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The Development and Evaluation of Pharmacy-led Medication Adherence Services

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Abstract

Keywords

Medication adherence, pharmacy services, domiciliary medicines support, health behaviour change, cognitive-based techniques, theoretical domains framework.

Background

Medication non-adherence has been described as a worldwide problem of striking magnitude yet a gold-standard adherence intervention remains elusive and current interventions elicit modest improvements at best. Innovative, evidence-based approaches, grounded in theory and tailored to meet individual need are therefore required.

Methods

This thesis included four key elements: (1) a domiciliary medicines support service was evaluated to establish the effect of a pharmacy-led service targeting non-adherence of a primarily unintentional nature. (2) A review of health psychology theory was undertaken to provide a theoretical basis for intervention design. (3) A systematic review and meta-analysis of 'cognitive-based' behaviour change techniques designed to improve medication adherence was undertaken to identify effective behaviour change techniques for intentional non-adherence. (4) A theory-based questionnaire to identify barriers to medication adherence was developed as a precursor to an intervention to address patient identified barriers to medication adherence.

Results

Medication regimen simplification, provision of adherence support and implementation of care packages, appear to be effective in reducing patients' medication related risk of harm and improving unintentional non-adherence in domiciliary support recipients. However, these findings should be interpreted cautiously due to the 'before-and-after' study design. 'Cognitive-based' interventions may be capable of eliciting improvements in adherence beyond those yielded with the behavioural and educational interventions that form the mainstay of current practice. The theoretical domains framework has been used successfully to develop a questionnaire to identify medication adherence barriers.

Conclusions

At present, pharmacy-led adherence interventions tend to focus on resolving adherence difficulties of a practical nature. Whilst these approaches are of some benefit to unintentional non-adherence, intentional non-adherence requires a different approach. 'Cognitive-based' behaviour change techniques such as motivational interviewing could be delivered in routine pharmacy consultations to address adherence barriers identified using a theory-based questionnaire.

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Peer reviewed publications

Easthall C, Song F, Bhattacharya D (2013). A meta-analysis of cognitive based techniques as interventions to improve medication adherence. *BMJ Open,* **3:**e002749doi:10.1136/bmjopen-2013-002749

Conference abstracts accepted for poster presentations

Easthall C, Taylor N, Bhattacharya D (2013). The role of emotions as a barrier to medication adherence. Presented at the UK Society of Behavioural Medicine (UKSBM) 9th Annual Scientific Meeting, Oxford.

Easthall C, Scrimshaw P, Bhattacharya D (2013). Cambridgeshire Community Services (CCS) NHS Trust Domiciliary Medicines Management Service: a service evaluation. Presented at the Royal Pharmaceutical Society (RPS) Annual Conference, Birmingham.

Easthall C, Wright D, Taylor N, Bhattacharya D (2012). Developing the 'Identification of Medication Adherence Barriers (IMAB) instrument: A novel application of behaviour change theoretical frameworks. Presented at the UK Society of Behavioural Medicine (UKSBM) 8th Annual Scientific Meeting, Manchester.

Easthall C, Watson S, Wright D, Wood J, Bhattacharya D (2012). The impact of Motivational Interviewing (MI) as an intervention to improve medication adherence; a meta-analysis. *International Journal of Pharmacy Practice,* 20(S1): 49-50. Presented at the Health Services Research In Pharmacy Practice (HSRPP) International Conference, Cork, Ireland, April 2012.

List of abbreviations

ADR	Adverse Drug Reaction
BCC	Behaviour Change Counselling
BCT	Behaviour Change Technique
BMQ	Beliefs about Medication Questionnaire
	Brief Medication Questionnaire
BNF	British National Formulary
BPS	British Psychological Society
CAS	Composite Adherence assessment Score
CCG	Clinical Commissioning Group
CCS	Cambridgeshire Community Services
CHD	Coronary Heart Disease
CHF	Congestive Heart Failure
CI	Confidence Interval
CPPE	Centre for Pharmacy Postgraduate Education
CSQ-8	Client Satisfaction Questionnaire
DH	Department of Health
DOT	Directly Observed Therapy
DVLA	Driver and Vehicle Licensing Agency
GP	General Practitioner
HAART	Highly Active Anti-Retroviral Therapy
HAPA	Health Action Process Approach
HBM	Health Belief Model
HCP	Healthcare Professional
ICC	Intraclass Correlation Co-efficient
III	Implementation Intention Interventions
IMAB-Q	Identification of Medication Adherence Barriers Questionnaire
IQR	Interquartile Range
IRR	Inter-Rater Reliability
MAQ	Medication Adherence Questionnaire
MARS	Medication Adherence Rating Scale
	Medication Adherence Reasons Scale
MCA	Multi-compartment Compliance Aid
MDS	Monitored Dosage System
MEMS®	Medication Event Monitoring System
MESH	Medical Subject Headings
MI	Motivational Interviewing
MMAS	Morisky Medication Adherence Score

MRC	Medical Research Council
MUR	Medicines Use Review
NELM	National Electronic Library for Medicines
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NMS	New Medicine Service
NMSS	Norfolk Medicines Support Service
NPSA	National Patient Safety Agency
NSF	National Service Framework
OTC	Over The Counter
PCT	Primary Care Trust
PIL	Patient Information Leaflet
PMT	Protection Motivation Theory
PPA	Prescription Pricing Authority
PPI	Proton Pump Inhibitor
PPIRes	Public and Patient Involvement in Research
PSNC	Pharmaceutical Services Negotiating Committee
PST	Problem Solving Treatment
QOL	Quality of Life
RCT	Randomised Controlled Trial
RPS	Royal Pharmaceutical Society
RSPGB	Royal Pharmaceutical Society of Great Britain
SCM	Social Cognition Model
SD	Standard Deviation
SIMS	Satisfaction with Information about Medicines Scale
SPT	Specialist Pharmacy Technician
SRM	Self-Regulatory Model
TB	Tuberculosis
TDF	Theoretical Domains Framework
TPB	Theory of Planned Behaviour
TRA	Theory of Reasoned Action
TTM	Trans Theoretical Model
UEA	University of East Anglia
VAS	Visual Analogue Scale
WHO	World Health Organisation

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Dedication

This thesis is dedicated to the loving memory of

David William Anquish Simons

my much adored Grandad, true friend and hero, who passed away on 24th April 2013, aged 85 years.

Thank you so much for everything that you taught me, for showing me all that can be achieved when you are determined and for reminding me every day that "there's more than one way to skin a cat".

Thank you for giving me roots and for allowing me to know who I am, where I'm from and where my home will always be.

Of all that I've achieved and everything that I have to be proud of, nothing comes close to the pride of knowing that I am yours; that you were my Grandad and that I am your Grandaughter.

Love and miss you always Gramps x

Chapter One Medication Adherence

1.1 Chapter introduction

This thesis seeks to explore the development and evaluation of interventions to improve medicine taking behaviours (adherence) by considering:

- a home based medicines support service designed to improve how patients manage and use their medicines
- a systematic review and meta-analysis of cognitive-based adherence interventions
- the development of a novel questionnaire to identify barriers to medication adherence

The aim of this chapter therefore is to describe:

- the different terms used for medicines taking and related behaviours
- the magnitude and potential causes of non-adherence
- the complexity of the problem

1.2 Defining medication adherence

At present, the most commonly used and widely accepted term to describe medication taking behaviours is adherence, but historically, the term compliance was preferred. Numerous definitions of compliance exist, and whilst there is no 'official' definition, all have the common theme of patient behaviour corresponding with the prescriber's instruction. Urquhart described drug regimen compliance as:

'the extent to which a patient's actual history of drug administration corresponds with the prescribed regimen'[1]

The more classically cited Haynes definition describes compliance as:

'the extent to which a person's behaviour (taking medications, following a recommended diet or executing a lifestyle change) coincides with medical or healthcare advice'[2]

Despite its widespread use, the term compliance has been criticised, predominantly because of the negative connotations evoked by the definition of the term as 'the action or act of complying with a wish or demand'[3]. This definition suggests a submissive, patriarchal relationship between the patient and their prescriber, whereby a patient must passively follow their doctors orders without any form of therapeutic alliance[4]. Furthermore, non-compliance can wrongly be interpreted as patient incompetence, or as a deliberate, self-sabotaging behaviour[5].

The term 'adherence' emerged in an attempt to resolve the negative connotations associated with the term compliance. The Oxford English Dictionary defines the term adherence as a 'steadfast commitment to a belief or practice'[6]. With regard to medication taking, the term 'adherence' has been adopted to imply some form of negotiation between the patient and prescriber and the patient's willingness to participate in the agreed regimen[5]. The 2003 World Health Organisation (WHO) definition of adherence reflects the importance of implied agreement between the patient and healthcare provider[7]. The WHO definition of adherence will be used throughout this thesis:

'the extent to which a person's behaviour – taking medication, following a diet and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider' [7].

Despite the WHO definition, both compliance and adherence remain imperfect terms and are uninformative descriptions of medication taking behaviours[4]. Adherence is

widely accepted as a less judgemental term than compliance, yet it still holds implicit assumptions of practitioner power and their better judgement. Subsequently, in 1997, the Royal pharmaceutical Society of Great Britain (RPSGB) recommended a new term 'concordance'[8], to describe the relationship between prescriber and patient. When a prescriber and patient work together to reach a shared agreement and consider the beliefs and preferences of both parties, even when these may be opposing views, a concordant discussion has been achieved[5]. Concordance is defined by the RPSGB as:

'an agreement between the patient and healthcare professional, reached after negotiation that respects the beliefs and wishes of the patient in determining whether, when and how their medicine is taken, and (in which) the primacy of the patient's decision (is recognised)' [8].

The emergence of concordance in healthcare has been the subject of much debate and is still deemed to be a relatively novel concept. Whilst research has emerged in examining the feasibility of delivering a concordant consultation and the implications of this, it is imperative to recognise that adherence and concordance are not synonymous terms. Incorporation of concordance may be a fundamental aspect of improving medication adherence and the concept fits well with government objectives towards greater patient autonomy and choice. However, the degree to which patients want to be involved in decision making about their care is variable and thus, not all patients are suitable or ready for shared decision making in their healthcare, preferring instead to be led by their doctor[9].

A fourth term, 'non-persistence' is also used in research, referring to patients who start taking their medicines but then stop, without advice to do so from their healthcare provider. Cramer *et al.* suggest a definition for persistence as:

"the duration of time from initiation to discontinuation of therapy"[10]

The term non-persistence is commonly used for considering long term therapies such as tamoxifen, used in the treatment of breast cancer, where drop-out of the advised five year treatment course is common[11].

The extent to which medication taking behaviours can be deemed as 'adherent' or 'non-adherent' is variable and dependent upon many factors such as the treatment type, disease state and adherence measurement. Definitions of adherence in terms of percentages of patients forgetting their medicines or percentage of doses taken correctly are known as process-orientated outcomes; relating to the process of

adhering to prescribed medication regimens. Alternatively, outcome-orientated definitions emphasise the end results of the medication taking behaviour such as decrease in blood pressure or frequency of infection resolution. Whilst potentially useful in specific disease states, the generalisability of outcome-orientated definitions limits their widespread use. Process orientated outcomes such as the percentage of doses taken correctly, are therefore the most frequent means to define a patients adherence, although for ease, researchers will often dichotomise this inherently continuous variable into 'adherers' or 'non-adherers'. Dichotomisation is an attractive option for convenience and simplicity, but details of adherence patterns and a depth of data is lost through this approach[12].

Consensus as to a gold-standard value for 'good' adherence has not been reached, though conventionally, adequate adherence has been considered as 80% of doses taken as prescribed[2, 13]. The 'cut-off point' for 'good' and 'poor' adherence is however variable according to the medication taken and disease state. In conditions such as HIV, near perfect adherence is necessary to ensure therapeutic goals are obtained. Chesney reports that at least 95% adherence to Highly Active Antiretroviral Therapy (HAART) is necessary for successful long term treatment of HIV and AIDS[14]. Horne and colleagues suggest a more pragmatic definition of non-adherence, which supports the concept of clinically meaningful non-adherence as:

'the point below which desired preventative or therapeutic result is unlikely to be achieved'[12] .

Clear definitions of adherence are imperative to good research and an important consideration when comparing the outcomes of adherence studies.

1.3 The relevance and prevalence of medication non-adherence; why does it matter?

Assuming a correct diagnosis and choice of treatment has been made, adherence to an agreed agenda for medication taking is the key link to successful outcomes in medical care. Consequently, patient behaviours which lead to deviations from the prescribers intentions will inevitably lead to suboptimal treatment outcomes[7, 12, 15]. The World Health Organisation (WHO), suggest that the magnitude and gravity of non-adherence is such that greater worldwide health benefit could be gained through improving adherence to current medications than developing novel treatments[7].

1.3.1 The prevalence of non-adherence

Whilst the potential implications of non-adherence are severe , it is the prevalence of non-adherence that causes greatest concern amongst healthcare professionals and policy makers[15]. The cumulative findings of reviews and seminal reports have consistently concluded that between 30 and 50% of patients prescribed medication for chronic illnesses, do not take their medications as prescribed[12, 16, 17], with other studies suggesting a third or more of patients comply poorly with prescribed drug regimens, irrespective of the disease state or prognosis[1].

Whilst the seminal World Health Organisation (WHO) report (2003) suggested that 50% of patients with chronic diseases who live in the developed world are non-adherent, it rightfully identified that in the developing world, non-adherence may threaten the management of chronic illness to an even greater extent, when coupled with poorer access to healthcare, diagnostics and medicines[7]. Non-adherence was subsequently described by the WHO as “a worldwide problem of striking magnitude” and has been identified as a priority for healthcare researchers and policy makers[7].

1.3.2 The clinical consequences of non-adherence

The clinical consequences of non-adherence will largely depend upon the medicines concerned and the disease state in question, but patient related factors including co-morbidities can also be influential. As such, non-adherence in one patient could have far greater clinical implications than in others, and the impact across different chronic illnesses can range from minimal to highly significant[18].

The dosage and timing of the medicine administered will influence both the therapeutic and adverse effects. Taking a medicine at the wrong time of day may substantially reduce efficacy, for example, a 5mg dose of simvastatin has been shown to reduce

plasma cholesterol levels by 21% when taken in the evening, compared to 14% when taken in the morning, a difference that is significantly different ($p = <0.05$)[19]. Whilst this study shows an interesting perspective, the limitation of using a 5mg dose, which is seldom used in routine practice, should be borne in mind. Experience of side effects may also be increased by taking a medication at the wrong time of the day, for example, the diuretic effects of bendroflumethiazide, commonly prescribed for hypertension, will likely disrupt sleep if taken in the evening.

Non-adherence through taking inadequate or excessive doses will also have clinical implications. Taking too little medication may lead to treatment failure, for example inadequate adherence to immunosuppressive medications post organ transplant is likely to result in transplant rejection. Conversely, taking too much medication, for example taking double doses, can cause serious adverse events, such as toxicity. In addition, deviations in adherence by taking too much medication, or continuing with a therapy for longer than intended, can lead to problems with addiction, such as with opioid and benzodiazepines dependence.

Intermittent adherence, where patients stop and start their medications may also have profound clinical consequences, especially for medicines with a 'narrow therapeutic window', such as lithium used in the treatment of bipolar affective disorder. For these medicines, therapeutic and toxic blood plasma levels are very close to each other, therefore small deviations from complete adherence may have notable clinical effects. Sporadic adherence may also be hazardous in patients taking medications with substantial withdrawal or rebound effects.

Undetected non-adherence may lead to unnecessary additional investigations and dose adjustments[13] as the treatment may appear to be ineffective, incurring costs to both the patient and healthcare provider. In extreme cases, for example insulin dependent diabetes, non-adherence can result in life threatening hypo or hyperglycaemia. Increased morbidity and mortality have been observed in non-adherent patients suffering with hypertension, diabetes and HIV[18]. In 2006, Simpson *et al.* reported comprehensive meta-analytical evidence from 21 observational studies, to support the link between poor adherence and mortality; a mortality odds ratio (95% CI) of 0.56 (0.50, 0.63) was reported for 'good' adherence compared to 'poor' adherence[20]. The authors also report an association between good adherence to a placebo medicine and reduced mortality and so argue that this supports the notion of the "healthy adherer" effect, whereby adherence to a therapy may be a surrogate for overall healthy behaviours[20]. Whilst this study is well regarded and has been heavily cited, the

potential limitations of drawing data from observational studies rather than RCTs should not be overlooked.

Whilst the clinical consequences of non-adherence are important, it is worth noting that some medicines are more 'forgiving' than those with a narrow therapeutic window[15]. However, even when the clinical consequences of non-adherence to medicines may not be of notable concern, the financial implications of wasted medicines may still be apparent.

1.3.3 The economic consequences of non-adherence

The cost of wasted medicines; prescribed, dispensed and never used, poses a financial cost to the UK and worldwide healthcare systems. A recent report commissioned by the Department of Health (DH) estimated the cost of wasted medicines in community and primary care in England to be in the region of £300 million annually[21]. Although non-adherence may only account for a small proportion of this medicines wastage, the magnitude of medicines waste in the UK means that notable costs will still be incurred. As with all interventions utilising NHS resources, strategies to reduce medicines waste must demonstrate cost effectiveness.

Whilst medicines waste incurs some financial costs, it is the clinical consequences of non-adherence that contribute most heavily to the associated financial burden. Worsening health, failed therapy, unnecessary additional investigations or treatments, lost working days, increased hospital admissions or loss of treatment gain all contribute to notable financial costs. Urquhart highlights that omission of just three consecutive doses of furosemide, when used to treat congestive heart failure (CHF), can result in fluid retention sufficient to precipitate acute fluid overload, with pulmonary oedema and associated breathing difficulties[15]. The resulting hospital admission would have serious financial implications; O'Connell and Bristow report a cost of $10,400 US dollars for each CHF related hospital admission[22] and more recently, Stewart *et al.* estimated the total direct cost of heart failure to the NHS to be £905 million, of which, hospitalisation was the predominant cost [23]. Although it is impossible to determine what proportion of CHF admissions result from poor medication adherence, given the documented adherence rates for other chronic conditions [12, 16, 17], and the need for good adherence to this medication, it is likely to be a notable number. Whilst there is little evidence to support an association between disease severity and adherence, (as discussed in section 1.5.1) it is worth noting that the economic consequences of non-adherence may be greater for some medical conditions compared to others.

1.4 The nature of non-adherence

Non-adherence may exist through errors of omission or addition or by taking medicines at the wrong time. Incorrect administration of a medicine, for example poor inhaler technique, also constitutes non-adherence, as the patient will not be taking their medicines as agreed with their GP. The nature of non-adherence and the reasoning behind these deviations is variable. A patient who consciously chooses to omit doses of their medication is non-adherent for very different reasons to, for example, a patient with arthritis and insufficient manual dexterity to administer their medicines correctly.

Adherence to medication is a complex, multi-stage process, and there are many points at which a patient may deviate from the initial agreement made with their GP. For a patient to adhere to their prescribed medicine, pivotal processes must occur at key stages, the patient must therefore:

- Collect their medication from their GP or pharmacy
- Fully understand how and when to take it
- Be motivated to take the medication and have the intention to follow the directions
- Have the cognitive capacity to be able to remember to take the correct medication at the right time
- Have sufficient physical dexterity to be able to manipulate the medicine packaging and administer the medicine

Deviations in adherent behaviours at these key stages can therefore be classified in a number of ways. Non-adherence may either be primary or secondary in nature and intentional or unintentional.

1.4.1 Primary non-adherence

Primary non-adherence occurs when a patient fails to redeem their prescription. This may be an intentional decision or an unintentional memory failure whereby the patient simply forgets. The majority of adherence studies focus on the use of medicines in the patient's possession, therefore primary non-adherence is often overlooked. This form of non-adherence is also termed 'non fulfilment adherence'[24].

At present, UK based data on primary non-adherence relies heavily upon self-report measures and the numbers of prescriptions returned to the Prescription Pricing Authority (PPA) for verification of payment. Both measures are flawed due to potential for inaccurate data. However, the introduction of electronic prescribing has facilitated research to better identify the magnitude of primary non-adherence.

Early studies of primary non-adherence reported non-redemption rates of between 5 and 20%[25-28], however the methods used to provide the upper estimate of 20% have been criticised elsewhere for creating an overestimate[26]. More recent studies have shown similar variations in estimates, with rates ranging from 2.4% to 21.6%[29-31], though for the upper rate, a delay in filling a prescription was considered as primary non-adherence[29]. The most recent and comprehensive data are provided by analysis of 195,930 electronic prescriptions; primary non-adherence was reported at a rate of 22%[32]. It is therefore reasonable to conclude that primary non-adherence exists in variable magnitudes, with numerous factors such as patient age [25, 29, 30, 32, 33], gender [25, 30, 33] and socio-economic status [29, 33] influencing the effect.

In 2000, Matsui *et al.* studied primary non-adherence in parents of children who had attended a paediatric emergency department (n= 1222 children) and reported that 7.3% of parents had failed to redeem the prescription issued to their child. Reasons for this included believing the medicine was unnecessary, financial constraints and not having enough time[31]. Similarly, Ekedahl and Mansson, report that 61% of patients who failed to collect a prescription transmitted from their GP to their pharmacy, did so because they felt it was not necessary[30].

Worthy of note when considering rates of primary non-adherence, is the increasing availability of Over the Counter (OTC) medicines, which can often be purchased for less than a prescription charge. Primary non-adherence may therefore be a misnomer if a patient purchased an OTC equivalent instead of paying a prescription charge. Other factors which may lead to erroneous classifications of primary non-adherence or skew data collected on this matter include:

- Prescriptions for emergency use or delayed antibiotics which may not be needed, non-redemption therefore reflects adherence by following the prescribers guidance, yet according to electronic data, may appear as primary non-adherence
- Handwritten prescriptions are not recorded with electronic data and may therefore skew studies reliant on this measure

1.4.2 Secondary non-adherence

Secondary non-adherence occurs when a prescription is redeemed and the correct medicine is possessed but not taken as prescribed. Contrary to primary non-adherence, secondary non-adherence has been studied extensively, with a wealth of studies investigating both the magnitude and nature of secondary non-adherence. Monitoring of adherence to medication regimens dates back to as early as the time of

Hippocrates[2], but widespread research interest in the field didn't emerge until the 1970's[34]. Reviews to estimate the extent of non-adherence generally tend to conclude that about 50% of patients do not take their medicines as intended, although this estimate can vary. Such disparity reflects the complex nature of medication adherence but also the complexities of both defining and measuring it. Patient populations and disease areas studied can also account for the variations in the extent of non-adherence.

Similar to primary non-adherence, secondary non-adherence may be intentional, when patients willingly choose not to use their medications as prescribed or unintentional when physical or cognitive barriers prevent adherence. Irrespective of intentional or unintentional behaviours, most deviations in medicine taking occur as omissions of doses or delays in timing of doses rather than additional doses[35, 36].

1.4.3 Intentional non-adherence

Intentional non-adherence occurs when a patient makes a conscious decision not to follow the agreed recommendations of their healthcare provider. In 2005, Pound *et al.* reported that approximately half of all non-adherence is intentional [37] and that this can be both primary and secondary in nature.

Factors precipitating primary intentional non-adherence include health beliefs such as feeling the medicines are not needed[30, 31], lack of trust in the prescriber[29, 32], lack of satisfaction with the healthcare received[29, 31] and financial constraints[25, 26, 31, 33], although all of these reasons could also contribute to secondary non-adherence. Consistent evidence suggests that patient's health beliefs and illness perceptions may be amongst the strongest predictors[38, 39] of intentional non-adherence. Illness perceptions and health beliefs are likely to inform a conscious, intentional decision to use prescribed medicines in a way that differs from the prescriber's intentions, if they are used at all. Psychological theories of health behaviours are useful in understanding the complex interaction between health beliefs, illness perceptions and non-adherent behaviours and will be discussed in depth in chapter three.

Intentional non-adherence has also been displayed through strategic use of medicines to fit in with lifestyles. Documented examples of such behaviour include skipping doses of antihypertensive medicines before drinking alcohol due to fear of interactions[40] and moderating the dose of a Proton Pump Inhibitor (PPI) to manage acid reflux symptoms, after a 'triggering' meal such as heavily spiced foods[41].

1.4.4 Unintentional non-adherence

Intentional non-adherence is an active process based around informed decision making. Conversely, unintentional non-adherence is a passive process where specific barriers prohibit adherence in patients who would otherwise take their medicines.

For primary non-adherence, two unintentional behaviours are likely dominant; difficulties in getting to a pharmacy[29] and being unaware that an electronic prescription has been transmitted to a pharmacy[30]. Cognitive deficits may also be implicated in primary unintentional non-adherence, whereby a patient simply forgets to redeem their prescription or loses it. Language barriers, poor literacy or cognitive deficits may introduce another source of primary unintentional non-adherence, if a patient fails to understand the process of taking a prescription to a pharmacy for dispensing. Whilst financial constraints are widely regarded as a source of intentional non-adherence (choosing not to spend the money on a prescription and spending it elsewhere instead), it could be argued that in cases of severe deprivation, insufficient funds could be classified as unintentional non-adherence. The impact of financial constraints on medication adherence will vary according to the differing healthcare systems across different countries, as discussed in section 1.5.2.

Secondary unintentional non-adherence, can be broadly categorised into two domains; physical and cognitive barriers to adherence. Physical barriers to adherence describe functional limitations that prevent medication adherence and include swallowing difficulties and dexterity or visual problems. Cognitive barriers to adherence concern impairments of memory or understanding, leading to non-adherence through 'forgetting' or not understanding instructions.

1.4.5 Overlap in the classification of non-adherence

The complex multi-faceted nature of medication taking behaviours means that in most instances, non-adherence will have elements of both intentional and unintentional behaviours. Despite the nature of non-adherence, the outcome is still the same; the patient fails to use their medicines as prescribed. However, understanding the nature of non-adherent behaviours is imperative for formulating interventions to improve adherence. Consider for example the case of a patient who reports non-adherence due to forgetting to take their medicines. If the doses are forgotten due to genuine lapses in memory and the patient wishes to adhere but is struggling due to their memory deficits, an intervention such as reminder charts or alarms may be beneficial. Conversely, if the medicine is forgotten because the patient views it as unimportant and

does therefore not prioritise it in their mind, the same intervention is unlikely to yield benefit.

1.5 Factors influencing medication adherence

Reviews have identified more than 200 variables associated with medication non-adherence[34, 42] which can be broadly classified into three groups:

- Treatment related factors such as experience of side effects or duration of therapy
- Patient related factors such as motivation and health beliefs
- Prescriber related factors such as the patients trust in their prescriber and their satisfaction with the information given to them

Overlap between these classifications is evident, for example, oral chemotherapy is prescribed for life-threatening disease states but is associated with many side effects which may affect adherence (treatment related factors). Consequently, patients may need more information about the treatment (patient related factor) which may not be provided (prescriber related factor) which could in turn influence patients health beliefs (patient related factor). The existence of causal relationships must therefore not be overlooked.

1.5.1 Treatment related factors

The type of medicine prescribed, condition treated, duration of therapy, dosing regimen complexity and experience of side effects have all been identified as predictors of non-adherence in varying magnitudes. According to the WHO, experience of side effects and high dosage frequencies are the most prominent regimen related factors which impeded good medication adherence[7].

1.5.1.1 Disease area and type of medication

In 2004, DiMatteo and Robin reported that adherence rates were highest in patients with HIV, arthritis, gasterointestinal disorders and cancer, and lowest in pulmonary disease, diabetes and sleep disorders[43]. Similar results have been reported elsewhere by Fischer *et al.* who report that primary non-adherence to newly prescribed medicines was most common for hypertension, hyperlipideamia and diabetes[32]. Ekedahl and Mansson also report that primary non-adherence rates vary according to the type of medication prescribed, with medicines acting on the musculoskeletal system having higher than expected non-redemption rates and antibiotics lower[30]. Numerous inter-relating factors are likely to account for these findings, but the patient's perceived necessity of the medications and the weighted balance of perceived risks and benefits are likely notable.

The 2003 WHO report on medication adherence identified that the illness related demands of some conditions can strongly influence adherence, highlighting symptom severity, rate of progression, disease severity and availability of effective treatments as key determinants[7]. These factors are likely to inform patient health beliefs and perceived medication necessity and will therefore either encourage or abate intentional non-adherence.

Whilst the type of medication and condition treated can moderate adherence, the medicine dosage form can also be influential[44]. A study of barriers to HIV medication adherence identified that the taste, smell, size and shape of medicines could impede adherence[45]. The use of modified release formulations has been demonstrated to significantly improve adherence and reduce costs[46] through reduced dosage regimen complexity. Alternative dosage forms such as liquids, patches or suppositories can also aid adherence when physical barriers to adherence such as swallowing difficulties make more conventional dosage forms inappropriate. Conversely, patient acceptability and preferences may mean that the use of less conventional dosage forms are of detriment to medication adherence, though the definitions of conventional and unconventional dosage forms may be geographically and culturally variable. A recent questionnaire-based study (n= 485) which aimed to identify risk factors for non-adherence to medication in inflammatory bowel disease reported that oral therapy was associated with a significantly better adherence than rectal therapy (60% vs. 32%, $P = 0.001$)[47].

The presentation of a medicine, in terms of its appearance and packaging can also influence adherence. Solid dosage forms (tablets and capsules) are most frequently prescribed and will most commonly be packaged in either bottles with child resistant closures or blister packaging. These apparently simple devices can pose notable barriers to adherence for certain patients, who have difficulty retrieving their medicines from their packaging. Beckman *et al.* reported that 10% of patients were unable to access medication from a blister pack[48] and similar findings were reported by Nikolaus *et al.* with 10.1% of patients admitted to a geriatric ward being unable to open one of more medication container presented to them[49]. Both studies report that an inability to manipulate medication packaging is directly related to visual, cognitive or physical deficits in the patient[48, 49], therefore any patient, of any age may be affected if these difficulties prevail.

Whilst difficulties with tablet packaging have reportedly caused problems for approximately 10% of patients, breaking scored tablets in half was found to be a

problem for 78.3% of older patients admitted to a geriatric ward. The same study also reported that 41.4% of patients were unable to perform one or more tasks necessary to gain access to their own medications[50]. Dexterity problems which prohibit access to medicines and administration problems are therefore notable barriers to adherence.

1.5.1.2 Duration of therapy

Patient persistence with therapy is known to decline dramatically after the first six months of therapy[51, 52]; adherence to medication for the treatment of chronic conditions is therefore likely to be poorer than that for acute conditions. Benner *et al.* report that only 25% of older patients prescribed a statin to lower cholesterol maintained adequate adherence (defined as 80% of days covered) after five years[52]. DiMatteo reports that non-persistence with a prescribed medication is most likely for asymptomatic conditions, prophylactic treatments or when the consequences of stopping treatment are delayed[43]. This observation has important implications for long term adherence to medications such as anti-hypertensives and lipid regulating drugs, which are widely prescribed and constitute a notable proportion of UK prescriptions.

1.5.1.3 Dosing regimen complexity

The complexity of a medication regimen is defined by the number of medicines taken and the frequency of doses. Additional requirements such as taking the medicines at specific times and in a specific way (e.g. with or without food) may augment the complexity. Medication adherence has been shown to decline as the medication regimen complexity and number of different medicines increases[18]. In part, this observation is related to the increased cognitive burden associated with more complex regimens. However, accommodation of complex regimens requires greater lifestyle changes on the patient's part and may be inconvenient, intentional elements of non-adherence may therefore prevail in patients with low motivation, lack of support or disordered lifestyles. Horne and colleague suggest that it is not the complexity of the regimen per se that influences adherence, but more how this fits with the patients routines, lifestyles and expectations[12], making clear the potential for both intentional and unintentional behavioural influences.

Evidence synthesis suggests that reducing the number of daily doses in a medication regimen should improve adherence[42, 51], though individual studies have shown variation in the point at which further dose reduction continues to have an effect. Claxton *et al.* report significantly greater adherence in patients taking once daily regimens compared to thrice daily or more frequently, though no differences were observed been once and

twice daily dosing regimens[53]. This systematic review included 76 different studies and was restricted to studies that used electronic monitoring, the gold-standard, as the adherence measure. The size and robust inclusion criteria therefore increase the confidence with which these findings can be regarded. Richter *et al.* report similar findings, though in this study, single doses were found to be preferable to multiple doses[54]. However, the number of studies included in this review is not directly reported and the search strategy is comparatively less robust. Further studies have also shown that simplifying a medication regimen can improve adherence with Fish and Lung reporting that once or twice daily dosing led to better adherence compared to regimens where doses were taken three or four times per day[55].

1.5.1.4 Experience of side effects

Experience of side effects from a medicine is widely regarded as a predictor for non-adherence[56]. A US based cohort study (n=303) of tamoxifen discontinuation in women with breast cancer revealed that experience of side-effects increased the likelihood of tamoxifen discontinuation four-fold[57]. However, tamoxifen therapy is indicated for five years following breast cancer as a prophylactic therapy, therefore the long therapy duration and prophylactic nature may be contributory factors to the non-adherence, in addition to the experience of side effects. Experience of side effects has been significantly associated with non-adherence in HIV[58] and interfered with medication adherence in diabetes, as adherence is significantly lower for medicines deemed problematic in causing side effects, compared to those which are not[59]. Medication side effects are also a notable problem for adherence to medicines used in psychiatry[60], especially antipsychotics where side effects are common and can have a durable negative impact on adherence[61].

Concerns about medicine side effects can also be influential in non-adherence; Gallagher *et al.* report a questionnaire based study where over two thirds of migraine sufferers (n = 2444) had delayed or avoided taking their prescription medicines due to concerns about adverse effects[62]. General concerns about medicines will be discussed in greater depth in section 1.5.2.3.

Whilst experience of side effects is a reliable predictor of non-adherence, inter-relating factors such as the patient's coping skills, motivation and perceived necessity for the medicine will likely influence whether experience of side effects precipitates non-adherence. For example, experience of side effects to an antihypertensive medicine where the patient perhaps doubts the need for treatment may be more likely to cause

non-adherence than experience of side effects to life saving chemotherapy where the patient's perceived necessity is likely higher.

1.5.2 Patient related factors

Medication taking is a patient determined event therefore many predictors of non-adherence can be classed as patient related factors. Illness perceptions and health beliefs have been identified as powerful predictors of adherence[38, 39] whereas socio-demographic factors are much weaker predictors[34, 39]. Patient doubts as to the necessity of their medication and concerns about adverse effects have been shown to correlate with poor adherence across a wide range of diseases including asthma, diabetes, cancer and coronary heart disease[38], hypertension[63], renal disease[64], depression[65], HIV/AIDS[66] and haemophilia[67]. Other patient related factors include their cognitive and physical capacity to adhere to medication regimens.

1.5.2.1 Cognitive abilities

Medicines' taking requires an understanding and correct interpretation of directions plus the ability to remember to execute the behaviour; a patient's cognitive capacity to undertake these processes will therefore influence adherence. Forgetfulness is the most commonly cited reason for non-adherence[4], even in patients without formally diagnosed memory problems.

Notable research into non-adherence due to cognitive incapacity has been undertaken in the field of HIV medication adherence as low literacy levels and cognitive impairment are widely accepted as strong predictors of non-adherence in this domain[68]. Becker *et al.* report that declining neuropsychological function in HIV patients correlates with worsening medication adherence[69]. The extent of worsened adherence with cognitive impairment was elucidated by Hinkin *et al.* who report that neurocognitive impairment confers a 2.5 times greater risk of poor adherence[70].

Whilst the manifestation of cognitive impairments is frequently attributable to the HIV infection, the effect of the cognitive impairments described in HIV studies are generalisable to cognitive deficits in any population. Wider conclusions about the impact of poor cognitive function on medication adherence can therefore be surmised and research in other conditions supports this. Salas *et al.* report that mild cognitive impairment increases the risk of non-adherence to anti-hypertensive therapy and this risk increase is significant for patients living alone[71].

Related to the concept of cognitive capacity, is that of health literacy, a relatively new concept in health promotion[72]. Definitions of health literacy are widespread[73], but the widely cited WHO definition is largely considered to be the broadest, defining health literacy as:

"the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health" [74]

In 2003, the 'Skills for Life Survey' was commissioned by the Department for Education and Skills to provide a national profile of adult literacy and numeracy across five broad levels of competence. The literacy test was completed by 7873 randomly selected adults, residing in England and between the ages of 16 and 65; literacy levels were classified into three key groups; entry level (comprised of three subgroups), level one and level two. The survey reported that 56% of the respondents (equating to 17.8 million adults in England) had a literacy skills at level one or below, meaning their understanding was limited to short and straightforward texts at best. The lowest possible grading (entry level one or below) was awarded to 3% of respondents (equivalent to 1.1million adults in England) meaning these people were classed as functionally illiterate[75]. Patients with poor health literacy are at greater risk of non-adherence, poor health and hospitalisations[76] and health literacy has been identified as a predictor of adherence in cardiovascular disease[77, 78], HIV[79] and glaucoma[80].

The correlation between poor adherence and low health literacy is likely to manifest through poor understanding of dosing regimens. A study of ethnic minority patients with low health literacy (n =87) reported that the inclusion of pictograms on medication labels improved understanding and adherence, with 18% more adherent patients in the intervention group compared to control[81]. Kalichman *et al.* also suggest that patients with poor health literacy are more likely to hold health beliefs which impede adherence[79].

1.5.2.2 Illness perceptions

The severity with which a patient perceives their illness and their experience of symptoms will influence both their perceived necessity of the medicine and interpreted sense of treatment efficacy. Experience of symptoms can prompt adherence if the patient perceives the medicine as necessary and efficacious[12]. However, symptom experience can also be detrimental to adherence if the patient wrongly attributes this to medication side effects[82]. Non-adherence is particularly problematic in asymptomatic

chronic conditions, as an absence of symptoms may lead a patient to question the severity of their illness and necessity of their medicine[83].

Non-acceptance of illness is a known predictor of non-adherence[84] as patients who do not believe themselves to be ill are unlikely to perceive their medicines as a necessity[39]. Patients' 'common sense beliefs' are therefore pivotal in influencing their actions to cope with an illness[12, 85]. 'Downplaying' of symptom severity and non-acceptance of illness has been noted as particularly relevant in asthma where adherence to prescribed regimens is notoriously problematic[37]. Horne *et al.* report better adherence to inhaled corticosteroids in patients who perceive asthma as a chronic condition than those who understand asthma in a symptomatic sense and therefore do not perceive preventative therapy as necessary when symptoms are absent[39].

Illness perceptions can also be influenced by the social stigmas attached to certain illnesses such as depression, schizophrenia, HIV and epilepsy. Patients with these conditions, especially HIV have reported a reluctance to take their medicines due to the fear of disclosing their illness[12]. Rintamaki *et al.* report that HIV positive patients are 3.3 times more likely to be non-adherent if they express high social stigma concerns and that patients will skip doses of their medicines due to fear that it would disclose their HIV status to friends and family[86]. For epilepsy, lower levels of adherence with higher levels of perceived social stigma has been reported[87], though Horne poses that stigmatisation could increase adherence in this condition as fear of seizures and the associated stigma may increases the perceived necessity of good adherence[12]. In contrast to the concept of social stigmatisation, social factors such as the expression of positive attitudes by other members of the community, can improve adherence[88].

1.5.2.3 Health and medication beliefs

Research suggests that people tend to view medicines as unnatural and harmful substances that are frequently over prescribed[89], these negative beliefs may adversely affect adherence[8]. In 2005, Pound *et al.* reported a synthesis of qualitative research which identified the main reason for non-adherence as concerns about medicines[37].

Horne's seminal work in understanding the influence of medication beliefs in non-adherence reveals that patients who hold negative beliefs about medicines tend to have greater concerns about taking them and are therefore less likely to be adherent[12, 38, 90]. The original work conducted by Horne and colleagues considered medication beliefs in both general and specific contexts, and a questionnaire with well-regarded psychometrics was tested in over 800 patients across multiple disease areas[38, 90]. In

December 2013, Horne *et al.* published a meta-analysis of studies which had utilised this questionnaire and included data from 94 different studies (n = 25,072)[91]. Horne *et al.* report that across these studies, higher adherence was significantly associated with stronger perceptions of treatment necessity and fewer concerns.

Negative beliefs about medicines have also been shown to affect interpretation of subsequent events, for example, experience of new symptoms are more likely to interpreted as side effects of the medicine rather than a worsening condition, in patients that hold preconceived negative beliefs[92]. Public perceptions and media influences can also shape beliefs about medicines. Media scares about, for example, anti-depressants being addictive, may feed in to a 'general schema' that assumes most medicines are addictive[85], a belief which is likely to be of detriment to good medication adherence.

Horne's work has also identified that the balance between a patient's perceived necessity of a medicine and their concerns about taking it predicts non-adherence to a greater extent than socio-demographic and clinical factors[90]. Therefore, when a patient's concerns about a medicine outweigh their perceived necessity for it, non-adherence is more likely[38]. Horne notes that the concept of medication efficacy is related to perceived necessity although the two concepts are not synonymous[12]. However, doubt over efficacy may evoke an evaluation of continued necessity and lead patients to 'experiment' with their medicine doses to 'test' whether they are still necessary[37].

Concerns about experiencing adverse effects from medicines are consistent across disease states, with evidence suggesting that a third of all patients hold such concerns [38, 90]. Other medicine related concerns may be more specific, such as concerns about weight gain with inhaled corticosteroid use[93] or reduced efficacy and addiction with prolonged regular use of analgesics[94]. However, concerns about addiction or dependence have been expressed by patients in many disease states including asthma[95, 96], hypertension[97, 98], epilepsy [99] and depression [100, 101]. Blenkinsopp *et al.* have identified that medicine related concerns include the fear of masking more sinister symptoms and fears of unknown cumulative effects with prolonged use[102]. Such concerns are often based around ill-informed beliefs therefore educational interventions may be important in alleviating concerns and thus facilitating improved adherence.

Another factor known to influence patient's medication beliefs is the prescribing of generic rather than branded medicines and therapeutic substitutions to reduce prescribing costs[103]. A recent qualitative study by Chambers *et al.* reported that some

patients felt that generic medicines caused more side effects, whilst others doubted the therapeutic content of generic medicines which augmented their fear of side effects[103]. Such concerns may be of detriment to good adherence.

1.5.2.4 Social and economic factors

Socio-demographic factors such as age, gender, socio-economic status, marital status and ethnicity undoubtedly have the potential to influence medication adherence through various mechanisms, yet research has identified such factors as generally poor and inconsistent predictors of adherence[39, 43].

Age

The WHO identify 'age' as a complex and unpredictable determinant of adherence[7]. Paediatric adherence is largely determined by the child's primary caregivers and is subsequently often high, especially in the case of acute emergency prescriptions[31]. However, in other paediatric conditions, adherence may be lower[104, 105] and as children age, they assume increasing responsibility for their own health[106]. An influential report in 2004 concluded that adherence is generally lower in children than adults, especially in adolescents approaching independence, children with learning disabilities and infants[107]. Numerous studies have therefore considered medication adherence in adolescent populations[107-110] and specific guidelines to involve children in decisions about their care where possible, have been issued in the 2004 National Service Framework (NSF) for children[111]. Policy guidance linked to the NSF has also been issued to facilitate medicines use in schools[112].

Medication non-adherence in older patients is also of concern. Declining health, poor dexterity and cognitive capacity, co-morbidities and polypharmacy with complex regimens all contribute to the vulnerability of older people to medication non-adherence[13].

Ethnicity and culture

Ethnicity has been identified as an important predictor for non-adherence in numerous settings including hypertension[113-115] and HIV [116, 117], with patients from ethnic minorities often being more susceptible to non-adherence[118]. Monane *et al.* report significantly better adherence in patients of white race[114] and similar findings have been reported elsewhere[113]. Postulated reasons for this tend to focus on differing cultural beliefs although health inequalities may co-exist adding a further contributory factor[114].

Differing cultural backgrounds have also been shown to influence medication beliefs. In 2004, Horne *et al.* reported that students of an Asian background were significantly more likely to hold negative beliefs about medicines, perceiving them as intrinsically harmful, addictive substances that are best avoided. Conversely, students with European cultural backgrounds had significantly more experience with medicines and were more likely to endorse their benefits[119].

Social support

DiMatteo's meta-analysis of 122 studies identified a significant relationship between social support and adherence to medical treatments. The analysis encompassed both emotional and practical support plus factors such as marital status and living arrangements. The most notable correlation to adherence was practical support, with a 3.6 fold increase in the likelihood of adherence for those patients receiving practical support compared to those who did not. Correlates to other forms of support were also identified[120]. Though influential, this report did not specifically focus on medication adherence and instead included adherence to other medical treatments and appointment keeping which may have biased the findings. Based on this evidence, Horne concludes that social support may be an important factor in reducing barriers to adherence in some patients[12]. Based on the best evidence available, Horne's conclusions appear to be valid; social support should therefore be acknowledged as a potential moderator of medication adherence, though further work is needed to establish the circumstances in which this is most important.

Whilst receipt of social support is commonly deemed to positively influence medication adherence, social pressure to adhere may induce 'imposed compliance' whereby patients feel forced to adhere to their medication regimens[121]. This phenomenon is most prevalent in mental health, with schizophrenic patients reporting feelings of powerlessness with regard to their medicines due to the extreme pressures that they felt to adhere[121]. Whilst contrary to the ideals of informed decision making and concordance, 'imposed compliance' may be a necessity in conditions such as a schizophrenia where adherence is frequently poor[122].

Medication costs

The cost of medication has been identified as an important precipitator for primary non-adherence, especially in countries where state-provision of healthcare is inadequate[7, 29, 33]. In the UK, patients that pay a prescription charge are more likely to display non-adherence compared to patients that are exempt from charges[25, 27]. However, it is

worth noting that the cost of medicines may be secondary to the patient's illness perceptions and medication beliefs. Therefore, if a patient considers themselves gravely ill and that a medicine is necessary they are likely to find means to pay for the prescription as their perceived necessity for it will outweigh the financial sacrifice. A patient in identical financial circumstances prescribed a medicine perceived by them as unnecessary to treat a condition they think not so serious may, however, be much less likely to pay the prescription charge.

1.5.2.5 Patient co-morbidities

Co-morbidities such as depression and anxiety or drug and alcohol abuse have been identified as important modifiers of medication adherence. DiMatteo's seminal meta-analysis reported a threefold increase in the odds of non-adherence for patients suffering with depression compared to those who did not, an effect that was consistent across differencing disease states[123]. Horne notes that the direction of causality with such observations remains unknown and so the mechanisms through which depressive symptoms moderate medication adherence are not fully understood[12].

Illicit drug use has also been linked to poor adherence, with a study of illicit drug use in HIV positive patients showing that individuals using illicit substances were over four times more likely to display suboptimal medication adherence compared to those with negative urine toxicology screenings[124].

Co-morbidities that engender visual, physical or cognitive deficiencies can also be detrimental to adherence, as mediated through administration difficulties. Reduced visual acuity will affect accuracy in reading prescription labels and identifying medicines whilst dexterity problems may impair manipulation of tablet packaging[50]. Swallowing difficulties may also impede oral administration of medicines[125] and mobility problems could prevent collection of medicines from a pharmacy and thus contribute to primary non-adherence.

1.5.3 Prescriber and healthcare team related factors

A good relationship with healthcare providers and trust in the prescribing practitioner are important moderators of medication adherence. The trust that a patient has in the abilities of the person issuing their prescription can greatly influence the beliefs held about both their illness and medications, as can satisfaction with the consultation.

1.5.3.1 Patient and prescriber interaction

In their seminal review of medication adherence, Vermeire *et al*. report that the quality, frequency and duration of interactions between the patient and prescriber will influence adherence[34]. A prescriber's attitude towards their patient, their ability to elicit and respect patient concerns, provide appropriate information and demonstrate empathy have been shown to be of utmost importance[88].

1.5.3.2 Provision of information

Evidence suggests that better informed patients are more likely to be committed to their treatment regimens and adhere to decisions that they have been actively involved in[126]. To facilitate adherence, information regarding newly prescribed medicines must be delivered in a comprehendible manner that meets the patient's information needs. This approach should evoke patient satisfaction, which has been identified as an important predictor of medication adherence in numerous chronic conditions. Satisfaction with information provision is linked to lower medication concerns and subsequent improved adherence[127, 128].

Poor communication can also make understanding of complex instructions difficult, especially in older patients[129], leading to a lack of knowledge. The role of patient knowledge in determining adherence, has been described as complex[12] with some studies reporting a strong link, but many more studies failing to identify definitive causality[130]. Discrepancies in the influence of patient knowledge on adherence may in part be accountable to conceptual and methodological disparities in the definition of patient knowledge. Moreover, Horne *et al.* note that the cross sectional study designs assumed in this domain do not enable determination of a direction of causality. It is therefore impossible to determine whether non-adherence is caused by a lack of knowledge or whether non-adherent patients are less interested in their medicines and do therefore not seek knowledge or pay attention when it is offered[12]. Despite inconsistent evidence, a certain level of knowledge regarding a treatment and how to use it is a prerequisite for appropriate use[131] and therefore relevant to adherence.

Information delivery can also influence patient recall of instructions for taking medicines, another prerequisite for adherence[132]. Evidence suggests that patients are able to recall less than 50% of prescription information presented to them[133]. Whilst individual factors such as cognitive ability and intelligence have been shown to influence information recall[134], the information delivery style, length and complexity all influence recall[135].

The communication style assumed by a GP when prescribing a medicine has also been shown to influence adherence. Barry *et al.*[136] and Britten *et al.*[137] have published qualitative work highlighting that when consultations are rushed, patients may leave their appointments with unmet concerns and feel worried and misguided; factors that may subsequently impede adherence. A consultation style that involves patients in the decision making and where lay terminology is used is also known to improve adherence[137, 138].

1.6 Measuring adherence

Measurement of adherence is notoriously difficult and an important consideration in the evaluation of adherence research as differing methods can produce dissimilar results. Broadly speaking, adherence assessment methods can be grouped as direct and indirect measures. Each method has advantages and disadvantages as summarised in table 1.1 and described in the following sections.

1.6.1 Direct measures

Direct measures of adherence commonly involve the measurement of a biological marker or drug metabolite in blood plasma or urine to detect the presence of a medicine in the body[137]. Biological markers can be added to a formulation for this specific purpose. Such techniques are expensive, labour intensive, invasive and susceptible to distortion by the patient[4]. Direct measures of adherence are therefore an unpopular choice for many adherence studies, though for some medicines these approaches are widely used as an effective adherence measure. Plasma lithium levels are routinely measured in primary care to avoid toxicity and medicines used in the treatment of epilepsy, such as phenytoin and valproic acid, are also amenable to plasma monitoring, with sub-therapeutic levels indicative of poor adherence[4].

Whilst monitoring of drug plasma levels provides an objective measure of adherence, few medicines are suitable for this approach as metabolism and other patient related factors may affect readings. Moreover, patient behaviour may change if they know their plasma levels are soon to be monitored, sporadic non-adherence is therefore less likely to be detected.

Direct measures of adherence also include the observation of medicines taking, commonly known as Directly Observed Therapy (DOT). This technique is commonly used as an adherence assessment for conditions such as Tuberculosis (TB) where perfect adherence is essential yet commonly poor[138] and is considered to be an accurate method of measuring adherence[139] . Patients are observed whilst taking their medication, which should ensure adherence, though patients have been known to retain the medicines in their mouth and then discard it surreptitiously post observation[4]. Whilst used in clinical practice to ensure adherence, DOT is seldom used as an adherence assessment tool in research studies. It is worth noting that DOT is also used as an intervention to improve adherence, though evidence from a recent systematic review suggests the effectiveness of this approach may be limited[138].

1.6.2 Indirect measures

Whilst direct measures of adherence are seldom used in research, the opposite is true for indirect measures, which tend to provide accurate and convenient adherence data[34].

1.6.2.1 Self-report

Patients self-reports remain one of the simplest measures of adherence and can provide accurate data that correlates well with more precise measures such as electronic monitoring[140]. Self-report measures include patient interviews, questionnaires and diaries which represent fast, flexible and inexpensive approaches that are generally acceptable to patients. However, self-report can be subject to recall problems and social desirability bias, whereby a patient provides the 'expected' response of adherence, in order to please the researcher or their practitioner. Moreover, questionnaires assume patient understanding and honesty, which can be particularly problematic in patients who do not understand their regimen or are unaware of their non-adherence. Good questionnaire design and administration are key to eliciting accurate adherence data and extensive guidelines have been issued on this topic[141]. Patient interviews are more likely to overestimate adherence as social desirability biases are stronger, therefore postal questionnaire may provide greater accuracy[142, 143].

One of the most widely used self-report adherence questionnaires is the four item Medication Adherence Questionnaire (MAQ) developed by Morisky *et al.* in 1986 for use in antihypertensive therapy[144]. The four non-adherent behaviours included in the questionnaire; forgetting, carelessness, stopping when feeling better and starting when feeling worse, were created using a theoretical approach. The statements are phrased to minimise social desirability bias and good psychometrics properties have been established[144]. The MAQ has been validated against a clinical outcome measure (blood pressure) and displays both concurrent and predictive reliability. Despite these important credentials, the tool has been widely criticised as an overly simplistic assessment of an inherently complex behaviour. This limitation is augmented by dichotomous response options which yield limited data and no indication of the frequency or magnitude of non-adherence.

The Morisky Medication Adherence Scale (MMAS) evolved from the 4-item Morisky scale in response to its criticisms and has documented reliability, with greater sensitivity than the four-item scale used previously[145]. MMAS considers seven non-

adherent behaviours with dichotomous response options but also includes an additional item with a five-point Likert scale response, to establish the frequency with which the respondent has difficulties remembering to take all of their medicines.

In 1999, Svarstad *et al.* developed the Brief Medication Questionnaire (BMQ) which utilised questionnaire development theory to specify a recall time period, thus increasing accuracy[146]. The authors report specifically selected wording to reduce perceptions of threat or embarrassment and the tool has been validated using electronic monitoring. The BMQ considers three different aspects of non-adherence relating to regimen, recall and beliefs and enables differentiation between sporadic and repeated non-adherence.

Another commonly used self-report tool is the Medication Adherence Rating Scale (MARS) developed by Horne and Hankins[147, 148]. Whilst formal validation of the tool remains unpublished, it has been reliably used to assess adherence across numerous domains[90, 127, 149]. Similar to Morisky, MARS uses carefully selected wording to reduce social desirability pressures and assumes a non-judgemental and non-threatening stance[127]. Respondents are asked to rate the frequency with which they engage in five non-adherent behaviours, using a five-point Likert scale ranging from 'always' to 'never'. This continuous rather than dichotomous measure of adherence is widely regarded as a positive attribute[150]. MARS has demonstrated good internal and test re-test reliability when used to assess adherence across a variety of chronic conditions and has also shown good correlation to dosage unit counts[151].

Table 1.2 provides a summary of the overlapping constructs of these four most widely used self-report tools and highlights that 'forgetting to take doses' is the only non-adherent behaviour common to all four tools.

Less commonly used self-report adherence assessment tools include:

- The Adult AIDS Clinical Trials Group (AACTG) Adherence Instrument[152] – developed by Chesney *et al.* to identify non-adherence to medication for HIV
- The Medication Adherence Self-Report Inventory (MASRI)[140] - developed by Walsh *et al.* also in the domain of HIV, which incorporates a visual analogue scale to record adherence
- The Medication Adherence Rating Scale (MARS)[153] – developed by Thompson *et al.* for use in psychosis, specifically schizophrenia

- The Medication Adherence Reasons Scale (MARS)[154] – developed by Unni and Farris in response to a literature review of reported reasons for non-adherence

With numerous self-report adherence assessment tools, a synthesis of research was necessary to determine the suitability of these measures; this need was addressed with a systematic review in 2011[155]. Garfield *et al.* identified 58 self-report adherence assessment tools suitable for use in primary care and 93% of these were reportedly validated. Whilst a plethora of tools therefore exist, Garfield and colleagues note that few distinguish between intentional and unintentional behaviours, thus limiting their use in clinical practice. Despite these limitations, self-report measures continue to be widely used in research.

1.6.2.2 Patients' clinical response

The clinical correlates of non-adherence will depend upon the medication taken, disease state and severity plus patient co-morbidities[15] and is therefore unlikely to represent a reliable adherence measure. However, clinical response data such as blood pressure or blood cholesterol levels are commonly collected as part of routine care and may therefore represent an easily accessed 'indicator' of non-adherence rather than definitive measure[4]. Clinical responses are not recommended as sole measures of adherence as they assume that the medicine is the only determinant of the outcome and do not account for the numerous confounders that may exist[156].

1.6.2.3 Pill counts

Second to patient self-report questionnaires, pill counts are the most common method of adherence assessment[4]. Prior to the emergence of electronic monitoring it was considered a gold-standard technique, but the method is not without flaws. Whilst the process of counting the number of pills remaining in a patient's bottle at the end of a designated time period (e.g. one month) is relatively simple it is time consuming and reliant on the patient retaining their medicines containers. Moreover, the process assumes that uncounted pills have been ingested correctly. Such assumptions are fallible as patients have been known to dispose of their unused medicines in an attempt to appear adherent[4]. A comparison of pill count data to electronic monitoring, found pill counts to be unreliable[157], detailed data of adherence patterns and dose timings are also unavailable using this technique. Finally, pill counts are also subject to the Hawthorne effect, where patients change their behaviour when they know their adherence is being monitored[158].

1.6.2.4 Prescription refills

Prescription refill rates can be a reliable method of assessing adherence, in closed pharmacy systems whereby the patient can only obtain their medicines from one source. In the UK, patients are free to obtain their prescription from any pharmacy; refill rates are therefore unlikely to be a reliable adherence measure. In addition, refill rates only infer adherence as collection and possession of a medicine at the correct time points will not always equate to perfect adherence[4]. Prescription refill data has been demonstrated to both under and overestimate adherence[159].

1.6.2.5 Electronic monitoring

Electronic monitoring devices are available to record the time of opening a medicines bottle, dispensing eye drops (for glaucoma) or activation of a canister (for asthma) and are a reliable adherence assessment tool[4]. Electronic monitoring avoids the notable biases introduced by tablet counts and other methods which enable the patient to disguise omitted doses by removing them prior to be counted[15]. Precise and detailed insights into patients' patterns of medicine taking are offered by this method, though the indirect method means details of whether the medicine was actually taken, or how many tablets were taken are still absent[4]. Raynor reports that the use of electronic monitoring devices has been pivotal in furthering our understanding of non-adherent behaviours, leading to the discovery of 'drug holidays' and 'white coat adherence'[160]. Whilst the costs associated with this method prohibit its routine use, electronic monitoring of adherence is widely considered as the 'gold-standard' approach[161].

Test	Advantages	Disadvantages
Direct measures of adherence		
Directly observed therapy (DOT)	Generally considered as accurate method	Impractical for routine use, patients can deceive observer
Measurement of drug or metabolite blood plasma levels	Objective measure	Expensive process, variations in metabolism can give false readings, sensitive to Hawthorne effect
Measurement of biological marker in blood	Objective measure, can be used to assess placebo in clinical trials	Expensive assays and sample collection
Indirect measures of adherence		
Patient questionnaires and self-report	Simple and inexpensive measure, practical approach in clinical settings, good level of data can be elicited including differentiation between intentional and unintentional non-adherence	Subject to self-report bias and Hawthorne effect
Pill counts	Objective, quantifiable and relatively easy to perform	Patients can manipulate data (pill dumping), details of whether correct medicines were taken at correct time not captured
Prescription refill rates	Objective and relatively easy to obtain	Assumes patient visits regular pharmacy and has not obtained medicines elsewhere, does not provide information on whether medicines were actually taken
Assessment of patients clinical response	Simple assessment, data often collected as part of routine care	Non-response does not mean non-adherence as other factors may be causative
Electronic monitoring (e.g. MEMS®)	Provides detailed and precise data about timings, adherence tracked over period	Expensive method, assumes opening and closing of bottle correlates with medicines taking, patients need to return packing to allow data download.
Patient diaries	Process of self-monitoring/recording adherence may improve it	Easily falsified, may be subject to recall bias

Table 1.1 Summary of adherence measures (based on Osterberg and Blaschke[4])

	MARS	Morisky (MAQ)	Morisky (MMAS)	BMQ
Primary intentional non-adherence				
Choosing not to redeem a prescription due to not wanting to take medicine				
Choosing not to redeem a prescription due to unwillingness to pay prescription charge				
Secondary intentional non-adherence				
Choosing not to take a medicine or reducing the dose because of health beliefs/illness perceptions/confidence in prescriber				
Choosing not to take a medicine or reducing the dose due to experience or fear of side effects				
Choosing to stop a medicine or reducing the dose due to feeling better		✓	✓	
Choosing to stop a medicine due to perceived lack of efficacy				
Choosing to increase the dose of a medicine due to perceived lack of efficacy				
Choosing to take a medicine differently to prescribed because of increased convenience/fitting in with lifestyle/ knowing best				
Altering the dose of a medicine	✓			
Stop taking for a while	✓			
Deciding to miss a dose	✓			
Taking less than instructed	✓			
Stopping medicine or reducing dose due to feeling worse		✓	✓	
Being careless about taking medicines		✓		
Primary unintentional non-adherence				
Forgetting to redeem a prescription				
Failure to redeem a prescription due to insufficient funds				
Forgetting to order a medicine and running out of it				
Forgetting to collect a dispensed prescription from the pharmacy/doctors surgery				

Table 1.2 Summary of non-adherent behaviours assessed by commonly used self-report questionnaires

	MARS	Morisky (MAQ)	Morisky (MMAS)	BMQ
Secondary unintentional non-adherence				
Not understanding the dosage instructions				
Confusion in differentiation between different medications				
Forgetting doses	✓	✓	✓	✓
Forgetting to take medication with them when they stay away			✓	
Forgetting whether they have already taken a dose				
Unable to administer medication due to dexterity problems				✓
Unable to administer medication due to visual problems				✓
Unable to take medication due to inappropriate formulations				
Non-specific non-adherent behaviours				
Not taking medication in last two weeks			✓	
Not taking medication yesterday			✓	

Table 1.2 (continued) **Summary of non-adherent behaviours assessed by commonly used self-report questionnaires**

1.7 Interventions to enhance medication adherence

Widespread research interest in the most effective interventions to improve medication adherence exists, yet no single method has been shown to be inherently superior[162]. A series of highly influential systematic reviews have been conducted by Haynes *et al.* to explore the efficacy of Randomised Controlled Trials (RCTs) designed to increase medication adherence, the most recent being in 2008[163]. Undertaken to Cochrane standards, this meticulous review identified 83 interventions to increase adherence for long term conditions, reported in 70 RCTs. A mere 43% of these interventions improved adherence and only 30% led to an improvement in at least one treatment outcome. Haynes *et al.* conclude that whilst these interventions are mostly complex, they are also largely ineffective and subsequently call for the prioritisation of innovative research in the field[163].

The studies included within the Haynes systematic reviews were deemed too disparate to warrant synthesis through meta-analytic techniques. In 2003, Peterson *et al.* accommodated the disparity in studies by specifically focusing on educational and behavioural interventions[164]. The resulting meta-analysis reported an overall effect size (95% confidence interval (CI)) of 0.07 (0.04 to 0.09), 0.11 (0.06 to 0.15) and 0.08 (0.04 to 0.12) for behavioural, educational and combined interventions respectively. Similar to the Haynes reviews, modest improvements in adherence were therefore reported, further highlighting the need for novel approaches in this domain.

1.7.1 Educational strategies

Educational interventions to improve medication adherence were defined by Peterson *et al.* as 'those that taught the patient about the medication or disease through oral, written or audio-visual communication in an individual, one-to-one or group format'[164]. The focus on imparting knowledge to patients tends to yield conflicting effects, largely because patients' information needs differ and untailored information delivery fails to consider individual attitudes and beliefs. Provision of information may also be detrimental to adherence if negative aspects of therapy such as side effects are highlighted, which had not previously been considered[165].

Educational interventions are most likely to be efficacious in patients who are willing to take their medicines but who need information on how to do so, though it may also be of use in cases of intentional non-adherence, due to misunderstandings about medicines or ill-informed beliefs[164].

In English community pharmacies, two nationally commissioned adherence intervention services are available, the New Medicines Service (NMS) and Medicines Use Reviews (MURs). Whilst neither service is specifically classified as educational interventions, both have a fundamental element of increasing patient's knowledge about their medicines. MURs are not a clinical medication review but instead have the more modest aim of establishing a patient's medication use and increasing patient knowledge and understanding of their medication[166]. MURs have been a routinely delivered adherence intervention in community pharmacies nationwide since the inception of the new pharmacy contract in 2005 yet robust, comprehensive evidence to document their value remains elusive[167].

Despite the paucity of evidence in supporting the value of MURs, large amounts of NHS expenditure has been streamed into funding this intervention. Data from the NHS prescription services showed that in the financial year, from April 2010 to March 2011, just over 2.1 million MURs were undertaken in community pharmacies in England alone which cost the NHS almost £58.9 million; a figure that continues to rise[168]. Whilst the fundamental premise of a community pharmacy based medicines use review is intuitively useful and provides ample opportunity to identify, discuss and resolve adherence barriers, the outcome of these basic and limited techniques is unknown and the limited evidence available does not look promising.

Contrary to MURs, the NMS service is theoretically based, with research evidence to support its design and rationale[169, 170]. Designed to identify and resolve any adherence difficulties within the first few weeks of initiating a new therapy, promising early results from the service have been reported[171]. A full economic evaluation and qualitative appraisal of the service is currently being undertaken[172]. However, the NMS represents an educational intervention that is not targeted to meet individual needs and does not encompass a clear strategy for resolving adherence barriers, especially those of an intentional nature. The deficit in community pharmacy based adherence interventions is therefore evident.

1.7.2 Behavioural Strategies

In the meta-analysis of adherence interventions reported by Peterson *et al.* behavioural interventions included the use of any tool or action that would change a patient's skill level or normal routine, such as pillboxes, calendars, reminders and dose-schedule changes[164]. Behavioural strategies are based on the assumption that medication taking behaviours can be learnt, modified and practised to improve medication adherence. Provision of clear instructions as to how to adhere plus support strategies

such as provision of adherence aids and reminders are therefore commonly utilised in community pharmacy practices.

1.7.2.1 Reminder charts

Computer generated reminder charts are provided by community pharmacies as a prompt to encourage adherence, especially in patients with mild to moderate cognitive impairments. Reminder charts commonly involve a list of the medicines prescribed in the left-hand column, with four daily time points (based around mealtimes) across the top of the chart, indicating the number of each medicine to be taken at each time point. An RCT reported by Raynor *et al.* demonstrated that recipients of a reminder chart were more likely to display adequate adherence compared to non-recipients (86% Vs 63% p= <0.0001)[131]. Reminder charts may therefore be a useful and relatively simple intervention in cases of unintentional non-adherence associated with cognitive impairment. However, they are less likely to yield benefit in non-adherence of a more intentional nature.

1.7.2.2 Simplification of dosing regimens

Evidence, as described in section 1.5.1.3, demonstrates that as a patient's dosing regimen increases, adherence is likely to decrease. Interventions which aim to reduce the number and frequency of daily medicine doses are therefore an intuitive strategy to improve adherence. Simplification of dosing regimens, in conjunction with the prescribing practitioner, is commonly deployed as a 'first line tactic' by community pharmacists wishing resolve identified adherence difficulties. A meta-analysis of educational and behavioural interventions to improve medication adherence reported that dosage-schedule changes were the most frequently used behavioural type intervention[164].

1.7.2.3 Adherence aids

When reminder charts and dose simplifications have failed to remedy adherence difficulties, adherence aids may be utilised and are often recommended by community pharmacists. A wide range of devices are available and are designed to make it easier for patients to administer and remember their medicines. Adherence aids may therefore be a useful strategy to overcome both cognitive and physical barriers to adherence.

Multi-compartment compliance aids (MCAs)

MCAs assume many different designs but in essence comprise of a box divided into multiple compartments to represent the days of the week and differing times points during the day. A patient's medicines can be dispensed into the device, usually on a weekly basis, so that each tablet is set out at a specified time point. Whilst most solid oral dosage forms (tablets) are suitable for inclusion in an MCA, many are not including those that are sublingual, dispersible or hydroscopic. These medicines, along with non-oral formulations such as inhalers, creams or eye drops must therefore be supplied separately.

MCAs are primarily designed to act as a reminder in cases of non-adherence due to memory impairment. However, dispensing in an easily accessible device can also improve adherence for patients with dexterity problems that inhibit access to medicines in blister packs or with child resistant closures. Though most commonly filled in community pharmacies, MCAs can also be purchased or supplied directly to patients or their carers/family members for self-filling with existing supplies of medicines.

Evidence to support the use of MCAs is mixed but tends to acknowledge that these are costly interventions with limited evidence to support their use[173]. In 2001 Nunney and Raynor conducted a questionnaire based study to evaluate the use of MCAs in primary care. Responses from 123 pharmacies revealed that MCA use was common, but that initiation and supply were not always focussed towards the patient's needs. Interviews with 56 patients receiving an MCA revealed that 39% felt they would still be able to cope without their MCA and 18% had difficulty accessing their medicines from the device. The authors conclude that MCAs should not always be the default option for support[174]. Whilst this study provides valuable information, the limitations of questionnaire-based methods in just one UK region, must be considered. Green and McCloskey also conducted a questionnaire based study, but focused on the provision of MCAs in UK hospitals rather than community dwelling patients. This study was strengthened by the large number of UK hospitals contacted; a 74% response rate provided data from 160 acute hospitals across the UK, meaning the results from this study are likely generalisable to the wider UK population. The authors report that whilst the majority of UK hospitals supply MCAs, only 16.3% reported use of a formal system to target MCA provision to the most suitable patients[175].

In 2005, Ryan-Woollley and Rees reported the use of MCAs in a more favourable light by focusing on reduced medicines waste and improvements in patient-prescriber communication following dispensing of medicines. The authors report an 'exploratory

controlled, matched study' in which medicines wastage was reduced from 18.1% to pre study to 1% 12 months after a switch from conventional packaging to an MCA[176]. However, as medicines wastage data were not reported for the group of patients who continued to receive their medicines in conventional packaging, it is prudent to interpret these results with caution. The study is further limited by the small sample size of 62 sheltered housing residents from just one UK region.

More recently, Nunney and colleagues reported a qualitative study using grounded theory to establish the attitudes and beliefs of 15 older people living independently and using MCAs and 17 HCPs from all sectors of care regarding the use of MCAs. Maintenance of independence was paramount to the older patients but there was mixed views on whether the use of MCAs supported this; patients largely agreed that the aids did not help with memory problems and the MCAs were often initiated without patient consultation which was viewed by the patients as paternalistic. In their conclusion, the authors rightly call for further evidence for the use of MCAs in older patients and emphasise the importance of careful multi-disciplinary evaluations before an MCA is initiated and the need to consider and respect patients views[177].

Whilst there is a paucity of evidence regarding the use of MCAs, the evidence that is currently available has led to the recent issuing of guidance which advises that other avenues of support, such as reminder charts and dose simplification should be explored before considering an MCA[178].

Administration aids

Specific aids to facilitate administration of medicines have been developed including the pill press® to facilitate de-blistering of tablets, the haleraid® to support co-ordination of inhaler actuations with breathing and the auto-dropper® to aid administration of eye drops. These devices are intended to address physical barriers to adherence where dexterity problems associated with conditions such as Parkinson's disease or arthritis may be prohibitive.

Salyani and Birt describe an evaluation of eye drop administration aids and conclude that whilst useful to some patients, some found them to be counterproductive[179]. This evidence highlights the importance of rejecting a "one size fits all" approach to adherence interventions and the need to tailor support to meet the needs of an individual.

Modern technology

In recent years, advances in technology have enabled internet and text message based reminded systems to be trialled and with smartphone use now common place, 'Apps' to support adherence are also commonly available. Whilst formal evaluation of these techniques is still to be provided, indications show great promise and such techniques are likely to increase their precedence in the future[180, 181].

1.7.3 Cognitive based strategies

In recent years, an interest in improving non-adherence using psychological based techniques has emerged. Techniques to improve patients' motivation to adhere, or address negative illness and medicines perceptions are likely to be more effective for intentional non-adherence. The health psychology theory underpinning these techniques is considered in detail in chapter three of the thesis.

1.8 Chapter summary

The WHO has summarised the consequences of non-adherence in simplistic terms as waste, morbidity and hospital admissions[7]. Medication adherence is a complex and multifaceted process and a plethora of factors may determine patient behaviours in this domain. Though research in this field is wide-spread, the deficit in effective interventions to improve adherence is well noted.

Educational and behavioural techniques may have some effect and practical strategies such as reminders, adherence aids and dose regimen simplification may prove to be effective in cases of unintentional non-adherence where memory and dexterity problems prevail. However, the efficacy of such interventions is likely modest and is not always predictable. For intentional non-adherence, there is a deficit in an appropriate and effective armoury of interventional strategies to modify behaviour. This deficit may be addressed by the emergence of newer 'cognitive based techniques' which employ psychological theory to modify patient behaviours. The potential application of these newer techniques to pharmacy-led adherence intervention is considered in greater depth in chapters three, four and five. However, before considering future adherence interventions, an evaluation of current practices was prudent. Chapter two therefore describes the evaluation of a domiciliary medicines support service which is primarily designed to support unintentional non-adherence.

Chapter Two Domiciliary Medicines Management Service Evaluation Study

2.1 Introduction and background

Non adherence to prescribed medicines is both complex and multifaceted, causing a notable problem in healthcare provision. In chapter one, the nature of non-adherence and strategies to improve it were described. This chapter evaluates a domiciliary medicines management service and its impact on non-adherence of a primarily unintentional nature.

2.1.1 Cambridgeshire Community Services (CCS) NHS Trust Domiciliary Medicines Management Service

Cambridgeshire Community Services (CCS) NHS Trust provides an established domiciliary medicines management service in the East Cambridgeshire and Fenland area, which is reportedly valued by both service users and healthcare professionals (HCPs). The aim of the service is to provide support to patients having difficulties with the management of their medicines.

The majority of patients visited are older and confused; however, any patient experiencing medicine related difficulties can be referred into the service, which is delivered by a specialist pharmacy technician (SPT). The service takes a patient-centred approach, tailoring resolution strategies to meet individual needs whilst considering the patient's overall circumstances and views. In light of the evidence for effective adherence interventions[16, 173], a patient-centred service which is holistic in nature is appropriate. Recommendations from The National Institute for Health and Clinical Excellence (NICE) relating to adherence support, namely that patients should be involved in decisions about their care[182] are also complemented by the patient-centred service design. This approach differs from many medicines support services, which focus purely on provision of assistive technology such as reminder alarms or multi-compartment compliance aids (MCAs). Such devices are often costly interventions with limited evidence of effectiveness[173-176].

Delivery by a SPT is relatively unique as domiciliary medicines support services are usually provided by pharmacists[183, 184]. Using SPTs compared to pharmacists, plus implementation of support strategies other than assistive technology, are potentially effective approaches to reducing costs.

Whilst numerous reports of successful outcomes from the CCS NHS Trust service are encouraging, anecdotal reports are insufficient to scientifically evaluate the efficacy and value of the service. A rigorous service evaluation was therefore undertaken.

2.1.2 Pharmacy Technician led services

To work as a pharmacy technician, a level three NVQ Diploma in Pharmacy Service Skills is required, taking approximately two years to complete[185]. Senior technicians can specialise in areas such as medicines management, recording whether patients are adherent to their medicines and ensuring patients know how to take their medicines correctly[186]. Accredited training to enable this specialisation, includes consultation skills, pharmaceutical care planning, adverse drug reactions, clinical topics and care of older people[187]. Many Primary Care Organisations have employed specialist technicians to work alongside pharmacists in providing medicines support services[188].

Despite evidence of pharmacy technician involvement in current medicines support services, there are no published reports of domiciliary visiting services delivered solely by pharmacy technicians. An evaluation of a technician led service, or at least description of activities undertaken, will enable comparisons to be made with previously reported pharmacist led services.

2.1.3 Pharmacy domiciliary visiting services

2.1.3.1 Definition

Domiciliary visits provide an opportunity for a pharmacist or pharmacy technician to visit a patient in their own home and support their medication taking and pharmaceutical care needs.

2.1.3.2 Context and background

The premise of a domiciliary visit stems from the founding principles of the National Health Service (NHS), whereby a universal and comprehensive service should be provided with equal access to all[189]. In an aging population, an ever growing number of older, frail or housebound patients are unable to receive the same pharmaceutical care as ambulatory patients who can easily visit their community pharmacy. In 1999, Oxley reported that 58% of UK based older people receiving multiple medicines, were unable to collect their prescription in person, and were thus unable to directly access pharmaceutical care[190]. It is often these patients, who may be vulnerable, confused and prescribed numerous medicines that need additional support to adhere. A lack of direct contact with pharmacy services may lead to compounding of simple problems (such as misunderstandings) over time[191], with a subsequent detrimental impact on medication adherence, efficacy and safety.

Domiciliary visits also enable assessment of medicines management practices in the patient's own home. This provides a broader perspective and allows detection of adherence related issues that may otherwise go unobserved such as inappropriate storage of medicines or hoarding[192]. The increased privacy provided by home-based reviews may also encourage more honest and open adherence discussions[193].

