.0 (SD 17.6) to 76.1 (SD 16.7) (adjusted mean difference 4.5, 95% CI 0.6-8.3, *P*=.03).	2. Adherence from baseline to 30-days: 27.9% to 3.5% vs. 22% to 23.2% (adjusted difference 16.6%; 95% CI 2.8%-30.4%, *P<0.001).*	Both medication adherence and HRQL were significantly improved using the intervention, with patients also accepting the intervention to a favourable level.
16	1. OAC (N/S) adherence at 1-year: 0.85 ± 0.26 vs. 0.75 ± 0.31 (P< 0.001).	2. OAC persistence at 1-year: 88.2% vs. 75.6% (adjusted odds ratio of 2.42, 95% CI 1.72–3.41, P<0.001). 3. Treatment gaps: Continuous OAC use 59.6% vs. 41.8% (95% CI 1.60-2.67, P<0.001)	Motivational interviewing during OAC treatment for non-valvular AF can improve adherence, reduce

		Transient treatment gap 23.6% vs. 26.9% (95% CI 0.88-1.57, P=0.275). Major treatment gap 16.8% vs. 31.2% (95% CI 1.76-3.26, P<0.001). 4. Clinical events: All-cause death 27.4% vs 29.5% (95% CI 0.75-1.19, P=0.605). Cardiovascular death 19.4% vs 22.2% (95% CI 0.67-1.16, P=0.361). Thromboembolic death 3.9% vs. 4.8% (95% CI 0.43-1.63, P=0.600). Major bleeding 4.1% vs. 5.0% (95% CI 0.43-1.56, P=0.545). Myocardial infarction 1.4% vs. 2.0% (95% CI 0.28-2.50, P=0.259).	treatment gaps, and increase persistence to a significant level.

INR; International normalized ratio, MMAS-8; 8-part Morisky Medication Adherence Survey, OAC; Oral anticoagulation, DOAC; Direct oral anticoagulant, CHA2DS2-VASc; Congestive heart failure, hypertension, age ≥75 years, diabetes, stroke/transient ischemic attack, thromboembolism, vascular disease, age 65–74 years, sex category, HRQL; Health-related quality of life, AF; Atrial fibrillation, BP; Blood pressure, BMI; Body max index, PDC; Proportion of days covered, TTR; Time in therapeutic range, PAM; Patient activation measure, PHR; Personal health record, AFEQT; Atrial fibrillation effect on quality of life.

*Discrepancies between the values provided in the results section (shown) and in the abstract.

Table 8 – Quality of reporting assessment.

Study number	Domain 1: B**ias related to study design and implementation of study procedures (40) ***	Domain 2: **Bias related to randomisation and blinding procedures (30) ***	Domain 3: **Bias related to adherence outcome measurement and reporting (35) ***	Domain 4: **Bias related to data analysis and interpretation (45) ***	Overall judgement
1	Moderate (29)	High (17)	Serious (8)	Moderate (34)	Serious
2	Moderate (26)	Moderate (21)	High (19)	Moderate (32)	High
3	Moderate (26)	Low (24)	High (16)	Moderate (32)	High
4	Moderate (26)	High (17)	High (15)	High (26)	High
5	Moderate (26)	High (13)	High (20)	Low (38)	High
6	Moderate (29)	Moderate (19)	High (14)	Low (38)	High
7	Moderate (29)	High (17)	Moderate (21)	Low (37)	High
8	Moderate (26)	Very low (30)	High (14)	Moderate (28)	High
9	Moderate (26)	High (17)	High (14)	Moderate (31)	High
10	Moderate (26)	Very low (30)	High (20)	Moderate (32)	High
11	Moderate (26)	High (17)	High (17)	Moderate (29)	High
12	High (22)	High (13)	Moderate (22)	Moderate (29)	High
13	Moderate (29)	Moderate (18)	High (19)	Moderate (29)	High
14	Moderate (26)	High (14)	Moderate (24)	Moderate (34)	High
15	High (22)	High (14)	High (19)	Moderate (29)	High
16	Moderate (29)	Moderate (18)	Moderate (24)	Moderate (34)	Moderate

*Maximum score in each domain.

2.5 Discussion

Statement of principal findings

This review identified 16 studies that randomised 8,492 participants to mHealth interventions (or control) to improve adherence to OACs. The results of these trials indicate the potential for mHealth interventions to be effective in promoting adherence; however, the quality of the trials were poor, both from a methodological perspective and their risk of bias, and in terms of reporting.

The findings of our review aligns with a previous systematic review which aimed to investigate the impact of smartphone-based applications in the broader context of cardiovascular disease management (Al-Arkee *et al.,* 2021). Although only one study was in common to both reviews, Al-Arkee *et al.,* (2021) also report that the quality of most trials were poor, with just two trials being reported as being of '*fair'* quality (Santo *et al.,* Sarfo *et al.,* 2019).

Among the mHealth interventions considered, telephone calls or text messages were most frequently associated with statistically significantly improved medication adherence, consistent with the review by Bond *et al.,* (2021), in the context of adherence to statins. Bond *et al.,* (2021) concluded that to achieve the best results, multiple different mHealth interventions should be employed together. Despite this, our review identified that only 3 of the 9 which used multiple components led to significant improvements in adherence (studies 3, 9, 13).

Strengths and limitations of the review process

The detailed search strategy, as well as the rigorous screening and selection process performed supports our contention that the reviewing methods used were robust and likely to not to have missed many relevant studies. It should be acknowledged, however, that limiting the inclusion criteria to only studies published in the English Language may have excluded some results. Distinct strengths include our application of the RoBIAS tool to assess bias, and rigorous critique of the methods of adherence measurement, analysis and reporting.

Strengths and limitations of the studies

Generally, study quality was poor and the results liable to bias. The lack of methodological rigour was apparent, as was the incompleteness of reporting. This included the poor reporting of the medication adherence phase studied (initiation, implementation, persistence) (Vrijens *et al.,* 2012). The description of the measure, metric and method of data aggregation of adherence data, for instance, was complete for only one study (study 10). Study sample sizes were often small and not calculated formally suggesting that many trials were underpowered. Follow-up period was relatively short, with no study follow-up exceeding one year which limits evaluation of the impact of mHealth interventions on persistence. The need for more robust research methods to improve the design, conduct and reporting of clinical trials that investigate medication adherence has been highlighted previously (Anderson *et al.,* 2020, Jang. 2021); and improvements in these would allow for more definitive conclusion that the observed effects are solely due to the mHealth intervention that was tested.

Generalizability of the results

Participants of the included studies were relatively comparable in age and had similar, cardiovascular-related health conditions that qualify them for OAC treatment. Recently published literature, however, has alluded to differences in the adherence rates for once and twice-daily OACs (Ingason *et al.,* 2023), and this may have important implications concerning the effectiveness of the mHealth interventions. Table 5 refers to which OAC is being studied in each trial included in this review. While all participants likely had their medications subsidised for the duration of the study, the behaviours and beliefs in relation to disease and treatment may differ for other contextual reasons, including socioeconomic and healthcare system factors (Wilder *et al.,* 2021). Most of the studies included in this review were conducted in high-income countries with insurance-funded, private healthcare systems.

2.6 Conclusions

This review suggests that mHealth interventions may be effective in promoting OAC adherence in adults – with more evidence favouring telephone calls and messages for follow-up support or as medication intake reminders. This may reflect that more of the studies used telephone calls and messages as the mHealth intervention. Future research in this respect should focus on identifying how telephone calls and messages can be optimized within the specific context studied – to define, for instance, the optimal frequency of delivery, the content of calls or messages and whether there is an opportunity for automation. Research should also focus on conducting larger, longer-term trials that are of better methodological quality. Improved methodological rigour needs to be applied in the design, conduct and reporting of clinical trials involving mHealth interventions to improve medication adherence.

2.7 Other information

2.7.1 Protocol registration

The protocol for this review (Appendix B) is registered with the International Prospective Register of Systematic Reviews (PROSPERO). Registration number: CRD42022372863.

2.7.2 Support

Knowledge Economy Skills Scholarships (KESS 2) is a pan-Wales higher level skills initiative led by Bangor University on behalf of the higher education sector in Wales. It is part funded by the Welsh Government's European Social Fund (ESF) convergence programme for West Wales and the Valleys.

CHAPTER 3 – DEVELOPING HEALTH-PROMOTING MESSAGES IN CHATGPT-3.5

3.1 Introduction

There is a growing body of evidence supporting the use of short-message service (SMS) to promote positive behavioural changes in healthcare, for example, medical appointment attendance, quitting smoking, and the implementation of a healthy diet (Orr and King. 2015). There is evidence of the benefit of mobile phone messaging for the self-management of long-term illnesses including hypertension, asthma, and diabetes, but further research is warranted (de Jongh *et al.,* 2012). SMS messaging is used increasingly to support medication adherence (initiation, implementation, persistence) for patients taking long-term medications for chronic diseases (Thakkar *et al.,* 2016; Vrijens *et al.,* 2012). The literature describes push-based approaches, comprised of users receiving text- or notification-based information (Kornfield *et al.,* 2022), and app-based events (Hernández-Reyes *et al.,* 2020).

One challenge in developing content for SMS messages relates to methodology. Bartlett *et al.*, (2020) described the methods used to develop BCT messages for supporting the adherence of individuals with type 2 diabetes. The research was comprised of a message development workshop, attended by behavioural change researchers and healthcare professionals, a focus group of individuals with type 2 diabetes to determine acceptability, and two online surveys. The first survey aimed to determine the acceptability of a portion of the messages in people with type 2 diabetes, whilst the second survey aimed to determine how well a portion of the messages adhered to the specified BCT (Bartlett *et al.*, 2020).

This work also extends to other publications, including prior research to determine the needs of individuals with type 2 diabetes regarding messaging support (Bartlett *et al.,* 2019), as well as more recent research to gather the opinions of general practice staff regarding the implementation of messaging support for individuals with type 2 diabetes (Butler *et al.,* 2023). As this body of research was both extensive and very detailed, it can be considered the gold-standard. Despite this, it is also hard to replicate in every context, hence presenting a potential role for AI to facilitate this.

Dobson *et al.,* (2015) described the development of a diabetes text-message self-management support programme. A multidisciplinary team was employed, informed by existing literature and mHealth interventions, as well as recourses already available to patients. Clinicians with expertise in the management of diabetes, together with individuals with type 2 diabetes, subsequently reviewed the messages. Despite a total of 180 different messages being generated, with participants only receiving the same message once, this was not the case for reminder messages, with participants receiving the same nine messages throughout the study (Dobson *et al.,* 2015).

According to Bartlett *et al.,* (2020), studies aiming to develop health-messaging support, excluding those explicitly outlined in this paper, often lack basic detail, such as the methods used to generate the messages, as well as message content, presenting a gap needing to be addressed within the field.

A nascent approach to developing health-promoting messaging, which has the potential to overcome some of these specific challenges, is the use of AI. With the ability to produce large amounts of text in short periods of time, and the potential to address the resource-intensive nature of creating health messages (Dergaa. 2023), using AI to develop health-promoting messages may facilitate increased diversity, including in message number, phrasing, and content, which offers a promising prospect.

AI describes *"the use of computers and technology to simulate intelligent behavior and critical thinking comparable to a human being"* Amisha (2019). The applications of AI in healthcare are widespread (Topol. 2023), from supporting the analysis of radiological assessments in oncology (Hosny *et al.,* 2018), to aiding blood glucose monitoring in the management of diabetes (Jin *et al.,* 2023; Khodve and Banerjee. 2022), and supporting patients to adhere with their medicines (Davenport and Kalakota. 2019; Aharon *et al.,* 2022). The potential for interactive and personalised health messaging support by combining AI technologies with patient data presents a further opportunity (Jungwirth and Haluza. 2023).

There is a growing body of evidence supporting the use of OpenAI's ChatGPT for developing health messages, with Schmälzle and Wilcox (2022) using ChatGPT-2 to develop health messages for social media campaigns, applying folic acid as an example. After evaluation, the generated messages were determined to be of equal standard to real Twitter tweets (Schmälzle and Wilcox. 2022). Similarly, Karinshak *et al.,* (2023) used ChatGPT-3 to develop pro-COVID-19 vaccination messages for public health, using ChatGPT-3, which were determined to be more effective than messages created by humans at the Centers for Disease Control and Prevention (Karinshak *et al.,* 2023).

This chapter aims to develop messages to support medication adherence using an open-source AI platform, ChatGPT-3.5. A systematic methodological approach is undertaken, in which the reproducible steps used will be outlined, including the initial prompts inputted, the iterative refinement of the outputs, and the screening criteria used to generate the final list of messages.

3.2 Methods

ChatGPT, arguably the progenitor of publicly-accessible AI models that uses natural language processing, was launched in November 2022 (Ruksakulpiwat *et al.,* 2023). Described as a chatbot, ChatGPT responds to prompts inputted by users that can be likened to those of a human (Dave *et al.,* 2023), in several different languages (Sallam. 2023).

Our methods for prompt generation in ChatGPT followed those of Karinshak *et al.,* (2023), who trialled variations of the prompt and rated the outputs generated by each version across different criteria (accuracy, relevancy, attempted persuasion), before determining which prompt was to be inputted into ChatGPT-3. This ensures that our methods are inclusive, being easily reproducible by most individuals. We combined this approach with current evidence, which underlies our choices for the audience, writing style and message length chosen for the initial prompt, as outlined below. After iterative refinement of the messages generated, the messages were screened against pre-defined criteria (Table 10) to produce a final list, drawing similarities with the criteria used by Karinshak *et al.,* (2023).

3.2.1 The initial prompt

Audience

The population of interest was poly-medicated patients recruited from community pharmacies (see Chapter 4).

Writing style

Literacy ability is often grouped into various levels. For instance, the 2011 Skills for Life survey assesses literacy across five different levels (Table 9) and estimates that approximately 1 in 7 adults in England are at Entry level 3, otherwise defined as having the literacy skills of a nine- to 11-year-old child (National Literacy Trust. 2023). In this way, when defining the reading age for the writing style of the inputted prompt, the age range corresponding to Entry Level 3 was chosen, which according to the Skills for Life survey, is nine to 11 years old. Thus, without pre-existing knowledge of an individual's literacy level, using the ages that correspond with Entry Level 3 should ensure that the majority will be able to read and comprehend the messages generated. As this research was conducted in Wales, The United Kingdom, as well as to further ensure sufficient comprehension, the writing style was specified to be plain, United Kingdom English.

Table 9 – Literacy levels and their equivalents, according to the 2011 Skills for Life survey.

Level	Equivalent
Entry Level 1	5-7 years of age
Entry Level 2	7-9 years of age
Entry level 3	**9-11 years of age**
Level 1	GCSE grades D-G
Level 2	GCSE grades A*-C

Information taken from The National Literacy Trust (2023).

Message length

According to the UK Government, when writing content for an audience, short sentences of around 25 words should be used. They base this on existing evidence, including research reporting that at 25 words sentences become more challenging to understand, and become highly complicated at 29 words or more (GOV.UK. 2023). To align with this, when specifying the message length of the inputted prompt, a maximum of 25 words was noted.

Context

Reminder messages prompt individuals to successfully complete health-related tasks, in this case, to remind participants to take their medication as prescribed (O'Leary *et al.,* 2018). All the while, motivational messages empower individuals, whilst instilling them with the confidence needed to evoke positive behaviour changes (Bedrov and Bulaj. 2018), whilst messages grounded in health psychology put tested theories into practical application (Hilton and Johnston. 2017).

The following prompt was inputted into ChatGPT-3.5 to generate an initial list of messages (see Appendix C). All elements of adherence were considered so that the generated messages were not restricted and could be related to all phases of medication adherence (initiation, implementation, persistence) (Vrijens *et al.,* 2012). For the context, the search term 'reminder,' was replaced by 'motivational,' and then by 'health psychology theory' and the search re-ran, to generate a total of 300 messages. Despite this, the subsequent categorisation of the generated messages was beyond the scope of this project.

Context = create a list of 100 **reminder** messages to support adherence to medication(s).
Audience = patients from community pharmacies.
Writing style = plain UK English, reading age of 9 to 11 years old.
Message length = limit each message to a maximum of 25 words.
Example message: Don't miss your meds, stay on track.

3.2.2 Iterative refinement

After an initial list of messages was generated for each different type of message context (reminder, motivational, health psychology theory), further instructions were inputted to refine the content of the messages, as shown below.

Change ‘medication’ or ‘meds’ to medicine(s). Change ‘pill’ or ‘pills’ to medicine(s). Change medicine to medicine(s).   Example message: Don't miss your medicine(s), stay on track.

3.2.3 Screening the messages

After all searches were completed in ChatGPT, the lists generated were screened by the student and her supervisor. This was based on the criteria below (Table 10), with messages that did not fit within the criteria either edited where possible or eliminated where messages were determined to be entirely irrelevant or were essentially duplicates of other, better-worded messages. The removal of duplicates was performed manually by the student. This produced a final, refined, list of messages.

Table 10 – The criteria used to screen the messages.

Delete (or edit where possible) messages that:	Refer to setting digital reminders (as a reminder app would already do this).
	Include content that is too specific i.e., for a certain medication (including dosing frequency) or condition.
	Are unclear or include language and content that is too complex.
	Are not clinically appropriate (including misleading statements e.g., your medicine(s) will improve the quality of your life).
Merge messages that are too similar in content.	

3.3. Results

Of the 300 health-promoting messages initially generated using ChatGPT-3.5 (see Appendix C), 108 duplicate messages were removed. Subsequently, after the messages were screened by the criteria outlined in Table 10, a total of 47 messages were removed. Of these, 8 messages referred to setting digital reminders, 17 messages were too specific, 3 messages were unclear, and 29 messages were not clinically appropriate, as outlined in Figure 3. This produced a final list of 145 messages, with all messages remaining after manual refinement (Table 11).

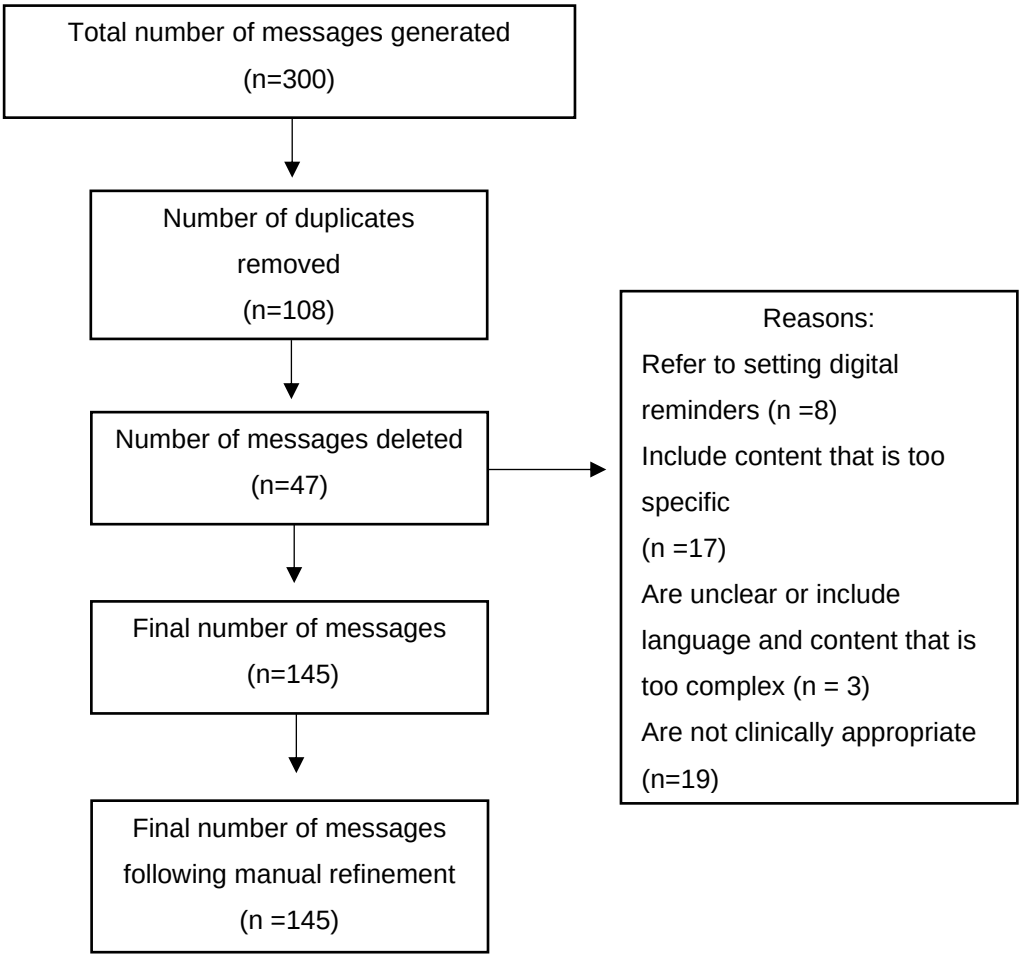

Figure 3 **–** Flow diagram.

Table 11 – Final list of messages

1.	Remember to take your medicine(s) as prescribed!
2.	Keep your medicine(s) where you can see them. Always keep out of reach of children.
3.	Don't forget to take your medicine(s)!
4.	Ask your clinician for help with taking your medicine(s) if needed.
5.	Use a special medicine organizer.
6.	Mark it off on a calendar.
7.	Medicine(s) may help you feel better.
8.	Take your medicine(s) on time.
9.	Keep your medicine(s) at room temperature. Always read the storage instructions on the packaging carefully.
10.	Get a cute medicine(s) box to use.
11.	Put a reminder note on the fridge.