2.1.3.3 Health policies and government guidelines

In 2001, The Department of Health released The National Service Framework (NSF) for Older People, a key policy document outlining proposed objectives for improving the quality of care received by older people. Recommendations included moving towards person-centred care, whereby all older people are treated as individuals and a range of medicines management interventions. The most notable recommendation impacting on the provision of domiciliary services was the direction that all Primary Care Trusts (PCTs) should have schemes in place to allow older people to get more help from pharmacists with managing their medicines by April 2004[194]. As a consequence, PCT pharmacists and technicians developed medicines support services to fulfil the requirements of the NSF, effectively providing an adherence intervention as a domiciliary visiting service. Domiciliary services shifted from being novel, experimental, community pharmacy-led services towards PCT delivered services to target older patients with medicine management problems. The NSF for older people also recommended regular medication reviews for older patients to maximise therapeutic benefits and minimise potential harm. Pharmacy based domiciliary services therefore enable housebound patients to receive medication reviews and address other medicine related aspects of the NSF[195].

More recent publications and policy guidelines have maintained the move towards supporting older people to continue living in their home and with such changes, the need for domiciliary services is ever growing. In 2004, The Public Service Agreement[196] set targets for increasing the number of people aged over 65 living in their own homes, through supported care. These targets were supported by the government White Paper, 'Our health, our care, our say', published in 2006[197], which recommended changes that would lead to more integrated health and social care systems, enabling the delivery of services that better meet the needs of local populations. Subsequently, the provision of care for older people increasingly shifted from secondary to primary care. Further publications have reiterated the need for this shift[195,196,198,199].

2.1.4 Research evidence relating to domiciliary visiting services

Studies concerning domiciliary medicines support services and home-based medication reviews are predominantly UK based. A mixture of Randomised Controlled Trials (RCTs), before and after studies and cohort studies provide insights into the medicines management problems encountered by patients, the types of interventions made and the associated health outcomes. A brief summary of the current research base for domiciliary medicines support services is provided in table 2.1 and summarised in the subsequent sub-sections.

2.1.4.1 Medicines management difficulties experienced by patients; the need for domiciliary services

A small, UK based observational study (N=39), reported that 54% of participants had one or more medicine related problem which may lead to non-adherence and/or administration errors. The main reasons for non-adherence were forgetfulness, confusion, poor understanding and side effects[200]. Whilst this study provides some useful insights, it is limited by the small sample size and study methods. In a prospective cohort study of 100 patients visited at home by their community pharmacist, 160 interventions were made and later classified as medicines management issues (55%), health beliefs and concordance (26%) and therapeutic problems/adverse effects (19%)[201].

2.1.4.2 Nature and types of interventions made

The interventions made in domiciliary visits are most frequently to facilitate improved medication adherence, commonly achieved via some form of medication review. Formats have included semi-structured interviews[201-203], informal discussions[200] or more structured, formal medication reviews[204-207].

In Schneider and Barber's 2006 study, the majority of interventions focused on simplification and clarification of medication regimen, clarification of any medication ambiguities and implementation of adherence support such as provision of non-child resistant closures to reduce dexterity problems[200]. Holland's HOMER study, a large RCT of home-based medication reviews in older people, reported similar interventions including organising large print labels for the visually impaired, non-childproof closures for patients with dexterity problems and, as far as feasible, ensuring dosing regimens fitted with patients routines[208]. However, the primary focus of the HOMER intervention was to provide medication review. The intervention also aimed to provide education to patients and carers, remove out of date drugs, report possible drug reactions and the

need for compliance aids. The interventions made in other studies tend to focus on similar support such as patient education about their medication[202, 207] and assessing the need for adherence aids[207]. Hawksworth and Chrystyn's intervention focused on a more clinical design, including medication reviews, therapeutic drug monitoring and checking other biochemical parameters. The service also assessed patients' healthcare needs, checked medication adherence and examined excessive medication stocks, removing any unwanted medicines where necessary[204].

2.1.4.3 Position of services within the care pathway

A proportion of research tends to focus on the period immediately following hospital discharge[202, 205]; a particularly hazardous time in terms of potential confusion and the risk of medication errors. Other studies have focused on patients living in the community who were referred into the service by their GP[191, 200] or other healthcare professionals[191], identified by their pharmacist[203] or who met predefined inclusion criteria[204 201 207].

2.1.4.4 Effect of domiciliary based interventions

Reported benefits of pharmacist domiciliary visiting services include potential prevention of unplanned hospital readmissions[204] and improved medication adherence[191 202, 203]. Further benefits also include, improved clinical outcomes and cost reductions[209] plus significant reductions in medicines related problems[203]. The mean number of medicines prescribed has been significantly reduced following a pharmacy-led medication review of older patients in their own homes[207] and reductions in inappropriate medicines storage and hoarding also elicited[208]. Recommended changes to therapy have also been deemed valuable by GP's[204]. A before and after study (N=143) of a tailored, pharmacist-led, home-based adherence intervention for older patients, reported significantly fewer medication related problems at follow up and significant improvements in adherence[203].

A large RCT of a home-based intervention delivered by both pharmacists and nurses (n= 762) reported a reduction in hospital admissions and deaths outside hospital[210], however it is not possible to establish whether it was the pharmacist or nurse led components which were effective. The follow-on study published by Stewart *et al.* a year later, did however only include nurse-led home visits[211].

A larger, UK based RCT (N=190), evaluated the impact of domiciliary visits on medication management in older patients who had recently been discharged from hospital[202]. Patients in the intervention group received five domiciliary visits over a

twelve month period and demonstrated significantly better adherence, better medicine storage practices and a decreased tendency to hoard medicines. They also required fewer GP visits or consultations than patients in the control group, who received standard care. The authors concluded that the service was effective in detecting medicine related problems in a potentially high risk group. In this, and all of the aforementioned studies, participants were identified by selecting patients matching pre-defined inclusion criteria from either hospital or pharmacy records. This method is not comparable to 'real-life' services where patients are identified by healthcare providers based on their individual need. This limitation in the current body of knowledge is an important consideration, as this deficit could be addressed by formally evaluating a domiciliary service provided in a naturalistic setting.

The HOMER trial (N= 872) was an RCT to determine whether a pharmacist-led home-based medication review affected hospital readmission rates in older people[205]. Older patients, recently discharged from hospital and who met broad pre-defined inclusion criteria were randomised to intervention or standard care. Intervention group patients received two home visits to provide medicines education and remove any unwanted medicines. Liaisons with the patients GP's and community pharmacists were also made to rectify any medication related problems. The intervention was associated with a significantly higher rate of hospital readmissions and did not significantly improve quality of life. Although there were fewer deaths in the intervention group, this was also non-significant. The authors of the HOMER study acknowledge that the reasons for these counter-intuitive findings are not known but suggest four possible explanations:

1) The possibility of chance effects

2) That the advice given enabled patients to present to their GP with problems earlier

3) That the improved adherence increased previously avoided side effects/ adverse events

4) That the intervention increased patient anxiety and confusion leading to greater dependence on health services

A follow-on report to HOMER[208], identified positive impacts from the pharmacists' visits, including identification of adverse drug reactions (ADR's) in 33% of patients and a significant reduction in inappropriate medicine storage and hoarding. These findings, especially the detection of ADR's may support Holland's previously postulated notion[205] that the increase in hospital readmissions were actually warranted, to address issues such as ADR's that may otherwise have gone undetected. The economic evaluation of

the HOMER study reported a 25% probability of intervention cost effectiveness and therefore concluded that the likelihood of cost effectiveness is low[212].

A small number of other domiciliary medicines support studies have also included some form of simple cost analysis. Hawksworth and Chrystyn's clinical domiciliary pharmacy service (n=50) was crudely evaluated from a financial perspective by assessing the costs saved through avoided hospital admissions, based on data from a clinical panel that assessed the likelihood of readmissions. The estimated cost saved, exceeded the remuneration necessary to fund the service and cost savings made through removal of excess, unwanted and out of date stock also inferred cost efficacy[204]. Whilst the inclusion of an independent clinical panel to assess the importance of the interventions made, strengthens the study design, the conclusions made may have been premature generalisations based on a sample size of just fifty patients. The subjective method of valuing the intervention also introduces a limitation.

Removal of unwanted medicines and a reduction in the number of regularly prescribed medication, has also been used to demonstrate that such services represent a good use of NHS resources[203]. More recently, Desborough *et al.* undertook a simple cost-consequences analysis of the Norfolk Medicines Support Service; a pharmacist-led service based on provision of MCAs[183]. The evaluation, which assumed a before and after study design and was based on 117 patients, reported a mean cost saving of £307 per patient following the intervention, plus reduced hospital admissions and improved medication adherence. Whilst these studies provide a useful insight into the potential cost savings associated with domiciliary support services, the limitations of the before-and-after study design should be acknowledged.

2.1.4.5 Outcome measures used to determine effect

A common aim of pharmacy-led domiciliary services is to improve medication adherence, therefore, it is unsurprising that medication adherence is a commonly used outcome measure[183, 200, 202, 203] as demonstrated in table 2.1. Two of these studies assessed medication adherence via self-report[183, 203], one used pill counts[200] and one used both pill counts and patient interviews[202]. Other outcome measures have included emergency hospital readmissions[205-207], care home admissions[207], healthcare utilisation data[206, 209], medication related risks of harm[213], patient deaths[205-207] and patient quality of life[183, 205, 207, 209].

Whilst multiple studies provide evidence for improvements in outcome measures such as adherence, reducing medicine related problems and reducing inappropriate

medicine storage and hoarding, when outcome measures such as quality of life and hospital admissions are used, the evidence for positive effects becomes less clear. It is therefore evident that no single, gold-standard outcome measure is available for evaluation of domiciliary medicines support services.

Paper	Year	Location	Sample size	Study type	Intervention details	Outcome measures	Delivered by	Delivered to	Key results
Begley *et al.*[202]	1997	UK	190	RCT	Assessment of knowledge, dexterity & cognitive functioning plus advice on storage & use of medicines	Adherence (pill counts and interviews). GP consultations.	Pharmacist	Older patients recently discharged from hospital	Significantly better adherence, better drug storage & decreased hoarding. Fewer GP consultations or visits.
Coleman *et al.*[201]	2001	UK	100	Cohort study	3 home visits	Peer assessed impact on patient care	Community pharmacist	Older patients	Favourable/ important impact on patient care in most cases.
Desborough *et al.*[183]	2012	UK	117	Before & after study	Home-based medication review	Self-reported adherence and quality of life	Pharmacists	Non-adherent patients aged >65 years	Increased medication adherence. No significant changes in health-related QOL.
Dilks[184]	2007	UK	468	Service evaluation	General medication review, stock checks, counselling, adherence support & clinical monitoring	None – characterisation of practice	Domiciliary pharmacists	At risk housebound or older patients	Unnecessary medicines stopped, new medicines recommended & medicines synched
Foulsham & Goodyer[191]	1999	UK	90	Cohort study	Semi-structured interview to assess medicines difficulties	Appropriateness of referrals	Pharmacist	Community patients	Little difference in appropriateness of referral between GP, nurse & social services
Hawksworth & Chrstyn[204]	1997	UK	50	Cohort study	Medication review, TDM, adherence checks, removal of excessive stocks & unwanted medicines	Patient risk of harm, unplanned hospital readmissions	Community pharmacist	Older patients	Prevention of unplanned hospital readmissions. Reduced likely harm to patients.
Holland *et al.*[205]	2005	UK	872	RCT	Medication review, education & removal of unwanted drugs.	Emergency hospital readmissions, death & QoL (EQ-5D)	Community and hospital pharmacists	Older patients recently discharged form hospital	Significantly higher rate of hospital readmissions in intervention group.

Table 2.1 Summary of research evidence relating to domiciliary medicines support services

Paper	Year	Location	Sample size	Study type	Intervention details	Outcome measures	Delivered by	Delivered to	Key results
Lenaghan *et al.*[207]	2007	UK	136	RCT	Education, ID pharmaceutical care issues, assess need for adherence aids	Admissions to hospital or care homes, deaths, & QoL (EQ-5D)	Community pharmacists	Patients aged >80 years, living at home	No difference in hospital admissions, care home admissions or death.
Raynor *et al.*[203].	2000	UK	143	Before and after study	ID of adherence problems. Individual action plans to revise medication regimens.	Self-reported adherence	Community pharmacists	Patients aged >65 years, living alone	Significant reduction in medication problems and improved patient adherence
Schneider & Barber[200]	1996	UK	39	Cohort study	ID adherence problems and hoarding	Adherence (pill counts)	Community pharmacists	Housebound patients	Non-adherence due to forgetfulness, confusion, poor understanding & side effects
Sorensen *et al.*[209]	2004	Australia	400	RCT	Education, medication review, multidisciplinary action plans	Health-related QoL, ADRs, GP visits	GPs and pharmacists	At risk community based patients	No differences in health related QoL. ADRs and GP visits reduced
Stewart *et al.*[211]	1999	Australia	200	RCT	Multidisciplinary, home-based intervention	Unplanned hospital readmissions, out-of-hospital deaths	Cardiac nurse	Heart failure patients discharged from hospital	Significant reduction in unplanned hospital readmissions and out-of-hospital deaths in intervention group
Waddingham[213]	2012	UK	50	Service evaluation	Domiciliary medicines management service	Patient risk of harm from medicines	Specialist pharmacy technician	Community based patients	Reduction in risk of harm from medicines following intervention

Table 2.1 (continued) **Summary of research evidence relating to domiciliary medicines support services**

2.1.5 The need for a service evaluation; application of background knowledge to research methods and study design

The deficit in reports of pharmacy technician led domiciliary medicines support services, coupled with the need to provide more conclusive evidence of service benefit, beyond anecdotal reports, highlights the need for formal evaluation of such a service.

In addition to providing evidence of service efficacy and patient value, this service evaluation will provide an opportunity to characterise service provision, and gather valuable data regarding the recipients of a technician-led service and the interventions utilised in supporting their adherence. This will provide a 'snap-shot' assessment of community pharmacy-based services to improve non-adherence of a primarily unintentional nature.

Outstanding methodological questions with regard to choice of outcomes measures in this domain can also be considered in undertaking the service evaluation.

2.1.5.1 Selection of outcome measures

The primary aim of the CCS NHS Trust domiciliary services is to improve medication adherence, therefore, inclusion of an adherence based outcome measure is necessary. Whilst electronic monitoring is the gold-standard approach, the frequent provision of MCAs in these services is problematic. Technologies to enable electrionic monitoring with MCAs are available, but costly. Moreover, changes to packaging to accommodate electronic monitoring had potential to confuse an already vulnerable population with cognitive impairments. Electronic monitoring of medication adherence was therefore rejected as a feasible outcome measure. Pill counts require multiple home visits thus are costly and as described in chapter one, the monitoring may alter patient behaviour[158]. Whilst self-reported medication adherence has known problems of bias and recall difficulties, it is inexpensive and of low burden to participants and thus deemed to be an appropriate measure of medication adherence for this study.

Table 2.2 summarises the desirable characteristics of the self-report adherence assessment tool which were carefully considered to ensure appropriate data collection and suitability for use in the population in question.

Characteristic	Rationale
Simplicity and brevity of use	To ensure a good response rate, especially in population with cognitive impairments
Well designed and unambiguous	To facilitate ease of use
Assessment of adherence to all medicines prescribed, not individual medicines	Replication of tool for each medicine would be unacceptably long and complex given the expected poly-pharmacy & cognitive impairments
Continuous scale rather than dichotomous responses	To ensure sufficient sensitivity for identification of changes in frequency of non-adherent behaviours
Detection of broad range of non-adherent behaviours	To identify non-adherence of both an intentional and unintentional nature
Non-threatening, non-judgemental and open phrasing of questions	To encourage a good response rate and honesty

Table 2.2 Desirable characteritsics for an adherence assessment tool

The self-report adherence assessment tools identified in chapter one, were deemed too brief to elicit sufficiently detailed information[144] or too complex and lengthy for the population in question[146, 152, 154]. They were also rejected for their lack of relevance to this study[153] and dichotomous type responses[144, 145]. None of the tools evaluated were intended for use on generalised medication adherence rather than specific medications, therefore tools such as Horne's Medication Adherence Rating Scale (MARS), were also rejected. The deficit in appropriate, validated tools demonstrated a need to develop a novel adherence assessment tool for use within the population likely to receive a domiciliary visit.

Previously reported outcome measures such as healthcare utilisation data, emergency hospital admissions and patient deaths were deemed unintuitive and potentially misleading in a population where progressive decline is anticipated. Health-related quality of life was also rejected as an outcome measure, due to an anticipated lack of sensitivity for the intervention in question and general irrelevance which could confuse respondents.

Beyond improving medication adherence, a key focus of the service is to improve patient safety and support patients to keep living in their own homes by reducing the risks associated with medicines mismanagement. A means of detecting any reductions in the patient's risk of harm following the intervention was therefore an intuitive outcome measure, in addition to self-reported medication adherence. The National Patient Safety Agency (NPSA) have developed a commonly used risk matrix tool[214], where risk scores are calculated by combining estimates of consequence (severity or outcome) and likelihood (frequency or probability) to produce an overall score ranging from 1 indicating rare negligible harm through to 25 indicating almost certain

catastrophic harm. Although not validated for use in research, reports of the NPSA risk matrix's use in assessing medication related risks of harm are available[215, 216]. However, the methods used to assign the risk scores in these studies are either not described[215] or lacking in both rigour and detail[216]. In this study, an indication of validity was obtained by comparison of the risk scores obtained with the NPSA risk matrix, to those obtained with the Fuller's risk tool. This tool was validated and refined for use in April 2004[217, 218] to identify medicine related risks of harm and consists of seven domains. The reliability of the NPSA risk tool, amongst multiple raters was also explored, representing a novel research application.

Beyond self-reported medication adherence and patient's risk of harm from their medicines, additional outcome measures included:

- Patient satisfaction with the service – an intuitive outcome for a service evaluation, assessed via the Client Satisfaction Questionnaire (CSQ-8)[219]; a widely used a validated tool which is simply worded and easily understood[220].
- Patients' perceived changes in confidence and ability to manage their medicines following the intervention – to assess the anecdotally reported additional benefits of the service, using an adaptation of a previously validated tool[221].
- Caregiver satisfaction with the service – using an adapted version of CSQ-8[219] to enable alternate data collection where cognitive impairment is prohibitive of patient self-completion of the CSQ-8 questionnaire.
- Changes to caregiver feelings following the intervention - to assess the anecdotally reported additional benefits of the service, using an adaptation of a previously validated tool[221].

The adaptations to the patient confidence[221] and satisfaction tools[219] are summarised in the methods section and table 2.3.

2.2 Service evaluation aims and study methods

2.2.1 Aims

To describe the interventions within a pharmacy technician-led domiciliary medicines management service and to assess service impact on patient adherence and medication related risk of harm.

2.2.2 Objectives

- To describe the nature of the pharmacist technician intervention, including visit, patient and medication details
- To describe and quantify any changes in patient adherence and risk scores following intervention
- To establish the level of agreement between healthcare professionals in assigning risk assessment scores to patients pre and post intervention
- To explore agreement between the Fullers and NPSA risk assessment tools
- To quantify patient satisfaction with the service and changes in patient ability and confidence with the management of their medicines
- To quantify and describe patient caregiver satisfaction with the service and their feelings about providing care following the intervention

2.2.3 Methods overview

The UEA's Faculty of Health Ethics Committee confirmed that as a service evaluation study, full NHS ethical approval was not necessary (appendix 2.1). Given that the study involved an evaluation of a routinely provided service and would (primarily) involve analysis of existing data, the study was classified as a service evaluation according to the National Research Ethics Service (NRES) definitions[222].

A service evaluation of the CCS NHS Trust Domiciliary Medicines Management Service was undertaken using routinely collected and patient reported data. Patients were referred into the service in the standard way and received the usual domiciliary visit, during which routine data were collected. Additionally, pre-intervention self-reported adherence was elicited using a patient questionnaire. Following the intervention, patients and where appropriate patients' caregivers, were posted a service evaluation questionnaire to determine service impact and satisfaction. In addition to the data from the questionnaires, information gathered from the domiciliary visits was used to calculate each patient's risk of harm from their medicines at both the pre and post intervention stage.

2.2.4 Patient identification and recruitment

Patients could:

- self-refer
- be referred by a carer or relative
- be referred by a healthcare professional such as a GP or district nurse
- be referred by a paid carer, support worker or social services representative

2.2.5 Inclusion criteria

Patients referred into the CCS NHS Trust service and who received their initial visit during a four month recruitment period from February to June 2012.

2.2.6 Exclusion criteria

There were no exclusion criteria for study participation.

2.2.7 Outcome measures

Two primary outcome measures were used in the study:

1. Change in patient adherence following the intervention
2. Change in patient's medication related risk of harm following the intervention

Secondary outcome measures included:

- Patient and patient caregiver satisfaction with the service
- Changes in patients perceived confidence and ability to cope with medicines
- Changes in patient caregiver feelings

2.2.8 Domiciliary visiting process

A flow chart summarising the study procedures and methods is provided in figure 2.1.

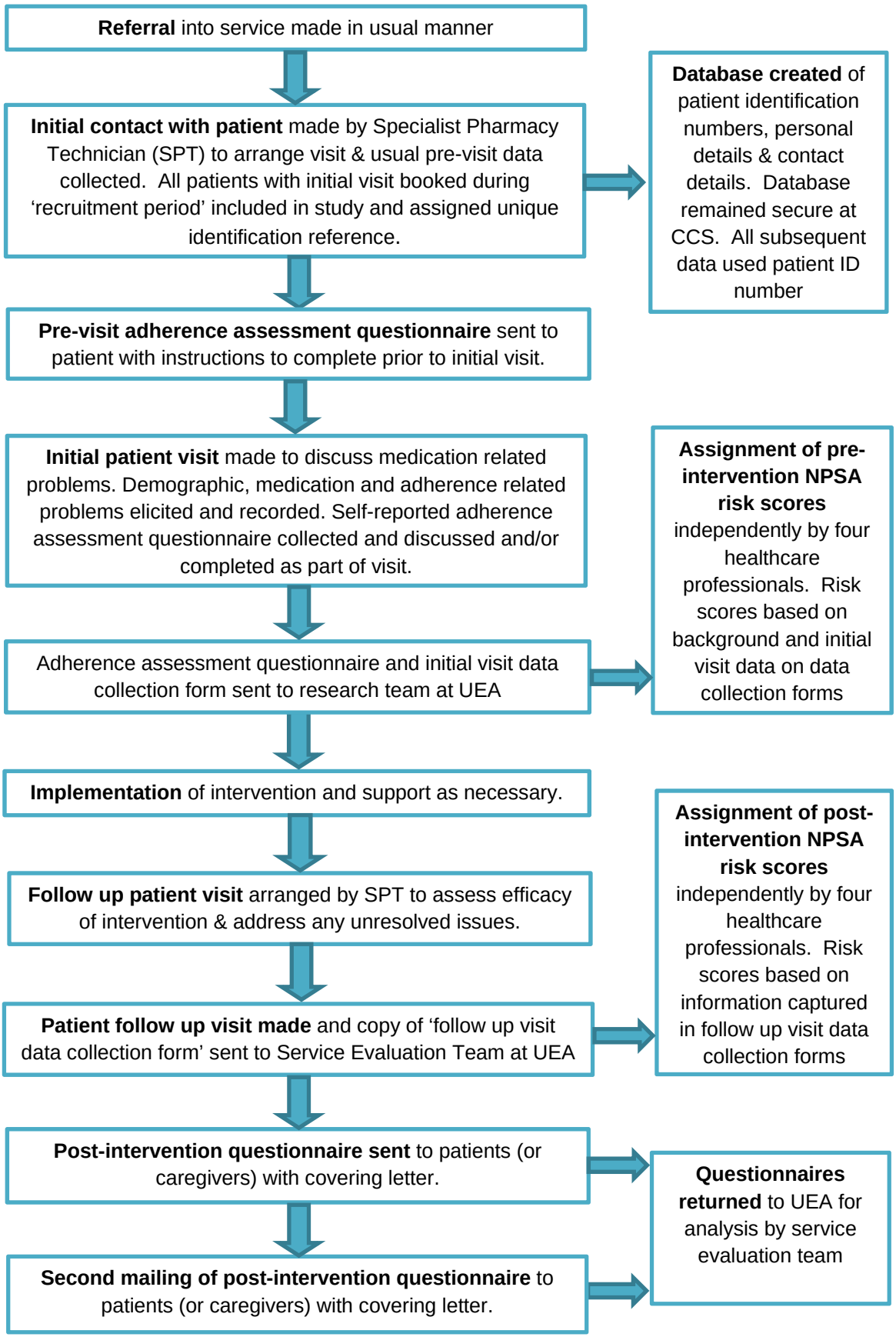


Figure 2.1 Data collection and analysis flow chart

2.2.8.1 Patient referral into the service

The Specialist Pharmacy Technician (SPT) prioritised referrals according to details of the medicine related problems provided at the point of referral. Before visiting the patient, the SPT gathered the relevant information needed, such as details of prescribed medicines from the patient's GP and frequency of prescription collection from the local pharmacy.

2.2.8.2 Arranging the initial visit

All patients were contacted via telephone to arrange an initial visit and asked to complete the adherence assessment questionnaire prior to the SPT's visit to enable its discussion. The adherence assessment questionnaire was posted to patients once the initial visit had been confirmed, with instructions for completion. A unique patient identification reference was assigned to each patient to ensure all data were anonymous. The corresponding patient details to identify the patient reference were securely stored at CCS NHS Trust.

2.2.8.3 The initial visit

During the visit the SPT elicited further details about the difficulties experienced by the patient in taking their medicines. All potential avenues of support and assistance were fully explored, and the intervention provided was tailored to meet individual needs. Where possible, patients were involved in all decision making processes. Detailed notes of the visit were recorded on a data collection form (appendix 2.2) which included:

- Demographic data including patient age, gender and whether they lived alone or with a carer or relative
- Number of regularly prescribed medicines
- Details of the medicine related problems and likely risks
- Details of any physical and cognitive difficulties experienced and their current level of support provision
- Details of the intervention

The design and content of the initial visit data collection form was informed by the Fuller's risk screening tool (see figure 2.5), as this data would be used to assign risk scores later. For details such as cognitive or physical difficulties, formal assessment tools were not used as this was deemed to be beyond the remit of the study and not advised for use with the Fuller's risk tool[223]. Instead a subjective assessment was

made by the SPT based on the patient and pre-visit data, for example, for a patient who appeared to be muddled with their medicines, confused by the days of the week and who confessed forgetting to take their medicines, the SPT would record this patient as 'confused and forgetful'.

The adherence assessment questionnaire was also, where possible, discussed during the initial visit to further clarify the nature and magnitude of patient non-adherence. In instances where the patient had not completed the questionnaire in advance, where possible, the SPT administered the questionnaire verbally during the visit.

After the initial visit, the SPT sent the anonymised 'initial visit data collection form' and adherence questionnaire to the UEA research team.

2.2.8.4 Implementation of the interventions recommendations

The processes of intervention implementation were variable according to the patient's needs, for example, some patients needed their medication dispensed in a compliance aid, in which case the SPT liaised with the patient's GP and local pharmacy to arrange for provision. Alternatively, some patients needed simplification of their medication regimen, in which case the SPT liaised with the patient's GP to suggest changes.

2.2.8.5 Follow up visit

Post intervention implementation, the SPT re-visited the patient to assess intervention effect and whether any further support was necessary. The interval between the initial and follow up visit varied according to patient need. Details of the follow up visit were recorded on a data collection form (appendix 2.3) and posted to the UEA service evaluation team for data extraction and the dissemination to the panel of risk scorers.

2.2.9 Content and design of questionnaire based tools

2.2.9.1 Pre-intervention adherence screen

Figure 2.2 shows the adherence assessment tool that was developed by critique of pre-existing adherence assessment tools, (described in chapter one) and consideration of the study population. The tool consisted of nine statements to represent commonly cited reasons for non-adherence, such as 'I forget to take my medicines' or 'I have difficulty swallowing my medicines'. For each statement, the patient was asked to indicate how often this led to them taking their medicines differently to prescribed, using a five point Likert scale ranging from always to never. A five point scale

represented the best opportunity to capture meaningful data, without over burdening respondents with excessive options.

The chosen 'reasons' for non-adherence covered both intentional and unintentional non-adherence, with both primary and secondary unintentional non-adherent behaviours gaining representation. In any other population, more 'reasons' such as not taking medicines due to concerns over side effects or fear of embarrassment may have been included. However, given the limitation of needing to keep this tool as simple and brief as possible, a maximum of nine 'reasons' was chosen as this was deemed to be a reasonable compromise between eliciting comprehensive information and not overburdening respondents. Furthermore, by choosing a maximum of nine 'reasons', the tool could be kept to one side of A4 sized paper; a feature important to the overall questionnaire design and layout[141, 150].

Each statement on the questionnaire was scored on a five point scale with a response of 'always' scoring five points, through to a response of 'never' scoring one point. The scores for each statement were then added together to give an overall score ranging from nine to 45 with higher scores indicative of greater non-adherence.

Domiciliary Medicines Management Service – Initial Assessment

Many people have difficulty taking their medicines or find a way to use their medicines which best suits them.

- The statements listed below are common situations that people experience.
- For each statement, please tell us how often these lead to you taking your medicines differently to the instructions on the label or from your doctor. Please **tick (✓)** the response that best reflects how you feel.

I take my medicines differently to instructed because:	Always	Often	Some-times	Rarely	Never
I have difficulties opening medicine packaging, or using items such as inhalers or eye drops	❑	❑	❑	❑	❑
I have difficulties swallowing my medicines	❑	❑	❑	❑	❑
I struggle to read the instruction labels	❑	❑	❑	❑	❑
I have difficulties in remembering what time to take each medicine	❑	❑	❑	❑	❑
I forget to take my medicine	❑	❑	❑	❑	❑
I forget when to order or collect my medicines from the doctor or pharmacy	❑	❑	❑	❑	❑
I choose to alter the dose of my medicines if I feel better or worse	❑	❑	❑	❑	❑
I choose to miss out doses of my medicines if I feel better or worse	❑	❑	❑	❑	❑
I choose to stop taking my medicines for a while	❑	❑	❑	❑	❑

Figure 2.2 Adherence assessment tool developed for use in study

2.2.9.2 Patient questionnaire

The patient questionnaire (see appendix 2.4) was designed to elicit information that could not be gathered during the domiciliary visits and was posted to patients after their follow up visit, along with a covering letter (appendix 2.5). Each questionnaire was re-mailed two weeks after the original mailing with a slightly amended covering letter (appendix 2.6) explaining that the second mailing was a reminder in case the first questionnaire had been forgotten or misplaced. Patients were advised to ignore the second mailing if they had already returned the first questionnaire.

In recognition of the population in question and the possible levels of confusion, the salient points from a patient information sheet were incorporated into the covering letter. Patients were therefore provided with all of the information needed to decide whether to complete the questionnaire, but paperwork was kept to a minimum to reduce the likelihood of confusion. Patients were asked to complete the questionnaire and return it to the UEA using the pre-paid envelope provided. Provision was also made for completion of the questionnaire over the telephone to accommodate potential visual, literacy or dexterity difficulties.

The patient questionnaire comprised of three sections:

1. **Self-reported medication adherence** – to elicit post-intervention medication adherence, using the same tool as the pre-intervention adherence screen.

2. **Patient confidence and ability to manage their medicines and health** – to assess any changes in patients' feelings towards managing their medicines and health following the intervention. Based on a previously validated patient enablement tool[221].

3. **Patient satisfaction with the service** – based on the Client Satisfaction Questionnaire (CSQ-8)[219]

The second and third sections of the questionnaire were based on validated tools, but amended slightly to increase their relevance and to facilitate simplicity and brevity of use for the vulnerable questionnaire recipients. A summary of the changes made to and the rationale for these changes is provided in table 2.3.

Questionnaire section	Changes made	Rationale for changes
Patient confidence and ability	Removal of two statements relating to coping with and understanding illness	Deemed irrelevant to the purpose of the intervention
	Minor amendments to format and wording	To improve consistency and patient acceptability
	Splitting and rewording the 'same or less' response option	To enable differentiation between no improvements and worsening ability and/or confidence
	Removal of 'not applicable' response option	Deemed surplus to requirement as 'same' option could be used when statement did not apply, plus improved ease of scoring
Patient satisfaction	Removal of 'did you get the kind of service you wanted' statement	Considered irrelevant as majority of patients do not know what to expect
	Removal of 'to what extent has the service met your needs' statement	Removed due to potential confusion of patients
	Removal of 'if you were to seek help again would you choose the service again' statement	Removal due to irrelevance and potential confusion
	Changing response options to unidirectional format	To facilitate simplicity of patient use and reduce cognitive burden

Table 2.3 Summary of changes to validated tools used in patient questionnaire

2.2.9.3 Patient caregiver questionnaire

This questionnaire (appendix 2.7) was sent to patients' informal caregivers following the intervention, where deemed appropriate by the SPT and/or requested by the caregivers. A covering letter was mailed with the questionnaire (appendix 2.8). Patient caregivers were provided with a pre-paid envelope to return the completed questionnaire directly to the research team at UEA.

The caregiver's questionnaire comprised of two sections:

1. **The carer's feelings as a caregiver** – designed to establish any effects of the service in terms of the caregiver's anxiety, stress, confidence and time commitments. This section was developed from the 'confidence and ability' sections of the patient questionnaire.

2. **The carer's satisfaction with the service** - consisting of the same five questions used in the patient satisfaction questionnaire, with amended wording to reflect completion by the caregiver rather than patient.

2.2.10 Public and patient involvement

NHS Norfolk's Patient and Public Involvement in Research (PPIRes) service[224] was utilised to provide feedback on the questionnaires and study methods. Feedback from a panel of ten members of the public, from diverse backgrounds, led to minor formatting and wording amendments in the questionnaires and covering letters to improve readability and clarity of instructions. Changes to the questionnaire front page were also implemented to ensure that in the event of losing the covering letter, patients would still be able to complete and return the questionnaires.

2.2.11 Piloting

Data were collected for ten patients, prior to commencing full data collection to ensure feasibility of the data collection process and suitability of the questionnaires. The data collection forms were subsequently amended to improve ease of use and ensure all data were captured unambiguously.

Four patient questionnaires and five patient caregiver questionnaires were returned, with complete, accurate data and no suggestions for improvement, thus inferring questionnaire acceptability. The only questionnaire change was therefore to remove the 'not applicable' option from the section on confidence, as detailed previously.

The pilot phase also revealed that assignment of pre-intervention risk scores using both the NPSA and Fuller's tools was excessively labour intensive. As the Fuller's tool was comparatively more objective and also previously validated, the lead researcher assigned risk scores using the Fuller's tool, without the need to take a mean score from four HCPs.

2.2.12 Data analysis

2.2.12.1 Assignment of patient pre and post intervention risk scores using NPSA risk matrix[214]

Risk assessment scores were calculated independently, by a panel of four healthcare professionals (HCPs) using the data collected on the initial and follow up visit data collection forms. The panel of four HCPs comprised of a GP, nurse, community pharmacist and hospital pharmacist, selected from a convenience sample. This

process was informed by the work of Dean and colleagues[225, 226] who reported that only four HCPs comprised of; doctors nurses and pharmacists were needed to give high generalisability of hospital medication administration error scores. A mean score from any four HCPs (ideally including a doctor, nurse and pharmacist) was both a reliable and valid approach [225].

For each patient included in the service evaluation, the HCPs were asked to calculate a pre and post intervention risk score using the NPSA risk matrix as illustrated by figure 2.3. The risk scores assigned by each HCP were collated by the service evaluation team at UEA to determine the mean risk score pre and post intervention for each patient. To allow for mean risk scores that did not fall within the NPSA's specified ranges, the risk category boundaries were adjusted as detailed in figure 2.4. The 'low' risk category remained unchanged, but the 'medium' risk group increased by one to include risk scores of 7. The 'high' risk category was also extended by one to include risk scores up to 13 and the 'extreme' risk group was altered to include risk scores of 14.

In addition to the pre and post intervention risk scores assigned using the NPSA risk matrix, a pre-intervention risk score was also assigned using the Fuller's risk screening tool, as detailed in section 2.2.12.2.

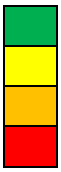
	Likelihood				
Consequence	**1**	**2**	**3**	**4**	**5**
	Rare	**Unlikely**	**Possible**	**Likely**	**Almost certain**
5 Catastrophic	**5**	**10**	**15**	**20**	**25**
4 Major	**4**	**8**	**12**	**16**	**20**
3 Moderate	**3**	**6**	**9**	**12**	**15**
2 Minor	**2**	**4**	**6**	**8**	**10**
1 Negligible	**1**	**2**	**3**	**4**	**5**

Risk scoring = consequence x likelihood (C x L)

For grading risk, the scores obtained from the risk matrix are assigned grades as follows:

1 – 3	Low risk
4 – 6	Moderate risk
8 – 12	High risk
15 – 25	Extreme risk

Figure 2.3 NPSA Risk matrix[214]



1-3	Low risk
4-7	Medium risk
8-13	High risk
14-25	Extreme risk

Figure 2.4 Risk score category boundaries for NPSA risk matrix (altered to accommodate for mean scores assuming full range of values)

The use of the NPSA risk matrix can be exemplified by considering a hypothetical patient, typical of those evaluated in the service. The pre-intervention data could describe an 82 year old female living alone with moderate cognitive impairment who is prescribed multiple medicines including antihypertensives, opioid analgesics and warfarin. This patient has formal carers who administer her medicines but the carers have noticed that the patient tampers with her medicines in between care calls and often takes additional doses or hides the medicines so that the carers can then not administer them. Based on this pre-intervention data and using figure 2.2, a risk scorer may consider the consequence of harm to be 'major' (scoring 4) given the potential for under or overdosing on medicines such as opioids and warfarin and the likelihood of harm to be 'possible' (scoring 3) given the carers concerns. This risk scorer would therefore assign a pre-intervention risk score of 12 (4x3). However, based on the same data, another risk scorer may consider the consequence to be 'catastrophic' (scoring 5) given the risk of warfarin overdose and the likelihood to be 'almost certain' (scoring 5) given the additional doses known to be taken between care calls; this risk scorer would therefore assign a pre-intervention risk score of 25 (5x5). The remaining two risk scorers may perhaps assign pre-intervention risk scores of, for example, 15 and 16, therefore this patient's mean pre-intervention risk score would be 17. Figure 2.3 shows that a risk score of 17 would be considered as 'extreme risk'.

At the post-intervention stage, the data provided to the risk scorers summarises the intervention. Whilst there have been no changes in the patients cognitive state, prescribed medicines or social circumstances, the SPT intervened to provide a locked briefcase for storage of the medicines, to which only the carers had access. This intervention meant that the patient could no longer tamper with their medicines in between care calls, could not take additional doses and all medicines were safely administered by the carers. Based on this data, one of the risk scorers may now consider the likelihood of harm from medicines (in this instance taking additional doses) to be 'rare' (scoring 1) given the new intervention but, given the medicines prescribed, consider the consequence to still be major (scoring 4); this risk scorer would therefore

assign a post-intervention risk score of 4 (1x4). A different risk scorer may however take a different stance and instead of focusing on the risk of overdose which has now been negated, question the clinical appropriateness of the medicines, given that a clinical review was not performed. This risk scorer may consider that medicine related harm is 'possible' (scoring 3) which could have 'moderate' consequences (scoring 3) and therefore assign a post-intervention risk score of 9 (3x3). If the remaining two risk scorers assigned risk scores of 5 and 6, then mean post-intervention risk score for this patient would be 6, placing them in the 'medium' risk category.

2.2.12.2 Assignment of patient pre intervention risk scores using Fuller's risk tool[223]

Data collected during the initial visits were used by the principle investigator to assign pre intervention risk scores to all patients, using the Fuller's risk scoring tool detailed in figure 2.5.

					Score
Number of prescribed medications	**1** 1 drug	**2** 2 drugs	**3** 3 drugs	**4** 4 or more drugs	
Mental state	**1** Alert and orientated	**4** Orientated but sometimes forgetful	**8** Confused, muddled/ disorientated/ very forgetful	**12** Very confused/ forgetful	
Vision	**1** Can see to read with no aids	**2** Needs glasses/aids to read print	**4** Difficult to read print with glasses/ aids	**6** Unable to see	
Social circum-stances	**1** Living with others who can fully support medication needs	**2** Living with others who usually/ sometimes support medication administration	**3** Living alone with some help from paid carers or family/ friend	**4** Living alone with no help	
Physical condition	**1** Can manage to open bottles/ packets independently	**2** Weakness of hand/ poor co-ordination, but can manage to open bottles/ packets with difficulty	**3** Disabled. Requires some help to open bottles/ packages	**4** Severely disabled unable to manage	
Attitude and knowledge about medicines	**1** Interested about prescribed medicines and knows all about them, believes they are important	**2** Fairly interested about prescribed medicines and knows enough about them to administer them safely/ believes they are important	**8** Not very interested in prescribed medicines. Does not believe they are important/ unable to recall medicines regime	**12** Disinterested and/or unwilling to take prescribed medication	
6-13 Low risk 14-16 Medium risk 17-22 High risk 23-42 Very high risk					**TOTAL**

Figure 2.5 Fuller's self-medication risk assessment screening tool[223]

2.2.12.3 Statistical analysis and data manipulation

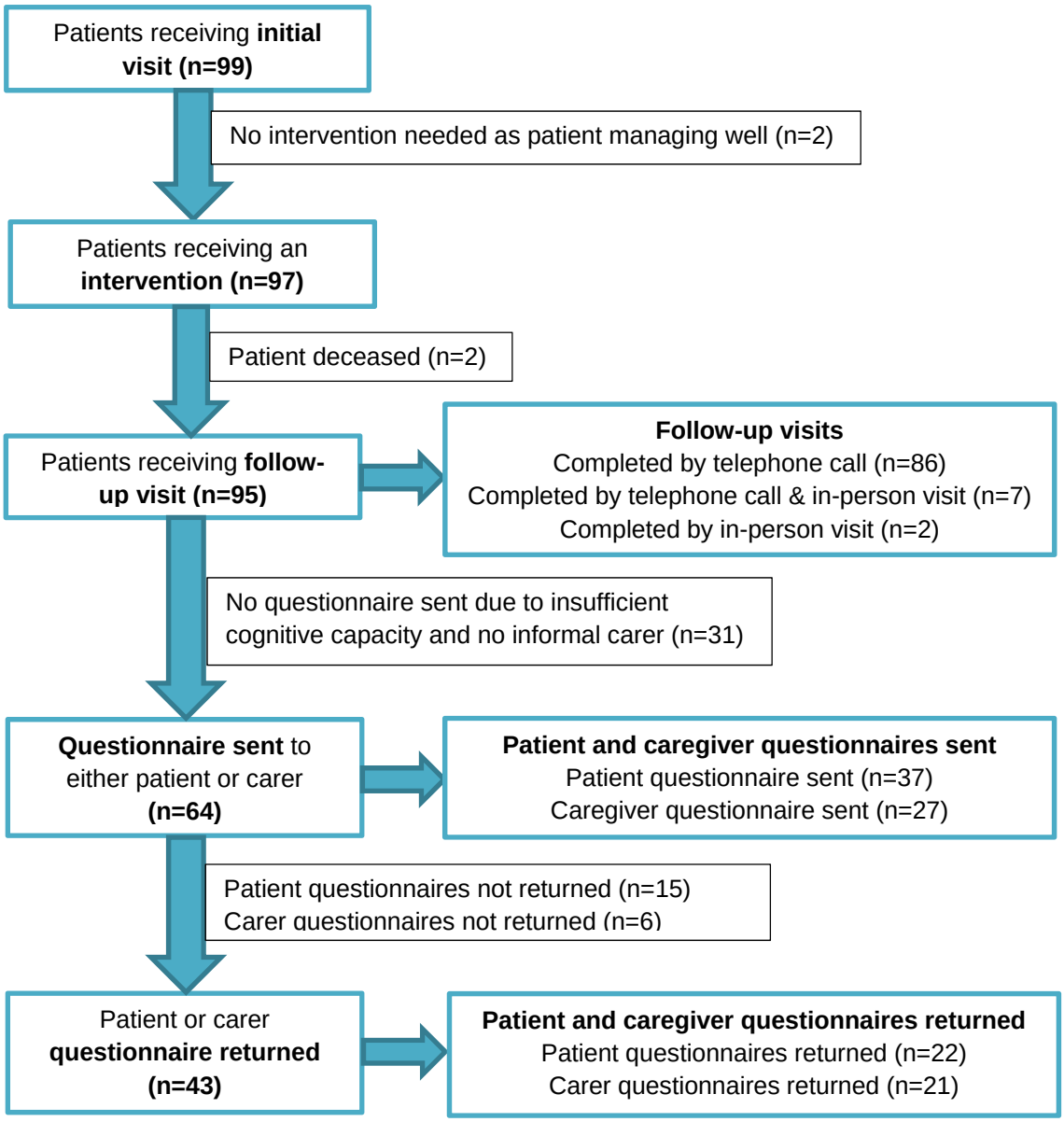
Appropriate descriptive statistics were used to characterise the population in terms of demographics, medication related problems, types of intervention, patient risk assessment scores pre and post intervention, patient adherence pre and post intervention, patient and caregiver satisfaction with service, patient confidence with their medicines and health and patient caregiver feelings following the intervention. A summary of the statistical analyses undertaken is provided in table 2.4.

Objective	Variables	Statistical test	Rationale
To determine significance of changes in SPT reported adherence post intervention	Proportion of patients categorised as fully adherent pre & post intervention	McNemar's chi-squared	Dichotomised, nominal repeated measures data
To determine significance of changes in patient reported adherence	Median adherence score pre intervention and post intervention	Wilcoxon Signed Ranks	Repeated measures non-parametric data
To assess agreement between patient and SPT reported adherence problems	All patient and SPT reported adherence problems	Kappa co-efficients with average proportions of agreement for positive (P_{pos}) and negative responses (P_{neg}).	Kappa suitable for two raters, and nominal data. High prevalence of negative responses (no adherence problems) meant P_{pos} and P_{neg} were needed to avoid biased interpretations of kappa [227, 228]
	Adherence problems reported by patients 'always'		
	Adherence problems reported by patients 'often'		
	Adherence problems reported by patient 'sometimes'		
To determine significance of any changes in the ranking of NPSA risk score categories post intervention	Risk score categories pre and post intervention	Wilcoxon matched pairs test	Repeated measured ordinal data
To establish inter-rater agreement for NPSA risk scores	NPSA risk scores assigned by four different HCPs	Kendall's co-efficient of concordance (*W*)	Literature recommended test for ordinal data and multiple raters[229]
To establish inter-rater reliability between HCPs in assigning NPSA risk scores	NPSA risk scores assigned by four different HCPs	Two-way, random, consistency, average-measures Intra-Class Coefficient (ICC)	Literature recommended assessment of inter-rater reliability[230]
To establish agreement between risk scores assigned using two different risk assessment tools	Pre-intervention risk scores assigned using NPSA risk matric and Fuller's risk tool	Two-way, random, absolute agreement, average-measures Intra-Class Coefficient (ICC)	ICC equivalent to weighted kappa (for ordinal data) under general conditions[231]
To compare degree of reported cognitive function between recipients and non-recipients of the patient questionnaire	Number of patients in each cognitive function category and whether or not they received a questionnaire	Mann-Whitney U	Two independent groups (recipients and non-recipients) with ordinal dependent variable

Table 2.4 Summary of statistical analyses undertaken

2.3 Results

A flow diagram summarising the patients included and data collected is provided in figure 2.6. Whilst the majority of patients provided both pre and post intervention data, post-intervention questionnaires from either the patient or their informal carers were only returned for 43.4% of patients.



Note all 99 patients receiving an initial visit had a pre-intervention risk score using the NPSA risk matrix and Fuller's risk screening tool plus SPT adherence assessment

All 95 patients receiving a follow up visit had a post-intervention risk score calculated using the NPSA risk matrix plus SPT adherence assessment

Figure 2.6 Flow diagram to summarise patients included in the study and data collected

Figure 2.7 shows the flow of data for patients' self-reported adherence. Loss to follow up caused a notable problem for this outcome measure as pre and post intervention data were only available for ten patients.

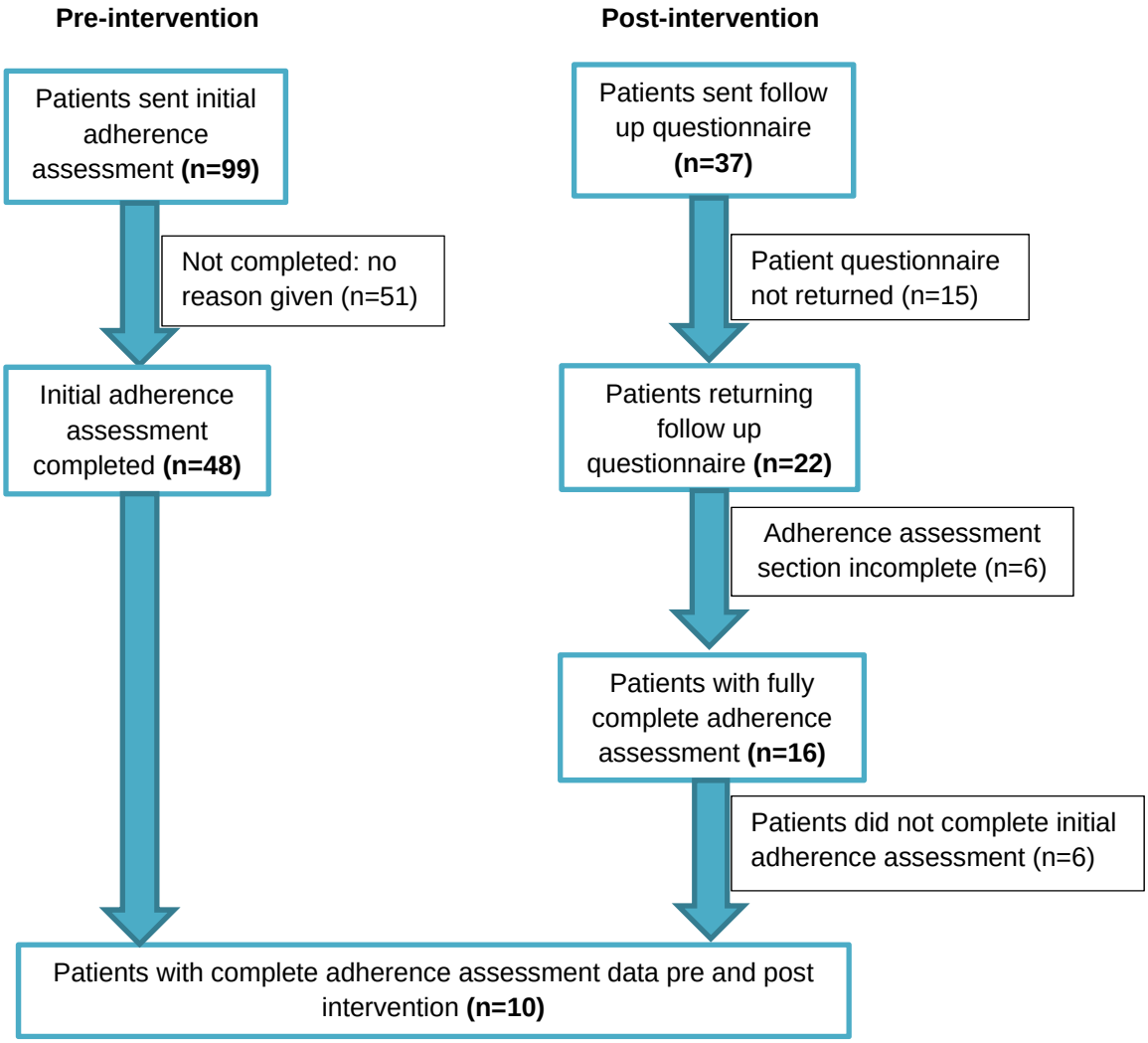


Figure 2.7 Summary of data collection for patient reported adherence data

2.3.1 Domiciliary support service recipients

In total, 99 patients were included in the study; 69 (69.7%) of patients were female. Table 2.5 summarises the key patient characteristics, as captured on the data collection forms. Patients were primarily older, with a median age (IQ range) of 82 (76 to 86) years. Of the 83 (83.8%) patients with some degree of cognitive impairments, 47 (48.5%) were slightly confused and/or slightly forgetful, 12 (12.1%) were very confused and/or forgetful and 23 (23.2%) had a formal diagnosis of dementia (or under investigation).

Patients tended to be living alone and this was the case for 63 (63.6%) patients; 22 of whom (34.9%) had no additional help or support in their medicines taking. Whilst most

patients could access their medicines independently and with ease, 14 (14.6%) patients reported struggling to do so and 22 (22.9%) required assistance with accessing or administering their medicines.

The majority of patients were interested in their medicines, thought their medicines were important and were willing to take their medicines. However, 53 patients (54.5%) were not knowledgeable about their prescribed medications and could not recall their regimens. A majority of patients were reported as being unable to administer their medicines safely, and this was the case for 58 patients (59.8%).

2.3.2 Prescribed medicines

All patients were prescribed multiple medicines, with a median (IQR) of 9 (7 to 12) medicines per patient at the pre-intervention stage. The median number (IQR) of doses taken daily, for regular use was 12 (7 to 19).

The most commonly prescribed group of medicines, according to British National Formulary (BNF) chapter, were those affecting the cardiovascular system totalling 35.4% of all prescriptions. Medicines affecting the central nervous, endocrine and gastro-intestinal systems accounted for 19.1%, 15.7% and 11.2% of all prescriptions respectively. Proton Pump Inhibitors (PPIs) were found to be the most commonly prescribed therapeutic group, accounting for 6.5% of all prescriptions. The most commonly prescribed medicine was paracetamol; 39.4% of patients had this medicine on their repeat list.

Patient Characteristic	Categories & number (%) of patients				
Co-habitation status	Living alone 63 (63.6%)	Living with partner 33 (33.3%)	Living with family member 1 (1.0%)	Living in care home 1 (1.0%)	Other 1 (1.0%)
Mental state	Alert and orientated 17(17.2%)	Slightly confused and/or slightly forgetful 47 (48.5%)	Very confused and/or very forgetful 8 (8.2%)	Dementia under investigation 4 (4.1%)	Formal diagnosis of dementia 23 (23.7%)
Vision	Able to read without aids 70 (75.3%)	Needs glasses or aids to read print 6 (6.5%)	Struggles to read print even with aid or glasses 9 (9.7%)	Illiterate 4 (4.3%)	Registered blind 3 (3.2%)
Social circumstances	Living alone but with help from friends, family or carers 46 (47.4%)	Living alone without any help 22 (22.7%)	Living with someone who supports their medication needs 15 (15.4%)	Living with someone who does not support their medicines needs 9 (9.3%)	Other 5 (5.2%)
Physical condition	Can access all medicines independently and with ease 60 (62.5%)	Requires assistance with accessing or administering medicines 17 (17.7%)	Can manage to access all medicines but struggles 14 (14.6%)	Has difficulty swallowing medicines 3 (3.1%)	Severely disabled and unable to mange 2 (2.0%)
Attitude towards medicines	Shows interest in medicines 76 (79.2%)	Believes medicines are important 92 (95.8%)	Willing to take medicines 91 (93.8%)	Able to administer medicines safely 35 (35.6%)	Able to recall medication regimen 35 (36.5%)

Table 2.5 Summary of patient characteristics at pre-intervention stage

2.3.3 Details of the domiciliary visits

2.3.3.1 Referrals into the service

Healthcare professionals (HCPs) accounted for 42 (42.9%) referrals. Within this group, nurses accounted for 19 referrals (45.2%) and there were 11 GP referrals (26.2%). Other sources of referral within the group of HCPs included psychiatrists, occupational therapists and speech and language therapists.

Referrals from 'social' based sources, such as care-agency co-ordinators and housing scheme managers, accounted for 27 (27.6%) referrals in total. Friends and family members accounted for 12 (12.2%) referrals and there were six (6.1%) self-referrals. The remaining 11 referrals (11.2%) came from pharmacy staff or prescription clerks at the local surgery.

2.3.3.2 Reasons for referral into the service

Figure 2.8 provides a summary of the reasons for referral into the service. The majority of referrals related to some kind of cognitive impairment with 39 referrals (39.4%) made due to concerns over the patient's failing memory, confusion, being known to forget to take their medicines or because of a recent diagnosis of dementia.

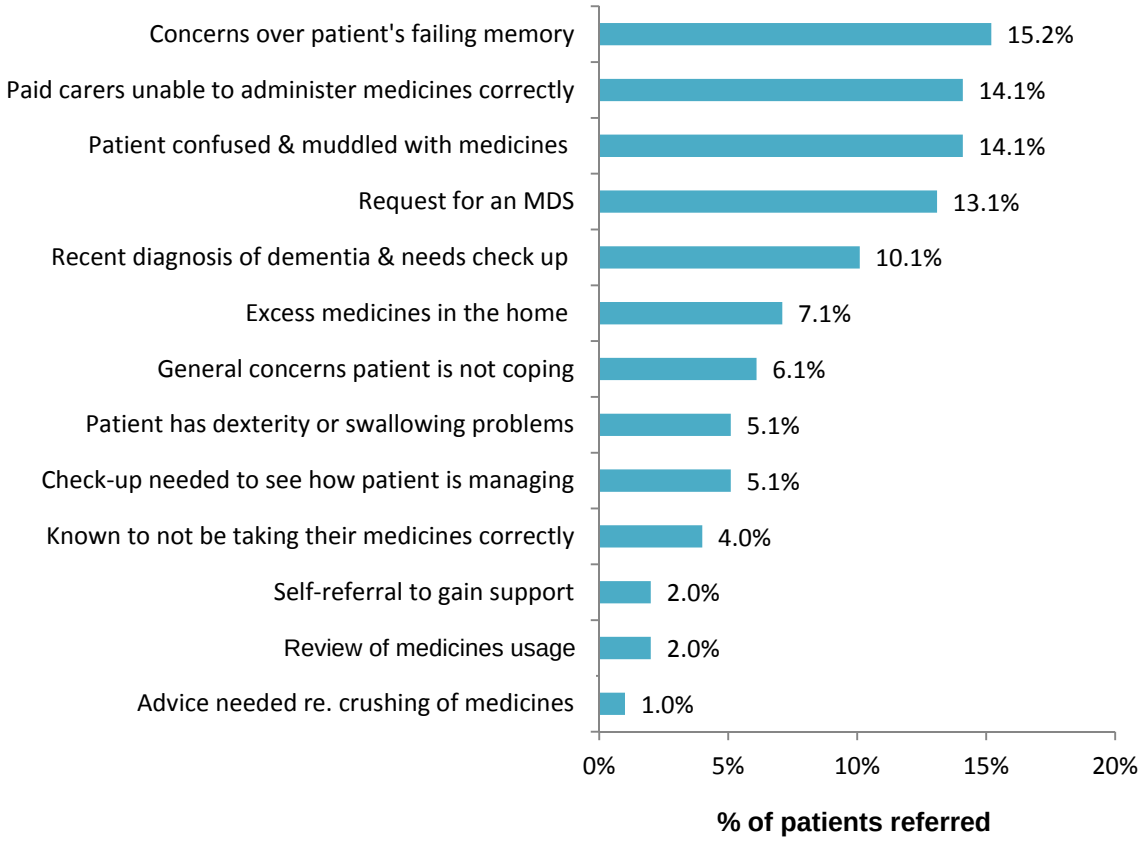


Figure 2.8 Summary of reasons for patient referral into service

2.3.4 Identification and management of medication difficulties

A wide range of medication related difficulties were identified, with all bar two patients experiencing some form of difficulty which required intervention. The vast majority of medication related difficulties were associated with non-adherence, as reported in section 2.3.5.1.

2.3.4.1 Medication difficulties unrelated to adherence

In addition to the medication difficulties associated with non-adherence, 29 patients (29.3%) also experienced difficulties which were not specifically associated with adherence such as excessive stock holding and inaccurate repeat medication lists. Table 2.6 provides a summary of the medication difficulties experienced that were unrelated to adherence and the resolution strategies deployed by the SPT to overcome these. The most common medication difficulty that was not directly related to adherence was the presence of discontinued medicines on the patient's medication repeat list, followed by the presence of excessive stocks of medicines in the patient's home. On four occasions, the build-up of excessive medication was due to community pharmacies automatically reordering all of the patient's medicines each month, without checking what was required first. For the 29 patients that had medication problems unrelated to non-adherence at the initial visit stage, 89.7% had these problems resolved by the follow up stage.

Medication difficulty	No. (%) patients affected	Resolution strategy utilised by SPT	Outcome
Discontinued medicines on repeat list	10 (10.1%)	Query need for medication at GP surgery (n=10)	Re-initiation of medication considered necessary (n=4)
			Redundant medicines removed from repeat list (n=6)
Excessive medication stocks in patients home	8 (8.1%)	Removal of excess medicines (n=8)	Excessive medicines stocks avoided (n=8)
		Patient counselled not to order each month (n=1)	Prevention of recurrence of excessive stock build up (n=1)
		Medication added to an MCA (n=2)	Prevention of recurrence of excessive stock build up (n=1)
		Locked box provided to stop patient access to medicines (n=1)	Only carers can access medicines so patient cannot interfere or stockpile (n=1)
		Community pharmacy based automatic reordering stopped (n=4)	Prevention of recurrence of excessive stock build-up of unwanted items (n=4)
Packaging difficulties	2 (2.0%)	De-blistering device provided (n=1)*	Improved access to medicines (n=1)
Sight impairment	2 (2.0%)	Provision of a filled MCA (n=1)	Patient able to take medicines safely (n=1)
		District nurse to visit and monitor blood glucose levels (n=1)	Blood glucose monitoring could resume safely (n=1)
Experience of side effects	2 (2.0%)	Discuss problem with patient's GP	Patient switched to an alternative without side effect
Swallowing problems	1 (1.0%)	Discuss problem with patient's GP	Patient switched to liquid formulation
Inappropriate prescribing	1 (1.0%)	Discuss problem with patient's GP	Patient switched to an alternative medicine
Medication not on repeat	1 (1.0%)	Discuss problem with patient's GP	Medication added to patient's repeat list

* The other patient with difficulties accessing their packaging had passed away by the follow up visit

Table 2.6 Summary of medication difficulties experienced by patients (unrelated to adherence), resolution strategies deployed by the SPT and outcomes

2.3.4.2 Interventions recommended for medication related difficulties

Table 2.7 provides a summary of all interventions recommended following the initial visit. Of the 190 recommended interventions, the two most common types were provision of some form of MCA and provision of some form of advice to patients.

Intervention delivered	No (%) patients receiving intervention	% of total interventions delivered
Provision of advice to patient	43 (43.4%)	22.6%
Provision of an MCA	43 (43.4%)	22.6%
Liaison with other parties to resolve issues	34 (34.3%)	17.9%
Provision of a locked box/briefcase for storage of medicines in patients' home	23 (23.2%)	12.1%
Removal of unnecessary/inappropriate/unused medicines from repeat medication list	12 (12.1%)	6.3%
Provision of an adherence aid (reminder watch or chart, de-blistering device or Haleraid®)	9 (9.1%)	4.7%
Removal of unused/excess medication from patient home	8 (8.1%)	4.2%
Stopping unnecessary/confusing systems e.g. pharmacy filled MCA or repeat ordering system	6 (6.1%)	3.2%
No intervention needed	5 (5.1%)	2.6%
Other practical solutions e.g. synchronisation of medication or switching pharmacy	4 (4.0%)	2.1%
Arranging a second follow up visit to check on patient progress	2 (2.0%)	1.1%

Table 2.7 Summary of interventions delivered

Of the 43 MCAs supplied as an intervention, 22 (51.2%) were standard devices, without reminder technology, and were filled in a community pharmacy. A further six (14.0%) 'standard' MCAs were supplied to willing informal carers (patients friends or family) for self-filling rather than being filled in a pharmacy. The remaining MCA recommendations were for the Pivotell® device; there were seven (16.3%) recommendations for a pharmacy filled device and eight (18.6%) recommendations to loan a Pivotell® to willing informal carers to fill.

Patient advice included demonstration of how to use inhalers and compliance aids plus advice regarding the importance of taking medicines as prescribed and appropriate dosing regimens. Another common intervention was provision of a locked box/briefcase for storage of medicines in the patient's home so that only the carers could access the medicines, preventing the patient from accessing additional doses

between care calls or tampering with the medicines. This intervention occurred on 23 occasions, accounting for 12.1% of all interventions.

2.3.5 Patient adherence

2.3.5.1 SPT reported adherence at the initial visit stage

The majority of patients (66.7%) were recorded as either fully or partially non-adherent. Although almost a quarter of patients (24.2%) were classified as 'fully adherent', 14 of these patients (58.3%) still had problems to resolve, including patient worries about excessive medicines stocks and difficulties with local pharmacies. Fully adherent patients had also requested support because they wanted to manage their medicines independently without need for carers or were referred by family members who could no longer cope with providing the level of support necessary to facilitate adherence.

Twenty-two patients were classified as 'partially adherent' with deviations including taking some medicines at an incorrect dose or time, forgetting to take some medicines and failing to take medicines (e.g. eye drops) that were not in a Pivotell® device.

Of the 44 patients classified as 'non-adherent' 13 patients (29.5%) were identified as 'forgetting'. Non-adherence was also attributed to taking additional doses of medicines in between carer visits, which affected 11 patients (25.0%). Patients were also reported as being too confused to take their medicines, hiding their medicines from their carer so that they could not be administered and refusing to take their medicines in four (9.1%), three (6.8%) and two (4.5%) instances respectively. There were individual cases of swallowing difficulties, packaging problems, taking the wrong dose, forgetting and taking excessive doses and forgetting if medicines have been taken.

2.3.5.2 SPT reported adherence at the follow up visit stage

At the follow up visit stage, 88 patients (88.9%) were classified as fully adherent. All 24 patients reported as being 'fully adherent' at the initial visit stage were still fully adherent at follow up. Although all of these patients had maintained full adherence throughout the study, 15 patients (62.5%) had gained benefit from the SPT's visit, beyond confirming that they were taking their medicines correctly.

Improvements in medication adherence were also reported for the group of patients classified as 'partially adherent' at the initial visit stage with 17 of these patients (77.3%) recorded as fully adherent by the follow up visit.

At the initial visit stage, the SPT reported that it was unclear whether or not eight patients were adherent. At the follow up visit stage, seven of these patients (87.5%) were classified as fully adherent.

Of the 44 patients initially recorded as non-adherent, 35 (79.5%) had become fully adherent by the follow up visit, however, two patients (4.5%) remained non-adherent as they openly declared that they 'wished to die'. The remaining seven initially non-adherent patients included two patients (4.5%) who moved into residential care (becoming fully adherent though this was not directly related to the SPT's intervention) and two patients (4.5%) where their adherence remained unclear. Finally, one patient was deceased, one patient had their medicines administered via GP authorised covert administration and one patient was partially adherent as they took all of their medicines bar one from a Pivotell® device.

2.3.5.3 Comparisons between SPT reported adherence at pre and post intervention stage

Table 2.8 summarises the proportion of patients classified into each adherence category at the pre and post intervention stage, exemplifying the clear trend towards increased adherence following the intervention. With exclusion of cases where adherence was 'unclear' or the patient had died, 21 patients (25.0%) were fully adherent at the pre intervention stage, compared to 81 patients (96.4%) at the post intervention stage. This difference was statistically significant (*McNemar's X^2 = 58.02, 1df, p-value of <0.001*).

Adherence category	No. (%) patients at pre-intervention stage	No. (%) patients at post-intervention stage
Fully adherent	24 (24.2%)	88 (88.9%)
Partially adherent	22 (22.2%)	1 (1.0%)
Non adherent	44 (44.3%)	2 (2.0%)
Unclear/uncertain	8 (8.1%)	6 (6.1%)
Unreported	1 (1.0%)	0 (0.0%)
Deceased	0 (0.0%)	2 (2.0%)

Table 2.8 Patient adherence at the pre and post intervention stages

2.3.5.4 Patient self-reported adherence at the initial visit stage

Of the 99 patients receiving an initial visit, 48 initial adherence screens were completed (48.5%), of which 18 (37.5%) were completed by the patient prior to the visit and five (10.4%) were completed by a patient caregiver. Twenty patients (41.7%) completed

the adherence screen with the SPT's assistance during the initial visit. For five patients, the person completing the adherence screen (10.4%) was not recorded.

Figure 2.9 summarises the patient responses to the adherence statements, highlighting the variation in adherence difficulties causing non-adherence. The most common cause of non-adherence was 'struggling to read the instruction labels' with 14 patients (33.3%) stating that they 'always' or 'often' experienced this problem.

The mean (95% CI) medication adherence score pre intervention could be calculated from 42 (87.5%) questionnaires with complete data and was 37.3 (35.5 to 39.1) out of a possible 45 with higher scores indicating better adherence. Only two patients (4.8%) reported being perfectly adherent.

2.3.5.5 Patient self-reported adherence at the follow up visit stage

In total, 22 (59.5%) patient questionnaires were returned providing self-reported adherence data at the post-intervention stage of which 14 (63.6%) were completed by the patient themselves. A family member was responsible for the completion of four patient questionnaires (18.2%) with a friend/carer or somebody else each completing 2 of the returned patient questionnaires (9.1%).

The adherence assessment section was fully completed by 16 patients (72.7%), providing a mean (95% CI) total adherence score was 38.3 (36.0 to 40.6) out of a possible score of 45, with higher scores indicative of better adherence.

A summary of the patient responses is provided in figure 2.10 which highlights patients' tendency to report 'rarely' or 'never' engaging in the non-adherent behaviours represented by the questionnaire statements; this was the case for 79.6% of responses. Struggling to read instruction labels was the most frequent cause of non-adherence, with 10 patients (45.5%) reporting 'always', 'often' or 'sometimes' experiencing this problem.

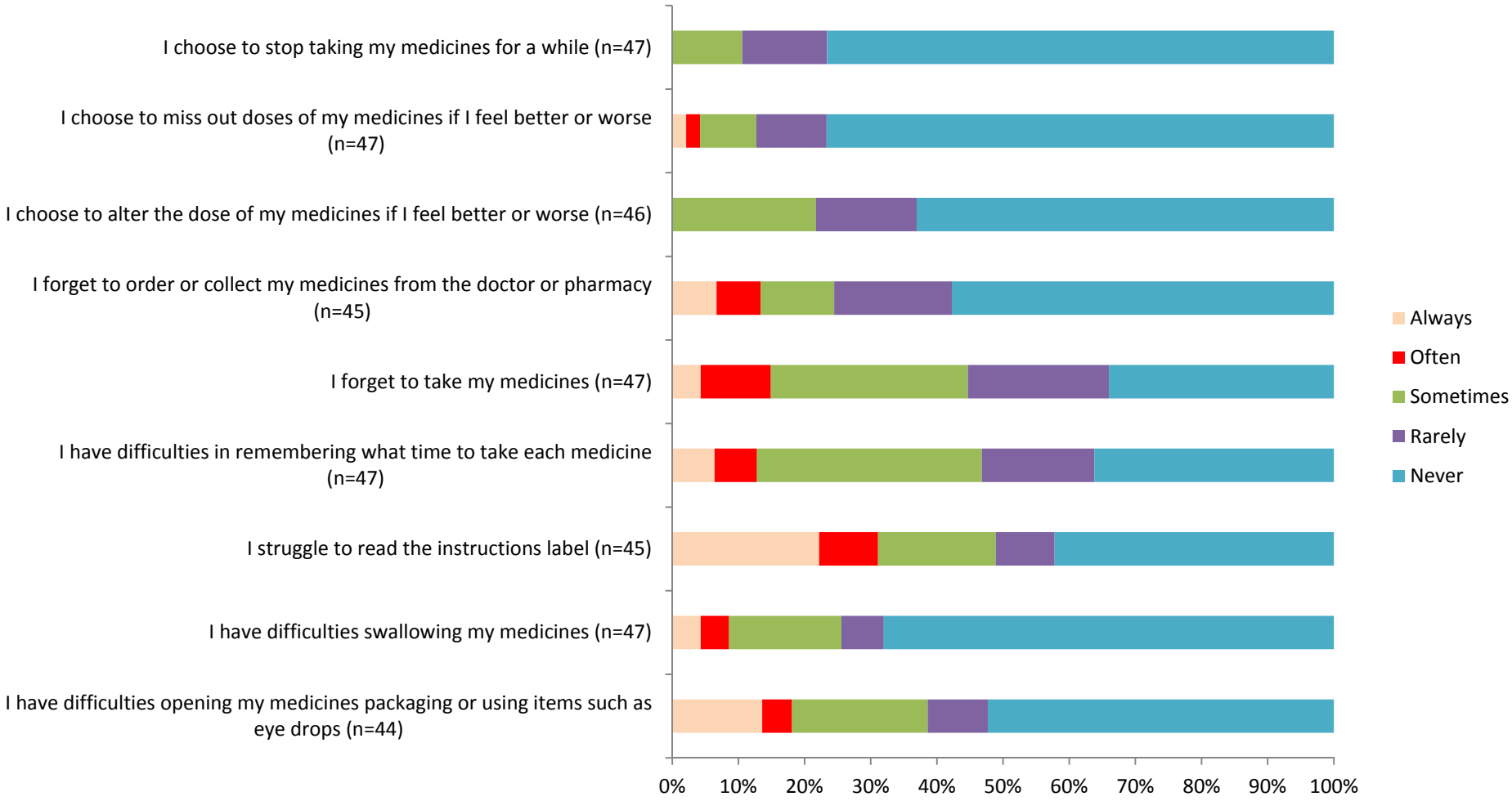


Figure 2.9 Summary of patient self-reported adherence pre-intervention

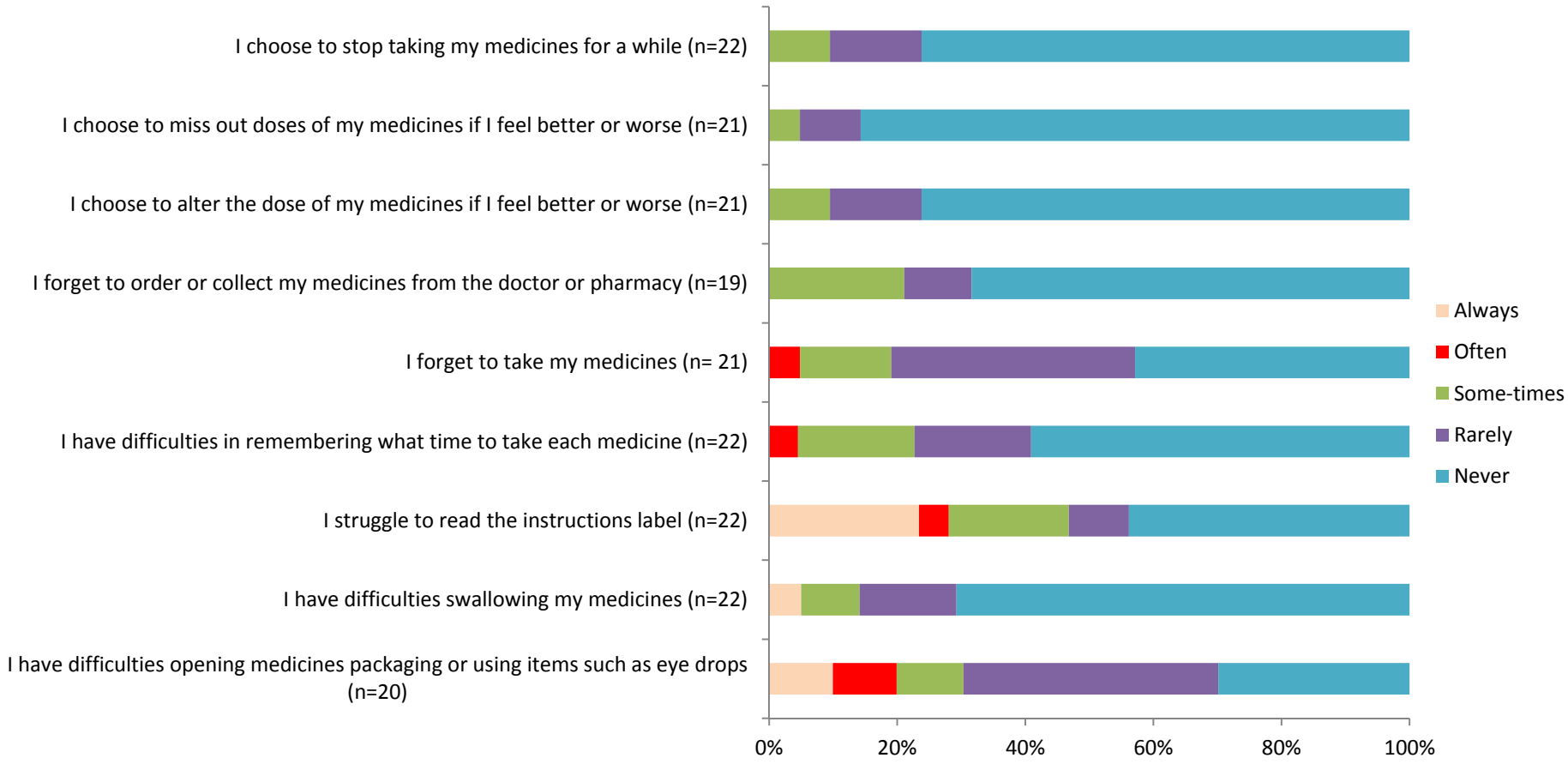


Figure 2.10 Summary of patient self-reported adherence post-intervention

2.3.5.6 Comparisons between patient self-reported adherence pre and post intervention

Due to the limitations of the questionnaire distribution process at the post-intervention stage, pre and post intervention self-reported adherence data were only available for ten patients. The data for these ten patients are summarised in table 2.9 and are consistent with the strong overall tendency for adherence at both the pre and post intervention stage and a lack of notable difference between the pre and post intervention data. The median (Interquartile range (IQR)) adherence score for these ten patients pre-intervention was 38.0 (36.0 to 40.6) with a post-intervention median (IQR) adherence score of 40.0 (34.5 to 44.0). This difference was not statistically significant (*P= 0.735, Wilcoxon signed ranks*).