12.	Why not try and pair taking your medicine(s) with a regular activity, such as brushing your teeth.
13.	Medicine(s) may help make you strong.
14.	Don't skip your medicine(s).
15.	Medicine(s) are good for you.
16.	Get a fun timer to use with your medicine(s).
17.	Ask a friend to remind you to take your medicine(s).
18.	Keep your medicine(s) in plain sight. Always keep out of reach of children.
19.	Medicine(s) may help you heal.
20.	Take your medicine(s) with a smile.
21.	Don't forget your medicine(s) routine.
22.	If you will be out of the house during your dosing time(s), remember to take you medicine(s) with you! Use a colourful medicine(s) box.
23.	Mark your medicine(s) time on a chart.
24.	Medicine(s) may help make you feel better.
25.	Remember your medicine(s) always.
26.	Keep your medicine(s) in a cool place. Always read the storage instructions on the label carefully.
27.	Get a cute medicine(s) reminder bracelet.
28.	Put a sticky note reminder on the mirror.
29.	Medicine(s) may help you get well.
30.	Keep your medicine(s) in your room. Always read the storage instructions on the label carefully and keep out of reach or children.
31.	Ask your family for support with your medicine(s).
32.	Use a medicine(s) box with pictures.
33.	Mark your medicine(s) on a chart.
34.	Take your medicine(s) with a treat.
35.	Medicine(s) may help keep you strong.
36.	Remember your medicine(s) schedule.
37.	Keep your medicine(s) in a safe place out of reach of children.
38.	Put a reminder on the door.
39.	Medicine(s) may help you feel good.
40.	Don't miss your medicine(s) dosage time(s).
41.	Keep your medicine(s) routine, even on weekends!.
42.	Ask a friend or family member to help with your medicine(s).
43.	Use a colourful timer for your medicine(s).
44.	Medicine(s) may help keep you healthy.
45.	Keep your medicine(s) in the kitchen. Always read the storage instructions on the label carefully and keep out of reach or children.

46.	Put a note on your bedroom door to remind you to take your medicine(s).
47.	Medicine(s) may help you get better.
48.	Use a fun medicine(s) organizer.
49.	Don't skip your medicine(s) routine.
50.	Use a box to store your medicine(s) so that they are all in one place!
51.	Put a sticky note on the fridge to remind you to take you medicine(s).
52.	You're a medicine(s) superstar!
53.	Medicines(s) may help you stay strong.
54.	You've got this, take your medicine(s).
55.	Medicines(s) may help make you healthier.
56.	Don't forget, medicine(s) are important.
57.	Keep going, you're doing great!
58.	Medicine(s) may bring healing power.
59.	Stay on track with your medicine(s).
60.	Remember, medicine(s) are your pals.
61.	Be a medicine(s) champion.
62.	Medicine(s) may help boost your well-being.
63.	You're a medicine(s) hero!
64.	Medicine(s) may help keep you well.
65.	Keep up the good work!
66.	Take your medicine(s) with care.
67.	Medicine(s) support your journey.
68.	Stay strong, take your medicine(s).
69.	Medicine(s) may help improve the quality of your life.
70.	You're a medicine(s) rockstar!
71.	Medicine(s) are your friends.
72.	Take medicine(s) like a pro.
73.	Medicine(s) bring healing vibes.
74.	You've got the medicine(s) magic.
75.	Remember, medicine(s) are your allies.
76.	Stay on track, take your medicine(s).
77.	You're a medicine(s) superstar!
78.	Medicine(s) are your secret weapon.
79.	Taking medicine(s) may help your body heal.
80.	Remembering to take your medicine(s) may help keep you well.
81.	Routines make taking your medicine(s) easier.
82.	Habit makes taking your medicine(s) simpler.
83.	Your efforts matter for health.
84.	Consistency with medicine(s) is key.

85.	Believing in medicine(s) is powerful.
86.	Your commitment supports health.
87.	Mindset matters for medicine(s).
88.	Health may come from taking your medicine(s) as prescribed.
89.	Your choices impact wellness.
90.	Stick to medicine(s) for better health.
91.	Thinking positively about medicine(s) may help you take them as prescribed.
92.	Small steps lead to wellness.
93.	Your routine impacts taking your medicine(s) as prescribed.
94.	Staying strong with medicine(s) is important.
95.	Wellness may come from taking your medicine(s) as prescribed.
96.	Consistent habits aid wellness.
97.	Your commitment helps medicine(s) work.
98.	Sticking to medicine(s) may bring health.
99.	Wellness comes from your efforts.
100.	Consistency impacts medicine(s).
101.	Your choices impact medicine(s).
102.	Believe in medicine(s) for better health.
103.	Staying strong supports wellness.
104.	Trust in medicine(s) for a healthier you.
105.	Health comes from consistency.
106.	Trusting in medicine(s) aids health.
107.	Your mindset can affect your ability to take your medicine(s) as prescribed.
108.	Staying committed may support healing.
109.	Belief in medicine(s) aids wellness.
110.	Trusting in medicine(s) supports health.
111.	Consistent routines can positively impact your ability to take your medicine(s) as prescribed.
112.	Your commitment aids medicine(s).
113.	Wellness can come from positive thoughts.
114.	Consistency impacts wellness.
115.	Belief in medicine(s) may support healing.
116.	Your routine influences medicine(s).
117.	Trust in medicine(s) for better health.
118.	Your mindset aids wellness.
119.	Sticking to medicine(s) for a healthier you.
120.	Believing in medicine(s) may aid health.
121.	Confidence in medicine(s) may support your healing.
122.	Consistent habits aid medicine(s).

123.	Trusting in medicine(s) may aid wellness.
124.	Wellness comes from your commitment.
125.	Your choices influence medicine(s).
126.	Trust in medicine(s) may support wellness.
127.	Patience aids medicine(s) success.
128.	Small steps can lead to a healthier you.
129.	Staying committed aids wellness.
130.	Positive thoughts may impact health.
131.	Consistency supports medicine(s) success.
132.	Believing in medicine(s) for a healthier you.
133.	Confidence may support healing.
134.	Trusting in medicine(s) may influence health.
135.	Wellness may come from consistency in taking your medicine(s) as prescribed.
136.	Your routine impacts healing.
137.	Belief in medicine(s) supports wellness.
138.	Consistent habits aid health.
139.	Positive thoughts may influence wellness.
140.	Wellness may come from your mindset.
141.	Believing in medicine(s) may support healing.
142.	Consistency may support better health.
143.	Trust in medicine(s) may influence healing.
144.	Positive mindset aids medicine(s) success.
145.	Your choices impact health..

3.4 Discussion

Our research shows that using the AI platform, ChatGPT-3.5, to develop health-messaging support is a feasible option, that has the potential to overcome some of the specific challenges involved with health message generation, including its resource-intensive nature (Dergaa. 2023), and a lack of diversity in message number, phrasing and content. The literature also alludes to the feasibility of using ChatGPT to generate health resources, with a recent paper by Modal *et al.,* (2023) investigating the potential of using ChatGPT (January 2023 version) to generate educational materials for common public health issues in India, including malnutrition and tuberculosis, reporting positive results (Mondal *et al.,* 2023). Despite these findings, it is also evident that there are persisting mixed attitudes regarding AI adoption in healthcare, which may potentially affect the practical implementation of using platforms, such as ChatGPT, for health-message generation (Gao *et al.,* 2020; Nitiéma. 2023).

Strengths of our study in relation to other studies include the speed and cost at which a large number of messages were generated, with 145 messages being included in our final list. This differs from a study conducted by Karinshak *et al.,* (2023), which used ChatGPT-3 to develop pro-COVID-19 vaccination messages. Their testing of different prompt variations and subsequent rating of the generated outputs was a relatively time-consuming process. Despite this, our study lacks scrutiny and clinical check to compare our work with others, with Karinshak *et al.,* (2023) implementing a survey to gather people's opinions of the generated messages.

Different methods are used by studies for prompt generation in ChatGPT. For instance, before inputting any prompts, Schmälzle and Wilcox (2022) fine-tuned ChatGPT-2 by inputting existing tweets from X (Twitter) on the topic of folic acid supplementation in pregnancy. A new set of messages on folic acid were then generated using this fine-tuned version of ChatGPT-2. This method required either a degree of coding knowledge or associated training (Schmälzle and Wilcox. 2022). In contrast, our study did not involve the fine-tuning of ChatGPT-3.5 prior to inputting the prompts. This ensured that the methods used in our research, if not the messages, were reproducible by others, regardless of their coding ability, and irrespective of any training. Nevertheless, this might also have resulted in the responses provided by ChatGPT-3.5 in our study being less specific, but this is only a minor concern as our messages were intentionally designed to be generic, meaning that the prompts were designed to generate messages that were suitable for various medication types and health conditions, as well as be appropriate for different dosing schedules and phases of adherence (initiation, implementation, persistence) (Vrijens *et al.,* 2012).

The speed, cost, and ease at which a large number of messages were generated is a clear strength of this study. The systematic methodological approach undertaken presents a further strength, with the prompts inputted, and criteria used to screen the messages clearly defined. Additionally, the number of messages merged and edited, as well as deleted, according to the reason for doing so, are outlined in Figure 3. The initial list of messages generated is included as an appendix, with the final list of messages included within the Chapter itself. This represents a transparent process that is reproducible by other researchers.

Limitations of our study might include the reliability, relevance, and reproducibility of the messages. Additionally, despite removing a high number of duplicate messages, some of the final messages remain relatively similar in wording. This is likely due to the tight constraints of the initial prompt inputted, including for the reading age and message length. This might have meant that creating 300 entirely distinct messages that fit within these criteria might have been challenging, even for AI. Furthermore, our research did not extend to the validation of the health-promoting messages generated using ChatGPT-3.5 in real patients or professionals, such as clinicians and health psychologists, which can be considered a limitation. Doing this would have improved our interpretation of the results, whilst allowing us to truly validate the messages in clinical practice.

Our research demonstrates that using ChatGPT-3.5 to develop health-messaging support is a feasible option that has the potential to overcome some of the specific challenges involved with generating health messages, including its resource-intensive nature (Dergaa. 2023), and a lack of diversity in message number, phrasing and content. This was achieved by undertaking a systematic methodological approach, in which the prompts inputted and screening criteria used were clearly defined. Our findings should be used to inform future research, specifically in improving the reporting of the methods used to generate health messages using AI platforms, such as ChatGPT. This would increase the transparency of future research, which might, in turn, improve acceptability and therefore its implementation in clinical practice.

Future research should focus on the improved reporting of the methods used to develop health-promoting messages using AI platforms, such as ChatGPT, ensuring that they are transparent and reproducible. The acceptance of the messages in actual patients remains unknown, and therefore future research should also prioritize their validation through this approach, as well as through clinical confirmation. As part of this, focus should be placed on how their delivery might be enhanced, whilst addressing concerns to enhance acceptability. Future research could also consider the impact of targeting health-promoting messages to the specific phases of medication adherence (initiation, implementation, persistence) (Vrijens *et al.,* 2012). Future work may also explore how the AI messages compare to messages generated using theory-based approaches. Our research might also have regulatory implications, such as those concerning medical devices. Lastly, future research should focus on how the generated messages could be diversified, whilst still producing a sizeable number, which might be achieved by adjusting the constraints of the initial prompt.

CHAPTER 4 – FEASIBILITY TESTING OF THE ATOM5™ APP

4.1 Background

There are currently over 11,000 community pharmacies within the UK (Statista. 2023), with over 700 of these based in Wales (Community Pharmacy Wales. 2023-a). Within rural landscapes, community pharmacists are often the most accessible healthcare provider available to patients, highlighting their significance within these contexts (Carpenter *et al.,* 2021). Pharmacists play an essential role in caring for patients, providing expert advice on medicines and other treatments, whilst also dealing with key clinical issues, including medication adherence (initiation, implementation, persistence) (Nazar *et al.,* 2015; Vrijens *et al.,* 2012). Patient education is a key element of promoting medication adherence, which might include advising patients on how to correctly take a medication, as well as discussing any potential side effects (Ilardo and Speciale. 2020).

The Community Pharmacy Contractual Framework (NHS England. 2023), and The Community Pharmacy NHS Wales Contractual Framework (Welsh Government. 2023), describe the contractual agreement between community pharmacies and the NHS in England and Wales. As part of this, community pharmacies are contracted to provide a wide range of services – including those deemed to be essential that all community pharmacies are required to provide – as well as advanced services that community pharmacies can opt to provide if they have gained the correct accreditation to do so. Whilst essential community pharmacy services include dispensing repeat medicines, the disposal of medicines and healthy lifestyle promotion, advanced community pharmacy services in Wales include the discharge medicines review service (Welsh Government. 2020), which supports patients after they are discharged from a care setting (Community Pharmacy Wales. 2023-b).

Medication reviews aim to support patients in adhering to their medication, with the key elements including enhancing the quality, safety, and proper utilization of medications (Blenkinsopp *et al.,* 2012). In Wales, The Welsh National Standards for Medication Review were developed to facilitate healthcare professionals when conducting medicines reviews. It is hoped that the quality of medicine reviews will become improved when healthcare professionals adhere to these standards, whilst also presenting a more unified approach to undertaking medication reviews. Five standards are outlined (Involving patients and caregivers, Safety, Review of medicines, Reducing waste, and Medication review documentation) (All Wales Medicines Strategy Group. 2020).

Evidence suggests that pharmacists are adept in supporting patients in improving their medication adherence, with the literature abundant with papers reporting the positive impacts of pharmacist-led interventions on medication adherence. For instance, in a systematic review by Conn *et al.,* (2017), which looked at interventions promoting medication adherence, the interventions deemed to be most effective in improving adherence were those delivered by pharmacists. There is also evidence specifically supporting the use of pharmacist-implemented smartphone applications for improving

medication adherence. For instance, in a study investigating the impact of a pharmacist-implemented smartphone application in women with gestational diabetes, a statistically significant improvement in medication adherence was reported in the intervention group, when compared with the control group (Zhuo *et al.,* 2022).

Betsi Cadwaladr University Health Board (BCUHB) is the local health board of NHS Wales for the north of Wales. It is the largest health organisation in Wales, providing a full range of primary, community, mental health, and acute hospital services for a population of more than 700,000 people (Betsi Cadwaladr Health Board. 2023). BCUHB is currently working on service evaluation entitled '*Supporting the safe and effective use of medicines in patients' own homes*' (for the specification see Appendix D). This project was initiated in response to the National Guiding Principles for Medicines Support in the Domiciliary Care Sector, released by the All Wales Heads of Adult Services and NHS Wales in 2019. These guidelines aim to provide a unified approach to the medicines support provided in domiciliary care settings and are endorsed by a wide range of agencies, including Care inspectorate Wales, Social Care Wales, The National Institute for Health and Care Excellence, and The Royal Pharmaceutical Society. Reference is made to medicines optimisation, including medicine reviews and monitored dosage systems. Despite this, the guidelines caution the use of monitored dosage systems due to their inherent disadvantages, which include not being able to easily identify the different types of medications, which may have implications if a tablet is dropped (ADSS Cymru. 2023).

This chapter describes a bolt-on feasibility study, linked to the BCUHB '*Supporting the safe and effective use of medicines in patients' own homes*' service evaluation – specifically in line with aim 3, which is to '*Improve patient understanding of, and adherence to, their medicine regimens*', and the objective of creating an adherence-enhancing tool. As part of the main service evaluation, pharmacists are assessing both new and existing patients for medication adherence (for the assessments see Appendices E and F). Patients being assessed as part of the BCUHB service evaluation were offered the opportunity to take part in the feasibility testing of the Atom5™ app, which was developed as an mHealth technology to support patients in adhering to their medication in the form medication-intake reminders, as well as daily digital messaging combined with gamification (bronze, silver, and gold badges) (for the protocol of this feasibility testing see Appendix G).

The Medical Research Council provides guidance on the development and evaluation of complex interventions, with the assessment of the feasibility of an intervention described as a stage of complex intervention research. According to this guidance, a feasibility study should be guided by predefined criteria, including elements relating to the design of the evaluation, such as reducing data collection uncertainty, as well as elements relating to the intervention, such as its optimisation and acceptability (Skivington *et al.,* 2021).

The student's Master of Science by Research (MScRes) project is funded by The Knowledge Economy Skills Scholarship 2 (KESS 2), which is supported by the European Funds (ESF) through the Welsh Government (KESS 2. 2023). This unique scholarship opportunity pairs students based at higher

education institutions with industry partners to collaborate on various research projects. In this case, the student was paired with the North Wales-based digital health company, Aparito Ltd, which is why Atom5™ was the mHealth technology chosen for this feasibility testing.

The Atom5™ app is the flagship product of Aparito Ltd and is a highly configurable smartphone-based app which now has over 800 configurations. Aparito Ltd focuses on digitalising clinical trials, with the Atom5™ app allowing remote patient data to be captured via electronic patient-reported outcomes, video, and voice recording. Remote patient data can also be captured via wearable devices, made possible through their partnership with Garmin Ltd. The Atom5™ app is connected to an online portal, which allows data to be accessed and visualised, most often by clinicians or study personnel. The app has been used in a wide range of conditions, with Aparito Ltd now largely focusing on using Atom5™ in paediatric, rare disease, ataxia, and neurodegenerative studies (Aparito. 2023). This feasibility testing of Atom5™ will provide insight into whether interventions like these can work alongside existing community pharmacy services, such as medication reviews, to support patients in adhering to their medicines.

Aim and Objectives

This chapter aimed to determine whether a bespoke mHealth intervention (the Atom5™ app) can support medication adherence in patients recruited from community pharmacies.

This was achieved through the following objectives:

1. Evaluation of whether the Atom5™ app is a feasible tool to implement in community pharmacies for supporting patients in adhering to their medication.
2. Evaluation of the feasibility of collecting remote medication adherence data in patients recruited from community pharmacies using the Atom5™ app.
3. Evaluation of the acceptability of using the Atom5™ app for supporting patients recruited from community pharmacies in adhering to their medication, from both a patient and pharmacist perspective.

4.2 Methods

4.2.1 Development of Atom5™

The student worked alongside colleagues at Aparito Ltd to develop a novel configuration of the app to support patients in adhering to their medication. This configuration of the Atom5™ offered alerts in the form of medication-intake reminders, as well as daily digital messaging combined with gamification (bronze, silver, and gold badges). Badges corresponded with the completion of two (bronze), four (silver) and six (gold) weekly adherence questionnaires. The app allowed patients to self-onboard via a QR code (for the onboarding instructions see Appendix H) meaning that no personal identifiable information such as name, email, phone number and date of birth was collected. The app was made available in

two languages (English/Welsh) and selected by participants upon onboarding (for app screenshots see Appendices I and J). The app, as well as the daily digital messages, were translated into Welsh by Bangor University's Translation Unit.

4.2.2 Development of the daily digital messages

Whilst an initial pool of daily digital messages was generated using ChatGPT-3.5 (April 2023 version) in this chapter, due to the time constraints of this feasibility testing, the inputted prompts did not follow the same structured design and robust methods that were used in Chapter 3. Any future work would aim to follow the methods used in Chapter 3. When using ChatGPT-3.5 to generate the initial pool of messages for this chapter, only the message type and number were specified in the inputted prompt.

The messages were then developed using input from surveys created in Jisc (for the survey see Appendix K), in which pharmacists across BCUHB were asked to rate the appropriateness of the messages. Dr Adam Mackridge (BCUHB Strategic Lead for Community Pharmacy) distributed a link to the survey landing page (for the survey landing page see Appendix L) to BCUHB pharmacists via a newsletter. The survey landing page subsequently (block) randomised pharmacists to one of 10 sub-questionnaires, each containing eight messages. This avoided burdening the pharmacists with too many messages, whilst reducing the time commitment required to complete the survey.

Pharmacists were asked to anonymously rate eight messages on a 5-point scale (from very good to very poor). For each message, they were asked to assess its accuracy (clinical appropriateness), the clarity of its wording, and whether it was sufficiently generic (i.e. not specific for any particular medicine or class of medicines). A total of 20 responses were collected and, using this feedback, the messages were edited, with some deleted altogether, to generate the final list that was used in the Atom5™ configuration (for the final list of messages see Appendix M). The messages were configured so that one message was delivered per day, at a random time (daily digital messages).

4.2.3 Ethical approval

This feasibility study, forming part of a service evaluation was deemed as *'NOT research'* by the Medical Research Council's *'Is my study research?'* online tool (for the tool outcome see Appendix N). An application for secondary data collection analysis was submitted for ethical approval and subsequently approved, by Bangor University's School of Medical and Health Sciences Academic Ethics Committee Chair (for the secondary data analysis application form see Appendix O).

4.2.4 Informed consent

Before patient recruitment began, the student met with the pharmacists. This involved the student explaining the support provided by Atom5™ (facilitated by screenshots of the app), as well as instructing

the pharmacists on the patient onboarding process and providing them with QR codes and patient information sheets. Verbal consent was taken from patients for the usability testing of the Atom5™ app by the community pharmacists. Before verbally consenting to take part, participants were asked to read a participant information sheet (for the participant information sheet see Appendix P). When onboarding onto Atom5™, participants were also required to consent to take part, as well as consent to Aparito's privacy policy via a tick box.

4.2.5 Participants

Patients

Patients were those who were already taking part in the main service evaluation who also consented to take part in our feasibility testing of Atom5™, contacted via pharmacies located in Blaenau Ffestiniog (Moelwyn Pharmacy and Fferyllwyr Llŷn, Blaenau/D Powys Davies).

Pharmacists

Pharmacists were those based at Moelwyn Pharmacy and Fferyllwyr Llŷn, Blaenau/D Powys. These pharmacists were selected to take part as they were already taking part in the main service evaluation, whilst also accepting our invitation to take part in our feasibility testing of Atom5™. An invitation to take part in the feasibility testing of Atom5™ was sent to three pharmacists via email, and followed up via telephone, with one of these pharmacies declining to take part.

4.2.6 Recruitment procedures

Participants were those invited to take part in the service evaluation and offered the opportunity to take part in the usability testing of the Atom5™ app.

4.2.7 Data management

Patients were navigated to a URL to connect with a QR code that onboarded them onto the Atom5™ app. No personal identifiable information such as name, email, phone number and date of birth was collected. Aparito was responsible for data collection via the Atom5™ platform and then transferred this data to the student for analysis. Data was held on a Bangor University, encrypted and password-protected laptop computer, accessible only to the student and supervisor.

4.2.8 Assessments

All patient assessments were conducted, and thus all data were collected, within the Atom5™ app. These assessments were in the form of self-reported questionnaires. The student drafted the initial versions of these questionnaires, facilitated by colleagues at Aparito Ltd explaining the different configurable answer options (free text boxes, Likert scales etc). Supervisor input refined the phrasing and content of the questionnaires.

Participants were asked to fill in a medication adherence questionnaire at the end of each week, detailing their medication taking using a 5-point Likert scale of whether they have taken ‘all’ or ‘none’ of their prescribed medication for that week. If a value of less than five was inputted, patients were asked to provide a reason for not taking all their medication as prescribed. Patients could select a reason from a list of nine options but could also select ‘other’ to provide a different reason in a free text box. At the end of the feasibility testing, participants were also asked to complete a questionnaire detailing their experience of using the Atom5™ app.

Participant engagement with the app was also assessed using data from Atom5™ (time spent on questionnaires, missed questionnaires). All anonymous data collected by Atom5™ was transferred to the student for analysis via Aparito and not the NHS.

The community pharmacists involved in the project were also asked to complete a questionnaire expressing their views and opinions of the Atom5™ app. The pharmacist experience questionnaire (for the pharmacist experience questionnaire see Appendix Q) was created in Jisc and distributed via a URL link, with the responses collected being anonymous. The student drafted the initial version of this questionnaire, with supervisor input refining its content and phrasing.

4.2.9 Data analysis

Data analysis was limited to the data collected by Atom5™. This data was analysed descriptively and includes a summary of the Likert scale responses. Age and sex were used to describe the cohort. No statistical inference testing was performed.

4.3 Results

4.3.1 Participant characteristics

A total of 10 participants were onboarded onto the Atom5™ app from 02/10/2023 to 26/10/2023, with the last data collection point being on 07/11/2023. Follow-up periods ranged from 12 days to 36 days, with the mean follow-up period being 22.5 days. Seven participants were female, with five participants opting to use the Welsh version of the app. Three participants were aged 18-29 years, three aged 40-49 years, two aged 30-39 years, and two aged 50-59 years.

When onboarding, most participants (seven) selected that they needed medication-intake reminders once per day, with two participants needing medication-intake reminders once per week, and one participant needing medication-intake reminders three times per day.

4.3.2 Participant medication adherence and engagement

The number of weekly adherence questionnaires completed throughout this feasibility testing totalled six, which were completed by four different participants. Completion times ranged from 34 seconds to 1

minute and 27 seconds, with a median of 55.5 seconds. Five of the weekly adherence questionnaires reported participants taking all their medication as prescribed (a value of 5), with one questionnaire reporting a value of 4. This participant (patient number 7) was a female aged 18-29 years, with the reason provided for not taking all their medication as prescribed being '*I forgot.'* Only two participants completed two weekly adherence questionnaires and therefore earned a bronze badge. A total of 39 daily digital messages were delivered throughout this feasibility testing, with seven participants opening a daily digital message over periods ranging from one day to 14 days.

Table 12 – Summary of results

Patient	Age category (years)	Gender	Language	Frequency of medication-intake reminders	Number of daily digital messages opened	Number of weekly adherence questionnaires completed	Time spent on weekly adherence questionnaire(s)	Time spent on patient experience questionnaire	Badge(s) earned	Follow-up period (days)
1	40-49	Female	English	Three times per day	2	1	53 seconds	Not completed	None	36
2	18-29	Female	English	Once per day	3	0	None completed	34 seconds	None	36
3	40-49	Male	English	Once per week	0	0	None completed	Not completed	None	35
4	30-39	Male	Welsh	Once per day	3	0	None completed	Not completed	None	19
5	50-59	Female	Welsh	Once per day	0	0	None completed	Not completed	None	18
6	50-59	Female	English	Once per week	0	0	None completed	Not completed	None	18
7	18-29	Female	Welsh	Once per day	7	2	➢ 38 seconds ➢ 34 seconds	Not completed	Bronze	18
8	18-29	Female	Welsh	Once per day	14	2	➢ 58 seconds ➢ 1 minute and 17 seconds	28 seconds	Bronze	18
9	30-39	Male	Welsh	Once per day	1	0	None completed	Not completed	None	15
10	40-49	Female	English	Once per day	13	1	1 minute and 27 seconds	44 seconds	None	12

4.3.3 Participant experience questionnaire

A total of 3 participants completed the participant experience questionnaire. Completion times ranged from 28 seconds to 44 seconds, with a median of 34 seconds. Two participants agreed that the app was easy to navigate, with one participant strongly agreeing. All participants agreed that the daily digital messages and medication-intake reminders were useful. When asked if the badges encouraged participants to complete the weekly adherence questionnaires, one participant strongly agreed, and one participant agreed, with one participant providing a neutral response. One participant strongly agreed that the questionnaires were easy to read and understand, one participant agreed, and one provided a neutral response. Two participants disagreed that more digital messages and medication-intake reminders would have been useful, with one participant strongly disagreeing. When asked if they would recommend using an app like this in the future, two participants agreed, with one strongly agreeing. No responses were provided on how the app experience could be improved.

4.3.4 Pharmacist experience questionnaire

The pharmacist experience questionnaire was completed anonymously by the three community pharmacists who participated in the feasibility testing. All pharmacists rated the Atom5™ app as being *'useful'* for their patients, whilst also agreeing that they see the value in their patients using the app to support medication adherence. When asked if referring patients to self-onboard onto the Atom5™ app increased their workload too much, two pharmacists selected *'disagree,'* whilst one pharmacist selected *'neither agree nor disagree.'* Two pharmacists outlined the daily reminders to be useful elements of the app. When asked what changes they would make to Atom5™, one pharmacist described a technical issue that involved the onboarding screen reappearing when a medication-intake reminder was clicked, which would need to be resolved upon its further implementation. Another pharmacist would have liked having the option of only receiving reminders on specific days, that did not correlate with medication dosage, such as weekends. All pharmacists agreed that the Atom5™ app is a practical and feasible option for supporting medication adherence in community pharmacies, whilst also agreeing that they would recommend using an app like this in the future.

4.4 Discussion

4.4.1 Principal findings

This study aimed to determine whether a bespoke mHealth intervention, in the form of a novel configuration of the Atom5™ app, is a feasible option for supporting participants recruited from community pharmacies in adhering to their medication. The limited sample size of both pharmacies and patients achieved within the recruiting period meant that feasibility is indeterminate. However, for those who engaged with the study, feedback was positive even if engagement did not persist, with the daily digital messages past 2 days, and the questionnaires past 7 days.

These findings were preliminary in nature, and as such could not substantiate those of other studies investigating the effectiveness of a smartphone app. Studies that aim to assess outcomes, such as improved hypertensive control through combining education with digital reminders (AlerHTA) (Márquez Contreras *et al.,* 2019), recruited more patients (148), who were followed-up for a longer period (12 months). Aligning with the findings of Márquez Contreras *et al.,* (2019), improved adherence to treatment was reported in a study investigating the effectiveness of a digital reminder app (MediSafe) for the non-antibiotic treatment of viral upper respiratory tract infection (Brinker *et al.,* 2022). The reminders were tailored for each treatment type, drawing similarities with the Atom5™ medication-intake reminders, which were configured for each participant's dosing schedule. Their study was limited to a follow-up period of 14 days, and therefore provided no real benefit over our feasibility testing in this respect. Furthermore, their study failed to report on participant app usage, which limits the ability to directly relate the positive findings as being due to participants using the app (Brinker *et al.,* 2022).

4.4.2 Strengths and limitations

Participants being able to self-onboard onto the Atom5™ app is a strength of this feasibility testing, which reduced the time burden for the recruiting pharmacies, as well as the research team. This also meant that participants could remain completely anonymous to the research team, with no personal identifiable information data needing to be collected. Being able to collect all data via the Atom5™ app presents a further strength, which allowed data collection to be a streamlined process, whilst again keeping the time commitment for the pharmacies, research team, and participants minimal. Furthermore, making the app available in two languages (English/Welsh) allowed participants could choose to interact with Atom5™ in the language they felt most comfortable using.

The small number of recruited participants is a limitation of this feasibility testing, with recruitment also being restricted to two community pharmacies serving largely rural areas, within the same area of North Wales. This has implications in terms of the diversity of the studied population and therefore our ability to relate the results to other, more diverse populations. The small number of participants also limits our ability to observe the impact of gender, age, and language on the ability of participants to adhere to their medication. The relatively short follow-up period presents a further limitation, restricting our ability to assess the feasibility of the Atom5™ app for supporting patients in adhering to their medication on a longer-term basis. The anonymous recruitment process, with participants only being required to input their age, gender, and how often they needed medication-intake, limited our ability to interpret other factors which might have impacted the results, such as medication type. The lack of tailoring of the daily digital messages in response to the answers provided by participants in the questionnaires presents a further limitation. The response to the surveys distributed to pharmacists across BCUHB to gather their opinions on the daily digital messages was poor, which somewhat restricted our ability to edit the messages. The lack of patient co-creation when developing the messages can also be considered a limitation, with this being beyond the scope of the project.

Lastly, participant engagement in completing the weekly adherence and participant experience questionnaires was generally poor. This limits our ability to interpret the medication-taking behaviours of participants, including their reasons for being nonadherent, with only one participant reporting sub-optimal adherence. As the badges were linked to the completion of the weekly adherence questionnaires, this also meant that only two participants earned a badge (bronze), which might explain why the usefulness of the badges was rated *'neutral'* by one participant, and not rated at all by several more.

4.4.3 Future directions

Further research is needed to assess the longer-term impact of a novel mHealth intervention for supporting patients recruited from community pharmacies in adhering to their medication. In doing this, a larger, more diverse pool of participants would be required, which would improve our ability to generalize the results to wider clinical practice. Future research should also focus on the potential of optimizing the mHealth support, such as by personalizing the intervention by reasons for being nonadherent, which might be achieved through a pre-screening process. In doing this, patient engagement, including in completing the questionnaires, might become improved.

CHAPTER 5 – DISCUSSION

How the thesis met the stated aims

The main aim of the research presented within this thesis was to determine the feasibility of using a digital health intervention to support patients in adhering to their medications.

The systematic review of the literature (Chapter 2) aimed to assess existing evidence concerning using mHealth interventions for improving adherence to OACs, which included both DOACs and VKAs. This involved searching the databases PubMed, Embase, CENTRAL and Web of Science using terms capturing mHealth, OACs, medication adherence and randomised controlled trials. Of the 2,319 records that were initially identified, 16 studies were included in the final review. Of these, seven reported statistically significant improvements in medication adherence, describing a total of five different mHealth interventions (telephone calls/text messages, reminders, apps, electronic medication dispensers/smart pill bottles, web-based portals/interventions). Telephone calls and text messages were the mHealth intervention most frequently associated with statistically significant improvements in medication adherence, used in four of the seven studies that reported statistically significant improvements in adherence.

Most of the studies included in our systematic review were of poor methodological quality, with most being of *'serious'* risk of bias. Most of the studies were also of poor reporting quality, with only one study explicitly reporting the adherence phase studied (implementation). Future studies should therefore focus on appropriately defining the phase of medication adherence being studied (initiation, implementation, persistence) (Vrijens *et al.,* 2012). Chapter 2 therefore reports that mHealth interventions, specifically telephone calls and text messages, could be effective in improving OAC adherence, but that this needs to be confirmed in larger, longer-term trials, with emphasis placed on improved trial design, conduct and reporting.

Chapter 3 aimed to develop novel and efficient methods of generating health-messaging support using Artificial Intelligence (ChatGPT-3.5). Initial prompts were inputted into ChatGPT-3.5, with iterative refinement refining the content of the generated messages. Of the 300 initial messages that were generated, 108 duplicates were removed, with a further 47 messages removed after manual refinement against a pre-defined criterion. This produced a final list of 145 messages. Chapter 3 determined that using AI to develop health-messaging support is an efficient and feasible option that also has the potential to overcome some of the specific challenges involved with health message generation, including limited message number and diversity. Despite this, Chapter 3 also reports that a degree of human input is still required when using AI to generate health-messaging support, particularly during the final screening process.

Chapter 4 aimed to develop a novel mHealth intervention for improving medication adherence (the Atom5™ app) and test the feasibility of this intervention for supporting patients recruited from community pharmacies in adhering to their medications. The results of the systematic review (Chapter 2) guided the design of the app. This novel configuration of Atom5™ offered medication-intake reminders and daily digital messages combined with gamification (badges). A total of 10 patients were recruited from two community pharmacies within the same area of North Wales (Blaenau Ffestiniog), with patient follow-up periods ranging from to 12 to 36 days. Despite an enthusiasm for adopting and using the Atom5™ app, poor recruitment of patients, and retention for longer-term follow-up meant that limited data were available to reach a more definitive conclusion regarding its feasibility.

5.2 Overview of the main findings in totality

mHealth interventions may be feasible options for supporting patients to adhere to their medications

There are common themes and findings amongst the different chapters of this thesis, which can be contextualised within current evidence in the literature. Together, the findings of the systematic review, as well as the feasibility testing of the Atom5™ app, allude to the potential benefit of using mHealth interventions for supporting patients in adhering to their medications (initiation, implementation, persistence) (Vrijens *et al.,* 2012). Specifically, the results of the systematic review predominantly supported the use of telephone calls and text messaging for supporting OAC adherence, with four of the seven studies associated with significant improvements in adherence. Telephone calls and text messages were conducted or sent either as follow-up support or as medication-intake reminders. The feasibility testing of Atom5™ reported a limited amount of initial evidence alluding to the potential acceptability of using a smartphone app, which combined medication-intake reminders, as well as daily digital with gamification (bronze, silver, and gold badges), for supporting patients recruited from community pharmacies in adhering to their medications. Despite this, the limited number of participants means that further research would be required to reach a more definitive conclusion regarding the app's feasibility.

Somewhat consistent with our findings, a study focusing on elderly participants with AF determined that a smartphone app (Smart AF), which combined education with digital reminders and patient engagement, was largely successful in improving adherence to OACs (Senoo *et al.,* 2022). For instance, the study reports that 72% of patients placed in the low adherence group at baseline moved to either the medium or high adherence groups after using the app for six months. Smart AF provided similar support to that of Atom5™, but their tailoring of Smart AF to the elderly population provides an advantage over our feasibility testing, which did not tailor Atom5™ app to any specific groups of people, including specific age groups or medication type, which potentially presents a missed opportunity. Presenting a further advantage over our feasibility testing is their longer follow-up period of six months (Senoo *et al.,* 2022), compared with the longest follow-up period in our study being limited to 36 days.

Similarly, a study using the TeleClinical care app in individuals with cardiac disease during the transition from hospital to the community, reported higher rates of medication adherence in the intervention group, when compared with the control group (75% vs. 50%, *P*=.002) (Indraratna *et al.,* 2022). The app released educational push notifications three times per week, which is less frequent than our feasibility testing's once-per-day daily digital messages. Providing an advantage over our feasibility testing, the app was connected via Bluetooth to a digital blood pressure monitor, digital weighing scale, and a wearable fitness device. Their study also had a larger sample size of 164 patients and a mean follow-up period of 193 days (Indraratna *et al.,* 2022).

Medication adherence is often poorly reported in trials

The systematic review conducted as part of this thesis detailed that medication adherence (initiation, implementation, persistence) (Vrijens *et al.,* 2012) is often poorly reported in trials. Several guidelines have been published in an attempt to combat the issue of poor reporting in adherence-related trials. In response to the lack of uniformity in how adherence is defined in the literature, the ascertain barriers to compliance (ABC) project proposed a new taxonomy for defining adherence to medications, with initiation, implementation, and discontinuation being identified as the three key phases (Vrijens *et al.,* 2012). In response to the issue of poor reporting, the ESPACOMP Medication Adherence Reporting Guideline (EMERGE) was designed to supplement other recommendations, outlining four criteria that should be reported as a minimum in adherence research, as well as a further 17 recommended criteria (De Geest *et al.,* 2018). Furthermore, the Timelines–Events–Objectives–Sources (TEOS) framework was developed to focus on the operationalization of adherence in drug trials (Dima *et al.,* 2021). Despite some of the studies included in our systematic review pre-dating these guidelines, many were published after their creation. In this way, greater care should be taken to ensure that such guidelines are used and implemented into practice, which would in turn increase the quality of reporting in adherence-related trials, and therefore our ability to interpret their results.

In addition to poor reporting quality, most of the studies included in our systematic review were of poor methodological quality, with most being of *'serious'* risk of bias, as determined by the risk of bias instrument for interventional adherence studies tool (Sinnappah *et al.,* 2023). These findings are consistent with those of the literature, with an overview of systematic reviews, investigating the impact of interventions to support participants in adhering to their medications, reporting that the studies included were generally of poor methodological quality (Anderson *et al.,* 2020). This was also the case in a systematic review investigating the impact of apps and text messaging on the adherence of adolescents with chronic conditions, with most of the studies being of low or moderate methodological quality (Badawy *et al.,* 2017).

Using AI to generate health-messaging support presents a new opportunity

Chapter 3 reports that using AI platforms, such as ChatGPT-3.5, may be feasible options for developing health-messaging support, whilst also having the potential to overcome some challenges involved with health message generation, such as limited message number and diversity.

This finding is consistent with that of the limited literature in this area, including a study testing a similar tool, described as an automated software (Trial Promoter) for generating, distributing, and assessing health messages for social media platforms, reporting positive results (Reuter *et al.,* 2019). Despite generating a larger number of messages than our research (1275 vs. 145 messages), the simplicity of use of ChatGPT-3.5 presents an advantage over their study, with our research not requiring processes such as data import or the adjustment of parameters (Reuter *et al.,* 2019).

Despite these findings, our research required human input to screen the messages against a pre-defined criterion before the list could be finalised. We therefore conclude that using AI to develop health messaging support does not yet fully replace humans. This finding is consistent with that of the literature, with authors reporting that AI platforms should not replace humans, such as healthcare professionals, but should rather enhance and optimise the support that they already provide (Bohr. 2020; Sezgin. 2023). Furthermore, concerns regarding the use of AI in healthcare remain, and therefore to truly maximise the potential of AI, including for health message generation, concerns like these will need to be addressed and minimised where possible to enhance acceptability (Khan *et al.,* 2023).

5.3 Critical review of the methodology highlighting strengths and weaknesses

The methods used to conduct the systematic review of the literature, investigating the effectiveness of mHealth interventions for improving adherence to OACs were rigorous, with the publication of a protocol with the International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42022372863) representing a transparent process. The review was also reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The search terms inputted, as well as the inclusion and exclusion criteria used were clearly defined, allowing the work to be reproducible by other researchers. Furthermore, restricting our use of field tags when conducting searches in the literature databases allowed our searches to be as broad as possible, minimising the likelihood that potentially relevant studies were missed. Using the RoBIAS tool to assess the risk of bias of the included studies meant that a tool specifically designed for interventional adherence studies was employed, which was therefore fit for purpose. A limitation of the systematic review process was that only studies published in the English language were included, which could have meant that potentially relevant studies were missed. Also at the time of analysis, the RoBIAS tool was in its unpublished, draft form.

Chapter 3 aimed to assess the feasibility of using AI (ChatGPT-3.5) to develop health-messaging support. The methods used were robust and clearly outlined, which included the prompts inputted and screening criteria used. The number of messages merged, and deleted according to reason, was also

clearly defined, with the initial list of messages generated included as an appendix and the final list of messages included in Chapter 3. This means that our research is transparent, as well as being reproducible for future researchers. Our methods were guided by current evidence in the literature, which included reviewing the methods used by previous studies to develop health messaging support using AI platforms, which presents an evidence-based approach. Our methods did not require the fine-tuning of ChatGPT-3.5 before inputting the prompts, meaning that our research is inclusively reproducible, regardless of coding ability. Limitations of the research include the lack of tailoring of the messages to patient needs, as well as the lack of validation of the messages by patients. By asking patients to validate the messages, the robustness of the results would have been further increased.

Chapter 4 assessed the feasibility of using the Atom5™ app to support the adherence of participants recruited from community pharmacies. The findings of the systematic review were used to guide the design of the app, presenting an evidence-based approach. Furthermore, the methods used for participant onboarding and data collection were both very efficient. Using QR codes to onboard participants not only reduced the time commitment needed by the community pharmacies involved in the onboarding process but also allowed for the participants to remain anonymous to the research team. Collecting all data via questionnaires within the Atom5™ app meant that data collection was simplified and secure, and again, time- and labour-saving for the community pharmacies, as well as the research team and participants. Lastly, the number and types of messages used in the app presents a further advantage, with a total of 64 messages being used.

The feasibility study of the Atom5™ app only recruited a small number of participants and pharmacists, who were recruited from two largely rural community pharmacies based in the same area in North Wales (Blaenau Ffestiniog), limiting the diversity of the population studied and therefore the generalisability of the study findings. Retention also proved difficult, with only a limited number of questionnaires being completed by recruited patients. The short follow-up periods means that we cannot interpret the longer-term effects of using the Atom5™ app for supporting the adherence of patients recruited from community pharmacies. Furthermore, due to this being a service evaluation, more information might have been gained from a research study. For instance, participants were not asked what medication they were taking during the onboarding process, only their age category and gender, and how often they needed reminders, which limited our ability to relate and interpret the findings to medication type. Due to the increased complexities of personalizing the app configuration for each participant, everyone received the same configuration of the app, with the language (English/Welsh) being the only exception, which perhaps presents a missed opportunity to optimize the support. Lastly, only a small number of pharmacists across BCUHB responded to the surveys gathering their opinions on the messages before these were incorporated into the app. More feedback would have allowed the messages to be developed further, which might have further increased their quality.

5.4 Challenges in implementing/generalising the research findings to clinical practice

As the health-promoting messages generated using AI (ChatGPT-3.5) were not validated in patients, the ability to relate our results from this research to clinical practice is somewhat limited. Furthermore, as the feasibility testing of the Atom5™ app only recruited a limited number of patients and pharmacists from two community pharmacies within the same area of North Wales, the ability to generalise the research findings to wider clinical practice is limited as the population studied lacks diversity, including in the recruitment setting. Additionally, as participants were only followed for a short period, with the longest follow-up period being 36 days, it is difficult to generalise our findings to longer periods. Due to this being a service evaluation, participants were only asked about their gender, age category, and how often they needed medication-intake reminders. In this way, trying to relate the results to other factors in clinical practice, such as medication type, would be difficult. Due to only a small number of BCUHB pharmacists answering the surveys that gathered their opinions on the daily digital messages, the opportunity for the messages to be further developed and edited was missed. More responses would be required for the messages to be truly validated for use in wider clinical practice.

5.5 Recommendations for future research

There are several ways in which researchers could build upon the findings of this thesis and implement them into practice. Firstly, future research should prioritize optimizing the mHealth support provided, with emphasis placed on tailoring the intervention according to individual needs. This necessitates the examination of these interventions in larger, longer-term trials, that include a more diverse pool of participants. In doing this, focus should be placed on enhancing methodological quality, particularly by improving the measurement, reporting and analysis of medication adherence. Lastly, future research should explore the potential of using AI platforms, such as ChatGPT, to develop health-messaging support as it may overcome some of the specific challenges involved with health message generation.