	% of patients responding…									
	Always		Often		Sometimes		Rarely		Never	
I have difficulties opening medicines packaging or using items such as eye drops	0.0%	10.0%	0.0%	0.0%	40.0%	20.0%	10.0%	40.0%	50.0%	30.0%
I have difficulties swallowing my medicines	20.0%	0.0%	0.0%	0.0%	20.0%	20.0%	10.0%	20.0%	50.0%	60.0%
I struggle to read the instructions label	20.0%	30.0%	0.0%	10.0%	20.0%	0.0%	0.0%	10.0%	60.0%	50.0%
I have difficulties in remembering what time to take each medicine	0.0%	0.0%	0.0%	10.0%	20.0%	20.0%	30.0%	20.0%	50.0%	50.0%
I forget to take my medicines	0.0%	0.0%	0.0%	10.0%	20.0%	10.0%	20.0%	30.0%	60.0%	50.0%
I forget to order or collect my medicines from the doctor or pharmacy	0.0%	0.0%	0.0%	0.0%	0.0%	10.0%	30.0%	10.0%	70.0%	80.0%
I choose to alter the dose of my medicines if I feel better or worse	0.0%	0.0%	0.0%	0.0%	30.0%	10.0%	0.0%	10.0%	70.0%	80.0%
I choose to miss out doses of my medicines if I feel better or worse	0.0%	0.0%	0.0%	0.0%	10.0%	0.0%	0.0%	10.0%	90.0%	90.0%
I choose to stop taking my medicines for a while	0.0%	0.0%	0.0%	0.0%	10.0%	10.0%	0.0%	10.0%	90.0%	80.0%

Table 2.9 Pre and post intervention self-reported adherence (n=10)

2.3.5.7 Agreement between SPT and patient reported adherence problems at the initial visit stage

Table 2.10 summarises the agreement between the SPT and patient reported adherence problems at the pre-intervention stage. Multiple problems were frequently reported by both the SPT and patients. There were 11 cases where the SPT reported a problem that the patient did not**,** 59 cases where the patient reported a problem that the SPT did not and 64 cases where both the SPT and the patient reported a problem.

Whilst there was 'moderate' agreement between the SPT and patients for 'all cases', agreement was more likely on negative reports (no adherence problems) compared to positive reports (adherence problems) as highlighted by the P_{neg} and P_{pos} values respectively, though this difference is not vast. Moreover, with a narrow confidence interval around the kappa value, it is reasonable to conclude that agreement overall was 'moderate'.

For patients who reported 'always' experiencing an adherence difficulty, this problem was, in the majority of cases, also reported by the SPT, providing 'substantial' agreement that was statistically significant. Patients reported three cases of 'always having difficulties reading medicines instructions labels' and four cases of 'always having difficulties with medicines packaging or devices' that were not recorded as difficulties by the SPT.

Instances of patients reporting 'often' experiencing adherence difficulties were reported by the SPT less frequently, yielding a lower kappa value in the 'fair' range. The imbalance of agreement between negative reports and positive reports is also more notable at this stage, reducing the confidence with which the Kappa value is trusted, as reflected in the wider confidence interval. The favouring of agreement in negative cases over positive may infer that the kappa value is exaggerated.

Instances of a patient reporting 'sometimes' experiencing an adherence problem were also commonly not recorded by the SPT, though the Kappa value falls in the 'moderate' range. This could however be elevated by the higher proportion of agreement on negative ratings compared to positive. The adherence difficulty of 'sometimes struggling to swallow medicines' was the most commonly reported problem that the SPT had not recorded with all seven patient reported cases not having this documented in the patients notes.

Patient reported adherence problems	No. problems reported by patients	No. (%) also reported by SPT	Kappa (95% CI)	P-value	Agreement *	P_{pos}	P_{neg}
All cases	123	64 (52.0%)	0.55 (0.46 to 0.64)	<0.001	Moderate	0.65	0.89
'Always'	26	19 (73.1%)	0.66 (0.51 to 0.80)	<0.001	Substantial	0.68	0.98
'Often'	17	7 (41.2%)	0.37 (0.16 to 0.59)	<0.001	Fair	0.40	0.97
'Sometimes'	77	37 (48.1%)	0.53 (0.41 to 0.64)	<0.001	Moderate	0.59	0.93

*Landis and Koch scale[232]

Table 2.10 Agreement between patient and SPT reported adherence problems at the pre- intervention stage

Figure 2.11 summarises the percentage of patient reported adherence problems that were not documented by the SPT. 'Struggling to swallow tablets' was the most common patient reported adherence difficulty that was not documented by the SPT accounting for 15.5% of all cases.

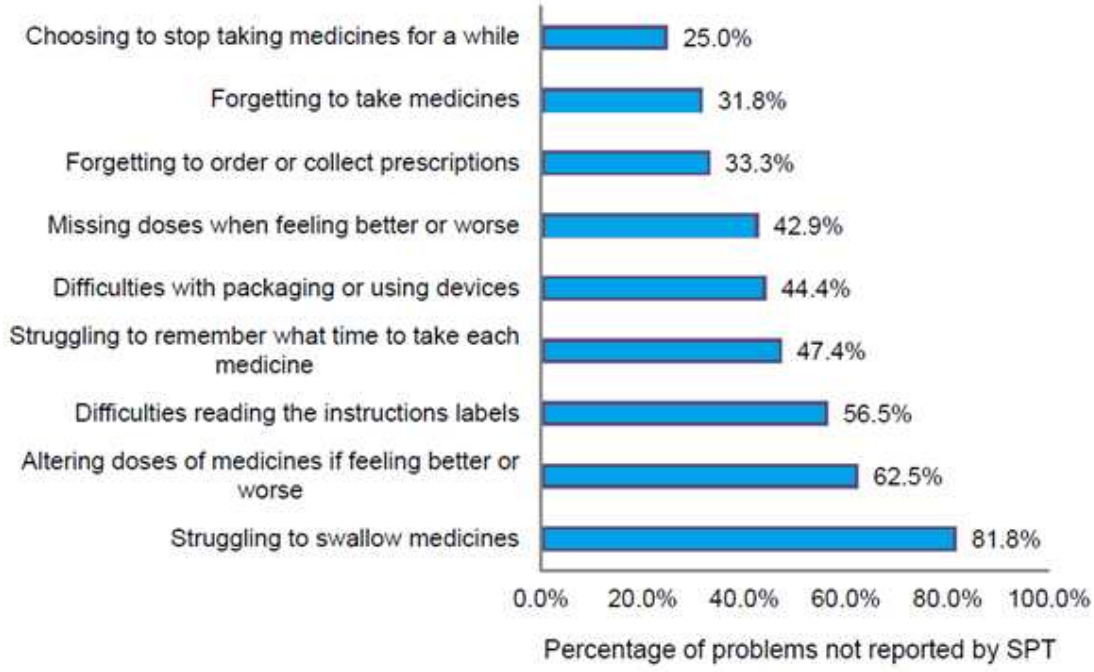


Figure 2.11 Patient reported adherence problems not recorded by the SPT

2.3.5.8 Agreement between SPT and patient reported adherence problems at the post intervention stage

Table 2.11 summarises the agreement between patient and SPT reported adherence at the post-intervention stage. The majority of adherence problems reported by patients at the post-intervention stage were not recorded by the SPT, yielding low agreement. In all cases bar those reported as 'always' causing an adherence problem, the SPT and patients agreed on negative cases (no adherence problems) far more frequently than positive cases (adherence problems) meaning the calculated kappa values are subject to notable bias. Whilst 'moderate' agreement was obtained when patients 'always' experienced an adherence problem, the 95% confidence interval associated with the kappa statistic is very wide, making meaningful interpretations problematic.

Despite the limitations of interpretation of these data, it is reasonable to infer that agreement between patient and SPT reported adherence was negligible, and unlikely to exceed that which would have occurred by chance.

Patient reported adherence problems	No. problems reported by patients	No. (%) also reported by SPT	Kappa (95% CI)	P-value	Agree-ment*	P_{pos}	P_{neg}
All cases	35	3 (8.6%)	0.12 (-0.02 to 0.25)	0.005	Slight	0.15	0.90
'Always'	6	2 (33.3%)	0.43 (0.02 to 0.84)	<0.001	Moderate	0.44	0.99
'Often'	4	0 (0.0%)	-0.01 (-0.02 to 0.00)	0.879	Poor	0.00	0.97
'Sometimes'	26	1 (3.8%)	0.05 (-0.07 to 0.17)	0.152	Slight	0.07	0.92

*Based on Landis and Koch scale[232]

Table 2.11 Agreement between patient and SPT reported adherence problems at the post- intervention stage

2.3.6 Patients' risk of harm from their medicines

A summary of the mean risk scores calculated pre and post intervention for each patient, using the NPSA risk matrix is provided as appendix 2.11.

2.3.6.1 Pre-intervention risk scores using the NPSA risk matrix

Pre-intervention risk scores (mean of four HCPs for each patient) ranged from 2 to 21 with higher scores indicative of a greater risk of harm. The group median (IQR) was 12.0 (9.0 to 15.0) indicating that on average, patients receiving their initial visit were considered to be at a 'high' risk of harm from their medicines. According to the NPSA risk categories, the majority of patients (82.8%) were considered to be at either a 'high' or 'extreme' risk of harm from their medicines.

2.3.6.2 Post-intervention risk scores using the NPSA risk matrix

Post-intervention risk scores (mean of four HCPs for each patient) ranged from 2 to 16 and the group median (IQR) was 5.0 (3.0 to 6.0); a 'medium' risk of harm. The majority of patients (92.9%) had either a 'low' or 'medium' risk of harm from their medicines.

2.3.6.3 Comparison between pre and post intervention risk scores using the NPSA risk matrix

A reduction in risk score following the intervention was achieved for 92 patients (92.9%). The median risk scores were significantly lower post intervention (P= <0.001, Wilcoxon matched pairs test) with a median (IQR) change of -7.0 (-3 to -10) points following receipt of the domiciliary medicines support service. For 83 patients (83.8%) the reduction in risk score following the intervention was sufficient to also reduce their risk score category.

Figure 2.12 provides a comparison between the percentage of patients falling into each risk score category at the pre and post intervention stages and highlights the switch of patients from 'high and extreme' risk at the pre-intervention stage to 'medium and low' at the post-intervention stage. The error bars representing the 95% CI around each point estimate highlight that true differences between the proportion of patients in each category pre and post intervention are likely, given that the confidence intervals do not overlap in all cases. For all four HCPs, risk score categories were ranked significantly lower following the intervention (p = <0.001, Wilcoxon matched pairs).

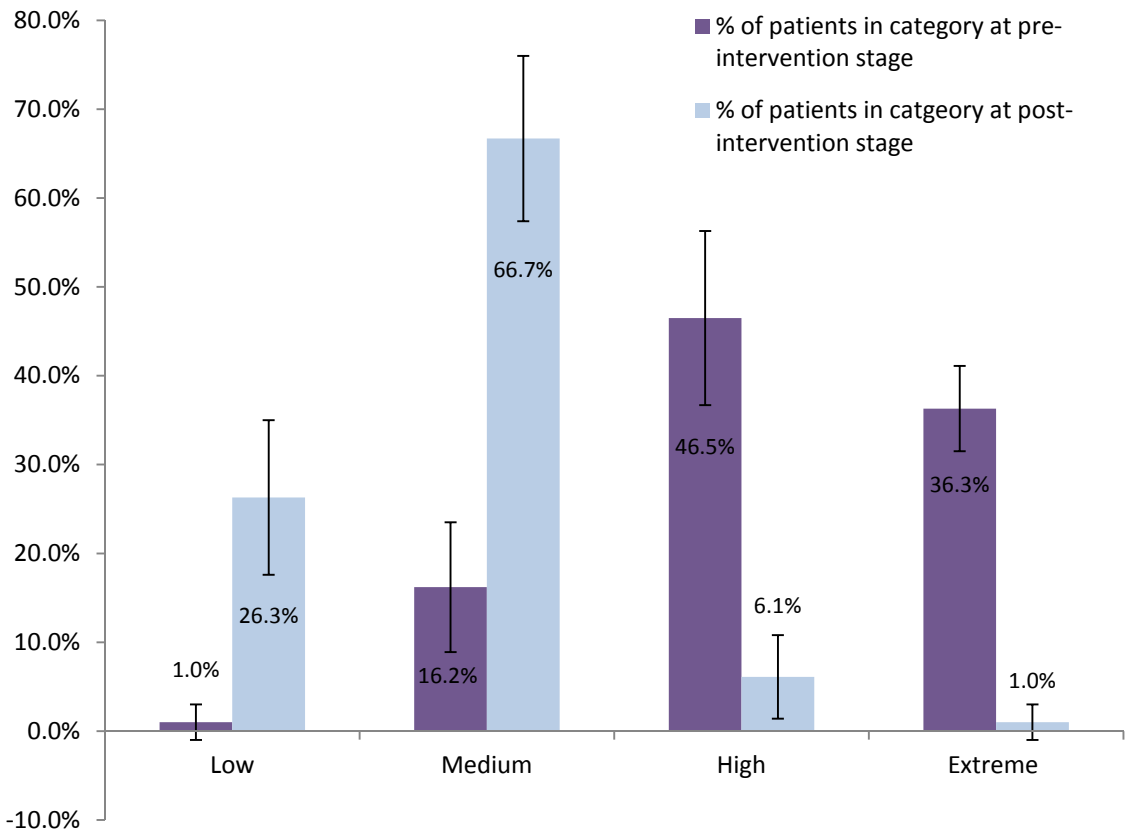


Figure 2.12 Comparison of percentage of patients in each risk score category at the pre and post intervention stage

2.3.6.4 Agreement in NPSA risk scores assigned by different healthcare professionals

Pre-intervention risk scores

For inter-rater agreement, a Kendall's *W* statistic of 0.67 indicated good agreement and this was statistically significant (p = <0.001). For the measure of inter-rater reliability (IRR), an ICC value (95% CI) of 0.83 (0.77 to 0.88) was calculated, representing excellent IRR[233]. This average measure of reliability notably exceeded the single measure (95% CI) of 0.55 (0.46 and 0.65), highlighting the improved reliability achieved by taking an average of the risk scores assigned by four different HCPs.

Post-intervention risk scores

There was significant agreement between the risks scores assigned by the four HCPs (p = <0.001) and according to the Kendall's *W* statistic of 0.56, this agreement was considered to be 'reasonable'. For the inter-rater reliability measure, an ICC value

(95% CI) of 0.78 (0.70 to 0.84) was calculated, representing excellent IRR[233]. As with the pre-intervention stage, this average measure of reliability notably exceeded the single measure (95% CI) of 0.47 (0.37 and 0.58), highlighting the improved reliability achieved by taking an average of the risk scores assigned by four different HCPs.

2.3.6.5 Pre-intervention risk scores using Fuller's risk assessment tool

Difficulty with the use of the Fuller's tool was reported, as patients frequently fell in between the category boundaries, especially for the 'patient's attitude towards their medicines' section. The tool was therefore adapted so that data could be recorded in a consistent manner, for example, where a patient was interested in and willing to take their medicines but unable to recall their regimen, a score of '6' was assigned.

A pre-intervention risk score was calculated for 92 patients where sufficient data were provided. The median (IQR) risk score was 18.5 (13.0 to 23.0) and so on average, patients were considered to have a 'high' risk of harm. The percentage of patients categorised as 'low' and 'very high' risk was equal, with each category accounting for 24 patients (26.1%). Eight patients (8.7%) were classified as having a 'medium' risk of harm from their medicines and the remaining 36 patients (39.1%) were classified as having a 'high' risk of harm.

2.3.6.6 Comparison between risk score categorisation using the NPSA and Fuller's risk tools

Figure 2.13 compares the percentage of patients assigned to each risk score category at the pre-intervention stage, using the NPSA and Fuller's risk tools. The percentage of patients classified as low risk using the Fuller's risk tool is notably higher than that for the NPSA risk tool. Likewise, the proportion of patients classified as 'high' or 'very high' are lower for the Fuller's risk score compared to the NPSA risk score.

The 95% CI around each point estimate (represented by error bars) highlight that whilst there may be differences in the proportions of patients in each category using the two tools, it is only the 'low' risk category where true differences are likely to exist.

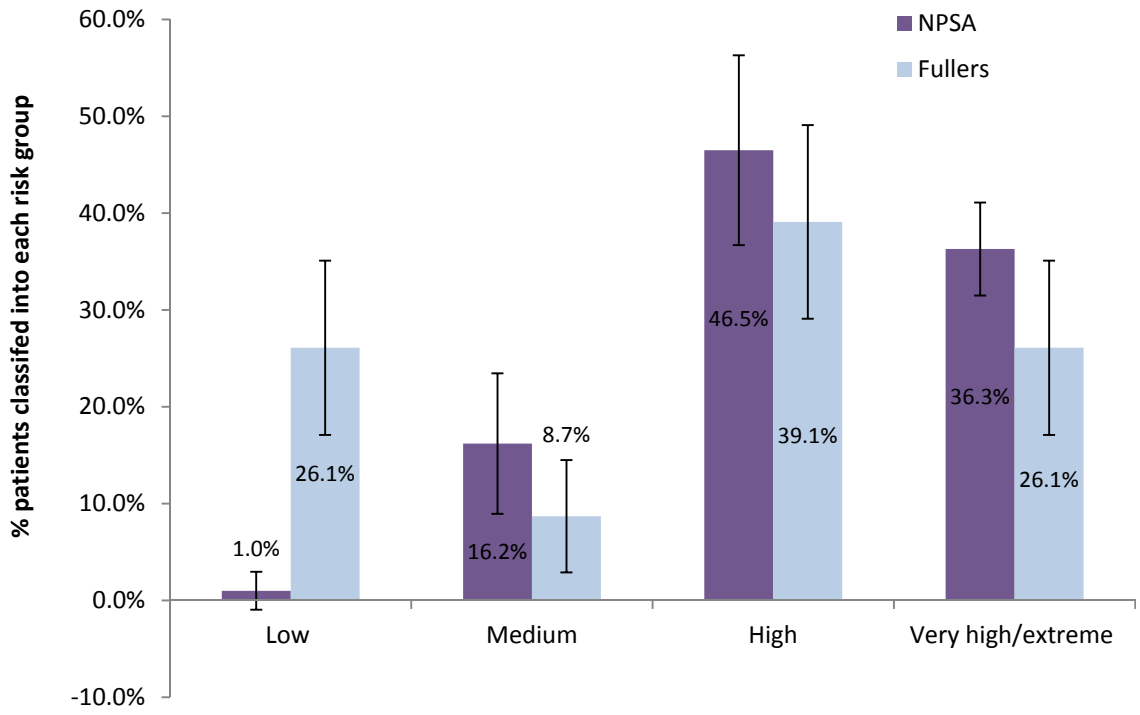


Figure 2.13 Percentage of patients in each risk score category using NPSA and Fuller's risk tools

The ICC (95% CI) value calculated to assess agreement between the two tools was 0.36 (0.05 to 0.57). The equivalence of the ICC value to weighted kappa means that agreement between the two tools can be considered as 'fair'. The associated p-value of 0.008 confirmed significant agreement between the two tools.

2.3.7 Patient questionnaires

Thirty-six questionnaires were sent directly to patients, of which 22 (61.1%) were returned. Twenty-seven questionnaires were sent to a patient's caregiver and the remaining 31 patients were not eligible for either questionnaire due to poor cognitive function and receipt of formal rather than informal care.

Table 2.12 provides a comparison of questionnaire recipients and non-recipients, according to their SPT reported cognitive state. This comparison was made to determine whether, as per protocol, the SPT had only sent the questionnaires to patients deemed to have sufficient cognitive capacity for completion.

In the group of patients who received a questionnaire, 2 (5.6%) had notable cognitive impairment, as defined as being 'very confused, 'very forgetful' or having a formal diagnosis of dementia. Comparatively, for the group of patients who were not sent a questionnaire, 38 (65.5%) had notable cognitive impairments. Differences in the mean

rankings of cognitive impairment for questionnaire recipients and non-recipients was significantly different (MWU P=<0.001); non-recipients of the questionnaire therefore had significantly poorer cognitive function.

SPT reported cognitive state	No. (%) patients sent a questionnaire	No. (%) patients NOT sent a questionnaire
Alert and orientated	15 (41.7%)	0 (0.0%)
Slightly confused and/or slightly forgetful	18 (50.0%)	21 (36.2%)
Slightly confused AND very forgetful	0 (0.0%)	6 (10.3%)
Very confused and/or very forgetful	1 (2.8%)	9 (15.5%)
Formal diagnosis of dementia or awaiting tests	1 (2.8%)	23 (39.7%)

Table 2.12 Questionnaire distribution according to patients' cognitive state

The data concerning patient reported adherence is reported in section 2.3.4.5 with the rest of the adherence related data.

2.3.7.1 Patient confidence with managing their medicines and health

Table 2.13 summarises the patient responses to the six questionnaire statements relating to the patient's confidence with managing their medicines and health after receiving the intervention.

An overall section score could be calculated for 19 patients (86.4%) with fully completed data for this section. The mean (SD) total confidence score was 17.3 (4.9) out of a possible 24, with higher scores indicating greater improvements in confidence and perceived ability post intervention. Cumulatively, 60.2% of patients reported an improvement in their overall confidence and ability to manage their medicines and health.

The majority of responding patients thought that their confidence in taking their medicines correctly had improved following the intervention and this was the case for 81.0% of respondents. In a similar vein, 66.7% of responding patients thought that their ability to take their medicines correctly had improved following the intervention. A majority of patients also reported that their ability to cope with life had improved following the intervention.

In relation to the patient's perceived ability to keep themselves healthy, a smaller margin of 42.8% of responding patients reported an improvement, with a majority of patients reporting that their ability to keep themselves healthy had stayed the same. An improvement in the patient's ability to help themselves was reported by 60.0% of

patients and 55.0% of patients thought their confidence in managing their health had improved.

Confidence/ability statement: As a result of my recent home visit to help me with my medicines, I feel:	No. (%) of participants giving a response of…			
	Much better	Better	The same	Worse
My confidence in taking my medicines correctly is…	8 (38.1%)	9 (42.9%)	4 (19.0%)	0 (0.0%)
My ability to take my medicines correctly is…	8 (38.1%)	6 (28.6%)	7 (33.3%)	0 (0.0%)
My ability to cope with life is…	7 (35.0%)	4 (20.0%)	8 (40.0%)	1 (5.0%)
My ability to keep myself healthy is…	5 (23.8%)	4 (19.0%)	11 (52.4%)	1 (4.8%)
My ability to help myself is…	4 (20.0%)	8 (40.0%)	8 (40.0%)	0 (0.0%)
My confidence in managing my health is…	6 (30.0%)	5 (25.0%)	8 (40.0%)	1 (5.0%)
Overall response (n=123)	38 (30.9%)	36 (29.3%)	46 (37.4%)	3 (2.4%)

Table 2.13 Summary of patient responses to confidence with managing medicines and health section of questionnaire

2.3.7.2 Patient satisfaction with the service received

All 22 of the returned patient questionnaires had complete satisfaction data and could therefore be used to calculate the average overall satisfaction score. The median (IQR) total satisfaction score was 19 (16 to 20) out of 20, with higher scores indicating greater satisfaction.

Table 2.14 summarises the patient responses to each of the satisfaction statements and highlights the positive trend towards satisfaction with the service. The quality of the service received was rated as good or excellent by 90.0% of responding patients. In addition, 100% of responding participants:

- Would recommend the service to a friend in need of similar help
- Were satisfied with the amount of help they had received
- Reported that the services they had received had helped to deal with their medicines more effectively
- Reported that overall, they were satisfied with the service they had received

Satisfaction statement	Questionnaire responses Number (%) of patient responses			
How would you rate the quality of the service you have received?	Excellent 11 (50.0%)	Good 9 (40.9%)	Fair 2 (9.1%)	Poor 0 (0.0%)
If a friend were in need of similar help, would you recommend the same service you received?	Yes, definitely 16 (72.7%)	Yes, I think so 6 (27.3%)	No, I don't think so 0 (0.0%)	No, definitely not 0 (0.0%)
How satisfied are you with the amount of help you received?	Very satisfied 13 (59.1%)	Mostly satisfied 9 (40.9%)	Indifferent or mildly dissatisfied 0 (0.0%)	Quite dissatisfied 0 (0.0%)
Have the services you received helped you to deal more effectively with your medicines?	Yes, they have helped a great deal 13 (59.1%)	Yes, they helped somewhat 9 (40.9%)	No, they didn't really help 0 (0.0%)	No, they seemed to make things worse 0 (0.0%)
In an overall, general sense, how satisfied are you with the service you have received?	Very satisfied 14 (63.6%)	Mostly satisfied 8 (36.8%)	Indifferent or mildly dissatisfied 0 (0.0%)	Quite dissatisfied 0 (0.0%)

Table 2.14 Summary of patient responses to satisfaction section of questionnaire

2.3.7.3 Comments provided in patient questionnaires

Ten (45.5%) questionnaires were returned with additional written comments. Eight of these comments (80.0%) were positive, describing the effectiveness of the service and the patient's satisfaction with the SPT delivering the service. One comment was neither positive nor negative, and one comment related to unresolved problems. A selection of statements to support these findings are provided in appendix 2.12.

2.3.8 Patient caregiver questionnaires

Questionnaires were returned by 21 caregivers giving a response rate of 77.8%. Twelve caregiver questionnaires (57.4%) were completed by the offspring of a patient and five (23.8%) were completed by the patients spouse. For four caregiver questionnaires (19.0%) the caregivers relationship to the patient was not recorded.

2.3.8.1 Caregiver feelings following the intervention

Complete data for this section were available for 20 (95.2%) of the returned caregiver questionnaires. The median (IQR) overall score for the caregiver's feelings post

intervention was 27 (22 to 30) out a possible 32 with higher scores indicating greater confidence and lower concerns following the intervention.

A summary of the caregiver responses to each statement in this section is provided in table 2.15. An increase in the caregiver's confidence in the ability of the patient to take their medicines as prescribed was reported by 95.2% of responding caregivers. A large majority (85.7%) of caregivers also felt more confident in the patient's ability to manage their medicines independently. An improvement in the patient's ability to manage their health and well-being was reported by 60.0% of responding caregivers and 95.2% of responding caregivers reported a reduction in the patient's difficulties with taking their medicines.

In terms of the caregiver's own feelings, 90.4% reported reduced levels of anxiety and 81.0% reported a reduction in the amount of time that spent worrying about medicines taking. The majority of caregivers also reported a reduction in the amount of time the spent helping the patient with their medicines and this was the case for 76.2% of responding caregivers. Just over half of the responding caregivers (52.4%) reported a reduction in the level of reliance that the patient had on them.

As a result of the recent Medicines Management visit received by the person that I care for, I feel :	No. (%) of patient caregivers giving a response of…			
	Much better	Better	The same	Worse
My confidence in their ability to take their medicines correctly is…	12 (57.1%)	8 (38.1%)	1 (4.8%)	0 (0.0%)
My confidence in their ability to manage their medicines independently is…	12 (57.1%)	6 (28.6%)	3 (14.3%)	0 (0.0%)
My confidence in their ability to manage their health and well-being is…	6 (30.0%)	6 (30.0%)	8 (40.0%)	0 (0.0%)
	Much less	Less	The same	More
My level of anxiety about them taking their medicines wrongly is…	12 (57.1%)	7 (33.3%)	2 (9.5%)	0 (0.0%)
The difficulties that they had in taking their medicines are…	12 (57.1%)	8 (38.1%)	1 (4.8%)	0 (0.0%)
The amount of time I have to spend helping them with their medicines is…	9 (42.9%)	7 (33.3%)	3 (14.3%)	2 (9.5%)
The amount of time I spend worrying about them taking their medicines is…	11 (52.4%)	6 (28.6%)	4 (19.0%)	0 (0.0%)
The level of reliance that they have on me is…	3 (14.3%)	8 (38.1%)	9 (42.9%)	1 (4.8%)
Total no. (%) of responses given	**77 (46.1%)**	**56 (33.5%)**	**31 (18.6%)**	**3 (1.8%)**

Table 2.15 Caregiver feelings and confidence following the intervention

2.3.8.2 Caregiver satisfaction with the service

All 21 returned questionnaires were fully complete for this section and therefore used to calculate the average overall satisfaction scores. The median (IQR) total satisfaction score for caregivers was 20 (19 to 20) out of a possible score of 20 with higher scores representing greater satisfaction. Table 2.16 summarises the caregiver responses to the satisfaction section of the questionnaire and highlights a positive response to the service, with 100% of caregivers rating the service as 'good' or 'excellent' and recommending the service. 100% of caregivers also thought that the service had helped the patient to deal with their medicines more effectively and were satisfied with the overall service. 95.2% of caregivers were happy with the amount of support received.

Satisfaction statement	Questionnaire responses Number (%) of patient responses			
How would you rate the quality of the service received?	Excellent 18 (85.7%)	Good 3 (14.3%)	Fair 0 (0.0%)	Poor 0 (0.0%)
If a friend were in need of similar help, would you recommend the same service to them?	Yes, definitely 20 (95.2%)	Yes, I think so 1 (4.8%)	No, I don't think so 0 (0.0%)	No, definitely not 0 (0.0%)
How satisfied are you with the amount of help received by the person that you care for?	Very satisfied 18 (85.7%)	Mostly satisfied 2 (9.5%)	Indifferent or mildly dissatisfied 1 (4.8%)	Quite dissatisfied 0 (0.0%)
Have the services received by the person that you care for, helped them to deal more effectively with their medicines?	Yes, they have helped a great deal 15 (71.4%)	Yes, they helped somewhat 6 (28.6%)	No, they didn't really help 0 (0.0%)	No, they seemed to make things worse 0 (0.0%)
In an overall, general sense, how satisfied are you with the service received by the person that you care for?	Very satisfied 17 (81.0%)	Mostly satisfied 4 (19.0%)	Indifferent or mildly dissatisfied 0 (0.0%)	Quite dissatisfied 0 (0.0%)

Table 2.16 Caregiver responses to satisfaction section of questionnaire

2.3.8.3 Caregiver comments from returned questionnaires

Ten (47.6%) of the returned caregiver questionnaires had additional written comments. Eight of the comments were positive (80.0%) and two comments (20.0%) detailed problems that were still occurring.

Comments focused on feelings of less worry and greater confidence about correct medicines taking plus general satisfaction and the personable approach and care offered by the SPT. A selection of statements to support these findings are provided in appendix 2.13.

2.4 Discussion

The service evaluation was focused around describing the effects of the CCS NHS Trust Domiciliary Medicines Management Service on medication adherence and patients' risk of harm from their medicines. The results have highlighted that the service yields significant improvements in patient adherence and significant reductions in the patients' risk of harm. Whilst this observation is seemingly positive, limitations must be considered when appraising this study, these limitations are discussed within the relevant sections below and can be summarised as:

- The omission of the patients clinical details means that full characterisation of the service recipients is not possible
- The study design means that we have no way of knowing how the patients may have progressed without intervention
- The lack of outcome measures beyond adherence and risk means that limited data is portrayed; the intervention could have conceivably increased healthcare utilisation and decreased quality of life but this is unknown.
- Poor follow up with self-reported adherence prohibits the utility of this data in drawing meaningful conclusions
- The study is limited by notable risk of bias, namely:
    - The risk scores were assigned using data provided by the SPT who delivers the service
    - The SPT adherence data should be interpreted with caution as this is also directly provided by the SPT delivering the service
    - There is potential for bias in the questionnaire distribution process which was co-ordinated by the SPT delivering the service.
- The omission of long-term follow up data means that the duration of effect from the intervention is unknown

2.4.1 The nature of the pharmacist technician intervention, including patient, medication and visit details

2.4.1.1 Patient details

Service recipients were primarily of an older age, experiencing some degree of cognitive impairment, living alone and unable to administer their medicines safely. In comparison to national statistics, recipients of this service were:

- Older - 31.2% were aged over 85 years compared to 2.0% in the wider population[234]

- Had a greater degree and prevalence of cognitive impairment – 23.2% had a formal diagnosis of dementia compared to 12.1% and 13.5% of males and females in this age range respectively[235, 236]
- More likely to be living alone – 63.6% compared to 49.0% of patients of a similar age in the wider population[237].

Numerous factors associated with increasing age, such as declining cognitive and physical capacity plus a lack of social support have been reliably associated with medication difficulties and non-adherence[4, 238]. As such, it is reasonable to infer that the service was targeted towards those at greatest risk of non-adherence and other medication related difficulties. This is supported by the high risk scores observed in the majority of patients at the initial visit and serves to communicate the potential fragility and vulnerability of the population receiving this service and the need to intervene.

Although the majority of patients were unable to administer their medicines safely, many were considered competent, which may cause question as to the need for intervention. It is however, important to note that an ability to take medicines safely does not necessarily equate to execution of the behaviour and thus, patients with an ability to take their medicines as prescribed were not necessarily doing so. This implies that there were elements of intentional non-adherence amongst the population.

2.4.1.2 Medication details

Patients were taking a median of nine medicines per day and multiple daily doses, inferring complexity of regimens. This is unsurprising given the evidence to support an association between regimen complexity and non-adherence[18, 53].

In 1999, Golden *et al.* reviewed prescribing of medicines in homebound older adults in the USA[239]. The large cohort, whose mean age was comparable to the patients in this service evaluation, were on average prescribed 5.3 +/- 2.9 drugs (range 0-22), which is notably less than the recipients of this service. Data from other studies, including the HOMER trial[205] and Hawksworth and Chrystyn's study[204] report similar numbers of medicines per patient. Recipients of the CCS NHS Trust service were therefore taking more medicines on average, highlighting their increased vulnerability and need for support.

Whilst details of the medicines taken were essential for calculating the risk scores and provide useful data to characterise the recipients, it would also have been useful to collect clinical data to establish for which conditions the medicines were taken for. The absence of this data therefore marks a study limitation.

2.4.1.3 Visit details

Referrals into the service were from a diverse range of sources with a variety of different referral reasons. The volume of patients visited per month appears to be admirable for a sole full-time technician, given that follow up visits and intervention implementations for patients already in the system, but not included in this evaluation would also be necessary during this time. The number of patient visits is also comparable to that described in a similar study[184] over a similar time period, supporting the idea that patient turnover in this service is appropriate.

The number of patients visited during the data collection period also implies that this is a well utilised service, as does the diversity of referral sources. It is unsurprising that almost all referrals came from primary care, as it would be expected that patients experiencing problems with their medicines would be in their own homes. However, it is interesting to note that there were also referrals from secondary care. In both cases these referrals concerned patients currently in hospital but who were soon to be discharged. This cross-setting referral system is encouraging as recent government policies have encouraged improved hospital discharge processes to ensure continuity of care and reduce the risk of harm at the healthcare interface[199, 240]. The SPT is ideally placed to liaise between primary and secondary care services. Assuming the SPTs capacity was allowing, greater referrals from secondary care, in instances of patient discharge could be an intuitive means for expansion of the service.

The list of referral sources includes almost all healthcare providers involved in primary care. Family members, friends and the patients themselves were also represented as sources of referral. In 2007, Bhattacharya *et al*. reported that services with more referral sources were more likely to remain operational beyond a year of initiation[189]. The wide range of referral sources for this service is therefore a likely contributory factor to its continued service provision.

The only referral source that is potentially under represented is community pharmacists, who are ideally placed to identify patients experiencing adherence problems. Whilst implementation of interventions requires considerable liaison between the SPT and community pharmacists, exploration of increased referrals from this source may also be an intuitive route to expansion of the service.

In 1999, Foulsham and Goodyer reported that referrals made into a new domiciliary medicines support service were predominated by GPs and nurses, with far fewer referrals from social services[191]. Comparatively, for the referrals made via this service

evaluation, the relative proportion of referrals made by these three sources was more alike. It encouraging to see that the SPT has forged good interdisciplinary relationships and that social services are closely involved, as this agency is likely to most frequently see how patients are coping in their own homes.

The prevalence of referrals from care agency co-ordinators and housing scheme managers reflects the difficulties experienced by paid caregivers in administering patients' medicines. Patients were tampering with their medicines, hiding them from their carers or taking inappropriate additional doses between care calls which triggered the referrals. It is encouraging to see that carers made referrals to the SPT in these circumstances and positive that additional referrals were made for patients where there were concerns about coping and declining memory. This infers that patients in receipt of paid care or who were living in sheltered housing were well monitored, with efficient referral systems in place to address any concerns.

The reason for referral related to cognitive impairments in a majority of cases which is unsurprising given the prevalence of cognitive deficits in the sample population. Dexterity or swallowing problems, excess stock build ups and requests for MCA all also accounted for multiple referrals, though the proportion of referrals attributed to dexterity problems may have been expected to be higher, given the age of the sample populations. It is interesting that multiple referrals were made to request an MCA as this suggests that some referrers had preconceived ideas about an appropriate intervention. This may be an artefact of the many domiciliary medicines support services that are primarily focused on provision of an MCA.

At the initial visit stage, a range of problems, unrelated to medication adherence were identified, further highlighting the diversity of problems experienced and range of referral reasons. Whilst problems such as difficulties with tablet packaging, out-dated repeat medication slips and excess medication stocks were identified, such difficulties were only reported for a minority of patients, meaning the majority of patient's problems were more directly associated with medication adherence. This supports the concept that the medicines management service is primarily, but not exclusively a medication adherence intervention.

Provision of some form of MCA or advice were the most common interventions, however each only accounted for just under a quarter of all interventions respectively. A wide range of interventions were therefore recommended which is encouraging and likely a reflection of the holistic, patient-centred approach adopted. Moreover, the

range of interventions recommended and consideration of alternate options supports the SPT's ethos that supply of an MCA should not be a default option.

The utility and necessity of MCAs has long been disputed and recent guidelines have emphasised the importance of only using MCA where necessary and exploring all avenues of support rather than assuming the use of an MCA as a default resolution strategy[178]. Whilst many patients received some form of MCA, given the frequency of cognitive impairments, it is likely that in the vast majority of cases, this represented an appropriate intervention. Furthermore, the data collected suggests the SPT considered other avenues of support as over a third of the MCAs provided were to be filled by either a friend or family member. This demonstrates that alternate sources of support were utilised where possible, tailoring the intervention to meet the individual's need and adjusting it to individual circumstances.

Though the initiation of an MCA is seemingly appropriate for the patients reviewed in this service, a lack of detail as to how these MCAs were implemented may be cause for concern. It is important to consider the clinical safety of initiating MCAs in instances where patients' medicines may not have been fully reviewed or optimised. For example, a patient may have been prescribed a 10mg dose of Ramipril and been non-adherent for some time, meaning their blood pressure would need to be reviewed and dose titration of the Ramipril, as if the patient was treatment naïve, would be necessary. However, if this 10mg dose was added to an MCA, without review and without dose titration, adverse effects such as postural hypotension are probable, which would significantly increase the patient's risk of falls. Given that patients in receipt of this service were predominantly frail and older, such risk increases are unacceptable. In the absence of details regarding the review processes before initiation of an MCA and more importantly without long-term follow up details of adverse effects, it is not possible to establish whether such problems occurred. These deficits therefore mark further study limitations.

In 2012, Desborough *et al.* reported an economic evaluation of the Norfolk Medicines Support Service (NMSS) as a before and after study[183]. The recommended intervention was dispensing of medicines in an MCA for 90 patients (76.9%); a notably greater proportion than the 43.4% of patients in the CCS NHS Trust service. In addition, 32.6% of the MCAs supplied as an intervention in the CCS NHS Trust service, were supplied to be filled by friends or family members rather than the pharmacy. Desborough *et al.* reported that in 2007, the unit cost of filling an MCA was £78 per patient, for six months. In the CCS NHS Trust service, there were therefore 14

patients, who could have had an MCA filled in a pharmacy, but instead friends or family members were utilised. This represents a potential cost saving of £1092 over six months, however, there is little comparative evidence regarding the safety of MCA filling by non-pharmacy staff. Such costs savings and utilisation of alternate sources are important credentials for the CCS NHS Trust service. However, without formal economic evaluation, inferences with regard to cost effectiveness of the service must be drawn with caution.

The interventions recommended also highlight that, in almost all cases, referral into the service was appropriate as some form of intervention was needed. Only two patients did not receive a follow up visit as no intervention was necessary.

Problems identified at the initial visit stage that were not specifically related to non-adherence, had, in the main part been resolved following the intervention, highlighting the benefits of the service, beyond improvements in adherence. All patients with an outdated medication repeat list had this problem resolved by the follow-up stage, either by removal of the redundant medicine or re-initiation where appropriate. An accurate repeat medication list is an important aspect of patient safety, especially at the healthcare interface as they are routinely used as a primary resource upon hospital admission. In the instances of removing a medication that was no longer needed, this may have saved a medication being erroneously administered if the patient was admitted to hospital. Conversely, in instances of a medication that was thought to be redundant (by the patient) but that was reinitiated following the intervention, the SPT had resolved confusion and ensured continuation of appropriate medicines.

The SPT's intervention also resolved instances of excessive stock build ups and in all cases, additional measures were taken to prevent reoccurrence of this. Interestingly, in three cases of excessive stock build-ups (37.5%), the problem had occurred due to poorly managed pharmacy repeat ordering services. These services are intended to improve medication adherence and reduce medicines waste by a nominated community pharmacy contacting the patient each month to see which items they would like to order. It would seem however, that for some patients, all items were automatically ordered each month, irrespective of whether or not they were needed. This not only represents poor professional practice, but also a notable waste of resources; these cases were reported back to the SPT for further investigation. One specific case in this service evaluation related to a patient who was sent all of their diabetic blood testing strips and associated paraphernalia each month, despite visual impairments which precluded the use of these items. The cumulative cost of lancets,

test strips, monitoring devices and waste disposal units for this patient would amount to substantial costs. Whilst the SPT's intervention of stopping all of these items and arranging for a district nurse to test the patient's blood sugar regularly is, in itself a costly intervention, it is likely to be more cost efficient and certainly far safer than wasting the supply of these valuable resources each month.

Beyond reducing medicines waste and ensuring safety with accurate medication repeat lists, the SPT's intervention also resolved patient side effects, packaging problems and inappropriate prescribing, plus improved medication access for patients with sight impairments. This demonstrates the wide range of benefits associated with the service, though the long-term benefits elicited are unknown.

2.4.2 The development and acceptability of a new adherence assessment tool

The first draft of a novel adherence assessment tool, for use in this specific population was developed and tested. The potential adherence problems represented in the tool were selected with the population in mind and are based on the plethora of existing validated adherence assessment tools which increases confidence in content validity.

Assessment of face validity in the target population, was however, more problematic. Less than a quarter of the patients receiving an initial visit completed the adherence assessment questionnaire prior to the SPT's visit. This observation could be indicative of poor face validity (the patient's did not understand what they had to do or could not answer the questions). However, given the magnitude of cognitive impairment in the service recipients, forgetfulness and confusion may have been more likely contributory factors. Of the questionnaires completed, high proportions were completed fully, indicating that the patients were able to understand the instructions and questions. However, it is important not to overlook the possibility that those who did not understand the instructions and questions simply did not complete the questionnaire and were therefore 'non-responders'.

Post intervention data on the adherence assessment tool was captured for roughly a quarter of all patients receiving the service, augmenting the difficulty in establishing the face validity of the tool in the full sample. However, there was a good response rate for the limited number of patients who were sent a questionnaire and high proportions were completed in full. This suggests that in patients with sufficient cognitive capacity, the face validity of the questionnaire was adequate.

Whilst patient responses were predominantly 'rarely' or 'never' as is often found with medication adherence self-reports, there were a notable number of patients reporting adherence problems. This suggests that the adherence assessment tool was capable of detecting adherence related difficulties. The choice of a continuous rather than dichotomous scale may have facilitated these detections.

The comparison between the patient and SPT reported adherence sheds an interesting light on the questionnaire and brings into question whether the patients completed the questionnaires appropriately. There are however, multiple possible explanations for these discrepancies:

1. That the SPT did not feel it pertinent to record problems that occurred 'often' or 'sometimes', especially if there were more pressing issues that occurred 'always'
2. That the SPT did not check experience of certain adherence barriers with patients and therefore failed to establish some adherence difficulties
3. That the patients felt more confident in reporting adherence problems on the self-report questionnaire than in discussing them in person with the SPT
4. That patients filled in the questionnaires inaccurately

It is likely, that the disagreement between the patient and SPT reported adherence is an amalgam of the four outlined explanations. The data collected offers some support for the second proposed explanation, as a very high proportion of patients reporting swallowing difficulties did not have this problem documented by the SPT, yet a notably lower proportion of patients reporting 'stopping their medicines for a while' did not have this problem documented by the SPT. These data suggest that adherence barriers such as swallowing difficulties, altering doses of medicines and difficulties reading the instructions labels were overlooked more commonly than others such as forgetting to take or order medicines, especially when the problems occurred 'often' or 'sometimes'.

Whilst it may be worth reviewing the procedures undertaken by the SPT for adherence problems that 'often' or 'sometimes' cause difficulties, it is worth considering the potential of the fourth explanation too; that the questionnaires were not completed as intended. Agreement between the SPT and patients was lower at the post-intervention stage compared to the pre-intervention stage, which supports the proposal of insufficient questionnaire sensitivity to detect change. This may also be augmented by the subjective nature of the response options on the questionnaire, as 'sometimes' may be interpreted differently by different people.

Some adherence tools[140, 146, 152] have attempted to overcome the problem of subjective response options by asking how often each adherence difficulty has caused non-adherence over, for example, the last three or seven days. Whilst these approaches have proved to be appropriate in their target populations, it is likely that such specific recall may increase the cognitive burden of completion and thus be inappropriate for the population in this study.

At the post-intervention stage, the adherence questionnaire was identical to that given to patients at the pre-intervention stage. Therefore, a patient with, for example, swallowing difficulties, may still report that they 'always' or 'often' have difficulties swallowing their medicines, despite receiving an intervention whereby their medicines were all switched to liquid forms. From the patient's perspective, they have difficulties swallowing their medicines and therefore need to have them in an alternate form. For all other statements, an ambiguity of interpreting the situation, as described above may be possible. An alternate form of the questionnaire, focussing on changes in medicines taking since the initial visit may therefore have been more appropriate, although it is common practice to use standardised self-report measures pre and post intervention without changes.

Overall, it would seem that the questionnaire can identify adherence related difficulties and is acceptable to patients with sufficient cognitive capacity to allow questionnaire completion. The acceptability and utility of the questionnaire in patients with cognitive deficits remains unestablished. However, it is worth considering whether any questionnaire based tool, no matter how simple would be acceptable to patients with notable cognitive impairments.

2.4.3 Changes in patient adherence following the intervention

The SPT reported that the majority of patients were either fully or partially non-adherent at the initial visit stage, highlighting the need for the service. This need is augmented by the data which demonstrated that over half of the patients deemed to be fully adherent, required some form of intervention to ensure their adherence could be safely maintained. The proportion of patients classified as partially adherent at the initial visit stage reflects the variable nature of non-adherence.

The most common cause of non-adherence was 'forgetting' which is expected given the cognitive impairments of the service recipients and is similar to the findings of a comparable study[200]. The notable proportion of non-adherence that was attributable to patients taking additional doses in between care calls is also likely to reflect the

documented cognitive impairments in the sample population. However, it is worth considering that there could also be elements of intentional non-adherence, especially in taking additional doses. The cases of hiding medicines from carers may also reflect intentional non-adherence, although this may be more likely to be a facet of altered behaviours arising from dementia or other cognitive impairments.

With consideration of the intentional or unintentional nature of the adherence behaviours encountered, there is a strong likelihood that the non-adherence observed was dominated by unintentional factors. Both cases of 'refusing to take medicines' were likely intentional and for some behaviours such as hiding medicines and taking additional doses it is unclear whether such behaviour is intentional in nature. More likely, as discussed previously, is that such behaviours are related to the high prevalence cognitive impairments which may account for such behaviours. 'Forgetting' was, in all likelihood an unintentional behaviour, especially given the prevalence of known cognitive impairments. However, as highlighted in chapter one, 'forgetting' can, in some circumstances be defined as an intentional behaviour. Despite clearly defined classifications, it is reasonable to conclude that the medication non-adherence encountered in this evaluation was almost exclusively unintentional in nature.

The SPT reported a statistically significant increase in the proportion of adherent patients following the intervention. This data is encouraging for the service as it portrays its efficacy favourably. However, two important limitations must be considered. Firstly, these data were gathered by the SPT providing the service and may thus be subject to strong potential reporting bias. Secondly, whilst the SPT reported that patients had become adherent following the intervention, the longevity of these adherence improvements is unknown. A further follow up of patients at, for example, a six month or one year time point post intervention would therefore be useful to establish whether the intervention achieved long term adherence improvements.

Whilst the potential for reporting bias in SPT gathered data should not be overlooked, there is evidence to suggest this is unlikely. In many cases, for example those involving patients that were tampering with their medicines in between care calls, the SPT intervention of providing a locked box for medicines storage that only the carers can access, prohibited the patient's non-adherent behaviour thus a genuine positive outcome is extremely likely. Furthermore, the magnitude of the adherence improvements, coupled with the supporting descriptive data and information on the interventions recommended cumulatively suggest that the intervention truly did improve adherence.

Beyond improving adherence for those classed as non-adherent or partially adherent at the initial visit stage, patients who were adherent but who were experiencing medicines related difficulties also received benefit from the service. This inclusivity and commitment to supporting all patients in need also represents the service favourably.

Whilst the SPT reported data showed large and statistically significant improvements in medication adherence following the intervention, this was not so for the patient reported data. However, pre and post intervention self-reported adherence data were only available for ten patients, meaning the value of the statistical test is questionable due to insufficient power. With greater numbers, the improvement in median adherence score following the intervention may have been significant. In addition, the adherence tool may not have been sufficiently sensitive to detect changes in adherence, as discussed previously.

A further point of consideration with the patient reported adherence data is that the person completing the pre-intervention adherence screen may not have been the same as the person completing the questionnaire at the post-intervention stage. Patients were frequently supported by the technician at the pre-intervention stage, and many returned questionnaires at the post-intervention stage had been completed by a caregiver rather than the patient themselves. It is therefore difficult to draw meaningful conclusions from the patients' self-reported adherence data and this is a notable limitation of the study.

The questionnaire dissemination process, whereby the SPT decided which patients received a questionnaire based on their cognitive capacity also introduces potential selection biases. However, statistical tests confirmed that significantly more patients had poorer cognitive function in the group on non-recipients. Whilst this observation cannot exclude the potential of selection bias, it does increase our confidence that questionnaire distribution procedures were followed correctly, whereby questionnaires were not sent to patients considered to have insufficient cognitive function. A dissemination process whereby all patients were sent a questionnaire would overcome this potential bias, however the ethical implications of potentially confusing vulnerable older adults with known cognitive impairments would have to be considered. In a similar vein, there is also potential selection bias in the questionnaire distribution process for caregivers. Whilst it is assumed that all eligible caregivers received a questionnaire, data to support this assumption was not collected. An auditable, more robust caregiver questionnaire dissemination process is therefore recommended to alleviate the potential for this source of bias.

2.4.4 Changes in patient risk assessment scores following the intervention

Pre and post intervention risk scores were successfully assigned to each patient by four different health care professionals (HCPs) using the NPSA risk matrix, representing novel utilisation of the risk matrix tool. Whilst the tool has been reported for use in assigning medication related risks of harm, this is, to the best of our knowledge the first time that a multiple-rater approach has been utilised.

The variation in risk scores across patients both pre and post intervention reflects the diversity of patients receiving this service and their complex and varying healthcare needs. On average, the patients' risk of harm at the pre-intervention stage was 'high', indicating the need to intervene and appropriateness of referral. Following the intervention, the vast majority of patients achieved a reduction in their risk score and the average risk score was reduced to 'medium'. The difference in median risk scores pre and post intervention was statistically significant, and thus suggests beneficial effects of the service. There was also a significant reduction in the proportion of patients categorised as 'high or extreme' risk following the intervention, adding further weight to the evidence of beneficial service effect.

In cases where reductions in risk scores were not achieved, consideration of the circumstances surrounding these patients makes a strong case for understanding the limitations of the SPTs capacity to make changes. Overall therefore, there is strong evidence for the efficacy of the service in reducing the patients' risk of harm. Whilst there is statistical evidence to suggest service benefit in terms of risk reduction, it is essential to consider how meaningful the data were, given that the risk scores are based on data provided by the SPT delivering the service. The limitations of the before and after study design must also be considered.

2.4.5 Agreement between healthcare professionals in assigning NPSA risk assessment scores to patients' pre and post intervention

The measures of inter-rater agreement (IRA) and inter-rater reliability (IRR) for the risk scores assigned by the four HCPs demonstrate that overall, HCPs were able to consistently differentiate between different risks of harm (IRR), even if they didn't always agree of the severity of the risk (IRA). The high ICC values suggest that, whilst the coders did not always reach perfect agreement in their risk scores, the process of assigning risk scores was undertaken in a consistent manner and that a minimal amount of measurement error was therefore introduced by the independent coders

(HCPs)[241]. Whilst inter-rater reliability was considered excellent at both stages, inter-rater agreement was less impressive, although still at an acceptable level and of statistical significance.

The comparison between single and average measures of ICC at both the pre and post intervention stage highlights that reliability of risk score assignment is greatly improved by taking an average of the scores provided by four different HCPs than a single risk scorer. This observation supports the selected method of taking an average of four different risk scores and adds confidence to the interpretation of a reduction in risk score following intervention.

The statistically significant and (moderately) high statistics for Kendall's *W* mean that the four different HCPs were essentially applying the same standard of rankings for the patients included in the study[229]. Agreement was slightly poorer at the post-intervention stage compared to the pre-intervention stage which may suggest that the HCPs struggled to agree on the value of the intervention and the extent to which it had reduced the risk of harm. However, closer analysis of the data may also account for this observation. At the pre-intervention stage the risk scores assigned by the HCPs were clustered around the midpoint of the scale without substantial variance. Comparatively, there was less clustering of data around a central point at the post-intervention stage, with a greater range of risk scores across patients. The slightly higher value for Kendall's *W* at the pre-intervention stage may therefore be an artefact of an overall narrower range of scores between different patients. This being so, a clustering of scores around the central point of the scale could imply that the HCPs felt uncertain of their risk score assignments and had a tendency to 'hedge their bets' around the central point.

Qualitative interviews with the HCPs who assigned the risk scores would have been a useful addition to the data, to inform an understanding of how decisions about risk scores were made and whether there were any differences in the perceived ease of assigning risk scores at the pre and post intervention stage.

Whilst the method of taking an average risk score from four HCPs has been shown to improve the reliability of the measure, the implications for future use of this method must be considered as it is a labour intensive approach. In terms of the sole technician model utilised in this study, if utilisation of this measure were to continue, the reliability of risk scores being assigned by one individual alone must be questioned, or at least be carefully assessed before conclusions about risk reductions are drawn. For teams of technicians or other HCPs utilising the NPSA risk matrix in their practice, robust

training must be provided and assessments of inter-rater agreement and reliability should be undertaken before assuming the team will utilise the tool in comparable ways[242] .

One important note of consideration is that the high and statistically significant value of Kendall's *W* simply shows that there was good agreement between the HCPs in the risk scores assigned. It does not infer that the risk scores assigned were accurate 'predictors' of the patient's risk of harm.[229] Further work to establish the validity of this method in accurately predicting a patient's risk of harm is therefore recommended. Additional data such as mortality or hospital admissions would be necessary to establish a relationship between risk and outcome, although the ethical implications of such work may be prohibitive.

2.4.6 Agreement between the NPSA and Fuller's risk assessment tools when used to calculate pre-intervention risk scores

Overall, the Fuller's risk tool offered a more conservative estimate of patients' risk of harm from their medicines compared to the NPSA risk matrix. Whilst there was significant agreement between the two tools, the magnitude of agreement may be cause for concern and further investigation is warranted to establish why agreement between the two tools was not greater.

The 'fair' agreement between the two tools may therefore leave the validity of the NPSA risk matrix in question, as the Fuller's risk tool is reported as being validated for use in identifying a patients' risk of harm associated with medicines. However, upon closer inspection, the validation process for the Fuller's tool comprised only of establishing inter- and intra-rater reliability. It's content and criterion validity and hence the extent to which the tool actually predicts patient harm therefore remains unknown.

For both tools, further research is therefore necessary, to establish whether the risk scores calculated are indicative of actual harm, such as hospital admissions, increased healthcare utilisation, mortality or adverse drug reactions. The ethical implications of such research may however, as previously noted, make such data collection problematic.

2.4.7 Patient satisfaction with the service plus changes in ability and confidence to manage their medicines

Patient satisfaction with the service was captured from approximately a quarter of the service recipients. Whilst this is lower than ideal and may therefore not reflect a

representative sample of the service recipients, it is an artefact of the difficulties associated with capturing questionnaire based data in a population where cognitive impairments are so prevalent. A potential source of bias with this data could be that the SPT delivering the service, decided which patients would receive a patient questionnaire, based on their known levels of cognitive capacity. This was an intuitive approach to overcoming the ethical concern of confusing patients with known cognitive deficits by sending them a questionnaire. However, the SPTs 'selection' process has potential to introduce bias via preferential selection of patients who were expected to give favourable responses. Whilst it is important to acknowledge these potential biases and study limitations, analysis of the data gathered suggests such bias was unlikely as the patients who were sent a questionnaire were significantly less likely to have notable cognitive impairments compared to those who were not sent a questionnaire.

The patient reported satisfaction highlights the quality of the service, with almost all patients rating the service as good or excellent. The comments provided by patients also highlight this satisfaction and proved to document that the humility, compassion and generosity with time provided by the SPT were pivotal to its success and the patients' satisfaction. This overwhelming positive response suggests that the continuity of care and expertise of a sole SPT model are important attributes.

Positive effects of the service were also communicated by the favourable improvements in the patients confidence and ability to adhere and manage their health. This data has added a valuable depth of information to the service evaluation and has enabled realisation of improvements beyond reduced risks and improved adherence. Empowering patients to manage their own health and well-being is an important priority for healthcare and thus, the service is again represented favourably.

2.4.8 Patient carergivers' satisfaction with the service and their feelings about providing care following the intervention

The high caregiver questionnaire response rate (77.8%) and excellent completion rates (only one questionnaire had one section that was not fully complete) imply adequate face validity. Almost all caregivers reported an increased confidence in the patient's ability to take their medicines as prescribed and manage their medicines independently plus reduced difficulties with taking their medicines, highlighting the benefits of the service. The questionnaire also captured the positive influence of the service on the caregiver's own feelings, with a large majority of patients reporting reduced anxiety levels and less time spent worrying about medicines taking. Whilst these positive effects are laudable, it is worth noting that only half of the caregivers reported a

reduction in the level of reliance that the patient had on them. This observation may be worthy of further investigation as it implies that caregivers still felt relied upon for medicines support. Whilst this reliance may intuitively be perceived negatively, involving informal caregivers in the continuation of patient care may have benefits and it is known that some caregivers struggle to relinquish all responsibility[243].

The median satisfaction score for caregivers was 20, indicating that on average, caregivers expressed complete satisfaction with the service and could not have rated it more highly; this observation portrays the service auspiciously. This satisfaction is also portrayed in the caregiver comments, which, as with the patient comments, are focused around the personable and supportive nature of the SPT. Caregiver comments also captured the reduced levels or anxiety associated with being a caregiver confirming the all-round benefits of receipt from this service.

2.5 Conclusion

An evaluation of the CCS NHS Trust Domiciliary Medicines Support Service has highlighted that the service is capable of improving medication adherence and reducing patient's risk of harm from their medicines. However, there are substantial limitations to this data, most notably that both primary outcome measures were informed by data supplied by the SPT delivering the service. These findings must therefore be interpreted with caution. Further to these potential biases, the overall method imposes a limitation in so much as we cannot be sure how the patients would have progressed without intervention. A follow-on RCT study would enable this data to be captured, offering a more robust evaluation of service effect. However important ethical concerns (i.e. not intervening to resolve identified difficulties in the control arm) would need to be carefully considered.

Despite numerous study limitations, high levels of patient and patient caregiver satisfaction were reported, plus improvements in the patient's confidence and ability to manage their medicines and health. The possibility of selection bias with the questionnaires must however be considered though additional analyses suggests this is unlikely.

Based on the data gathered (whilst acknowledging the aforementioned limitations), this service may seemingly be providing effective domiciliary medicines support to its recipients. However, the longevity of these positive effects is unknown and further work is therefore recommended. Establishing the prolonged effects of this service may however be difficult in a population prone to natural declines in their ability to manage, especially those with cognitive impairment. The cost-effectiveness of the intervention has also not been established, which, given the reduced use of MCAs and technician led basis compared to pharmacists, may be useful. Further inferences of service efficacy could also have been captured through additional data such as health related quality of life, healthcare utilisation data and adverse events. Whilst the rationale for not eliciting this data is provided, its absence represents a further study limitation.

The work undertaken posed numerous methodological concerns and further work is necessary to continue resolving these. Self-reported adherence in a population with known cognitive impairment remains problematic, although the tool developed for this study shows promise in those patients with sufficient cognitive capacity. Further exploration the utility of this new adherence assessment tool and validation by comparison to electronic measurements of adherence such as the Medication Event Monitoring System (MEMS®) devices is therefore recommended. For patients with

cognitive impairments, self-report is unlikely to be an appropriate measure of adherence, even when bespoke assessment tools are used. Alternatives measures such as pill counts and MEMS® devices should therefore be explored. In relation to the assessment of a patient's risk of harm from their medicines, neither tool used was without limitations. The subjective nature of risk assessment and the difficulties in establishing validity of the processes leaves the utility of such approaches in question. At best, the NPSA tool may be a brief and easily utilised means of capturing a patients risk and comparing this at different time points to establish intervention effects. It should not however, be seen as an absolute proxy for risk and the scores produced from its use should therefore be interpreted with caution.

The work undertaken has contributed to the deficits in knowledge regarding domiciliary support services by providing a wealth of data to characterise service recipients, their adherence difficulties and the interventions recommended to resolve these. Such data has not been widely reported and, whilst possibly collected via audits and service evaluations for each individual service offered in the UK, is rarely shared amongst service providers to establish best practice. Dissemination of this work to providers of similar services may therefore facilitate shared knowledge and best practices. However, this data could have been supplemented by information regarding the patients' clinical conditions.

The service provision model utilised in this evaluation has demonstrated positive effect and is clearly well regarded by its recipients and their caregivers, however it is not known whether this model is optimal. Provision of the service by a sole SPT appeared to have benefits, as supported by the questionnaire comments which focused on the specialist expertise, generosity with time and attention plus continued support enabled by this model. It is clear therefore, that, with the right personnel, a sole SPT model can work well. However, the limitations of this model and risk of dependence on one individual should be borne in mind. Further collaborative practice and sharing of knowledge amongst providers of domiciliary support services, via forums and dissemination of research may help to establish the optimal model for service delivery.

The contribution of this chapter to the overall thesis is centred on understanding the role of community pharmacy based adherence services in addressing non-adherence that was almost exclusively of an unintentional nature. The evidence highlights that, with this particular service, non-adherence can seemingly be managed effectively, with a range of interventions utilised to address these deficits. Whilst the strength of this service was its holistic focus and commitment to ensuring all avenues of support were

considered it is reasonable to conclude that as a profession, pharmacists and pharmacy technicians are well equipped to address non-adherence of an unintentional nature. Memory and physical impairments can be remedied with assistive techniques such as reminders and devices, and advice with regard to appropriate dosing and administration can be offered with expertise. Overall, community pharmacies are well equipped to support their patients in overcoming intentional non-adherence, although such services may be further improved by sharing of knowledge and best practice.

Chapter three Theoretical models of behaviour and behaviour change techniques

3.1 Chapter introduction

Chapter two focused on a domiciliary support service to resolve adherence difficulties of a primarily unintentional nature. In this service, patients experiencing cognitive and/or physical deficits were supported via a variety of resolution strategies including additional support plus provision of advice and adherence aids. Whilst improvements can still be made, in the main part, pharmacy services appear to be reasonably well equipped to resolve non-adherence that assumes this unintentional nature.

The remainder of this thesis will therefore concern strategies to resolve intentional non-adherence. The adherence interventions routinely delivered in community pharmacies such as Medicines Use Reviews (MURs) are not well designed to challenge complex patient preferences to intentionally deviate from their prescriber's intentions. Encouraging adherence in these situations is likely to need a different approach, capable of facilitating behaviour change. In this chapter, different techniques to change behaviour will be explored. However, to understand the techniques that can be used to resolve intentional non-adherence, we must first consider the psychology underpinning these behaviours.

3.2 Health psychology and its application to medication adherence

Health behaviours can be thought of as actions that we engage in with the intention of maintaining, attaining or regaining good health, or actions taken in order to prevent illness[244]. By this definition, the action of taking a medicine as prescribed is a health behaviour. In 1980, the biopsychosocial model of health behaviour was first proposed by Engel, who suggested that biological, psychological and social factors interact[245]. This model therefore accounts for the potential impact of thoughts, feelings, culture and environment on a person's behaviour and can be used as a framework to 'understand the person in the context of their life'[246]. The biopsychosocial model is therefore essential for understanding the plethora of factors that may influence a patient's medication taking behaviours.

In chapter one, the importance of a patient's health beliefs to medication adherence were described. Health beliefs can be considered in four different ways[247]:

1) **Attribution theory** – individuals need to view their world as predictable and controllable; an individual's level of perceived control over their illness may therefore influence health behaviours such as adherence to medications.

2) **Risk perception** – individuals will develop a sense of whether or not they are susceptible to a given health problem. Continuation of unhealthy behaviours may be explained by unrealistic optimism where an individual feels confident that they are not susceptible to the risks associated with the behaviour. In a similar way, risk compensation frameworks suggest that an individual may engage in one set of risky behaviours (for example medication non-adherence) as they perceive that this can be compensated for by an alternate healthy behaviour (such as eating fruit).

3) **Motivation and self-determination theory** – autonomous motivations drive personally relevant goals and convey a sense of wellbeing and persistence with health behaviours. Controlled motivations are driven by external factors such as pressure to please peers and may be associated less personal satisfaction and subsequent avoidance of health behaviours.

4) **Self-efficacy** – describes an individual's sense of belief and confidence in their abilities; a deficit in self-efficacy may prevent engagement with health related behaviour change such as implementing a new medicines regimen.

The application of health psychology theory to medication adherence is apparent as patient behaviour (taking medicines as prescribed) is the pivotal link between effective prescribing and achieving a therapeutic outcome. In an attempt to understand and predict the complexities of human behaviour, several psychological theories have emerged to integrate these four key aspects of health beliefs and behaviour. Whilst the theories tend to have similarities and overlapping components, differences also prevail.

3.2.1 Leventhal's Self-Regulatory Model (SRM)[248]

Leventhal's Self-regulatory Model (SRM) describes the key factors which influence health behaviours when an individual encounters ill-health, by assuming a problem-solving approach[248]. The model suggests that individuals deal with illness and illness symptoms in the same way as any other problem; by maintaining an equilibrium. In the presence of a threat to psychological or physical being (an illness), individuals will be motivated to engage in activities to resolve this so that an equilibrium is restored[244].

Illness representations, defined by Leventhal and colleagues as 'a person's own common-sense belief about their illness'[248] provide a framework of five dimensions for coping with and understanding an illness, as described in figure 3.1.

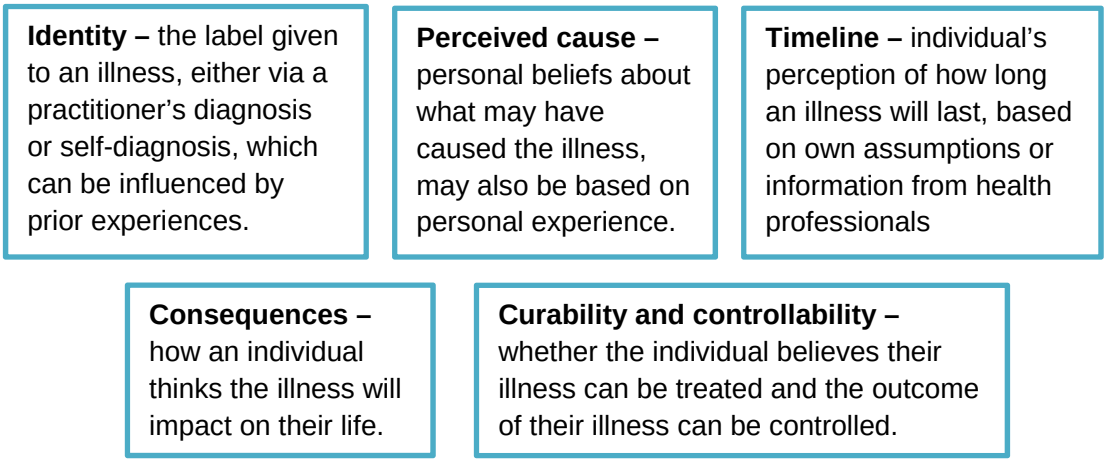


Figure 3.1 Illness representations included in Leventhal's SRM

The SRM is divided into three stages; interpretation, coping and appraisal. During the interpretation phase, the five dimensions (detailed in figure 3.1) are assessed to create an illness representation. An emotional response may also be evoked during the interpretation phase as the implications of an illness may lead to anxiety, stress and fear. The second phase, coping, is the point at which an individual will begin to act upon their interpretation of the illness, this may involve advice seeking from friends, family or healthcare providers, or for example, taking time off of work. In the third stage, appraisal, the individual will assess their chosen coping strategies and decide whether

to continue with this or adopt an alternative strategy. Some individuals may not reach the appraisal stage, especially if they opt for an avoidant strategy or only know of one coping strategy[246].

The SRM has been widely used to understand how people respond to the threat of illness and is useful in its acknowledgement of the dynamic interaction between the way an individual thinks, experiences and copes with an illness. Illness responses will commonly involve consultation with a healthcare provider, which in turn will often yield a prescription. An individual's illness representations may therefore be pivotal to their decision whether to adhere to their prescribed medicine and heavily influenced by previous experiences and lay health beliefs.

In more recent years, the SRM has been reviewed, with new research identifying that treatment beliefs are more strongly associated with behaviour than illness beliefs[249]. This self-regulatory approach to treatment beliefs is supported by recent work, relating to predictors of adherence to preventative medicines for patients who have experienced a stroke[250]. It was reported that whilst illness perceptions were not predictors of poor adherence to preventative medicines, high specific concerns and low perceived benefits of medicines were strongly associated with poor adherence.

3.2.2 Social Cognition Models (SCMs)

Social cognitive approaches to behaviour emphasise that individuals play an active role in interpreting the information around them, focusing on the social context of behaviour change and the cognitive processes that determine whether or not an individual engages with behaviour change[244]. Fiske and Taylor defined social cognitions as 'individual cognitions or thoughts which intervene between observable stimuli and responses'[251]. They therefore represent modifiable determinants of health behaviour and have attracted interest in the fields of health psychology and behaviour change.

Social Cognition Models (SCMs) assume that the major determinants of behaviour are an individual's attitudes and beliefs, which in turn influence the interpretation of experiences and information, which guide behaviour. Many models have emerged and new theories continue to be presented, however, the three most commonly applied social cognitive models are described in the following sections.

3.2.2.1 The Health Belief Model (HBM)[252]

The Health Belief Model was one of the first SCMs and remains one of the best known health behaviour change models[253], despite almost forty years passing since its original conception by Rosenstock[252]. Later elaborations developed the model further[253, 254], maintaining its position as a core model of health behaviour. Rosenstock and colleagues worked as a small team of social psychologists during the 1950's as part of the US Public Health Service, where they were tasked with developing a theoretical model to better understand the widespread failure of screening programmes for tuberculosis[255]. The HBM model was therefore developed in the context of understanding preventative health behaviours. Central to the underpinning of this model, is the importance of health beliefs in determining whether or not an individual engages with protective health behaviours.

According to the HBM, the likelihood of an individual engaging in a health behaviour (for example taking a prescribed medication) is determined by the perceived health threat and an evaluation of the recommended action. Figure 3.2 provides a summary of the Health Belief Model, and highlights that the core elements of the model are:

- **Perceived susceptibility** - an individual's assessment of the likelihood of succumbing to the illness in question
- **Perceived severity** - an individual's assessment of the severity of a condition and its consequences
- **Perceived barriers/costs** - an individual's assessment of likely influences that may discourage adoption of the health behaviour and the implications of adopting (or not adopting) the behaviour
- **Perceived benefits** – an individual's assessment of the positive consequences of adopting the behaviour
- **Cues to action** – prompts that trigger the behaviour, including internal cues (such as symptoms of illness) and external cues (such as health promotion)
- **Health motivation** – the value that an individual attaches to their health and their willingness to take part in health promoting activities

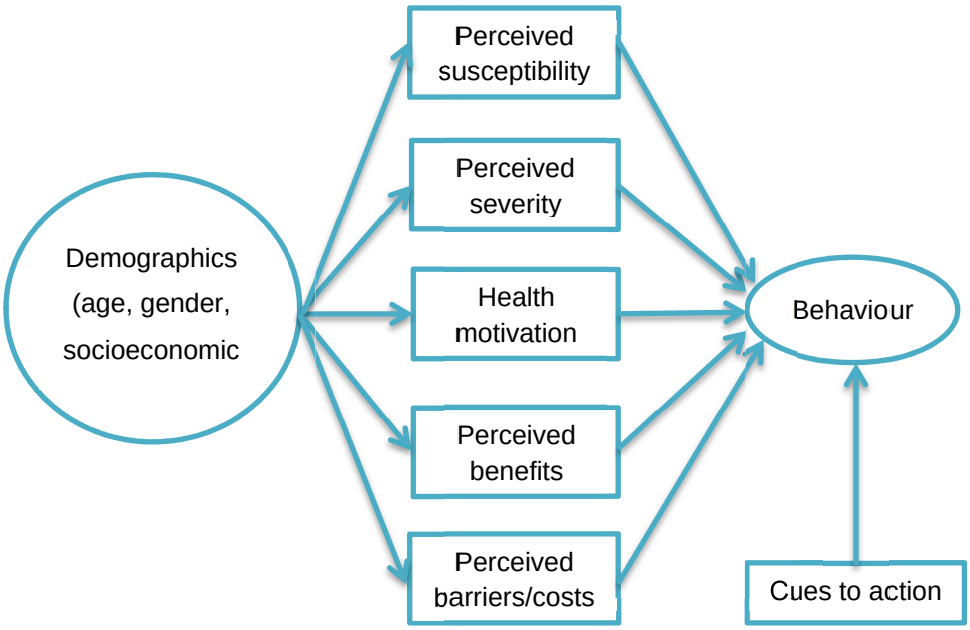


Figure 3.2 The Health Belief Model (HBM)

Figure sourced from Conner, M. and P. Norman (2005). Predicting Health Behaviour: Research and Practice with Social Cognition Models. Oxford University Press[256].

The perceived susceptibility and seriousness of a condition feed into a cognition of perceived threat, whereas the perceived benefits and barriers of an action feed into a cognition of outcome expectation. In essence, the HBM explains that people create a risk/benefit analysis of perceived threat and balance this against their outcome expectations. The balance between these two factors will determine behaviour.

With regard to medication adherence, for a patient to adhere they must believe they are susceptible to an illness and that they will become unwell if they do not adhere to their prescribed therapy. They must also believe that taking the medicine will infer benefits, that there are few personal costs resulting from adherence and that any barriers to non-adherence are not insurmountable. They must also be motivated to engage in the necessary behaviours. Whilst medicines can be used to both treat and prevent symptoms (for example beta-agonist inhalers and steroid inhalers respectively for asthma) and protect against disease manifestation (for example statins to protect against cardiovascular disease), patients must always believe that they are susceptible to the illness and that treatment will confer greater benefits than costs, plus have sufficient motivation in order to adhere. The HBM is therefore useful in understanding patient behaviour in relation to medication adherence.

The HBM has been applied to a wide range of health behaviours[257] though conflicting findings have been reported[244]. Criticisms of the HBM have focused on its emphasis on individual rather than social and environmental factors plus the assumption that individuals are rational processors of information, which does not account for the influence of emotions such as fear. Despite these criticisms, the HBM remains the most cited and researched of the SCMs.

3.2.2.2 Protection Motivation Theory (PMT)[258]

The PMT model was originally conceived to explain the effects of 'fear appeals' on health attitudes and behaviours[258]. Whilst this theory builds upon the HBM, PMT includes 'fear' and thus attempts to incorporate an emotional component within the understanding of health behaviours. The components of the PMT (as depicted in figure 3.3) predict behavioural intentions which are closely related to behaviour.