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Appendix A – Ful search strategy

Database	Search strategy
PubMed	1. Mobile application* 2. Mobile health 3. mHealth 4. ehealth 5. Telemedicine 6. Messag* 7. Smart phone* 8. Smartphone* 9. Cell phone* 10. Mobile phone* 11. Home monitoring 12. Technolog* 13. Digital health 14. App 15. Application* 16. Wearable* 17. Smart watch 18. Smart device 19. Electronic 20. Reminder* 21. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 22. Oral anticoagul* 23. Anticoagul* 24. Dabigatran 25. Rivaroxaban 26. Apixaban 27. Edoxaban 28. Betrixaban 29. Warfarin 30. 22 OR 23 OR 24 OR 25 OR 26 OR 27 28 OR 29 31. Medication adherence 32. Adhere* 33. Complian* 34. Persistence 35. Non adherence 36. Non compliance

	37. Non persistence 38. Complier* 39. 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 40. Randomized controlled trial 41. Randomised controlled trial 42. Controlled clinical trial 43. Randomized 44. Randomised 45. Randomization 46. Randomisation 47. 40 OR 41 OR 42 OR 43 OR 44 OR 46 48. 21 AND 30 AND 39 AND 47
Embase	1. 'mobile application*' 2. 'mobile health' 3. mHealth 4. ehealth 5. telemedicine 6. messag* 7. 'smart phone*' 8. smartphone* 9. 'cell phone*' 10. 'mobile phone*' 11. 'home monitoring' 12. technolog* 13. 'digital health' 14. app 15. application* 16. wearable* 17. 'smart watch' 18. 'smart device' 19. electronic 20. reminder* 21. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 22. 'oral anticoagul*' 23. anticoagul* 24. dabigatran 25. rivaroxaban 26. apixaban 27. edoxaban

	28. betrixaban 29. warfarin 30. 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 31. 'medication adherence' 32. adhere* 33. complian* 34. persistence 35. 'non adherence' 36. 'non compliance' 37. 'non persistence' 38. Complier* 39. 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 40. 'randomized controlled trial' 41. 'randomised controlled trial' 42. 'controlled clinical trial' 43. randomized 44. randomised 45. randomization 46. randomisation 47. 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 48. 21 AND 30 AND 39 AND 47
	1. ALL=(Mobile application*) 2. ALL=(Mobile health) 3. ALL=(mHealth) 4. ALL=(ehealth) 5. ALL=(Telemedicine) 6. ALL=(messag*) 7. ALL=(Smart phone*) 8. ALL=(Smartphone*) 9. ALL=(Cell phone*) 10. ALL=(Mobile phone*) 11. ALL=(Home monitoring) 12. ALL=(Technolog*) 13. ALL=(Digital health) 14. ALL=(App) 15. ALL=(Application*) 16. ALL=(Wearable*) 17. ALL=(Smart watch) 18. ALL=(Smart device) 19. ALL=(Electronic)

Web of Science	20. ALL=(Reminder*) 21. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 22. ALL=(Oral anticoagul*) 23. ALL=(Anticoagul*) 24. ALL=(Dabigatran) 25. ALL=(Rivaroxaban) 26. ALL=(Apixaban) 27. ALL=(Edoxaban) 28. ALL=(Betrixaban) 29. ALL=(Warfarin) 30. 22 OR 23 OR 24 OR 25 OR 26 OR 27 28 OR 29 31. ALL=(Medication adherence) 32. ALL=(Adhere*) 33. ALL=(Complian*) 34. ALL=(Persistence) 35. ALL=(Non adherence) 36. ALL=(Non compliance) 37. ALL=(Non persistence) 38. ALL=(Complier*) 39. 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 40. ALL=(Randomized controlled trial) 41. ALL=(Randomised controlled trial) 42. ALL=(Controlled clinical trial) 43. ALL=(Randomized) 44. ALL=(Randomised) 45. ALL=(Randomization) 46. ALL=(Randomisation) 47. 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 48. 21 AND 30 AND 39 AND 47
	1. (“mobile application*”) 2. (“mobile health”) 3. (mHealth) 4. (ehealth) 5. (“telemedicine”) 6. (messag*) 7. (“smart phone*”) 8. (smartphone*) 9. (“cell phone*”)

Cochrane	10. (“mobile phone*”) 11. (“home monitoring”) 12. (technolog*) 13. (“digital health”) 14. (app) 15. (application*) 16. (wearable*) 17. (“smart watch”) 18. (“smart device”) 19. (electronic) 20. (reminder*) 21. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 22. (“oral anticoagul*”) 23. (anticoagul*) 24. (dabigatran) 25. (rivaroxaban) 26. (apixaban) 27. (edoxaban) 28. (betrixaban) 29. (warfarin) 30. 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 31. (“medication adherence”) 32. (adhere*) 33. (complian*) 34. (persistence) 35. (“non adherence”) 36. (“non compliance”) 37. (“non persistence”) 38. (complier*) 39. 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 40. (“randomized controlled trial”) 41. (“randomised controlled trial”) 42. (“controlled clinical trial”) 43. (randomised) 44. (randomized) 45. (randomization) 46. (randomisation) 47. 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 48. 21 AND 30 AND 39 AND 47

Systematic review

Please select one of the options below to edit your record. Either option will create a new version of the record - the existing version will remain unchanged.

A list of fields that can be edited in an update can be found here

1. * Review title.

Give the title of the review in English

What is the effectiveness of mobile health interventions that aim to improve adherence to oral anticoagulant treatment in adults?

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

07/11/2022

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

31/01/2023

5. * Stage of review at time of this submission.

This field uses answers to initial screening questions. It cannot be edited until after registration.

Tick the boxes to show which review tasks have been started and which have been completed.

Update this field each time any amendments are made to a published record.

The review has not yet started: Yes

Review stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No

Risk of bias (quality) assessment	No	No
	No	No

Data analysis

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Non Wyn Davies

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:
Miss Davies

7. * Named contact email.

Give the electronic email address of the named contact.

nnd22ppy@bangor.ac.uk

8. Named contact address

PLEASE NOTE this information will be published in the PROSPERO record so please do not enter private information, i.e. personal home address Give the full institutional/organisational postal address for the named contact.

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

Bangor University

Organisation web address:
https://www.bangor.ac.uk/

11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.
NOTE: email and country now MUST be entered for each person, unless you are amending a published record.

Miss Non Davies. Bangor

University Professor Dyfrig

Hughes. Bangor University

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

KESS2 East funded.

Grant number(s)

State the funder, grant or award number and the date of award

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

What is the effectiveness of mobile health interventions that aim to improve adherence to oral anticoagulant treatment in adults?

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

The following databases will be searched: PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science.

The search strategy will include terms relating to (i) mobile health (mhealth), (ii) oral anticoagulants (OAC), (iii) medication adherence and (iv) randomised controlled trials (RCTs). These search terms will be combined using Boolean operators.

The search will be restricted to publications since 1/1/2000, as well as to only those published in English.

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible.

Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

Warfarin has been the mainstay of anticoagulation treatment to prevent stroke and other thromboembolic diseases, however, direct oral anticoagulants (DOACs) are now becoming increasingly used. The reduced need for frequent blood monitoring, as well as increased safety, when compared with warfarin, makes DOACs an increasingly attractive option for most individuals (Turakhia et al., 2021). Despite this, adherence to oral anticoagulants (OAC) remains poor (Banerjee et al., 2019). In response to this, mobile health (mhealth) interventions aiming to promote OAC adherence are becoming increasingly popular, but their significance remains unclear.

In this review, we aim to investigate the impact of mhealth interventions on OAC adherence in adults.

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

The target population will be adults ≥ 18 years of age who are prescribed oral anticoagulation (OAC) therapy. This will include both warfarin and direct oral anticoagulant treatment (DOACs).

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

The World Health Organization (2017) defines mobile health (mhealth) as “medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices.”

This review will focus on identifying studies where one or more intervention aligns with this definition of mhealth, where the intent is to improve medication adherence. This will include, but not be limited to, interventions involving mobile phone applications and their associated content and reminders, telemedicine and text messaging services, wireless devices such as wearable technology, and other internet resources that are supported by mobile devices.

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Comparison with standard care (treatment as usual/routine practice), or with another intervention.

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Studies will be considered eligible for inclusion if they (i) involve a population who are self-responsible for taking oral anticoagulants (including vitamin K antagonists as well as direct oral anticoagulants [non-vitamin K antagonists]), (ii) are designed as randomized control trials, (iii) involve randomising patients to one or more mHealth intervention that aims to improve medication adherence, and (iv) measure adherence as an outcome measure.

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

The review will focus on identifying studies where the population are self-responsible for taking their medicines.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

OAC medication adherence.

Measures of effect

The review will include any measures of adherence. These might include direct measures (such as drug/metabolite concentration in blood/urine), secondary database analysis (for example using data from electronic prescription services), electronic medication packaging (EMP) devices, pill count, clinician assessments, self-reports (such as from diaries, questionnaires or interviews), as well as multi-measure approaches (Lam and Fresco. 2015).

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

Clinical outcomes, including:

- Bleeding events, hospitalization/re-hospitalization, death, stroke and systemic embolism, venous thromboembolic events(VTE), transient ischemic attack (TIA).

Patient self-reported outcomes, including:

- Patient knowledge of - medication, mhealth programme, and disease.
- Quality of life (QoL).
- Patient experience of mhealth intervention – engagement, motivation, satisfaction, usability, acceptance, and feasibility.
- Cost effectiveness/economic outcomes.

Measures of effect

The review will be inclusive of measures including self-reports, routine clinical records and case report forms.

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Following databases searching, studies will be exported into 'Zotero' and duplicate results removed. Subsequently, the titles and abstract of the remaining studies will be screened by one reviewer against the inclusion criteria. Studies will be included if they are designed as RCTs, the participants are adults taking OACs and published in English since 1/1/2000. Following the initial process of screening, the full texts of the remaining studies will be screened for the same inclusion criteria as previously described.

Data extraction will focus on identifying:

1. Study characteristics (including author, year of publication, country, sample demographics, sample size, inclusioncriteria, duration, control/comparator, study design).
2. Characteristics of mhealth intervention (including type/format of mhealth, purpose/aim, developing organization, durationof implementation).
3. Details of the outcomes measured and metric applied.

4. Results.
5. Author's interpretation of the results.

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

The risk of bias and quality of the studies will be assessed using a novel tool, designed specifically to assess the bias and quality of studies investigating medication adherence.

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data.
If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

The review will be assessed for appropriateness for quantitative analysis. A meta-analysis will be performed if sufficient homogeneous studies of similar outcome, design and measure are found. If too much clinical or statistical heterogeneity is present, a narrative synthesis will be followed, with presentation being in both tabular and written formats. Focus will be placed on study characteristics, mhealth intervention characteristics, and the outcomes assessed, results, and the author's interpretation, as described in the data extraction section of this protocol.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

If important subgroups are identified, they will be analysed separately.

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness	No
Diagnostic	No
Epidemiologic	No
Individual patient data (IPD) meta-analysis	No
Intervention	No
Living systematic review	No
Meta-analysis	No
Methodology	No
Narrative synthesis	No
Network meta-analysis	No
Pre-clinical	No

Prevention	No
Prognostic	No
Prospective meta-analysis (PMA)	No
Review of reviews	No
Service delivery	No
Synthesis of qualitative studies	No
Systematic review	Yes
Other	No

Health area of the review

Alcohol/substance misuse/abuse	No
Blood and immune system	No
Cancer	No
Cardiovascular	No
Care of the elderly	No
Child health	No
Complementary therapies	No
COVID-19	No
Crime and justice	No
Dental	No
Digestive system	No
Ear, nose and throat	No
Education	No
Endocrine and metabolic disorders	No

Eye disorders	No
General interest	No
Genetics	No
Health inequalities/health equity	No
Infections and infestations	No
International development	No
Mental health and behavioural conditions	No
Musculoskeletal	No
Neurological	No
Nursing	No
Obstetrics and gynaecology	No
Oral health	No
Palliative care	No
Perioperative care	No
Physiotherapy	No
Pregnancy and childbirth	No
Public health (including social determinants of health)	No
Rehabilitation	No
Respiratory disorders	No
Service delivery	No
Skin disorders	No
Social care	No
Surgery	No
Tropical Medicine	No
Urological	No
Wounds, injuries and accidents	No
Violence and abuse	No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error. English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved. Wales

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them.
If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

No I do not make this file publicly available until the review is complete

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

Mobile health; oral anticoagulants; medication adherence; randomised controlled trials.

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

38. * Current review status.

Update review status when the review is completed and when it is published.

New registrations must be ongoing so this field is not editable for initial submission.

Review_Ongoing

39. Any additional information.

Provide any other information relevant to the registration of this review.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission).

List authors, title and journal details preferably in Vancouver format.

Appendix C – Initial list of messages

1.	Take your medicine(s) with a glass of water.
2.	Remember your medicine(s) every day.
3.	Set an alarm to help you remember.
4.	Keep your medicine(s) where you can see them.
5.	Don't forget your medicine(s) before bed.
6.	Ask a grown-up for help if needed.
7.	Take your medicine(s) after breakfast.
8.	Use a special medicine organizer.
9.	Take your medicine(s) with a snack.
10.	Mark it off on a calendar.
11.	Medicine(s) help you feel better.
12.	Take your medicine(s) on time.
13.	Keep your medicine(s) at room temperature.
14.	Get a cute medicine(s) box to use.
15.	Remember your medicine(s) after school.
16.	Put a reminder note on the fridge.
17.	Take your medicine(s) before brushing teeth.
18.	Medicine(s) make you strong.
19.	Don't skip your medicine(s).
20.	Take your medicine(s) in the morning.
21.	Medicine(s) are good for you.
22.	Get a fun timer to use with your medicine(s).
23.	Ask a friend to remind you.
24.	Take your medicine(s) with dinner.
25.	Keep your medicine(s) in plain sight.
26.	Set a daily alarm on your phone for your medicine(s).
27.	Medicine(s) help you heal.
28.	Take your medicine(s) with a smile.
29.	Don't forget your medicine routine.
30.	Ask your teacher to help you.
31.	Keep your medicine(s) in your backpack.
32.	Take your medicine(s) after playtime.
33.	Use a colourful medicine(s) box.
34.	Mark your medicine(s) time on a chart.
35.	Take your medicine(s) after a school snack.
36.	Medicine(s) make you feel better.
37.	Remember your medicine(s) always.

38.	Keep your medicine(s) in a cool place.
39.	Get a cute medicine(s) reminder bracelet.
40.	Take your medicine(s) before bedtime.
41.	Put a sticky note on the mirror.
42.	Medicine(s) help you get well.
43.	Don't miss your medicine(s) dose.
44.	Take your medicine(s) each morning.
45.	Keep your medicine(s) in your room.
46.	Set a reminder on your tablet for your medicine(s).
47.	Ask your family for support with your medicine(s).
48.	Take your medicine(s) with lunch.
49.	Use a medicine(s) box with pictures.
50.	Mark your medicine(s) on a chart.
51.	Take your medicine(s) with a treat.
52.	Medicine(s) keep you strong.
53.	Remember your medicine(s) schedule.
54.	Keep your medicine(s) in a safe place.
55.	Get a fun alarm clock for your medicine(s).
56.	Take your medicine(s) before play.
57.	Put a reminder on the door.
58.	Medicine(s) make you feel good.
59.	Don't miss your medicine(s) time.
60.	Take your medicine(s) with a smile.
61.	Keep your medicine(s) routine.
62.	Set an alarm on your watch for your medicine(s).
63.	Ask a family member to help with your medicine(s).
64.	Take your medicine(s) before dinner.
65.	Use a colourful timer for your medicine(s).
66.	Mark your medicine(s) time on a chart.
67.	Take your medicine(s) with a snack.
68.	Medicine(s) keep you healthy.
69.	Remember your medicine(s) every day.
70.	Keep your medicine(s) in the kitchen.
71.	Get a cute reminder phone app for your medicine(s).
72.	Take your medicine(s) before school.
73.	Put a note on your bedroom door.
74.	Medicine(s) help you get better.
75.	Don't forget your medicine(s) dose.
76.	Take your medicine(s) each night.

77.	Keep your medicine(s) where you can see them.
78.	Set an alarm on your tablet for your medicine(s).
79.	Ask a friend to remind you.
80.	Take your medicine(s) after breakfast.
81.	Use a fun medicine(s) organizer.
82.	Mark your medicine(s) time on a chart.
83.	Take your medicine(s) with a treat.
84.	Medicine(s) make you healthy.
85.	Remember your medicine(s) always.
86.	Don't skip your medicine(s) routine.
87.	Take your medicine(s) with a smile.
88.	Keep your medicine(s) in your backpack.
89.	Set an alarm on your phone for your medicine(s).
90.	Ask your teacher to help you with your medicine(s).
91.	Take your medicine(s) before bedtime.
92.	Use a medicine(s) box with stickers.
93.	Mark your medicine(s) on a chart.
94.	Take your medicine(s) after a school snack.
95.	Medicine(s) help you heal.
96.	Remember your medicine(s) every day.
97.	Keep your medicine(s) in plain sight.
98.	Get a cute medicine(s) reminder bracelet.
99.	Take your medicine(s) after playtime.
100.	Put a sticky note on the fridge.
101.	You're a medicine(s) superstar!
102.	Medicines(s) help you stay strong.
103.	You've got this, take your medicine(s).
104.	Medicines(s) make you healthier.
105.	Don't forget, medicine(s) are important.
106.	Keep going, you're doing great!
107.	Medicine(s) bring healing power.
108.	Take medicine(s) with a smile.
109.	Stay on track with your medicine(s).
110.	Medicine(s) help you feel better.
111.	Remember, medicine(s) are your pals.
112.	Be a medicine(s) champion.
113.	Don't miss your medicine(s) time.
114.	Medicine(s) boost your well-being.
115.	You're a medicine(s) hero!

116.	Medicine(s) keep you well.
117.	Keep up the good work!
118.	Take your medicine(s) with care.
119.	Medicine(s) support your journey.
120.	Stay strong, take your medicine(s).
121.	Medicine(s) make life better.
122.	You're a medicine(s) rockstar!
123.	Don't skip your medicine(s).
124.	Medicine(s) are your friends.
125.	Keep your medicine(s) in sight.
126.	Take medicine(s) like a pro.
127.	Medicine(s) bring healing vibes.
128.	You've got the med magic.
129.	Remember, medicine(s) are your allies.
130.	Stay on track, take your medicine(s).
131.	Medicine(s) keep you healthy.
132.	You're a med superstar!
133.	Medicine(s) are your secret weapon.
134.	Be a medicine(s) champion.
135.	Don't miss your medicine(s) time.
136.	Medicine(s) make you strong.
137.	Keep going, you're doing great!
138.	Take your medicine(s) with a smile.
139.	Medicine(s) help you feel better.
140.	You're a medicine(s) hero!
141.	Medicine(s) keep you well.
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179.	Remember, medicine(s) are your allies.
180.	Stay on track, take your medicine(s).
181.	Medicine(s) keep you healthy.
182.	You're a med superstar!
183.	Medicine(s) are your secret weapon.
184.	Be a medicine(s) champion.
185.	Don't miss your medicine(s) time.
186.	Medicine(s) make you strong.
187.	Keep going, you're doing great!
188.	Take your medicine(s) with a smile.
189.	Medicine(s) help you feel better.
190.	You're a medicine(s) hero!
191.	Medicine(s) keep you well.
192.	Keep up the good work!
193.	Take medicine(s) with care.

194.	Medicine(s) support your journey.
195.	Stay strong, take your medicine(s).
196.	Medicine(s) make life better.
197.	You're a medicine(s) rockstar!
198.	Don't skip your medicine(s).
199.	Medicine(s) are your friends.
200.	Keep your medicine(s) in sight.
201.	Taking medicine(s) helps your body heal.
202.	Remembering medicine(s) keeps you well.
203.	Routines make medicine(s) easier.
204.	Believing in medicine(s) aids recovery.
205.	Habit makes medicine(s) simpler.
206.	Trust in medicine(s) brings wellness.
207.	Your efforts matter for health.
208.	Understanding medicine(s) supports healing.
209.	Positive thoughts help medicine(s) work.
210.	Consistency with medicine(s) is key.
211.	Believing in medicine(s) is powerful.
212.	Your commitment supports health.
213.	Mindset matters for medicine(s).
214.	Health comes from taking medicine(s).
215.	Your choices impact wellness.
216.	Stick to medicine(s) for better health.
217.	Confidence aids medicine(s) success.
218.	Thinking positive about medicine(s) helps.
219.	Small steps lead to wellness.
220.	Your routine impacts medicine(s).
221.	Faith in medicine(s) brings better health.
222.	Staying strong with medicine(s) is important.
223.	Patience supports medicine(s) effectiveness.
224.	Trusting in medicine(s) aids recovery.
225.	Mind over medicine(s) helps healing.
226.	Wellness comes from taking medicine(s).
227.	Positive thinking supports medicine(s).
228.	Consistent habits aid wellness.
229.	Your commitment helps medicine(s) work.
230.	Understanding aids medicine(s) effectiveness.
231.	Sticking to medicine(s) brings health.
232.	Belief in medicine(s) aids recovery.

233.	Confidence in medicine(s) aids wellness.
234.	Wellness comes from your efforts.
235.	Consistency impacts medicine(s).
236.	Trust in medicine(s) supports healing.
237.	Positive mindset aids medicine(s) effectiveness.
238.	Stick to medicine(s) for better health.
239.	Your choices impact medicine(s).
240.	Believe in medicine(s) for better health.
241.	Staying strong supports wellness.
242.	Trust in medicine(s) for a healthier you.
243.	Patience helps medicine(s) work.
244.	Positive thoughts boost medicine(s).
245.	Health comes from consistency.
246.	Trusting in medicine(s) aids health.
247.	Your mindset affects medicine(s).
248.	Small steps lead to wellness.
249.	Your routine impacts medicine(s).
250.	Staying committed supports healing.
251.	Belief in medicine(s) aids wellness.
252.	Confidence supports medicine(s) success.
253.	Positive thoughts aid medicine(s) effectiveness.
254.	Trusting in medicine(s) supports health.
255.	Consistent routines impact wellness.
256.	Mind over medicine(s) for a healthier you.
257.	Your commitment aids medicine(s).
258.	Wellness comes from positive thoughts.
259.	Positive thinking supports medicine(s).
260.	Consistency impacts wellness.
261.	Belief in medicine(s) supports healing.
262.	Your routine influences medicine(s).
263.	Trust in medicine(s) for better health.
264.	Positive thoughts impact medicine(s).
265.	Your mindset aids wellness.
266.	Sticking to medicine(s) for a healthier you.
267.	Believing in medicine(s) aids health.
268.	Confidence in medicine(s) supports healing.
269.	Consistent habits aid medicine(s).
270.	Trusting in medicine(s) aids wellness.
271.	Positive mindset aids medicine(s) effectiveness.