PMT postulates that when an individual is confronted with a threat (for example ill health), two mediating cognitive processes are stimulated; threat appraisal and coping appraisal[259]. Threat appraisal is influenced by an individual's perceived severity of a threat, their perceived susceptibility to it and their fear. Coping appraisals combine the individuals assessment of the efficacy of the threat responses (actions), and their perceived sense of self-efficacy in executing these threat responses[258]. Environmental and intrapersonal information influence the core components of the PMT, which then elicit either an adaptive or maladaptive coping response. For an adaptive behaviour to be performed an individual must perceive the threat to be severe, something they are susceptible to and that there is an effective response (behaviour) that will negate the threat and which they are confident they will be able to execute.

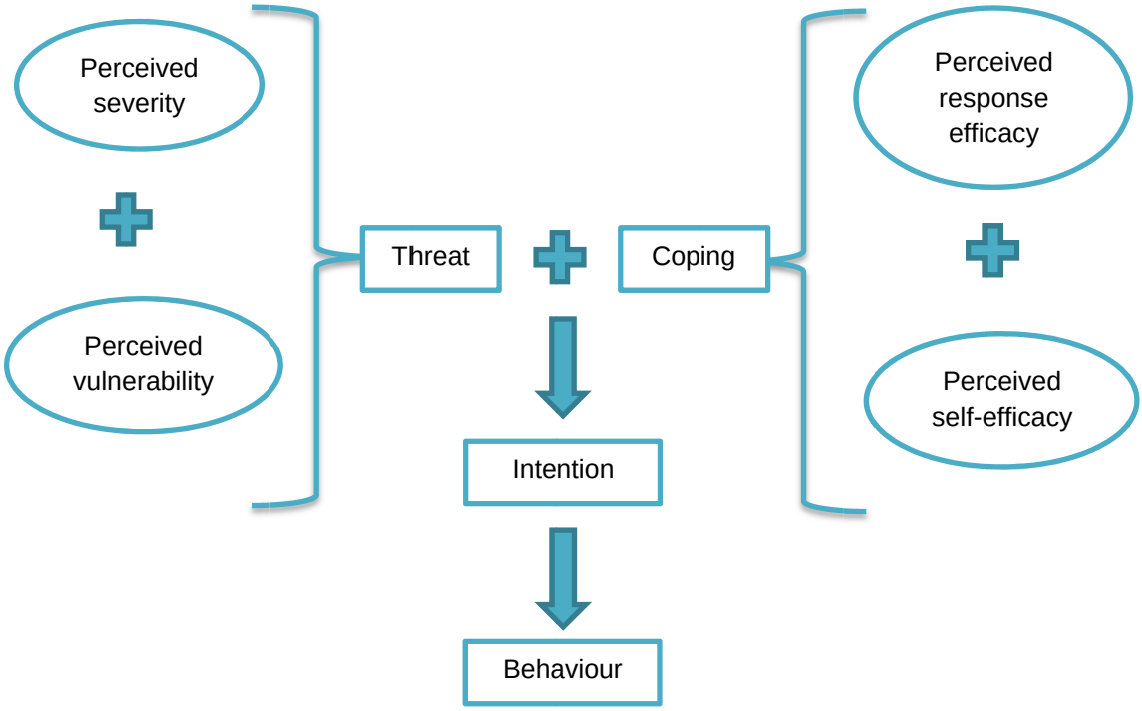


Figure 3.3 Protection Motivation Theory (PMT)

Figure sourced from Lee et al. (2007)[260]

In the application of PMT to, for example, adherence to medication for the prevention of cardiovascular disease, PMT would predict that information about the role of medicines in preventing cardiovascular disease would increase the individual's fear and perceived severity of the disease, as well as their belief regarding how susceptible they are to experiencing adverse cardiovascular events. If the individual felt confident that they could adhere to their medicines (self-efficacy) and that taking their medicines would reduce their risk of cardiovascular disease (response effectiveness), then high intentions to change their behaviour and adhere to their regimen will prevail, yielding an adaptive coping response.

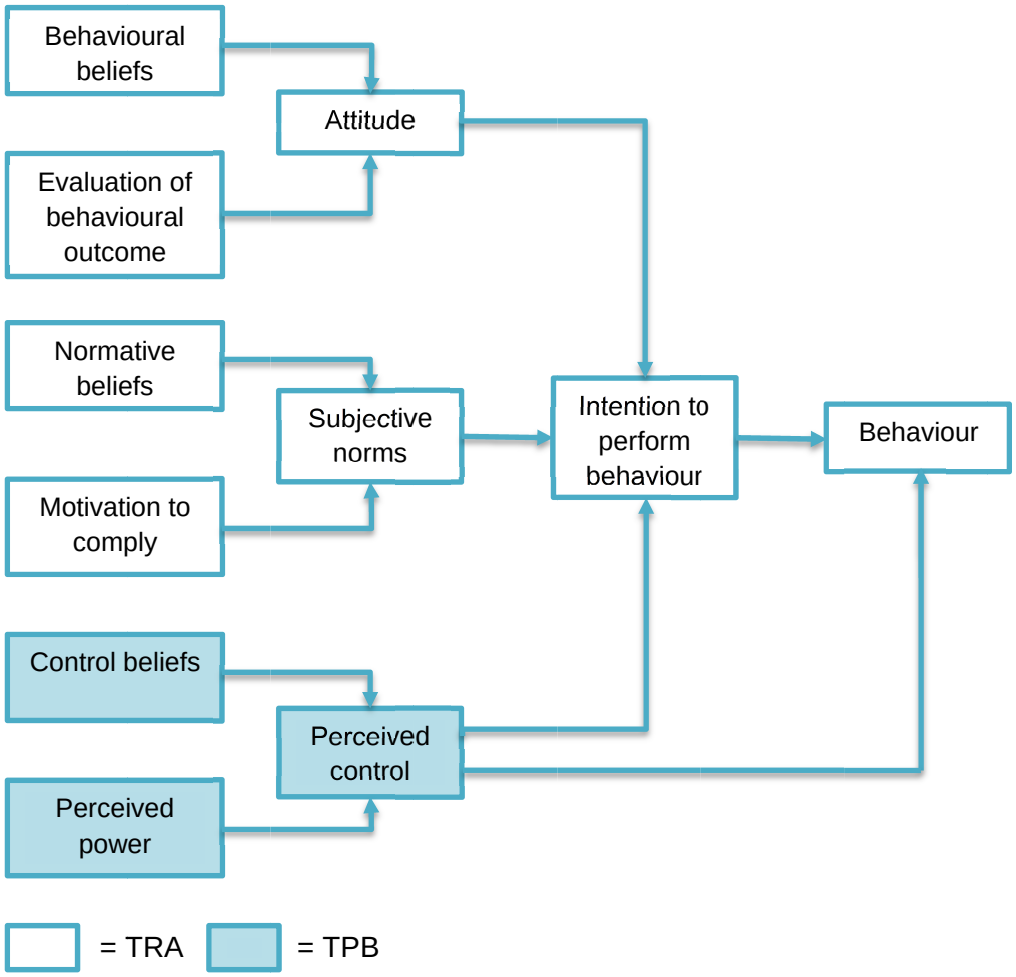
Whilst reports of the use of PMT in predicting health behaviours are apparent[247] it has been criticised for its failure to include social and environmental factors. Similarities to the HBM are apparent and the same limitations exist. As such, the PMT model is unlikely to provide the best explanation of medication taking behaviours.

3.2.2.3 The Theory of Planned Behaviour (TPB) and the Theory of Reasoned Action (TRA)

The TRA also has similarities with the HBM but differs in that it accounts for social influences. Social influences such as what friends and family think, what is perceived as 'normal' and perceived pressure to please others are likely determinants of

medication taking behaviours and thus the TRA is relevant to this domain. The premise of the TRA is that intentions precede behaviours and that these intentions are shaped by attitudes towards the behaviour (likely outcomes and values) and subjective norms (patient beliefs about the views of others with respect to the behaviour and their perceived expectations)[261, 262].

The TRA is useful in its inclusion of intention formation and social influences; however, it fails to encompass the effect of factors outside of the patient's control. The TPB addresses this deficit, by adding perceived behavioural control (self-efficacy) and perceived barriers[262]. Perceived behavioural control, the extent to which an individual believes they can successfully engage in a particular behaviour, is shaped by both previous experience and beliefs about ability[244]. Figure 3.4 depicts the TRA and its adaptation, to the TPB.



Adapted from Montano and Kasprzyk[263]

Figure 3.4 Theory of Reasoned Action (TRA) and Theory of Planned behaviour (TPB)

An adherence study to psychiatric medication, using the TPB to aid understanding, reported that perceived behavioural control and intentions to adhere both significantly predicted adherence, accounting for 38.1% of the variance in adherence[264]. These research findings, amongst others support the application of the TPB to understanding medication adherence. As such, it is clear to see that interventions seeking to change a patient's beliefs about taking their medicines or enhance their motivation to do so are likely to yield changes in behaviour. If an individual believed that adhering to their medication would be beneficial to their health (attitude towards the behaviour) and believed that other people thought they should take their medicine (subjective norm), plus, if they believed that they were capable of adhering to their prescribed medication regimen (behavioural control) then this would predict high intentions to adhere (behavioural intention). The TPB also predicts that perceived behavioural control can directly influence behaviour without influencing intentions, for example, in instances where deficits in manual dexterity affect a person's ability to access or administer their medicines (behavioural control), this is a better predictor of adherence than whether or not they intended to adhere.

Whilst the positive aspects of the TPB, especially with regard to medication adherence are apparent, limitations have also been suggested. Most notably, the intention-behaviour gap is of concern, as intentions are not always translated into behaviours[244].

3.2.2.4 Summary of Social Cognition Models

All of the models of behaviour proposed are based on cognitions that are consciously thought out before the behaviour occurs. Whilst useful in allowing an understanding of conscious behaviours, habitual or irrational behaviours which do not involve conscious pre-emptive thoughts cannot be explained by these theories. The theories therefore provide a foundation point from which we can begin to understanding the complexity of explaining medication taking behaviours. Rather than being a definitive explanation of human behaviour, SCMs represent a tool to facilitate our understanding, providing a structured approach to understanding health beliefs and predicting health behaviours.

In light of the limitations of the SCMs, suggestions for the addition of further variables have been posed, including[247]:

1) **Expanded norms** – such as moral norms, descriptive norms (perceptions of whether other people carry out the behaviour) and injunctive norms (whether other people may approve or disapprove of the behaviour)

2) **Affective beliefs** – to include the influence of emotions and their affect upon behaviour, beyond the inclusion of 'fear' in PMT
3) **Anticipated regret** – as an alternative approach to emotions
4) **Self-identity** – as individuals will only intend to perform a behaviour if it fits with their own image of themselves
5) **Ambivalence** – to accommodate for behavioural attitudes that are indifferent rather than positive or negative
6) **Personality** – certain aspects of personality are associated with health behaviours and may influence motivation

3.2.3 Stage models

A notable limitation of the Social Cognition Models is that cognitions and behaviours change over time**.** Stage models attempt to address this problem by considering health behaviours as processes which occur in a series of stages.

3.2.3.1 The stages of change model

The stages of change model, also known as the Transtheoretical Model of behaviour change (TTM) is the most widely applied stage model and assumes that different cognitions take precedence at different stages of change. Developed in 1983 by Prochaska and DiClemente[265] and based on the analysis of different theories of psychotherapy[266] the TTM recognises that individuals change their behaviour in gradual and often non-linear fashion.

The TTM proposes five key stages of change:

1. **Pre-contemplation** – an individual is unaware of the need to change or unwilling to do so, they will not be thinking about changing their behaviour and will not be interested in any help to do so.
2. **Contemplation** – the individual becomes aware of the consequences of their current behaviour and their personal susceptibility and begin to weigh up the costs and benefits of changing the behaviour. Whilst thinking about the behaviour, they are not as yet fully committed to changing it.
3. **Preparation** – the individual has made the decision to change their behaviour and intends to do so in the near future. This is the period of psychological preparation for change, small changes may be tried first to ease the behavioural transition.

4. **Action** – the individual implements the plans made in the preparation stage and attempts to change their behaviour, though the risk of relapse is high.
5. **Maintenance** – the individual develops strategies to maintain their new behaviour and resist temptations which would prompt relapse.

Ideally, relapse will be avoided and the new 'healthier' behaviour will be maintained. However, in reality, it may take several attempts before a patient is able to fully maintain their new behaviour. Decisional balance, the way in which an individual weighs up the costs and benefits of a behaviour is also key to the TTM, as an individual's focus will shift according to the different stages of change. For example, an individual who has stopped smoking is likely to focus on the benefits of this behaviour at the action and maintenance stages, but comparatively, at the pre-contemplation stage, they are more likely to focus on the costs.

In relation to medication adherence, the TTM is useful in understanding the processes necessary to convert a non-adherent patient into an adherent one. Moreover, it is useful in prioritising service delivery so that interventions to support behaviour change are delivered at the appropriate stage, when a patient feels ready and is a willing recipient of support and help.

3.2.3.2 The Health Action Process Approach (HAPA)

Developed by Schwazer in 1992[267], the HAPA stage model of health beliefs and health behaviours, emerged following a review of literature in an attempt to address recognised deficits. The model emphasises the importance of self-efficacy and shares many constructs with the SCMs described earlier. The HAPA differs from other models in its distinction between a decision making/motivation stage and an action/maintenance stage. In the motivation stage, an individual decides whether or not to carry out a behaviour and then makes plans to initiate and maintain the behaviour in the action phase. Figure 3.5 summarises the HAPA.

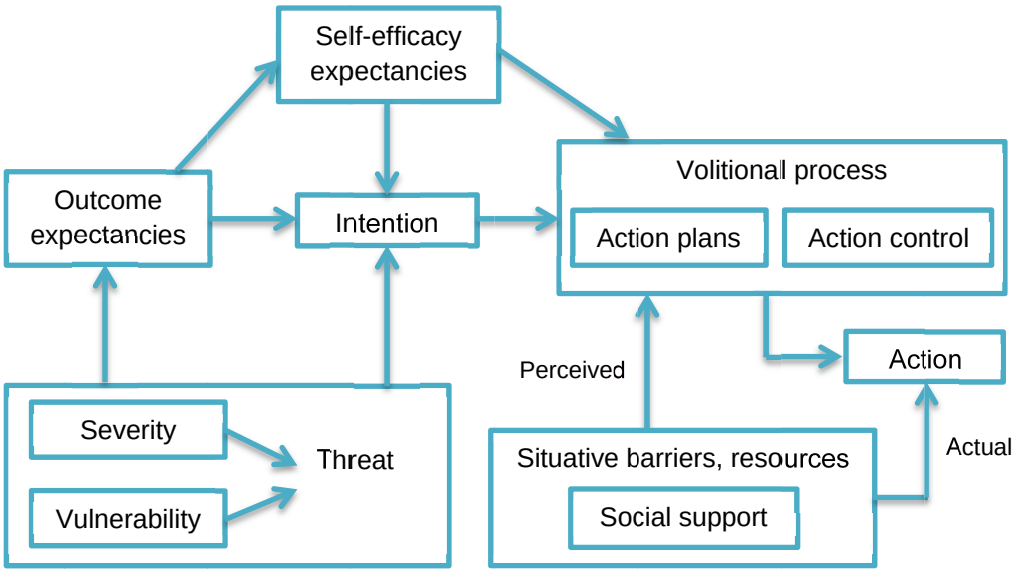


Figure 3.5 The Health Action Process Approach (HAPA)

Figure sourced from Ogden, J. (2012). Health psychology, McGraw-Hill International.[247]

The motivational phase is comprised of:

- Self-efficacy – confidence in ability to perform the behaviour
- Outcome expectancies – anticipated benefits associated with performing the behaviour such as improved health or approval from peers
- Threat appraisal – individual beliefs about the severity of an illness and perceived susceptibility

The action phase is comprised of:

- Cognitive (volitional) factors – action plans and action control which determine the individuals willpower
- Situational factors – including social support and the absence of barriers such as costs

These cognitive and situational factors integrate with behavioural factors to determine the extent to which a behaviour is initiated and maintained. Schwatzer has argued that self-efficacy has consistently been shown to be the best predictor of behavioural intentions for numerous health related behaviours[267] and the HAPA model has been used to predict breast self-examination behaviours in a large population of women[268]. It has however been criticised for failing to stipulate the role social and environmental factors[247].

3.2.4 Summary of theories of behaviour

Considering medication adherence in the context of health behaviour theories is a useful tool in understanding how to modify patient behaviour by supporting adherence. The SCMs and stage models have shown that social cognitions predict behaviour, therefore, if practitioners wish to influence patient behaviour, aiming to amend these social cognitions, where possible, is intuitive.

Interventions grounded in psychological theory have also been shown to elicit larger behavioural effects than interventions that are not designed with a theoretical basis. In their systematic review and meta-analysis of internet based health promotion strategies, Webb *et al.* reported that more extensive use of theory was associated with statistically significant increases in effect size (p= 0.049). In particular, Webb and colleagues report that interventions based on the theory of planned behaviour tended to elicit the most substantial effects on behaviour[269]. Similarly, Taylor *et al.* have recently published a meta-analysis of worksite physical activity programmes and reported that interventions which explicitly used more theory, elicited larger effects[270].

Whilst the most commonly and widely accepted theories of behaviour have been considered, there are many other models, each focusing on slightly different or overlapping constructs. The complexities of the different models and their overlapping concepts, limit their use in the wider field outside of theoretical psychology. Moreover, the different models place precedence on different cognitions, therefore it can be difficult to know which cognitions are priorities for intervention targeting. Many models (including the TPB) also explain and predict behaviour rather than providing information on how best to modify it which augments the usability difficulties. Given these problems, it is not surprising that so few interventions have a strong grounding in theory; the complexities, poor accessibility and confusing overlaps of the theoretical models act as a barrier to their efficient incorporation in intervention design.

In order for behaviour change interventions to be theoretically based and therefore better designed, the psychological models of behaviour which underpin the theory need to become more accessible. In recent years, novel work has emerged which aims to address these deficits and provide a theoretical framework for the models of behaviour and integrate the models to form a singular, definitive model comprised of the core constructs of behaviour.

3.2.5 Integrated models of behaviour

Integrated models of health behaviour have included Lippke and Plotnikoff's integration of PMT with the SOC to predict exercise[271] and the work of Jacobs *et al.* who integrated the TPB with self-determination theory in the context of diet and physical activity[272]. Whilst these approaches have generated research interest, the most notable integrative model to emerge in recent years, 'the major theorist's model' emerged from a workshop attended by prominent psychologists who identified eight key variables which they believed to account for variance in any given behaviour[273]. These variables were divided into those directly impacting upon behaviour (environmental constraints, skills and intentions) and those relating to intentions (self-discrepancy, self-efficacy, social pressure, advantages/disadvantages, emotional reactions).

Conner and Norman note that although this model is logical and includes well-tested constructs from the SCMs, it also contains new, untested constructs and those which have previously shown poor predictive validity such as self-discrepancy[256]. Further criticisms of the model extend to the omission of variables such as risk perception and perceived severity, which are known predictors of behaviour plus a failure to bridge to intention-behaviour gap[256]. Fishbein and colleagues' work with the 'major theorist's model' did however represent the first theoretical framework of individual behaviour change, from which notable research has stemmed.

3.2.6 Theoretical frameworks of individual behaviour change

In recent years, two theoretical frameworks have emerged[274, 275], pooling the different models of behaviour and identifying common domains to form a scaffold for identifying individual patient barriers to behaviour change. These frameworks are therefore the logical mediator between understanding theories of behaviour and developing a theory based novel adherence intervention.

The frameworks have been designed to have high usability and an accessible nature, to facilitate the incorporation of health psychology theory into intervention design in a robust, but far simpler way.

3.2.6.1 The 'Fishbein Framework'[274]

Fishbein's framework for individual behaviour change was developed in the context of health promotion, with specific relation to HIV preventative behaviours. The framework

consists of eight domains, which have been identified as the key moderators of patient behaviour, as shown in figure 3.6.

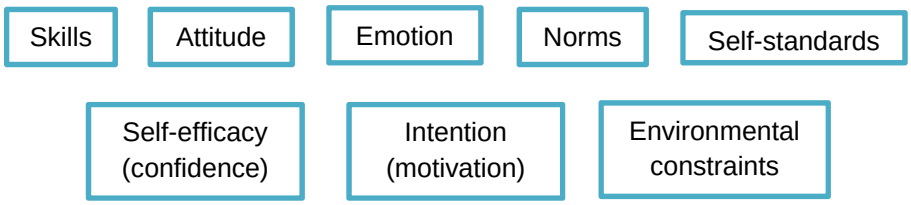


Figure 3.6 Domains of the 'Fishbein Framework'

In order to adhere, a patient requires practical skills to be able to take their medicines (skills) plus confidence in their ability to do so (self-efficacy). They also need to be motivated to adhere and intend to take their medicines (intention) and they must not be hindered by difficulties such as being unable to collect their medicines (environmental constraints). Adherence will also be supported by a positive attitude towards taking the medicine (attitude), positive social influences (norms) and placing importance on undertaking the behaviour (self-standards). Experience of stress and anxiety associated with medicines taking may hinder adherence (emotions).

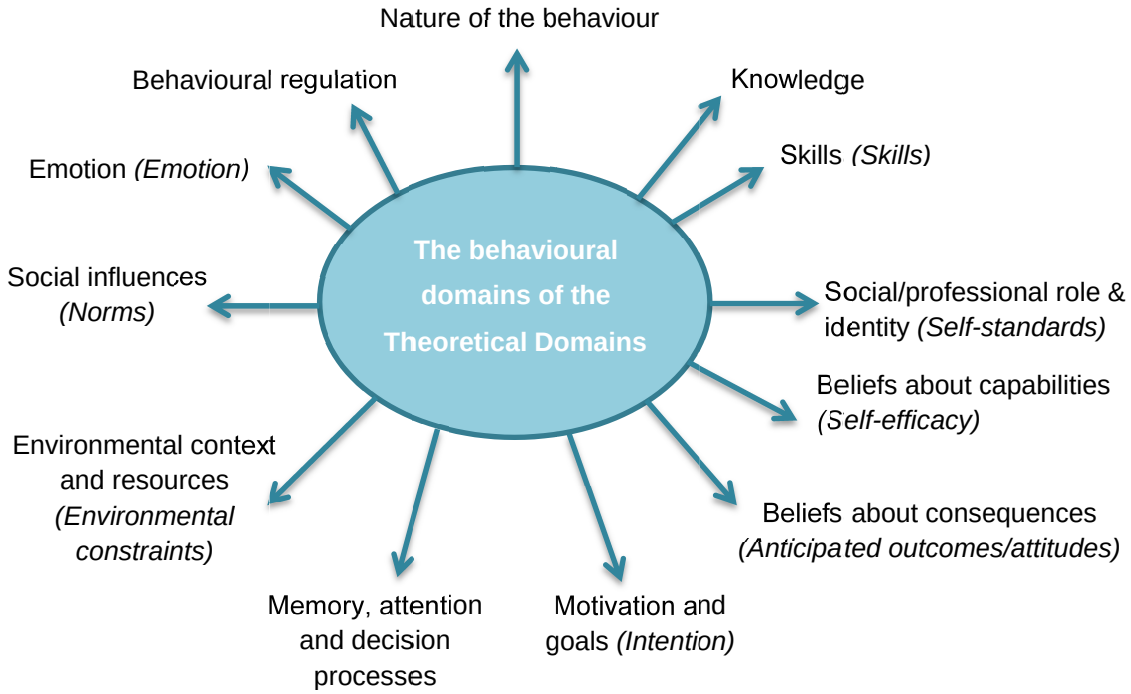
Fishbein *et al.* suggested that just three domains were necessary and sufficient prerequisites for performing a specified behaviour; a strong intention to perform the behaviour, no environmental constraints that would make performing the behaviour impossible and the skills necessary to perform the behaviour. The remaining domains are considered to be determinants of intention strength. Fishbein and colleagues used a consensus approach to arrive at these domains, but precise methodological details are absent. The framework was also published for psychological readership, which may limit its accessibility to non-psychologists, responsible for research on the implementation of evidence based practice. The Fishbein Framework therefore represents a useful foundation for collating health behaviour models, but may not be sufficient to provide a fully accessible and widely used tool.

3.2.6.2 The Theoretical Domains Framework (TDF) [275]

Unlike Fishbein's work, the Theoretical Domains Framework (TDF) was developed in the context of professional behaviour change, but has later been adapted for patient health behaviours. This seminal work was undertaken in 2005 by Michie *et al.* on behalf of the Psychological Theory Group and was later adopted as the British Psychological Society's (BPS) Framework. Michie and colleagues used a multi-stage consensus approach over a 14 month period to develop a theoretical framework that could be used in implementation research. The multiple stages included work with 18

experts in health psychology theory, 16 international health service researchers with expertise in implementation research and 30 delegates at a health psychology conference.

Figure 3.7 summarises the final 12 domains of the TDF and highlights the overlap with Fishbein's framework[274]. Full details of the constructs associated with these domains are provided in appendix 3.1. Given that consensus for the TDF was achieved independently of the Fishbein Framework and in the context of different behaviours, the similarity between the two frameworks can be argued to further validate the work of Michie *et al*. Whilst the two frameworks are largely similar, the TDF includes four additional domains: 'knowledge', 'memory, attention and decision processes', 'behavioural regulation' and 'nature of the behaviour'. Michie *et al.* suggest that the inclusion of four additional domains may be reflective of the wider group of expertise employed, but also developments in the research field since Fishbein's work[275].



* Domains in parenthesis show corresponding domains of 'Fishbein framework'

Figure 3.7 Behavioural domains of the Theoretical Domains Framework (TDF)

In 2012 the TDF was refined following a comprehensive three-step validation process[276] to contain 14 domains and 84 component constructs. The refined framework provides explicit behavioural domain definitions, informed by the use of the American Psychological Associations' Dictionary of Psychology[277], as summarised in appendix 3.2. Further refinements to the TDF are summarised in table 3.1.

Nature of change	Rationale
'Motivation and goals' domain separated into 'intentions' and 'goals'	Domain split to differentiate between 'goals' which focus on a preferred outcome or end state and 'intentions' which concern the resolve to initiate or terminate a behaviour.
'Beliefs about consequences' domain split into two domains, one retaining the original name and one termed 'reinforcement'	Domain split to differentiate between 'reinforcement' which focuses on the constructs of associative learning and 'beliefs about consequences' which focuses purely on beliefs.
'Beliefs about capabilities' domain split into two domains, one retaining the original name and one termed 'optimism'	Domain split to differentiate between 'optimism' which concerns a general disposition and 'beliefs about capabilities' which focuses on specific capabilities
'Behavioural regulation' domain clarified	Clarification enables focus on self-regulatory processes
'Nature of the behaviours' domain removed	Analysing the nature and influences of behaviour are two distinct processes

Table 3.1 Summary of key changes to updated TDF[276]

3.2.6.3 Research applications of the TDF

Whilst the refined TDF is yet to be widely used in research, the original TDF has generated marked research interest. In their 2012 commentary, Francis *et al.* identify 133 papers which cite the TDF, including 17 studies which have used the TDF to explore health professionals' behaviours[278]. The TDF has been used successfully to develop theoretically derived behaviour change interventions for the management of acute low back pain in primary care[279] and to identify barriers to the implementation of best practice guidelines in schizophrenia[280]. Further uses of the TDF include the identification of enablers and barriers to incorporation of evidence based guidelines, in acute low back pain[281, 282] and to classify the behavioural determinants of clinicians' blood transfusion practices[283, 284] .

Whilst these qualitative studies highlight the variety of health behaviours to which the TDF is applicable, interesting work has also emerged from the application of the TDF to the development of health related questionnaires. Questionnaires have emerged to identify barriers and promoters to behaviours such as the implementation of smoking cessation guidelines in midwives[285] and dentists[286], following hand hygiene behaviours in hospital workers[287] and following guidelines the positioning of nasogastric (NG) tubes in healthcare providers[288]. The questionnaire relating to positioning of NG tubes was later used to highlight the feasibility of using the TDF as a framework to guide the implementation of patient safety interventions[289].

More recently, a patient based questionnaire, grounded in the TDF and designed to identify determinants of physical activity has been reported[290]. In this work, previously identified barriers to physical activity were mapped to the behavioural domains of the TDF then questionnaire statements developed to reflect these barriers. Psychometric testing of the questionnaire, following its completion by 832 UK based university staff and students highlight the promising credentials of this tool.

3.2.6.4 Strengths and limitations of the TDF

The theoretical domains framework has assimilated common and overlapping constructs of the plethora of health behaviour and social cognition models, into a simple framework to identify key determinants and constructs of health related behaviours. This approach, which aims to provide easier access to health psychology theory, has been applied to a variety of health behaviours and in many different ways. Michie *et al.* comment that the TDF is intended for use by health services researchers and other practitioners, without expertise in health psychology and note that this is a key point of differentiation from other theoretical models which tend to be intended for use by psychologists[275]. Whether or not the aim of improving access to psychological theory has been realised is yet to be established as to date, publications reporting the use of the TDF are still predominated by psychologists[278]. However, by providing a singular and comprehensive framework, covering multiple overlapping theories, it is feasible that the TDF could be utilised more easily by non-psychologists. If nothing else, use of the TDF has the potential to remove the complex decision of identifying which theory of behaviour should be used as a model. The utility of the TDF by pharmacists rather than psychologists is explored in chapter five.

Taylor *et al.* have highlighted that the TDF is also amenable to adaptation for specific behaviours offering a degree of flexibility to its application[290]. The original TDF and its later update are therefore promising tools both in behaviour change and implementation research. However, the TDF is not without limitations. Whilst approaches such as the theory of planned behaviour specify relationships between the detriment areas, such as the link between intention and behaviour, the TDF does not specify such relationships. The TDF does therefore not attempt to replace such theories[283] but instead offers an alternate approach.

3.2.6.5 Applying the TDF to the design of a novel adherence intervention

In their hand hygiene behaviours work, Dyson *et al.* comment that identification of the barriers to behaviour change is a significant step forward in designing targeted and

effective interventions to modify behaviour[287]. More recently, in their physical activity questionnaire, Taylor *et al.* note that their questionnaire has the potential to be adapted to other health domains to facilitate tailoring of interventions to meet individual needs[290].

Whilst the TDF has been applied to numerous health behaviours and promising work has emerged to utilise the TDF to identify barriers to behaviour change, to date, the TDF has not been applied to medication adherence. If the barriers to medication adherence could be identified and mapped to the behavioural domains of the TDF, a questionnaire to represent these barriers could be developed, similar to that developed by Taylor *et al.* Such a questionnaire, enabling identification of an individual's barriers to medication adherence could be a pivotal precursor to delivery of a theory-based adherence intervention targeted to meet individual needs by resolving their identified adherence barriers. The notion of developing an Identification of Medication Adherence Barriers Questionnaire (IMAB-Q) was therefore conceived, as described in chapter five of this thesis.

3.3 Facilitating behaviour change; a taxonomy of behaviour change techniques

Whilst understanding that the theories of medication taking behaviours are fundamental in designing adherence interventions, the primary aim of such interventions will be to improve medication adherence by changing patient behaviours. As such, the challenge in designing effective adherence interventions is in understanding how to influence and change patient behaviour[12]. Behaviour change is notoriously difficult, requiring considerable time, effort and motivation on the patient's part.

In 2011, the term Behaviour Change Technique (BCT) was defined as:

"an observable, replicable and irreducible component of an intervention designed to alter or redirect causal processes that regulate behaviour"[291]

BCTs can therefore be thought of as the 'active ingredients' of an intervention and the components that yield behaviour change. A plethora of BCTs to change health behaviours are available and many of these, such as provision of education and demonstrating the behaviour, are routinely used in community pharmacy consultations to support medication adherence.

One of the most widely cited criticisms of health behaviour change research is the lack of a 'common language' to describe intervention components[292, 293]. As such, similar terms may be used for very different techniques or different terms used for identical techniques. An example of ambiguous terminology, applicable to medication adherence is that of the term 'self-monitoring' which could refer to diary keeping to record medicines taken. However, the term could also refer to monitoring the benefits of medication adherence by recording, for example, home monitored blood pressure or blood glucose readings.

Guidance for the development and evaluation of complex interventions, issued by the Medical Research Council (MRC), has called for improved methods for specifying and reporting intervention content[294]. Developing a common vocabulary for intervention components, as a taxonomy of behaviour change techniques was an intuitive approach to addressing this problem. In 2008, Abraham and Michie developed the first cross disciplinary behaviour change technique taxonomy, comprised of 26 BCTs as detailed in appendix 3.3. In the same year, Michie *et al.* linked 35 defined BCTs to the behavioural domains of the TDF[295], as summarised in appendix 3.4. This mapping work represents the first steps towards practitioners being able to select a behaviour change technique according to the problem that they are trying to address and thus

represents an important milestone in health behaviour change research. With application to medication adherence this preliminary work poses that, for example, if a patient was known to be non-adherent due to a deficit in their skills such as an inability to correctly use their inhaler, the BCT termed 'modelling/demonstrating the behaviour' would be appropriate as the patient would likely benefit from being shown how to use the inhaler correctly. Conversely, BCTs such as motivational interviewing have been mapped to the TDF behavioural domain of 'motivation and goals' which is intuitive as motivational interviewing is known to be an effective approach to increasing a patient's motivation. For some behavioural domains such as 'skills' and 'beliefs about capabilities', numerous BCTs were identified as potential tools for behaviour modification. Conversely, for other behavioural domains such as 'knowledge' and 'emotions', far fewer BCTs were identified. These differences are likely influenced by the type of behaviour to be targeted. For example, in order to increase a patients knowledge, there is little more to be done other than to provide education. Similarly, to overcome emotional barriers to behaviour change such as feeling negative, few BCTs are readily available; Michie and colleagues suggest BCTs termed 'stress management' and 'coping skills' as effective techniques[295].

Whilst this work was intended as a preliminary taxonomy and mapping exercise it represents a pivotal progression in the quest for well defined, theory based behaviour change interventions. For the interventions grounded in the TDF, such as the barriers to physical activity questionnaire designed by Taylor *et al.* an opportunity to select BCTs according the behavioural domain containing the greatest prominence of barriers is created. This approach is also applicable to the proposed questionnaire that will be developed to identify barriers to medication adherence, representing an exciting opportunity to develop an evidence and theory based intervention tailored to meet individual need.

The preliminary nature of the work presented with Abraham, Michie and colleagues is represented by the notable developments and refinements that have emerged in recent years. The original BCT Taxonomy has been applied to behaviours such as physical activity and healthy eating[296], smoking cessation[297] and excessive alcohol use[298]. In 2013 the first full BCT Taxonomy was published, comprised of 93 BCTs clustered in 16 groups[293]. Work to map the new 93 BCT taxonomy to the behavioural domains of the TDF is due for publication imminently[299] and will provide explicit detail of interventions appropriate for moderating barriers to behaviour change in the domains of the TDF. As the taxonomy continues to be refined, its potential application to medication adherence research should therefore be borne in mind.

3.4 Behaviour change techniques to resolve intentional non-adherence

The 26 BCTs defined by Abraham and Michie[292] and detailed in appendix 3.3 highlight that the nature of the BCTs and the behaviours for which they may be useful in moderating are variable. BCTs such as 'providing instructions' would be useful in cases of unintentional non-adherence, where a patient does not know how to adhere to their medicines. Similarly, BCTs such as 'teach to use prompts or cues' would also be useful to address barriers to adherence such as forgetfulness which often assumes an unintentional nature. Conversley, BCTs such as 'motivational interviewing', 'prompting intention formation' and 'prompting barrier identification' may be more useful in intentional non-adherence, whereby an individual's, motivations and intentions may need to be altered. As the remainder of this thesis concerns strategies to resolve intentional non-adherence, BCTs that may be applicable to the endeavour will be considered in greater depth. Firstly, consideration is given to the intervention approach that may be needed to facilitate change of intentional behaviours.

3.4.1 A patient centred approach to behaviour change

Substantial developments in understanding health related behaviour changes came with the seminal work of Rollnick who identified that the challenging nature of behaviour change is augmented by patient ambivalence towards making the changes[300].

For many years, healthcare practitioners' attempts to encourage lifestyle changes, such as those needed to adhere to medication regimens, were heavily focused around the provision of persuasive advice, which whilst beneficial for some patients, tended to demonstrate poor efficacy[301]. These poor results may be a reflection of the ambivalence experienced by patients contemplating change and their lack of readiness to do so. Consequently, provision of advice when it has not been requested, in patients who are not ready to receive it is likely to have detrimental effects by instigating or increasing a patient's resistance to change[302]. In the BCT Taxonomy, techniques such as 'providing information on consequences' and 'providing information about behaviour-health link' have the potential to evoke resistance, if delivered to patients who are unwilling recipients of such information. In contrast to the patriarchal perceptions evoked through unwanted advice from health care professionals wishing to instigate behavioural changes in their patients, the move towards more patient-centred approaches produced far better outcomes[301].

Despite the move towards patient centred care, routine community pharmacy services, such as MURs and the NMS are still heavily focused on the provision of advice and education. For patients who, for reasons of health beliefs, illness perceptions or lack of motivation have willingly chosen to not take their medicines as prescribed, education as to why they 'should' take their medicines is unlikely to evoke behaviour change.

Included within the aforementioned behaviour change taxonomy, are a number of behaviour change techniques, such as Motivational Interviewing (MI) which are targeted towards behaviour change using a psychological or cognitive based approach. These techniques are of particular interest for resolving non-adherence of an intentional nature as they are designed to change the way individual thinks and feels about the behaviour and their motivation to do so.

3.4.2 Motivational Interviewing (MI)

Motivational interviewing (MI) is a patient-centred technique that has gathered increasing interest in health care settings[303] since its conception by Miller in 1983[304] and subsequent elaborations[302]. Rollnick and Miller describe the main focus of MI as the facilitation of behaviour change by enabling patients to resolve and explore their ambivalence related to the behaviour[305]. MI is a directed technique with clear goal setting and deployment of systematic strategies to guide the patient towards choosing to change their behaviour in the desired direction[302]. A supportive rather than argumentative approach is imperative, with a persuasive rather than coercive stance enabling an increase in the patient's intrinsic motivation[306].

Miller and Rollnick describe the five clinical principles upon which MI is based as expressing empathy, developing discrepancy, avoiding argumentation, rolling with resistance and supporting self-efficacy[302]. Without empathy, rapport may be low and clients may be resistant to change and less likely to explore their inner thoughts and motivations. Likewise, developing discrepancy is essential in exploring the patient's ambivalence and formulating arguments for and against their problematic behaviours with avoidance of argument and rolling with resistance imperative in ensuring ambivalence and reluctance is respected and that defensive or resistant behaviours are avoided. Finally, supporting the patients self-efficacy is essential in building upon their confidence in their ability to change, without which, change cannot be elicited[307]. Miller and Rollnick describe rolling with resistance metaphorically as 'dancing' with the patient rather than 'wrestling' with them, and note that by de-escalating expressed resistance rather than challenging it, further resistance to change may be avoided[302]. Additional strategies, such as listing the positive and negative points of both current

behaviour and changed behaviour can be used within this framework to tailor the intervention towards an individual's needs[301]. Through accumulation of these five clinical principles and utilisation of additional strategies, two core phases of MI can be differentiated; the first being increasing motivation to change, the second, consolidating a verbalised commitment to make the change[306].

3.4.2.1 The theoretical basis of MI

The conception of MI was heavily based on Miller's experience of treatments for problem drinkers[304] rather than being grounded in any one specific theory of behaviour. However, the interest generated from his early work and subsequent modifications with Rollnick[302] have facilitated the linking of MI to the trans-theoretical model of change[301]. MI can also be linked to the core themes of other theories of behaviour, such as the health belief model, where MI can influence a patients perceptions about their health behaviour[301]. As such, MI draws upon several other theories in order to understand motivation, the most essential component of the behaviour change process[307]. Miller's and Rollnick's MI theories are also inspired by Carl Roger's work on non-directive counselling[308], where examination and resolution of ambivalence are core. MI also builds on Festinger's cognitive dissonance theory[309] and Bem's self-perception theory[310] which both describe the processes involved with attitudinal changes.

3.4.2.2 Evidence for MI in health related behaviour change; systematic reviews and meta-analyses

Comprehensive evidence for the efficacy of MI in healthcare is provided by reviews[311, 312] systematic reviews[313, 314] and meta analyses[307, 315-318], as summarised in table 3.2. From the wealth of evidence presented it is clear that a large and growing body of research has examined the effectiveness of MI, across a range of different healthcare settings. The earliest studies are predominated by small reviews of non-randomised studies; conclusions should therefore be drawn with caution. However, as the body of evidence has grown, comprehensive and well conduced systematic reviews and meta-analyses of RCTs have been provided, offering high quality evidence.

The reviews summarised in table 3.2 highlight that MI consistently yields statistically significant positive effects in the small to medium effect size range. Whilst the reviews provide conflicting evidence as to the longevity of MI effects, the effects appear to be maintained up to at least one year beyond treatment. Beyond establishing the efficacy of MI, the reviews also provide insights into the optimal means of MI based intervention delivery. Evidence suggests that MI is less effective when delivered in group sessions

compared to one-to-one and that better outcomes are achieved through greater exposure to MI. In terms of the wider application of MI and scope for its routine use, the evidence has shown that MI is not solely indicated for substance abuse problems or very troubled clients. It is successful in motivating clients to change, across of range of health behaviours, from various different groups and backgrounds and with delivery from practitioners of differing levels of experience and training.

Whilst these reviews describe the evidence for MI in facilitating healthcare related behaviour change, no reviews have specifically focused on the domain of medication adherence.

Author	Type of evidence	Setting	Evidence for efficacy	Other key findings
Noonan and Moyers (1997)[311]	Review article of 11 clinical trials	Problem drinking and substance abuse	Over 80% of studies demonstrated efficacy in addictive behaviours	MI worthy of further development in healthcare settings
Dunn *et al.* (2001)[313]	Systematic review of 29 studies	Focus on brief interventions adapted from MI across four behavioural domains; substance abuse, smoking, HIV risk and diet and exercise	60% of studies demonstrated at least one significant behaviour change effect size	MI particularly useful to enhance entry into and engagement with intensive substance abuse treatment programmes. Positive effects did not diminish over time
Burke (2003)[315]	Meta-analysis of 30 studies	Adaptations of MI (AMI) for alcohol, drugs and diet/exercise	AMIs equivalent to other active treatments and yield moderate, sustained effects (0.25 to 0.57)	MI effects equivalent to other active treatments and achieved in considerably less time; cost effectiveness therefore likely
Britt *et al.* (2004)[301]	Review article	MI use in healthcare settings	Individual studies described no research synthesis	Paucity of information describing MI interventions noted as problematic
Rubak *et al.* (2005)[316]	Systematic review and meta-analysis of RCT's using MI (72 methodologically sound studies)	Various healthcare settings	74% of RCTs reviewed had a positive effect	Individual support superior to group support. 81% efficacy for interventions lasting 60 minutes or more compared to 61% efficacy for interventions lasting 20 minutes or less. 40% of RCTs with only one session were effective, compared to 87% with 5 or more sessions

Table 3.2 Summary of evidence for the use of MI in healthcare settings

Author	Type of evidence	Setting	Evidence for efficacy	Other key findings
Hettema *et al.* (2005)[317]	Meta-analysis of 72 clinical trials	A range of healthcare problems across ten different behaviours	Small to medium effect sizes achieved via MI	Greater effects in ethnic minorities and when interventions are not manual guided. Efficacy not influenced by MI purity or methodological quality. Effects established early and diminish over time
Knight *et al*. (2006)[314]	Systematic review	MI in physical healthcare settings including asthma, hypertension, heart disease & hyperlipidaemia	Physiological and psychological positive lifestyle changes elicited	Generally poor quality trials; better research needed
Lundahl and Burke (2009)[307]	Practice friendly synthesis of prominent meta-analyses	Variety of health behaviours including problem drinking	MI significantly (10-20%) more effective than no treatment and generally as effective as other active treatments but with results achieved in less time than comparators.	Client related variables unrelated to treatment outcomes. Group based interventions less effective than one-to-one sessions. Durability of MI effects is variable but on average, durable for at least one year beyond treatment.
Lundahl (2010)[318]	Meta-analysis of 119 studies over 25 years	Various health behaviours	Average effect size (95% CI) = 0.22 (0.17 to 0.27); small but statistically meaningful effect	Effect size greater when compared to weak comparison groups rather than specific treatments

Table 3.2 (continued) **Summary of evidence for the use of MI in healthcare settings**

3.4.2.3 Adaptations of motivational interviewing

MI can be delivered as a stand-alone intervention or motivational prelude to other cognitive based interventions[317]. When MI in its purest form is combined with elements of other therapeutic interventions, the term adaptations of MI (AMIs) is commonly used, a term first coined in Burke's meta-analysis in 2003[315].

Behaviour Change Counselling (BCC) is an adaptation of MI, suitable for brief consultations in healthcare settings[319]. Although derived from MI, the brevity of the consultations, intervention aims and information exchange style are all pertinent to the distinct classification of BCC away from MI, as described by Rollnick's taxonomy[320]. Whilst the fundamental aim of MI is to elicit 'change talk' and develop discrepancy, the aims of BCC are more modest, and hence more fitting for brief interventions. BCC simply aims to provide a patient with the opportunity to talk through the why and how of change and for the practitioner to understand how the patient is feeling and what plans they have for change[320]. Although well described in the work of both Rollnick *et al.*[320] and Broer *et al*[321], literature searching revealed a substantial paucity of evidence for BCC in any health domains including medication adherence. Instead, published work has tended to focus on the practicality of training GPs to use BCC to improve asthma medication adherence[321] and the development of a tool to assess changes in practitioner behaviour before, after and during BCC training[319]. Whilst BCC appears to be an interesting and relevant modification of MI, evidence is therefore needed to assess its efficacy as a stand-alone intervention to facilitate behaviour changes such as improved medication adherence.

3.4.2.4 Other 'cognitive-based' techniques

Whilst the Behaviour Change Taxonomy specifically refers to MI, other cognitive based techniques include many of the behaviour change techniques included in the taxonomy. Whilst MI focuses on the readiness for change, other cognitive based techniques explore and enhance a patient's ability to change[317].

Problem solving treatment (PST) is a brief psychological intervention derived from cognitive behavioural principles. Designed to increase a patient's ability to solve their problems in a structured way, PSTs also improve patient confidence in dealing with future problems and encourage realistic and specific goal setting[322, 323]. To date, the evidence base for PST efficacy is centred in the treatment of major depression and a wide range of emotional disorders[323]. More recently, an RCT of community pharmacy based interventions to reduce drug related problems and increase medication

adherence has combined PST with MI during a community pharmacy based medication review[324]. The application of these techniques to improving medication adherence and for use in community pharmacies highlights that such techniques are amenable to use in a variety of settings. Ahmad *et al.* report that whilst MI was used to increase a patients motivation towards better medication adherence, PST was used to address difficulties in achieving adherence, and equip patient with the tools to overcome adherence barriers[324]. Whilst data from this study is, as yet limited to publication of the study protocol, this work represents the potential to apply PSTs to health scenarios beyond treatment of emotional disorders.

In a similar way to PST, the technique of forming implementation intentions, otherwise known as 'if-then planning' has been used to improve goal attainment and change individual behaviours[325, 326]. Implementation intentions interventions (III) recognise that self-regulatory problems may impede goal achievement, even when goal intentions are strong[326]. As such, a patient may have, for example, a strong intention to take their medicine as prescribed, but self-regulatory problems such as time-management or forgetfulness may mean that non-adherence prevails.

The formation of an implementation intention provides a preconceived 'action-plan' to link anticipated critical situations to goal directed responses which ensure goals are still attained[327]. With regard to medication adherence, the 'chosen critical situation' could be, for example, consuming a cup of tea in the morning. If the 'goal directed response' is taking medication at an appropriate time then the 'preconceived action-plan' (the if-then plan) could be 'If I have my morning cup of tea, and I've not taken my medicines then I must do so'. Formation of an implementation intention therefore encompasses specifying exactly when, where and how a goal will be obtained so that encountering specific situations automatically triggers behaviours, thus avoiding the need for further decision making[328]. Meta-analytical evidence has demonstrated that 'if-then-planning' has beneficial effects in a wide range of health behaviours [326].

In recent years, literature reporting the use of III to improve medication adherence has emerged. A recent UK based study utilised 'if-then planning techniques' to improve adherence to contraceptive use in teenagers and reported that consultations for emergency contraception and pregnancy testing reducing by 15% after 'if- then plans' had been made[329]. Also based in the UK, Jackson *et al.* aimed to increase adherence to short-term antibiotics via formation of implementation intentions at the point of prescribing. Although no significant improvements in adherence were reported, the authors identify methodological limitations and recognise the potential of III as a simple

strategy to promote medication adherence that can easily be deployed by pharmacists and other healthcare professionals in a cost and time effective way[330].

More conclusive evidence to support the efficacy of III in improving medication adherence is provided by a UK based RCT to enhance adherence to epilepsy medication[331]. In this study, written implementation intentions were made as part of a worksheet based intervention and adherence assessed via electronic monitoring. Statistically significant improvements in adherence were reported for intervention group patients compared to the control group, highlighting notable improvements from a straightforward and easily implemented intervention. Following these encouraging findings, the III worksheet utilised in this study has recently been utilised in a pilot RCT to increase medication adherence in 62 stroke survivors[332, 333]. This brief intervention, delivered over two sessions aimed to utilise III to assist patients in establishing better medication taking routines. Additional techniques were also utilised to address erroneous illness perceptions and medication beliefs, identified via a brief questionnaire[332]. O'Carroll *et al.* report a 10% increase in the percentage of doses taken on time for recipients of the brief intervention, a difference that was statistically significant in comparison to control group patients[333].

These studies highlight the potential of III, in conjunction with other 'cognitive-based' techniques as brief interventions to improve medication adherence and highlight the relevance of grounding interventions in theory and evidence. In their protocol for the III RCT in stroke survivors, O'Carroll *et al.* make good reference to the frameworks used in developing the intervention and the need to identify processes which target both intentional and unintentional non-adherence[332]. Whilst III are an exciting opportunity for medication adherence research, their efficacy in patients who are unmotivated to adhere is likely to be poor, as an intention to adhere may be non-existent. For intentionally non-adherent patients, with low motivation to adhere, it would seem logical to combine techniques; using motivational interviewing or its derivatives such as BCC to increase to patient's motivation and confidence to adhere and then other cognitive based techniques such as III to equip patients with the tools to implement their intended behaviour changes.

3.5 Chapter summary

3.5.1 Incorporating theory into a novel adherence intervention

A plethora of theories to explain and predict health behaviours exist and interventions gain benefit from being grounded in such theory. Recent work to synthesise these complex theories into a cohesive framework and develop a taxonomy of BCTs represents an exciting opportunity to advance the incorporation of theory into intervention design. Similar to the approach used in other healthcare domains, there is ultimately potential to deliver evidence based BCTs to address specific adherence barriers, with selection of the BCT determined by the behavioural domain to which an identified barrier has been mapped to. The first stage of this process is to develop a questionnaire, grounded in the TDF that will enable identification of individual barriers to medication adherence. The development of such a questionnaire is described in chapter five.

3.5.2 Using MI and other 'cognitive-based' techniques as interventions to improve adherence

Literature has demonstrated that appropriate deployment of MI techniques can facilitate behaviour change in a wide range of health settings. These techniques are likely to be useful in facilitating medication related behaviour change to improve adherence. However, unlike the application of MI to many health behaviours, evidence to support the use of MI in improving medication adherence is relatively sparse and to date, meta-analytic synthesis of this research has not been undertaken. In 2005, Broers *et al.* reported a PubMed search of MI based interventions to improve medication adherence. Ten studies, all describing medication adherence in either HIV or psychiatry and with MI delivered by specially trained counsellors were sourced, with three studies describing positive adhere effects[321]. Although useful as a preliminary indicator for the evidence of MI in facilitating improved medication adherence, the limitation of searching just one database must be considered and highlights the need for more comprehensive and robust literature searching and reviews for the role of MI in medication adherence.

Chapter Four 'Cognitive-Based' Interventions to Improve Medication Adherence; a systematic review and meta-analysis

4.1 Chapter introduction

In chapter three, the psychological theories underpinning health related behaviours were explored, highlighting the complexity and plethora of factors which may influence a patient's behaviour. Chapter three also considered some of the 'cognitive-based' behaviour change techniques that utilise psychological processes to change a patient's health behaviour by altering their thoughts, feelings, confidence or motivation to follow specific health behaviours.

Whilst cognitive-based behaviour change techniques such as motivational interviewing may be efficacious in improving a wide range of health related behaviours, evidence for their application to medication adherence is not cohesive. Such studies are diverse in terms of interventions evaluated and patients included and have shown promising but often heterogeneous results. Any form of robust or conclusive evidence for this application of these techniques to medication adherence remains elusive.

A systematic review and meta-analysis of MI and other cognitive-based behaviour change techniques as interventions to improve medication adherence was therefore necessary to estimate the overall efficacy of these approaches. This chapter describes the methods, results and conclusions of the systematic review and meta-analysis.

4.2 Systematic review and meta-analysis methods

Standard systematic review methods[334] were employed for this review and used to inform the development of the registered study protocol (PROSPERO register reference CRD42011001721). The protocol development was led by Claire Easthall (CE) with supervisory guidance from Debi Bhattacharya (DB), David Wright (DW) and Fujian Song (FS).

4.2.1 Aims and objectives

4.2.1.1 Aims

To describe and evaluate the use of motivational interviewing and other cognitive-based behaviour change techniques as interventions to improve medication adherence.

4.2.1.2 Objectives

1) To estimate the effect size of these interventions on medication adherence

2) To describe:

- from where such interventions have been delivered and by whom
- the training received by practitioners delivering the interventions
- the nature of the interventions
- the delivery of the interventions in terms of duration and number of sessions
- which patient groups have been targeted with these interventions

4.2.2 Literature search strategy

Preliminary literature searching identified that classification of interventions as motivational interviewing or otherwise, is a contentious issue. Similar interventions are often termed differently and conversely, different interventions can sometimes be given similar names. Searches beyond specific terminology such as motivational interviewing or behaviour change counselling were therefore conducted, to include a broader search of cognitive-based behaviour change techniques.

Studies were identified through comprehensive electronic and manual searches with use of appropriate subject headings and text words. Scoping searches were conducted prior to finalising the search strategy.

The following databases were searched without language or date restrictions:

1. MEDLINE
2. EMBASE
3. PsychINFO
4. CINAHL
5. The National Electronic Library for Medicines (NELM)

The references of included studies and the motivational interviewing website were also searched to identify additional studies.

4.2.3 Search terms used in literature retrieval

Search terms were devised using MESH (Medical Subject Headings) terms for 'medication adherence' and other key variables such as 'motivational interviewing'. Papers identified though preliminary literature searches were used to identify keywords for searches, as were previously identified systematic reviews and meta-analyses.

Truncations (*), wild cards ($), hyphens and other relevant Boolean operators were used where appropriate and permitted. The search terms applied to the Embase, Medline and PsychINFO databases using the OVID interface on the 4th of August 2011, and the CINAHL database on the 5th of August 2011 are provided in appendix 4.1. The NeLM database did not permit combinations with Boolean operators, so an alternative search strategy was applied to account for the differing syntax rules (appendix 4.1). Language and date restrictions were not applied to the search strategies.

4.2.4 Inclusion criteria

As guided in the Cochrane Handbook for systematic reviews[334], the study inclusion criteria were based around four parameters:

1) Study populations and sites

Population Any patient receiving an intervention to improve adherence to a prescribed medication

Site No restrictions were applied as this study aimed to describe from where these interventions have been delivered

2) Types of interventions

Any interventions that described motivational interviewing or other cognitive-based behaviour change techniques as an intervention to improve or facilitate medication adherence including (but not restricted to) motivational interviewing, motivational enhancement therapy, behaviour change counselling and implementation intentions/if-then planning.

In the case of interventions that did not explicitly use a defined technique, studies were included if the intervention pertained to using some form of cognitive or psychological technique. Such techniques included (but were not exclusively restricted to):

- Altering a patient's beliefs, attitudes or feelings towards their medication and adherence
- Increasing a patient's motivation to adhere
- Increasing the patient's confidence and sense of self-efficacy to adhere
- Using problem solving strategies to identify and resolve adherence barriers

3) Study design

Inclusion was not restricted to randomised controlled trials (RCTs) as this was considered likely to exclude too many studies and thus prohibit statistical synthesis through a meta-analysis. Any evaluative study designs were therefore eligible. For studies with a comparison or control group, comparators such as usual care or an alternative intervention were included.

4) Outcomes

The outcome measure of interest was intervention efficacy, defined as medication adherence. Studies measuring adherence by self-report, observation, pill counts, prescription refill rates, electronic devices such as MEMS™ or surrogate markers such as drug plasma levels were included.

4.2.5 Exclusion criteria

In order to facilitate inclusion of a diverse range of studies, exclusion criteria were restricted to two domains:

- Interventions where adherence was not assessed or reported

- Interventions targeted specifically towards adherence to medication for mental illnesses or for the treatment of addiction; these studies were excluded as the techniques used tend to be specific to mental health and addiction problems.

4.2.6 Screening and selection

Titles and abstracts were screened independently by two reviewers, who then compared their findings. Disagreements were resolved through discussion and, if necessary, referred to a third reviewer. CE led the review process and DB acted as the third reviewer. The second reviewer was Estelle Payerne, a research assistant working at UEA. Agreement in abstract screening between the two reviewers (prior to discussion) was assessed by calculation of Cohen's Kappa. Study selection was conducted in two stages:

1) For the abstracts identified via the electronic database searches, an abstract screening tool was used to screen the abstracts against the inclusion criteria.

   For the abstracts identified from the reference sections of included or other relevant papers, preliminary screenings of titles was undertaken to enable elimination of obviously irrelevant titles. Abstracts were then obtained for the titles of interest, and subjected to the same screening tool as detailed above.

At this stage, potential papers were grouped into four classifications:

1. Papers for full text retrieval
2. Papers where the abstract was insufficient to determine inclusion
3. Papers that were not suitable for inclusion but which could be used as a reference source to identify additional papers
4. Papers that were excluded

2) Full texts were obtained for all papers falling into the first three classifications. The number of papers excluded at each stage was recorded, with details of the reason for exclusion.

4.2.7 Data extraction

A bespoke data extraction tool was used to extract the following data from each study:

- Author name, publication date, journal and country of origin

- Study design, disease area, intervention type and whether or not the intervention was delivered alone or in conjunction with non-MI/cognitive-based components such as education
- Whether the study was a pilot, if the intervention was targeted towards non-adherent patients and if participants were paid or reimbursed for participation
- Who the intervention was delivered by, where it was delivered from and what training was received by the personnel delivering the intervention
- The initial and final sample size
- The number of participants in the intervention group and where applicable control group and the control group type
- The average number of sessions over which the intervention was delivered, the average length of each session and time period over which it was delivered
- Whether the intervention was delivered entirely in person, over the telephone or by a combination of these methods and whether the intervention was delivered by one facilitator alone or multiple facilitators
- The intervention follow up period
- The definition of adherence and tool used to assess this
- Adherence rates with standard deviations and confidence intervals where applicable and relevant statistics such as p-values.

Independent, duplicate data extraction of each included study was undertaken. The data extraction forms were piloted using a representative sample of studies. Inter-rater reliability was checked for the recording of outcome data and quality assessment. Where differences occurred, these were resolved through discussion and referral to a third independent reviewer if necessary. Where necessary, additional information was obtained by contacting the study authors.

4.2.8 Quality assessment

Independent, duplicate quality assessment of each study was undertaken as part of the data extraction process. Because different study types were included, it was not possible to use a standardised tool to assess the quality of all the study types. Instead, validated tools such as those developed by the Critical Appraisal Skills Programme[335], were used to determine the criteria for critiquing the studies, which enabled key variables or indicators of methodological quality to be considered in a structured manner. The Cochrane Reviewer's Handbook[334] was also used as a guide to assess the quality of studies in terms of bias. The criteria selected for assessing the

methodological quality of included studies are summarised in table 4.1, which highlights that the studies were critiqued on 12 different criteria.

Studies were not excluded based on methodological quality. Following comparison of the quality assessment data extracted by the two reviewers, an overall methodological quality assessment was agreed upon. Studies were classified into five groups:

1. Methodologically sound papers without concerns and of good overall quality
2. Generally good papers with only minor problems that are of no real concern
3. Papers with moderate problems and concerns
4. Papers with notable problems and serious concerns
5. Seriously questionable papers with extensive methodological flaws

Indicator of methodological quality	Questions to assess methodological quality
Undertaking fidelity checks	• Were fidelity checks undertaken to ensure the intervention delivered actually matched the intended intervention?
Research question and aims/objectives	• Was a clearly focused question asked? • Was the research question clearly focussed in terms of the population studied, the intervention delivered and the outcomes considered? • Were the aims of the study clear and transparent?
Study design	• Was an appropriate study design used? • Was it the correct approach for the research question to be answered?
Recruitment	• Was the recruitment process appropriate and well executed? • Were participants recruited in a logical and fair way which is likely to minimise bias? • Was the recruitment process well described and transparent?
Randomisation	• Were subjects randomised into intervention and control groups in an appropriate way? • Did the process used minimise the risk of bias and is the process well described? • Were the intervention and control group comparable at baseline in terms of demographics and treatments related factors, or any other factors that may have influenced the results?
Blinding	• Were participants and/or researchers blinded?
Loss to follow-up/attrition	• Were all of the patients entering the study accounted for at conclusion? • Does the study report reasons for and numbers of any participants that dropped out/did not finish the study?
Sample sizes	• Were power calculations or sample size calculations undertaken?
Reporting	• Are the results reported in a systematic and comprehendible way, do they make sense and are they clearly reported? • Has the data been analysed in a sensible and fair way?
Outcome reporting	• Were all of the important outcomes considered and reported? • Are all of the outcome measures described in the methods section reported? • Have the authors considered all variables that are pertinent to the results?
Outcome measures	• Were the outcome measures chosen appropriate and well measured? • Did they use the most appropriate tool to assess adherence and was a sensible adherence definition used?
Follow up	• Was the follow up study appropriate and likely to be long enough to fully assess the intervention effect?

Table 4.1 Quality assessment criteria for studies included

4.2.9 Data analysis

Descriptive statistics were used to convey the identification, retention and exclusion of studies. Details of the included studies in terms of publication particulars, study design and disease area were also reported via descriptive statistics as were all other data variables extracted from the included papers.

Study types were reported and the interventions grouped with reference to the following criteria:

- Primary intervention component and number of components
- For MI based interventions, whether pure MI was delivered or an intervention based on MI techniques
- The disease area for which the prescribed medication studied was taken
- The person delivering the intervention
- The training of the person delivering the intervention
- The setting from which the intervention was delivered
- The communication methods (face-to-face or telephone) used in the intervention
- The number of sessions received
- The total length of sessions received
- The total duration over which interventions were delivered
- The follow up period for data collection post intervention
- The targeting of interventions towards non-adherent patients
- The payment or reimbursement of participants
- The type of comparison group used
- The overall methodological quality of the study

4.2.10 Meta-analysis

The decision to statistically pool data from studies in a meta-analysis was based upon the likely comparableness of interventions and their data, as pooling of results from a diverse range of non-randomised studies is not recommended[334].

Although many different adherence definitions and measures were used, in interventions delivered from a wide range of settings, by differing personnel to differing populations, ultimately all interventions shared one common theme; their use of some form of psychological based intervention to improve medication adherence. As this common theme formed the fundamental premise of each study, the decision to

undertake a meta-analysis was made. This decision was supported by the large number of methodologically robust RCTs included in the study.

The adherence outcome data from individual studies were statistically pooled in a meta-analysis which assumed a random effects model. A computerised programme was used to calculate effect sizes and produce forest plots[336]. A random effects model was chosen as the studies were pooled from a heterogeneous sample. A random effects model assumes that the treatment effect really does vary across studies, and that the results from individual studies were randomly distributed[337]. The weighting assigned to each study under a random effects model is therefore based upon both within study and between study variance.

The outcome measures from each study were frequently measured on different scales, so an effect size based on the standard difference in means (*d*) was calculated. The standard difference in means (*d*) is calculated by dividing the mean difference in each study by the standard deviation for that study, transforming the effect size into a common metric[338]. Quantitative results of each meta-analysis undertaken were reported as a point estimate with associated 95% confidence intervals and p-values, in line with recommended guidelines[339].

An important aspect of the meta-analysis was heterogeneity; the difference in results between individual studies beyond those attributable to chance[340] and hence whether they were sufficiently similar to enable a meaningful combination. As studies were pooled from a diverse sample, an assessment of the heterogeneity was undertaken. Given the small sample sizes in this meta-analysis, especially in the instance of sub-group analyses, the I^2 statistic was used to assess heterogeneity. The I^2 statistic describes the percentage of variation across studies that is attributable to heterogeneity rather than chance[341], providing a far simpler and inherently more intuitive assessment of heterogeneity than comparator such as Cochrane's *Q*. Moreover, low power due to small samples sizes will not influence this statistic in the same way that it would *Q*. The I^2 statistic allows heterogeneity to be calculated independently of scale, as a ratio of excess to total dispersion and is calculated as:

$$I^2 = \left(\frac{Q - df}{Q}\right) \times 100\%$$

A very small I^2 value, close to zero infers that any observed between-study variance is spurious, with tentative benchmarks of 25%, 50% and 75% reflecting low, moderate

and high heterogeneity respectively[338, 341]. These suggested benchmarks were referred to throughout the meta-analysis.

A forest plot was used to display variation in effect size across studies and the estimate of mean effect size[342]. The effect size from each individual study is represented by a solid square, with squares located to the right indicating a positive effect and squares to left indicating a negative effect. The relative size of the square is proportional to the precision of the study and horizontal lines extend either side of the square to represent the 95% confidence interval (CI) around the effect size[337]. The combined mean effect size across all included studies is represented by a diamond at the bottom of the plot, with the centre of the diamond representing the pooled point estimate and its width reflecting the confidence interval around this point estimate[342].

Assessment of publication bias was necessary to account for potential small study effects. In a random effects model, small studies still receive a notable weighting of contribution to the overall effect size, therefore if missing, an exaggeration of effect size can be seen. Funnel plots were therefore created to visually explore potential publication bias[343]. In each funnel plot, the effect size for each study was plotted against the inverse of the standard error for that study. The standard error was an intuitive measure of precision, reported on the same scale as the effect size and calculated as the square root of the variance. The inverse of the standard error was used so that the larger (more precise) studies are clustered close to the mean effect size and are therefore found towards the top of the funnel.

The funnel plot provides a visual means of checking for publication bias as a deficit in small studies with a small or negative effect size will be clearly visible. An unbiased sample will be represented by a 'cloud' of effect size estimates symmetrical around the mean population effect size. This 'cloud' assumes a funnel shape[344], given by widely scattered smaller studies at the bottom of the funnel, which narrows as the studies become larger and more precise to form the top of the funnel. Whilst funnel plots are a useful tool, careful interpretation is imperative as asymmetry can be attributable to other factors beyond reporting bias, including heterogeneity, methodological quality and chance[340, 345]. Concrete conclusions were therefore not made from the funnel plots, which were instead used as a tentative guide to visually inspect the spread of studies and a generic tool to examine small study effects[345].

Despite recommendations that funnel plots should only be used when there are a minimum of ten studies in the meta-analysis[334], funnel plots are still useful to assess publication bias in each subgroup where the covariates are discrete[346]. Moreover,

funnel plot asymmetry can arise from heterogeneity caused by distinct sub-groups of studies, each with a different intervention effect[340, 346]. A funnel plot was therefore created for each sub-group analysed to ensure a consistent analytical approach.

The funnel plot produced for the main meta-analysis (all included studies) was indicative of publication bias which was further investigated using advanced meta-analytical techniques via the STATA software programme. Egger's test for funnel plot asymmetry[343] was deployed to determine whether the association between estimated effect size and study size was greater than would be expected by chance. Egger's test was selected as it is suitable for use on outcome measures assessed on a continuous scale and recommended for data based on means differences[340]. The test is based on weighted linear regression of the effect estimates on their standard errors. A p-value of <0.1 indicates significant funnel plot asymmetry[343].

Duval and Tweedie's trim-and-fill method was used to calculate a population effect size, which was adjusted for publication bias[347, 348]. The widely used technique is an iterative procedure to remove the most extreme small studies from the positive side of an asymmetrical funnel plot. The effect size is re-computed at each iteration, until the funnel plot becomes symmetrical around the 'new' effect size. This 'trimming' process corrects the point estimate in light of publication bias, but reduces the variance of the effects to a point where the confident intervals around the point estimate become too narrow. To combat this, an algorithm is used to add the original studies back into the analysis and a mirror image for each reinserted study is imputed to ensure symmetry. Whilst this 'filling' stage does not affect the adjusted point estimate, it does correct the narrowed variance[338, 347, 348]. Duvall and Tweedie's technique has been praised as it enables a best estimate of an unbiased effect size to be calculated[338].

4.2.11 Sub-group analyses and meta-regression

Sub-group analysis enabled variation in effect size across different sub-groups of studies to be explored and facilitated further exploration of potential sources of heterogeneity. In line with methodological recommendations possible sub-groups were defined before under-taking the meta-analysis to enable a robust and transparent approach which avoided the temptation for 'data dredging' in the analysis phase[334, 349].

The study grouping variables listed in section 4.2.9 provided the premise for the sub-groups created, with planned analyses detailed in table 4.2. For variables, such as the person delivering the intervention, sub-groups were pre-defined as they could easily be

predicted. For other variables such as the intervention types, the sub-groups could not be fully defined until the data were gathered.

Sub-group analyses were restricted to variables deemed pertinent to exploring likely influences of intervention efficacy. Restricting the number of sub-groups analysed improved the methodological robustness, as multiplicity testing increases the likelihood of generating spurious results through chance[339]. Differences in results between subgroups were checked for statistical significance by means of the Z-statistic.

Meta-regression was used to explore the magnitude, direction and significance of any linear association between treatment effect and intervention exposure. Analyses based on the number of sessions, total intervention time (in hours) and total duration over which the intervention was delivered (in weeks) were undertaken using a random effects meta-regression. Scatter plots for each co-variant were created to visually explore any linear correlations. The meta-regression was undertaken using SPSS software with additional syntaxes[350] as described by Lipsey and Wilson[351].

Variable of interest	Planned sub-groups
Primary intervention component	Unable to define fully pre-data collection; likely to include MI and III
MI 'purity'	Pure MI (delivered in full original form)
	Adaptations of MI
Disease area	Unable to define fully pre-data collection; likely to include HIV compared to other disease areas
Person delivering the intervention	Routine healthcare professionals (e.g. nurses, GPs and pharmacists)
	Specialists (e.g. psychologists and researchers)
Training of person delivering intervention	Unable to define fully pre-data collection; likely comprehensive and superficial
Setting from which the intervention delivered	Unable to define fully pre-data collection; likely community and hospital, clinical and non-clinical
Communication method	Unable to define fully pre-data collection; likely in person and via telephone
Follow up period	Unable to define fully pre-data collection; likely prolonged beyond intervention and follow up at end of intervention
Targeting of interventions towards non-adherent patients	Targeted towards patients with known non-adherence
	Delivered to all patients (no targeting)
Payment or reimbursement of participants	Interventions offering payment/reimbursement for participation
	Interventions that did not offer any payment/reimbursement for participation
Comparison group type	Standard care (treatment as usual)
	Alternative form of intervention (e.g. no cognitive-based component)
Methodological quality	Good methodological quality
	Poor methodological quality
	Fidelity checks undertaken
	No fidelity checks undertaken

Table 4.2 Summary of planned sub-group analyses

4.3 Results

In total 34 papers were included in the systematic review giving an overall sample size of 3554 participants. Five papers could not be included in the meta-analysis leaving a sample size of 3247 for this stage of the review.

4.3.1 Flow of articles identified

Figure 4.1 shows the flow articles excluded and retained at the different screening stages, this figure conforms to the requirements of the PRISMA statement for reporting systematic reviews[352]. Of the 242 citations excluded at the abstract screening stage, 58 (24.0%) were not an intervention to improve medication adherence, 51 (21.1%) did not use MI or other cognitive-based techniques, 27 (11.2%) did not report medication adherence as an outcome measure and 65 (26.9%) related to the treatment of addiction or mental health. Thirty-four of the full-text articles retrieved were included in the qualitative review[330, 331, 353-384] and 29 contributed to the quantitative phase of the meta-analysis[331, 353, 354, 357, 359-378, 380-384].

Five studies [330, 355, 356, 358, 379] could not be included in the meta-analysis due to insufficient data for calculating the standard difference in means (effect size), most commonly because a sample size or assessment of dispersion (confidence intervals or standard deviation) were missing. These five papers were however included in the systematic review as an indication of intervention effect was offered.

Abstracts were screened with 76% agreement between the two reviewers and all cases of disagreement were resolved by discussion without need for referral to a third independent reviewer. Disagreement between reviewers was most frequently attributed to conflict in classifying an intervention as a cognitive-based technique, which accounted for 55.1% of all discrepancies. A Kappa statistic of 0.473 indicated moderate agreement[232].

Of the 16 studies identified through manual rather than electronic searches, ten (62.5%) related to 'anti-retroviral therapy adherence' or abbreviations of this and were therefore not detected by the more generic terms used for medication adherence. Three (18.8%) studies were referred to 'treatment adherence'; a variant that was not included in the search terms and three studies did not mention 'adherence' at all

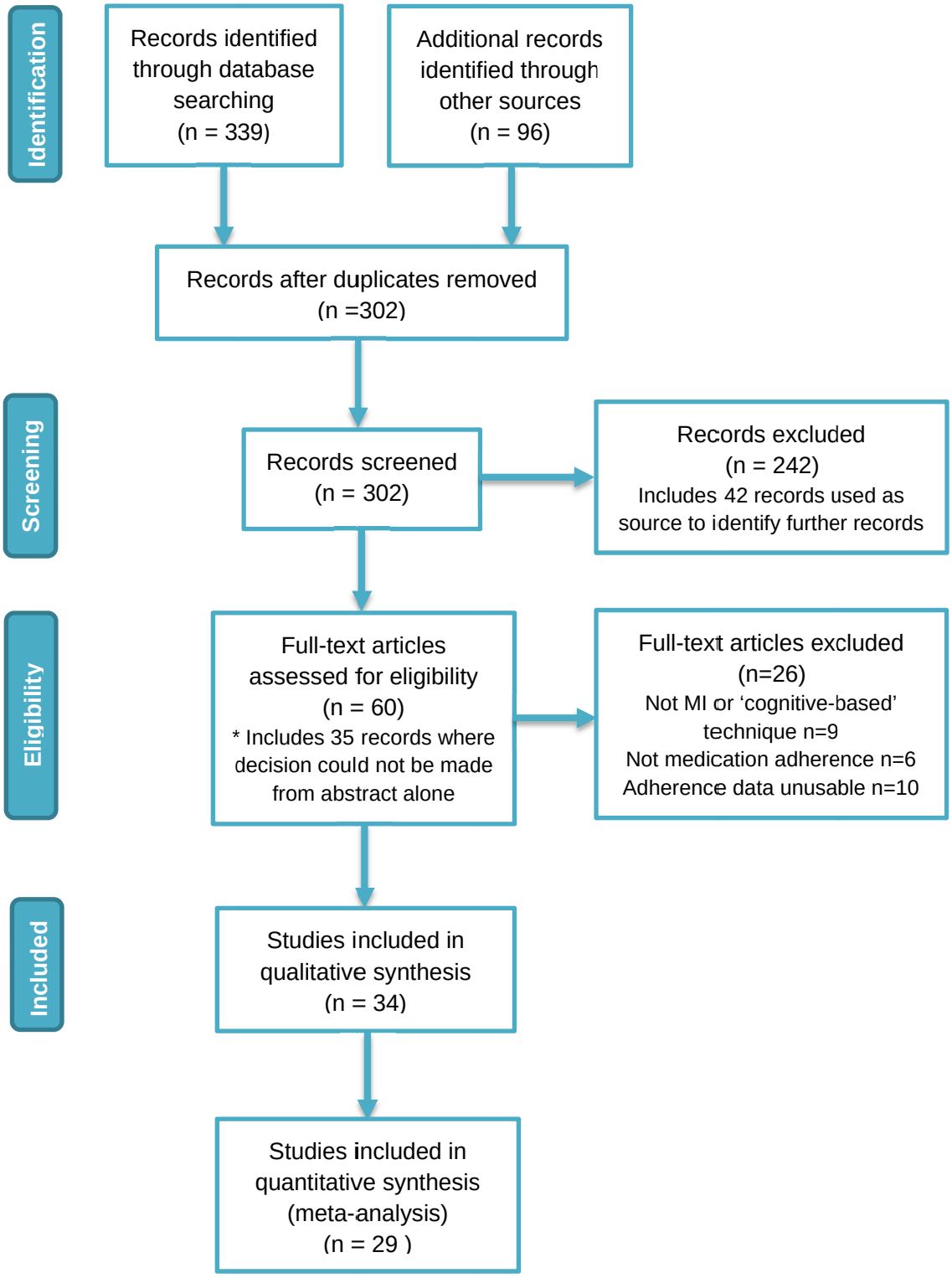


Figure 4.1 Flow of articles identified and studies included in review

4.3.2 Source and range of studies included

Of the 34 studies included in the review, 16 (47.1%) were sourced from the references of other papers and 18 (52.9%) came from the electronic database searches.