272.	Wellness comes from your commitment.
273.	Your choices influence medicine(s).
274.	Trust in medicine(s) supports wellness.
275.	Patience aids medicine(s) success.
276.	Small steps lead to a healthier you.
277.	Staying committed aids wellness.
278.	Positive thoughts impact health.
279.	Consistency supports medicine(s) success.
280.	Believing in medicine(s) for a healthier you.
281.	Confidence supports healing.
282.	Mind over medicine(s) aids wellness.
283.	Trusting in medicine(s) influences health.
284.	Positive mindset aids medicine(s).
285.	Wellness comes from consistency.
286.	Your routine impacts healing.
287.	Trust in medicine(s) for better health.
288.	Belief in medicine(s) supports wellness.
289.	Confidence aids medicine(s) success.
290.	Consistent habits aid health.
291.	Trusting in medicine(s) aids medicine(s).
292.	Positive thoughts influence wellness.
293.	Wellness comes from your mindset.
294.	Believing in medicine(s) supports healing.
295.	Confidence in medicine(s) aids wellness.
296.	Consistency supports better health.
297.	Trust in medicine(s) influences healing.
298.	Positive mindset aids medicine(s) success.
299.	Small steps lead to wellness.
300.	Your choices impact health

Community Pharmacy Medicines Adherence Support Service

Supporting the safe and effective use of medicines in patient's own home

Prepared by: Ellen Lanham
March 2023

Updated April 2023

Aims & Objectives

Aim

This project aims to:

- develop a pathway to support patients to safely take medicines in their own homes, improving adherence to medicines and achieving better therapeutic outcomes
- ensure that every patient receives the appropriate patient-centred support to increase adherence
- Improve patient understanding of, and adherence to, their medicine regimes
- Reduce adverse events associated with non-adherence and the potential associated medicines related harm
- Reduce waste by optimising the use and therapeutic outcomes of prescribed medicines and highlighting prescribed medication that is not being used

Objectives

The above aim will be realised through the following objectives:

1. Develop a standardised assessment tool to be used by all community pharmacies in BCU
2. Develop a Community Pharmacy Additional Service to complete assessments (using tool above) and provide the appropriate support to each patient
3. Pilot and roll out the service in an agile cluster-by-cluster manner reviewing and refining the service and associated tools at 3-monthly intervals and after each new cluster is added
4. Wider engagement campaign to launch assessment tool, provide information on the options for support that may be available and the patient pathway for obtaining such support, and issue guidance to help Allied Healthcare Professionals to supporting their patients

Methods

Phase 1 – Initial test of concept

The service will be commissioned in a small cluster with one surgery and two community pharmacy contractors who have established relationships to test the tools and associated guidance on patients requiring support with taking their medicines.
Initial engagement of the following local stakeholders will be undertaken by project lead:

- Area team
- Community Pharmacy Contractors
- GP practice
- Community Resource Team
- District Nursing colleagues

The pharmacies will invite patients currently receiving support taking their medicines, mainly patients currently receiving some or all of their medicines in MCCA for review assessments and use the assessment form for any new patients who may present with adherence problems. We will use analysis of the assessments and quantitative techniques to provide data on:

- Number of patients assessed (existing and new)

- Summary of the adherence issues
- Initial support provided
- Outcome of the review
- Cost of the interventions provided and the service

The project will include regular check-in meetings with the stakeholders as a group to review progress as well as one-to-one interviews with pharmacy colleagues undertaking the reviews. We will review the service specification, guidance documents and tools.
This phase will address objective (1-3)

Phase 2 – Roll out

Following the reviews undertaken in Phase 1, the specification, guidance and tools will be updated to reflect any learning and feedback. The service will then be rolled out in an agile phased manner at cluster level with further reviews after each cluster implementation.
The following stakeholders/groups will be engaged as the roll out progresses:

- Community Pharmacists
- GP practices
- Community Resource teams
- Primary Care teams
- Cluster Leads
- Nursing leads for Community Hospitals & District Nursing
- Local Authority /Carer network

Continuous reviews of the service and associated documents/tool and interviews stakeholders at cluster level will continue to be undertaken as the roll out progresses and the necessary amendments made before the next cluster starts. Interviews will be transcribed and thematically analysed to identify relevant themes.

This phase will address objective (1-3)

Phase 3 – Wider engagement / roll out of the service

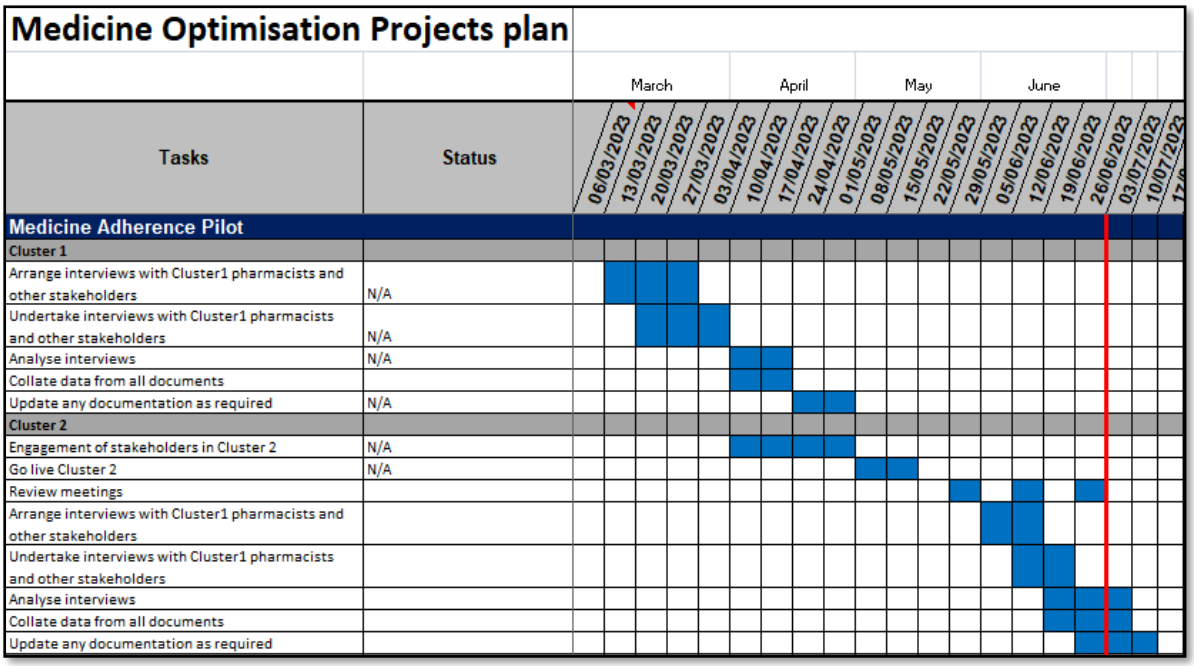
Once the service has been rolled out across all areas, this phase will include a campaign to raise awareness of the community pharmacy service, launch the Assessment Tool with the wider Allied and Secondary Healthcare professionals. This engagement activity will support creating a BCU pathway for patients requiring support with medicines.

This activity will be undertaken by the Community Pharmacy Team.

This phase will address objective (4)

Timeline

This project will require a robust engagement plan as well as continuous review to support the agile roll out. The current projection is that the end-to-end activity for each cluster will be 13 weeks. On current resource the activity will be limited to one cluster at a time.



Budget/Cost:

A provisional amount of £20K of the ring-fenced Community Pharmacy Services budget has been allocated for implementation to the first 20 pharmacies. The financial impact will be assessed as part of the continuous review and a business case for further funding will be submitted for roll-out beyond the initial agreed allocation.

Appendix E – BCUHB medication adherence assessment (existing patient)

Medication Adherence Assessment – Existing Patient

This assessment should be used by the pharmacy team to review patients who are currently receiving support with taking medicines.

The assessment and the decision/ agreement of the support required/ to be provided must **only** be completed by the patient's regular **community pharmacy** following a discussion with the patient*.

* where it has not possible to discuss adherence and potential options with the patient or their nominated **representative, please document the reason for this.**

PART 1:

PATIENT DETAILS	
Name:	**Address:**
Date of Birth:	**Telephone number:**
Hospital/NHS Number (in known):	

PATIENT CONSENT	
I confirm that the patient (or their representative**) has provided consent to this assessment and to the sharing this information with the community pharmacist, GP, social services and home carers. ☐ Tick to confirm	
Name of person confirming consent:	**Date of initial conversation:**
****Name of patient representative:** **Relationship/authority to provide consent:**	
Is the patient/representative happy to be contacted by a Local Health Board representative to give them an opportunity to give feedback about the service? (provide contact details if different from above) ☐ Tick to confirm	

KEY CONTACTS (if known)			
GP		Next of Kin/Relative	
Does the patient have a carer?	Yes ☐ No ☐ If yes, are they (circle): Formal (paid) Informal (Unpaid)		
Name of Care Agency/Organisation/Individual:		Telephone Number:	

Days and time of calls (tick)

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Morning							
Lunch							
Tea-time							
Night							

OR provide details of care visits:

CURRENT MEDICATION ARRANGEMENTS		
How does the patient currently obtain their repeat medicine? *(tick as appropriate and provide comments)*		
Patient self-orders		
Pharmacy Managed Repeats		
Batch/Repeat dispensing		
Family or Representative orders		
Patient / Representative Collects		
Pharmacy Delivers		

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Access to repeat medicines		
Do you have problems ordering or remembering to order your medication?	Yes/No	
Do you have problems collecting your medication from the pharmacy?	Yes/No	

CURRENT MEDICATION ARRANGEMENTS		
How medicines are currently supplied? (tick all appropriate or provide comments) Where medicines are supplied in more than one method, how are these managed?		
In original boxes and bottles		
Dosette box filled by patient or representative. Please state filled by		
MDS/blister pack from pharmacy		
Other medicine packing device(s) Please state which and filled by:		
MAR chart used by patient		
MAR Chart Used by Patient Representative		
MAR Chart used by formal Carer		
Reminder chart		
Other reminder device including apps		

How many times a day do you take medication?		
Does the patient have any issues reading and understanding the instructions to take their medicines?	Yes/No	*If Yes, specify*
What issue is the above support addressing?		

Does the patient currently get support with taking their medicines? *(tick as appropriate and provide comments)*		
Self-administration		
Prompting (by who?)		
Administration (by who?)		
Other (provide detail)		

Medication Adherence Assessment PART 2:

Using medicines:							
Current Medicines (including over the counter & complementary therapies)		Is the patient able to retrieve this medicine from original and current packaging? *If No, specify*	Does the patient know how to use this medicine? *If No, specify*	Does the patient always use the medicine as prescribed? *If No, specify*	Does the patient know why they take this medicine?	Does the patient believe that this medicine is helping? *If No, specify*	Does the patient believe that this medicine is causing side effects? *If No, specify*
1	*Name, form & strength:* *Dose:*						
2	*Name, form & strength:* *Dose:*						
3	*Name, form & strength:* *Dose:*						
4	*Name, form & strength:* *Dose:*						
5	*Name, form & strength:* *Dose:*						
6	*Name, form & strength:* *Dose:*						
7	*Name, form & strength:* *Dose:*						
8	*Name, form & strength:* *Dose:*						

Further Space on last page

Medication Adherence Assessment PART 2 *(continued):*

ADHERENCE/ATTITUDE TO MEDICATION:		
Do you think you need help to remember take your medication?	Yes/No	
How often do you forget to take your medication? *(include which medicines are regularly forgotten)*	Daily, once or twice a week, once a month less often	
What time do you most often forget to take your medicines?		
Why do you think you forget to take your medicines?		
Do you have a strategy to remind you to take your medicines? or How do you remember to take your medicines?		
Where do you keep your medicines?		
Do you have concerns/worries about your medication?	Yes/No	
Do you have any old/unused medication that that you no longer take or surplus medication at home? *(does this need removing from house?)*	Yes/No	
Notes:		

Medication Adherence Assessment PART 3:

This part of the assessment must be completed by the community pharmacy to document the actions agreed with the patient or their representative* and the agreed date for the review of this agreement.

* In exceptional circumstances where it has not been possible to discuss the assessment, explore options and agree potential solutions, the reason for this, the decision of what support will be provided and how this will be communicated with the patient or their representative must be documented.

If the patient is to continue receiving their medicines in a blister pack, please provide the rationale:			
Action required			
What:	**By who:**	**By when:**	**Date to be reviewed:**

I confirm that I have explored the options available with the patient (or their named representative) and have agreed to the action documented here.

Name of Pharmacy colleague completing assessment:

Signature of pharmacy colleague: **Date of assessment:**

Medication Adherence Assessment Review of Support:

Review of support previously agreed:			
Review with patient or representative?		**Length of time since initial assessment?**	
Has the previously agreed actions been completed/Implemented?			
Discuss the support previously agreed with the patient or representative. Has this addressed the adherence issue previously identified? If not, discuss alternative options and agree further support/action. *Document this in the action section below.*			
Further Action(s) agreed			
What:	**By who:**	**By when:**	**Date to be reviewed:**

I confirm that I have explored the options available with the patient (or their named representative) and have agreed to the action documented here.

Name of Pharmacy colleague completing assessment:

Signature of pharmacy colleague: **Date of assessment:**

Medication Adherence Assessment PART 2 *(continued)*:

Using medicines:							
Current Medicines (including over the counter & complementary therapies)		Is the patient able to retrieve this medicine from packaging? *If No, specify*	Does the patient know how to use this medicine? *If No, specify*	Does the patient use the medicine as prescribed? *If No, specify*	Does the patient know why they take this medicine?	Does the patient believe that his medicine is helping? *If No, specify*	Does the patient believe that this medicine is causing side effects? *If No, specify*
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						

Appendix F – BCUHB medication adherence assessment (new patient)

Medication Adherence Assessment – New Patient

This assessment should be used to support patients who may be experiencing problems taking medicines as prescribed.

Part 1 and Part 2 Column A of the assessment to be completed by the community pharmacy but may be completed by **any** health or social care colleague prior to referral to the patient's regular community pharmacy.

Part 2 Column B and Part 3 of the assessment and the decision/ agreement of the support required/ to be provided must **only** be completed by the patient's regular **community pharmacy** following a discussion with the patient*.

* where it has not possible to discuss adherence and potential options with the patient or their nominated **representative, please document the reason for this.**

PART 1: *(to be completed by the community pharmacy or any health or social care colleague when referring a patient)*

PATIENT DETAILS	
Name:	**Address:**
Date of Birth:	**Telephone number:**
Hospital/NHS Number (in known):	
Details of colleague completing initial assessment (Part 1 and Part 2 Column A):	
Name:	**Job role:**
Contact number:	**Email:**

PATIENT CONSENT	
I confirm that the patient (or their representative**) has provided consent to this assessment and to the sharing this information with the community pharmacist, GP, social services and home carers. ☐ Tick to confirm	
Name of person confirming consent:	**Date of initial conversation:**
****Name of patient representative:** **Relationship/authority to provide consent:**	
Is the patient/representative happy to be contacted by a Local Health Board representative to give them an opportunity to give feedback about the service? (provide contact details if different from above) ☐ Tick to confirm	

KEY CONTACTS (if known)			
GP		Next of Kin/Relative	
Does the patient have a carer?		Yes ☐ No ☐ If yes, are they (circle): Formal (paid) Informal (Unpaid)	
Name of Care Agency/Organisation/Individual:		Telephone Number:	

Days and time of calls (tick)

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Morning							
Lunch							
Tea-time							
Night							

OR provide details of care visits:

CURRENT MEDICATION ARRANGEMENTS					
Taking medicines (tick as appropriate or provide comments)		**How medicines are supplied (tick all appropriate or provide comments)**		**Obtaining medicines(tick as appropriate or provide comments)**	
Self-administration		In original boxes and bottles		Patient self-orders	
Prompting (by who?)		Dossete box filled by:		Pharmacy Managed Repeats	
				Batch/Repeat dispensing	
Administration (by who?)		Other eg. devices: Please state which and filled by:		Family or Representative orders	
				Patient Collects	
				Family or Representative collects	
				Pharmacy delivers	
Other Support/Comments:					

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Medication Adherence Assessment PART 2:

	COLUMN A: (to be completed by community pharmacy or other colleague doing initial assessment)		COLUMN B: (to be completed by community pharmacy)
	Response:	Comments / Preferences (if any):	Community Pharmacist Actions:
Access to repeat medicines			
Do you have problems ordering or remembering to order your medication?	Yes/No		
Do you have problems collecting your medication from the pharmacy?	Yes/No		

Using medicines:

	Current Medicines (including over the counter & complementary therapies)	Is the patient able to retrieve this medicine from packaging? *If No, specify*	Does the patient know how to use this medicine? *If No, specify*	Does the patient always use the medicine as prescribed? *If No, specify*	Does the patient know why they take this medicine?	Does the patient believe that this medicine is helping? *If No, specify*	Does the patient believe that this medicine is causing side effects? *If No, specify*
1	*Name, form & strength:* *Dose:*						
2	*Name, form & strength:* *Dose:*						
3	*Name, form & strength:* *Dose:*						
4	*Name, form & strength:* *Dose:*						
5	*Name, form & strength:* *Dose:*						
6	*Name, form & strength:* *Dose:*						

Further Space on last page

Medication Adherence Assessment PART 2 *(continued)*:

Using medicines:

	Current Medicines (including over the counter & complementary therapies)	Is the patient able to retrieve this medicine from packaging? *If No, specify*	Does the patient know how to use this medicine? *If No, specify*	Does the patient use the medicine as prescribed? *If No, specify*	Does the patient know why they take this medicine?	Does the patient believe that his medicine is helping? *If No, specify*	Does the patient believe that this medicine is causing side effects? *If No, specify*
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						
	Name, form & strength: *Dose:*						

Medication Adherence Assessment PART 3:

This part of the assessment must be completed by the community pharmacy to document the actions agreed with the patient or their representative* and the agreed date for the review of this agreement.

* In exceptional circumstances where it has not been possible to discuss the assessment, explore options and agree potential solutions, the reason for this, the decision of what support will be provided and how this will be communicated with the patient or their representative must be documented.

Action required			
What:	By who:	By when:	Date to be reviewed:

I confirm that I have explored the options available with the patient (or their named representative) and have agreed to the action documented here.

Name of Pharmacy colleague completing assessment:

Signature of pharmacy colleague: **Date of assessment:**

Medication Adherence Assessment Review of Support:

Review of support previously agreed:			
Review with patient or representative?		Length of time since initial assessment?	
Has the previously agreed actions been completed/Implemented?			
Discuss the support previously agreed with the patient or representative. Has this addressed the adherence issue previously identified? If not, discuss alternative options and agree further support/action. *Document this in the action section below.*			

Further Action(s) agreed			
What:	By who:	By when:	Date to be reviewed:

I confirm that I have explored the options available with the patient (or their named representative) and have agreed to the action documented here.

Name of Pharmacy colleague completing assessment:

Signature of pharmacy colleague: **Date of assessment:**

Medication Adherence Assessment PART 2 *(continued)*:

	COLUMN A: (to be completed by community pharmacy or other colleague doing initial assessment)		COLUMN B: (to be completed by community pharmacy)
	Response:	**Comments / Preferences (if any):**	**Community Pharmacist Actions**
How many times a day do you take medication?			
Does the patient have any issues reading and understanding the instructions to take their medicines?		*If Yes, specify*	
ADHERENCE/ATTITUDE TO MEDICATION:			
Do you think you need help to remember take your medication?	Yes/No		
How often do you forget to take your medication? *(include which medicines are regularly forgotten)*	Daily, once or twice a week, once a month less often		
What time do you most often forget to take your medicines?			
Why do you think you forget to take your medicines?			
Do you have a strategy to remind you to take your medicines? or How do you remember to take your medicines?			
Where do you keep your medicines?			
Do you have concerns/worries about your medication?	Yes/No		
Do you have any old/unused medication that that you no longer take or surplus medication at home? *(does this need removing from house?)*	Yes/No		
Notes:			

Appendix G – Feasibility testing of Atom5™ protocol

Protocol

Service evaluation title: Supporting the safe and effective use of medicines in patient's own home.

Master's project title: Digital Health Solutions for Medication Adherence Support.

Key contacts:

Master of Science by Research (MScMRes) student:

Non Wyn Davies, Bangor University, UK.

nnd22ppy@bangor.ac.uk

Academic supervisor:

Professor Dyfrig Hughes, Centre for Health Economics and Medicines Evaluation (CHEME), Bangor University, UK.

d.a.hughes@bangor.ac.uk

Company supervisor:

Dr Elin Haf Davies, Aparito Ltd, UK.

elin@aparito.com

Master's degree funder:

Knowledge Economy Skills 2 (KESS2) Scholarship.

Research ethics committee review has been deemed as not being required for research involving NHS staff recruited as research participants by virtue of their professional role.

Project background and rationale

Betsi Cadwaladr University Health Board (BCUHB) is currently working on a service evaluation titled 'Supporting the safe and effective use of medicines in patient's own home.' The student plans to work alongside BCUHB colleagues on this project, specifically in line with aim 3 of the main service evaluation, which is to "Improve patient understanding of, and adherence to, their medicine regimens", and the objective of creating a tool (see 'objective and measures' subsection for further details). As part of the main service evaluation, pharmacists will be assessing both new and existing patients for medication adherence (appendices 1 and 2). Data capture is restricted to the assessments conducted within the pharmacies as defined in the service evaluation protocol and will be retained by BCUHB employees. Neither Aparito nor Atom5™ will have visibility of this data and will not be involved in this aspect of the project. Please refer to the appendix 3 for the BCUHB service evaluation specification.

Patients being assessed under the BCUHB service evaluation will be offered the opportunity to take part in the co-creation and usability testing of the Atom5™ app which is being developed as an mHealth technology to support patients in adhering to their medications. No personal identifiable information (PII) such as name, email, phone number or date of birth will be captured within the Atom5™ system but patients will be offered the opportunity to input age and sex. Aparito will be responsible for all the data that is collected via Atom5™ and all data that is collected will be transferred to the student for analysis via Aparito and not the NHS.