The earliest publication date was 1990 and most recent 2011. Only three (8.8%) studies were published prior to the year 2000. Fifteen (44.1%) studies were published between 2000 and 2005 and 16 (47.1%) between 2006 and 2011. Studies came from nine different countries, with 21 (61.8%) from the USA and 4 (11.8%) from the UK.

4.3.3 Types of studies included

RCTs accounted for 24 (70.6%) of the included studies, before and after studies eight (23.5%) and non-randomised trials two (5.9%). Thirteen (38.2%) studies were reported as pilot or feasibility studies.

4.3.4 Intervention characteristics

4.3.4.1 Intervention type

Table 4.3 shows the number of studies falling into the groups created according to the primary intervention type, number of intervention components and in the case of MI based interventions, the purity with which the MI element was delivered.

In total, 18 studies (52.9%) used MI in some form. The studies classified as a 'multi-component intervention' that did not contain any definable techniques such as MI, BCC or III, combined various elements such as increasing motivation and perceived self-efficacy, problem-solving and identification of strategies to overcome adherence barriers. A total of 12 (35.3%) studies used only one or two components whereas 22 (64.7%) had multiple components. Interventions with multiple components frequently combined the MI or cognitive-based component with strategies such as education, pill reminders and monitoring.

Intervention type	Number (%) of studies
Multi-component intervention using non-specific motivational and/or cognitive-based techniques	13 (38.2%)
Multi-component intervention using MI	7 (20.6%)
Multi-component intervention MI-based techniques	2 (5.9%)
Intervention with only one or two components based on application of MI techniques	2 (5.9%)
MI + CBT (SCRIPTASSIST)	4 (11.8%)
MI alone (pure MI)	2 (5.9%)
MI as feedback with III	1 (2.9%)
Implementation Intention Intervention (III)	3 (8.8%)

Table 4.3 Intervention type in included studies

4.3.4.2 Disease area

Interventions targeted medication non-adherence across 12 different disease areas; 17 (50%) focused on HIV. Five (14.7%) studies concerned asthma medication and three (8.8%) targeted medication adherence in patients with hypertension.

4.3.4.3 Person delivering the intervention

Interventions were primarily delivered by routine healthcare providers, with 18 (52.9%) studies delivered by nurses, clinicians or pharmacists. Nurses and nurse practitioners constituted the majority of this group accounting for 13 (72.2%) of the 18 interventions delivered by a healthcare professional and 38.2% of interventions overall. Community pharmacists were responsible for delivering 2 (5.9%) interventions. A specialist, such as a psychologist or psychotherapist delivered the intervention in 8 (23.5%) studies and research personnel were used in 5 (14.7%) studies. In 2 (5.9%) studies, the intervention was delivered via a computer based programme or questionnaire.

The number of individuals involved in the intervention delivery could not be determined for the majority of studies due to a paucity of information. However, 4 (11.8%) interventions were delivered by one person alone, whereas 23 (67.6%) were delivered by a team of people.

4.3.4.4 Training of personnel involved in intervention delivery

A summary of the training provided to intervention delivery personnel in the included studies is provided in table 4.4. Training for intervention delivery was described in 17 (50%) studies, although for 9 (26.5%) studies details of the training were insufficient to determine appropriateness. Two studies (5.9%) did not require any personnel training as they were delivered via computer programmes and no specific training was given in 4 (11.8%) studies since the intervention was delivered by somebody with 'experience in the field'. Details about training of any type were absent for 7 (20.6%) studies.

Training deemed to be comprehensive and appropriate included full training on the research background and interventional components, role plays and case scenarios to practice the techniques, training by certified practitioners and recording of sessions with provision of coaching and performance feedback. Studies without comprehensive and appropriate training were mostly commonly classified in this way due to a paucity of information, although brief sessions, delivered by inexperienced or unqualified personnel also fell into this category.

Type of training	Number (%) of studies
No reference to any type of training	7 (20.6%)
No training needed as intervention not delivered in person	2 (5.9%)
No training needed as intervention delivered by specialists e.g. psychotherapist	3 (8.8%)
Intervention delivered by 'trained' personnel but no details provided	4 (11.8%)
Training mentioned but no detail provided	5 (14.7%)
Well described training which appears comprehensive and appropriate	11 (32.4%)

Table 4.4. Summary of training provided to intervention delivery personnel

Information regarding the amount of training received was available for nine studies; all involved a minimum of a full days training. A single day of training was offered for two studies, and five studies offered training over three full days. The maximum amount of training provided was a 'five day intensive course' and this was the case for one study. Six studies described training delivered by certified MI trainers and the training for one study was delivered by a specialist psychologist.

4.3.4.5 Setting from which the intervention was delivered

Table 4.5 shows the number of studies delivered from different settings. A majority of 22 (64.7%) interventions were delivered from community or hospital based clinics. Nine interventions (26.5%) involved contact with patients in their own home.

Setting from which intervention was delivered	Number (%) of studies
Community based clinic	9 (26.5%)
Hospital based clinic	13 (38.2%)
Specialist psychotherapy clinic	1 (2.9%)
Community based non-clinical setting e.g. research office	2 (5.9%)
Phone calls to patients home	7 (20.6%)
Visits to patients own home	2 (5.9%)

Table 4.5 Intervention delivery setting for included studies

4.3.4.6 Intervention delivery style

Interventions were delivered in person in 23 (67.6%) studies and only 2 (5.9%) studies involved group sessions. Five (14.7%) studies were delivered over the telephone and 4 (11.8%) involved sessions both in person and over the telephone. One study (2.9%) was delivered by completion of a questionnaire.

4.3.4.7 Number and length of sessions received

The mean length of sessions for each intervention could not be calculated from the data available. However, the mean total length of the intervention could be estimated for 18 (52.9%) studies. The intervention total length ranged from less than 30 minutes for two (11.1%) studies through to one (5.6%) study being 6.5 hours in duration. Ten (55.6%) studies described an intervention lasting less than 3 hours in total.

The mean number of sessions over which each intervention was delivered ranged from one off interventions, which was the case for 5 (15.2%) studies, through to 2 (5.9%) studies delivered over a mean of 12 sessions.

Figure 4.2 shows the distribution of the mean number of sessions over which interventions were delivered. A majority of 21 (63.6%) studies described an intervention delivered in between two and five sessions.

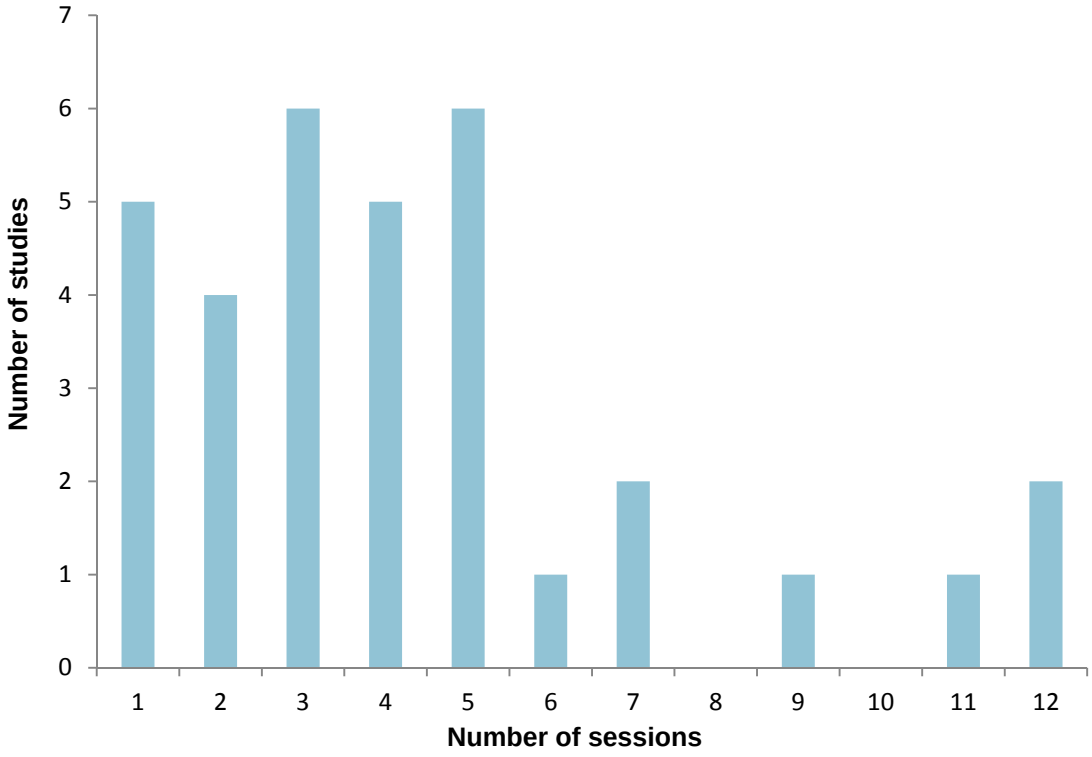


Figure 4.2 Number of sessions over which interventions were delivered

4.3.4.8 Intervention delivery and follow up period

The maximum intervention delivery period was 12 months and this was the case for 4 (11.8%) studies. An intervention delivered over a time period of six months or less was recorded for 27 (79.4%) studies.

The follow up period was extended beyond the intervention period in 16 (47.1%) studies.

4.3.4.9 Targeting of interventions towards non-adherent patients

Interventions were targeted towards non-adherent patients in 23 (67.6%) studies. Of these, 16 (47.1%), concerned patients with documented or reported non-adherence, and 7 (21.9%) concerned patients deemed to be 'at risk' of non-adherence such as those with recent changes to complex drug regimens and populations where adherence tends to be low.

4.3.4.10 Payment for study participation

Patients did not receive payment or reimbursement for participation in 25 (73.5%) studies. Four (11.8%) studies reported payment for completion of each session or questionnaire and one (2.9%) study paid participants upon study completion and reimbursed their costs. Three (8.8%) studies described reimbursing participants for costs incurred such as travelling costs and loss of time and one (2.9%) study reported 'incentivisation' for study completion.

4.3.4.11 Comparison group types

Six (17.6%) studies assumed a before and after study design and did therefore not have a control group. Treatment as usual or standard care was the control group type for 9 (26.5%) studies and 3 (8.8%) studies compared their data other studies with comparable demographics. The remaining 6 (17.6%) studies had control groups who received the intervention in an alternate form, for example education alone, compared to education plus MI in the intervention group.

4.3.5 Measures of adherence

A summary of the adherence measures used in the included studies is provided in table 4.6. In total, electronic monitoring was used to assess adherence in 10 (29.4%) studies and self-report questionnaires were used in 12 (35.3%) studies. Five studies (14.7%) used patient interviews and three (8.8%) assessed adherence via prescription refill data. A Composite Adherence Assessment Score (CAS) and pill count were used in 2 (5.9%) and 1 (2.9%) studies respectively.

Adherence assessment measure	Number (%) of studies
Electronic monitoring	8 (23.5%)
Patient self-report	7 (20.6%)
Patient self-report plus an additional method (e.g. pill counts of plasma monitoring)	5 (14.7%)
Patient interviews	5 (14.7%)
Prescription refill data	3 (8.8%)
Electronic monitoring plus patient self-report/interview	2 (5.9%)
Composite Adherence Assessment Score (CAS)	2 (5.9%)
Pill counts	1 (2.9%)

Table 4.6 Summary of adherence assessment methods used in included studies

4.3.6 Quality assessment of included studies

Eighteen (52.9%) studies were considered to be of generally good methodological quality with only minor deficits that were not of any real concern and 14 (41.2%) studies were deemed to have moderate methodological concerns. Two studies had notable problems which imparted serious concerns due to unreported data, anomalies in the flow of patients in the study, missing baseline adherence data and self -selection bias in patient recruitment.

Missing or ambiguous study details were the primary cause of study classification as 'minor deficits of no real concern', although studies with a less robust design such as non-randomised trials also fell into this group. Studies deemed to have moderate methodological concerns included those with complex or ambiguous data analysis, missing data or poor choice of adherence assessment tool. Fidelity checks were reported in 10 (34.5%) studies.

4.3.7 Data extraction agreement between independent reviewers

Agreement in data extraction between the two independent reviewers was matched for 42 different points, with an average agreement rate of 89.5%. Differences between the two reviewers were largely due to differing interpretations of the data extraction form, for example the 'total length' column was intended to record the total length of the sessions in hours but one reviewer used this column to record the total time period over which the intervention was delivered.

4.4 Meta-analysis

Data from 29 studies were statistically pooled in the meta-analysis; the main characteristics of these studies are summarised in appendix 4.2. The results data from each included study is summarised in table 4.7.

The studies included within the meta-analysis were predominantly RCTs and sample sizes ranged from 6 to 367, with 12 (41.4%) studies including at least 100 participants. Adherence outcome measures were variable but included the percentage of doses taken in a given time period in nine (31.3%) studies and the percentage of patients reaching a specified adherence level in six (20.7%) studies. Three (10.3%) studies showed a non-significant negative effect on medication adherence. Conversely 26 (89.7%) studies showed a positive adherence effect and this was found to be significant in 21 (72.4%) studies.

Multi-component intervention using non-specific techniques							
Study	**Study type**	**Total Sample Size (n)**	**Intervention group (n)**	**Control group (n)**	**Adherence definition**	**Adherence measure**	**Outcome summary**
Bailey *et al* 1990[353]	RCT	225	124	101	% of patients scored as adherent on all 6 items of a self-report scale	Self-report questionnaire	Significantly better adherence in intervention group
Hovell *et al* 2003[364]	RCT	188	92	96	Cumulative number of doses taken over 9 months	Patient interview	Significantly better adherence in intervention group
Molassiotis *et al* 2003[369]	Cohort	6	6	0	% of doses taken in last 4 days	Self-report questionnaire	Significantly better adherence post intervention
Murphy *et al* 2002[370]	RCT pilot	33	17	16	% of doses taken during intervention period	Self-report questionnaire	Better adherence in intervention group – non-significant
Pradier *et al* 2003[372]	RCT	202	100	102	% of patients deemed to be adherent (taking 100% of doses)	Self-report questionnaire	Significantly more adherent patients in intervention group
Put *et al* 2003[373]	RCT	23	12	11	Frequency of non-adherent behaviour over the last 3 months	Self-report questionnaire	Significantly less frequent non-adherence in intervention group
Remien *et al* 2005[374]	RCT	215	106	109	% of doses taken during previous 2 weeks	Electronic monitoring	Significantly higher proportion of doses taken in intervention group
Smith *et al* 2003[378]	RCT	17	8	9	% of participants taking ≥ 80% of their weekly doses	Electronic monitoring	Significantly more adherent participants in intervention
Tuldra *et al* 2000[381]	RCT	77	36	41	% of patients with monthly adherence ≥ 95%	Self-reported no. of pills taken	Significantly more adherent participants in intervention
Van Es *et al* 2001[382]	RCT	67	33	34	Adherence score on self-report scale	Self-report questionnaire	Significantly better adherence in intervention group
Wagner *et al* 2006[383]	RCT	135	97	48	% of doses taken during intervention period	Electronic monitoring	Better adherence in control group – non-significant.
Weber *et al* 2004[384]	RCT pilot	53	29	24	% of patients with monthly adherence ≥ 95%	Electronic monitoring	Significantly more adherent participants in intervention group

Table 4.7 Data extracted from individual studies for pooling in meta-analysis

Interventions using MI alone as one component							
Study	**Study type**	**Total Sample Size (n)**	**Intervention group (n)**	**Control group (n)**	**Adherence definition**	**Adherence measure**	**Study outcome summary**
DiIorio et al 2008[361]	RCT	213	107	106	% of doses taken during intervention period	Electronic monitoring	Better adherence in intervention group – non-significant
Lavoie et al 2011[367]	RCT	25	10	15	% increase in prescription refill rate during intervention period	Prescription refill data	Significantly better increase in prescription refill rate for intervention group
Multi-component intervention using MI							
Study	**Study type**	**Total Sample Size (n)**	**Intervention group (n)**	**Control group (n)**	**Adherence definition**	**Adherence measure**	**Study outcome summary**
Cook et al 2007[357]	Non-RCT	255	225	0	% of patients still adherent (taking medication) at end point	Pharmacy prescription refill data	Significantly better adherence in intervention group
George et al 2010[362]	RCT	343	170	173	% of participants classed as adherent	Morisky self-report scale questionnaire	Better adherence in intervention group – non-significant
Golin et al 2006[363]	RCT	117	59	58	% of prescribed doses taken take in month prior to study endpoint	Composite Adherence Assessment Score (CAS)	Better adherence in intervention group – non-significant
Ireland et al 2010[365]	Before & after	20	20	0	% of patients who did not miss one or more medicines in an average week	Self-report	Significant increase in adherence post intervention
Lawrence et al 2008[368]	Non-RCT	199	123	76	% of prescription drugs re-initiated following a period of non-adherence	Pharmacy prescription refill data	Significantly better medication re-initiation in intervention group
Riekert et al 2011[375]	Before & after	37	37	0	% of patients taking their medication every day	Self-report in patient interviews	Adherence decreases post intervention, non-significant
Safren et al 2000 [376]	RCT pilot	53	28	25	% of prescribed doses taken over the last 2 weeks	Self-report questionnaire	Better adherence in control group – non-significant
Thrasher et al 2006[380]	Before & after	30	30	0	% of prescribed doses taken	CAS	Significantly better adherence post intervention

Table 4.7 (continued) **Data extracted from individual studies for pooling in meta-analysis**

Interventions using techniques based on MI							
Study	**Study type**	**Total Sample Size (n)**	**Intervention group (n)**	**Control group (n)**	**Adherence definition**	**Adherence measure**	**Study outcome summary**
Berger et al 2005[354]	RCT	367	172	195	% of patients discontinuing treatment by study endpoint	Patient interview	Significantly better adherence in intervention group
De Bruin et al 2005[359]	Before & after	19	19	0	% of patients with adherence ≥ 95%	Electronic monitoring	Significantly more participants adherent post intervention
DiIorio et al 2003[360]	RCT pilot	17	8	9	Mean number of missed medicines in the last 30 days	Self-report questionnaire	Better adherence in intervention group – non-significant
Kalichman et al 2005[366]	Before & after	23	23	0	Mean number of doses missed in the last three days	Patient interview	Significantly fewer doses missed post intervention
Ogedegbe et al 2008[371]	RCT	160	79	81	% of days during two month period in which medication was taken correctly	Electronic monitoring	Significantly better adherence in intervention group
Interventions using III							
Study	**Study type**	**Total Sample Size (n)**	**Intervention group (n)**	**Control group (n)**	**Adherence definition**	**Adherence measure**	**Study outcome summary**
Brown et al 2009[331]	RCT	69	36	33	% of prescribed doses taken over a month	Electronic monitoring	Significantly better adherence in intervention group
Sheeran et al 1999[377]	RCT	78	38	40	Number of once daily doses missed over a 3 week period	Self-report questionnaire	Significantly fewer doses missed in intervention group

Table 4.7 (continued) **Data extracted from individual studies for pooling in meta-analysis**

4.4.1 Estimates of overall effect size

Figure 4.3 shows the forest plot for all 29 studies, separated by study design type. Whilst the figure exemplifies the strong overall trend towards positive adherence effects with intervention, it also highlights that before and after studies elicited the strongest summary effect size. The pooled estimate of standardised difference in mean (95% CI) for all 29 studies was 0.38 (0.28, 0.48) with moderate heterogeneity (I^2 = 48.5%).

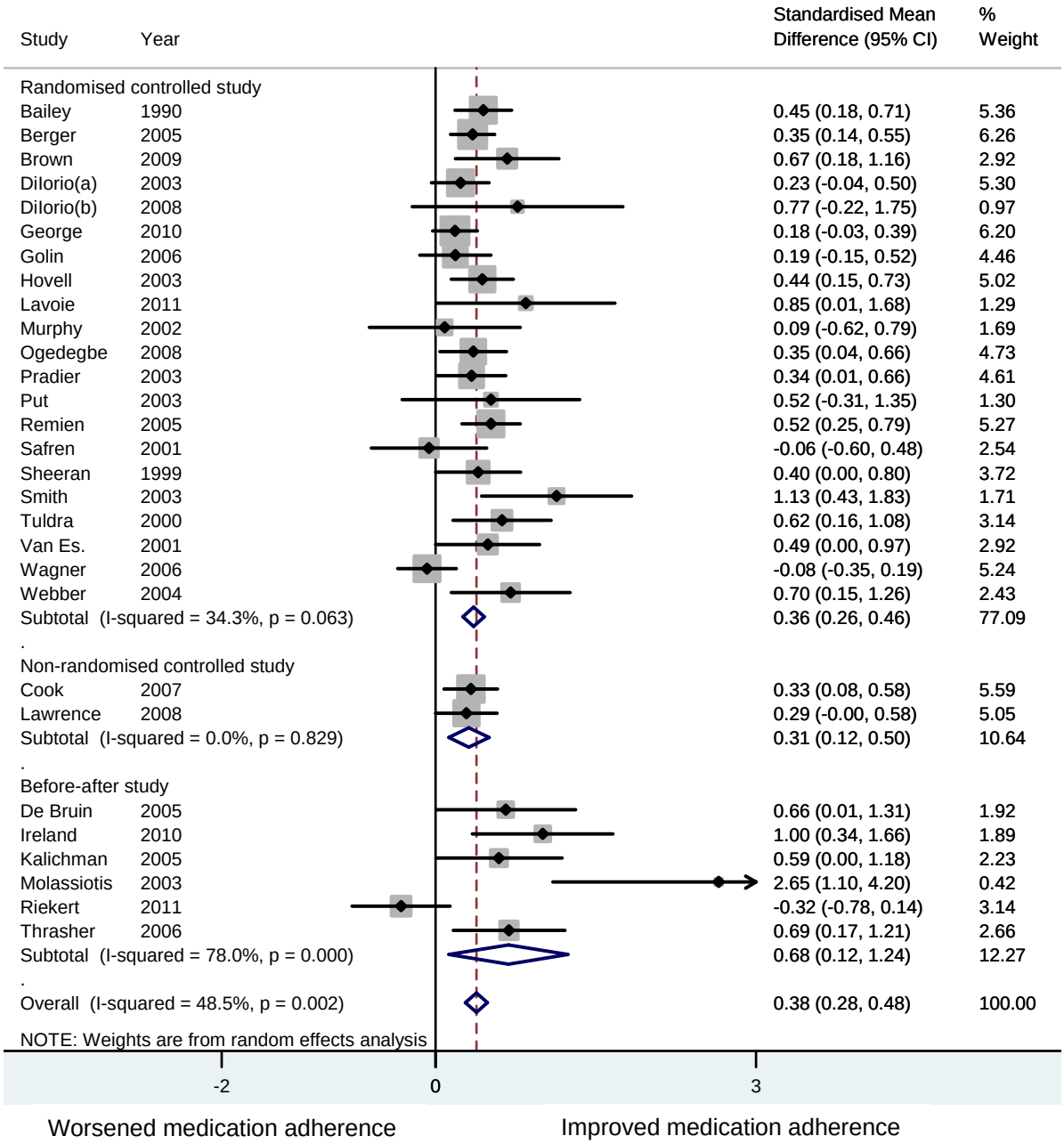


Figure 4.3 Calculated intervention effect sizes and summary effect size for all studies, separated by study design type

A funnel plot for the 29 included studies is shown in figure 4.4, suggesting publication bias, as noted by the deficit in small studies of a small or negative effect size. Egger's test confirmed statistically significant funnel plot asymmetry (p= 0.005) and the trim and fill technique elicited a re-computed effect size (95% CI) of 0.30 (0.19, 0.41).

Figure 4.5 shows the funnel plot for studies assuming an RCT design and also suggests publication bias; significant funnel plot asymmetry was found (p= 0.05) and the re-computed effect size (95% CI) was 0.31 (0.20, 0.41).

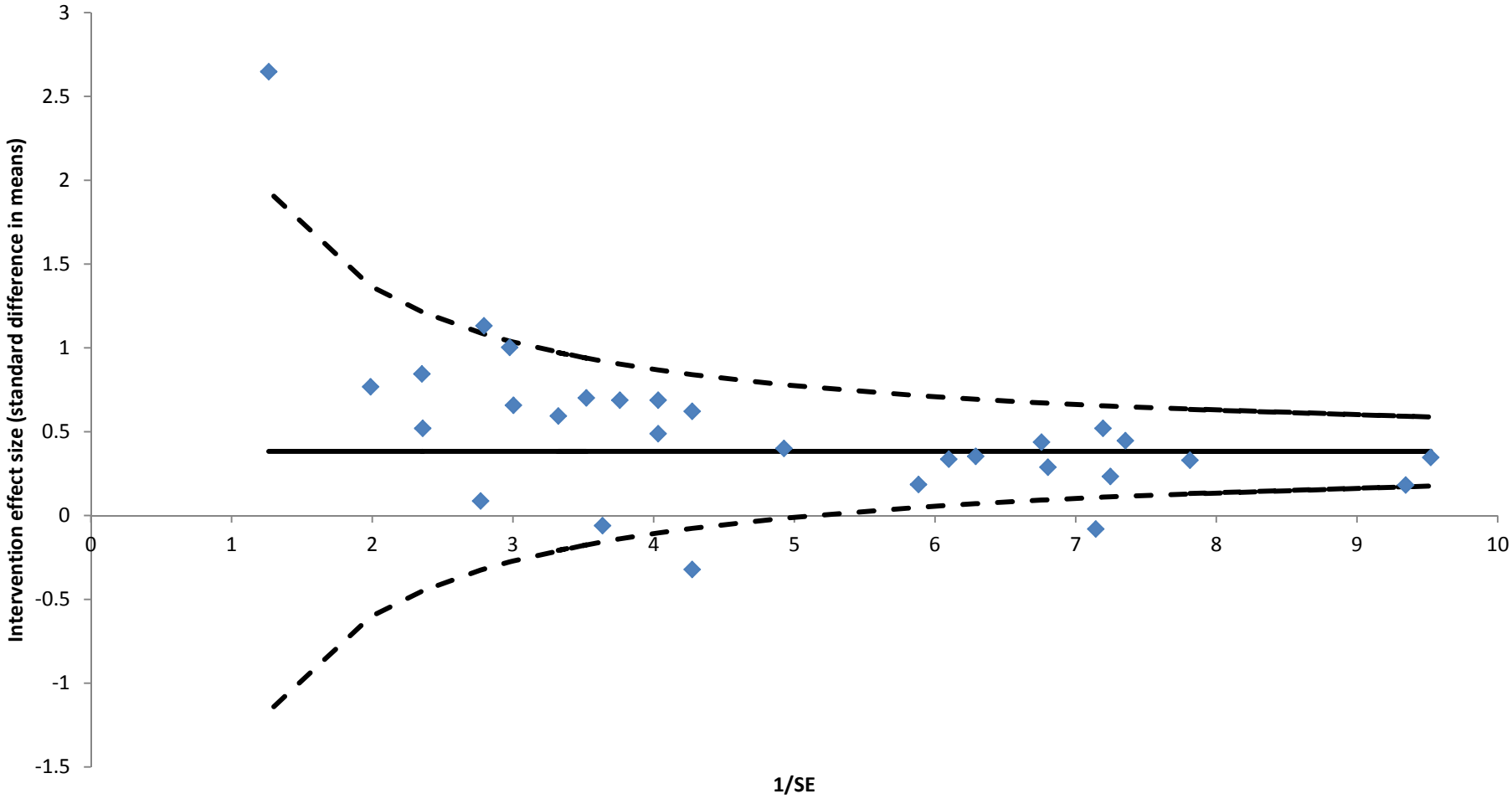


Figure 4.4 Funnel plot for meta-analysis of all included studies

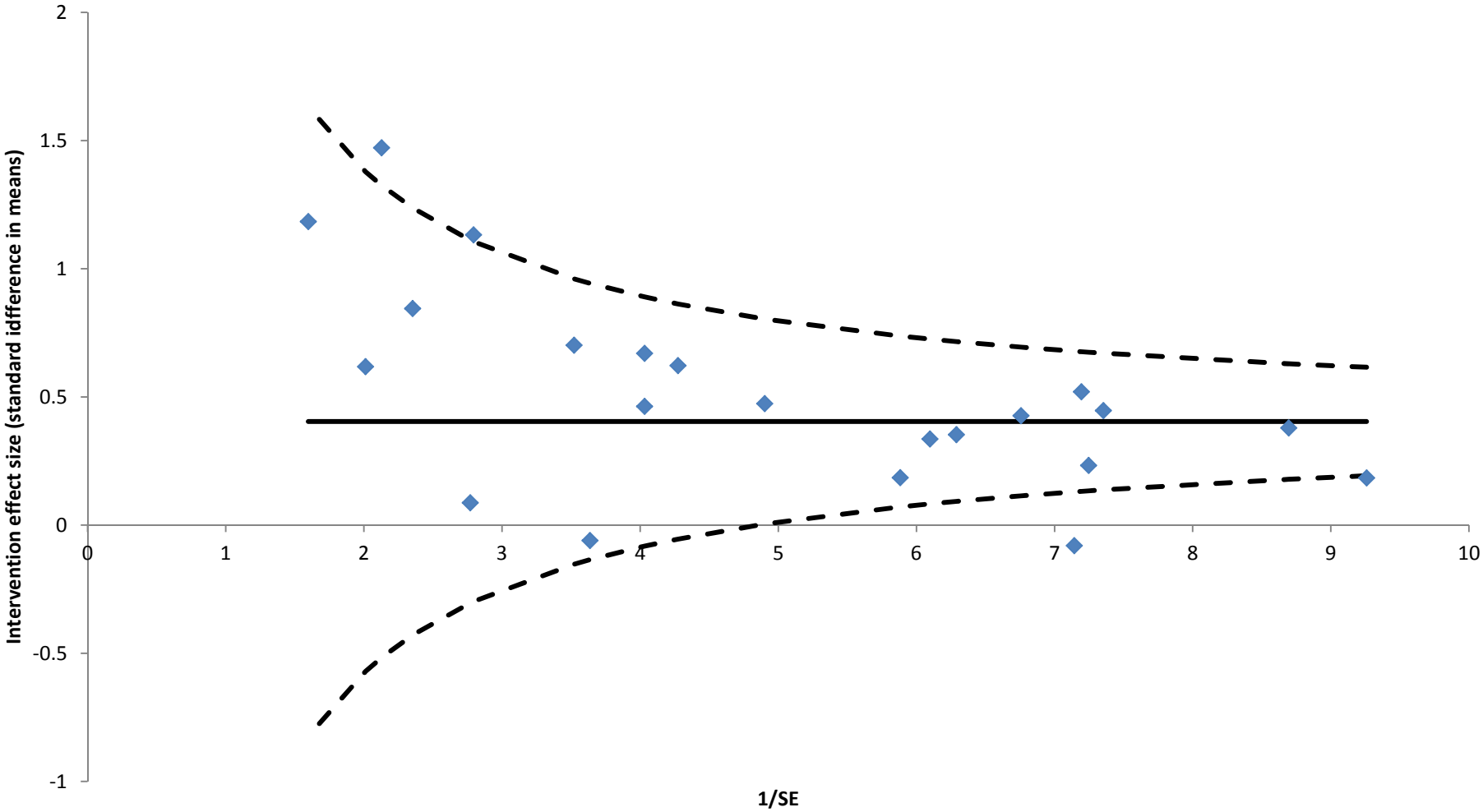


Figure 4.5 Funnel plot for meta-analysis of all studies with an RCT design

4.4.2 Sub-groups analyses

Table 4.8 summarises the main sub-group analyses. In the majority of cases, differences in effect size between sub-groups were not statistically significant, as represented by a p-value of >0.05. The exception to this was the sub-group analysis based around intervention delivery sites, which suggested that hospital based interventions achieved significantly greater effect than community based interventions.

Whilst the majority of planned sub-group analyses were undertaken, the data extracted for facilitator training was too subjective to form meaningful sub-groups as differentiation between poor reporting and poor training could not be made. Sub-groups based on the duration of facilitator training and number of facilitators delivering the intervention were also subject to a paucity of information which prohibited meaningful analyses. The data extracted on receipt of payment or reimbursements for participation were also deemed too unreliable for creation of sub-groups.

4.4.2.1 Funnel plot asymmetries

For the majority of sub-groups, the funnel plots created were not indicative of publication bias. For these sub-groups, the effect sizes detailed in table 4.5 can therefore be accepted with reasonable confidence. Publication bias was suggested by the funnel plots for both sub-groups relating to disease area, though this was more prominent for the group of interventions in disease areas other than HIV. This publication bias infers that the true effect size for the group of interventions delivered in disease areas other than HIV may have been lower, as the small studies of negligible or negative effect that are missing (as indicated by the asymmetrical funnel plot) would have pulled the mean effect size closer to zero. The difference in effect size between these two groups may therefore have been greater in the absence of publication bias and thus HIV based interventions could yield greater adherence improvements. Both funnel plots for the sub-groups based on clinical and non-clinical delivery settings were also suggestive of possible publication bias. Potential publication bias was also suggested by an asymmetrical funnel plot for the sub-groups of studies:

- delivered from secondary care
- that did not target the interventions towards non-adherent patients
- where control group participants received standard care
- without methodological concerns
- without fidelity checks

Subgroup A Studies included	No. of studies (sample size)	Effect size (95%CI)	I^2 (%)	Subgroup B Studies included	No. of studies (sample size)	Effect size (95%CI)	I^2 (%)	p-value
Multi-component interventions using non-specific techniques	12 (1222)	0.47 (0.27, 0.67)	60.8	Interventions using some form of MI	15 (1878)	0.29 (0.21, 0.38)	36.8	0.12
Interventions using some form of MI	15 (1878)	0.29 (0.21, 0.38)	36.8	Interventions using MI in its full, classically defined pure form	10 (1292)	0.27 (0.10, 0.43)	49.9	0.76
Interventions targeting adherence to HIV medication	15 (1191)	0.43 (0.24, 0.62)	60.3	Interventions targeting adherence to other conditions	14 (2056)	0.36 (0.25, 0.47)	31.8	0.52
Interventions delivered by routine healthcare professionals	17 (2067)	0.33 (0.18, 0.47)	55.4	Interventions delivered by specialists or the researchers	9 (1008)	0.41 (0.28, 0.53)	11.7	0.40
Interventions delivered in person	19 (1556)	0.38 (0.21, 0.55)	59.6	Interventions delivered by telephone calls/mixed methods	7 (1467)	0.36 (0.26, 0.47)	0.0	0.87
Interventions delivered from community-based settings	17 (2113)	0.30 (0.18, 0.43)	50.8	Interventions delivered from hospital-based settings	12 (1134)	0.51 (0.35, 0.66)	31.2	0.05
Interventions delivered from clinical settings	22 (2271)	0.40 (0.28, 0.53)	47.9	Interventions delivered from non-clinical settings	7 (796)	0.33 (0.13, 0.54)	56.4	0.57
Interventions where the follow-up period is identical to the intervention period	15 (1269)	0.39 (0.23, 0.55)	46.4	Interventions where the follow-up period is extended beyond the intervention period	12 (1676)	0.36 (0.21, 0.51)	55.4	0.78
Interventions targeted towards non-adherent patients	20 (2262)	0.37 (0.22, 0.51)	60.8	Interventions not targeted towards non-adherent patients	9 (925)	0.41 (0.29, 0.53)	0.0	0.66
Controlled studies with a comparison group receiving treatment as usual/standard care	17 (2658)	0.37 (0.28, 0.45)	0.0	Controlled studies with a comparison group receiving an intervention in an alternate form	6 (589)	0.38 (0.15, 0.62)	48.3	0.94
Studies deemed to have methodological concerns	13 (1348)	0.45 (0.25, 0.65)	63.8	Studies without any notable methodological concerns	16 (1899)	0.36 (0.25, 0.47)	28.8	0.43
Studies which undertook fidelity checks	10 (1140)	0.25 (0.07, 0.42)	55.3	Studies which did not undertake fidelity checks	19 (2107)	0.45 (0.33, 0.58)	38.4	0.06
Studies assuming an RCT design	21 (2658)	0.36 (0.26, 0.46)	34.3	Studies assuming a before & after design	6 (135)	0.68 (0.12, 1.24)	78.0	0.27

Table 4.8 Summary of sub-group analyses undertaken

4.4.2.2 Variation in effect size with differing intervention types

Whilst the sub-group analyses based on intervention type revealed no statistically significant differences, the types of intervention used were of particular interest and therefore further explored. Table A4.3 (appendix 4.3) provides further detail about the main intervention components and demonstrates how these relate to the intervention type classifications made. The majority of interventions utilised numerous different techniques and the most frequently occurring components were patient education, identification and resolution of adherence barriers, developing problem solving skills, increasing a sense of self-efficacy and encouraging effective social support.

Table 4.9 provides a comparison of the most commonly occurring intervention components in the 'non-specific multi-component' group of interventions and the 'MI based multi-component interventions'. Interventions that occurred more commonly in the 'non-specific multi-component' group aimed to:

- increase social support
- deliver education
- challenge negative thoughts and beliefs
- develop coping strategies
- increase a sense of self-efficacy
- improve communication with healthcare professionals

Conversely, intervention components including diary keeping and self-monitoring, pill reminders, dosing aids or memory cues and medication reviews were all used more frequently in the group of interventions based on MI.

Intervention component	No. (%) studies using component in 'non-specific' group	No. (%) studies using component in 'MI' group	% difference between 'non-specific' group and 'MI' group
Interventions components more commonly used in the non-specific group of interventions			
Improving social support	8 (66.7%)	1 (11.1%)	55.6
Challenging negative thoughts/changing attitude	4 (33.3%)	0 (0%)	33.3
Education	10 (83.3%)	5 (55.6%)	27.7
Increasing sense of self-efficacy	6 (50%)	3 (33.3%)	16.7
Developing coping strategies	2 (16.7%)	0 (0%)	16.7
Improving communication with healthcare providers	3 (25.0%)	1 (11.1%)	13.9
Encouraging self-care/self-management/adherence skills	4 (33.3%)	2 (22.2%)	11.1
Intervention components where there is no notable difference in use between the two groups			
Increasing confidence	1 (8.3%)	0 (0%)	8.3
Identifying and resolving adherence barriers	6 (50.0%)	4 (44.4%)	5.6
Identifying and addressing concerns	2 (16.7%)	1 (11.1%)	5.6
Problem solving skills	4 (33.3%)	3 (33.3%)	0
Increasing knowledge	1 (8.3%)	1 (11.1%)	-2.8
Behaviour rehearsal	1 (8.3%)	1 (11.1%)	-2.8
Regimen simplification/tailoring	2 (16.7%)	2 (22.2%)	-5.5
Goal setting/action planning	3 (25.0%)	3 (33.3%)	-8.3
Interventions components more commonly used in the 'MI' group			
Diary keeping/self-monitoring	1 (8.3%)	4 (44.4%)	-36.1
Pill reminders/dosing aids/adherence cues	1 (8.3%)	3 (33.3%)	-25.0
Medication review	1 (8.3%)	2 (22.2%)	-13.9

Table 4.9 Comparison of intervention components between 'non-specific' group and 'MI' group

4.4.3 Meta-regression

Inverse variance weighted regression of the number of sessions over which the interventions were delivered was based on 25 studies. Figure 4.6 shows a scatter plot of the number of sessions against the effect size, suggesting that a notable correlation between the two variables is unlikely. The meta-regression confirmed this with a beta weight value (95% CI) of 0.021 (-0.019, 0.061) indicating that for each additional session, the effect size may increase by just 0.021. With a wide confidence interval which crosses zero, any consistent increase in effect size with an increasing number of sessions is unlikely. This result is supported by a non-significant p-value of 0.299.

Inverse variance weighted regression was also used to explore a linear association between the number of weeks over which the intervention was delivered and the intervention effect size. This analysis was based on 23 studies and the scatter plot obtained is shown in figure 4.7, indicating that any association is unlikely. The meta-regression revealed no indication of any significant association with a beta weight value (95% CI) of -0.004 (-0.012, 0.005) and a p-value of 0.412.

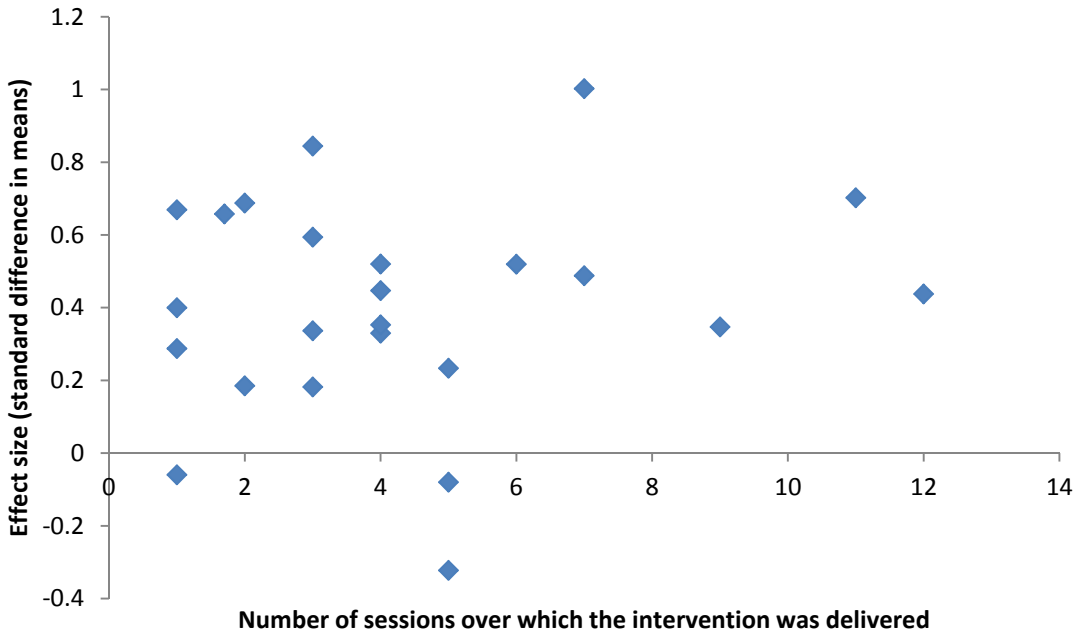


Figure 4.6 Scatter plot for number of intervention sessions and effect size

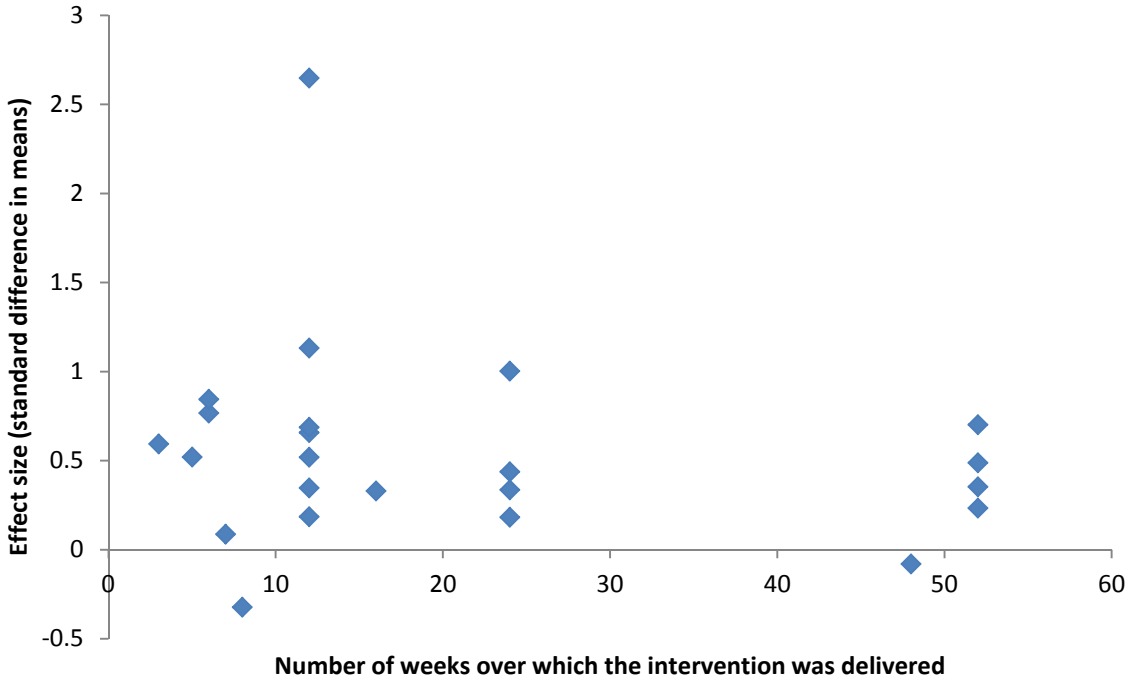


Figure 4.7 Scatter plot for intervention duration (no. weeks) and effect size

The total intervention length was also explored as a covariate which may have influenced the effect size, although no associations were found based on the data from the 15 studies with available data. The scatter plot shown in figure 4.8 indicates no association between increasing intervention length and effect size, as confirmed by a beta weight value (95% CI) of 0.001 (-0.001, 0.020) and p-value of 0.476.

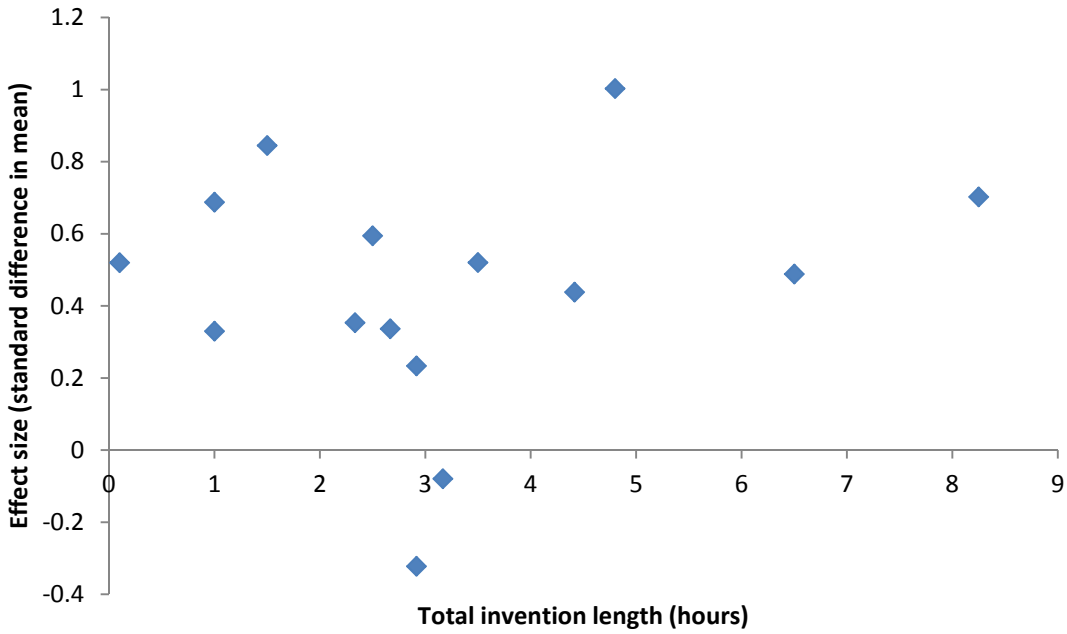


Figure 4.8 Scatter plot for total intervention length and effect size

4.5 Discussion

Thirty-four studies have been described in narrative, with 29 of these combined in a random effects meta-analysis. Given the diverse range of studies included, moderate heterogeneity was anticipated. Whilst implying the effect sizes across the different studies are likely different, the moderate heterogeneity does not impart notable concerns regarding the trust with which we can accept the overall effect size. Whilst the techniques used, patients studied and persons delivering the interventions varied, their ultimate aim and study premise remained consistent. Statistical combination of these studies in a meta-analysis was therefore both intuitive and meaningful.

Techniques to provide an unbiased, best estimate of effect which accounts for heterogeneity and publication bias increased the confidence placed in the effect size estimated. This value of 0.31 (0.20, 0.41) infers that these interventions achieved a significant positive effect of the small to medium range[385]. This study represents the first meta-analysis of MI and cognitive-based behaviour change techniques as interventions to improve medication adherence. The effect size calculated in this study, is however higher than effects achieved for comparable adherence interventions delivered over similar time periods and in similar settings. A meta-analysis reported by Peterson *et al.*[164], comprised of educational and behavioural interventions to increase medication adherence in a range of illnesses, reported a correlation coefficient *(r)* equivalent to a Cohen's *d* effect size of 0.16 (0.08, 0.24). The interventions evaluated in Peterson's meta-analysis are representative of the mainstay of current practice, thus, the novel motivational and cognitive-based techniques explored in this study seemingly improve medication adherence beyond traditional approaches.

For MI, the effect size calculated in this review, closely matches the effect size calculated in the most recent and comprehensive meta-analysis of MI as an intervention in substance abuse, health-related behaviours, gambling and treatment engagement[318]. Novel evidence for the wider use of MI, beyond these domains has therefore been provided. Whilst any inferences are tentative, the similarity in effect sizes established in this study and that of Lundal *et al.* increases the confidence with which this study's findings can be trusted. Moreover, it may tentatively add further support to the hypothesis that it is the cognitive-based intervention elements, or the synergy between cognitive and motivational elements that enhance the effect sizes further.

4.5.1 Number, range and source of included studies

The number of included studies was greater than anticipated from preliminary searches and is likely influenced by the fact that over a third of the included studies did not use specific techniques but instead combined multiple non-specific components. The large number of studies relating to mental health or addiction represented a notable reduction in studies that were otherwise potentially suitable for inclusion. However, the original justification for excluding these studies remains and has allowed a clearer picture of intervention impact to be obtained.

Full text articles were most commonly excluded due to unusable adherence data and further studies, included in the systematic review but not in the meta-analysis, were subject to similar inappropriate reporting of data. Whilst disappointing, it is not surprising that poor study reporting is problematic in this field, as many reviews of MI have previously identified this weakness, specifically stipulating that poor reporting and detail made intervention definition problematic[301, 314-316].

Whilst the exclusion of one study[386] due to an inability to access the full text is not ideal, inclusion was dubious as it was unclear whether adherence data were reported and whether the intervention used MI or a cognitive-based technique. The study was also published in 1980, long before the intervention types of interest became main stream, further decreasing the likelihood of suitability for inclusion. The inability to access this study in full text was therefore not considered a notable limitation of the review.

Whilst 'moderate' agreement for abstract screening may seem disappointing, perfect agreement was obtained following discussion. This 'moderate' level of agreement can largely be explained by considering the differing levels of experience, knowledge and expertise between the two reviewers. The main reviewer had extensive background knowledge of MI, cognitive-based techniques and medication adherence and had been responsible for the study protocol development since its inception. In comparison, the second reviewer came into the review much later, with minimal background knowledge. This point is exemplified by the perfect agreement achieved by discussion, as many cases of disagreement had arisen from misunderstandings of the material. Given this disparity in experience and knowledge, achieving moderate agreement is a reasonable accomplishment. A paucity of information in screened abstracts also heavily influenced the agreement rate between reviewers.

Discrepancies in data extraction for the meta-analysis were largely attributable to ambiguities on the data extraction form, though there were some sample size

discrepancies in the instances of intention-to-treat analyses. The strong level of agreement between the reviewers, especially after discussion increases the confidence placed in the data extracted and therefore strengthens this study.

Almost half of the studies included were not found via the electronic database screen, suggesting a possible deficit in the electronic database search terms. Including the search term 'treatment adherence' and incorporating a search term to accommodate HIV adherence studies may therefore have increased the number of studies identified via the electronic database searches. However, extensive manual searching of appropriate reference sources provided good coverage of the published material; study limitations in this domain are therefore unlikely.

The vast majority of studies were published after the year 2000; this finding was anticipated as the use of MI and cognitive-based behaviour change techniques for medication adherence has only generated interest in more recent years. Whilst studies were undertaken in a total of nine different countries, the majority of studies (61.8%) came from the USA, suggesting that international, widespread use of these novel concepts and techniques is not yet apparent. Interestingly, whilst the UK was the second most prominent country of study origin, only 4 (11.8%) studies originated in the UK, indicating these techniques are scarcely used in UK based research.

4.5.2 Types of studies included

Due to the novel research concepts used in the studies, it was anticipated that the majority of studies would be small in size and of a before and after study design. However, the majority of studies assumed an RCT design; the most methodologically robust, gold-standard study design. With a predominance of RCTs, increased confidence can be placed upon the data from which conclusions are drawn.

4.5.3 Intervention components

Defining the intervention type proved to be complex and numerous studies could not be grouped into a specific category, with 13 (38.2%) studies grouped as 'multi-component non-specific interventions'. The difficulties in defining whether an intervention used 'true' MI as previously detailed in other reviews[301, 314-316] was also evident. Despite the difficulties in classification of MI based interventions, just over half of the included studies described an intervention which used MI in some form. A prominence of MI type studies was anticipated as MI is the most widely studied cognitive-type intervention in other health-related behaviours. The marginal majority observed may

therefore be slightly lower than expected, but this is largely accounted for by the large group of 'non-specific' interventions, constituting over a third of the included studies. A minority of studies used III as their intervention or described CBT as a definable component, indicating that these newer, lesser developed strategies are as yet, not widely utilised in the medication adherence domain. MI purity was not associated with intervention efficacy, an observation consistent with the findings of Hetemma *et al.* for MI across a range of target problems[317].

Interventions also tended to refer to MI rather than BCC, indicating that this brief adaptation of MI is yet to be widely used. The concept of BCC dates back to 1999[387] with further developmental work over the next five years [320, 321] and has therefore existed in a comprehensive form for almost ten years. Given the promising potential of BCC, it is perhaps surprising that more interventions have not utilised this technique. However, it is possible that some of the interventions that pertained to use MI may actually have used a format that better reflected the premise of BCC, once again highlighting the problematic nature of defining interventions appropriately.

The majority of included studies involved multiple components and this observation is not surprising as previous evidence suggests that complex, multi-faceted interventions are the most effective[16] and that a combination of cognitive, behavioural and affective components is more effective than single focus interventions[388].

A larger difference in effect size was noted when interventions with multiple non-specific components were compared to those which used MI in some definable way, though this difference was not statistically significant. However, interventions occurring more commonly in the 'non-specific' group may be more strongly associated with efficacy compared to interventions occurring more commonly in the MI group.

It is unsurprising that increasing social support appears to be an important intervention component as comprehensive meta-analytical evidence has identified a significant positive relationship between social support and adherence[120], findings that mirrored earlier reports in a seminal systematic review[42] and it's later update[163]. Di Matteo's work identified that practical support in adherence elicited the greatest positive influence, with patients receiving practical support being 3.6 times more likely to be adherent than patients who did not[120]. It is therefore not surprising that practical elements such as developing coping strategies also prevailed as 'strong' intervention components.

With extensive literature describing the detrimental effects of negative beliefs about medications on adherence[38, 90], it is also unsurprising that 'challenging negative thoughts' appeared to be effective intervention component. Likewise, it is intuitive that 'increasing a sense of self-efficacy' was an intervention component more common in the 'non-specific' group of interventions associated with greater efficacy, as self-efficacy is a core component of many of the theoretical models described in chapter three. It is also interesting to see that interventions which addressed patient and prescriber relations and communications appear to be associated with efficacy. Whilst consideration of research evidence[83, 88] means this observation may have been expected, it is interesting to see adherence interventions have taken a specific focus on improving patient and prescriber communication, as this was not identified in the prominent review by Haynes *et al.* in 2008[163].

Whilst Haynes' review suggested self-monitoring and pill reminders were common themes in adherence interventions[163], evidence has suggested these are not always particularly effective interventions and more importantly not always appropriate[173-176]. It is therefore interesting to see that this review has also hallmarked these components as potentially being associated with lower efficacy. The evidence for the benefit of medication review has also been variable and fraught with controversy in recent years, as previously described in chapter one. This meta-analysis tentatively suggests that adherence interventions based upon a medication review may be less effective than interventions based on other components such as increasing patient support and sense of self-efficacy. Given the evidence relating to the value of medication review, this observation may not seem at all surprising. However, this does impart notable questions around the value of current adherence interventions such as the nationally commissioned Medicines Use Review (MUR) service, also described in chapter one. Whilst the evidence suggests that interventions based on medication review may be less effective than those with more cognitive-based components, it is pertinent to consider the importance of reviewing medication appropriateness before intervening to improve adherence. Improving adherence to a medication regimen that is clinically inappropriate has the potential for detrimental rather than positive health effects.

The evidence provided in literature and more specifically in this review suggests that reviewing a patient's medicines use, providing education and suggesting resolutions to non-adherence are unlikely to yield positive effects of a notable magnitude, especially in complex cases and in the instance of intentional non-adherence. In such instances, the novel motivational and cognitive-based techniques explored in this review are seemingly more likely to elicit the desired outcome of improved medication adherence.

These techniques are however, far from widespread in their use even in an experimental domain, and represent an unknown concept to the majority of healthcare professionals. This observation is disappointing given that sixteen years have now passed since Haynes and colleagues first identified the need for innovative approaches to improving medication adherence[389]. The current format of routinely delivered adherence interventions may therefore represent a 'missed opportunity' in eliciting maximal outcome effectiveness. Further research is therefore warranted.

Whilst this review provides some tentative inferences as to which intervention components may be associated with greatest efficacy, further work is needed to fully identify the most effective intervention components with confidence. However, the aforementioned paucity of well described studies prohibits the undertaking of this work. Without being able to describe the intervention components in a consistent and methodologically robust manner, teasing out the most effective intervention components is difficult. At the time of completing this review, the BCT taxonomy V1[293], as described in chapter 3, had not been published. However, with the publication now available and online sessions to train researchers as 'coders' soon to be available, this work will be possible in the near future.

4.5.4 Intervention delivery characteristics

4.5.4.1 Intervention delivery personnel

It is encouraging to see that over half of the interventions were delivered by routine healthcare professionals such as nurses, pharmacists and clinicians, as routine healthcare delivery is an important facet for wider application of these techniques. Whilst the effect sizes calculated suggest that interventions delivered by specialists may achieve greater effects than those delivered by routine HCPs, overlapping confidence intervals around the effect size estimates and a p-value of 0.40 infer that true differences between the two groups are unlikely.

In their seminal review of MI research, Lundhal *et al.* reported that the practitioner training level did not influence intervention efficacy[318]. These findings are echoed by the present systematic review of MI and other cognitive-based behaviour change techniques to enhance medication adherence. Although the number of studies with interventions delivered by a community pharmacist was too small to determine an effect size via meta-analysis, it is still encouraging to see that the skills and expertise of community pharmacists can be utilised in this way.

Interventions were more commonly delivered by 'multiple personnel' but sufficient data to enable sub-group analyses were not available, further exemplifying the aforementioned reporting problems. It is not surprising that delivery by multiple personnel rather than one facilitator working alone was more common as this is a more realistic model for service delivery in the wider healthcare domain.

4.5.4.2 Intervention exposure

Data relating to the intervention length proved difficult to elicit and were obtained for just over half of studies. Linear associations between the intervention effect size and three co-variates of intervention exposure were found to be highly unlikely; intervention exposure does therefore not appear to influence intervention efficacy in any way. It is intuitive to anticipate improved efficacy with prolonged intervention exposure as this relationship has been reported for MI interventions in other health domains[316, 318]. However, whilst Ruback *et al.*[316] and Lundhal *et al.*[318] both focused on one technique alone (MI), this study included numerous different techniques which likely contributed to the heterogeneity observed. It is therefore plausible that any intervention exposure effects may have been over-shadowed by the differing intervention components. It is also worth considering whether the poor study reporting regarding intervention duration may have accounted for the surprising observation of no increase in efficacy with greater intervention exposure.

Further investigation of the observation that efficacy was not increased by intervention exposure is warranted as, if found to be true, questions over causality may be inferred. In 1965, Sir Austin Bradford Hill provided a classic essay on causal evidence where the minimal conditions necessary to provide adequate evidence of a causal relationship were defined[390]. One of these minimal conditions for causality is, as termed by Bradford Hill, 'biological gradient' or in other words a dose-response effect. Whilst these minimum criteria for causality are heavily focused on a medical model of factors which are causative in disease, there may be some useful application to explore a causal relationship between receipt of cognitive-based interventions such as MI and an increase in adherence.

In consideration to the wider application of these techniques as routine healthcare interventions, it is encouraging to see that brief interventions, delivered in only one or two sessions can elicit small to medium sized, significant effects. Routine healthcare professionals are unlikely to have sufficient resources to deliver an intervention over many sessions, lasting several hours, so the findings reported here may be supportive of practical and feasible delivery in the wider domain.

Extension of the follow up period beyond the intervention delivery period was not associated with any statistically significant changes in effect size. It could therefore be argued that durability of effect may be evident as the effect size had not dropped when adherence was assessed beyond the end of the intervention. This is however a tentative conclusion as robust inferences about the durability of the treatment effects could not be made from the data gathered. Further work to determine the durability of these techniques is therefore warranted.

4.5.4.3 Intervention targeting and comparison group type

The majority of studies targeted the intervention towards non-adherent patients, which is unsurprising given the intervention aims. Although the summary effect size for the 'non-targeted group' was slightly higher than that for the 'targeted group', the closely matched effect sizes and overlapping confidence intervals suggest that the effect size in these two groups is unlikely to truly differ. This hypothesis is supported by the publication bias in the 'not-targeted' group which may in part account for the slightly larger effect size observed, given the use of a random effects model. Furthermore, a p-value of 0.66, confirms that any differences between the effects sizes calculated for the two sub-groups were not statistically significant. It would however, seem logical to expect a greater effect in patients who were non-adherent and this may well still be the case. The observations seen here could therefore be an artefact of the way 'non-adherent' patients were identified, after all a wide range of tools were used to do this and some studies simply targeted the intervention towards patients at risk of non-adherence.

For controlled studies, the comparison group was most frequently standard care or treatment as normal which is to be expected as comparison to usual care is generally considered to be the gold standard. However in terms of comparing effect sizes, standard care may be considered as a 'weak' comparator whereas delivering an alternate intervention may be considered as a 'strong' comparator, as the latter option enables determination of the most effective intervention type. In this study, interventions using standard care or treatment as usual as the comparator elicited a near identical effect size to interventions where the comparison group received the intervention in an alternate form. A p-value of 0.94 offered robust evidence to confirm that any differences in effect size between these two sub-groups were not statistically significant. Other meta-analyses in similar domains have identified the comparison group type as an effect size moderator, with strong comparators such as other interventions eliciting greater effect sizes[318]. Given the possible publication bias in the

group of studies using treatment as usual, it is possible that these finding could be mirrored in this study. Advanced meta-analytical techniques to explore the impact of publication bias may therefore be warranted, however, resource limitation did not permit this.

4.5.5 Study settings

Half of the included studies were for HIV medication adherence which is not surprising given the documented adherence challenges in this group[391-393] and need to maintain high adherence levels to ensure therapeutic benefit[14]. Other disease areas with multiple studies included asthma and hypertension which are also known to attract adherence problems[37, 43, 63, 105, 394]. Despite the predominance of HIV based studies, the meta-analysis included medication adherence across 12 different diseases, implying the techniques used are widely applicable across different domains. Whilst studies relating to the treatment of addiction or mental health were excluded, the rationale for this decision is sound given the known differences in adherence behaviours for these conditions. A limitation, in as much as this study is not applicable to these conditions has however been introduced. Further work to consider the application of these techniques to these specific domains is therefore advised.

The closely matched summary effect sizes, overlapping confidence intervals and non-significant p-values for interventions targeting HIV adherence compared to those for other disease areas, also supports the wider application of these techniques. However, the inferred publication bias for studies in 'other diseases' may have artificially elevated the effect size for this sub-group, in which case a true difference between the two groups may have been observed. Interventions targeting non-adherence to HIV therapy may be expected to be more efficacious as the perceived necessity of these drugs and consequences of non-adherence may be greater than in other disease areas.

The majority of interventions were delivered from hospitals, which is unsurprising given the prominence of interventions targeting adherence to HIV medication. Interventions delivered from secondary care appeared to be more efficacious than those delivered from primary care and the confidence intervals around these two notably different effect sizes overlapped only minimally. These inferences of true differences were supported by a p-value of 0.05, indicating a statistically significant difference in effect size between these two groups. Publication bias in the sub-group of interventions delivered in secondary care, may however have caused an exaggeration of this effect which should ideally be further investigated, though resource limitations did not permit this.

Based on the evidence available, our best estimates suggest that whilst interventions delivered from hospitals may be more effective, community based interventions are still capable of eliciting small, statistically significant effects. This is encouraging in terms of the widespread use of the techniques in community based settings. However, if hospital based interventions really are more effective than those delivered in community, further investigation to establish the reasoning for this would be warranted. It may be feasible that the conditions treated in secondary care (such as HIV for example) are more amenable to benefit from such interventions or perhaps the practitioners working in secondary care are better able to implement the interventions. More likely however, is the possibility that there is no true difference; the potential for spurious findings as a result of multiplicity testing must therefore be considered.

The majority of interventions were delivered in person, which is unsurprising given the counselling styles and techniques used in these interventions which intuitively benefit from face-to-face contact[395]. Interventions delivered entirely in person were slightly more effective than interventions delivered by mixed methods (including telephone calls), however the p-value of 0.87 provides no evidence of a statistically significant difference in effect size between these two groups. The differences observed may therefore have been due to chance, though with relatively small numbers of studies, there may also have been a lack of power to detect statistically significant differences. Intuitively, it may be expected that interventions delivered in person would elicit a greater effect as the facilitator may find it easier to build a rapport with the patient. Evidence of this has not been provided by this study.

A systematic review of telephone based medical consultations identified that public satisfaction with telephone consultations is high and the effectiveness of health promotion interventions delivered over the telephone, are comparable to those achieved via face-to-face communication[396]. Similar findings were also reported in a Cochrane review of telemedicine versus face-to-face care, however the need for further work to elucidate the full effect of telecommunications on health outcomes was also identified[397]. Whilst further work in this domain is required, delivery of interventions via the telephone or other telecommunications such as web-based interventions may well be a useful tool in dissemination of these techniques, offering effectiveness comparable to that of face-to-face communications.

The practical delivery of these interventions is an important factor that should not be overlooked as accessible delivery, that can easily be fitted into a busy healthcare provider's hectic daily schedule, is likely pertinent to the widespread use of such

interventions. Delivery methods such as the telephone may be an important factor in determining how accessible and deliverable an intervention is and is therefore an interesting concept worthy of further, more robust investigation.

4.5.6 Methodological quality of studies

Reporting of studies was variable but information was frequently absent, indicating poor reporting for many studies. Subsequently, only half of the studies were considered to be of good quality with only minor deficits of no real concern. Studies with methodological concerns elicited a slightly greater effect size than those without concerns, though a p-value of 0.43 confirmed that the methodological quality of each study does not significantly influence the effect size. This observation is encouraging; a greater effect from poorer quality studies would infer bias from the methodological quality of the studies, but evidence of this has not been presented. However, this could also suggest that the critical appraisal techniques were not effective. Based on the evidence available it is impossible to say which of these explanations is most probable. However, a comprehensive checklist, based on recommended tools was used to assess methodological quality by two independent reviewers, therefore, we can be confident that all reasonable steps to ensure a robust methodology assessment were taken.

The sub-group of studies that undertook fidelity checks produced an effect size notably lower than that for the sub-group of studies that did not undertake fidelity checks, with 95% confidence intervals that overlapped marginally. A p-value of 0.06 is close to statistical significance suggesting that true differences in effect size between the two sub-groups may exist. However, the 'no fidelity checks' group's effect size could be exaggerated by publication bias; advanced meta-analytical techniques such as Egger's test for funnel plot asymmetry[343] and Duval and Tweedie's trim-and-fill methods[347, 348] could be used to investigate this further if resources permitted. Reduced efficacy with fidelity checks may appear counterintuitive. However, when fidelity checks are undertaken, facilitators will commonly follow an intervention manual or protocol; practice that may introduce a meticulous and rigid delivery style. In comparison, studies without fidelity checks may be more fluid and amenable to adaptation and targeting to meet an individual's needs, without concern for the rigidity of following a manual. If this is so, these results would in part mirror the earlier work of Hettema[72] and Lundhal[106] who independently provided meta-analytical evidence to suggest manual guided interventions were less effective than interventions which did not use manuals.

4.5.7 Study strengths and limitations

A meticulously designed and executed study with a registered study protocol has been undertaken, with data largely drawn from RCTs covering a total of 3554 participants. Cumulatively, these factors act as study strengths. However, the study has limitations, which largely centre on a paucity of information and a potential lack of statistical power due to small numbers of studies in the sub-group analyses. The risk of obtaining spurious significant results due to the relatively large number of sub-group analyses undertaken (multiplicity testing) should also be acknowledged as a potential limitation. Such limitations have however been carefully considered throughout the data analysis and interpretation.

Whilst an 'adherence effect' has been estimated, data to estimate a treatment and clinical effect are absent, adding further limitation to this work. It is therefore unknown whether the adherence improvements yielded through use of these techniques translate into therapeutic and clinical benefits. Scope for future work has therefore been identified, though given the documented paucity of information in many studies, eliciting these details may prove challenging.

4.6 Conclusion

The evidence provided suggests that motivational and cognitive counselling techniques can effectively be delivered by routine healthcare professionals, in both primary and secondary care settings, and that positive effect is not restricted to diseases such as HIV. Evidence also suggests that efficacy is not related to treatment exposure and that brief interventions, delivered over few sessions demonstrate comparable efficacy to interventions of far greater duration. Interestingly, the results also suggest that these interventions can be delivered via telephone contact with comparable efficacy to similar interventions delivered via face-to-face contact. Such factors are likely pertinent to the scope of these techniques as widespread, routinely utilised adherence interventions, and suggests that the techniques are adaptable to a wide range of settings and amenable to tailoring to meet individual need. However, numerous sub-group analyses were undertaken which often related to relatively small numbers of studies; the potential for multiplicity testing and a lack of power to detect statistically significant differences must therefore be acknowledged.

Despite the promising evidence provided for these techniques, their widespread use remains uncommon, especially in the UK where only four studies were undertaken. Publication of research in this domain has however seen steady growth in the last ten years, and looks set to continue expanding in the near future. In comparison to common place interventions such as medicine use reviews, adherence checks and patient education, provided through the extensively funded MUR and NMS services, or provision of compliance aids which are also a costly intervention, the techniques evaluated in this study may represent a more effective intervention. However, as details of cost effectiveness have not been established in this study, conclusions about likely cost-effectiveness cannot be made.

Further research into the use of these techniques as medication adherence interventions is warranted in order to elucidate which techniques are most strongly associated with improved medication adherence. Feasibility studies to determine both patient and healthcare practitioner satisfaction and acceptance of these techniques is also necessary as tentative work in establishing the role of these techniques in the widespread delivery of evidence-based, effective adherence interventions.

This review has also highlighted that the quality of study reporting in this field is frequently problematic and thus represents a further marker for improvement in future research. Future research in this field therefore needs to provide methodologically robust, well conducted and appropriately reported studies, with clearly articulated and

well defined interventions. Such developments are likely pivotal in furthering the use of these techniques to the wider healthcare domain.

The contribution of this chapter to the overall thesis is to provide substantial evidence that these novel cognitive-based behaviour change techniques are worthy of further pursuit in the quest to develop a gold-standard adherence intervention. Whilst we can now be confident that these techniques are useful tools to improve adherence, the challenge, as referenced in chapter three, is to establish how these techniques can be incorporated into an intervention.

With a plethora of techniques available, evidence based methods to establish which techniques are best used when, is pertinent to further development. Chapter five considers the development of an adherence barriers identification questionnaire, which would in turn be used to determine which cognitive-based behaviour change technique would be most appropriate to address an individual patient's adherence barriers.

4.7 Addendum

In April 2013, the literature search for this meta-analysis was updated for publication. The original search, identified 21 RCTs suitable for inclusion in the meta-analysis; a figure that had increased to 26 RCTs 16 months later, highlighting the continued interest in these techniques and increase in quality publications within the field.

For these 26 RCTs an effect size (95% CI) of 0.34 (0.23 to 0.46) was achieved with high heterogeneity (I^2 = 68%). Adjustment for publication bias was necessary due to statistically significant funnel plot asymmetry yielding a more conservative estimate of summary effect size as 0.21 (0.08 to 0.33). As with the original meta-analysis, sub-group analyses suggested that the interventions were amenable to use across different populations and in differing manners, without loss of efficacy.

This update was published in August 2013 in BMJ Open and is available at:

http://bmjopen.bmj.com/content/3/8/e002749.full

Included within the update, was a UK based RCT involving 211 patients with type two diabetes who received an Implementation Intention Intervention (III) to improve adherence as a nurse delivered, one-off session[398]. A further UK based study of 62 stroke survivors prescribed medication for the prevention of further cardiac events, also based on III[333] narrowly missed inclusion within the update due to publication in May 2013. Both studies were of high quality and achieved promising improvements in medication adherence. This highlights that UK based research is, albeit gradually, starting to shift its research focus toward a more psychological basis for adherence improvements.

Chapter Five The 'Identification of Medication Adherence Barriers Questionnaire (IMAB-Q)'; developmental processes

5.1 Chapter introduction

5.1.1 The need for a tool to identify patient barriers to adherence

Chapter one detailed the nature, magnitude and implications of non-adherence to prescribed medication. Whilst a gold standard, evidence-based adherence intervention is elusive, a wealth of literature describing the predictors of adherence exists. Synthesis of this material, with a specific focus on adherence barriers, is an intuitive first step towards designing a questionnaire to enable identification of an individual's adherence barriers, as proposed in chapter three. A questionnaire, grounded in the TDF, will enable theory-based identification of medication adherence barriers and the interventions delivered to resolve these identified barriers can be targeted accordingly. Development of this questionnaire therefore represents an important step towards theory based adherence interventions that are targeted to meet individual needs. The proposed questionnaire would form a pivotal part of an intervention whereby adherence barriers identified in the questionnaire would then be discussed with the patient.

The best approach to resolving non-adherence, especially that of an intentional nature, is still unknown and a clear strategy for approaching this problem has not been defined. Through an understanding of the complexities of medication taking, it is clear to see that behaviour change is challenging, especially when the non-adherent behaviour is influenced by factors such as attitudes, confidence, motivation and health beliefs. Chapter four provided a systematic review and meta-analysis of cognitive-based behaviour change techniques to resolve these issues and improve adherence. Techniques such as MI and III were shown to improve medication adherence beyond the educational and behavioural strategies routinely used in practice.

The evidence for cognitive-based behaviour change techniques is encouraging, however, much work is still needed to develop a robust, theory and evidence-based means of utilising these techniques appropriately to improve adherence. Chapter three focused on theories to understand the psychology of intentional non-adherence. It also summarised recent developments led by Michie *et al.* which propose a mechanism for mapping behaviour change techniques to the theoretical domains of behaviour to which they relate. This novel approach would allow targeting of the interventions delivered to meet an individual's needs by selecting the most appropriate evidence-based behaviour change technique(s) for the adherence difficulties identified.

To be able to deliver an intervention to address a patient's adherence barriers, we must first have a robust, theory based tool to identify these barriers. Questionnaires

grounded in the Theoretical Domains Framework (TDF) to identify barriers to behaviour change have been described in chapter three. This chapter will focus on the application of this approach to develop the 'Identification of Medication Adherence Barriers Questionnaire' (IMAB-Q).

5.1.2 Questionnaire design; consideration of theory and methods

5.1.2.1 General principles and questionnaire content

Questionnaire development is a multi-stage process involving meticulous design to assure confidence in its rigour[150]. The process can be loosely categorised into content development, presentation, refinement, pilot work and psychometric analysis. Pilot work is an essential component to enable evolution of an appropriate questionnaire and the time needed to adapt and refine the questionnaire should not be overlooked[150].

Qualitative work such as interviews and focus groups are often undertaken in order to inform content development[399]. Such work is particularly necessary when there is little existing evidence to support determination of questionnaire content. Interviews offer an in depth exploration of ideas and are particularly useful for sensitive subject matters, where group discussions are less appropriate[400]. On the other hand, focus groups can encourage group discussion and debate about the topics raised and highlight a wider range of experiences and understanding[401, 402]. Individual views can also be collated to explore group perspectives and seek consensus, plus prioritisation of content can also be facilitated through group discussion[401]. Focus groups are therefore a widely used component in the development of valid and reliable survey instruments, representing a cost effective and flexible tool to explore participants' attitudes and responses[399].

Content development can be further expedited if a large evidence base is already in existence[150]; the evidence can be synthesised and supplemented with qualitative work to enable tailoring to meet the specific needs of the questionnaire being developed. In 2011, McEachan *et al.* reported identification of additional barriers plus a greater depth of understanding, when focus groups were used to supplement a list of literature identified barriers to worksite physical activity[403]. Similar findings were reported by Lacey *et al.* who undertook patient focus groups and semi-structured interviews to identify obstacles to and motivations for adherence to glaucoma therapies[404].

Qualitative work with members of the public during the development of a questionnaire provides an opportunity to explore their understanding of the material developed. The face and content validity of the questionnaire can therefore be checked in this way. Sofaer *et al.* note that consultation with members of the public provides an opportunity

to elicit the 'commonplace' and 'lay' language used to describe the questionnaire's material. The questionnaire content can subsequently be refined to reflect patient terminology and expression[399]. Involving patients or members of the public in the design of a questionnaire (which will subsequently be used in a behaviour change intervention) also enables incorporation of NICE guidelines, which advise a partnership with individuals from the target population to take account of lay wisdom[405].