Non Wyn Davies is undertaking a Master of Science by research (MScRes) degree titled 'Digital Health Solutions for Medication Adherence Support' at the School of Medical and Health Sciences, Bangor University, which is funded by the Knowledge Economy Skills 2 (KESS2) Scholarship (reference number BUKE027). As part of this scholarship, students work alongside a partner company, which, in this case, is Aparito Ltd. Aparito Ltd is a global digital health company based in Wrecsam, Wales, that focuses on the use of mobile apps, video assessments and wearable devices to collect patient data.

MScRes sub-study

The purpose of this protocol is to provide detail of the MScRes component of the service evaluation, and describe the aims and objective of including an app-based tool (Atom5™) to improve medication adherence.

Atom5™ will offer alerts in the form of reminders and motivational messaging combined with gamification (badges). The value add of this will be assessed by engagement rates and self-reported questionnaires.

AIM

This project aims to determine whether a bespoke mHealth intervention (the Atom5™ app) can support medication adherence in patients recruited from community pharmacies.

OBJECTIVES

1. Co-creation of a bespoke app (the Atom5™) that combines alerts in the form of reminders and motivational messaging with gamification (badges).
2. Testing of the Atom5™ app in patients already taking part in the ongoing BCUH service evaluation (approximately 15-30 patients).
3. User evaluation of the Atom5™ app.

Design

The sub-study will align with aim 3 of the service evaluation (To improve patient understanding of, and adherence to, their medicine regimes) and the objective of creating a tool (see 'objective and measures' subsection for further details) through early patient input and usability assessment. Please refer to appendix 3 for the BCUHB service evaluation specification.

Participant identification

Participants

Participants will be those who are invited to take part in the service evaluation, contacted via pharmacies located in Blaenau Ffestiniog (Moelwyn Pharmacy and Fferyllwyr Llŷn, Blaenau/D Powys Davies).

Procedures

Recruitment

Participants who are invited to take part in the service evaluation will be offered the opportunity to take part in the co-creation and usability testing of the Atom5™ app.

Description of Atom5™

The Atom5™ is an app developed by Aparito Ltd. Atom5™ will offer alerts in the form of reminders and motivational messaging combined with gamification (badges). The motivational messages will be developed using input from surveys, in which pharmacists across BCUH will be asked to rate the messages. Patient will self-onboard onto the app meaning that no personal identifiable information (PII) such as name, email, phone number and date of birth will be collected. Please refer to appendix 4 for preliminary screenshots of the Atom5™ configuration, appendix 5 for a preliminary list of the motivational messages, and appendix 6 for survey screenshots.

Assessments

All assessments will be conducted, and thus all data collected, within the Atom5™ app. Assessments will be in the form of self-reported questionnaires completed by participants. Participant engagement with the app will be assessed using data from Atom5™ (such as time spent on questionnaires, missed questionnaires). Please refer to appendix 4 for app screenshots showing the design of provisional questionnaires, and appendix 7 for a draft copy of the questionnaire intended to gather the views and opinions of the community pharmacists. All data that is collected by Atom5™ will be transferred to the student for analysis via Aparito and not the NHS.

Details of provisional questionnaires:

- Participants will be asked to fill in a questionnaire at the end of each week, detailing their medication adherence using a 5-point Likert scale of whether they have taken 'all' or 'none' of their prescribed medication for that week. They will also be asked to provide a reason for not taking their medication as prescribed if that is the case.
- At the end of the study period, participants will be asked to complete a questionnaire detailing their experience of using the Atom5™ app.
- The community pharmacists involved in the project will be asked to complete a questionnaire expressing their views and opinions of the Atom5™ app.

Informed consent

The BCUHB medication adherence assessments (appendices 1 and 2) require that the pharmacist confirms consents (verbal consent) with the patient or their representative:

4.1 The patient must be willing and able to participate in a review OR provide consent for a representative to participate on their behalf;

4.2 The patient must consent to the provider contacting the practice that he or she is registered with for the provision of General Medical Services;

Additional verbal consent will be taken for the co-creation and usability testing of the Atom5™ app. When onboarding onto Atom5™, participants will also be required to consent to take part via a tick box. They will also be required to tick a box to consent to Aparito's privacy policy, as seen in appendix 4.

Data management

Patient will be navigated to a URL to connect with a QR code that will onboard them onto the Atom5™ app. No personal identifiable information (PII) such as name, email, phone number and date of birth will need to be collected. Aparito will be responsible for data collection via the Atom5™ platform and will then transfer this data to the student for analysis. Data will be held on a Bangor University, encrypted and password protected laptop computer, accessible only to the student and supervisor.

The anonymized findings of this project (limited to the data collected by Atom5™) will be published in the student's master's thesis and may also be published in academic journals. Participants will not be identifiable in these publications (further details on this provided in the 'ethical considerations' subsection').

Data analysis

Data analysis by the student will be limited to the data collected by Atom5™. The data will be analysed descriptively and will include a summary of the Likert scale responses. If possible, age and sex will be used as variables but no statistical inference testing will be performed.

Reporting

The anonymized findings of this project (limited to the data collected by Atom5™) will be published in the student's master's thesis and may also be published in academic journals. Participants will not be

identifiable in these publications (further details on this provided in the 'ethical considerations' subsection').

Ethical considerations

Participant consent and anonymity

As part of the main service evaluation, verbal consent will be taken prior to the medication adherence assessments being carried out. Additional verbal consent will be taken for the co-creation and usability testing of the Atom5™ app. When onboarding onto Atom5™, participants will be required to consent to take part via a tick a box. They will also be required to tick a box to consent to Aparito's privacy policy, as seen in appendix 4.

Participation in the project is entirely voluntary and participants will be given adequate time to consider their decision before consenting. Participants are free to withdraw their consent at any point without providing reason or without experiencing repercussions. No personal identifiable information such as name, email, phone number and date of birth will be collected. All data that is collected will be anonymized, meaning that individual participants cannot be identified. Participants will alternatively be assigned subject codes. This complies with the General Data Protection Regulation (GDPR) and Data Protection Act (2018).

Approvals

The protocol, Atom5™ screenshots, preliminary versions of the pharmacist experience questionnaire and motivational messages, well as the BCUH project documents will be attached with the secondary data collection analysis application form to Bangor University's School of Medical and Health Sciences Academic Ethics Committee Chair. All investigators will be required to agree on any subsequent amendments to these documents.

Risks

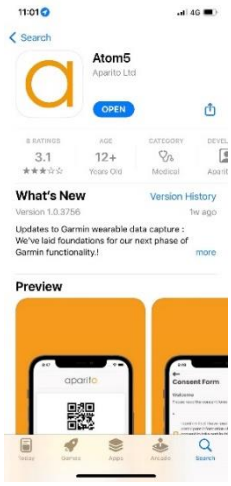
No risks are anticipated but participants are encouraged to contact the investigators if they have any concerns or questions.

Burden

The team will attempt to reduce the likelihood of participants experiencing burden because of the service evaluation. Study participants will be expected to dedicate approximately 5 minutes a week to complete the questionnaires.

Instructions for app download

1. **Download the Aparito Atom5™ app to your mobile phone or tablet device from the Google Play Store or the Apple App Store by searching for Atom5 by "Aparito".**

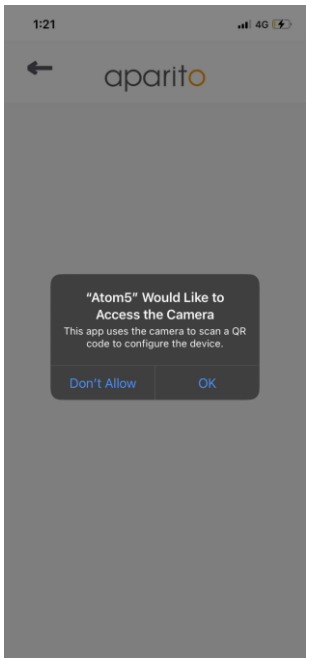


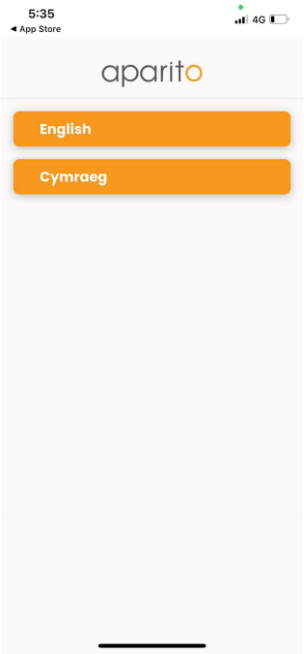
2. **Activate the Aparito Atom5™ app by scanning the QR code below**

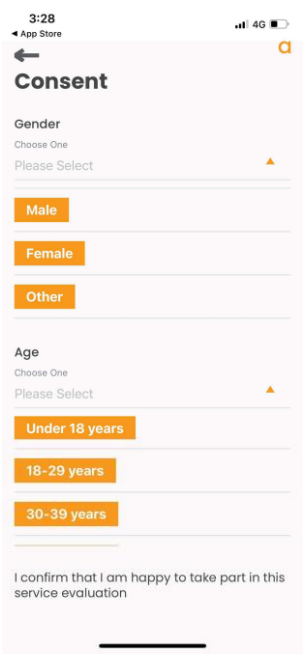
OR

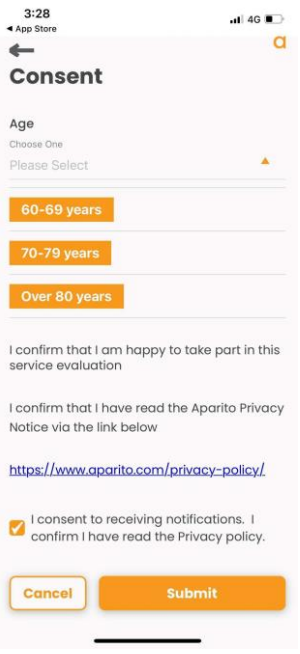
If you are unable to scan the QR code please enter the following code when prompted: h4198

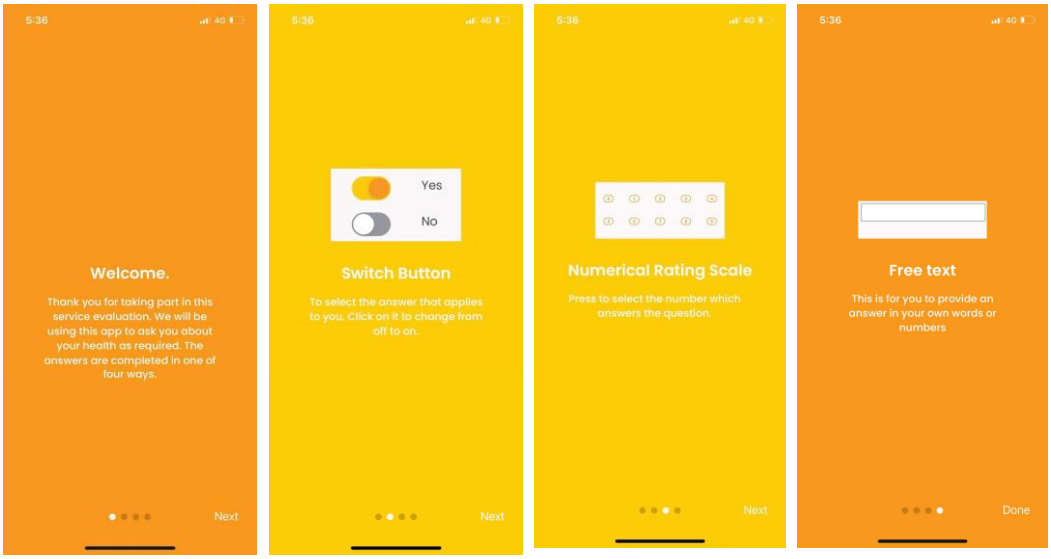
Appendix I – Screenshots of Atom5™ (English version)

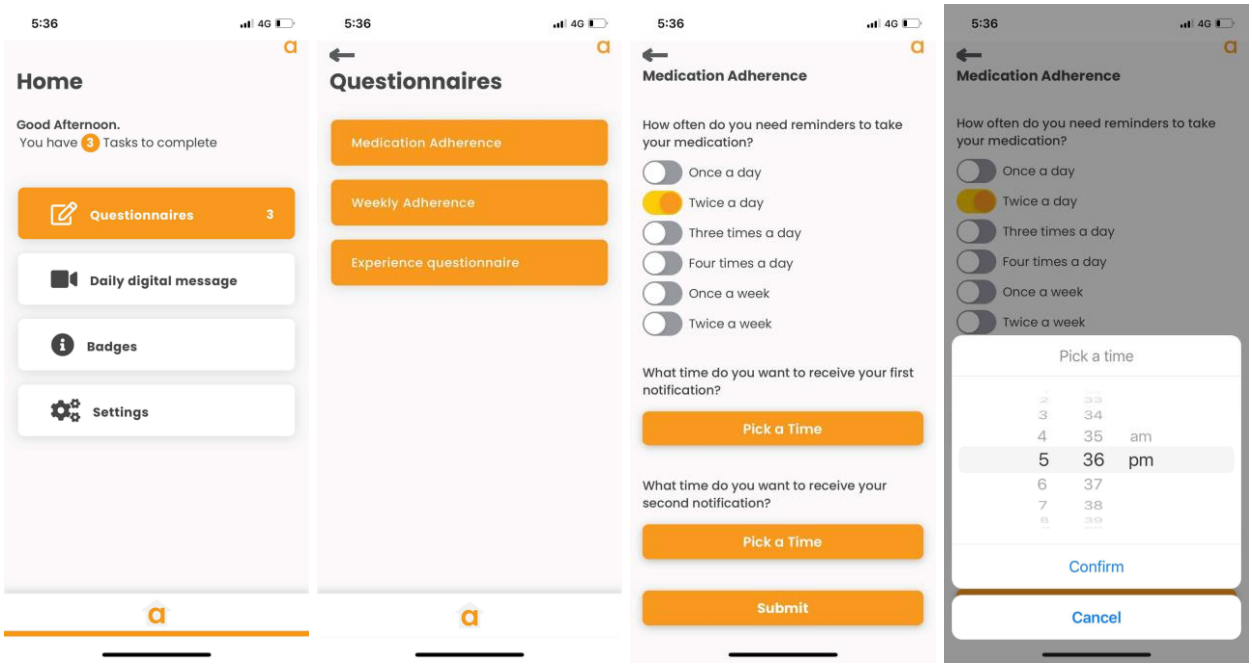


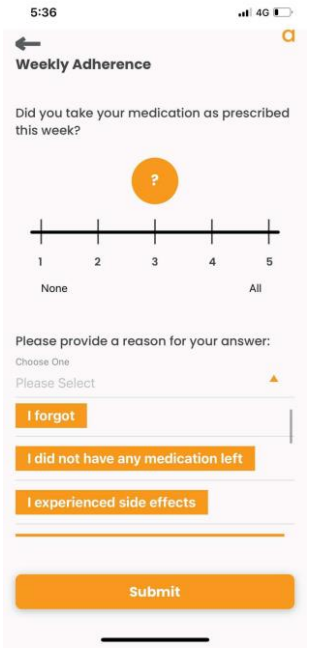


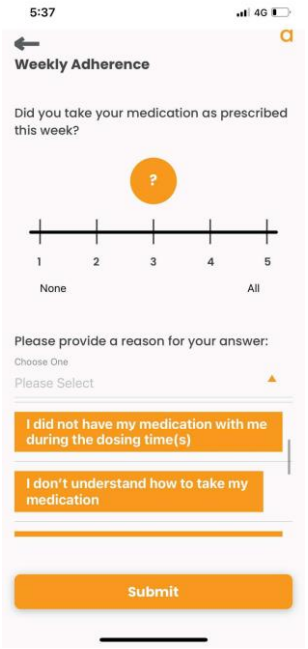


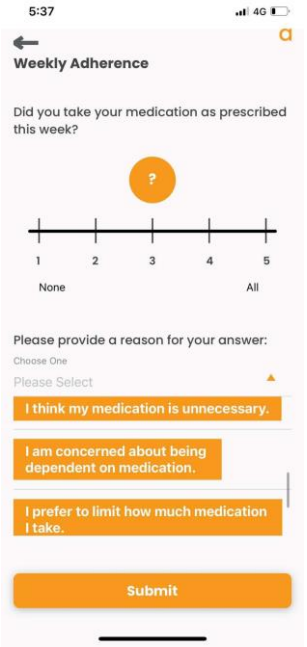


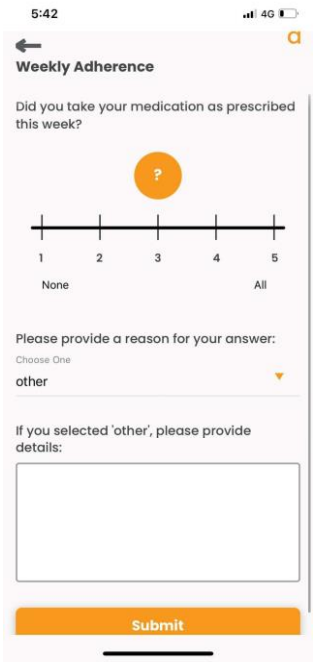

Welcome.
Thank you for taking part in this service evaluation. We will be using this app to ask you about your health as required. The answers are completed in one of four ways.
Next
Yes
No
Switch Button
To select the answer that applies to you. Click on it to change from off to on.
Next
Numerical Rating Scale
Press to select the number which answers the question.
Next
Free text
This is for you to provide an answer in your own words or numbers
Done


Home
Good Afternoon.
You have 3 Tasks to complete
Questionnaires 3
Daily digital message
Badges
Settings
Questionnaires
Medication Adherence
Weekly Adherence
Experience questionnaire
Medication Adherence
How often do you need reminders to take your medication?
Once a day
Twice a day
Three times a day
Four times a day
Once a week
Twice a week
What time do you want to receive your first notification?
Pick a Time
What time do you want to receive your second notification?
Pick a Time
Submit
Medication Adherence
How often do you need reminders to take your medication?
Once a day
Twice a day
Three times a day
Four times a day
Once a week
Twice a week
Pick a time
3 34
4 35 am
5 36 pm
6 37
7 38
Confirm
Cancel

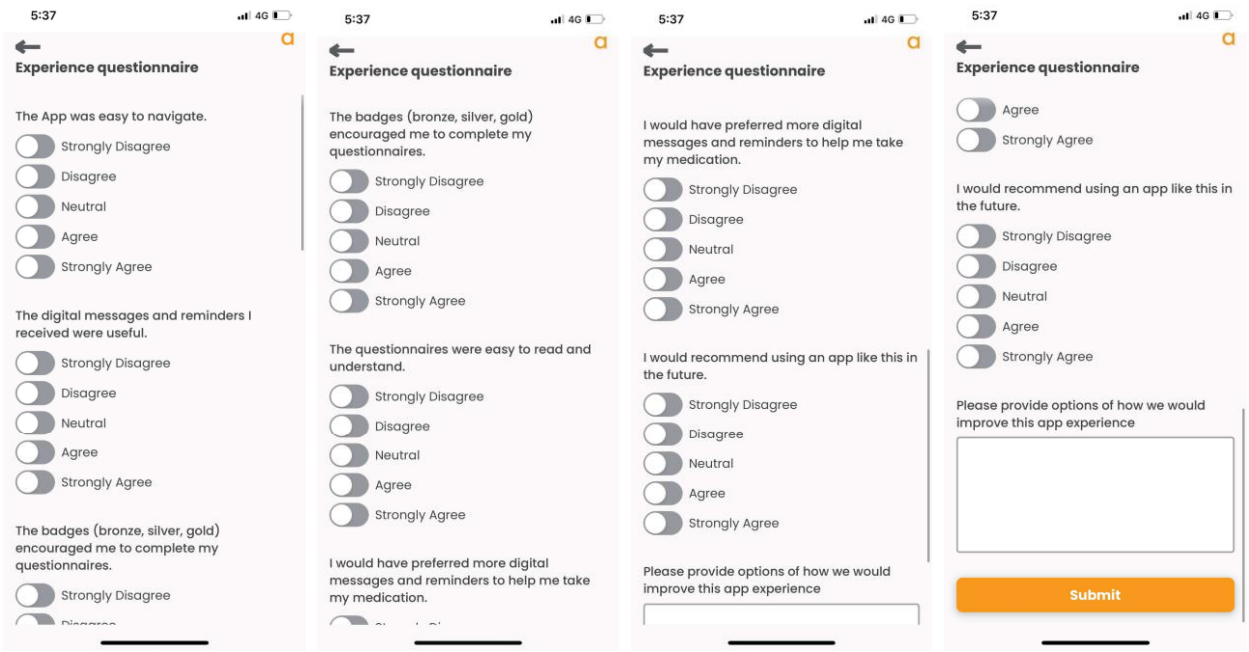

5:36
4G
Weekly Adherence
Did you take your medication as prescribed this week?
?
1 2 3 4 5
None
All
Please provide a reason for your answer:
Choose One
Please Select
I forgot
I did not have any medication left
I experienced side effects
Submit


5:37
4G
Weekly Adherence
Did you take your medication as prescribed this week?
?
1 2 3 4 5
None
All
Please provide a reason for your answer:
Choose One
Please Select
I did not have my medication with me during the dosing time(s)
I don't understand how to take my medication
Submit