To determine the content of a questionnaire to identify barriers to medication adherence, due consideration must be given to relevant literature. As described in chapter one, the existing body of quantitative and qualitative literature regarding medication non-adherence is vast. There is however, no recent synthesis of this information in order to elucidate the barriers to medication adherence.

In chapter one, non-adherence to medication for both acute and chronic conditions were considered and differences explored; this identified that the implications of non-adherence in acute conditions is likely to be less profound. The management of long term conditions is a UK priority due to its rising prevalence, negative health and social implications plus its significant impact on NHS and social care resources[406]. It is therefore most appropriate to focus an 'adherence barriers identification' questionnaire towards patients prescribed medicines for the management of chronic conditions. However, Gellad *et al.* report that the circumstances surrounding non-adherence to medication for the treatment of addiction and mental health problems is often condition specific[407]; exclusion of these two conditions is therefore warranted.

When questionnaire development is supplemented with qualitative work involving patients or members of the public, it is advisable to ensure a good coverage of people from differing backgrounds, to gain a diversity of perspectives on the material covered[408]. For medication adherence barriers, socio-demographic factors such as age may be influential, especially with regard to 'costs of medicines' as all patients in England over the age of 60 years are exempt from prescription fees. Inclusion of participants with differing medication regimen complexities and differing levels of health literacy would also be advisable as these parameters could influence perceptions of medication adherence barriers and comprehension of the questionnaire's content. Age and regimen complexity can be identified with relative ease by means of a simple questionnaire, but identification of varying levels of health literacy requires more consideration. Whilst a wealth of detailed health literacy screening tools are available, many of these tools such as the TOFHLA tool[409] and even its shortened version S-TOFHLA[410] are relatively complex and lengthy. The Single Item Literacy Screener

(SILS)[411] tool is less complex and consists of a single statement, relating to how frequently the participant needs assistance in reading health related materials, to which participants respond using a five-point Likert scale ranging from always to never.

5.1.2.2 Assessing patient attitudes

There are several approaches to measuring a respondent's attitude, each with advantages and disadvantages.

Dichotomous responses

Attitudinal statements should be designed so that participants can express their agreement or disagreement. The simplest attitudinal measure is therefore to offer a dichotomous response option of these choices. This approach offers simplicity and brevity, both for the respondent completing the questionnaire and researcher scoring it. However, such brief data provides limited detail. Oppenheim comments that attitudes have both intensity as well as content and that intensity is an important moderator of attitude function[150]. A dichotomous response option does therefore not elicit a patient's strength or intensity of agreement or disagreement with a statement.

Continuous and ordinal type responses

In order to establish the intensity with which a patient agrees or disagrees with a questionnaire statement, ordinal or continuous measurements are necessary. Ordinal attitudinal scales such as Likert scales serve to roughly divide people into a number of broad groups with respect to a particular attitude. They must be uni-dimensional, reliable, valid, linear and reproducible[150].

a) Visual analogue scales (VAS)

Visual analogue scales provide a continuous measure of attitudinal agreement, from which parametric statistical analysis can be undertaken. A VAS is a straight line, usually 10cm in length, with anchor points at each end labelling extreme boundaries of a sensation, feeling, attitude or response[412]. For attitudinal statements, the anchor points will likely be 'strongly disagree' and 'strongly agree'. Participants are asked to express their level of agreement with a statement by placing a mark along a 10cm which best reflects how they feel[413] This approach is of greatest value when assessing change within an individual, but less use in comparing a group of individuals at one time point[414]. Whilst elicitation of continuous data offer benefits for statistical analyses, the process of measuring where each mark has been placed is time consuming and in

clinical practice, this approach is therefore rarely permissive[415]. Problems with the validity and test-retest of this approach have also been reported[412].

b) Likert scales

Likert scaling is a frequently adopted attitude measuring technique requiring participants to indicate their level of agreement on a symmetric agree-disagree scale for a series of statements[150]. Of all the attitude measuring techniques, Likert scales are the most popular[150] and have been shown to have the best correlations with actual behaviour of the various attitude measurement techniques[416]. Likert scales use fixed choice response formats measuring attitude on an ordinal scale, for example, ranging from strongly agree to strongly disagree. These scales may or may not include a mid-point representing lack of an opinion, or ambivalence. The mid-point may be interpreted as the 'typical' response and thus be used by respondents as a reference for their own position[417]. Absence of a mid-point may lead to participants selecting a choice which does not reflect their own attitude and thus produce erroneous data[418 419].

5.1.2.3 Questionnaire presentation and length

Oppenheim's seminal text highlights the importance of good questionnaire design and layout[150], though McColl notes that there is little empirical evidence to guide the presentation of a questionnaire[141]. There is however evidence to highlight that small errors in design can have notable implications, for example, boxes that were out of line with their responses were found to be confusing for respondents and subsequently ignored, as were statements that were cramped together[420].

Key considerations for the presentation of the questionnaire therefore include:

- Inclusion of white space, to ensure the questionnaire appears less confusing, intimidating and difficult[419] as a cluttered questionnaire is known to elicit reduced response rates[421]
- Avoidance of separating a statement over two pages as this is more likely to increase the cognitive burden for completion[422, 423]
- Using a minimum of a 10-point font[141] in the general population, or 12-point for respondents of an older age[424]
- Use of an easily read typeface with a distinct separation between characters[141]
- Ensuring consistency in presentation[425] and an eye catching design to arouse interest[419]

Widespread literature offering guidelines for wording of questionnaires are available. Key considerations for the formation of questionnaire statements include:

- The avoidance of jargon, leading questions and ambiguity/multiple meanings[141, 150, 413, 422, 423, 426]
- The avoidance of double negatives and double-barrelled statements[427]
- The use of a conversational tone to facilitate rapport building with respondents[424]
- Minimising the cognitive burden associated with questionnaire completion[425]
- Using a mixture of both positively and negatively phrased statements to minimise the risk of acquiescent response bias in the questionnaire, whereby respondents have a tendency towards responding to each statement in a similar way[428]
- Giving due consideration to social desirability bias and therefore phrasing statements in an open and non-judgemental manner[150]

Further to considering the phrasing of the questionnaire statements, it is also pertinent to consider readability of the overall questionnaire. Williams reports that the average reading age in the UK is 12 years[75], therefore the questionnaire statements and instructions for completion must be comprehendible at this reading level to ensure respondent acceptability and accuracy of responses. It is also recommended that questionnaires should be comprehendible to respondents at the lowest end of educational backgrounds in the target population, not the average[422]. For all questionnaire components, a reading age of 12 must therefore be an absolute maximum. The Flesch formula, a commonly used metric to assess readability, can be applied to the questionnaire to determine the reading age necessary to permit comprehension, as recommended in literature[424].

With regard to questionnaire length, brevity is pertinent as excessively lengthy questionnaires are likely to yield lower completion rates. However questionnaires must not be so brief as to not elicit sufficient information. A balance between sufficient brevity to facilitate response and sufficient detail to enable data analysis and psychometric testing is therefore advised[150].

5.1.2.4 Psychometric properties

The psychometric properties of a questionnaire are those which describe how well the questionnaire performs, in terms of consistency, reliability and validity. Establishing such parameters is essential to documenting the suitability and scientific worth of a questionnaire. The process entails administering the questionnaire to a cohort of

patients that reflects the population for which it is intended and then analysing the questionnaire response data according to different parameters.

For the IMAB-Q, this chapter concerns the development of the tool and not its validation. Questionnaire validation is a time consuming and complex process which will therefore be undertaken as a separate study. Whilst this thesis chapter does therefore not concern questionnaire validation directly, it is pertinent to design the questionnaire in a way that will facilitate later psychometric testing.

Internal consistency

Internal consistency estimates the extent to which items within a scale assess a single construct and is assessed using Cronbach's alpha which gives a score of between 0 and 1. A score of 0 indicates no consistency whereas a score of 1 can be considered to mean the items are practically identical[150]. For a theory based questionnaire, internal consistency is important to check that similar statements assess the same construct. In designing a questionnaire it is therefore pertinent to ensure there are sufficient statements for each construct and that there is overlap between statements.

Test-retest reliability

This parameter concerns the likelihood of a questionnaire yielding the same result when repeated, for example two weeks after the first completion[150]. Whilst this important metric must be considered in validation stages, at the developmental stage, there are no factors to consider from this regard.

Validity

Validity, concerns the process of ensuring the questionnaire actually measures what it claims to. Oppenheim describes three main types of validity[150]:

1) **Content validity**

   Concerns:

   a. Face validity, achieved through discussion of questionnaire content and phrasing with representatives from the target population
   b. Content validity, achieved by consultation with experts in the field to ensure the questionnaire items are comprehensive and representative of the construct under consideration

2) **Criterion validity** concerns the comparison of the questionnaire to one or more external variables believed to measure the attribute under question

3) **Construct validity** concerns how well the statements measure the theoretical constructs that they are assumed to measure and involves looking at patterns of divergence and convergence using factor analysis

As described earlier, face and content validity can be determined through consultation with patients and/or members of the public. Criterion validity can be established via comparison to a gold-standard measure of the same construct measured in the new questionnaire. However, where such a measure is non-existent , criterion validity can be judged on the basis of relationships between the questionnaire and other relevant constructs[150]. A good example of the process of establishing criterion validity in such cases is the work of Horne *et al.* in the development of the Satisfaction with Information about Medicines Scale (SIMS)[127]. As there were no comparative validated tools to assess adherence, Horne and colleagues hypothesised that greater satisfaction would impart lower concerns and better adherence. The Beliefs about Medicines Questionnaire (BMQ)[38] and Medication Adherence rating Scale (MARS)[147] tools were therefore added to provide data on medication concerns and adherence respectively. The hypothesis about the relationship between these three constructs was then assessed with a Pearson correlation co-efficient. For construct validity, confirmatory factor analysis is a commonly used approach to determine how well the questionnaire statements fit a theoretical model. At the developmental stage the key consideration is to ensure sufficient data for later testing; due consideration should therefore be given to the questionnaire length and number of statements.

To ensure that psychometric testing of a questionnaire can be undertaken with optimal effect, minimising likely confounding factors is imperative. Due attention to potential moderators of medication adherence barriers must therefore be given. Beyond the differentiation between acute and chronic conditions, consideration of the differences between symptomatic and asymptomatic conditions is advisable (as detailed in chapter one). Non-adherence to asymptomatic conditions such as hypertension and hyperlipidaemia is known to be particularly problematic and is frequently intentional in nature[429]. Cardiovascular preventative medicines are amongst those most commonly prescribed in the UK[430] and non-adherence in often poor. A recent meta-analysis of over 376,000 patients taking cardiovascular preventative medications, reported a summary adherence estimate (95% CI) of 57% (50-64%) after a median of 24 months[431] post diagnosis. Restriction to patients taking medicines for the prevention of cardiovascular disease may therefore be appropriate to minimise confounding factors in the psychometric analysis of the questionnaire. This affords the additional benefits

of the potential for using clinical outcome measures (blood pressure and blood cholesterol levels) in subsequent studies.

5.2 Methods

Figure 5.1 summarises the multi-stage method for developing the 'Identification of Medication Adherence Barriers Questionnaire' (IMAB-Q).

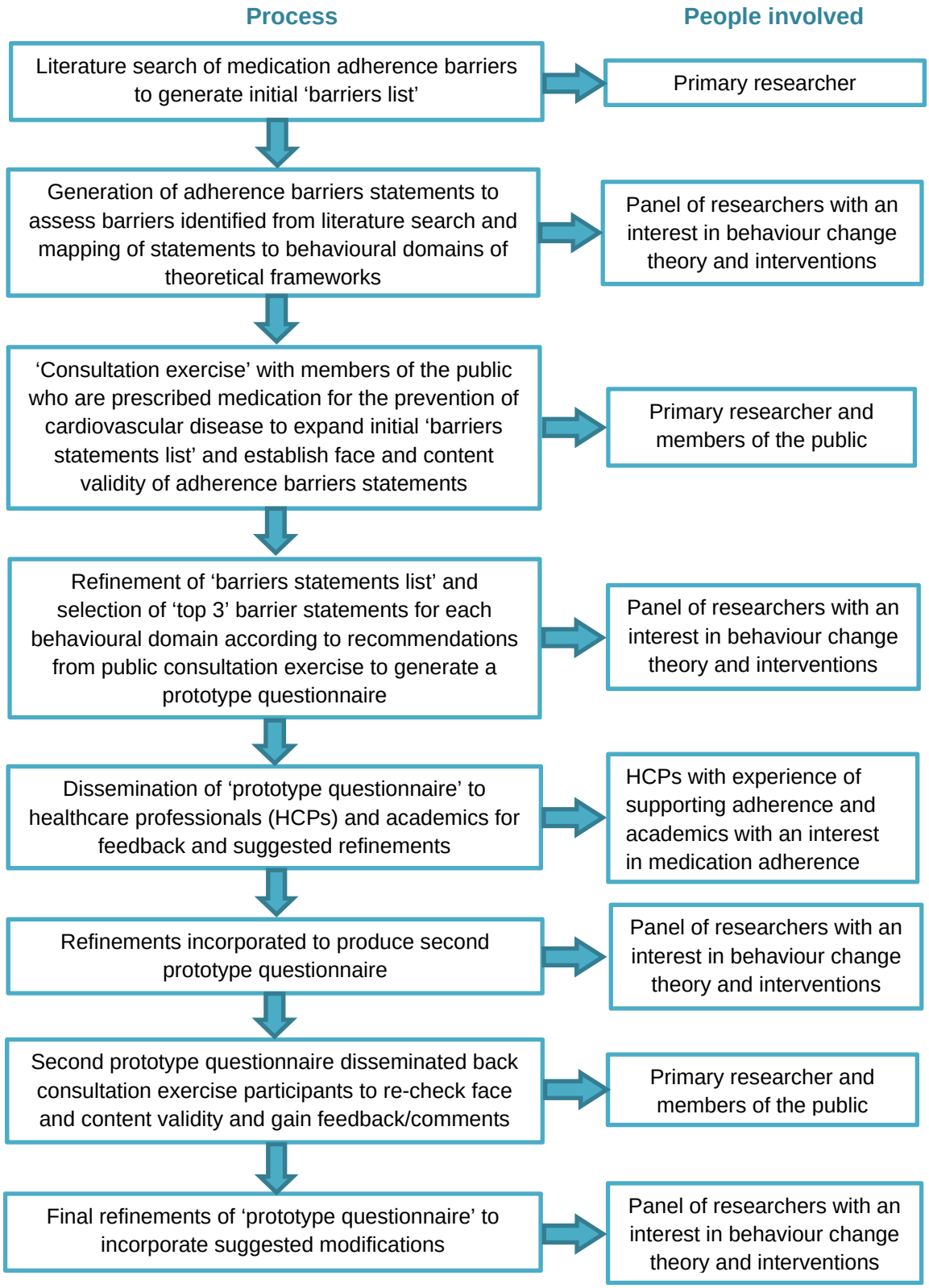


Figure 5.1 Summary of method for developing IMAB-Q

5.2.1 Literature search of barriers to medication adherence

Table 5.1 shows the literature search strategy applied to The Embase, Medline and PsycINFO databases via the Ovid interface on the 18th of September 2012. Abstracts relating to barriers to medication adherence in chronic conditions were selected for retrieval to elicit barriers.

Terms relating to 'medication' and 'non-adherence' were searched in both the titles and abstracts fields to ensure a good coverage of potential material. Terms relating to 'barriers' were restricted to the title search field only, as scoping searches identified that inclusion of these synonyms in the abstract field generated an excess of irrelevant papers. Scoping searches also revealed a number of key terms which yielded irrelevant papers and were subsequently stipulated in the search terms using the NOT operator, as detailed in table 5.1. The search was also restricted to abstracts written in the English language and a date restriction of 2005 to present was applied to ensure the most relevant material was selected. Prior to 2005, medication adherence research had focussed more heavily on compliance and thus the reasons for intentional non-adherence were little explored.

	Search terms
1	Medication*.ti,ab OR Drug*.ti,ab OR Medicine*.ti,ab
2	Adheren*.ti,ab OR Complian*.ti,ab OR Concordan*.ti,ab OR Non-adheren*.ti,ab OR Non-complian*.ti,ab
3	Barrier*.ti OR Difficult*.ti OR Problem*.ti OR Reason*.ti (NOT Tissue.ti, NOT epithelial.ti, NOT cream*.ti, NOT skin.ti, NOT platelet.ti, NOT guideline*.ti)
4	1 AND 2 AND 3
5	4 NOT letter, NOT editorial, NOT comment

Table 5.1 Search terms applied to electronic databases to identify barriers to medication adherence

Despite the search term restrictions, a large number of irrelevant abstracts were sourced. Abstract titles were therefore screened to remove duplicates and those that were obviously irrelevant. The remaining abstracts were screened in depth against the inclusion and exclusion criteria, using a bespoke abstract screening tool. Abstracts were eligible for inclusion if they:

- Reported barriers to medication adherence
- Concerned adherence to medication used to treat chronic conditions

Abstracts were excluded if they:

- Did not specifically focus on identification of barriers to medication adherence
- Did not consider medication for the treatment of long-term chronic conditions
- Concerned medication for the treatment of addiction or psychiatric problems
- Included participants known to be abusing non-prescription drugs, suffering with addiction or suffering with mental health problems
- Described a study which focused on the prevalence or further exploration of a specific barrier to medication adherence, for example cost or stigma
- Described a research protocol with no data yet available or a conference abstract without full data

As with the systematic review and meta-analysis reported in chapter four, studies reporting treatments for addiction or mental health problems were excluded as the nature of non-adherence is known to be condition specific.

Studies concerning a specific barrier were excluded as in depth data regarding a specific barrier and its prevalence in a specified population was not necessary for this study. Abstracts remaining after full screening were used to elicit barriers to medication adherence. Full texts were accessed where possible, but in instances where full texts were not available, barriers to adherence listed in the abstract were still extracted. Whilst it is not common practice to extract data from abstracts alone, for the purpose of this literature review, such practice was not deemed to be a notable limitation. The aim of the literature review was simply to identify studies which report barriers to medication adherence, and extract the main barriers identified in these studies; details provided in the abstract were sufficient to meet this objective.

The following data were extracted:

- Authors
- Date of publication
- Journal of publication
- Publication type – conference abstract or journal article
- Disease state studied (medication type taken)
- Population studied
- Method of establishing barriers to adherence
- Barriers to adherence

Adherence barriers were initially extracted using the exact terminology described in the article. Once all barriers had been extracted, similar barriers were grouped into themes to generate a single cohesive list.

5.2.2 Generation of adherence barrier statements and mapping to TDF

For each adherence barrier identified, potential adherence barrier statements were generated and mapped to the one of the twelve domains of the original TDF[275]. Whilst the updated TDF[276] was acknowledged, a notable amount of work for this project had already been undertaken by the time the TDF update was published. A collaborative decision to retain the original TDF was therefore made, however, following mapping with the original TDF, the updated TDF was considered to observe whether the updated version would have altered any decisions.

The principle investigator (CE) was responsible for the initial mapping of each adherence barrier to a theoretical domain and the generation of potential adherence barrier statements. The mapping and barrier statement generation process were undertaken in parallel as the phrasing of the adherence barrier statement was sometimes pertinent to the behavioural domain to which it was mapped. Adherence barrier statements were phrased to reflect the context of the original extracted barriers and in a non-confrontational, unambiguous way. The original literature was frequently referred to and research questions borne in mind throughout to ensure the adherence barriers statements remained relevant, as recommended in literature[150, 427].

The adherence barrier statements generated and behavioural domains to which these were initially mapped, were discussed over two telephone conferences between CE, NT and DB. Interpretation of the meanings of the theoretical domains was discussed extensively to achieve group consensus as to which theoretical domain each adherence barrier statement would be mapped. Discussion also enabled consensus as to the phrasing of each adherence barrier statement.

5.2.3 Consultation exercises with members of the public

Focus group style consultation exercises were undertaken

5.2.3.1 Aims

1) To assess the face and content validity of the generated adherence statements
2) To identify any additional barriers to medication adherence that were not elicited in the literature search

3) To assess members of the public's perspectives on which adherence barriers are most pertinent in each behavioural domain

5.2.3.2 Inclusion criteria

Eligible for inclusion were members of the public who were:

- Aged 18 years or over and able to provide informed consent
- Taking medication for the prevention of cardiovascular disease, which included, seven drug classes as recently defined in the literature[431]:
    - aspirin
    - angiotensin-converting enzyme inhibitors
    - angiotensin receptor blockers
    - beta-blockers
    - calcium-channel blockers
    - thiazides
    - statins

5.2.3.3 Exclusion criteria

Excluded from participation in the consultation exercises were members of the public who were:

- Receiving medication for the treatment of addiction or mental illness
- Unable to read or speak English

The previously documented rationale for exclusion of patients suffering with mental health or addiction problems was also applied here.

5.2.3.4 Participant recruitment

Ethical approval from the University's Faculty of Health (FoH) ethics committee was secured before recruitment commenced. Correspondence confirming ethical approval for the study can be found in appendix 5.1. Purposive sampling was undertaken to ensure a wide range of demographic characteristics were covered by the consultation exercise participants. Participants were recruited from the large pool of employees and students at the University of East Anglia (UEA).

Figure 5.2 summarises the participant recruitment process for the consultation exercises. Posters 'advertising' the study and asking for volunteers were placed across the university campus, in prominent places such as coffee shops and social areas. Electronic 'advertisement' of the study also occurred via a weekly bulletin which

is e-mailed to all staff and students. The study was advertised in the e-bulletin on two separate occasions separated by a four week interval to optimise recruitment. The study was also advertised on the university's social media sites such as 'Facebook' and 'Twitter'.

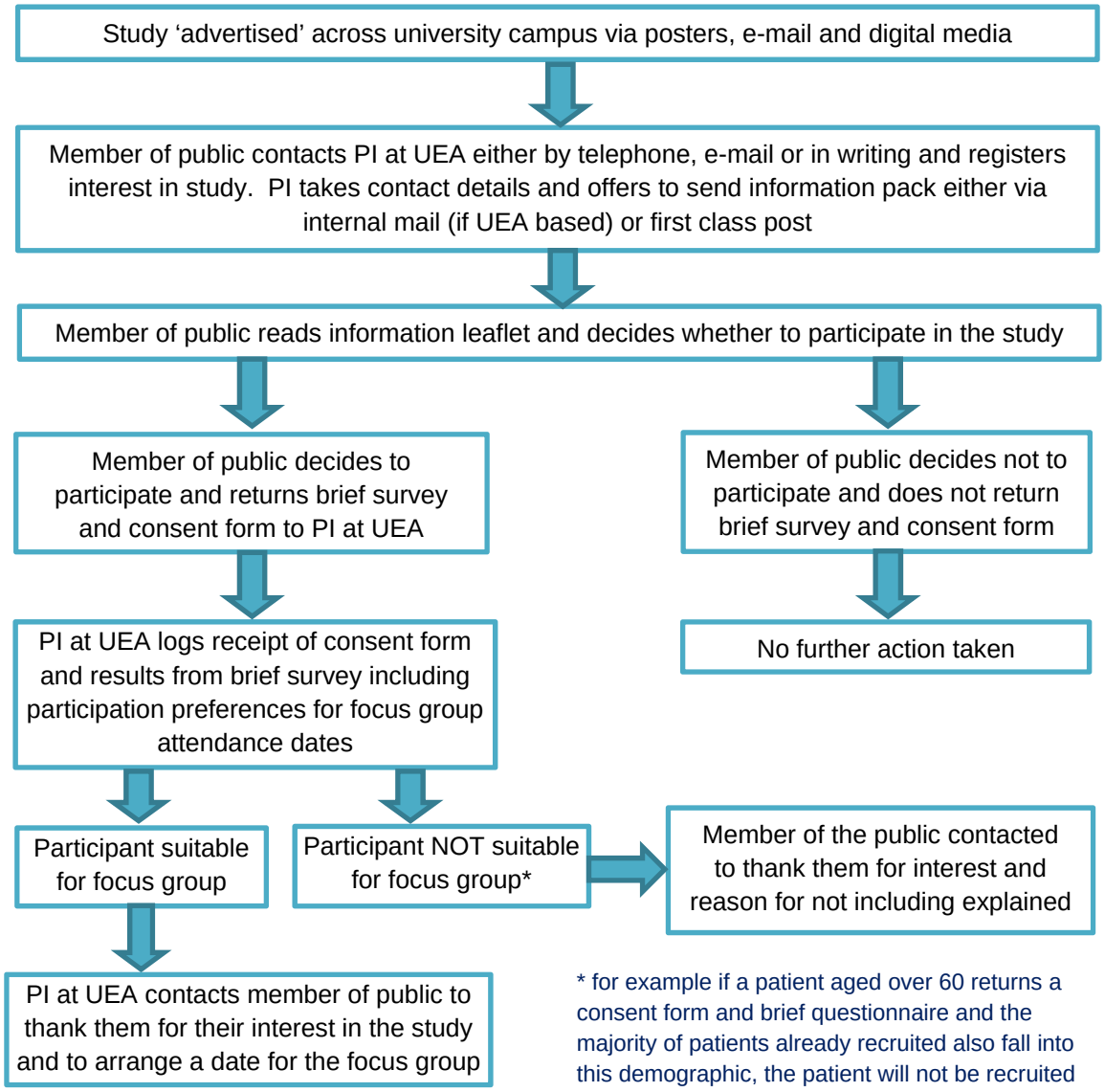


Figure 5.2 Consultation exercise recruitment process

The study 'advertisements' offered a brief synopsis of the study and described the types of participants needed. An example poster is shown in appendix 5.2. The 'advertisements' were carefully phrased to state 'would you or anybody you know like to participate in a study'. This wording extended the potential recruitment beyond UEA students and staff to include their friends and family and vastly extended the recruitment pool to an even wider, more diverse population. The advertisement asked

members of the public to contact the lead researcher (CE) if they would like more information about participation.

Members of the public making contact with the lead researcher were sent an information pack containing:

- A participant information leaflet – to explain the study
- A consent form – to complete and return to UEA if they wished to participate
- A brief survey to elicit demographic information and focus group preference information - to be completed and returned to UEA if they wished to participate
- A pre-paid envelope – for returning the consent form and brief survey.

The information leaflet, consent form and 'brief survey' are shown in appendices 5.3, 5.4 and 5.5 respectively. Members of the public wishing to participate were advised to complete the consent form and brief survey and then return these to the lead researcher at the UEA using the pre-paid envelope provided, or UEA internal mail.

Upon receipt of a consent form and brief survey CE recorded this information and used this to assign participants to one of two potential focus groups (on differing dates and times). The recruitment process continued until each focus group had between six and eight participants meeting the required inclusion criteria. Each focus group aimed to include:

- Participants of varying ages
- Both males and females
- Participants with low, average and high literacy levels
- Participants who were exempt from prescription charges and those who paid
- Participants with varying numbers of regularly prescribed medicines

5.2.3.5 Participant information packs

The information packs contained documents as shown in appendices 5.3, 5.4 and 5.5.

The brief survey (as shown in appendix 5.5) was used to elicit:

- basic demographic information from participants (age and gender)
- the number of regularly prescribed medicines taken
- whether or not the participant paid for their prescription
- basic literacy levels
- focus group attendance preferences

The inclusion of each section of the survey was explained to participants in the information leaflet so that the rationale behind the questions was understood. It was hoped that this transparency would encourage honest answers and an increased response rate, plus allay any concerns that the participants may have about completing the survey or any confusion experienced as to why the questions are being asked.

5.2.3.6 Consultation exercises

Each consultation exercise was moderated by CE with co-facilitation from either DB or an additional research colleague, with experience of focus group moderation. The co-facilitator was responsible for ensuring the focus groups ran to time and that all audio equipment was working correctly. They also made field notes during the sessions to record information (such as gestures and group interactions) that were not recorded by the audio equipment. Two focus groups were planned, to take place at the UEA as this is the base from which participants were recruited and was thus likely to be a convenient venue. Times and days were varied to give participants the option of attending at a time that was preferable to them.

Each consultation exercise lasted approximately two hours, with time allocated for a break midway. The sessions followed a structured format, whereby the adherence barriers statements for each behavioural domain were presented to the participants in turn. The first behavioural domain and barriers mapped to this was explained by the moderator and then each statement associated with this behavioural domain was visually presented to the participants one-by-one. For each statement the moderator asked the following of participants:

- Whether they understood the statement and what it meant to them
- Whether they thought the statement represented a legitimate barrier to medication adherence and how important they thought this barrier was
- Whether they would have changed the statement in any way to make it clearer, easier to understand, or more representative of the adherence barrier

After presentation of all of the barrier statements in one domain, participants were asked if they thought there were any additional barriers in the domain which were not represented. Participants were also asked to give an indication of which three adherence barrier statements in the list were the most important. Restriction to the three most pertinent barriers in each behavioural domain was made to generate a pool of statements sufficient in length to enable later psychometric testing and a

questionnaire that was comprehensive yet not excessively long. The next behavioural domain was then introduced and the above process repeated.

Due to the volume of material, it was not feasible to cover all of the behavioural domains in a two hour session and extension of the session beyond two hours was neither feasible nor advisable[401, 432]. The two sessions undertaken therefore considered barriers from differing behavioural domains. One behavioural domain was covered by both groups to enable an assessment of how comparable the findings of each group were.

5.2.3.7 Data analysis

Primary analysis of the data was undertaken by CE and validated by DB as recommended in literature[433]. Transcription of the focus groups audio data was undertaken by CE. Data were analysed purely for the purpose of refining the adherence barriers statements in light of participants' perceptions and understandings, using a framework analysis approach[434].

5.2.4 Refinement of adherence barrier statements and generation of prototype questionnaire

Each of the behavioural domains were considered in turn using a mind map approach to summarise the material necessary to inform decision making, into one cohesive document. These mind maps were informed by the transcripts from the participant consultation exercises and summarised:

- The definition of the domain from the updated TDF
- The definition developed by the research team for relation to medication adherence
- The barriers originally mapped to the behavioural domain
- The new barriers discussed during the consultation exercise
- Barriers moved to (or retained in) a different behavioural domain
- Barriers selected as most important
- Behaviour Change Techniques (BCTs) that would be used to address barriers from this domain[295]

Consideration to which BCT would be utilised (as described in chapter four) assisted the process by adding another dimension to the decision making strategy.

Data from the participant consultation exercises were used to refine the adherence barrier statements according to the participant's understanding of their meaning and

relevance. Any additional barriers generated during the consultation exercises were also considered. The same panel of researchers as used in the earlier stages of the questionnaires development (CE, NT and DB) were also used for this phase of the questionnaire development.

Participants' comments were used to influence selection of three statements from each behavioural domain for the questionnaire. The selected statements were combined to generate a prototype questionnaire. Instructions for completion of the questionnaire were written in clear and non-judgemental way to encourage honest responses.

5.2.5 Dissemination of prototype questionnaire for feedback

The prototype questionnaire was presented to a pre-selected panel of academic researchers with an interest in medication adherence research, for feedback and suggested amendments. Research colleagues, naïve to the TDF and adherence barrier mapping processes, were emailed the questionnaire prior to a research group presentation. Comments were collated by CE prior to delivery of a thirty minute presentation about the questionnaire's construction and its theoretical components.

A panel of healthcare providers including a GP, pharmacist and domiciliary medicine support technician also received the prototype questionnaire and were asked to provide suggestions for amendments based on their experience of consulting with patients with adherence difficulties. A second prototype questionnaire was generated from this feedback process.

5.2.6 Second consultation exercise with members of the public

The second prototype questionnaire was sent to the consultation exercise participants used earlier in the questionnaire's development. The face and content validity of the prototype questionnaire was established by asking participants whether they understood each statement and whether it accurately reflected a barrier to medication adherence. All participant comments were collated, reviewed and incorporated as necessary to generate a final IMAB-Q.

5.2.7 Readability testing of IMAB-Q

The Flesch-Kincaid readability test was applied to all sections of the completed IMAB-Q to indicate comprehension difficulty. The Flesch-Kincaid Grade Level was calculated using the following formula:

0.39 (total words/total sentences) + 11.8 (total syllables/total words) – 15.59

The resulting number corresponds with a US educational grade, for example a score of 7.1 would indicate that the material was suitable for comprehension by an average student in the 7th grade of the US education system. The US and UK educational system are equivalent in so much as 7th grade is equivalent to year 7 in UK high school. A Flesch-Kincaid score of 7.1 therefore means the material should be comprehendible to an average 11-12 year old in year 7 of UK high schools.

5.3 Results

5.3.1 Literature search to identify barriers to medication adherence

Figure 5.3 details the flow of studies from screening to inclusion. The literature search identified 515 abstracts; 323 of these (62.7%) were excluded after two rounds of brief screening to remove clearly irrelevant titles and duplicates. Of the remaining 192 articles, the main reasons for exclusion were articles not relating to identifying barriers to adherence or focussing on specific adherence barriers. These specific barriers included social stigmas, spiritual beliefs and medication costs.

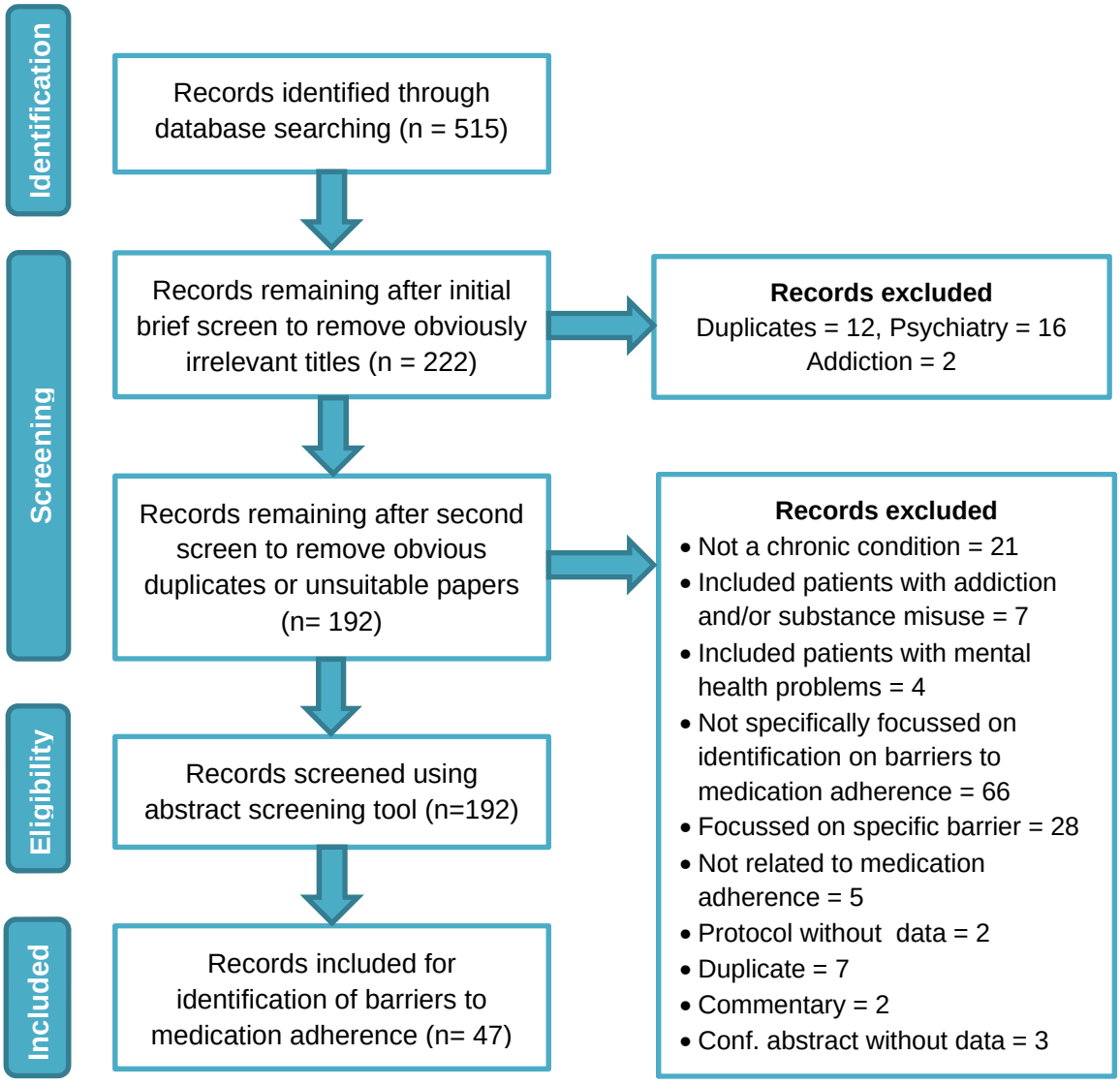


Figure 5.3 Flow diagram for selection of studies from database search

A summary of the 47 studies included in the review is provided in appendix 5.6. Full texts articles were available for 32 studies (68.1%); for the remaining 15 studies (31.9%), adherence barriers were extracted from the abstract alone. Medication adherence was considered in 11 diseases; HIV was the most frequently considered disease, accounting for 14 (29.8%) studies. Seven (14.9%) studies considered adherence to medicines for 'chronic conditions' and there were six studies (12.8%) each for hypertension and immunosuppressive therapy. Diabetes and cardiovascular disease, each accounted for three (6.3%) studies and inflammatory bowel disease, cystic fibrosis and glaucoma were each considered in two (4.3%) studies. Individual studies considered adherence to medication in dermatology and asthma.

Studies tended to consider adherence barriers in adult populations and this was the case for 32 (68.1%) studies; seven studies (14.9%) focussed on adolescents, five studies (10.6%) concerned paediatrics and three (6.2%) studies considered adherence in older patients. Participants were primarily from the USA (44.7%); four studies (8.5%) used patients based in India and two studies (4.3%) used UK based patients. The remaining studies involved patients from across the globe including Europe, Australia, Africa and Arabic nations.

Adherence barriers were most commonly elicited via questionnaires or surveys, 15 (31.9%) studies used patient questionnaires, two (4.3%) used patients and caregivers questionnaires and three (6.3%) studies used telephone surveys. Adherence barriers were also elicited via patient interviews in five (10.6%) studies, focus groups in four (8.5%) studies, systematic reviews in four (8.5%) studies and semi-structured interviews in three (6.4%) studies.

Table 5.2 summarises the adherence barriers extracted from the literature review, with grouping of similar barriers. The most frequently reported barrier was 'forgetting to take medicines or collect prescriptions' which was reported in 29 (61.7%) studies. Other frequently reported barriers included 'poor understanding of the disease regimen or instructions' and 'the cost of medication' which were each reported in 18 (38.3%) studies. 'Difficulties incorporating medicine taking into daily routines' and 'feeling negative emotions' were each reported in 13 (27.7%) studies and 11 (23.4%) studies each reported 'complex or confusing regimens', 'experience of side effects', 'difficulties getting to the pharmacy' and 'being too busy to take medicines'.

Adherence barrier grouping (total number of citations)	Themes included in barrier grouping
Denial of conditions existence or need for treatment (7)	Denying illness existence or denying having illness/inability to accept diagnosis[11, 27, 33]
	Not thinking there is a need for the medication[12, 18, 26, 48]
Communication barriers (4)	Speaking different language to HCP[11]
	Poor health literacy[19]
	Poor or complex medication instructions[45]
	Communication problems with pharmacy[9]
Drug and alcohol use (3)	Alcohol use[11]
	Concomitant substance abuse[17, 33]
Changes to usual routine (19)	Being away from home/travelling [6, 11, 21, 24, 29, 33, 36, 39, 41, 47]
	Disruptions to daily routine/chaotic lifestyle[6, 10, 15, 17, 25, 32, 33, 36, 42]
Treatment related factors (6)	Feeling better without treatment[11, 33]
	Decreased QOL/feeling worse with treatment[33]
	Stopping medicines when feeling better[6, 22]
	Stopping medicines as thought ineffective[22]
Healthcare provider related factors (5)	Poor relationship with healthcare provider[2, 19, 25, 46]
	Lack of trust in healthcare provider[33]
Regimen related factors (10)	Regimen too complex/ confusing[17, 33]
	Polypharmacy[15, 19, 23]
	Frequency of dosing[10, 33]
	Heavy pill burden/ too many treatments[4, 10, 13]
	Changes to regimen or dose[8, 17, 21]
Side effects of medicines (14)	Side effects (real or anticipated)[6, 10, 17, 22, 33, 35, 38, 40, 43, 47, 48]
	Perceived side effects of treatment[11]
	ADRs[19, 45]
Social factors (22)	Fear of stigma or discrimination[4, 11, 17, 20, 25, 37, 35]
	Fear of disclosure of illness[17, 33]
	Lack of social support/ support from friends & family/ living alone[2, 7, 17, 30, 33, 44]
	Negative publicity associated with medicines taking[33]
	Unwilling to take medicines in public[5]
	Social norms e.g. family rituals or social obligations[25]
	Concerns about image/perceptions of others/ bullying[20]
	Feeling embarrassed by taking medicines[13, 39]
Medicine administration problems (11)	Problems taking meds at specific times[41]
	Problems taking more than one medicine at the same time[41]
	Taste and/or size of medicines[6, 33, 42]
	Difficult characteristics of medicines[27]
	Difficulty administering medicines – practical problems[31, 43]
	Problems swallowing medicines or keeping them down[6, 24]
	Problems accessing medicines[12]
Patient preference for alternatives (2)	Choosing traditional or herbal remedies instead of prescribed medication [2, 11]
Patient confidence (5)	Doubting ability to adhere/ low self-worth[33]
	Not emotionally ready for taking meds[17]
	Self-blame of condition[17]

Table 5.2 Preliminary grouping of adherence barriers extracted from literature

Adherence barrier grouping (total number of citations)	Themes included in barrier grouping
Practical barriers (56)	Long waiting times at the clinic or pharmacy[11, 28]
	Running out of medicines[17, 29, 32, 41, 45-46]
	No time to obtain repeat prescription[33]
	Problems getting the medicines form the pharmacy e.g. medicine not available, problem getting a repeat, opening times [6, 8, 9, 12, 22, 33, 37]
	Transport difficulties for getting to clinics and appointments or pharmacy or being unable to get there[4, 9, 22, 33, 25, 28, 36, 40, 46]
	Logistical problems in accessing medicines[18, 19]
	Financial constraints/ cost of medicines[4, 10, 12, 14, 18, 25-26, 28, 30, 33, 36-38 43, 45-46 48,]
	No medical insurance/ insurance does not cover medicine[22, 26, 46, 48]
	Homelessness/concurrent illness[33]
	Poor nutrition/ lack of access to food[4, 16, 35, 40]
	No healthcare provider[48]
	Being away from medicine at time dose[3, 40]
	Reading the labels on medicines[37]
	Losing medication[13]
Knowledge related problems (19)	Poor disease related knowledge[7, 19]
	Lack of knowledge or understanding/ being misinformed[33, 35, 41, 44, 46,]
	Not understanding the implications of the disease[17, 35]
	Poor understanding of chronic nature of condition[14]
	Lack of understanding of medication benefit/ why prescribed[4, 28]
	Lack of information about disease and its treatment[2]
	Poor education[31]
	Poor counselling[25]
	Not understanding how to reconcile newly prescribed drugs or how to get repeats[28]
	Not understanding new directions/ how to take medicine[7, 28]
Beliefs about medicines (12)	Mistrust or beliefs[2, 25, 41]
	Suspicions about treatment[33]
	Not convinced of medicines efficacy[33]
	Uncertainty regarding long term effects[33]
	Medicines thought to be too harmful or toxic[33]
	Lack of belief in medicines[12]
	Concerns about safety of medicines/side effects[14,18]
	Influence of parents concerns about taking medicines[44]
	Fear of medicines adverse effects[26]

Table 5.2 (continued) **Preliminary grouping of adherence barriers extracted from literature**

Adherence barrier grouping (total number of citations)	Themes included in barrier grouping
Cognitive/memory related factors (32)	Poor cognitive function, poor memory[19, 45]
	Problems recalling regimen[12]
	Not remembering to refill prescription[21, 42]
	Forgetfulness/failure to remember[5, 6, 8, 10, 13, 15, 16, 18, 23, 24, 28, 29, 31-33, 36-38 40-44, 47, 48]
	Not emotionally ready for taking meds[17]
	Self-blame of condition[17]
Patient related factors (22)	Feeling low, depressed, angry, stressed, hopeless or overwhelmed[6, 17, 27, 35, 33, 39, 44, 47]
	Wanting to be free of taking medicines[33]
	Wanting to be 'normal'[13, 42]
	Wanting to maintain control[33]
	Not wanting to listen to authority figures[17]
	Being tired of taking pills[42]
	Treatment being a reminder of illness[33]
	Unwanted changes to body image/ effects on appearance[20, 33]
	Feeling ready to die[35]
	Wanting to be with friends rather than take medicines[5]
	Lack of motivation[31]
	Low priority assigned to medicines taking[44]
	Refusal to take[32]
Incompatibility of medicines taking with daily routine/lifestyle	Inconvenient or difficult to incorporate medicines taking/dosing time inconvenient[33, 43]
	Lifestyle restriction from taking so many doses[34]
	Work, family or caregiving responsibilities[33]
	Too busy/distracted, lack of time[5, 6, 8, 13, 17, 21, 22, 29, 33, 36, 39, 42]
	Falling asleep and missing medicines dose time/sleeping through dose[6, 29, 33]
	Fasting for Ramadan[15]
	Perceived burden of extra planning[27]
	Too tired or unwell to take medicines[6, 17, 42]
	Interference with other activities[24, 42]
	Skipping meals[39]
	Scheduling medicines administration into daily routine[7]
	Forgetting to bring medicines away with them/ being away from medicines at dose time[21, 42]

Table 5.2 (continued) Preliminary grouping of adherence barriers extracted from literature

5.3.2 Mapping the adherence barriers to the behavioural domains of theTDF[275] and generating the adherence barrier statements

During the mapping process it was pertinent to fully establish how each of the behavioural domains in the TDF relates to medication adherence. This process was undertaken collaboratively by the research team (CE, DB and NT) as part of the process of assigning barriers to the behavioural domains. For many adherence

barriers, such as experience of side effects, there were multiple behavioural domains to which the barrier could have been mapped. Decisions were discussed extensively, with reference to guiding literature where possible[290]. Using this collaborative approach, each of the behavioural domains of the TDF was considered as described in table 5.3.

During the process of assigning barriers to the behavioural domains, it was noted that a number of barriers related to competing goals, such as being too busy, being unable to fit medicines taking into a daily routine and forgetting to take medicines when there is a change in routine. An additional 'goal conflicts' behavioural domain was therefore created, as guided by relevant literature[290]. In addition, the 'social/professional role and identity' domain plus the 'nature of the behaviour' domain were excluded as none of the adherence barriers identified in the literature search pertained to these behavioural domains. As the entire study relates to the barriers to medication adherence, the behavioural regulation domain was also excluded.

Behavioural domain	Definition with relation to medication adherence
Knowledge	All aspects of knowing how to take medicines correctly and how to obtain prescriptions, plus a knowledge and understanding of why the medicines have been prescribed and how they will work
Skills	The patient's ability to take their medicines, including physical problems with administering medicines correctly and cognitive problems in understanding directions
Memory, attention and decision processes	All cognitive aspects of medication adherence e.g. remembering to take medicines and order prescriptions. The 'attention' aspect includes becoming easily distracted
Beliefs about capabilities	The patient's confidence in adhering to their regimen and perceived ability to take their medicines correctly. Also relates to how easy or difficult the patient finds adherence and their confidence and ability to overcome problems and difficulties.
Beliefs about consequences	Patient's beliefs about taking their medicines, specifically the consequences of taking (or not taking) their medicines, including denial of the existence of illness or need for medicines
Motivation and goals	The motivation expressed by a patient towards taking their medicines and how much of a priority this is to them
Environmental context and resources	Resource and material limitations which impede medication adherence; includes factors such as the cost of medications and access issues.
Social influences	Social factors or 'other people' that may influence the patient's adherence behaviours; includes discrimination/being treated differently and availability of social support
Emotion	The emotional elements of taking medicines such as stress, anxiety and other negative emotions
Social/professional role and identity	The extent to which a patient sees their medication taking as part of their identity
Behavioural regulation	Facilitators and barriers to medication adherence
Nature of the behaviours	Past behaviours and whether the behaviour occurs as an automatic process

Table 5.3 Behavioural domains of the TDF and their relation to medication adherence

Table 5.4 summarises the preliminary mapping of the adherence barriers to the behavioural domains. The number of barriers mapped to each behavioural domain ranged from two for the 'knowledge' domain to six for the 'belief about consequences' domain. The spread of studies amongst each behavioural domain was relatively even, with the exemption of the 'motivation and goals' domain which only contained barriers from eight studies. In comparison, the 'environmental constraints' domain contained barriers from 48 studies.

Behavioural domain	Medication adherence barriers mapped to domain
Knowledge	Poor understanding of regimen/instructions or disease
	Not understanding how to obtain prescriptions
Skills	Practical difficulties in administering medicines (e.g. difficulties with dexterity or swallowing)
	Difficulty in understanding directions (language barriers, low health literacy, unable to read directions)
Memory, attention & decision making processes	Forgetting to take medicines or refill prescription
	Running out of medicines or losing medicines
	Being distracted
Beliefs about capabilities	Regimen too complex, confusing or frequent / too many medicines
	Experience of side effects
	Frequent changes to doses and/or regimen
	Doubting own ability to adhere
	Wanting to maintain control
Beliefs about consequences	Mistrust in medicines or lack of belief in their efficacy
	Fear that medicines will be harmful
	Not thinking there is a need for treatment/medication
	Denial of existence of illness or non-acceptance of diagnosis
	Stopping medicines when feeling better
	Thinking medication is not working
Environmental context and resources	Cost of medication
	Transport difficulties with getting to pharmacy or clinic
	Being away from home/travelling
	Problems with pharmacy e.g. not stocking medicines or closing too early, long waiting times
	Wanting to be 'normal'
	Family rituals or social obligations
Emotions	Feeling 'negative emotions' (low/depressed/angry/helpless/ tired/overwhelmed or stressed)
	Embarrassment of taking medicines
	Wanting to be free of taking medicines
	Treatment being a reminder of illness
Goal conflicts	Being too busy or distracted to take doses/ too busy to pick up repeat medication
	Difficulties incorporating medicines taking into daily routine (e.g. disruption of other activities or being away from meds at dose times, need to undertake other duties)
	Disruptions to daily routine/having a chaotic lifestyle
Motivation and goals	Lack of motivation/ low priority assigned to medication taking
	Too tired to take medicines
	Preference of traditional or herbal remedies
	Refusal to take medicines
	Burden of adhering to regimen
Social influences	Lack of social support
	Fear of discrimination or social stigma, bullying, perceptions of other or disclosure of illness
	Embarrassment of taking medicines
	Poor relationship with or lack of trust in prescriber

Table 5.4 Preliminary mapping of medication adherence barriers to TDF

Difficulties with both side effects and complex regimens are 'externalities' that are not necessarily within the patient's control. However, as the focus of this work is on overcoming barriers, these factors were considered to be difficulties that patient's

should (ideally) have the ability to address and overcome, for example through seeking help from their GP. The adherence barriers 'experience of side effects' and 'complex regimens' were therefore included in the beliefs about capabilities behavioural domain.

Some of the barriers extracted from the literature review, (for example self-blame for condition) were excluded as these were specific to the individual study and disease area (in this case HIV). Other barriers such as no healthcare provider or no medical insurance were not included as they were not relevant in the UK. Some adherence barriers such as feeling better without treatment, were considered to be better represented by more general barriers such as those contained within the beliefs about consequences domain. Extracted barriers that were not mapped onto the behavioural domains included:

- Illicit substance or alcohol abuse
- Feeling better without treatment/worse with treatment/ decreased QOL
- Skipping meals
- Self-blame for condition
- Feeling ready to die
- Influence of parents concerns about taking medicines
- Not emotionally ready to take medicines
- Poor nutrition or lack of access to food
- Homelessness/ concurrent illness
- Falling asleep and missing dose time
- No healthcare provider
- No medical insurance/ insurance does not cover medicine needed
- Unwanted changes to body imagine/ effect of medication on appearance
- Not wanting to listen to authority figures
- Wanting to be out with friends rather than taking medicines

Proposed adherence statements for each included adherence barrier are provided in appendix 5.7 and are re-visited in sections 5.3.5 and 5.3.6.

5.3.3 Revisions to mapping of adherence barrier statements with consideration to the updated TDF[276]

Having adapted the original TDF[275] for relevance to medication adherence and mapped the adherence barrier statements to this, the mapping process was later reviewed in light of the recommended changes in the 2012 TDF update[276]. The detailed definitions

provided by the updated TDF are compared to the definitions created for the application of the original TDF to medication adherence in appendix 5.8.

The behavioural domain definitions using the original TDF closely mirrored the definitions provided by the updated version. For the 'knowledge', 'skills', 'environmental context and resources', 'social influences' and 'emotions' behavioural domains, a good match between the definitions from the updated TDF and the adopted definitions generated with the original TDF was observed. Consequently, no changes were made to the mapping of adherence barriers for these behavioural domains

The definition provided by the updated TDF for the 'social/professional roles and identity' behavioural domain added clarity to the meaning of the domain, but did not alter the group's decision to exclude the domain. In the updated TDF, the 'beliefs about capabilities' behavioural domain was divided into 'beliefs about capabilities' and 'optimism', with 'optimism' added to reflect a general disposition rather than specific capabilities[276]. Though the rationale for this distinction was acknowledged, the original TDF was maintained for this work, as it does not cover 'general dispositions' but instead concerns specific medication adherence barriers. The 'beliefs about capabilities' behavioural domain was also divided in the updated TDF to create 'beliefs about capabilities' and 'reinforcement'. The newly created 'reinforcement' domain reflects constructs of associative learning; however, none of the identified adherence barriers were relevant to this domain. The original TDF was therefore retained.

The updated TDF also split the 'motivation and goals' behavioural domain into 'intentions' and 'goals' to reflect a differentiation between an active decision to behave in a particular way (intention) and an end state viewed as a preferred option (goal). As the majority of the adherence barrier statements mapped to the 'motivation and goals' behavioural domain specifically focussed on motivation, the original TDF was retained.

For the 'memory, attention and decision making processes' domain, the definition provided by the updated TDF was comparable to the definition adopted by the research group, with the exception of the 'decision making processes' element which was not included as none of the identified adherence barriers concerning decision making processes fitted with this domain. The updated TDF therefore provides a useful definition of this aspect, though no changes were necessary. Interestingly, the 'behavioural regulation' domain which was excluded by the research group when using the original TDF was also excluded from the updated TDF. This infers further congruence between the two versions. The research group still felt that an additional

domain of 'goal conflicts' was necessary as the updated TDF did still not cover this aspect.

5.3.4 Participant recruitment for consultation exercises

Recruitment of participants commenced in January 2013 and lasted four weeks. In total, 32 members of the public expressed an interest in the study. The majority of interest was generated through 'word of mouth' with 20 (62.5%) members of the public hearing of the study through a third party. The original e-bulletin prompted contact from 6 (18.8%) members of the public and similar numbers were achieved when the study was re-advertised in the e-bulletin three weeks later, with 5 (15.6%) members of the public responding to this. One member of the public specifically mentioned seeing the study advertised on Twitter.

One respondent asked if they could be included despite a diagnosis of a mental health condition; with reference to the exclusion criteria detailed on the study advertisement, this respondent was excluded and therefore not sent an information pack. A total of 31 information packs to send to interested members of the public; 17 (54.8%) of which were returned with signed consent forms and completed brief surveys. There was a reasonable gender split between respondents with 9 (52.9%) males and 8 (47.1%) females. The ages of respondents ranged from 24 to 82 with a median (IQR) of 71.0 (54.0 to 74.5) years. The number of prescribed medicines per patient was also variable, ranging from one to 'at least ten' with a median (IQR) of 4 (2 to 8). Given the median age of the respondents it was unsurprising that 12 (70.6%) respondents did not pay for their prescriptions, with only one of these aged less than 60 years. Only one respondent reported 'rarely' needing assistance with reading written medical letters, the remaining respondents all stated that they 'never' needed assistance.

The participant consultation exercises were attended by 14 (82.4%) of the respondents. Two respondents could not attend either of the dates proposed and one could not be contacted.

5.3.5 Consultation exercise one

The first participant consultation exercise was held at UEA in March 2013 with three males and two females. One participant was unable to attend due to ill health but agreed to attend the second session instead. All five participants reported 'never' needing assistance in reading written material. The participants' ages ranged from 41 to 82, with a median (IQR) age of 70.0 (45.5 to 76.5) years. Two participants were aged less than 60 years and both paid for their prescriptions. The number of

medicines taken by participants was variable and ranged from two participants who only took one medicine, to one participant who took “in excess of ten”.

The following behavioural domains were discussed in this session:

1) Knowledge
2) Skills
3) Memory, attention and decision making processes
4) Social influences
5) Environmental constraints
6) Emotions

Full details of all topics discussed and comments made with regard to the questionnaire statements are provided in appendix 5.8 and summarised in the sub-sections below. For the first domain (knowledge), ranking the barriers in order of importance proved to be difficult as participants reported that many of the barriers were very similar. Ranking was therefore not requested in the subsequent sections; instead the facilitator guided conversation to highlight the important barriers.

The following sub-sections cover the behavioural domains discussed within the first consultation exercise. Each sub-section starts with a figure which replicates the adherence barriers presented to the participants; the topics of participant discussion regarding these adherence barriers are then summarised below this figure. The questionnaire statements that had been developed to represent the adherence barriers are then shown in a figure, with a summary of the participant comments relating to these provided below.

5.3.5.1 The ‘knowledge’ behavioural domain

As the first behavioural domain to be discussed, several topics were raised by the participants and not all were necessarily related to the ‘knowledge’ behavioural domain. In total, 20 minutes were spent on this section of the consultation exercise; the time was split evenly between discussion of the adherence barriers and potential questionnaire statements. The adherence barriers presented to participants for the ‘knowledge’ behavioural domain are shown in figure 5.4.

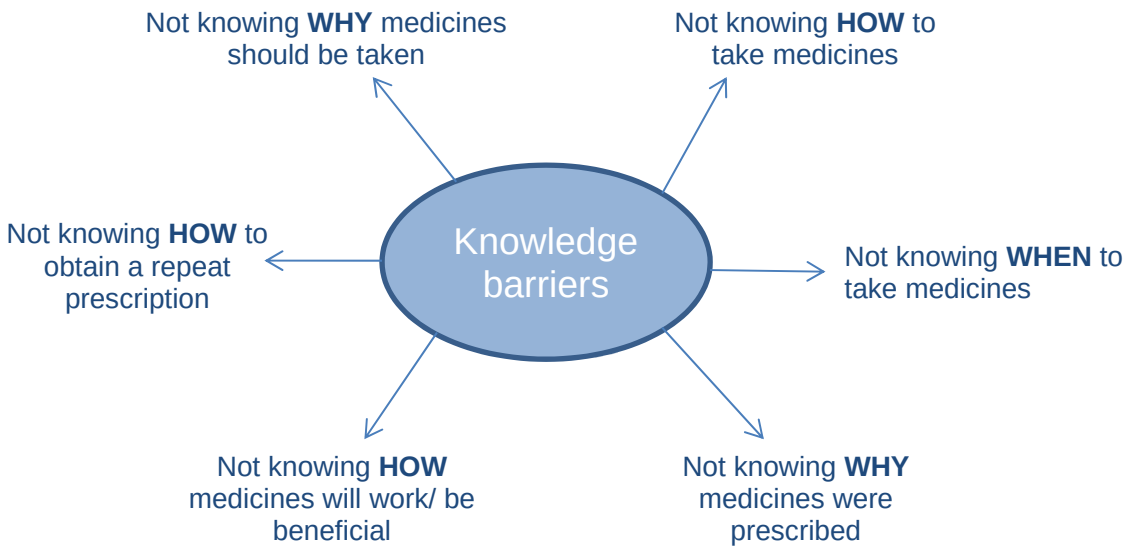


Figure 5.4 Adherence barriers discussed in 'knowledge' group

Topics raised by the participants within this section included:

- Frequent changes to medicines packaging and associated difficulties with medicine identification and differentiation
- Difficulties accessing medicines from their packaging
- Knowing what to do (i.e. going back to GP) in instances of not understanding medicines instructions
- The importance of knowing why medicines are prescribed and 'what to expect' from them, especially if there are concerns about side effects
- The importance of knowledge (for example from patient information leaflets (PILs)) in making informed decisions about the risks and benefits of taking medicines
- The complexity of the repeat medicines ordering process, specifically getting to a pharmacy or doctors surgery to order and collect prescriptions and the difficulties of balancing medicines ordering and collecting with other priorities
- The importance of knowing the 'systems' available to make the ordering and collecting process easier

Following the discussion of the adherence barriers, six questionnaire statements were displayed to the participants, as summarised in figure 5.5.

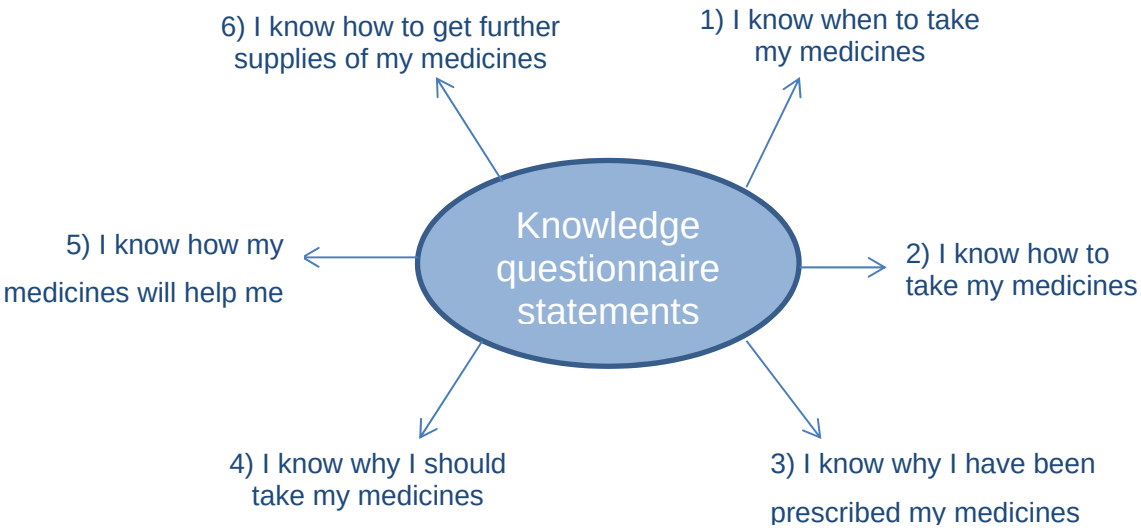


Figure 5.5 Questionnaire statements discussed in 'knowledge' group

Participants understood the concept of completing the questionnaire and the need to only tick one box for each statement. Comments relating to the questionnaire statements concerned:

- The similarity between statements four and five
- The disparity of statement six, which did not appear to 'fit' with the others

5.3.5.2 The 'skills' behavioural domain

The 'skills' behavioural domain was discussed for approximately 13 minutes, with an even split of discussion time between the adherence barriers and questionnaire statements. The adherence barriers presented to participants for the 'skills' behavioural domain are shown in figure 5.6.

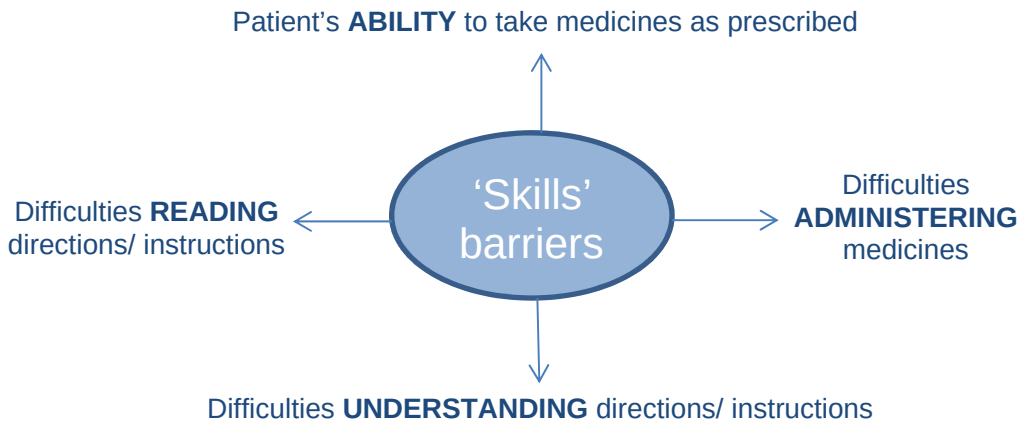


Figure 5.6 Adherence barriers discussed in 'skills' group

Topics raised by the participants within this section included:

- Difficulties with accessing medicines from the packaging and identifying tablets that have been dropped onto the floor
- The importance of 'having a system' and 'forward planning' as a skills for managing medicines, especially ordering to ensure sufficient supplies
- The 'skill' of knowing how to cope when there is a problem or difficulty and the importance of the PIL for resolving medicines difficulties
- The difficulty of reading the small print on PILs
- The difficulties of receiving medicines at the correct time when staying in hospital
- The problem of confusion associated with changes in medicines

Figure 5.7 summarises the questionnaire statements presented to participants to represent the adherence barriers in the 'skills' domain.

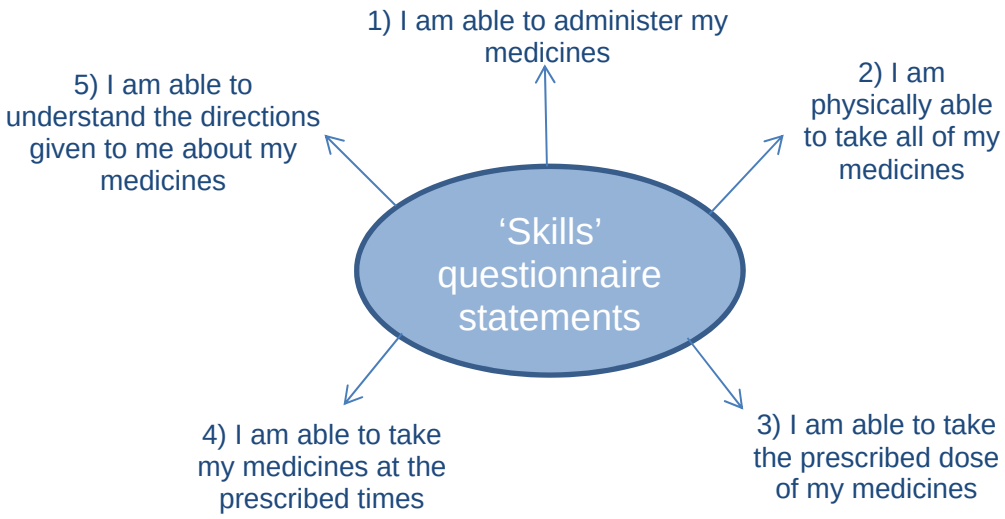


Figure 5.7 Questionnaire statements discussed in 'skills' group

For the questionnaire statements, participants commented that:

- There was overlap between statements four and five as one could not really be done without the other
- For statement one, the word 'administer' may be confusing for some patients
    - The words 'take' and 'use' were suggested as alternatives

5.3.5.3 The 'memory, attention and decision making processes' behavioural domain

The 'memory, attention and decision making processes' behavioural domain attracted comparatively more discussion than the other domains, with a total of 26 minutes spent on this section of the consultation exercise. The adherence barriers and questionnaire statements were discussed for 19 and 7 minutes respectively. The adherence barriers presented to participants for discussion in this section are displayed in figure 5.8.

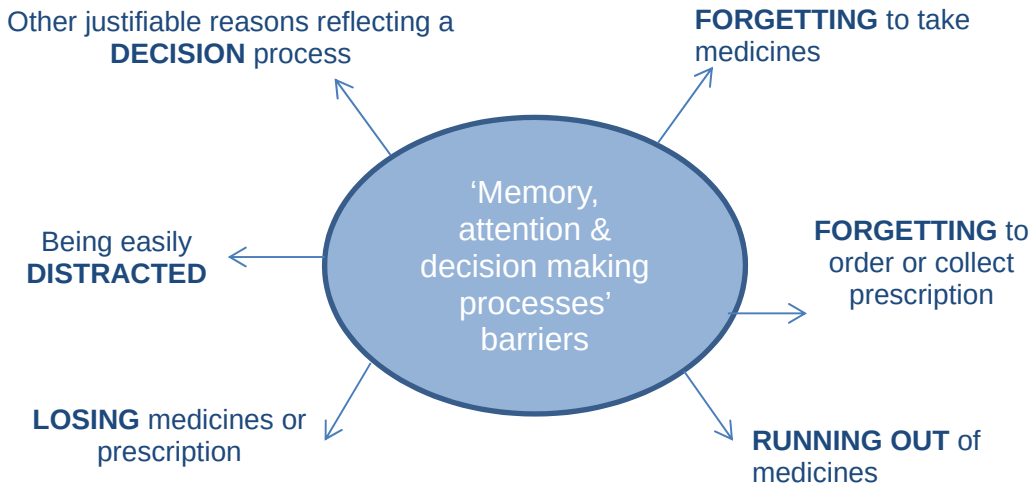


Figure 5.8 Adherence barriers discussed in 'memory, attention and decision making processes' group

Topics raised by the participants included:

- The decision making dilemma that can occur between a preference for managing health through health foods and yoga and a doctor's prescription for a medicine
- The difficulty of always remembering medicines doses, especially lunchtime doses which can particularly problematic as there is less routine at this time of day, unlike breakfast time and bedtime
- A hectic lifestyle and distractions such as 'getting the children ready for school', which can also impede adherence, especially in the mornings
- The barrier of forgetting to order and collect prescriptions
- The differing needs of patients for support with ordering their prescriptions
- The importance of having strategies for remembering and managing medicines
- The relevance of different 'life stages' as to whether or not medicines taking is seen as a priority

- Older patients tended to accept taking medicines as 'the norm' and important priority whereas younger patients tended assign less priority to it as they had other factors such as raising a family to consider.

Following discussion of these barriers, the potential questionnaire statements for this section were displayed to the participants, as summarised in figure 5.9

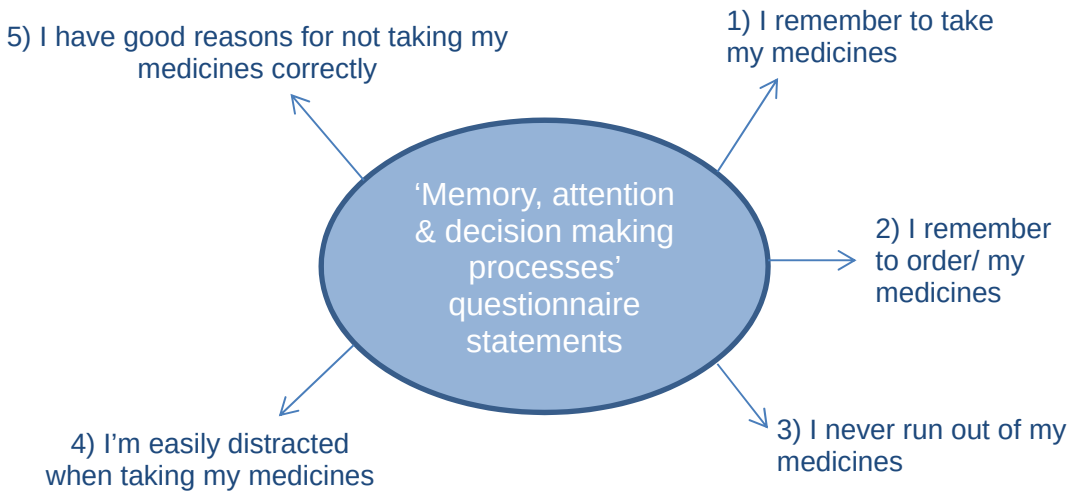


Figure 5.9 Questionnaire statements discussed in 'memory, attention & decision making processes' group

Comments made with regard to the questionnaire statements were that:

- Statement one could be improved by using the phrase 'I usually remember…'
- Statement four could be re-phrased to 'I can be easily distracted' to better reflect something that doesn't happen every day
- Statement three may be superfluous as it relates directly to statement two
- Statement five may need to be refined as personal reasons are not always 'good' reasons
    - A suggestion of 'I have my reasons for not taking my medicines as prescribed' was agreed to be the best option.

5.3.5.4 The 'social influences' behavioural domain

In this section of the consultation exercise, the adherence barriers and questionnaire statements were discussed for approximately 12 and 2 minutes respectively. The adherence barriers discussed for this behavioural domain are shown in figure 5.10.

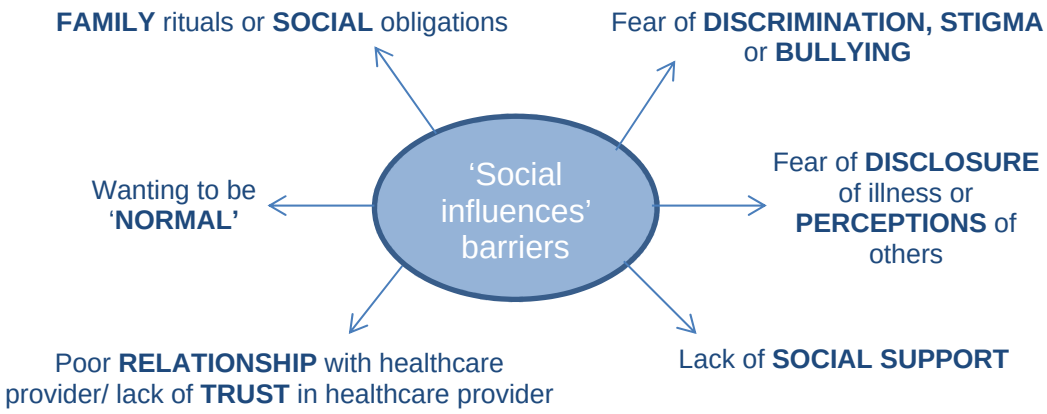


Figure 5.10 Adherence barriers discussed in 'social influences' group

The topics raised by the participants included:

- Discrimination had not been experienced and bullying was thought to be something only relevant to school children
    - Medicines taking was better accepted and seen as 'normal' for older people
- Lack of trust in prescribers was a barrier that participants could identify with
- Poor relationships with GPs receptionists and their 'hostility' can also be a barrier to adherence as they can be a barrier to seeing the GP and thus getting medicines
- Family obligations were a barrier to adherence in younger participants with families
- Social support was considered important and the relevance of various sources of support, including support groups acknowledged.

The potential questionnaire statements for this section were then displayed to the participants, as summarised in figure 5.11.

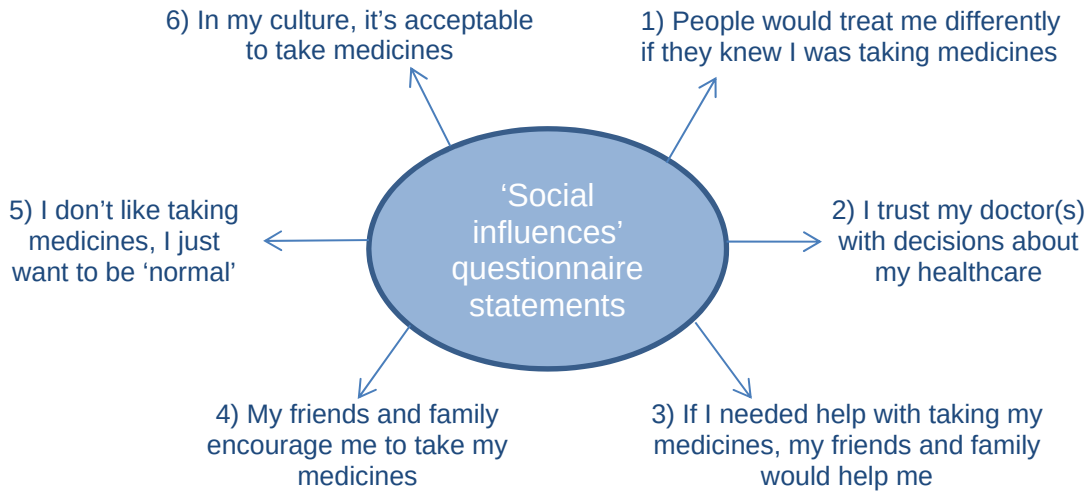


Figure 5.11 Questionnaire statements discussed in 'social influences' group

For the questionnaire statements, participants commented that:

- Statement six could be changed to 'my faith and religion' or 'my beliefs'

5.3.5.5 The 'environmental constraints' behavioural domain

The adherence barriers discussed in this section are shown in figure 5.12. With only four adherence barriers to discuss for this behavioural domain, the adherence barriers and questionnaire statements were discussed in just five and two minutes respectively.

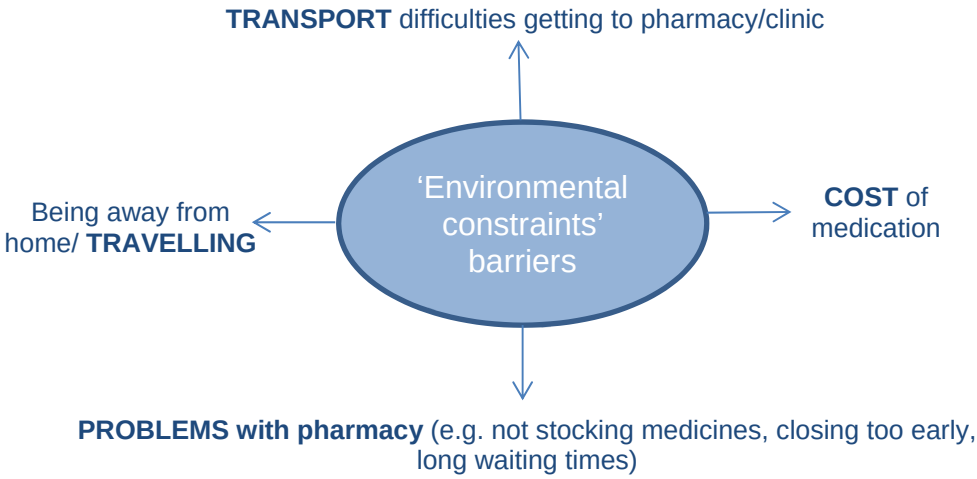


Figure 5.12 Adherence barriers discussed in 'environmental constraints' group

The key points of participant discussion for this section included:

- The expression of genuine shock by participants exempt from prescription charges at the current prescription charges; this was recognised as an important barrier
- 'Problems with pharmacy' could include difficulties getting to the pharmacy, frequent changes to packaging and inconvenient opening times
- Forward planning for travelling and being away from home were considered important skills for overcoming this potential barrier

The questionnaire statements displayed to the participants for this section are summarised in figure 5.13.

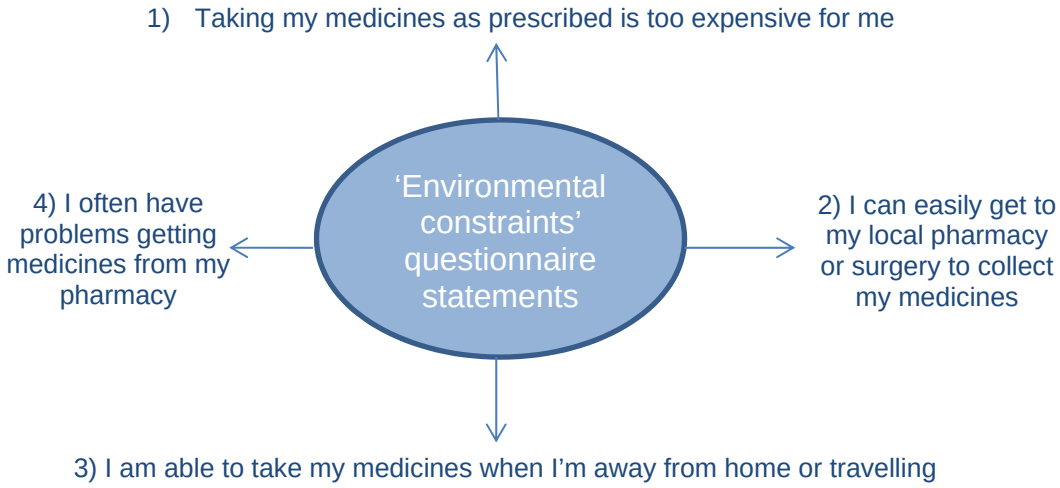


Figure 5.13 Questionnaire statements discussed in the 'environmental constraints' group

All of the statements were considered acceptable, though statement four was thought to only relate to stock issues and not wider problems as anticipated.

5.3.5.6 The 'emotions' behavioural domain

As the final behavioural domain to be discussed in the first consultation exercise, time was limited. Discussion of the adherence barriers and questionnaire statements for this behavioural domain therefore lasted just five and two minutes respectively. The adherence barriers discussed in this section are shown in figure 5.14.

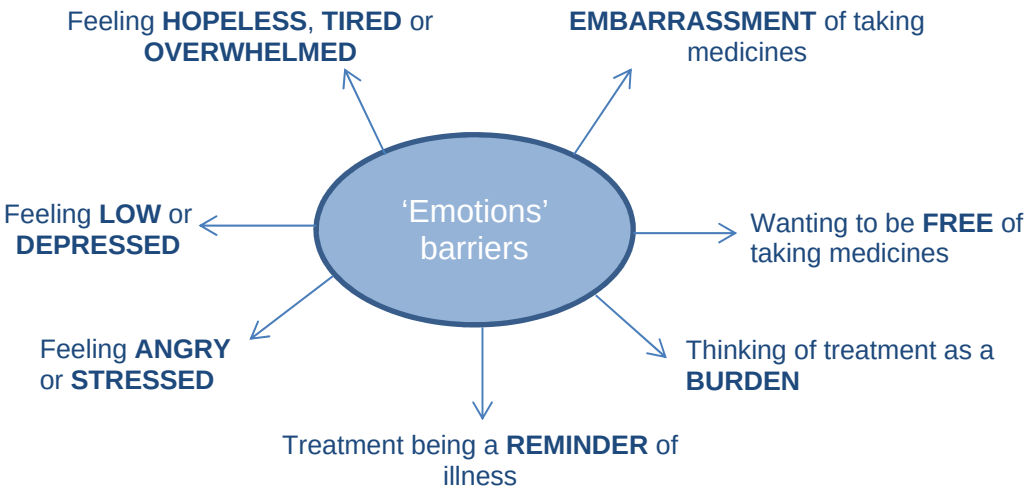


Figure 5.14 Adherence barriers discussed in 'emotions' group

The main points of participant discussion in this section were:

- Whether or not taking tablets is a reminder of illness is likely to be dependent upon the condition treated and individual concerned
- The 'negative emotions' listed could be caused by side effects of medicines
- Experiences of negative feelings could also act as a promoter of adherence if the negative feelings are a reminder of a need for treatment

The questionnaire statements discussed in this section are summarised in figure 5.15.

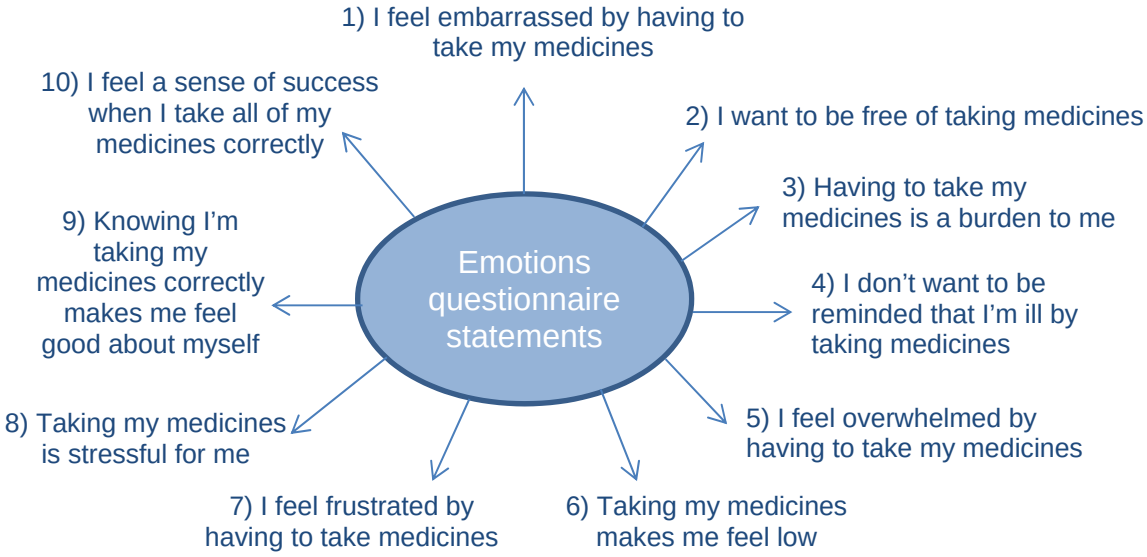


Figure 5.15 Questionnaire statements discussed in the 'emotions' group

Participants commented that:

- Statements three and seven were very similar
- Several of the statements could be combined to create a more general statement relating to experience of negative emotions

5.3.6 Consultation exercise two

The second participant consultation exercise was also held at the UEA, ten days after the first meeting. The meeting was moderated by CE, with DB assuming the assistant moderator role. Nine participants joined the meeting; five males and four females. The majority of participants reported 'never' needing assistance in reading written material, with only one participant stating that they 'rarely' needed assistance. Participant ages ranged from 24 to 81 with a median age (IQR) of 62.0 (54.0 to 75.5) years. Four participants were aged less than 60 years and all except one paid for their

prescriptions. The number of medicines taken by participants ranged from one to seven, with a median (IQR) of 2 (2 to 6).

The following behavioural domains were discussed in this session:

1) Motivation and goals
2) Goal conflicts
3) Beliefs about consequences
4) Beliefs about capabilities
5) Emotions

Full details of the topics discussed and comments made are provided in appendix 5.9 and summarised in the following sub sections.

5.3.6.1 The 'motivation and goals' behavioural domain

Similar to the first consultation exercise, as the first behavioural domain to be discussed, participants raised several topics that related to other domains. In total, 30 minutes were spent discussing the 'motivation and goals' behavioural domain; the adherence barriers and questionnaire statements were discussed in 20 and 10 minutes respectively. The adherence barriers discussed in this section are shown in figure 5.16.

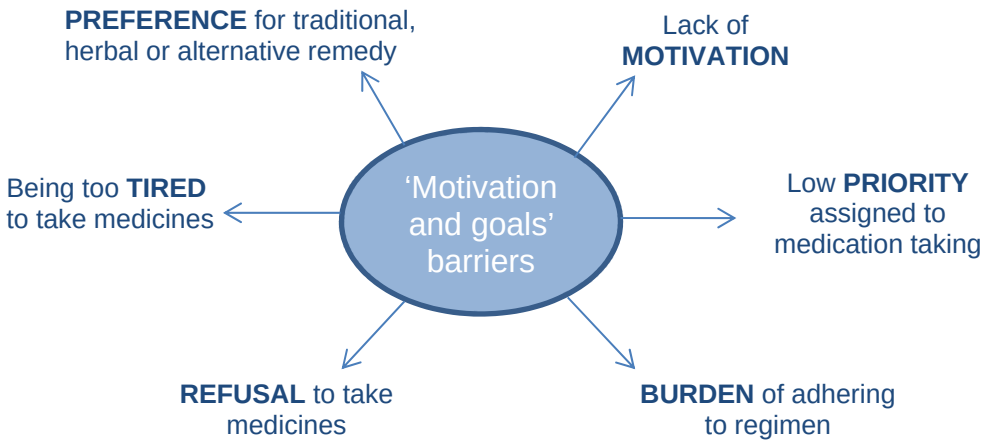


Figure 5.16 Adherence barriers discussed in 'motivation and goals' group

Key points of participant discussion included:

- 'Tiredness' seemed unintuitive as a direct barrier to adherence but may increase the likelihood of forgetfulness
- Motivation is often the single most important factor in taking medication

- Experience of side effects is an important barrier to medication adherence; previous experience may reduce motivation to adhere to a new regimen
- Even when motivation is strong, incapacity might inhibit adherence
- Questioning whether a prescribed medicines represents 'good value for money' can impinge upon motivation to adhere
- Negative feelings towards medicines could be evoked by a sense of getting a 'raw deal' with regard to medicines supply
- PILs could affect motivation to adhere by 'terrifying' patients and 'putting them off'

The questionnaire statements discussed in this section are summarised in figure 5.17.

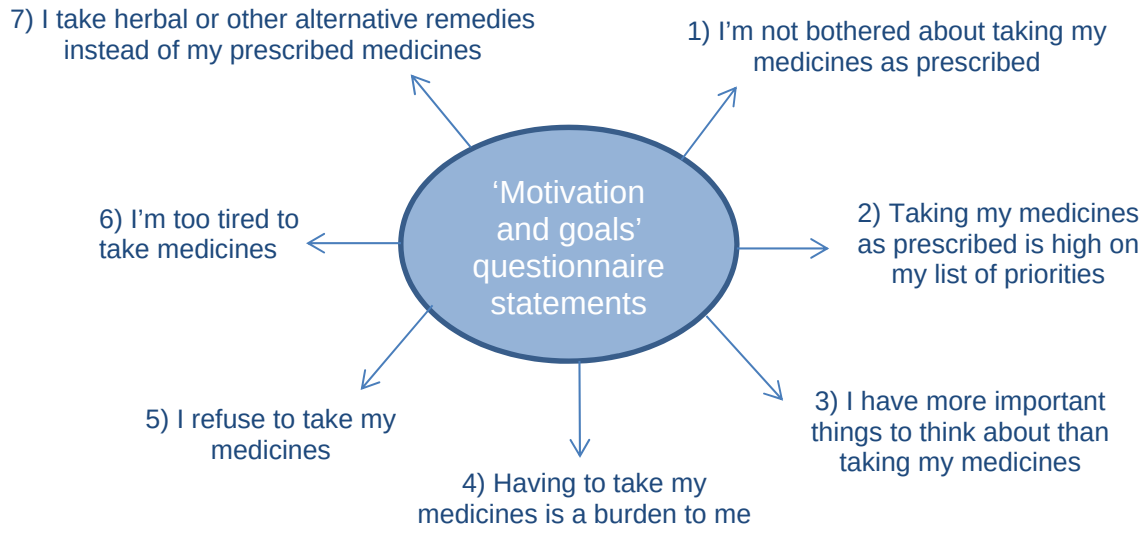


Figure 5.17 Questionnaire statements discussed in 'motivation & goals' group

Comments with regard to the questionnaire statements included:

- The term 'bothered' in statement one was considered to be ambiguous as it could mean worried as well as unmotivated
- For statement six, it was suggested that the term 'sometimes' could be added to reflect a problem that does not occur every day

5.3.6.2 The 'goal conflicts' behavioural domain

The adherence barriers and questionnaire statements for the 'goal conflicts' section were discussed in 8 and 1 minutes respectively. The adherence barriers presented to participants in this section are summarised in figure 5.18.

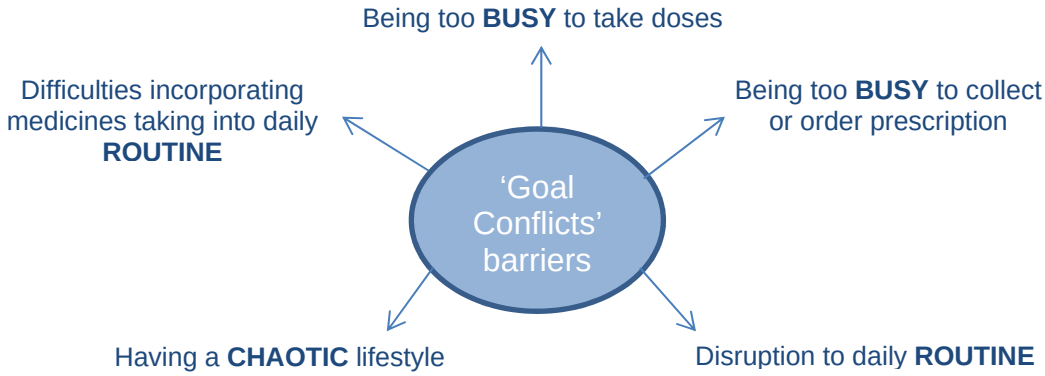


Figure 5.18 Adherence barriers discussed in 'goal conflicts' domain

Topics discussed by the participants within this section included:

- Ordering and collecting prescriptions can be problematic, posing a barrier to adherence for some people; being 'disciplined' and 'having a system in place' are therefore imperative to ensure adherence
- Changes in routine such as forgetting medicines when going away was perceived as a common barrier that many people would experience

Only three questionnaire statements were presented to participants for this section, as summarised in figure 5.19.

Figure 5.19 Questionnaire statements discussed in 'goal conflicts' group

With regard to the questionnaire statements, participants commented that:

- Statement two was 'too wordy'
    - 'changes' were thought to be easier than 'disruptions'

5.3.6.3 The 'beliefs about consequences' behavioural domain

In total, discussions for this section of the consultation exercise lasted approximately 25 minutes. The adherence barriers and questionnaire statements were discussed over 12 and 13 minutes respectively. The adherence barriers presented to the participants in this section are shown in figure 5.20.

Whilst there is clear overlap between the barriers 'mistrust in medicines' and 'fear that medicines will be harmful' both were included as the former represents a more general belief whilst the latter represents a specific concern (belief).

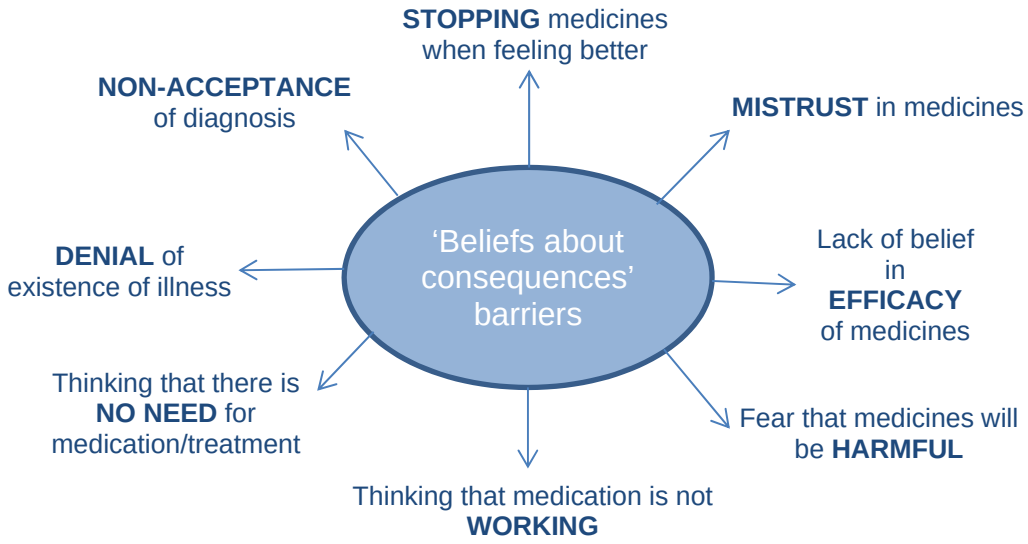


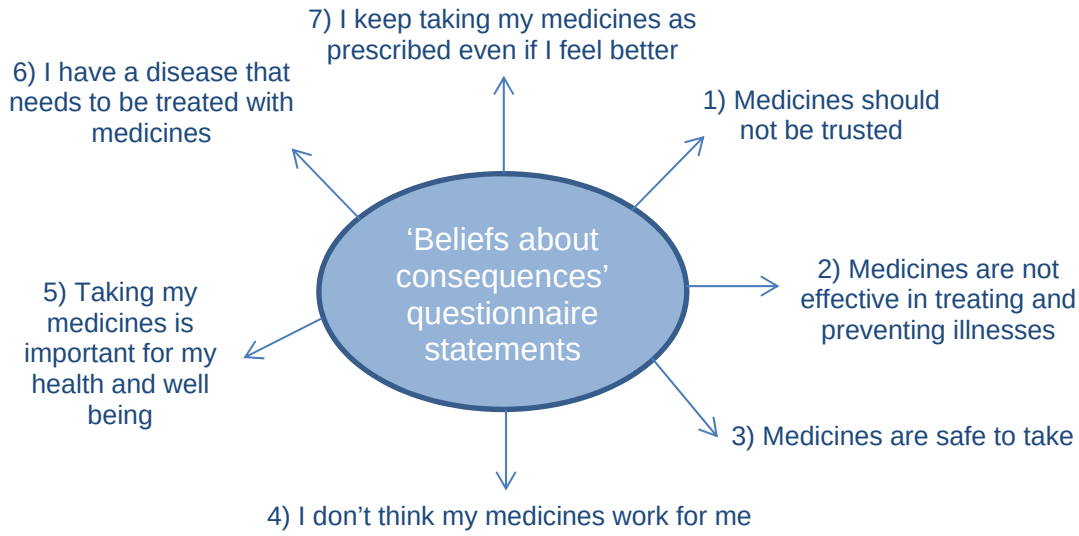
Figure 5.20 Adherence barriers discussed in 'beliefs about consequences'

Topics discussed by participants within this section included:

- 'Mistrust in medicines' and 'fear that medicines will be harmful' were strongly identified with by a participant who had previously experienced a severe adverse drug reaction that had led to hospitalisation
- Knowing what a medicine was for and why it had been prescribed were considered as important aspects of knowledge which in turn influence beliefs; this knowledge was subsequently described as "what drives confidence and motivation"
- Non-acceptance of a diagnosis was questioned, as a mistrust in the prescribers proficiency may be more pertinent
- Dose and brand changes were considered as factors which could evoke mistrust in medicines and prescribers
- Asymptomatic conditions were thought to be more likely to lead to questioning of whether a medicine was needed and doubting of a diagnosis

- Fear about the unknown, long term effects of medicines was also considered a barrier to medication adherence
- Prescribing of multiple medicines was deemed to be a factor that could augment fear of side effects as information regarding interactions is difficult to obtain
- Non-acceptance, denial and thinking there is no need for treatment were considered as phases that people might go through when they are first diagnosed with a condition.

The questionnaire statements presented to participants in this section are summarised in figure 5.21.



Figured 5.21 **Questionnaire statements discussed in 'beliefs about consequences' group**

Participant comments regarding these questionnaire statements included:

- Statement one was considered too emotive
- The wording of 'work for me' in statement four was considered to be ambiguous
    - 'beneficial' was suggested as a popular alternative
- The word 'disease' in statement six was considered unhelpful; 'medical condition' was considered more appropriate
- The term 'feel better' in statement seven was considered to be potentially confusing, especially in the context of preventative medicine such as cardiovascular disease.

5.3.6.4 The 'beliefs about capabilities' behavioural domain

The adherence barriers and questionnaire statements for this behavioural domain were discussed over 10 and 9 minutes respectively. The adherence barriers discussed in this section are summarised in figure 5.22.

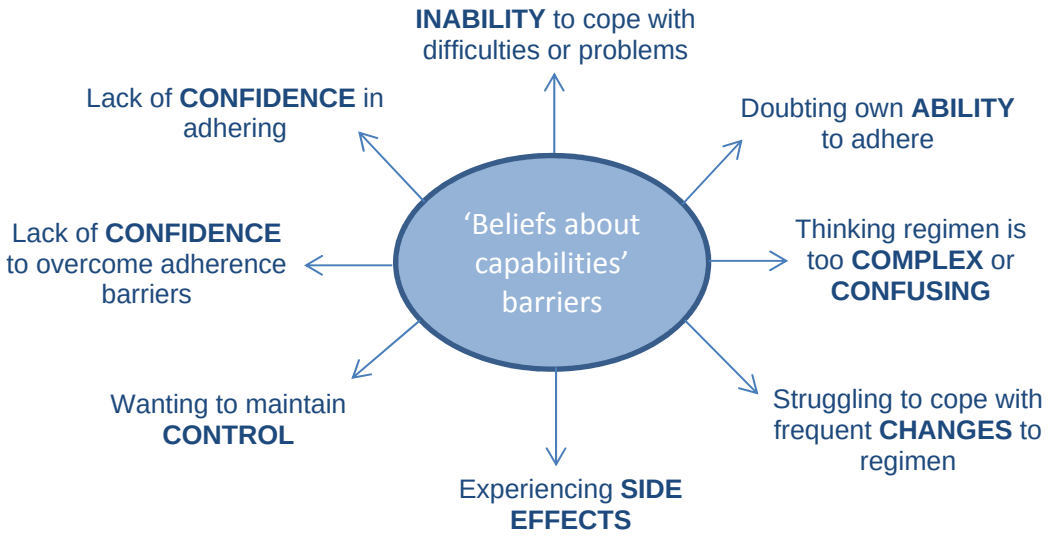


Figure 5.22 Adherence barriers discussed in 'beliefs about capabilities' behavioural domain

Topics discussed by the participants within this section included:

- Participants struggled with this domain and found the barriers difficult to relate to
- 'Wanting to maintain control' was identified as a potential cause of refusing to take medicines, but could also promote of adherence
- Lack of confidence was viewed as a potential barrier that could be overcome with appropriate support, such as pill organisers

Following discussion of the adherence barriers, eight questionnaire statements were presented as summarised in figure 5.23.

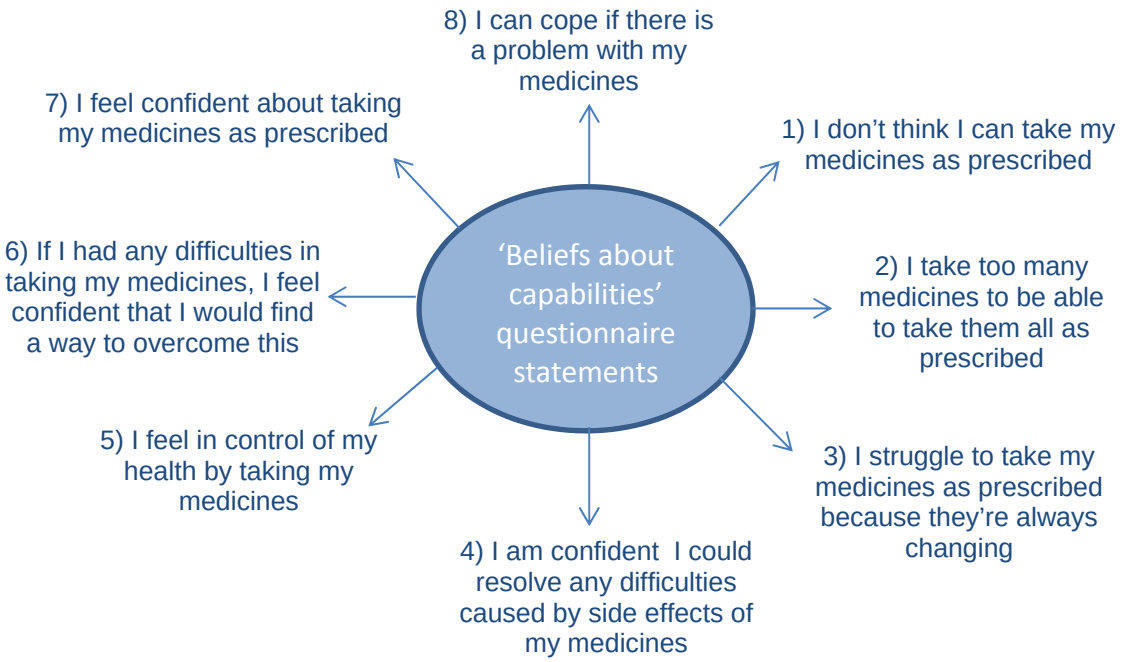


Figure 5.23 Questionnaire statements discussed in 'beliefs about capabilities' group

Participant comments regarding these questionnaire statements included:

- Statements four and six were thought to be verbose and in need of refinement
  - Participants were also confused by the 'I' element of these statements as overcoming problems was considered to be something done in collaboration with the prescriber
- Reluctance to take medicines as prescribed due to side effects was considered to be the key barrier for inclusion
- Statement eight was described as "adventurous" and inaccurate as resolution of problems would not be undertaken alone
- Statement three caused some confusion as for one patient it was his dose that regularly changed not his medicine.

5.3.6.5 The 'emotions' behavioural domain

Discussion of the 'emotions' group represented replication of material covered in the first session and enabled an opportunity to compare the data collected across the two sessions. The adherence barriers and questionnaire statements discussed were therefore identical to those displayed previously in figures 5.14 and 5.15 respectively. The adherence barriers and questionnaire statements for this section were discussed over 10 and 3 minutes respectively.

Topics discussed by the participants included:

- Participants could identify with the barrier of 'embarrassment'
- Seeing treatment as a burden could involve burden to carers and family members as well as to the patient
- Negative emotions were thought to be potential barriers to adherence
- Negative emotions associated with medicines taking may be more common in younger people who become 'depressed' at the prospect of having to take medicines for life
- Being reminded of an illness by taking medicines can be a motivating factor for some patients, reminding them of the importance of their medicines
- Annoyance from having to take medicines was suggested as another 'emotional' barrier to adherence with specific reference to declarations to the DVLA and holiday insurance forms creating a sense of frustration and grievance

With regard to the questionnaire statements, participants commented that for statement six, rephrasing was necessary as being reliant on taking a medicine is more likely to induce a low mood than the physical act of taking the medicine.

5.3.7 Selection and refinement of adherence barrier statements following the participant consultation exercises

Following the analysis of the consultation exercises, several adherence barriers were re-mapped to an alternative domain to better reflect the participants' comments and understanding. As this section represents an intermediary stage rather than end point, a summary of the key changes and decisions made are provided rather than full details. As previously detailed in the methods section, for each behavioural domain, three adherence barriers (and their corresponding questionnaire statements), were selected for progression to the next stage of the IMAB-Q's development. Three statements per domain were selected to provide a questionnaire appropriate for future psychometric evaluation.

The mind maps produced to summarise all ten behavioural domains are included in appendix 5.10. The changes made and adherence barriers selected following the consultation exercises are summarised in the following sub-sections. Each behavioural domain is considered in a separate sub-section. Each sub-section starts with a table to summarise the changes made to the barriers mapped to the behavioural domain. The three adherence barriers selected for the behavioural domain are then provided in

bullet points, followed by a table to summarise the questionnaire statements selected to represent the chosen adherence barriers.

5.3.7.1 Selection and refinement of adherence barrier statements for the 'knowledge' behavioural domain

Table 5.5 summarises the key refinements made to the mapping of adherence barriers to the 'knowledge' domain and provides a rationale for the changes made. Three barriers originally mapped to this domain were moved to alternate domains considered to be more appropriate.

Nature of change	Rationale
'Knowing how to identify medicines' barrier moved to skills behavioural domain	Behaviour represents an ability that can be acquired through practice more than direct knowledge
'Knowing how to access medicines from packaging' barrier moved to skills behavioural domain	As above
'Knowing how to overcome problems or difficulties' barrier moved to beliefs about capabilities behavioural domain	Barrier reflects a sense of perceived ability to undertake something that may or may not have happened and therefore better fits 'beliefs about capabilities domain'

Table 5.5 Summary of changes to 'knowledge' behavioural domain following participant consultation exercise

Review of the transcripts and the team's expertise allowed the following knowledge barriers to be preferentially selected for inclusion in the questionnaire:

- Not knowing how and when to take medicines
- Not knowing why medicines were prescribed and how they will be beneficial
- Not knowing the system of how to order repeat prescriptions

Details of the questionnaire statements selected to represent these barriers and the rationale for their selection is provided in table 5.6.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
I know how to take/use my medicines as prescribed	Not knowing how and when to take medicines	• 'How' considered sufficiently generalised to also cover 'when' • Although not ideal for readability, the phrasing 'take/use' was selected as both aspects considered important
I know enough about my medicines to decide whether to take them	Not knowing why medicines were prescribed and how they will be beneficial	• Aim is to capture provision of information to meet the individual's need, as this is known to vary between patients[127]. The phrasing of 'know enough' covers patients who do and do not wish to have extra information about their medicines
I know about the different ways to order and collect my repeat prescriptions	Not knowing the system of how to order repeat prescriptions	• Barrier received notable discussion in both consultation exercises, with patients expressing the importance of knowing about the systems such as delivery, repeat collection and online ordering services which make the process far easier

Table 5.6 Questionnaire barrier statements selected for 'knowledge' behavioural domain

5.3.7.2 Selection and refinement of adherence barrier statements for the 'skills' behavioural domain

Table 5.7 summarises the key barrier mapping changes made at this stage; three barriers, previously mapped to the 'skills' domain were moved to alternate domains.

Nature of change	Rationale
'Inability to overcome or resolve problems' barrier moved to 'beliefs about consequences' domain	Barrier most closely related to a perceived ability or confidence to undertake a task rather than direct ability (skill)
'Inability to cope with changes' barrier moved to 'beliefs about consequences'	As above
'Not being able to understand directions' barrier moved to 'knowledge' domain	Knowing how to take/use medicines statement in knowledge domain also covered this barrier, replication therefore unnecessary

Table 5.7 Summary of changes to 'skills' behavioural domain following participant consultation exercise

Three barriers were preferentially selected for inclusion in the questionnaire:

- Not being able to administer medicines
- Not having an ordering and management system in place
- Not being able to identify medicines

Table 5.8 summarises the questionnaire statements selected to represent these barriers and the rationale for their selection. Two new barriers that had not been

included prior to the consultation exercise are included, highlighting the enhanced information and insight provided through the consultation exercises.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
I am able to take/use all of my medicines as prescribed	Inability to take or administer medicines as prescribed	• Importance of barrier conveyed in consultation exercises • Minor re-phrasing to represent all medicines formulations including creams and inhalers
I am able to put a system in place to help me order, collect AND/OR take my medicines	Disorganisation (lack of system) with regard to medicines management	• Noted as important adherence barrier in both consultation exercises • Process components of ordering, collecting and taking should ideally be separated but this is not possible; and/or conjunction considered most reasonable compromise
I am able to identify each of my medicines from others	Inability to identify medicines and differentiate between them	• Barrier raised as a notable issue in both consultation exercises • Medicines identification considered to be an ability that could be acquired through practice and therefore met definition of 'skill'

Table 5.8 Questionnaire barrier statements selected for 'skills' behavioural domain

5.3.7.3 Selection and refinement of adherence barrier statements for 'memory, attention and decision making processes' domain

Table 5.9 summarises the barrier mapping changes made to this domain following the participant consultation exercises. Only two changes were made, with removal of one barrier and moving of another.

Nature of change	Rationale
'Not having a routine and strategy for managing medicines' barrier removed	Barrier already covered by amendments to 'skills' behavioural domain
'Medicines taking not being a priority' barrier moved to 'motivation and goals' behavioural domain	Priorities aspect clearly related to motivation and goals domain

Table 5.9 Summary of changes to 'memory, attention and decision making processes' behavioural domain following participant consultation exercise

The three barriers selected as the most important were:

- Being distracted
- Forgetting to order, collect or take medicines
- Preference for an alternative/ making an alternative decision

Table 5.10 summarises the questionnaire statements selected to represent these barriers and the rationale for their inclusion and phrasing.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
I struggle to remember to order, collect AND/OR take my medicines	Forgetting to order, collect or take medicines	• Statement is amenable to grouping as, for the purposes of the questionnaire, it does not matter at which process stage the forgetting occurs, simply that forgetting is an adherence barrier
I can easily be distracted from taking my medicines	Lack of attention to medicines taking	• Identified as potential adherence barrier in consultation exercises • 'Easily' added following consultation exercise to represent something that does not happen every day
I have my own reasons for not taking my medicines as prescribed	Decision making which impedes adherence	• 'Good reasons' removed following advice in consultation exercises to avoid perceived condolence of inappropriate behaviours • 'My own reasons' added to reflect personal decisions

Table 5.10 Questionnaire barrier statements selected for 'memory, attention and decision making' behavioural domain

5.3.7.4 Selection and refinement of adherence barrier statements for the 'social influences' behavioural domain

Changes to the adherence barriers mapped to this behavioural domain, following the participant consultation exercise are summarised in table 5.11. Only one change was necessary, and this was heavily influenced by the wealth of data elicited via the consultation exercises.

Nature of change	Rationale
'Family obligations' barrier moved to goal conflicts behavioural domain	Insights from consultation exercise clearly demonstrated 'conflict' with regard to wanting to adhere but family commitments sometimes impeding this

Table 5.11 Summary of changes to 'social influences' behavioural domain following participant consultation exercise

The three preferentially selected adherence barriers for the 'social influences' behavioural domain were:

- Poor relationships with (or lack of trust in) healthcare providers
- A lack of social support
- Religious or cultural obligations (concerns about others perceptions)

Table 5.12 summarises the three adherence barriers statements selected to represent these barriers and the rationale for their inclusion.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
I trust my doctor(s) with decisions about my healthcare	Lack of trust in prescriber	• Strong evidence for lack of trust in HCPs as a barrier to adherence plus notable discussion on topic in both consultation exercises
I have the support that I need from others to help me take my medicines as prescribed	Lack of support to adhere	• Lack of social support recently identified as a powerful predictor of non-adherence[120] • Statement modified to refer to support in a more general sense rather than specifically from friends and family and to capture element social support that was needed as patients having differing needs
I worry that other people will think badly of me if I take my medicines	Concerns of others perceptions	• More generic statement created to capture all concerns about other people's perceptions, including social pressures such as faith, religion and social stereotypes.

Table 5.12 Questionnaire barrier statements selected for 'social influences' behavioural domain

5.3.7.5 Selection and refinement of adherence barrier statements for the 'environmental constraints' behavioural domain

Table 5.13 summarises the key changes made to the barriers mapped to this domain; only one change was necessary; moving a barrier to a different behavioural domain.

Nature of change	Rationale
'Not having a system in place to cope with being away from home or changes' barrier moved to skills behavioural domain	Barrier best captured by 'not having a system in place' which had already been mapped to the skills behavioural domain

Table 5.13 Summary of changes to 'environmental constraints' behavioural domain following participant consultation exercise

Three adherence barriers were preferentially selected for inclusion in the questionnaire:

- Cost of medicines
- Problems with getting to the pharmacy (including inconvenient opening hours)
- Travelling and changes to routines

Table 5.14 summarises the adherence barrier statements selected to represent these barriers and the rationale for their inclusion in the questionnaire.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
Taking all of my medicines as prescribed is not good value for money	Cost of medicines	• Worded to reflect consultation exercise comments regarding perceived value for money • Generic statement represents any barrier associated with monetary value of medicines
I can easily get to my local pharmacy or surgery to collect my medicines	Difficulties getting to pharmacy	• Remains unchanged • Could also cover inconvenient opening hours
I struggle to take my medicines as prescribed when there are changes to my daily routine	Changes to daily routine	• Previously mapped to 'goal conflicts' domain • Updated TDF made clear that this domain included 'any circumstance, situation or environment' that could impede adherence

Table 5.14 Questionnaire barrier statements selected for 'environmental constraints' behavioural domain

5.3.7.6 Selection and refinement of adherence barrier statements for the 'emotions' behavioural domain

None of the barriers that were originally mapped to this domain were moved. The three barriers considered to be most important for this domain were:

- Experiencing negative emotions including frustration
- Feeling embarrassed
- Being reminded of illness by taking medicines

Table 5.15 summarises the adherence barrier statements selected to represent these barriers and describes the rationale for their inclusion in the questionnaire.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
Having to take my medicines makes me feel negative emotions (e.g. frustration, anger, embarrassment)	Experience of negative emotions	• Generic statement to capture a range of negative emotions, with example provided for clarity
Taking my medicines as prescribed is an unwelcome reminder of my illness	Medicines taking being a reminder of illness	• Re-phrased to provide greater clarity as recommended in consultation exercises
I feel positive about taking my medicines as prescribed	No sense of positive gain or reward from adherence	• Produced via merging of two similar statements presented in consultation exercise

Table 5.15 Questionnaire barrier statements selected for 'emotions' behavioural domain

5.3.7.7 Selection and refinement of adherence barrier statements for the 'motivation and goals' behavioural domain

Table 5.16 summarises the changes made to the mapping of adherence barriers following the participant consultation exercise, highlighting the utility of the participants' comments in fully elucidating the nature of the adherence barriers.

Nature of change	Rationale
'Feeling burdened' barrier moved to 'emotions' behavioural domain	Sense of burden regarded as a genuine emotion associated with medicines taking more than a lack of motivation manifested in an 'excuse'
'Feeling negative' barrier moved to 'emotions' behavioural domain	Experience of negative emotions regarded as a genuine emotion associated with medicines taking more than a lack of motivation manifested in an 'excuse'

Table 5.16 Summary of changes to 'motivation and goals' behavioural domain following participant consultation exercise

The three barriers preferentially selected for inclusion in the questionnaire were:

- Lack of motivation to adhere
- Low priority assigned to medicines taking
- Lack of intention to take medicines as prescribed

Table 5.17 summarises the questionnaire statements chosen to represent these adherence barriers and the rationale for their inclusion and phrasing. Whilst the first and third statements (regarding motivation and intention respectively), may seem similar, the two terms are not synonymous. Whilst motivation relates to 'a stimulus for action towards a goal directed response', intention concerns the 'mental application of effort'[6]. Put simply, the two terms are closely related but motivation focuses on the patient's desires whereas as intention concerns the planning of behaviour. With regard to medication adherence, a patient could, for example, be motivated to take their medicines as prescribed (they wish to do so and can see the benefits), however, they may not intend to take their medicines as prescribed as they know this is not possible, for example due to dexterity problems. The inclusion of items that are closely related to one another is also necessary to enable testing of construct validity at a later date.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
I am motivated to take my medicines as prescribed	Lack of motivation to adhere	• Newly written statement to reduce ambiguity of 'motivation' statement
Taking my medicines as prescribed is high on my list of priorities	Lack of priority assigned to medicines taking	• Addition of 'as prescribed' to ensure consistency between statements
I intend to take my medicines as prescribed	Lack of intention to adhere	• Recent evidence has highlighted the importance of intention in behaviour and therefore needed to be included

Table 5.17 Questionnaire barrier statements selected for 'motivation and goals' behavioural domain

5.3.7.8 Selection and refinement of adherence barrier statements for the 'goal conflicts' behavioural domain

Table 5.18 summarises the key barrier mapping changes made; two barriers, previously mapped to the 'goal conflicts' domain were excluded as they had already been re-mapped to more appropriate domains.

Nature of change	Rationale
'Changes to daily routine' barrier excluded from this domain	Barrier already covered by 'environmental constraints' behavioural domain
'Not having a system in for managing medicines' barrier removed from this domain	Barrier already covered by 'skills' behavioural domain

Table 5.18 Summary of changes to 'goal conflicts' behavioural domain following participant consultation exercise

The three adherence barriers selected for further development were:

- Being too busy
- Regimens not fitting in with daily routines
- Family commitments

Table 5.19 summarises the questionnaire statements selected to represent these barriers and provides a rationale for the wording of the selected statements.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
I'm too busy to order, collect AND/OR take my medicines	Being too busy – competing priorities	• Combines adherence process stages of ordering, collecting and taking to be consistent with rest of questionnaire
Taking my medicines as prescribed does not fit with my daily routine	Difficulty incorporating medicines regimen into daily routine	• Newly added statement to reflect comments regarding this barrier especially lunchtime doses
Life gets in the way of me taking my medicines as prescribed	Competing priorities	• Provides generic statement to encompass barriers such as family commitments

Table 5.19 Questionnaire barrier statements selected for 'goal conflicts' behavioural domain

5.3.7.9 Selection and refinement of adherence barrier statements for the 'beliefs about consequences' behavioural domain

Barriers such as 'misunderstanding' and 'insufficient information' were raised in this section but remained mapped to the 'knowledge' behavioural domain. No barriers originally mapped to the 'beliefs about consequences' behavioural domain were changed or remapped to an alternate domain following the consultation exercises.

The adherence barriers selected for development as questionnaire statements were:

- Fear that medicines will be harmful
- Not thinking there is a need for treatment
- Mistrust/lack of belief in medicines

Table 5.20 summarises the adherence barrier statements selected. All three statements were refined following the consultation exercise to improve clarity.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
Taking my medicines as prescribed is harmful to me	Belief that medicines are harmful	• Minor amendment from 'could be harmful' to 'is harmful' to better represent belief about consequences/ be clearer
If I don't take my medicines as prescribed my condition will get worse	Not thinking that medicines are necessary	• Re-phrased to provide stronger link between worsening health and non-adherence; original statement too vague
I don't think my medicines will help me with my condition	Lack of belief in medicines efficacy	• Re-phrased to convey clearer link between medicines taking and condition treated

Table 5.20 Questionnaire barrier statements selected for 'beliefs about consequences' behavioural domain

5.3.7.10 Selection and refinement of adherence barrier statements for the 'beliefs about capabilities' behavioural domain

All of the adherence barriers included within this domain were retained and unchanged following the consultation exercise. The three adherence barriers selected for further development into questionnaire statements were:

- Lack of confidence to adhere
- Lack of confidence in ability to overcome problems
- Inability to cope with problems/changes

Table 5.21 summarises the adherence barrier statements to represent these adherence barriers and provides a rationale for their phrasing and inclusion.

Questionnaire statement	Barrier represented	Rationale for statement & factors considered
I am confident about ordering, collecting AND/OR taking my medicines as prescribed	Lack of confidence in ability to adhere	• Newly introduced statement to reflect importance of confidence. All three stages of adherence combined to ensure comprehensiveness and questionnaire consistency
If I experienced difficulties with my medicines I would know what to do to overcome these	Inability to overcome difficulties	• Minor amendments to reflect confidence to undertake an active resolution strategy
I could easily overcome any difficulties that arise from side effects of my medicines	Inability to cope with side effects	• Side effects consistently identified as prominent adherence barriers; statement concerns confidence in ability to overcome this problem

Table 5.21 Questionnaire barrier statements selected for 'beliefs about capabilities' behavioural domain

5.3.7.11 Development of the first prototype questionnaire

The first prototype questionnaire is shown in appendix 5.11. The research team agreed that four sides of A4, printed on an A3 sheet to produce a booklet format would be an optimal design layout given the questionnaires length.

The front page was developed to create a professional appearance with background information added to provide clear expectations, collated into four brief bullet points to improve readability. In highlighting that there are no right or wrong answers, honest opinions were encouraged and any concerns about conforming to 'expected answers' minimised. Succinct and clear instructions for completion were provided and the non-judgemental nature of the questionnaire was further reinforced to encourage patients to see that non-adherence is common place and occurs for many different reasons.

Arial font size 12 was used throughout the questionnaire to provide a font size that was clear to read and (hopefully) large enough for any respondents with visual impairments. The text was non-justified as this is known to be problematic for certain populations such as people with dyslexia[141]. The adherence barrier statements were alternated in sequence between the behavioural domain that they related to, starting with the first 'knowledge' statement and ending with the third 'beliefs about consequences' statement.

5.3.8 Feedback from research colleagues and subsequent refinements

In total, ten research colleagues offered feedback, with eight also receiving the presentation about the theoretical construction of the questionnaire. In general the questionnaire was well received and colleagues recognised its importance in identifying barriers to adherence. Specific recommendations were covered by considering each behavioural domain in turn.

5.3.8.1 Recommendations for the overall layout and introductory section

Overall, the design and layout were pleasing, with experts in questionnaire design noting that it's clear layout and good readability should facilitate completion. The front cover was described as eye-catching and professional looking and the background statements were generally acceptable, with the exception of the statement providing an estimate of completion time, where changes were recommended. Whilst the time frame of 5-10 minutes was deemed appropriate, re-phrasing of the statement 'the questionnaire should not take any longer....' was recommended, as this could impose an expectation that would alarm patients if they needed longer. After considering these recommendations, the research team agreed to re-phrase this fourth bullet point as:

'*The questionnaire will take about 5-10 minutes to complete'*

Minor amendments to the instructions for completion were also recommended as this section was slightly verbose and at times repetitive.

5.3.8.2 Recommendations for the adherence barrier statements

A summary of the recommended changes to the adherence barrier statements and the research team's subsequent decisions is provided in table 5.22. In general, the recommendations largely related to rephrasing of statements to improve readability and reduce ambiguity. Recommendations that affected more than one statement included:

- For the statements *'I know how to take/use all of my medicines as prescribed'* and *'I am able to take/use all of my medicines as prescribed'*, changing the 'take/use' term to either 'take' or 'use', with 'take' generally considered most appropriate as most patients will have oral preparations and the term 'take' should not be unduly confusing for any non-oral preparations such as creams or inhalers
- For the statements containing '*AND/OR*' (e.g. remember to order, collect and/or take my medicines) replacing this with three distinct statements to represent each adherence process stage (ordering, collecting and taking) separately

Whilst the first of these recommendations was easily implemented, the second proved more complex as creating three unique statements was not possible, due to the restraint of having three statements per behavioural domain. When the purpose of the questionnaire in terms of identifying which behavioural domains adherence barriers were primarily within, the group of colleagues became less anxious about the need to differentiate between each adherence process stage. For some statements, all three process stages were therefore retained and combined with the 'and' conjunction to reduce confusion. For other statements, the most pertinent process stage was selected, as described in table 5.22.

Beyond minor rephrasing of statements, more notable changes were also necessary for the 'memory, attention and decision making processes' behavioural domain. The third statement in this domain was:

'I have my own reasons for not taking my medicines as prescribed'.

Reflection identified that this barrier had been mis-mapped, and did not accurately reflect a decision making process as originally intended. Whilst choosing an alternative to prescribed medicines involves decision making processes, the factor which may impede adherence is the preference for alternatives, not the decision making process. A barrier relating to decision making processes would, for example, be an inability to choose between two or more options. For medication adherence, this is therefore irrelevant as there are not multiple options to choose between plus no barriers pertaining to this were identified in either the literature search or consultation exercises. No barriers relating to decision making processes were therefore included, leaving opportunity for a new, third statement in this domain. The research team agreed that splitting the first statement (*'I struggle to remember to order, collect AND/OR take my medicines as prescribed')* to distinguish between 'remembering to take medicines as prescribed' and 'remembering to order and collect medicines on time' was the most intuitive approach. The adherence barrier relating to decision making, specifically

having 'own reasons for not adhering', was retained and moved to the 'beliefs about consequences domain' as this represented an important barrier. The beliefs about consequences domain was chosen as the 'justifiable reason' for non-adherence would likely be informed by consideration of the consequences of this choice.

The 'environmental constraints' domain was also subject to more notable refinements, with the first statement, *('taking all of my medicines as prescribed is not good value for money')*, attracting notable debate. Discussion revealed that, in an attempt to incorporate aspects from the consultation exercise, the core of the adherence barrier had been lost. The group of research colleagues suggested that the concept of 'value for money' as proposed in the consultation exercises, was ambiguous and also unlikely to relate to 'environmental constraints', unlike the original barrier of not being able to afford a prescription. Upon closer inspection, the adherence barrier 'cost of medicines' proved to be complex and multifaceted as summarised in appendix 5.12. For the literature identified adherence barrier, 'cost of medicines' related to a genuine inability to pay for prescriptions; this data was primarily based on HIV studies based in the USA. The UK based healthcare system however, means that a genuine inability to pay for prescriptions may be less likely. More likely however, is an enforced choice between paying for a prescription and paying for something else deemed to be important, due to limited financial resources. This choice between two alternatives, imposed due to limited funds is better represented by the 'goal conflicts' behavioural domain. The 'cost of medicines' barrier was therefore switched from the 'environmental constraints' domain to the 'goal conflicts' domain where the following statement was included:

'I have to choose between paying for my prescription and paying for other things that are important to me'.

With the removal of the cost related barrier from the 'environmental constraints' section, only two barriers remained, the literature review and consultation exercise transcripts were therefore reviewed again to identify important adherence barriers in this domain. Barriers such as 'unfriendly' or 'unhelpful' staff, losing prescriptions, failed orders and so forth were captured in a new statement:

'My pharmacy or surgery provides an efficient service for ordering and collecting my medicines'.

For the 'emotions' behavioural domain, the third statement *('I feel positive about taking my medicines as prescribed')* did not appear to relate to a specific barrier. This barrier

was therefore replaced by a statement to reflect 'seeing treatment as a burden' as the literature review and consultation exercises identified this as an important adherence barrier. Changes were necessary for the 'goal conflicts' domain, to accommodate the 'cost of medicines' barrier which had been newly mapped to this domain. The first statement *('I'm too busy to order, collect AND/OR take my medicines')* was removed as this was represented well by other statements and therefore replaced with the 'cost of medicines' statement.

The third statement in the 'beliefs about capabilities' domain ('*I could easily overcome any difficulties that arise from side effects of my medicines')*, was also removed, as this was considered to be unnecessarily specific and duplicated the second statement in this domain (*'If I experienced difficulties with my medicines I would know what to do to overcome these')*. The removed statement was replaced by a new statement to reflect the important barrier of 'inability to cope with changes'.

The research team also agreed that the second and third statements in the 'beliefs about consequences' domain, *('If I don't take my medicines as prescribed my condition will get worse'* and *'I don't think my medicines will help me with my condition'* respectively), were sufficiently similar to warrant removal of the third statement. The removal of this statement enabled addition of the 'own reasons for not taking medicines' barrier to this domain.

5.3.8.3 Summary of questionnaire refinements following feedback from research colleagues

Aside from refinements in the phrasing of many statements, the feedback process also permitted a reflective process, whereby the team critically assessed the value of each statement and its accuracy in representing the intended barrier. Appendix 5.13 summarises this reflective process, adding transparency to the research team's rationale for the decisions made.

Behavioural domain	Adherence barrier statement	Recommended refinement	Outcome/changes
Knowledge	I know how to take/use all of my medicines as prescribed	'Take/use' term unanimously agreed to be unnecessarily confusing	'Take' selected as majority of patients will have oral formulations. Term should not be unduly confusing for those using non-oral formulations
		'All of my medicines' considered as unnecessary	Statement amended to 'I know how to take my medicines as prescribed'
Skills	I am able to put a system in place to help me order, collect AND/OR take my medicines as prescribed	'And/or' term unacceptable and far too complex to process. Inappropriate to combine three distinct processes in one statement; use three separate statements	Changed to 'and'
		'I have a system in place' would better represent a skill, current phrasing pertains more to a belief about capability	Changed to 'I have a system in place…' after referring to TDF definitions and agreeing with recommendations
	I am able to take/use all of my medicines as prescribed	'Take/use' term unacceptable, either term but not both should be used	Changed to 'take'
	I am able to identify each of my medicines from others	Not clear what this means and what barrier it relates to plus 'identify' is ambiguous; needs rephrasing	Changed to 'I am able to tell each of my medicines apart from each other' to improve clarity
Memory, attention and decision making processes	I struggle to remember to order, collect AND/OR take my medicines as prescribed	'AND/OR' conjunction unacceptable; three separate statements recommended	Re-phrased to 'I remember to order, collect and take my medicines as prescribed' as 'and' conjunction appears acceptable for positively phrased statements
	I can be easily be distracted from taking my medicines	Change to 'distractions can stop me from taking my medicines as prescribed' as currently unclear	Changed to 'I am easily distracted from taking my medicines' to optimise reflection of original barrier and participant comments in consultation exercise
	I have my own reasons for not taking my medicines as prescribed	No changes necessary	Re-evaluation led the team to agree this barrier was misplaced and better fitted with the 'beliefs about consequences' domain

Table 5.22 **Summary of recommended changes to barrier statements following feedback from research colleagues**

Behavioural domain	Adherence barrier statement	Recommended refinement	Outcome/changes
Social influences	I worry that other people will think badly of me if I take my medicines	Indistinguishable ambiguity around statement, various amendments suggested	Statement changed to 'I worry about what other people will think of me if they knew I took medicines'
Environmental constraints	Taking all of my medicines as prescribed is not good value for money	Value for money concept is confusing and does not relate to original barrier of inability to pay for prescriptions, needs to be refined extensively	Barrier moved to 'goal conflicts' domain and rephrased as 'I have to choose between paying for my prescriptions and paying for other things that are important to me'
	I can easily get to my local pharmacy or surgery to collect my medicines	None suggested	Refined upon reflection to 'I can easily get hold of my medicines from my pharmacy or surgery' to better represent adherence barrier to and covered multiple aspects including inconvenient opening hours
Emotions	Having to take my medicines makes me feel negative emotions (e.g. frustration, anger, embarrassment)	Anticipated guilt/regret is an important emotion that may have been overlooked, refinements to include this may be necessary	Importance of anticipated regret acknowledged though this may not directly represent an adherence barrier per se. Moreover, no literature identified barriers, nor consultation exercise comments related to this therefore statement remained unchanged.
	I feel positive about taking my medicines as prescribed	No changes recommended	Statement did not represent a specific barrier and was therefore removed. New statement of 'taking my medicines as prescribed is a burden to me' added to reflect importance of 'burden' barrier as expressed in literature and consultation exercises.
Goal conflicts	I'm too busy to order, collect AND/OR take my medicines.	'AND/OR' phrasing unacceptable and needs to be rephrased	Barrier represented adequately by other statements elsewhere therefore this statement was removed to make way for the 'cost of medicines' barrier which had been newly mapped to this domain.

Table 5.22 (continued) **Summary of recommended changes to barrier statements following feedback from research colleagues**

Behavioural domain	Adherence barrier statement	Recommended refinement	Outcome/changes
Beliefs about capabilities	I am confident about ordering, collecting AND/OR taking my medicines as prescribed	'AND/OR' phrasing unacceptable and needs to be rephrased	'OR' removed plus 'I am' replaced by 'I feel' to better reflect a belief about capabilities
	If I experienced difficulties with my medicines I would know what to do to overcome these	Slightly muddled, rephrase to improve readability	Statement changed to ' if I experienced difficulties with my medicines I would know how to overcome these'
	I could easily overcome any difficulties that arise from side effects of my medicines	No recommended changes	Duplication of second statement (see above) therefore replaced with 'I don't think I could cope if my medicines or doses kept changing' to reflect barrier of inability to cope with changes, as described in literature and the consultation exercises
Beliefs about consequences	Taking my medicines as prescribed is harmful to me	'is harmful' implies medicines have already been taken and caused adverse effect and does therefore not reflect a 'belief about consequences'	Changed to 'I worry about the harmful effects of taking my medicines or their side effects' to better reflect a belief and emphasise the relevance of side effects to this barrier
	I don't think my medicines will help me with my condition	No recommended changes	Removed to accommodate 'own reasons' barrier as deemed sufficiently similar to 'condition getting worse' statement.

Table 5.22 (continued) **Summary of recommended changes to barrier statements following feedback from research colleagues**

5.3.9 Feedback from healthcare providers and subsequent refinements

Feedback was provided by three hospital pharmacists two community pharmacists and one pharmacist employed by a Clinical Commissioning Group. Feedback was also received from two GPs, one pharmacy technician specialising in domiciliary medicines support and one nurse with a specialist interest in medicines for the elderly.

Feedback was largely positive, with only minor points of criticism and improvement. Positive comments related to the clear instructions and explanations, professional design, good layout and good use of font size. The HCPs reported that the majority of patients should be able to complete the questionnaire without undue difficulty, given the clear instructions and 'user-friendly' format. Both GPs also commented that they felt the right questions were being asked and that they would be interested to see the results. Other respondents also commented that they did not feel there were any surplus questions and that it had been well written, with a clear value to healthcare providers exploring the nature of non-adherence.

General recommendations included re-phrasing the terms 'doctor(s)', used at several points in the questionnaire to encompass the fuller range of potential prescribers such as nurses. Alternative terms such as 'prescribers' and 'healthcare providers' were considered, but neither option were thought to be suitably clear or unambiguous. A specific question to inform the resolution of this matter was therefore posed to the consultation exercise participants in the next round of feedback.

Further general recommendations included:

- Numbering the statements to give respondents a sense of progress and facilitate data entry/analysis
- Removing the first bullet point on the front page which thanks the respondent for completing the questionnaire; this assumption may be offensive
- Including barriers that consider problems with physical dexterity and difficulties with swallowing tablets or opening packages

Whilst the first two recommendations were implemented with ease, the third recommendation posed a problem, as the statement 'I am able to take my medicines as prescribed' had been included to represent these barriers. The research team had anticipated that if a patient were unable to swallow their medicines, access their medicines from their packets or collect their medicines due to mobility problems, then they would 'disagree' or 'strongly disagree' with this statement as they are not able to take their medicines as prescribed. However, the HCPs comments suggested that this

statement may not represent these barriers adequately and may not be interpreted as intended. The research team agreed to probe the consultation exercise participants for further information about their interpretation of this statement and it's appropriateness in detecting the intended barriers, in the next round of questionnaire feedback.

Table 5.23 provides a summary of the HCPs recommendations for specific statements and any changes that were subsequently made. In the 'goal conflicts' behavioural domain, the 'cost of medicines' barrier statement evoked feedback, with suggestions to remove this statement as it would be irrelevant to the large majority of respondents who do not pay for their prescription. Whilst this suggestion was acknowledged the research team felt outright removal of the statement was inappropriate as this statement represented an important barrier, albeit one which may only affect a minority of patients. Two resolution strategies were therefore considered:

1) Inclusion of a 'not applicable' response option
2) Use of two questionnaires, one for patients who pay for their prescription and one for patients who are exempt from payment, where the cost related statement would be replaced by an alternative 'goal conflicts' statement.

As 'not applicable' response options are controversial[141, 150] this option was rejected. The option of creating two different questionnaires according to patient prescription payment status was also rejected, as this would create unacceptable and unnecessary complications. Moreover, this strategy would also not directly resolve the underlying issue of a poorly phrased adherence barrier statement. In designing the statement, the research team had hoped that if a patient did not pay for their prescription they would respond 'disagree' or 'strongly disagree' as they do not have to make the choice between their prescription or something else because they do not pay. The HCPs feedback suggested that this aspiration was conceived in error and thus a problem with face validity may exist. The next round of feedback from the consultation exercise participants was used as opportunity to further explore this matter, by directly asking whether the statement posed a problem and had been answered as intended.

Behavioural domain	Adherence barrier statement	Recommended refinement	Outcome/changes
Memory attention & decision making processes	'I am easily be distracted from taking my medicines'	Typographic error identified with word 'be'	'Be' removed so that statement reads 'I am easily distracted..'
Goal conflicts	I have to choose between paying for my prescription and paying for other things that are important to me	May be redundant as so many patients do not pay for their prescriptions	Agreed statement will not be relevant for many respondents but that this was not adequate justification for its removal as this may be a notable barrier for some patients.
Beliefs about consequences	If I don't take my medicines as prescribed my condition will get worse	Statement appears to be a knowledge based factual statement rather than one grounded in patient beliefs	Agreed that this statement needed refinement and was changed to 'If I don't take my medicines as prescribed, I think my condition will get worse' to more accurately reflect a belief about consequences
Knowledge	I know how to take my medicines as prescribed	Many patients will 'think' they know what to do and not realise they are doing it wrong	Whilst this is a valid point, it was considered to be beyond the remit of the questionnaire's objectives. The statement was therefore unchanged.
Beliefs about capabilities	I don't think I could cope if my medicines or doses kept changing	Patients may not understand what doses are	Considered as unlikely to be problematic as the term had been used without problem in the consultation exercise. Agreed seek further advice on this statement in next round of feedback.
Skills	I have a system in place to help me order, collect and take my medicines as prescribed	Patients may think that 'having a system' only refers to using an MDS	Phrase was derived directly from consultation exercise and is therefore unlikely to be problematic. No changes were therefore made

Table 5.25 Summary of recommended changes following feedback from healthcare professionals

5.3.10 Feedback from consultation exercise participants and subsequent refinements

Of the fourteen consultation exercise participants involved in the earlier stages of the questionnaires development, 13 (92.9%) agreed to being sent the feedback documents. One participant did not respond to the contact e-mail and was therefore excluded from receipt of the documents. The prototype questionnaire, 'feedback booklet' and covering letter posted to participants are shown in appendices 5.16, 5.17 and 5.18 respectively.

Completed feedback booklets were returned by 12 (92.3%) participants.

5.3.10.1 General feedback

Overall, the questionnaire was well received and without notable concerns with regard to design, layout and instructions for completion. Several comments concerned the pleasing and professional layout, good use of font size and clear instructions, adding confidence to the suitability of the questionnaire. The feedback provided made clear that both the questionnaire and consultation exercise process were well received and highly regarded.

Suggestions for delivering the instructions for completion via bullet points and re-phrasing the questionnaire title to something less 'intimidating' were both actioned. The research team agreed to re-phrase the questionnaire title to 'You and your medicines', to provide a non-threatening title and generic sense of the content. Further recommendations included reconsidering the repetitiveness of the questionnaire and including an additional 'comments box'. Neither of these recommendations were actioned; a comments box was deemed unnecessary as the questionnaire will be used as part of a discussion, where fuller details will be elicited and patients will have ample opportunity to verbally confer additional comments. The repetitive nature of the questionnaire was considered necessary at this stage of the development, to enable psychometric testing and subsequent refinement in later developmental stages.

5.3.10.2 General questionnaire statements

Of the 30 questionnaire statements, 26 were included in a section for provision of general comments and feedback, a summary of the comments attracted for these statements is provided in appendix 5.19, which also describes the rationale for any changes made following this feedback.

Of the 26 statements included in this section, 18 (69.2%) attracted recommended changes, leaving eight without need for further development. Many of the recommendations related to minor rephrasing of the statements that were deemed superfluous. Consequently, for nine statements which such recommendations, the research team agreed that no changes were necessary. For the remaining nine statements, careful considerations were made to optimise the phrasing of statements and ensure the intended adherence barriers were adequately reflected.

5.3.10.3 Specific questionnaire statements

Questionnaire statements 2, 4, 8 and 29 were considered in greater depth in the consultation exercise participant's feedback form, as the HCPs feedback had highlighted these statements as in need of further refinement. Table 5.22 provides a summary of the changes that were made to these statements. No changes were necessary for statement four and the concerns with statements two and 29 were resolved through minor re-phrasing of the statements.

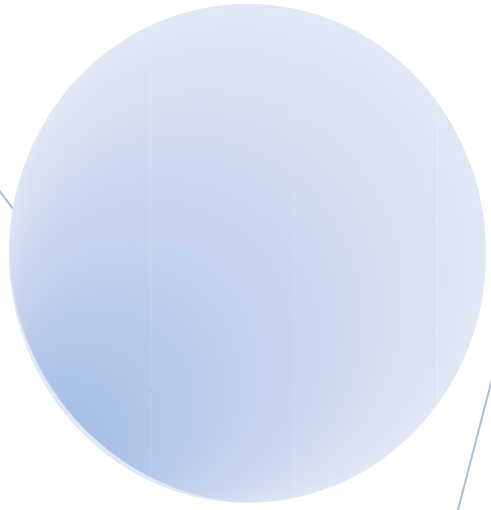
Statement eight, relating to choosing between paying for a prescription and other important things, required more extensive changes as only one participant (3.8%) completed this statement as intended and reported no need for refinements. Two participants (18.2%) responded 'neither agree nor disagree' providing a comment that it was hard to respond as they did not pay for their prescriptions and three participants (27.3%) left this statement blank, commenting that is was not applicable as they did not pay. Re-phrasing of this statement to 'I do not have to choose between paying for my prescriptions and paying for other things that are important to me' was selected as a resolution strategy. It was anticipated that this switched phrasing would make a response of 'strongly agree' or 'agree' more intuitive for participants who do not have to choose because they do not pay.

Questionnaire statement	Rationale for seeking specific feedback	Summary of feedback from consultation exercise participants	Agreed changes and rationale
2) I am able to take my medicines as prescribed	Statement did not appear to reflect intended barriers of dexterity and swallowing difficulties	Majority of participants did not consider physical difficulties for this statement and had assumed it related to knowledge and memory	Statement was changed to 'I am physically able to take my medicines as prescribed'. Additional of word 'physically' should better represent intended barrier
4) I trust my doctor(s) with decisions about my healthcare	Term doctor(s) may be problematic as some patients may have their medicines prescribed by a nurse	Two (16.6%) participants thought statement was fine, four (33.3%) conveyed a preference for the original term. 'Doctor or healthcare provider' suggested as resolution strategy	Phrasing of 'doctor or healthcare provider' made statement overly cumbersome and therefore unacceptable. Original wording therefore retained
8) I have to choose between paying for my prescriptions and paying for other things that are important to me	Majority of patients do not pay for their prescription and will therefore find this statement to be irrelevant	Majority of participants struggled with statement confirming the need for changes. All participants (bar one) felt that a 'not applicable' response option was needed	'Not applicable option' is best avoided for Likert scales[150] and therefore not adopted. Statement re-phrased to 'I do not have to choose between paying for my prescriptions and paying for other things that are important to me'.
29) I don't think I could cope if my medicines or doses kept changing	Term 'doses' thought likely to confuse respondents	Some suggestions for improved clarity provided but on the whole, participants did not struggle with this term	Statement re-phrased to 'I don't think I could cope if my medication regime kept changing' to overcome any potential ambiguity regarding the terms 'medicines' and 'doses'

Table 5.22 Summary of changes to specific questionnaire statements following consultation exercise participants' feedback

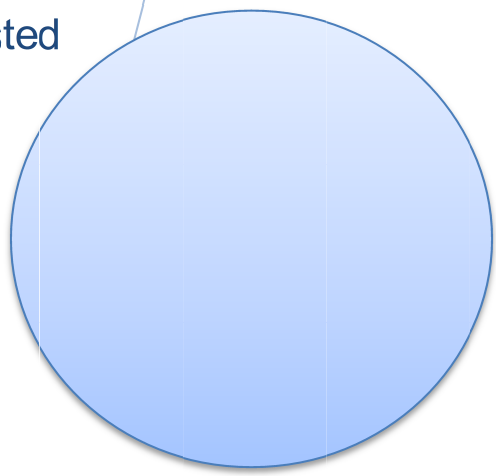
5.3.11 The IMAB-Q

Figure 5.24 shows the final version of the IMAB-Q, as agreed by the research team following the final round of consultation with members of the public. The layout has been amended slightly to accommodate incorporation within the margin restraints of this thesis; font size 11 has been used for the questions whereas font size 12 is used in the full version. The full version also fits neatly onto four sides of A4 so that a booklet layout can be used. These changes have only been used to allow inclusion within the thesis and do not reflect the final IMAB-Q.



You and Your Medicines

- This questionnaire will help us to understand more about any difficulties that you may have with taking your medicines
- There are no right or wrong answers to the questions asked, we're interested in your honest views
- The questionnaire will take approximately 5-10 minutes to complete



You and Your Questionnaire

Many people often struggle to take their medicines as prescribed, for many different reasons. We understand that different things can 'get in the way' of following your doctors recommendations about taking your medicines.

This questionnaire lists 30 different statements about taking your medicines. For each statement:

- Please tick (✓) the box that best reflects your level of agreement with the statement
- Please only tick ONE box per statement

Some of the statements may appear to be similar to others but please be sure to respond to each statement.

	Statement	**Strongly agree**	**Agree**	**Neither agree nor disagree**	**Disagree**	**Strongly disagree**
1	I know how to take my medicines as prescribed					
2	I am physically able to take my medicines as prescribed					
3	I remember to take my medicines as prescribed					
4	I trust my doctor(s) with decisions about my healthcare					
5	I can easily get hold of my prescribed medicines from the pharmacy or surgery					

	Statement	**Strongly agree**	**Agree**	**Neither agree nor disagree**	**Disagree**	**Strongly disagree**
6	I have negative emotions (e.g. frustration, embarrassment anger) about taking my medicines as prescribed					
7	I am motivated to take my medicines as prescribed					
8	I do not have to choose between paying for my prescriptions and paying for other things that are important to me					
9	I feel confident about all aspects of managing (ordering, collecting and taking) my medicines					
10	I worry about the unwanted effects (e.g. harmful effects or side effects) of taking my medicines					
11	I know enough about my medicines to decide whether to take them					
12	I have a system in place to help me order, collect and take my medicines as prescribed					

	Statement	**Strongly agree**	**Agree**	**Neither agree nor disagree**	**Disagree**	**Strongly disagree**
13	I am easily distracted from taking my medicines					
14	If I needed support from others to take my medicines as prescribed, I could get it					
15	Changes to my daily routine would not interfere with taking my medicines as prescribed					
16	Taking my medicines as prescribed is an unwelcome reminder of my condition					
17	Taking my medicines as prescribed is high on my list of priorities					
18	Taking my medicines as prescribed does not fit with my daily routine					
19	I am confident that I could find ways to solve any difficulties that I have with taking my medicines as prescribed					

	Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
20	If I don't take my medicines as prescribed I think my condition will get worse					
21	I have the information that I need to be able to easily order and collect my prescriptions					
22	Telling my medicines apart from each other would not be a problem for me					
23	I remember to order and collect my medicines on time					
24	I worry about what other people would think of me if they knew I took medicines					
25	My pharmacy or surgery provides an efficient service for ordering and collecting my medicines					
26	Taking my medicines as prescribed is a burden to me					
27	I intend to take my medicines as prescribed					
28	Life gets in the way of me taking my medicines as prescribed					

	Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
29	I don't think I could cope if my medication regime kept changing					
30	I have my reasons for not taking my medicines as prescribed					

Thank you for your time

Figure 5.24 **The identification of Medication Adherence Barriers Questionnaire (IMAB-Q) V1**

5.3.12 Calculations for the readability of IMAB-Q

Table 5.23 summarises the Flesch-Kincaid scores for each section of the questionnaire and the overall document. For the entire documents, the Flesch-Kincaid score is 7.5, indicating that it is comprehendible to an average UK student in year 7 or 8 of high school. This therefore covers a reading age of between 11 and 13 years, though an age of 12 years is most likely for the midpoint of year seven at high school.

Whilst the Flesch-Kincaid scores for the front page and instructions for completion are well represented by the score for the entire questionnaire, the individual questionnaire statements were more variable. Flesh-Kincaid scores for the questionnaire statements ranged from 2.3 to 13.5; at the lowest the questionnaire statements therefore require a reading age of 6 to 7 years, though for two statements, the reading age would be in excess of eighteen years.

Assuming the average UK reading age is 12 years[75], 19 questionnaire statements (63.3%) have a Flesch-Kincaid score equivalent to 12 years or less and can therefore be considered as suitable. For three statements (10.0%), whilst the reading age range encompasses the age of 12, it may also exceed it and for eight statements (26.7%) a reading age of 12 years is exceeded.

IMAB-Q section	Total words	Total sentences	Total Syllables	Flesch-Kincaid score	Equivalent UK reading age (years)
Front page	49	4	78	8.0	12-13
Instructions	93	8	146	7.5	11-13
Statement 1	9	1	12	3.7	7-9
Statement 2	10	1	16	7.2	11-12
Statement 3	8	1	13	6.7	10-12
Statement 4	9	1	14	6.3	10-11
Statement 5	14	1	21	7.6	11-13
Statement 6	14	1	28	13.5	18+
Statement 7	9	1	14	6.3	10-11
Statement 8	21	1	29	8.9	12-14
Statement 9	14	1	27	12.6	16-18
Statement 10	16	1	28	11.3	15-16
Statement 11	12	1	18	6.8	10-12
Statement 12	17	1	23	7.0	11-12
Statement 13	8	1	14	8.2	12-13
Statement 14	16	1	22	6.9	10-12
Statement 15	14	1	23	9.3	13-14
Statement 16	12	1	22	10.7	14-16
Statement 17	12	1	18	6.8	10-12
Statement 18	12	1	18	6.8	10-12
Statement 19	21	1	32	10.6	14-16
Statement 20	15	1	20	6.0	10-11
Statement 21	17	1	26	9.1	13-14
Statement 22	14	1	20	6.7	10-12
Statement 23	10	1	16	7.2	11-12
Statement 24	16	1	22	6.9	10-12
Statement 25	14	1	28	13.5	18+
Statement 26	10	1	15	6.0	10-11
Statement 27	8	1	10	2.3	6-7
Statement 28	12	1	16	4.8	8-10
Statement 29	12	1	17	5.8	9-11
Statement 30	11	1	16	5.9	9-11
Thank you	5	1	5	-1.8	
Entire questionnaire	**534**	**43**	**827**	**7.5**	**11-13**

Table 5.23 Flesch-Kincaid scores for IMAB-Q

5.4 Discussion

Best practices in questionnaire design have been utilised in a multi-stage process to develop a novel questionnaire to identify barriers to medication adherence using the theoretical domains framework. A multi-disciplinary approach and consultation with members of the public has added further robustness to this new tool. To be the best of our knowledge, the TDF has not previously been utilised to develop a theory based questionnaire to identify medication adherence barriers; a novel contribution to this field has therefore been made.

5.4.1 Literature review

The majority of adherence barriers extracted from literature were predictable, given the known moderators of adherence as described in chapter one. Given the breadth of literature reporting barriers to medication adherence, the choice to synthesise existing literature was intuitive and a good range of adherence barriers were extracted. However, a full systematic review rather than literature review may have added greater rigour to the study proceedings.

5.4.2 Mapping of adherence barriers and use of the TDF

The framework provided by the TDF offered a useful structure for grouping medication adherence barriers and has enabled incorporation of a theoretical approach in better understanding this domain. The TDF was designed to facilitate utility and allow non-psychologists easier access to health psychology theory. In this study, the TDF has been successfully utilised by two pharmacists (CE and DB) with collaborative guidance from a health psychologist (NT). Whilst the work was led by CE, it is unlikely that the mapping process would have been undertaken with such success, were it not for the guidance of the experienced psychologist on the team. Michie's ambition to create a tool that is accessible and useful to non-psychologists has therefore, in part, been met and the clarified definitions offered by the updated TDF may facilitate this further.

Despite both the experience and guidance offered within the research team, the mapping process was complex, with numerous iterations necessary to reach the final product. Mapping dilemmas were frequent with many barriers falling into more than one behavioural domain. However, as exemplified by the 'cost of medicines' barrier, such dilemmas were often created by overly generalist or ambiguous barriers. As such, it is not necessarily a deficit in the TDF that created these difficulties; precise and specific barriers are therefore key to effective mapping.

5.4.3 Participant, practitioner and researcher consultation

The participant consultation exercises were an invaluable aspect of the questionnaire's development, offering a first-hand account of adherence barrier perceptions and detailed advice for the phrasing of questionnaire statements. Barriers such as 'difficulties with ordering and collecting medicines' were of particular interest and an enhanced understanding was elicited through discussions. Participants expressed genuine discontent at the disparity in services offered by different GP surgeries and pharmacies, especially with regard to the quantity of medicines supplied. The concept of feeling "ripped off" with regard to medicines supply has received little attention in literature yet, from discussion, it became clear that such grievances can yield negative emotions that detrimental to good adherence. Many other adherence barriers were also clarified through discussion and provision of anecdotes. Consultation with members of the public is therefore a highly recommend strategy for similar work.