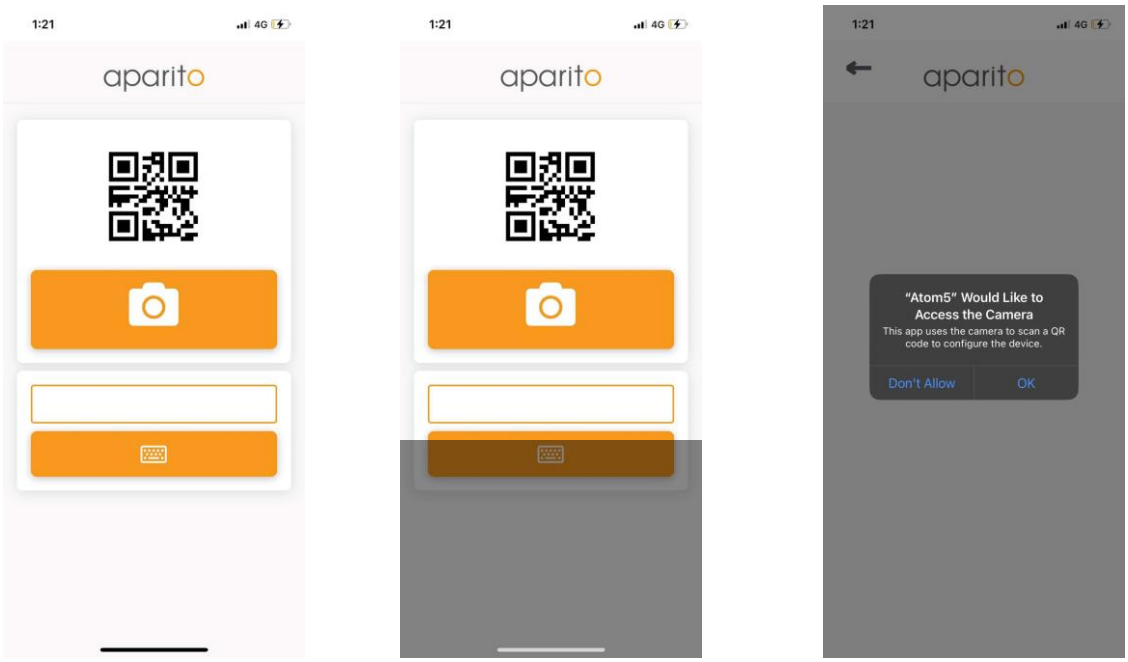

5:37
4G
Weekly Adherence
Did you take your medication as prescribed this week?
?
1 2 3 4 5
None
All
Please provide a reason for your answer:
Choose One
Please Select
I think my medication is unnecessary.
I am concerned about being dependent on medication.
I prefer to limit how much medication I take.
Submit

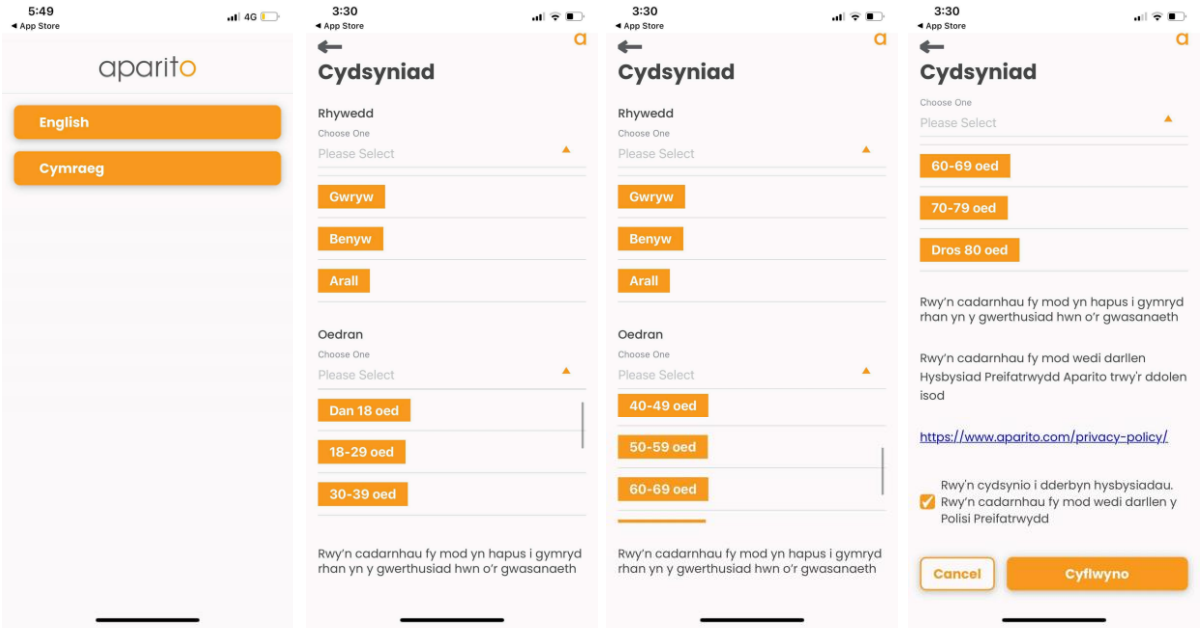

5:42
4G
Weekly Adherence
Did you take your medication as prescribed this week?
?
1 2 3 4 5
None
All
Please provide a reason for your answer:
Choose One
other
If you selected 'other', please provide details:
Submit

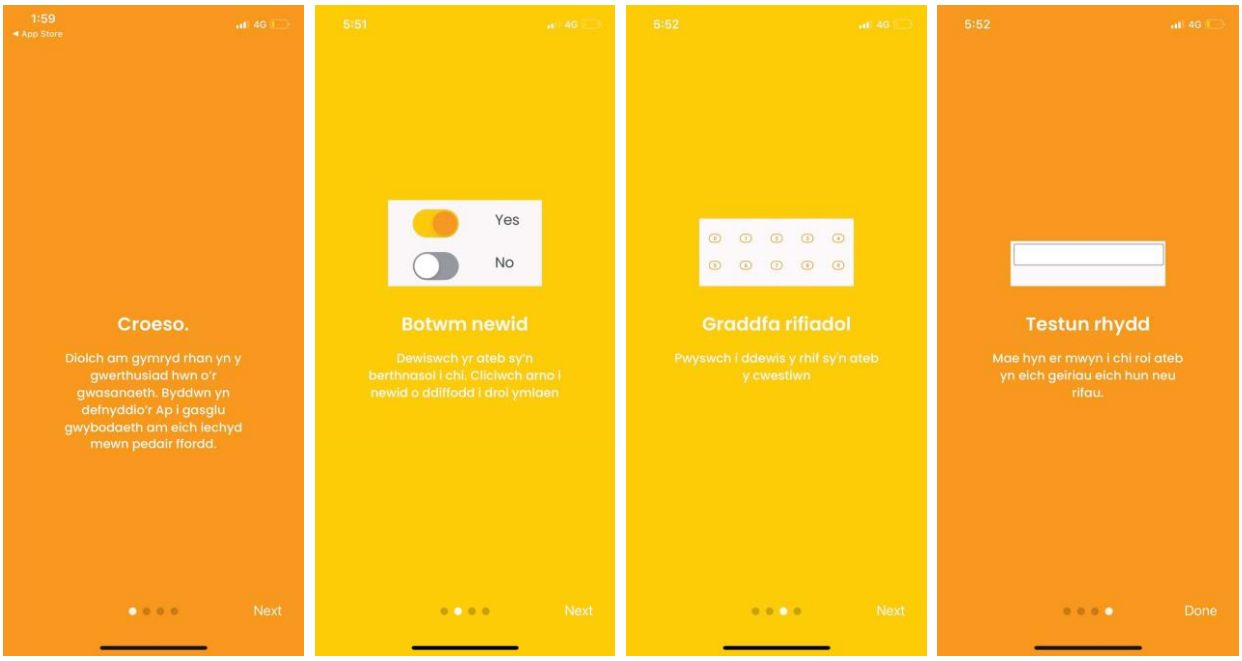

5:37
4G
Weekly Adherence
Did you take your medication as prescribed this week?
?
1 2 3 4 5
None
All
Please provide a reason for your answer:
Choose One
Please Select
I prefer to limit how much medication I take.
I am fearful of possible side effects.
other
Submit

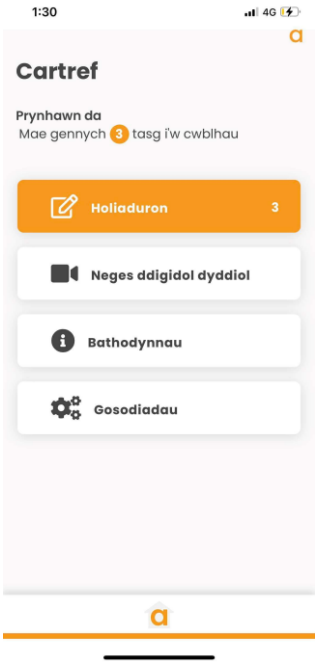

5:37
4G
Experience questionnaire
The App was easy to navigate.
Strongly Disagree
Disagree
Neutral
Agree
Strongly Agree
The digital messages and reminders I received were useful.
Strongly Disagree
Disagree
Neutral
Agree
Strongly Agree
The badges (bronze, silver, gold) encouraged me to complete my questionnaires.
Strongly Disagree
5:37
4G
Experience questionnaire
The badges (bronze, silver, gold) encouraged me to complete my questionnaires.
Strongly Disagree
Disagree
Neutral
Agree
Strongly Agree
The questionnaires were easy to read and understand.
Strongly Disagree
Disagree
Neutral
Agree
Strongly Agree
I would have preferred more digital messages and reminders to help me take my medication.
5:37
4G
Experience questionnaire
I would have preferred more digital messages and reminders to help me take my medication.
Strongly Disagree
Disagree
Neutral
Agree
Strongly Agree
I would recommend using an app like this in the future.
Strongly Disagree
Disagree
Neutral
Agree
Strongly Agree
Please provide options of how we would improve this app experience
5:37
4G
Experience questionnaire
Agree
Strongly Agree
I would recommend using an app like this in the future.
Strongly Disagree
Disagree
Neutral
Agree
Strongly Agree
Please provide options of how we would improve this app experience
Submit

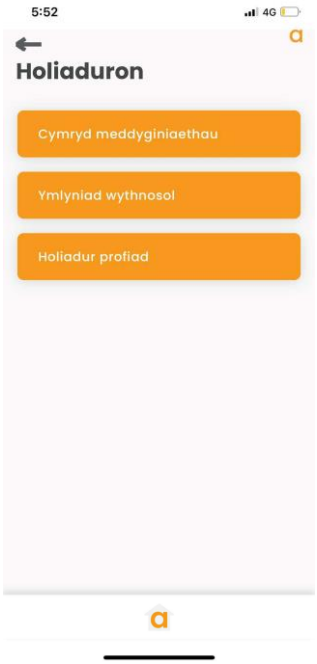
Appendix J – Screenshots of Atom5™ (Welsh version)

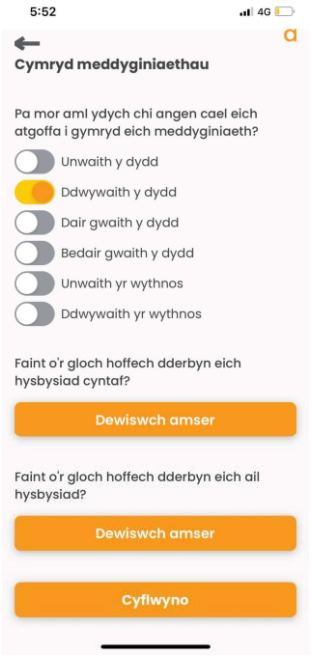


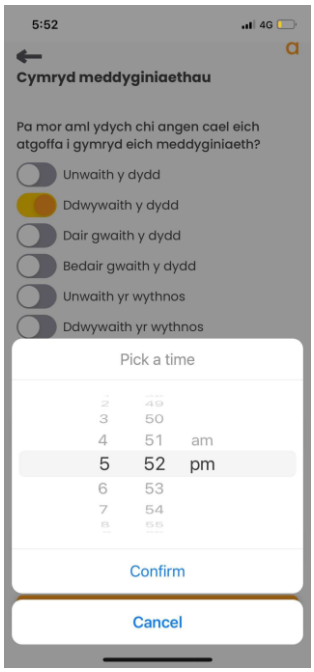



1:59
App Store
Croeso.
Diolch am gymryd rhan yn y gwerthusiad hwn o'r gwasanaeth. Byddwn yn defnyddio'r Ap i gasglu gwybodaeth am eich iechyd mewn pedair ffordd.
Next
5:51
Yes
No
Botwm newid
Dewiswch yr ateb sy'n berthnasol i chi. Cliciwch arno i newid o ddifflodd i droi ymlaen
Next
5:52
Graddfa rifiadol
Pwyswch i ddewis y rhif sy'n ateb y cwestiwn
Next
5:52
Testun rhydd
Mae hyn er mwyn i chi roi ateb yn eich geiriau eich hun neu rifau.
Done


1:30
Cartref
Prynhawn da
Mae gennych 3 tasg i'w cwblhau
Holiaduron 3
Neges ddigidol dyddiol
Bathodynnau
Gosodiadau


5:52
Holiaduron
Cymryd meddyginiaethau
Ymlyniad wythnosol
Holiadur profiad


5:52
4G
Cymryd meddyginiaethau
Pa mor aml ydych chi angen cael eich atgoffa i gymryd eich meddyginiaeth?
Unwaith y dydd
Ddwywaith y dydd
Dair gwaith y dydd
Bedair gwaith y dydd
Unwaith yr wythnos
Ddwywaith yr wythnos
Faint o'r gloch hoffech dderbyn eich hysbysiad cyntaf?
Dewiswch amser
Faint o'r gloch hoffech dderbyn eich ail hysbysiad?
Dewiswch amser
Cyflwyno

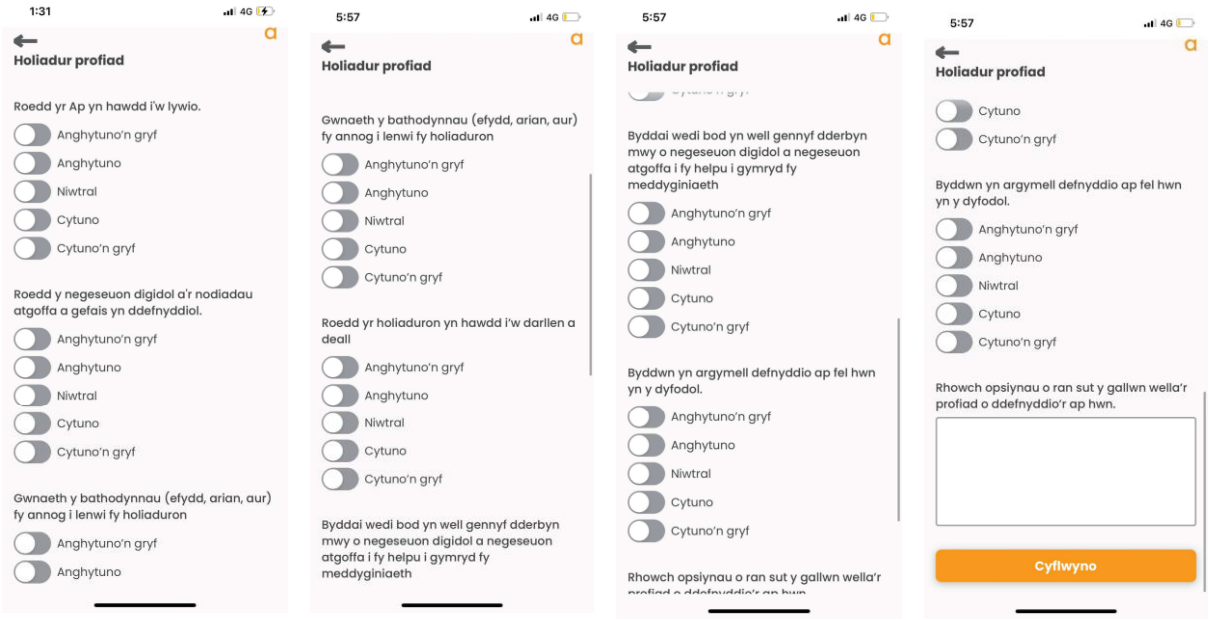

5:52
4G
Cymryd meddyginiaethau
Pa mor aml ydych chi angen cael eich atgoffa i gymryd eich meddyginiaeth?
Unwaith y dydd
Ddwywaith y dydd
Dair gwaith y dydd
Bedair gwaith y dydd
Unwaith yr wythnos
Ddwywaith yr wythnos
Pick a time
3 50
4 51 am
5 52 pm
6 53
7 54
Confirm
Cancel


5:52
4G
Ymlyniad wythnosol
A wnaethoch chi gymryd eich meddyginiaeth fel y rhagnodwyd yr wythnos hon?
?
1 2 3 4 5
Dim
Pob un
Rhowch reswm dros eich ateb
Choose One
Please Select
Wnes i anghofio
Nid oedd gennyf unrhyw feddyginiaeth ar ôl
Cefais sgîl-effeithiau
Cyflwyno


5:52
4G
Ymlyniad wythnosol
A wnaethoch chi gymryd eich meddyginiaeth fel y rhagnodwyd yr wythnos hon?
?
1 2 3 4 5
Dim
Pob un
Rhowch reswm dros eich ateb
Choose One
Please Select
Nid oedd fy meddyginiaeth gyda mi yn ystod yr amser/amseroedd eu cymryd
Dydw i ddim yn deall sut i gymryd fy meddyginiaeth
Cyflwyno


5:52
4G
Ymlyniad wythnosol
A wnaethoch chi gymryd eich meddyginiaeth fel y rhagnodwyd yr wythnos hon?
?
1 2 3 4 5
Dim
Pob un
Rhowch reswm dros eich ateb
Choose One
Please Select
Rwy'n meddwl bod fy meddyginiaeth yn ddiangen.
Rwy'n poeni am fod yn ddibynnol ar feddyginiaeth.
Cyflwyno


1:30
4G
Ymlyniad wythnosol
meddyginiaeth fel y rhagnodwyd yr wythnos hon?
?
1 2 3 4 5
Dim
Pob un
Rhowch reswm dros eich ateb
Choose One
arall
Os dewisoch 'arall', rhowch fanylion:
Cyflwyno


1:31
Holiadur profiad
Roedd yr Ap yn hawdd i'w lywio.
Anghytuno'n gryf
Anghytuno
Niwtral
Cytuno
Cytuno'n gryf
Roedd y negeseuon digidol a'r nodiadau atgoffa a gefais yn ddefnyddiol.
Anghytuno'n gryf
Anghytuno
Niwtral
Cytuno
Cytuno'n gryf
Gwnaeth y bathodynnau (efydd, arian, aur) fy annog i lenwi fy holiaduron
Anghytuno'n gryf
Anghytuno
5:57
Holiadur profiad
Gwnaeth y bathodynnau (efydd, arian, aur) fy annog i lenwi fy holiaduron
Anghytuno'n gryf
Anghytuno
Niwtral
Cytuno
Cytuno'n gryf
Roedd yr holiaduron yn hawdd i'w darllen a deall
Anghytuno'n gryf
Anghytuno
Niwtral
Cytuno
Cytuno'n gryf
Byddai wedi bod yn well gennyf dderbyn mwy o negeseuon digidol a negeseuon atgoffa i fy helpu i gymryd fy meddyginiaeth
5:57
Holiadur profiad
Byddai wedi bod yn well gennyf dderbyn mwy o negeseuon digidol a negeseuon atgoffa i fy helpu i gymryd fy meddyginiaeth
Anghytuno'n gryf
Anghytuno
Niwtral
Cytuno
Cytuno'n gryf
Byddwn yn argymell defnyddio ap fel hwn yn y dyfodol.
Anghytuno'n gryf
Anghytuno
Niwtral
Cytuno
Cytuno'n gryf
Rhowch opsiynau o ran sut y gallwn wella'r
5:57
Holiadur profiad
Cytuno
Cytuno'n gryf
Byddwn yn argymell defnyddio ap fel hwn yn y dyfodol.
Anghytuno'n gryf
Anghytuno
Niwtral
Cytuno
Cytuno'n gryf
Rhowch opsiynau o ran sut y gallwn wella'r profiad o ddefnyddio'r ap hwn.
Cyflwyno

Medication adherence messages survey v1

Page 1

Please read the messages below and record your responses.

1. **Your health is important and taking your medicine(s) is a crucial part of improving your health.**

Please don't select more than 1 answer(s) per row.

	Very good	Good	Neither good nor poor	Poor	Very poor
How would you rate the accuracy (clinical appropriateness) of this message?	☐	☐	☐	☐	☐
How would you rate the clarity of the wording of this message?	☐	☐	☐	☐	☐
Is this message sufficiently generic?	☐	☐	☐	☐	☐

1.a. Any other comments?

2. **Your medicine(s) is designed to help you manage your condition and reduce the impact it has on your daily life.**

Please don't select more than 1 answer(s) per row.

	Very good	Good	Neither good nor poor	Poor	Very poor
How would you rate the accuracy (clinical appropriateness) of this message?	☐	☐	☐	☐	☐
How would you rate the clarity of the wording of this message?	☐	☐	☐	☐	☐
Is this message sufficiently generic?	☐	☐	☐	☐	☐

2.a. Any other comments?

3. **People often forget to take their medicine(s) on weekends – why not try and make a special effort this week?**

Please don't select more than 1 answer(s) per row.

	Very good	Good	Neither good nor poor	Poor	Very poor
How would you rate the accuracy (clinical appropriateness) of this message?	☐	☐	☐	☐	☐
How would you rate the clarity of the wording of this message?	☐	☐	☐	☐	☐
Is this message sufficiently generic?	☐	☐	☐	☐	☐

3.a. Any other comments?

4. Make sure you take your medicine(s) as directed – some medicines are affected by food or drink.

Please don't select more than 1 answer(s) per row.

	Very good	Good	Neither good nor poor	Poor	Very poor
How would you rate the accuracy (clinical appropriateness) of this message?	☐	☐	☐	☐	☐

How would you rate the clarity of the wording of this message?	☐	☐	☐	☐	☐
Is this message sufficiently generic?	☐	☐	☐	☐	☐

4.a. Any other comments?

5. **Check how much medicine(s) you have left and order a prescription if you are running low!**

Please don't select more than 1 answer(s) per row.

	Very good	Good	Neither good nor poor	Poor	Very poor
How would you rate the accuracy (clinical appropriateness) of this message?	☐	☐	☐	☐	☐
How would you rate the clarity of the wording of this message?	☐	☐	☐	☐	☐
Is this message sufficiently generic?	☐	☐	☐	☐	☐

5.a. Any other comments?

6. **Always check the instructions on the label carefully.**

Please don't select more than 1 answer(s) per row.

	Very good	Good	Neither good nor poor	Poor	Very poor
How would you rate the accuracy (clinical appropriateness) of this message?	☐	☐	☐	☐	☐
How would you rate the clarity of the wording of this message?	☐	☐	☐	☐	☐
Is this message sufficiently generic?	☐	☐	☐	☐	☐

6.a. Any other comments?

7. **Think about what motivates you to take your medicine(s) and try to use those motivators to stay on track.**

Please don't select more than 1 answer(s) per row.

How would you rate the clarity of the wording of this message?	☐	☐	☐	☐	☐
Is this message sufficiently generic?	☐	☐	☐	☐	☐

8.a. Any other comments?

Appendix L – Pharmacist survey of app messages landing page

Messages to promote medication adherence

We are seeking the views of pharmacists across BCUHB to help design reminder and motivational messages that will be used within an app to help patients adhere to their medications.

What is this project's purpose?

This project aims to develop reminder and motivational messages, incorporating feedback gathered from pharmacists across BCUH. These messages will then be used within a bespoke app to help patients adhere to their medications. This is part of a larger project which aims to determine whether mobile health interventions can support medication adherence.

What am I being asked to do?

Your input will help us develop short messages to support patients in taking their medicines. The survey will ask for your opinion on 8 messages. It should take no longer than 5 minutes of your time to complete. There will be no payments for your time.

It is up to you to decide whether to take part. If you do decide to take part, we thank you and will assume that your proceeding to the survey implies your consent. You can withdraw from the survey at any time by exiting your browser page. This will have no negative consequences. Your responses to the survey will be anonymous and you will not be identified in any reports or publications. The anonymised responses to the survey will be kept for 3 years (until 14/06/2026).

According to data protection legislation, we are required to inform you that the legal basis we are applying to process your personal data is that 'processing is necessary for the performance of a task carried out in the public interest' (Article 6(1)(e)). Further information can be found in the University's Privacy Notice https://cheme.bangor.ac.uk/documents/gdpr/cheme-privacy-notice.pdf

Who is organising and funding the research?

This is being funded by a Knowledge Economy Skills 2 (KESS2) Scholarship (reference number BUKE027).

Who is the Data Controller?

Bangor University will act as the Data Controller for this project. This means that the University is responsible for looking after your information and using it properly.

Who has ethically reviewed the project?

Research ethics committee review has been deemed as not being required for research involving NHS staff recruited as research participants by virtue of their professional role.

What if something goes wrong and I wish to complain about the research?

If you wish to make a complaint about the conduct of this research project you can contact Professor Dyfrig Hughes E-mail: d.a.hughes@bangor.ac.uk in the first instance. If your complaint relates to how your personal data has been handled, you can contact Lynette Williams E-mail:

l.d.williams@bangor.ac.uk in the first instance. If you feel your complaint has not been handled to your satisfaction, you can contact the Information Commissioner's Office.

Contact for further information

Non Wyn Davies MSc student E-mail: nnd22ppy@bangor.ac.uk

Instructions for completing the survey

The messages that you will be asked to rate are meant to be generic, applicable to (typically) elderly people who may be prescribed a number of medicines. They are designed to help patient remember to take their medicines, and encourage adherence through motivational messaging.

For each of the 8 messages, you will be asked to rate, on a 5-point scale (from very good to very poor):

- the accuracy (clinical appropriateness) of the message
- the clarity of the wording of the message
- whether the message is sufficiently generic (i.e. not specific for any particular medicine or class of medicines)

Proceed

Appendix M – Full list of messages used in Atom5™

Welsh	English
Rwy'n meddwl bod fy meddyginiaeth yn ddiangen.	I think my medication is unnecessary.
Rwy'n poeni am fod yn ddibynnol ar feddyginiaeth.	I am concerned about being dependent on medication.
Mae'n well gen i gyfyngu ar faint o feddyginiaeth rydw i'n ei gymryd.	I prefer to limit how much medication I take.
Rwy'n ofni sgil effeithiau posib.	I am fearful of possible side effects.
Mae eich iechyd yn bwysig ac mae cymryd eich meddyginiaeth yn rhan hanfodol o wella eich iechyd.	Your health is important and taking your medicine(s) is a crucial part of improving your health.
Gall eich meddyginiaeth eich helpu i reoli eich cyflwr a lleihau'r effaith y mae'n ei gael ar eich bywyd bob dydd.	Your medicine(s) may help you manage your condition and reduce the impact it has on your daily life.
Cofiwch sicrhau eich bod yn cymryd eich meddyginiaeth yn ôl y cyfarwyddyd – mae bwyd neu ddiod yn effeithio ar rai meddyginiaethau.	Make sure you take your medicine(s) as directed – some medicines are affected by food or drink.
Gwiriwch faint o feddyginiaeth sydd gennych ar ôl ac archebwch bresgripsiwn os nad oes gennych lawer ar ôl!	Check how much medicine(s) you have left and order a prescription if you are running low!
Gwiriwch y cyfarwyddiadau ar y label yn ofalus bob amser.	Always check the instructions on the label carefully.
Meddyliwch am yr hyn sy'n eich cymell i gymryd eich meddyginiaeth a cheisiwch ddefnyddio'r cymhelliant hwnnw i gadw at y cyfarwyddiadau.	Think about what motivates you to take your medicine(s) and try to use those motivators to stay on track.
Meddyliwch am sut mae ffactorau personol neu ffactorau eraill yn dylanwadu ar eich arfer o gymryd meddyginiaeth, a cheisiwch ddefnyddio'r wybodaeth honno er mantais i chi.	Think about how personal or other factors influence your medicine-taking habits, and try to use that knowledge to your advantage.
Mae cymryd eich meddyginiaeth yn gam pwysig tuag at reoli eich iechyd.	Taking your medicine(s) is an important step to taking control of your health.
Gall eich meddyginiaeth eich helpu i reoli eich symptomau a byw bywyd i'r eithaf.	Your medicine(s) may help you manage your symptoms and live life to the fullest.
Gall cymryd meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn helpu i atal cymhlethdodau iechyd yn y dyfodol.	Taking medicine(s) as prescribed may help prevent future health complications.
Trwy beidio â chymryd meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn mae'n bosib y byddwch yn cynyddu'r risg y bydd y symptomau'n parhau.	By not taking medicine(s) as prescribed, you may be increasing the risk that symptoms continue.
Cadwch gofnod i olrhain pryd byddwch yn cymryd eich meddyginiaeth, fel y gallwch gadw eich hun yn atebol	Keep a record to track when you take your medicine(s), so that you can keep yourself accountable

Beth am geisio cymryd eich meddyginiaeth ar yr un pryd â gweithgaredd rheolaidd rydych yn ei fwynhau?	Why not try to pair taking your medicine(s) with a regular activity you enjoy?
Os byddwch allan o'r tŷ yn ystod yr amser byddwch yn arfer cymryd eich meddyginiaeth, cofiwch fynd â'ch meddyginiaeth gyda chi!	If you will be out of the house during your specified dosing time, remember to take your medicine(s) with you!
Gallai fod o gymorth os ydych yn cynllunio pryd a ble y byddwch yn cymryd eich meddyginiaeth.	It may help if you plan when and where you are going to be taking your medicine(s).
Mae cymryd eich meddyginiaeth yn fath o hunanofal a all eich helpu i deimlo bod gennych fwy o reolaeth dros eich bywyd.	Taking your medicine(s) is a form of self-care that may help you feel more in control of your life.
Ceisiwch gymryd eich meddyginiaeth ar yr un pryd â rhywbeth rydych yn ei wneud bob dydd, fel glanhau eich dannedd neu newid eich sanau!	Try and pair taking your medicine(s) with something you do every day, such as brushing your teeth or changing your socks!
Cofiwch bob amser fod cymryd eich meddyginiaeth yn rhan bwysig o'ch iechyd.	Always remember that taking your medicine(s) is an important part of your health journey.
Dewch i adnabod eich meddyginiaeth – beth am ddysgu am ei ddiben a phwysigrwydd ei gymryd?	Get to know your medicine(s) – why not learn about its purpose and the importance of taking it?
Cofiwch sicrhau bod gennych ddigon o feddyginiaeth trwy eu harchebu mewn da bryd.	Make sure you have enough medicine(s) to hand by ordering them in good time.
Cofiwch nad yw cymryd eich meddyginiaeth yn wendid, ond yn arwydd o gryfder ac ymrwymiad i'ch iechyd.	Remember that taking your medicine(s) is not a weakness, but a sign of strength and commitment to your health.
Peidiwch â gadael i ofn am y sgil effeithiau eich atal rhag cymryd eich meddyginiaeth - siaradwch â'ch clinigwr am unrhyw bryderon sydd gennych.	Don't let the fear of side effects stop you from taking your medicine(s) – talk to your clinician about any concerns you have.
Defnyddiwch ddyddiadur neu galendr i'ch helpu i gadw at amserlen cymryd eich meddyginiaeth.	Use a diary or calendar to help you stay on track with your medicine schedule.
Pan fyddwch yn cael nodyn atgoffa i gymryd eich meddyginiaeth, gweithredwch arno ar unwaith cyn i chi anghofio!	When you receive a reminder to take your medicine(s), act on it straight away before you forget!
Beth am wneud ymdrech weithredol unwaith yr wythnos i wirio faint o feddyginiaeth sydd gennych ar ôl?	Why not make an active effort once a week to check how much medicine you have left?
Peidiwch â bod ofn gofyn am help gan eraill i gymryd eich meddyginiaeth.	Do not be afraid to ask for help from others with taking your medicine(s).
Gall cymryd meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn helpu i gynyddu manteision y driniaeth.	Taking medicine(s) as prescribed may help improve the benefits of treatment.
Beth am greu eich system wobrwyo eich hun? Er enghraifft, os ydych yn cymryd eich meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn am wythnos, byddwch yn cael rhoi trît i chi eich hun!	Why not create your own rewards system? For example, if you take your medicine(s) as prescribed for a week, you earn yourself a treat!

Byddwch yn greadigol a meddyliwch am ffordd unigryw o atgoffa eich hun i gymryd eich meddyginiaeth, fel cân arbennig.	Get creative and come up with a unique way to remind yourself to take your medicine(s), such as a special song.
Os ydych yn ei chael yn anodd tynnu eich meddyginiaeth allan o'r pecyn, siaradwch â'ch clinigwr.	If you struggle with taking your medicine(s) out of their packaging, talk to your clinician.
Siaradwch â'ch clinigwr am yr amser gorau o'r dydd i gymryd eich meddyginiaeth.	Talk to your clinician about the best time of day to take your medicine(s).
Dychmygwch sut gallai cymryd eich meddyginiaeth wella eich iechyd a'ch lles.	Imagine how taking your medicine(s) might improve your health and wellbeing.
Meddyliwch am fanteision ac anfanteision cymryd eich meddyginiaeth a cheisiwch ddod o hyd i ffyrdd o oresgyn unrhyw rwystrau.	Think about the pros and cons of taking your medicine(s) and try to find ways to overcome any barriers you face.
Peidiwch â gadael i anghofrwydd neu anghyfleustra eich rhwystro rhag cymryd eich meddyginiaeth – rhowch flaenoriaeth iddi a dewch o hyd i ffyrdd o wneud iddi weithio i chi.	Don't let forgetfulness or inconvenience stop you from taking your medicine(s) – make it a priority and find ways to make it work for you.
Yn achos rhai meddyginiaethau, gall eu cymryd yn unol â'r cyfarwyddiadau ar y presgripsiwn leihau'r tebygolrwydd o orfod mynd i'r ysbyty.	For some medicines, taking them as prescribed can reduce the likelihood of hospitalization.
Meddyliwch am rywun rydych yn ei adnabod sy'n cymryd ei feddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn a cheisiwch ddysgu o'u hesiampl.	Think about someone you know who takes their medicine(s) as prescribed and try to learn from their example.
Ceisiwch ymgorffori cymryd eich meddyginiaeth yn eich trefn ddyddiol!	Try to incorporate taking your medicine(s) into your daily routine!
Ceisiwch feddwl pam nad ydych yn cymryd eich meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn ac ewch i'r afael â'r problemau hyn yn uniongyrchol!	Try and think of why you do not take your medicine(s) as prescribed and tackle these issues head on!
Gosodwch nodau bach i chi eich hun yn ymwneud â chymryd eich meddyginiaeth, fel y gallwch barhau i fod yn llawn cymhelliant.	Set small goals for yourself around taking your medicine(s), so that you can stay motivated.
Siaradwch â chi eich hun mewn ffordd gadarnhaol am gymryd eich meddyginiaeth ac atgoffwch eich hun pam ei fod yn bwysig.	Talk to yourself in a positive way about taking your medicine(s) and remind yourself why it's important.
Meddyliwch a ydych yn llwyddo i gymryd eich meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn a cheisiwch wella ar hynny.	Think about where you are in terms of being ready to take your medicine(s) as prescribed and try to make progress.
Cofiwch fod cymryd eich meddyginiaeth yn rhan bwysig o'ch cynllun iechyd cyffredinol.	Remember that taking your medicine(s) is an important part of your overall treatment plan.
Peidiwch â diystyru effaith cymryd eich meddyginiaeth (meddyginiaethau) - gall wneud gwahaniaeth sylweddol i'ch iechyd.	Don't underestimate the power of taking your medicine(s) – it can make a significant difference in your health.
Ysgrifennwch yr amser byddwch yn cymryd eich meddyginiaeth bob dydd i'ch helpu i gadw golwg ar eich cynnydd.	Write down the time you take your medicine(s) each day to help keep track of your progress.
Gwnewch restr wirio ddyddiol i sicrhau eich bod yn cymryd eich holl feddyginiaethau ar amser.	Make a daily checklist to ensure you take all of your medicine(s) on time.

Gall ymarfer technegau ymlacio fel anadlu dwfn neu adfyfyrio helpu i leihau straen a phryder sy'n gysylltiedig â chymryd eich meddyginiaeth	Practicing relaxation techniques like deep breathing or meditation may help reduce stress and anxiety about taking your medicine(s)
Meddyliwch am eich rhesymau dros gymryd eich meddyginiaeth(meddyginiaethau) a cheisiwch gymell eich hun trwy ganolbwyntio ar y rhesymau hynny.	Think about your reasons for taking your medicine(s) and try to stay motivated by focusing on those reasons.
Cofiwch mai eich cyfrifoldeb chi a'ch anwyliaid yw sicrhau eich bod yn cymryd eich meddyginiaeth.	Remember that taking your medicine(s) is a responsibility to yourself and your loved ones.
Mae eich clinigwr wedi rhoi'r feddyginiaeth i chi am reswm – peidiwch ag anwybyddu ei gyngor.	Your clinician prescribed your medicine(s) for a reason – don't ignore their advice.
Cofiwch fod cymryd eich meddyginiaeth yn ffordd o fuddsoddi yn eich iechyd a'ch lles yn y dyfodol.	Remember that taking your medicine(s) is a way of investing in your future health and wellbeing.
I rai pobl, gall cymryd meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn wella ansawdd eu bywyd a'u hymdeimlad o les.	For some people, taking medicine(s) as prescribed can increase their quality of life and sense of wellbeing.
Ewch i'r arfer o gymryd eich meddyginiaeth – dylai ddod yn haws dros amser!	Get into a routine with taking your medicine(s) – it should become easier over time!
Mae cymryd eich meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn yn bwysig i'ch iechyd.	Taking your medicine(s)as prescribed is important for your health.
Cofiwch fod cymryd eich meddyginiaeth yn ffordd o ofalu amdanoch chi eich hun a'ch iechyd.	Remember that taking your medicine(s) is a way to take care of yourself and your health.
Cofiwch adael 12 awr rhwng dosau meddyginiaeth sy'n rhaid eu cymryd ddwywaith y dydd.	Remember to leave 12 hours between twice-a-day medicine doses.
Mae eich iechyd yn bwysig ac mae cymryd eich meddyginiaeth yn rhan hanfodol o aros yn iach.	Your health is important and taking your medicine(s) is a crucial part of staying healthy.
Beth am gadw eich meddyginiaeth yn rhywle a fydd yn eich atgoffa i'w chymryd (e.e. mewn lle sych yn agos at eich brws dannedd). Cadwch eich meddyginiaeth mewn man diogel allan o gyrraedd plant bob amser.	Why not keep your medicine(s) some place that will remind you to take them (e.g. in a dry place close to your toothbrush). Always store your medicine(s) in a safe place out of reach of children.
Gwnewch gymryd eich meddyginiaeth yn arferiad trwy ei wneud ar yr un pryd bob dydd.	Make taking your medicine(s) a habit by doing it at the same time every day.
Siaradwch â'ch clinigwr os ydych yn cael trafferth cymryd eich meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn a gofynnwch am help.	Talk to your clinician if you're having trouble taking your medicine(s) as prescribed and ask for help.
Credwch ynoch chi eich hun a'ch gallu i gymryd eich meddyginiaeth yn unol â'r cyfarwyddiadau ar y presgripsiwn a cheisiwch feithrin eich hyder am hyn.	Believe in yourself and your ability to take your medicine(s) as prescribed and try to build your confidence around it.

Appendix N – Evidence the study would not be considered Research by the NHS

Medical Research Council

NHS Health Research Authority

Is my study research?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

Medication adherence project

IRAS Project ID (if available):

You selected:

- **'No'** - Are the participants in your study randomised to different groups?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the **HRA** to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at **Queries@hra.nhs.uk**

For more information please visit the **Defining Research** table.

Follow this link to start again .

Print This Page

NOTE: If using Internet Explorer please use browser print function.

Appendix O – Secondary data analysis ethics application form

PRIFYSGOL BANGOR UNIVERSITY

MHSAEC | Secondary Data Analysis

Please provide an outline of the project and attach the proposal for initial consideration. The first section is a questionnaire which requires you respond to the questions appropriately. The second section requires a brief summary.

Research Title: Digital Health Solutions for Medication Adherence Support

Name: Non Wyn Davies

Date 21/06/2023

secondary data analysis project

OVERALL ASSESSMENT OF SECONDARY DATA ANALYSIS PROJECT	RATING – CLICK ON ITEM BELOW
The data used in the project is completely anonymous when provided to the researcher	2 | Agree
It is impossible to identify participants from any resulting reports from the project	1 | Strongly agree
The use of the data in the project will not result in any damage or distress	1 | Strongly agree
THE ORIGINAL RESEARCH BEING USED FOR SECONDARY ANALYSIS	
The original participants are identifiable or recognizable	3 | Neutral
There is a need to get the original researchers or data collector's permission to use the data	3 | Neutral
The secondary analysis will utilise material that includes potentially sensitive personal data	4 | Disagree

SUMMARY OF PROJECT

Provide a summary of the project in no more than 150 words:
Participants collecting routine prescriptions from their local pharmacies will be asked to take part in a service evaluation of medication support tools under the BCUHB project 'Supporting the safe and effective use of medicines in patient's own home,' specifically a reminder and gamification app named Atom5. We are interested in their age, sex and medication frequency (number of times a day/ week/ month they need to take their medicines) and what features they may find useful.

secondary data analysis project

The MSc students will undertake a student placement in the local pharmacies to gather pharmacists' input and participants to user test the app.

POTENTIAL ETHICAL ISSUES

Provide a summary of any ethical issues you consider to be relevant as part of the project in no more than 150 words:

No personal identifiable information (e.g., name, email, phone number, DoB) will be collected.
We plan to publish the results at the end of the project and include descriptive overview of the age ranges and sex distribution of those that participated.

ADDITIONAL COMMENTS

Please see proposal and appendices for further information.

Optional comments
[Comments]

Appendix P – Participant information sheet

Participant Information Sheet

You have been invited to participate in an evaluation of a service provided via your pharmacy. Before deciding to take part, it is essential that you carefully read and understand the information provided below. Please contact the study team (details below) if you require any further clarification or information.

What is the purpose of the service evaluation?

The purpose of this service evaluation is to assess the feasibility of using an app to help you take your medicine(s) as prescribed.

What will you be required to do?

You will be asked to download an app onto your smartphone (or other compatible device). The app will send messages to remind you, and to help you with taking your medicines. You will be asked to complete questionnaires about your medicine-taking behaviour via the app, as well as provide feedback about your experience of using the app. The time commitment of this will be no more than 5 minutes a week.

Do you have to participate?

Participation in this service evaluation is entirely voluntary.

What will happen if you consent to participate, but later want to withdraw your consent?

At any point during the service evaluation, you are free to withdraw your consent. You will not experience any repercussions for doing this, and you are not required to provide a reason for withdrawing.

Will your information be treated as confidential?

Any information or data collected during the study period will be treated as confidential. Participants will be anonymized and will not be identifiable.

What are the advantages and risks of participating?

It is anticipated that the study will provide evidence about the feasibility of using an app to support people to take their medicines. No risks are anticipated, but please contact the study team if you have any concerns.

What will happen to the results of this service evaluation?

The results of the study will be used in a Master's Thesis and may also be published in academic journals. Any published information used will be anonymised and therefore participants will not be identifiable.

Who is conducting this service evaluation?

The service evaluation is organised by The Betsi Cadwaladr University Health Board (BCUHB), with Non Wyn Davies, who is a Master of Science through Research (MScRes) student based at Bangor University's Centre for Health Economics and Medicines Evaluation (CHEME), working alongside BCUHB colleagues on this. The service evaluation is being conducted in partnership with the digital health company, Aparito Ltd, who are responsible for the app. Non's degree is being funded by the Knowledge Economy Skills Scholarship 2 (KESS2) and she will be working under the supervision of Professor Dyfrig Hughes (CHEME, Bangor University) and Dr Elin Haf Davies (Aparito Ltd).

Who do you contact if you have any questions or concerns about the service evaluation?

You are free to contact the research team at any point if you have any questions, concerns or are at any point dissatisfied with the conduct of the service evaluation. Non Wyn Davies: nnd22ppy@bangor.ac.uk, Professor Dyfrig Hughes: d.a.hughes@bangor.ac.uk, Dr Elin Haf Davies: elin@aparito.com .

What happens next?

Please take your time to read and understand the above information before consenting to participate in the service evaluation.

We thank you for your time.

Pharmacist experience questionnaire

Page 1: Page 1

1. Overall, how useful do you think the Atom5™ was for your patients?

- Very useful
- Useful
- Neither useful nor poor
- Poor
- Very poor

2. I see value in my patients using the Atom5™ app to support medication adherence.

- Strongly agree
- Agree
- Neither agree nor disagree
- Disagree
- Strongly disagree

3. Referring patients to self-onboard onto the Atom5™ app increased my workload too much.

- Strongly agree
- Agree
- Neither agree nor disagree

- Disagree
- Strongly disagree

4. What elements of the Atom5™ app, if any, did you think were useful?

5. What changes would you make to the Atom5™ app, if any?

6. I think using an app like Atom5™ is a practical and feasible option for supporting medication adherence in community pharmacies.

- Strongly agree
- Agree
- Neither agree nor disagree
- Disagree
- Strongly disagree

7. I would recommend using an app like this in the future.

- Strongly agree
- Agree
- Neither agree nor disagree
- Disagree

Strongly disagree

8. Any other comments?