Despite the benefits of the consultation work with members of the public, there are limitations to the methods deployed. Most notably, the recruitment strategy provided a self-selecting sample of participants who may therefore not be representative of the wider population. There was however a good variety of people, from many different backgrounds and of differing ages, with varying medication regimen complexities, therefore the sampling procedure appeared to provide the variety of people intended. Having mixed groups within the consultation exercise was an important decision to ensure representation of different adherence barriers such as cost of medicines which would only be relevant to some participants.

There was however, poor diversity with regard to health literacy level as only one participant reported 'sometimes' needing assistance with reading health related material. Based on the depth and detail of feedback provided by the participants, it is likely that the reading comprehension abilities of the sample population were beyond the UK average. Therefore, whilst the questionnaire statements were largely acceptable to this group, this may not be so in the wider population. The lack of variation in health literacy could in part be attributed to the recruitment strategy from a university campus, where there is a predominance of well-educated people. However, UEA covers a wide range of non-academic employments and recruitment was also open to friends and family of university staff and students. Only three consultation exercise participants were directly associated with the university; one as a student, one as a professor and one as an administrative assistant. The remaining 11 consultation exercise participants heard of the study through friends or family members, or via the

social media advertisements. Any biases introduced by having a seemingly well-educated sample with good health literacy may therefore be more likely to be attributable to self-selection bias rather than flawed recruitment strategies, though the potential for this must be considered.

A further limitation of the study may be that the patients' clinical conditions are unknown. Whilst all patients were receiving treatments for the prevention of cardiovascular disease, it is likely that participants were also taking medicines for other clinical conditions. Such information may have been useful to characterise the participants and determine how representative the sample was. It is also worth considering whether discussion of the adherence barriers in just two consultation exercises may have also imposed a limitation. Duplication of the material across different groups or with greater numbers of participants may have added further robustness to the topics of discussion and yielded a greater depth of information. However, the information discussed was a synthesis of extensive qualitative work that had already been undertaken, replication of this was therefore not necessary and notable limitations are unlikely. As the emphasis was on facilitation of group discussion, the chosen methods of a focus group style consultation were appropriate. Individual interviews would have lacked the interactive component achieved through the methods deployed and the group discussions and shared idea generation aspects of this work were particularly useful. Finally, given the large volume of material discussed within each consultation exercise, it is reasonable to question whether each behavioural domain was discussed in sufficient depth to yield informative data. Whilst it is likely that a greater depth of information could be yielded through a slower pace of discussion, the time allocated was sufficient for the purpose of these consultation exercises, given the synthesis of an already extensive literature base.

Consultation with research colleagues and HCPs also proved useful and added a further dimension of robustness to the study procedures. However, the convenience sampling strategies deployed may be a limitation. Whilst a good range of HCPs provided feedback, it may have been beneficial to have included more GPs and also hospital prescribers. With regard to the research colleagues, feedback from a panel of medication adherence experts would have been preferable, though all colleagues had some experience in this field.

5.4.4 IMAB-Q (V1)

The IMAB-Q developed in this study represents a starting point, from which further refinements should yield a tool suitable for feasibility testing in routine community

pharmacy consultations. Once the mapping and adherence barrier selection phases had been completed, further refinement to the phrasing of the questionnaire statements was undertaken, representing a notable developmental phase of the questionnaire.

Calculation of the Flesch-Kincaid scores for the entire questionnaire and each statement highlighted the need for further developmental work. Refinement of almost a third of the questionnaire statements is advisable, as the calculated Flesch-Kincaid scores suggest that these statements are too complex for comprehension by average UK citizens. Two statements attracted particularly high scores, equivalent to a reading age of in excess of 18 years:

Statement 6: *"I have negative emotions (e.g. frustration, embarrassment anger) about taking my medicines as prescribed"*

Statement 25: "*My pharmacy or surgery provides an efficient service for ordering and collecting my medicines"*

For statement six, removal of one of the example emotions (embarrassment) would reduce the Flesch-Kincaid score from 13.5 to 11.3, which, whilst an improvement, is still not sufficient to ensure adequate readability. If all of the example emotions are removed the Flesch-Kincaid score reduces further to 8.4, which is equivalent to a reading age of 12-13 years and therefore at the upper end of acceptability. User testing would therefore be necessary to establish whether this was comprehendible, and whether the term 'negative emotions' is unambiguous without example emotions.

For statement 25, public consultation could be used to determine whether the term 'pharmacy' or 'surgery' is preferable so that both need not be used. However, such an amendment may not be sufficient, therefore re-phrasing to, for example, 'I receive an efficient service...' could be considered. It is however important to remember that the Flesch-Kincaid scores are just a guide for readability and should not be used instead of comprehensive user testing in the intended population.

The questionnaire statements for the 'beliefs about capabilities' domain were particularly troublesome as best efforts were made to avoid hypothetical or 'if-then' type statements. Oppenheim advises that hypothetical questions should be avoided as patients often make poor predictions about their future behaviour, especially if the behaviour has not been experienced previously[150]. However, as the 'beliefs about capabilities' domain concerns perceived self-confidence and ability, hypothetical statements can be difficult to avoid. With regard to avoidance of hypothetical statements, 'the belief about consequences' domain was also difficult as there was

frequent need to refer to future events. User testing will be necessary to establish whether any residual hypothetical statements are problematic with regard to accurate participant completion.

5.4.5 Future work

Whilst the first full version of the IMAB-Q opens exciting opportunities for future research, further work and refinements are still needed. With numerous amendments at the final stages, re-consultation with members of the public is advisable to check face and content validity.

Once the content of the questionnaire and its readability have been re-checked, the questionnaire must be validated in terms of criterion and construct validity. A grant proposal, to fund completion of the IMAB-Q in routine MURs in sufficient quantities to allow psychometric testing is currently under review.

Following validation, feasibility work will be necessary to establish whether the IMAB-Q can be used to identify adherence barriers in routine practice. Routine community pharmacy consultations such as MURs represent an ideal opportunity for deployment of the IMAB-Q. Moreover, given the paucity of evidence to support the benefits of an MUR and the lack of theoretical background (as described in chapter one) utilisation of the IMAB-Q in an MUR offers further potential benefits.

Chapter Six Conclusion

6.1 Conclusion

The 2008 systematic review of adherence interventions reported by Haynes *et al.* remains a seminal text and offers a bleak perspective on adherence interventions. Haynes *et al.* report that adherence interventions tend to elicit modest improvements at best and highlight the need for innovative approaches to provide complex, multi-faceted interventions that are tailored to meet individual needs[163]. Whilst MURs and the NMS promote routine, community pharmacy-based adherence interventions, neither are grounded in theory nor is there rigorous evidence to support efficacy and tailoring to meet individual need is minimal. Moreover, these interventions are ill equipped to resolve complex adherence difficulties, especially those of an intentional nature which requires a notably different approach. At present, we therefore find ourselves far removed from the gold-standard adherence intervention that is much needed.

In recent years strategies to improve medication adherence have become increasingly prominent in government agendas[182]. In May 2013, the Royal Pharmaceutical Society (RPS) issued the 'Medicines Optimisation' document as good practice guidelines for healthcare professionals in England[435]. Endorsed by cross-disciplinary professional bodies, this document sets out key recommendations to help patients gain maximal benefit from their medicines. Improving medication non-adherence is a core facet of this document, which calls for patient-centred approaches, multidisciplinary team working and an understanding of patients' beliefs and preferences about medicines. The document also highlights an important role for pharmacists in facilitating 'medicines optimisation'. Medication adherence is firmly set on government and research agendas providing an ideal backdrop to the work undertaken in this thesis.

Chapter one also highlighted that at present, pharmacy interventions to improve adherence are centred upon practical resolution strategies such as reducing regimen complexities and providing adherence aids. The service evaluation undertaken in chapter two supported this claim. The domiciliary service appeared to support medication adherence and reduce patients' risk of harm to good effect. However, this service may not be representative of other domiciliary support services as national provision is variable. Standardisation of these domiciliary support services and sharing of best practices is therefore advisable and within the last year, an active forum to facilitate this has emerged via the RPS website.

From chapter two it is reasonable to conclude that as a profession, pharmacists are reasonably well equipped to remedy simple adherence difficulties of a predominantly practical nature in older, vulnerable patients. Whilst patients over the age of 65 represent the greatest proportion of medicines users in the UK, there are many patients who do not fall into this demographic and many who will be intentionally non-adherent. For these patients, pharmacists are less well prepared and there is a notable deficit in strategies to resolve non-adherence that is influenced by illness perceptions, motivation and health beliefs.

Health psychology theory can be applied to medication adherence to better understand intentional behaviours and inform intervention development. Recent developments in this field have provided a taxonomy of behaviour change techniques and a theoretical framework, to enable greater access to this wealth of theory. These developments will undoubtedly facilitate incorporation of the MRC guidelines to ground complex behaviour change interventions in theory. Moreover, through application of this work there is potential to develop a theory based intervention to address medication adherence barriers using BCTs specific to the type of identified barrier.

Further potential benefits of the novel work described in chapter three include the increased ease with which health psychology theory can now be accessed by non-psychologists as the need to choose between multiple overlapping theories has been negated. Research from the realms of pharmacy practice (especially medication adherence research) and behavioural medicine are intrinsically linked and collaborations across psychology and pharmacy are therefore intuitive. Recent research has increasingly highlighted the relevance of psychology to medication adherence research including reports of the association between personality traits such as neuroticism with non-adherence[436] and conscientiousness with better adherence[437]. As a profession, pharmacists should embrace the expertise of psychology in the field of medication adherence. Facilitation of networking and collaborative opportunities across these two disciplines is therefore advised.

An understanding of the role of psychology in medication adherence research, allowed for consideration of psychological or 'cognitive-based' techniques as interventions to improve medication adherence in chapter four. A systematic review and meta-analysis of these techniques highlighted a potential to elicit improvements in adherence beyond the educational and behavioural strategies currently used in routine practice. Techniques such as MI and III have great potential as components

of adherence interventions and further exploration of these techniques is warranted. Chapter four also highlighted that the efficacy of these techniques is stable across many sub-groups, including delivery from routine HCPs rather than specialists. The potential role of pharmacists in delivering these techniques to improve adherence was therefore identified.

Following completion of the meta-analysis detailed in this thesis, the first full version of the BCT taxonomy has been published[293], which should enable accurate description of the intervention components using 'approved' terminology. Mapping of the identified intervention components to the BCT taxonomy is therefore advised to enable the wider application of this work. Following this, further statistical processes such as meta-regression should be deployed to establish which intervention components (BCTs) were associated with greatest efficacy.

With a strategy for incorporating theory into intervention design and preliminary data to identify effective BCTs in medication adherence, a questionnaire to identify medication adherence barriers (the IMAB-Q) was developed through an iterative, interdisciplinary approach. This questionnaire is the precursor to a novel adherence intervention to identify and resolve barriers to medication adherence. This approach is in accordance with NICE guidelines which recommend that health behaviour change interventions should identify potential barriers to change. These guidelines also recommend prioritisation of interventions that are tailored to tackle individual beliefs, attitudes, intentions, skills and knowledge associated with the target behaviour[405].

Validation of the IMAB-Q is essential before any feasibility work is started; a grant proposal to undertake this work is currently under review. Once validated, the best approach for feasibility testing and implementation of the IMAB-Q must be carefully considered. The MRC framework for complex interventions states that researchers often neglect the developmental and piloting phases of intervention development and do not give due consideration to the practical issues[294]. These aspects must therefore not be overlooked. At present the IMAB-Q is comprised of 30 statements and is therefore long, this may limit its routine use in healthcare consultations. However, it is pertinent to consider that the IMAB-Q currently has multiple statements to represent each behavioural domain so that subsequent validation and psychometric work can be undertaken. Following these essential stages, the IMAB-Q will be shortened to a more manageable length.

Utilisation of the IMAB-Q and the intervention that will follow is intended for routine community pharmacy consultations. Whilst the NMS has shown promising results for enabling smooth initiation of a medicine, patient behaviour and perceived barriers change over time. IMAB-Q will enable identification of barriers to medication adherence that may have emerged over time, capturing the variable and sometimes sporadic nature of non-adherent behaviours and supplementing the adherence support offered in community pharmacists. Consultation with pharmacists prior to implementation of the intervention is paramount to explore the facilitators and barriers to its use. In doing so, consideration of behaviour change at both the practitioner and patient level will be considered and guidance from novel theory sought[438]

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Appendix 2.1 Ethics approval for service evaluation study

Faculty of Medicine and Health Sciences Ethics Committee

Miss Claire Easthall
School of Pharmacy
University of East Anglia
Norwich
Norfolk
NR4 7TJ

Faculty of Medicine and Health Sciences
Elizabeth Fry Building, Room 2.30
University of East Anglia
Norwich NR4 7T

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3rd March 2011

Dear Claire

Domiciliary Medicines Management Service Evaluation – Reference: 2010/2011-29

The submission of your above proposal has now been reviewed by the Chair of the Faculty Research Ethics Committee and we can confirm that it is considered to be a service evaluation. There are no issues of confidentiality or harm to participants.

The Chair has requested that before your start your evaluation you add a final paragraph to the 'Patient questionnaire covering letter' at Appendix 3, as follows:

"When the results have been analysed we may try to publish them in an academic journal so people elsewhere can also learn from our evaluation. One of the researchers at UEA is studying for a PhD and may use the results for that."

Please could you ensure that any amendments to either the protocol or documents submitted are notified to us in advance and also that any adverse events which occur during your project are reported to the Chair. Please could you also arrange to send us a report once your project is completed.

The Chair would like to wish you good luck with your project.

Yours sincerely

Maggie Rhodes

Research Administrator

Cc Dr Debi Bhattacharya

Faculty of Medicine and Health Sciences Ethics Committee

Miss Claire Easthall
School of Pharmacy
University of East Anglia
Norwich
Norfolk
NR4 7TJ

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14th March 2011

Dear Claire

Domiciliary Medicines Management Service Evaluation – Reference: 2010/2011-29

Thank you for your e-mail dated 8th March setting out the amendments to your above proposal. These have now been considered by the Chair of the Faculty Ethics Committee and we can confirm that your amendments have been approved.

Please could you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance and also that any adverse events which occur during your project are reported to the committee. Please could you also arrange to send us a report once your project is completed.

Yours sincerely

Maggie Rhodes

Research Administrator

Appendix 2.2 Initial visit data collection form

Cambridgeshire Community Services Domiciliary Medicines Management Service Initial Visit Data Collection Form

Patient Details	**Patient background and referral information**
ID no: Age:	Referral Date:
Gender: Male ☐ Female ☐	Referral type: GP ☐ Nurse ☐ Family member ☐ Self-referral ☐
Co-habitation status: Living alone ☐ Living with partner ☐	Other (please specify) ☐
Living with other family member ☐ Other (please specify) ☐	Reason for referral:

Patient medication details

Name, dose, strength and form	**Taking as prescribed? (Y/N)**	**Difficulties reported and comments**

Patient's mental state

Formal diagnosis of dementia ☐ Alert and orientated ☐ Slightly forgetful ☐ Notes:

Slightly confused ☐ Very confused ☐ Very forgetful ☐

Patient's vision (with respect to reading medication labels and directions)

Can read with no aids ☐ Struggles to read print even with glasses or aid ☐ Notes:

Needs glasses or aids to read print ☐ Unable to see ☐ Registered blind ☐ Illiterate ☐

Patient's social circumstances

Living with someone who can fully support medication needs ☐ Living alone but has help from carers/friend/family ☐

Living with someone who usually or sometimes supports medication needs ☐ Live alone with no help ☐

Patient's physical condition

Can access all medications independently with ease ☐ Requires assistance with accessing or administering medicines ☐

Can manage to access all medication but struggles ☐ Severely disabled and unable to manage ☐

Patient has difficulty swallowing all/some of their medicines ☐ Comments:

Patient's attitude towards their medication

Shows interest in medicines: YES ☐ NO ☐ Believes medicines are important: YES ☐ NO ☐ Willing to take medicines: YES ☐ NO ☐

Able to administer medicines safely: YES ☐ NO ☐ Able to recall regimen and knowledgeable: YES ☐ NO☐

Details of domiciliary visit

Date of visit: Length of preparation time: Length of visit:

Intervention suggested & comments:

Appendix 2.3 Follow up visit data collection form

Cambridgeshire Community Services Domiciliary Medicines Management Service Follow-up Visit Data Collection Form

Patient ID:	**Date of referral:**	**Date of initial visit:**	**Date of follow up visit:** **Phone call:** ☐ **Visit:** ☐
Intervention costs: Time spent of follow visit and/or telephone call: Total amount of time spent implementing intervention (e.g. GP liaison time etc):			
Patient's co-habitation status No changes since initial visit ☐ Changes:			
Patient's mental state No changes since initial visit ☐ Changes:			
Patient's vision (with regard to reading medication labels and directions) No changes since initial visit ☐ Changes:			
Patient's social circumstances No changes since initial visit ☐ Changes:			
Patient's physical condition No changes since initial visit ☐ Changes:			
Patient's attitude towards their medication No change since initial visit ☐ Changes:			
Patient medication details All recommendations on initial assessment form implemented ☐ Some recommendations on initial assessment form implemented ☐ No recommendations on initial assessment form implemented ☐			

Intervention summary, outcomes and any other changes to patients medicines management:

Details of questionnaire dissemination:

Patient questionnaire sent to patient?: YES ☐ NO ☐

Patient Caregiver questionnaire sent to caregiver? YES ☐ NO ☐ Does the caregiver live with the patient? YES ☐ NO ☐

Caregiver relationship to patient: Husband/wife/partner ☐ Son/daughter ☐ Other family member ☐ Friend ☐ Other ☐

Appendix 2.4 Domiciliary project patient questionnaire

Patient No.			

Cambridgeshire Community Services NHS Trust - Domiciliary Medicines Management Service Evaluation Study

Service Evaluation Questionnaire

- This questionnaire has three sections
- It should take about 10 to 15 minutes to complete
- Please read the letter that came with this questionnaire before deciding whether to complete it as it contains useful information
- Please put your completed questionnaire in the pre-paid envelope provided and return it in the post to the Service Evaluation Team at the UEA.
- If you have any questions about this questionnaire, or you would like to arrange for somebody to help you complete it, please telephone Pippa Scrimshaw on 01353 652233

Thank-you for completing this questionnaire

Cambridgeshire Community Services NHS Trust

University of East Anglia

Section One: Using your medicines

- Many people have difficulty taking their medicines or find a way to use their medicines which best suits them.
- The statements listed below are common situations that people experience.
- For each statement, please tell us how often these lead to you taking your medicines differently to the instructions on the label or from your doctor. Please **tick (✓)** the response that best reflects how you feel.

I take my medicines differently to instructed because:	Always	Often	Some-times	Rarely	Never
I have difficulties opening medicine packaging, or using items such as inhalers or eye drops	❑	❑	❑	❑	❑
I have difficulties swallowing my medicines	❑	❑	❑	❑	❑
I struggle to read the instruction labels	❑	❑	❑	❑	❑
I have difficulties in remembering what time to take each medicine	❑	❑	❑	❑	❑
I forget to take my medicine	❑	❑	❑	❑	❑
I forget when to order or collect my medicines from the doctor or pharmacy	❑	❑	❑	❑	❑
I choose to alter the dose of my medicines if I feel better or worse	❑	❑	❑	❑	❑
I choose to miss out doses of my medicines if I feel better or worse	❑	❑	❑	❑	❑
I choose to stop taking my medicines for a while	❑	❑	❑	❑	❑

Section Two: Your confidence with managing your medicines and health

- We'd like you to think about how you feel about managing your medicines and general health and whether these feelings may have changed following your recent visit from the medicines support service.

- For each of the statements below, please **tick (√)** the response that best reflects how you feel:

As a result of my recent home visit to help me with my medicines, I feel:	**Much better**	**Better**	**The same**	**Worse**
My confidence in taking my medicines correctly is	❑	❑	❑	❑
My ability to take my medicines correctly is	❑	❑	❑	❑
My ability to cope with life is	❑	❑	❑	❑
My ability to keep myself healthy is	❑	❑	❑	❑
My ability to help myself is	❑	❑	❑	❑
My confidence in managing my health is	❑	❑	❑	❑

Section Three: Your satisfaction with the service

We would like to know more about your thoughts on the service you received when you were visited to get help with your medicines.

- We are interested in your honest opinions, whether they are positive or negative
- For the following questions please **tick (√)** the response that best suits you.

1. How would you rate the quality of the service you received?

❑	❑	❑	❑
Excellent	Good	Fair	Poor

2. If a friend were in need of similar help, would you recommend to them the same service you received?

❑	❑	❑	❑
Yes, definitely	Yes, I think so	No, I don't think so	No, definitely not

3. How satisfied are you with the amount of help you received?

❑	❑	❑	❑
Very satisfied	Mostly satisfied	Indifferent or mildly dissatisfied	Quite dissatisfied

4. Have the services you received helped you to deal more effectively with your medicines?

❑	❑	❑	❑
Yes, they have helped a great deal	Yes, they helped somewhat	No, they really didn't help	No, they seemed to make things worse

5. In an overall, general sense, how satisfied are you with the service you have received?

❑	❑	❑	❑
Very satisfied	Mostly satisfied	Indifferent or mildly dissatisfied	Quite dissatisfied

- Finally, please could you tell us who filled in this questionnaire:

❑ Myself (the patient)	❑ A family member	❑ A friend/carer	❑ Somebody else

If you have any other thoughts or comments about the medicines management support service you have received, please record these in the box below

Thank you for taking the time to complete this questionnaire

Please place the questionnaire in the envelope provided, and return it to the service evaluation research team at the university by putting it in the normal post using the pre-paid envelope provided.

The questionnaires will go straight back to the service evaluation research team and will not been seen by any of the healthcare team involved in your care

Appendix 2.5 Patient questionnaire covering letter – first mailing

Cambridgeshire Community Services (CCS) NHS Trust
Domiciliary Medicines Management Service Office (ECF)
Princess of Wales Hospital
Lynn Road, Ely
Cambs, CB6 1DN
01353 652233

<date>

<Patient name>
<Patient address>
<Patient address>
<Patient address>
<Patient address>

Dear <Patient name>,

I recently visited you to offer you help with managing your medicines at home. When I spoke to you on the telephone to discuss how you were getting on, we also talked about whether you would be happy to fill in a questionnaire about the service that you received. Please read this letter before you decide whether to fill in the enclosed questionnaire.

I explained on the telephone that Cambridgeshire Community Services NHS Trust, who provide the service are working with the Medicines Management Research Group at the University of East Anglia (UEA) in Norwich to find out the views of the people who have received the service, and that this is why we'd like you to fill in the questionnaire. We're working with the UEA so that all of the information you give is looked at independently. If you choose to fill in the questionnaire, it will go straight to the UEA and will not be seen by anybody involved with your care. Furthermore, the people at the UEA will not be able to identify you as the questionnaire you send back will just have a reference number on it, not your name.

By filling in the questionnaire, your views will be counted and these may help to further improve the service that we offer. However, it is entirely your decision whether you choose to fill in this questionnaire and whatever decision you make, it will not affect the care you receive in any way. You can talk to your friends, family or carers about completing the questionnaire if you are not sure what to do or if you would like any help completing it.

If you choose to complete the questionnaire, you will be asked to answer a series of questions by ticking boxes on the questionnaire. If you would like to answer the questions but have a difficulty which stops you from doing this, we can arrange for somebody to ask you the questions over the telephone and complete the questionnaire on your behalf. The person telephoning you would be a research assistant working for CCS NHS Trust. They would talk you through each question on the phone and then send your completed questionnaire straight off to the UEA, nobody involved in your care would see the responses you gave.

If you'd like to arrange for somebody to telephone you to help you complete the questionnaire then you can call me, Pippa Scrimshaw on 01353 652233 and I'll ask the research assistant to give you a call. If you have any other concerns or questions about this questionnaire and study, you can also speak to Pippa about these by calling the same number.

When the results have been analysed we may try to publish them in an academic journal so people elsewhere can also learn from our evaluation. One of the researchers at the UEA is studying for a PhD and may use the results from this study for that. If you would like a copy of the report once it has been written, this can be arranged by telephoning me, Pippa Scrimshaw on 01353 652233.

Yours Sincerely,

Pippa Scrimshaw
Specialist Pharmacy Technician – Domiciliary Medicines Management

Appendix 2.6 Patient questionnaire covering letter – second mailing

Cambridgeshire Community Services (CCS) NHS Trust
Domiciliary Medicines Management Service Office (ECF)
Princess of Wales Hospital
Lynn Road, Ely
Cambs, CB6 1DN
01353 652233

Dear <patient>

I recently visited you to offer you help with managing your medicines at home. When I spoke to you on the telephone to discuss how you were getting on, we also talked about whether you would be happy to fill in a questionnaire about the service that you received. I sent the questionnaire to you two weeks ago; however, I've included another copy of it with this letter today as I know people often misplace paperwork or forget to fill it in and I wanted to make sure you had another chance to express your views. If you've already returned the questionnaire then please ignore this letter and thank you very much for taking the time to give us your thoughts.

Please read this letter before you decide whether to fill in the enclosed questionnaire. I explained on the telephone that Cambridgeshire Community Services NHS Trust, who provide the service are working with the Medicines Management Research Group at the University of East Anglia (UEA) in Norwich to find out the views of the people who have received the service, and that this is why we'd like you to fill in the questionnaire. We're working with the UEA so that all of the information you give is looked at independently. If you choose to fill in the questionnaire, it will go straight to the UEA and will not be seen by anybody involved with your care. Furthermore, the people at the UEA will not be able to identify you as the questionnaire you send back will just have a reference number on it, not your name.

By filling in the questionnaire, your views will be counted and these may help to further improve the service that we offer. However, it is entirely your decision whether you choose to fill in this questionnaire and whatever decision you make, it will not affect the care you receive in any way. You can talk to your friends, family or carers about completing the questionnaire if you are not sure what to do or if you would like any help completing it.

If you choose to complete the questionnaire, you will be asked to answer a series of questions by ticking boxes on the questionnaire. If you would like to answer the questions but have a difficulty which stops you from doing this, we can arrange for somebody to ask you the questions over the telephone and complete the questionnaire on your behalf. The person telephoning you would be a research assistant working for CCS NHS Trust. They would talk you through each question on the phone and then send your completed questionnaire straight off to the UEA, nobody involved in your care would see the responses you gave.

If you'd like to arrange for somebody to telephone you to help you complete the questionnaire then you can call me, Pippa Scrimshaw on 01353 652233 and I'll ask the research assistant to give you a call. If you have any other concerns or questions about this questionnaire and study, you can also speak to Pippa about these by calling the same number.

When the results have been analysed we may try to publish them in an academic journal so people elsewhere can also learn from our evaluation. One of the researchers at the UEA is studying for a PhD and may use the results from this study for that. If you would like a copy of the report once it has been written, this can be arranged by telephoning me, Pippa Scrimshaw on 01353 652233.

Yours Sincerely,

Pippa Scrimshaw
Specialist Pharmacy Technician – Domiciliary Medicines Management

Appendix 2.7 Caregiver’s questionnaire

Patient No.			

Cambridgeshire Community Services NHS Trust - Domiciliary Medicines Management Service Evaluation Study

Patient caregiver's questionnaire

- This questionnaire has two sections
- It should take about 10 minutes to complete
- Please read the letter that came with this questionnaire before deciding whether to complete it as it contains useful information
- Please put your completed questionnaire in the pre-paid envelope provided and return it in the post to the Service Evaluation Team at the UEA.
- If you have any questions about this questionnaire, or you would like to arrange for somebody to help you complete it, please telephone Pippa Scrimshaw on 01353 652233

Thank-you for completing this questionnaire

Cambridgeshire Community Services NHS Trust

University of East Anglia

Section One: Your feelings as a caregiver

- We'd like you to think about how you feel as a care giver and whether these feelings may have changed since the person that you care for was visited by the Medicines Management Service.

- For each of the statements below, please **tick (√)** the response that best reflects how you feel:

As a result of the recent Medicines Management visit received by the person that I care for, I feel:	**Much better**	**Better**	**The same**	**Worse**
My confidence in their ability to take their medicines correctly is	❑	❑	❑	❑
My confidence in their ability to manage their medicines more independently is	❑	❑	❑	❑
My confidence in their ability to manage their health and well-being is	❑	❑	❑	❑
	Much less	**Less**	**The same**	**More**
My level of anxiety about them taking their medicines wrongly is	❑	❑	❑	❑
The difficulties that they had in taking their medicines are	❑	❑	❑	❑
The amount of time I have to spend helping them with their medicines is	❑	❑	❑	❑
The amount of time I spend worrying about them taking their medicines is	❑	❑	❑	❑
The level of reliance that they have on me is	❑	❑	❑	❑

Section Two: Your satisfaction with the service

- We would like to know more about your thoughts on the service that the person you care for received when they were visited to get help with the medicines that they take.
- We are interested in your honest opinions, whether they are positive or negative
- For the following questions please **tick (√)** the response that best suits you.

1. How would you rate the quality of the service received?

❑	❑	❑	❑
Excellent	Good	Fair	Poor

2. If a friend were in need of similar help, would you recommend the same service to them?

❑	❑	❑	❑
Yes, definitely	Yes, I think so	No, I don't think so	No, definitely not

3. How satisfied are you with the amount of help received by the person that you care for?

❑	❑	❑	❑
Very satisfied	Mostly satisfied	Indifferent or mildly dissatisfied	Quite dissatisfied

4. Have the services received by the person you care for helped them to deal more effectively with their medicines?

❑	❑	❑	❑
Yes, they have helped a great deal	Yes, they helped somewhat	No, they really didn't help	No, they seemed to make things worse

5. In an overall, general sense, how satisfied are you with the service received by the person you care for?

❑	❑	❑	❑
Very satisfied	Mostly satisfied	Indifferent or mildly dissatisfied	Quite dissatisfied

If you have any other thoughts or comments about the medicines management support service the person that you care for received, please record these in the box below:

Thank you for taking the time to complete this questionnaire

Please place the questionnaire in the envelope provided, and return it to the service evaluation research team at the university by posting using the pre-paid envelope provided.

The questionnaires will go straight back to the service evaluation research team and will not been seen by any of the healthcare team involved in the care of the person that you care for

Appendix 2.8 Covering letter for caregiver’s questionnaire

Cambridgeshire Community Services (CCS) NHS Trust
Domiciliary Medicines Management Service Office (ECF)
Princess of Wales Hospital
Lynn Road, Ely
Cambs, CB6 1DN
01353 652233
<date>

<Patient carer's name>
<Patient carer's address>
<Patient carer's address>
<Patient carer's address>
<Patient carer's address>

Dear <Patient's carer name>,

I recently visited <insert patients name>, who I know you care for, to offer help with managing medicines at home. We are undertaking an evaluation of this service and so are interested in the views of the people who care for patients that have difficulty in managing their medicines, as well as the views of patients themselves. The questionnaire is with this letter, but please read this letter first, before you decide whether to fill in the questionnaire as it contains some important information.

Cambridgeshire Community Services NHS Trust, who provided the service, is working closely with the Medicines Management Research Group at the University of East Anglia (UEA) in Norwich to review the service and the views of the people who have received it and their carers. We're working with the UEA so that all of the information you give is looked at independently and in a scientific way. If you choose to fill in the questionnaire, it will go straight to the UEA and will not be seen by anybody directly involved with the service. Furthermore, the people at the UEA will not be able to identify you as the questionnaire you send back will just have a reference number on it, not your name.

By filling in the questionnaire, your views will be counted and these may help to further improve the service that we offer. However, it is entirely your decision whether you choose to fill in this questionnaire and whatever decision you make, it will not affect the care received by the person that you care for.

If you choose to complete the questionnaire, you will be asked to answer some questions by ticking boxes. If you have decided you would like to answer the questions but have a difficulty which stops you from doing this, then we can arrange for somebody to ask you the questions over the telephone and complete the questionnaire on your behalf. The person telephoning you would be a research assistant working for CCS NHS Trust. They would talk you through each question on the phone and then send your completed questionnaire to the UEA, nobody directly involved in the service would see the responses you gave.

If you'd like to arrange for somebody to telephone you to help you complete the questionnaire, please call me, Pippa Scrimshaw on 01353 652233 and I will then ask the research assistant to telephone you. Furthermore, if you have been sent this questionnaire, but think that there is someone else who would be better suited to complete it; please telephone me on the number above. If you have any other concerns or questions about this questionnaire or study, you can also speak to me about these by telephoning the same number.

When the results have been analysed we may try to publish them in an academic journal so people elsewhere can also learn from our evaluation. One of the researchers at the UEA is studying for a PhD and may use the results from this study for that. If you would like a copy of the report once it has been written, this can be arranged by telephoning me, Pippa Scrimshaw on 01353 652233.

Yours Sincerely,

Pippa Scrimshaw
Specialist Pharmacy Technician - Domiciliary Medicines Management

Appendix 2.9 Summary of patient mean risk scores pre and post intervention using NPSA risk matrix

	Pre-intervention risk scores		Post-intervention risk scores	
Patient ID	Mean	Category	Mean	Category
01-PRI-D	18	EXTREME	4	MEDIUM
03-PRI-F	13	HIGH	5	MEDIUM
04-NOR-D	11	HIGH	4	MEDIUM
05-NOR-M	13	HIGH	2	LOW
06-COR-S	10	HIGH	4	MEDIUM
07-MER-L	5	MEDIUM	3	LOW
08-STM-M	19	EXTREME	13	HIGH
09-STM-R	13	HIGH	5	MEDIUM
10-STG-F	6	MEDIUM	3	LOW
11-TRI-C	14	EXTREME	5	MEDIUM
12-STM-S	12	HIGH	5	MEDIUM
14-NOR-M	14	EXTREME	5	MEDIUM
16-TRI-S	14	EXTREME	7	MEDIUM
17-GEO-S	12	HIGH	6	MEDIUM
18-CLA-D	8	HIGH	3	LOW
19-STM-R	13	HIGH	6	MEDIUM
20-STM-T	12	HIGH	5	MEDIUM
21-MER-P	14	EXTREME	6	MEDIUM
22-MER-H	12	HIGH	7	MEDIUM
23-RIV-F	10	HIGH	6	MEDIUM
24-COR-H	6	MEDIUM	4	MEDIUM
25-GEO-H	11	HIGH	5	MEDIUM
26-TRI-K	12	HIGH	7	MEDIUM
46-CAT-A	12	HIGH	6	MEDIUM

	Pre-intervention risk scores		Post-intervention risk scores	
Patient ID	Mean	Category	Mean	Category
29-PRI-C	6	MEDIUM	5	MEDIUM
30-RIV-H	14	EXTREME	6	MEDIUM
31-MER-B	6	MEDIUM	5	MEDIUM
32-MER-D	7	MEDIUM	5	MEDIUM
33-STM-H	8	HIGH	5	MEDIUM
36-STG-C	17	EXTREME	5	MEDIUM
38-STM-S	15	EXTREME	7	MEDIUM
39-STM-S	13	HIGH	4	MEDIUM
41-BUR-R	21	EXTREME	8	HIGH
43-STA-F	14	EXTREME	4	MEDIUM
44-STM-O	17	EXTREME	4	MEDIUM
47-STM-C	15	EXTREME	2	LOW
48-TRI-W	16	EXTREME	2	LOW
49-BUR-C	18	EXTREME	4	MEDIUM
50-STA-L	21	EXTREME	4	MEDIUM
51-STA-H	19	EXTREME	3	LOW
70-STA-C	17	EXTREME	11	HIGH
75-PRI-T	6	MEDIUM	4	MEDIUM
77-GEO-T	7	MEDIUM	4	MEDIUM
85-RIV-P	14	EXTREME	5	MEDIUM
13-NOR-M	5	MEDIUM	5	MEDIUM
27-MER-W	16	EXTREME	6	MEDIUM
28-MER-W	16	EXTREME	6	MEDIUM
34-GEO-S	12	HIGH	3	LOW

	Pre-intervention risk scores		Post-intervention risk scores	
Patient ID	Mean	Category	Mean	Category
52-CAT-B	14	EXTREME	6	MEDIUM
54-STM-P	14	EXTREME	6	MEDIUM
55-CAT-H	11	HIGH	6	MEDIUM
56-STG-S	6	MEDIUM	4	MEDIUM
57-STM-S	13	HIGH	4	MEDIUM
58-STM-M	12	HIGH	11	HIGH
59-BUR-S	15	EXTREME	6	MEDIUM
60-BUR-H	12	HIGH	5	MEDIUM
61-PRI-S	9	HIGH	5	MEDIUM
62-BUR-B	6	MEDIUM	5	MEDIUM
63-STA-R	8	HIGH	3	LOW
64-STA-H	6	MEDIUM	3	LOW
65-STM-T	7	MEDIUM	7	MEDIUM
66-MER-M	15	EXTREME	3	LOW
67-CAT-S	15	EXTREME	3	LOW
68-GEO-T	11	HIGH	5	MEDIUM
69-HAD-T	16	EXTREME	3	LOW
35-GEO-P	17	EXTREME	4	MEDIUM
37-STG-C	12	HIGH	5	MEDIUM
40-RIV-H	11	HIGH	4	MEDIUM
42-STM-S	11	HIGH	4	MEDIUM
45-GEO-D	11	HIGH	6	MEDIUM
86-HAD-E	20	EXTREME	7	MEDIUM
87-STG-E	17	EXTREME	5	MEDIUM

	Pre-intervention risk scores		Post-intervention risk scores	
Patient ID	Mean	Category	Mean	Category
88-TRI-S	10	HIGH	2	LOW
89-STM-B	13	HIGH	2	LOW
90-TRI-B	15	EXTREME	3	LOW
91-GEO-E	13	HIGH	2	LOW
92-CLA-J	15	EXTREME	2	LOW
95-PRI-N	11	HIGH	4	MEDIUM
96-STM-C	13	HIGH	2	LOW
72-JEN-D	8	HIGH	12	HIGH
80-STM-B	8	HIGH	5	MEDIUM

	Pre-intervention risk scores		Post-intervention risk scores	
Patient ID	Mean	Category	Mean	Category
97-JEN-D	10	HIGH	3	LOW
98-NOR-T	12	HIGH	2	LOW
99-NOR-C	8	HIGH	5	MEDIUM
73-HAD-G	8	HIGH	6	MEDIUM
76-MER-S	13	HIGH	7	MEDIUM
83-STM-S	14	EXTREME	12	HIGH
71-STA-S	15	EXTREME	3	LOW
93-MER-G	2	LOW	2	LOW
79-RIV-C	11	HIGH	7	MEDIUM

	Pre-intervention risk scores		Post-intervention risk scores	
Patient ID	Mean	Category	Mean	Category
100-CAT-W	9	HIGH	6	MEDIUM
101-STM-F	6	MEDIUM	5	MEDIUM
102-COR-H	7	MEDIUM	3	LOW
103-STM-W	13	HIGH	3	LOW
94-RIV-R	15	EXTREME	3	LOW
81-PRI-D	13	HIGH	4	MEDIUM
84-MER-R	10	HIGH	7	MEDIUM
74-NOR-T	6	MEDIUM	6	MEDIUM
78-RIV-W	16	EXTREME	16	EXTREME

Appendix 2.9 **Summary of mean risk scores assigned using NPSA risk matrix at pre and post intervention stage**

Appendix 2.10 Supporting data for ‘patient’s comments’ section of questionnaire

Comments provided in patient questionnaires

Positive comments described the effectiveness of the service but also focussed on the patient's satisfaction with the SPT delivering the service as highlighted in the example patient comments provided below:

"An excellent service which gave me great help (money well spent) when I was not able to cope with my drugs well and in a complete muddle".

"I would like to say my medicine lady is a really super person. She is so easy to take to; she makes me feel so comfortable because she explains things, not using a lot of medicines words I don't understand. She talks so that I understand what she is saying, I look forward to her visits she's a lovely lady and she makes me feel better too".

"This is the best support service I have received, what a wonderful asset to the NHS is Pippa Scrimshaw, she instantly put me at ease, she talked everything through with me and made sure that I had understood everything. I have severe hand problems and she found ways for me to manage things. I would thoroughly recommend Pippa to visit anyone who has problems with tablets".

Appendix 2.11 Supporting data for ‘caregiver’s comments’ section of questionnaire

Comments provided in patient caregiver questionnaires

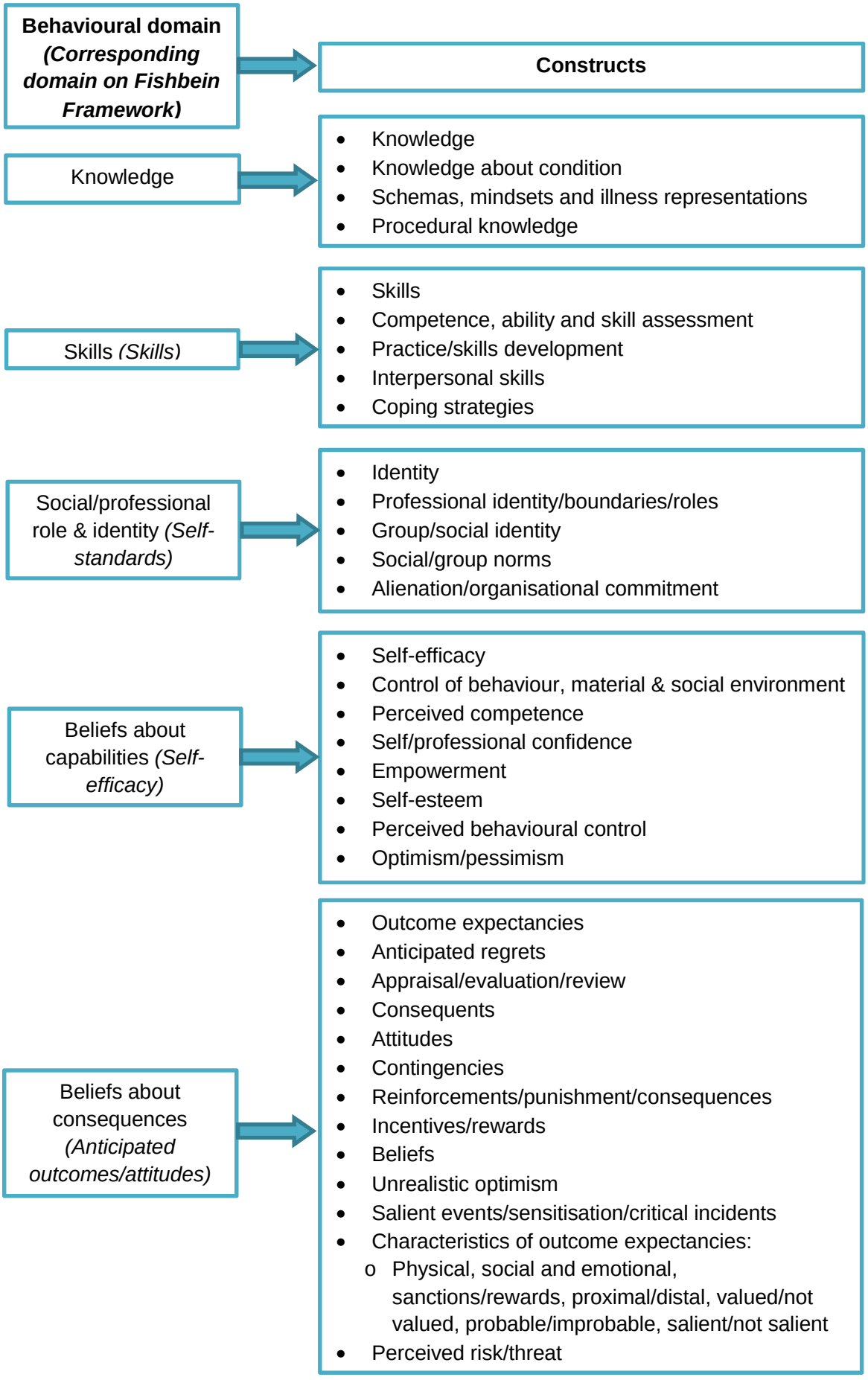
Comments focussed on feelings of less worry and greater confidence about correct medicines taking and also on general satisfaction and the personable approach and care offered by the SPT. The selected quotes highlight these points:

"This service has been a huge relief to me and my family. Pippa Scrimshaw was so nice to my parents on her visit; she made them feel so at ease and happy to try out her recommendations which are working very well for the both. Many thanks, a great service I say"

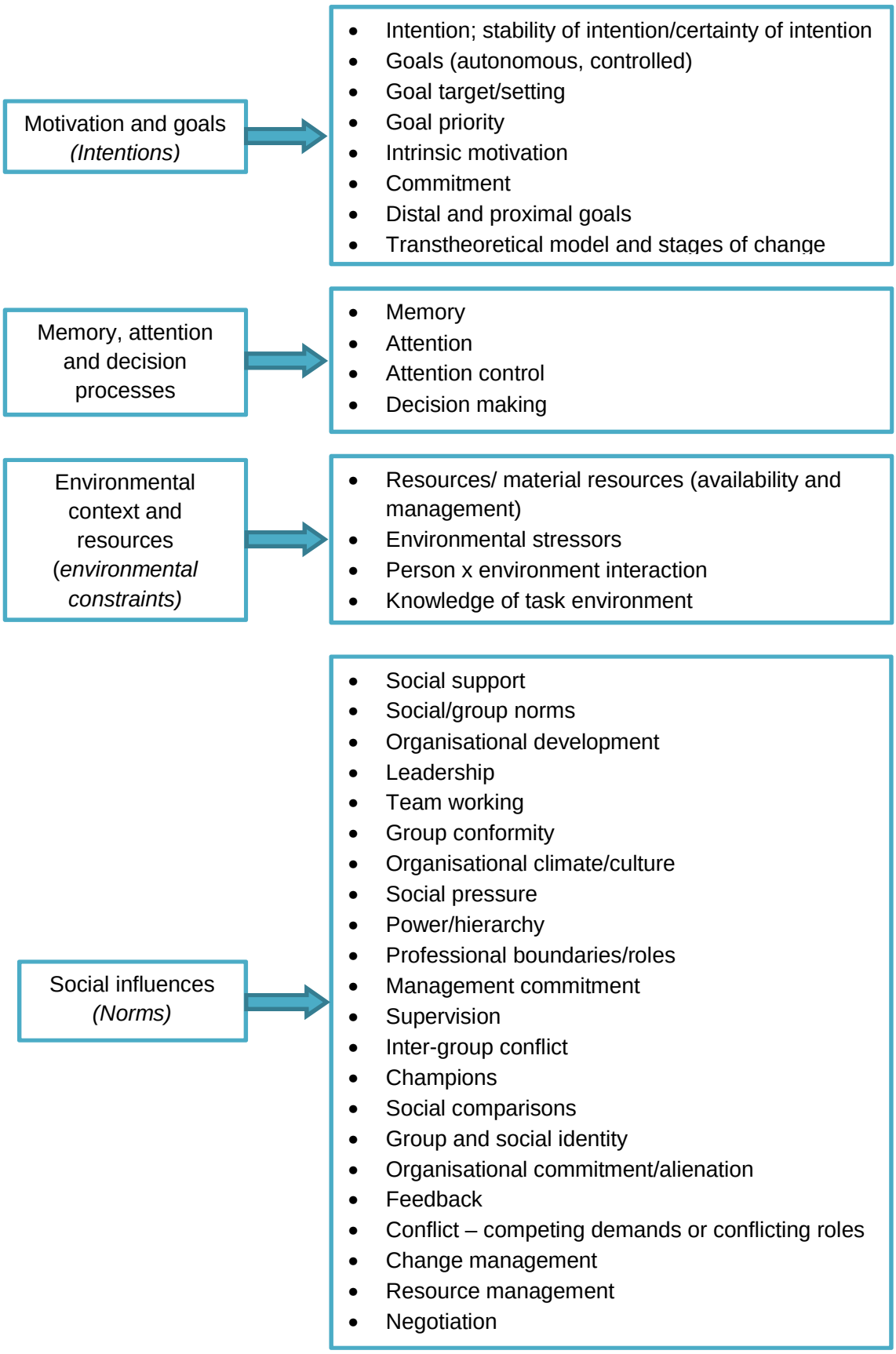
"I was so grateful for the help and advice given that I have given your number to a friend in a similar situation"

"I am more than pleased with the new arrangement and I am feeling more settled in my own piece of mind"

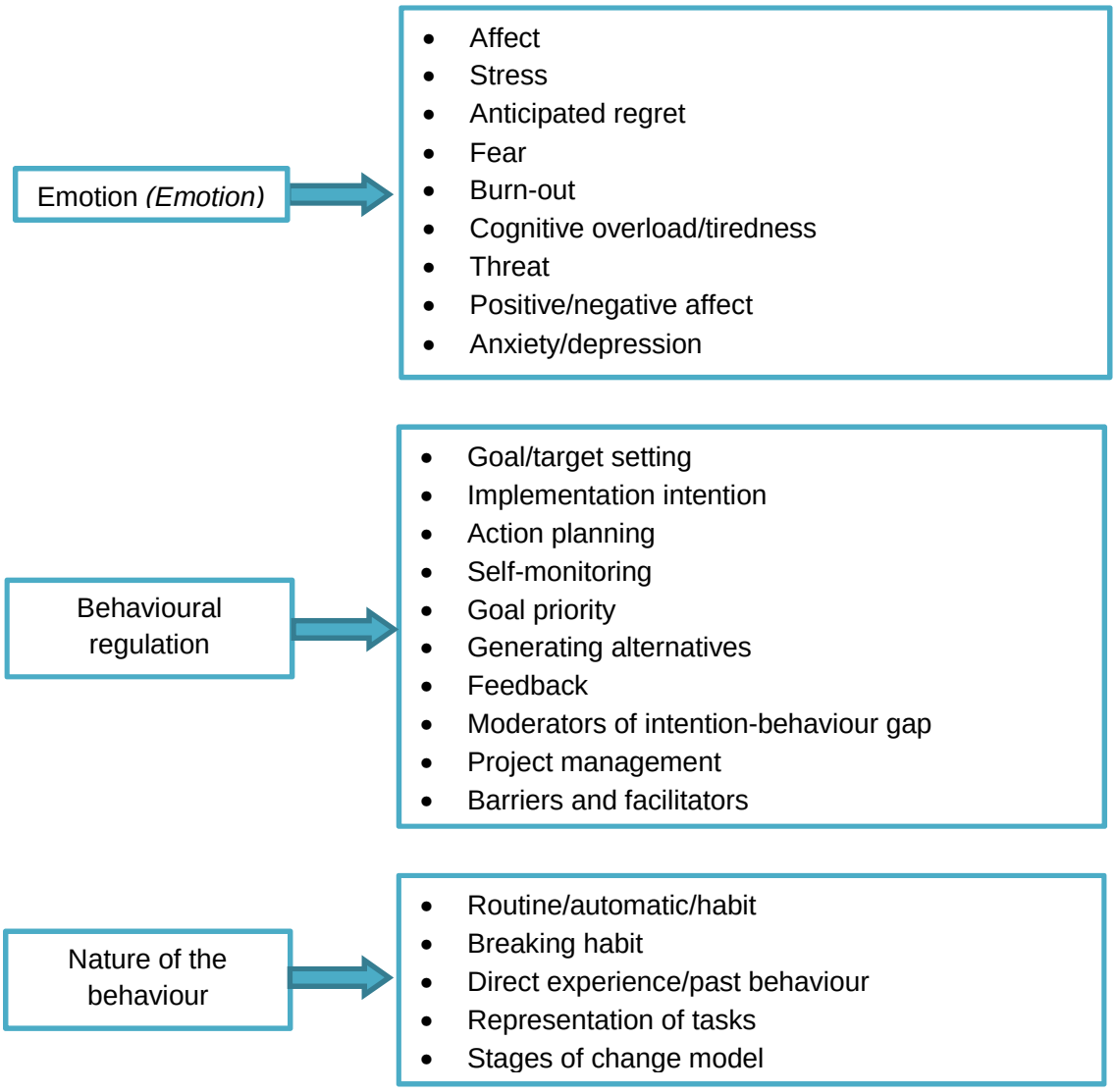
Appendix 3.1 Theoretical domains and component constructs of the original TDF[1]



Appendix 3.1 Theoretical domains and constructs of TDF[1]



Appendix 3.1 (continued) **Theoretical domains and constructs of TDF[1]**



Appendix 3.1 (continued) **Theoretical domains and constructs of TDF[1]**

Reference for appendix 3.1

1. Michie, S., et al. (2005). "Making psychological theory useful for implementing evidence based practice: a consensus approach." Quality and Safety in health care **14**(1): 26-33.

Appendix 3.2 Theoretical domains and refined definitions of updated TDF[1]

Domain	Definition
Knowledge	An awareness of the existence of something
Skills	An ability of proficiency acquired through practice
Social/professional role & identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting
Beliefs about capabilities	Acceptance of the truth, reality, or validity about an ability, talent or facility that a person can put to constructive use
Optimism	The confidence that things will happen for the best or that desired goals will be obtained
Beliefs about consequences	Acceptance of the truth, reality or validity about outcomes of a behaviour in a given situation
Reinforcement	Increasing the probability of a response by arranging a dependent relationship, or contingency between the response and a given stimulus
Intentions	A conscious decision to perform a behaviour or a resolve to act in a certain way
Goals	Mental representations of outcomes or end states that an individual wants to achieve
Memory, attention and decision processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives
Environmental context and resources	Any circumstances of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence and adaptive behaviour
Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings and behaviours
Emotion	A complex reaction pattern involving experiential, behavioural and physiological elements, by which the individual attempts to deal with a personally significant matter or event
Behavioural regulation	Anything aimed at managing or checking objectively observed or measured actions

Table A3.2 Domains and definitions of the refined TDF[1]

Reference for appendix 3.2

1. Cane, J., et al. (2012). "Validation of the theoretical domains framework for use in behaviour change and implementation research." Implementation Science **7**(1): 37.

Appendix 3.3 Summary of Abraham and Michie's 26 Behaviour Change Techniques (BCTs)[1]

Behaviour change technique	Description/definition
Provide information about the behaviour-health link	General information about behavioural risk, for example susceptibility to poor health outcomes or mortality risk in relation to behaviour
Provide information on consequences	Information about the benefits and costs of action or inaction, focussing on what will happen if the person does or does not perform the behaviour
Provide information about others approval	Information about what others think about the person's behaviour and whether others will approve or disapprove of any proposed behaviour change
Prompt intention formation	Encouraging the person to decide to act or set a general goal, for example, to make a behavioural resolution such as "I will take more exercise next week"
Prompt barrier identification	Identify barriers to performing the behaviour and plan ways to overcome them
Provide general encouragement	Praising or rewarding the patient for effort or performance without this being contingent on specified behaviours or standards of performance
Set graded tasks	Set easy tasks and increase difficulty until target behaviour is performed
Provide instruction	Telling the person how to perform the behaviour and/or preparatory behaviours
Model or demonstrate the behaviour	An expert shows the person how to correctly perform the behaviour, for example in a class or on video
Prompt specific goal setting	Involves detailed planning of what the person will do, including a definition of the behaviour specifying frequency, intensity or duration and specification of at least one context, that is, where, when, how or with whom
Prompt review of behavioural goals	Review and/or reconsideration of previously set goals or intentions
Prompt self-monitoring of behaviour	The person is asked to keep a record of the specified behaviour(s) (e.g. in a diary)
Provide feedback on performance	Providing data about the recorded behaviour or evaluating performance in relation to a set standard or others' performance, i.e. the person received feedback on their behaviour
Provide contingent rewards	Praise, encouragement or material rewards that are explicitly linked to the achievement of specified behaviours
Teach to use prompt or cues	Teach person to identify environmental cues that can be used to remind them to perform a behaviour including times of day or elements of contexts
Agree on behavioural contract	Agreement (e.g. signing) of a contract specifying behaviour to be performed so that there is a written record of the person's resolution witnessed by another
Prompt practice	Prompt the person to rehearse and repeat the behaviour or preparatory behaviours
Use follow-up prompts	Contacting the person again after the main part of the intervention is complete

Table A3.3 Summary of Abraham and Michie's taxonomy of behaviour change techniques used in interventions[1]

Behaviour change technique	Description/definition
Provide opportunities for social comparison	Facilitate observation of non-expert others' performance for example, in a group class or using video or case study
Plan social support or social change	Prompting consideration of how others could change their behaviour to offer the person help or (instrumental) social support, including 'buddy' systems and/or providing social support
Prompt identification as a role model	Indicating how the person may be an example to others and influence their behaviour or provide an opportunity for the person to set a good example
Prompt self-talk	Encourage the use of self-instruction and self-encouragement (aloud or silently) to support action
Relapse prevention	Following initial change, help identify situations likely to result in readopting risk behaviours or failure to maintain new behaviours and help person to plan to avoid or manage these situations
Stress management	May involve a variety of techniques (e.g. progressive relaxation) that do not target the behaviour but seek to reduce anxiety and stress
Motivational interviewing	Prompting the person to provide self-motivating statements and evaluations of their own behaviour to minimise resistance to change
Time management	Helping the person to make time for the behaviour (e.g. to fit into a daily schedule)

Table A3.3 Summary of Abraham and Michie's taxonomy of behaviour change techniques used in interventions[1]

Reference for table A3.3

1. Abraham, C. and S. Michie (2008). "A taxonomy of behavior change techniques used in interventions." Health Psychology **27**(3): 379.

Appendix 3.4 Summary of the BCTs deemed to be effect for changing the behavioural domains of the TDF[1]

Theoretical domain of TDF	BCTs agreed to be effective[1]
Social/ professional roles & identity	• Social processes of encouragement, pressure and support
Knowledge	• Information regarding behaviour, outcome
Skills	• Goal target specified: behaviour or outcome • Monitoring • Self-monitoring • Rewards; incentives (inc. self-evaluation) • Graded task, starting with easy task • Increasing skills: problem-solving, decision-making, goal-setting • Rehearsal of relevant skills • Modelling/demonstration of behaviour by others • Homework • Perform behaviour in different settings
Beliefs about capabilities	• Self-monitoring • Graded task, starting with easy task • Increasing skills: problem-solving, decision-making, goal-setting • Coping skills • Rehearsal of relevant skills • Social processes of encouragement, pressure and support • Feedback • Self-talk • Motivational Interviewing
Beliefs about consequences	• Self-monitoring • Persuasive communication • Information regarding behaviour, outcome • Feedback
Motivation and goals	• Goal target specified: behaviour or outcome • Contract • Rewards; incentives (inc. self-evaluation) • Graded task, starting with easy task • Increasing skills: problem-solving, decision-making, goal-setting • Social processes of encouragement, pressure and support • Persuasive communication • Information regarding behaviour, outcome • Motivational Interviewing
Memory, attention, decision and processes	• Self-monitoring • Planning, implementation • Prompts, triggers, cues
Environmental context & resources	• Environmental changes e.g. objects to facilitate behaviour
Social influences	• Social processes of encouragement, pressure and support

Table A3.4 Summary of effective BCTs for changing behaviours

Theoretical domain of TDF	BCTs agreed to be effective[1]
Emotion	• Stress management • Coping skills
Action planning	• Goal target specified: behaviour or outcome • Contract • Planning, implementation • Prompts, triggers, cues • Use of imagery

Table A3.4 (continued) **Summary of effective BCTs for changing behaviours**

Reference for table A3.4

1. Michie, S., et al. (2008). "From Theory to Intervention: Mapping Theoretically Derived Behavioural Determinants to Behaviour Change Techniques." Applied Psychology **57**(4): 660-680.

Appendix 4.1 Literature search strategy for systematic review

No.	Search term
1	medication* .ti,ab OR drug* .ti,ab OR medicine.ti,ab OR patient.ti,ab
2	adheren*.ti,ab OR complian*.ti,ab OR concordan*.ti,ab OR non-adheren*.ti,ab OR non adheren*.ti,ab. OR non-complian*.ti,ab OR non complian*.ti,ab. OR persist*.ti,ab.
3	1 AND 2
4	motivation* interview*.ti,ab OR motivation* enhancement therap*.ti,ab. OR behavio?r change counsel?ing.ti,ab OR implementation* intention*.ti,ab. OR if-then plan*.ti,ab OR if then plan*.ti,ab. OR motivation* counsel?ing.ti,ab. OR motivation* behavio?r.ti,ab OR motivation* change.ti,ab. OR motivation* intervention*.ti,ab. OR health behavio?r change*.ti,ab. OR brief intervention*.ti,ab. OR cognitive intervention*.ti,ab. OR cognitive technique*.ti,ab OR health behavio?r counsel?ing.ti,ab. OR problem solving treatment*.ti,ab. OR problem solving therap*.ti,ab
5	3 AND 4
6	Remove duplicates from 5

Table A4.1: Search terms applied to OVID interface and CINAHL database

The following terms were individually applied to the NeLM database:

Medication adherence cognitive techniques, medication adherence motivational interviewing, drug adherence motivational interviewing, cognitive intervention medication adherence, implementation intentions medicine, if then planning adherence, behaviour change counselling adherence, motivational behaviour change adherence, medication compliance motivational interviewing, motivational enhancement therapy adherence, motivational enhancement therapy.

Appendix 4.2 Summary of studies included in meta-analysis

Multi-component intervention using non-specific techniques								
Study	**Study type**	**Study setting**	**Disease area**	**Intervention personnel**	**Delivery personnel training**	**Intervention delivery style**	**Intervention length (average)**	**Follow up period**
Bailey *et al.* 1990[1]	RCT	Hospital clinic, USA	Asthma	Specialist	No details given	Telephone calls and in person	240 hours (4 x 60min sessions) over unknown period	12 months
Hovell *et al.* 2003[2]	RCT	Hospital clinic, USA	TB	Researcher	Trained research assistants used but no details provided	Telephone calls and in person	12 sessions of 15-30 minutes over 6 months	9 months
Molassiotis *et al.* 2003[3]	RCT	Hospital clinic, Hong Kong	HIV	Routine HCP	No details given	In person	12 sessions of unknown duration over 3months	6 months
Murphy *et al.* 2002[4]	RCT pilot	Community clinic, USA	HIV	Specialist	No details given as delivered by specialist	In person	Unknown number of sessions of unknown duration over 7 weeks	3 months
Pradier *et al.* 2003[5]	RCT	Hospital clinic, France	HIV	Routine HCP	Five day intense training course delivered by psychologists and monthly supervision	In person	3 sessions of 45-60 minutes over 3 months	6 months
Put *et al.* 2003[6]	RCT	Hospital clinic, Belgium	Asthma	Researcher	No details given	In person	360 hours (6 x 60 minutes sessions) over 3 months	6 months
Remien *et al.* 2005[7]	RCT	Community clinic, USA	HIV	Routine HCP	HCPs trained and supervised; no further details given	In person	4 sessions of 45-60 minutes over 5 weeks	8 weeks
Smith *et al*. 2003[8]	RCT	Community research office, USA	HIV	Routine HCP	No details given	In person	Unknown number of sessions of unknown duration over 12 weeks	12 weeks
Tuldra *et al*. 2000[9]	RCT	Hospital clinic, Spain	HIV	Routine HCP	Training delivered by a trained psychologist; no further details given	Unknown	No details provided	48 weeks

Table A4.2 Summary of interventions included in meta-analysis

Multi-component intervention using non-specific techniques								
Study	**Study type**	**Study setting**	**Disease area**	**Intervention personnel**	**Delivery personnel training**	**Intervention delivery style**	**Intervention length (average)**	**Follow up period**
Van Es *et al.* 2001[10]	RCT	Hospital clinic, Netherlands	Asthma	Routine HCP	Interventions delivered by 'specially trained asthma nurses'; no further details given	In person	7 sessions of 30-90 minutes over 12 months	2 years
Wagner *et al.* 2006[11]	RCT	Community clinic, USA	HIV	Routine HCP	Training delivered by trained research nurse and feedback offered; no further details given.	In person	Unknown number of sessions of 30-45 minutes over 48 weeks	48 weeks
Weber *et al.* 2004[12]	RCT pilot	Psychotherapy clinic, Netherlands	HIV	Specialist	Intervention delivered by trained psychotherapist; no further training described	In person	11 sessions of 45 minutes over 12 months	12 months
Interventions using MI alone as one component								
Study	**Study type**	**Study setting**	**Disease area**	**Intervention personnel**	**Delivery personnel training**	**Intervention delivery style**	**Intervention length (average)**	**Follow up period**
DiIorio *et al.* 2008 [13]	RCT	Hospital clinic, USA	HIV	Routine HCP	24 hours worth of training by certified MI trainers, skills assessment, on-going training & booster sessions as needed	Mostly in person with some telephone calls	5 sessions of 35 minutes over 12 months	12 months
Lavoie *et al.* 2011 [14]	RCT	Hospital clinic , Canada	Asthma	Unknown	No details given	In person	3 sessions of 30 minutes over 6 weeks	6 months

Table A4.2 (continued) **Summary of interventions included in meta-analysis**

Multi-component intervention using MI								
Study	**Study type**	**Study setting**	**Disease area**	**Intervention personnel**	**Delivery personnel training**	**Intervention delivery style**	**Intervention length (average)**	**Follow up period**
Cook *et al.* 2007[15]	Non-RCT	Telephone calls to patients at home, USA	Osteoporosis	Routine HCP	No details given, registered nurses used to deliver intervention	Telephone calls	1 hour (4 x 15 minute sessions) over 4 months	6 months
George *et al.* 2010[16]	RCT	Community pharmacies, Australia and Tasmania	Hypertension	Routine HCP	Face-to-face and online training, largely about study design and rationale, no other details given	In person	3 sessions of unknown duration over 6 months	6 months
Golin *et al.* 2006[17]	RCT	Community clinic, USA	HIV	Specialist	3 full days training by accredited MI trainers	In person	2 sessions of unknown duration over 2 months	3 months
Ireland *et al*. 2010[18]	Before & after	Hospital clinic , Canada	Hypertension	Routine HCP	Group training provided, no details given	In person and telephone calls	4.8 hours delivered over 7 sessions in 6 months	6 months
Lawrence *et al.* 2008[19]	Non-RCT	Telephone calls to patient's at home, USA	CVD	Routine HCP	Training on health behaviour change techniques, no other details provided	Telephone calls	One-off intervention of unknown duration	3 months
Riekert *et al.* 2011[20]	Before & after	Visits to patients own homes, USA	Asthma	Routine HCP	Two days MI training delivered by a specialist, role play training & bi-weekly supervision	In person	5 sessions of 30-40 minutes delivered over 8 weeks	10 weeks
Safren *et al.* 2001[21]	RCT pilot	Community clinic, USA	HIV	Routine HCP	No details given	In person	One-off intervention of unknown duration	12 weeks
Thrasher *et al.* 2006[22]	Before & after	Community clinic, USA	HIV	Specialist	3 full days training by MI experts, bi-weekly feedback and group meetings	In person	1 hour (2 x 30 minute sessions) delivered over 12 weeks	12 weeks

Table A4.2 (continued) Summary of interventions included in meta-analysis

Interventions using techniques based on MI								
Study	**Study type**	**Study setting**	**Disease area**	**Intervention personnel**	**Delivery personnel training**	**Intervention delivery style**	**Intervention length (average)**	**Follow up period**
Berger *et al.* 2005[23]	RCT	Telephone calls to patients at home, USA	Multiple Sclerosis	Researcher	8 hour training sessions on study background, role playing and case scenarios	Telephone calls	9 sessions of unknown duration delivered over 3 months	3 months
De Bruin *et al.* 2005[24]	Before & after	Hospital clinic, Netherlands	HIV	Routine HCP	Interventions delivered by trained HIV nurse; no further details provided	In person	2 sessions lasting 10-45 minutes delivered over 3 months	3 months
DiIorio *et al.* 2003[25]	RCT pilot	Community clinic, USA	HIV	Routine HCP	25 hours of training and practice sessions by MI trainer and evaluation of counselling skills	In person	5 x 35 minutes sessions delivered over 12 months	8 weeks
Kalichman *et al.* 2005[26]	Before & after	Community based non-clinical setting, USA	HIV	Routine HCP	Intervention delivered by 'staff with experience in the field'; no further details provided	In person	3 sessions lasting 2.5 hours in total delivered over 3 weeks	3 months
Ogedegbe *et al.* 2008[27]	RCT	Community clinic, USA	Hypertension	Researcher	2 full day training sessions delivered by experienced MI trainers plus one day booster session	In person	4 sessions lasting 30-40 minutes delivered over 12 months	12 months
Interventions using III								
Study	**Study type**	**Study setting**	**Disease area**	**Intervention personnel**	**Delivery personnel training**	**Intervention delivery style**		
Brown *et al.* 2009[28]	RCT	Hospital clinic, UK	Epilepsy	Not in person	Not delivered in person	Questionnaire completion	One-off intervention of unknown duration	1 month
Sheeran *et al.* 1999[29]	RCT	Visits to patient's at home, UK	Vitamin Supplements	Not in person	Not delivered in person	Questionnaire completion	One-off intervention of unknown duration	3 weeks

Table A4.2 (continued) **Summary of interventions included in meta-analysis**

References for table A4.2

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Appendix 4.3 Identified intervention components for studies included in meta-analysis

Multi-component intervention using non-specific techniques																														
Study	**Identified intervention components**																													
	Action planning	Adherence advice/support/cues	Adherence monitoring and feedback	Behavioural adaptations	Creating positive attitudes	Developing adherence skills	Developing problem solving skills	Developing coping strategies	Eliciting illness representations	Encouraging effective social support	Education	Encouraging self-care	Goal setting	Identifying/challenging negative cognitions	Identifying and resolving patient concerns	Identifying/overcoming adherence barriers	Improving communication with HCPs	Increasing cognitive skills	Increasing motivation	Increasing patient knowledge	Increasing positive attitudes	Increasing self-awareness	Increasing sense of control over health	Increasing sense of self-efficacy/confidence	Medication review	Praising and encouraging/positive feedback	Promoting support seeking behaviours	Psychotherapy	Rehearsing medication taking	Self-monitoring	Tailoring of dosing schedule to patient needs
Bailey et al 1990					✓					✓	✓	✓					✓	✓													
Hovell et al 2003		✓									✓		✓			✓										✓	✓				
Molassiotis et al 2003										✓	✓					✓										✓					
Murphy et al 2002	✓										✓					✓							✓								
Pradier et al 2003							✓	✓		✓					✓	✓						✓		✓							

Table A4.3 Identified intervention components for studies included in meta-analysis

Multi-component intervention using non-specific techniques																															
Study	**Identified intervention components**																														
	Action planning	Adherence advice/support/cues	Adherence monitoring and feedback	Behavioural adaptations	Creating positive attitudes	Developing adherence skills	Developing problem solving skills	Developing coping strategies	Eliciting illness representations	Encouraging effective social support	Education	Encouraging self-care	Goal setting	Identifying/challenging negative cognitions	Identifying and resolving patient concerns	Identifying/overcoming adherence barriers	Improving communication with HCPs	Increasing cognitive skills	Increasing motivation	Increasing patient knowledge	Increasing positive attitudes	Increasing self-awareness	Increasing sense of control over health	Increasing sense of self-efficacy/confidence	Medication review	Praising and encouraging/positive feedback	Promoting support seeking behaviours	Psychotherapy	Rehearsing medication taking	Self-monitoring	Tailoring of dosing schedule to patient needs
Put et al 2003				✓					✓		✓			✓															✓	
Remien et al 2005							✓			✓	✓					✓	✓							✓						
Smith et al 2003			✓			✓				✓	✓													✓	✓					
Tuldra et al 2000						✓	✓				✓			✓	✓					✓				✓						✓
Van Es et al 200								✓		✓	✓						✓				✓			✓						
Wagner et al 2006							✓			✓	✓			✓		✓			✓		✓			✓					✓		✓
Weber et al 2004													✓															✓			

Study	Identified intervention components																													
	Action planning	Adherence advice/support/cues	Adherence monitoring and feedback	Behavioural adaptations	Creating positive attitudes	Developing adherence skills	Developing problem solving skills	Developing coping strategies	Eliciting illness representations	Encouraging effective social support	Education	Encouraging self-care	Goal setting	Identifying/challenging negative cognitions	Identifying and resolving patient concerns	Identifying/overcoming adherence barriers	Improving communication with HCPs	Increasing cognitive skills	Increasing motivation	Increasing patient knowledge	Increasing positive attitudes	Increasing self-awareness	Increasing sense of control over health	Increasing sense of self-efficacy/confidence	Medication review	Motivational Interviewing (MI)	Praising and encouraging/positive feedback	Promoting support seeking behaviours	Rehearsing medication taking	Resolving ambivalence	Self-monitoring	Tailoring of dosing schedule to patient needs
Interventions using MI as sole component																														
DiIorio et al 2008	✓															✓			✓	✓				✓						✓		
Lavoie et al 2011																										✓					
Multi-component interventions using MI																															
Cook et al 2007						✓	✓									✓			✓				✓	✓								
George et al 2010		✓									✓														✓	✓					✓	
Golin et al 2006						✓									✓								✓			✓					

Table A4.3 (continued) **Identified intervention components for studies included in meta-analysis**

Multi-component interventions using MI																																
Study	**Identified intervention components**																															
	Action planning	Adherence advice/support/cues	Adherence monitoring and feedback	Behavioural adaptations	Counselling	Developing adherence skills	Developing problem solving skills	Developing coping strategies	Eliciting illness representations	Encouraging effective social support	Education	Encouraging self-care	Goal setting	Identifying/challenging negative cognitions	Identifying and resolving patient concerns	Identifying/overcoming adherence barriers	Improving communication with HCPs	Increasing cognitive skills	Increasing motivation	Increasing patient knowledge	Increasing positive attitudes	Increasing self-awareness	Increasing sense of control over health	Increasing sense of self-efficacy/confidence	Medication review	Motivational Interviewing (MI)	Praising and encouraging/positive feedback	Promoting support seeking behaviours	Rehearsing medication taking	Resolving ambivalence	Self-monitoring	Tailoring of dosing schedule to patient needs
Ireland et al 2010		✓			✓														✓					✓		✓				✓	✓	✓
Lawrence et al 2008				✓	✓											✓			✓					✓		✓				✓		
Riekert et al 2011	✓						✓				✓		✓			✓			✓											✓		
Safren et al 2001							✓				✓						✓		✓										✓		✓	
Thrasher et al 2006						✓					✓		✓						✓					✓		✓					✓	

Invention using MI-based techniques																																
Study	**Identified intervention components**																															
	Action planning	Adherence advice/support/cues	Adherence monitoring and feedback	Behavioural adaptations	Creating positive attitudes	Developing adherence skills	Developing problem solving skills	Developing coping strategies	Eliciting illness representations	Encouraging effective social support	Education	Encouraging self-care	Goal setting	Identifying/challenging negative cognitions	Identifying and resolving patient concerns	Identifying/overcoming adherence barriers	Improving communication with HCPs	Increasing cognitive skills	Increasing motivation	Increasing patient knowledge	Increasing positive attitudes	Increasing self-awareness	Increasing sense of control over health	Increasing sense of self-efficacy/confidence	Motivational feedback	Motivational Interviewing (MI)	Praising and encouraging/positive feedback	Regimen simplification/tailoring	Rehearsing medication taking	Resolving ambivalence	Self-monitoring/journal keeping	Implementation Intention Intervention (III)
Berger et al 2005											✓								✓											✓		
De Bruin et al 2005							✓												✓						✓							✓
DiIorio et al 2003											✓								✓											✓		
Kalichman et al 2005	✓	✓				✓	✓			✓	✓		✓			✓			✓	✓					✓			✓				
Ogedegbe et al 2008																✓			✓											✓		

Table A4.3 (continued) **Identified intervention components for studies included in meta-analysis**

Invention using Implementation Intention Interventions (III)																														
Study	**Identified intervention components**																													
	Action planning	Adherence advice/support/cues	Adherence monitoring and feedback	Behavioural adaptations	Creating positive attitudes	Developing adherence skills	Developing problem solving skills	Developing coping strategies	Eliciting illness representations	Encouraging effective social support	Education	Encouraging self-care	Goal setting	Identifying/challenging negative cognitions	Identifying and resolving patient concerns	Identifying/overcoming adherence barriers	Improving communication with HCPs	Increasing cognitive skills	Increasing motivation	Increasing patient knowledge	Increasing positive attitudes	Increasing self-awareness	Increasing sense of control over health	Increasing sense of self-efficacy/confidence	Medication review	Motivational Interviewing (MI)	Praising and encouraging/positive feedback	Promoting support seeking behaviours	Rehearsing medication taking	Implementation Intention Interventions (III)	Self-monitoring	Tailoring of dosing schedule to patient needs
Brown et al 2009																													✓		
Sheeran et al 1999																													✓		

Table A4.3 (continued) **Identified intervention components for studies included in meta-analysis**

Appendix 5.1 Ethics committee communications for consultation exercises

Claire Easthall
School of Pharmacy
University of East Anglia
Norwich Research Park
Norwich
NR4 7TJ

Research & Enterprise Services
REN West (SCI)
University of East Anglia
Norwich

NR4 7TJ

21 November 2012

Dear Claire

Project Title: Development of a screening tool to identify patient barriers to medication adherence.

Reference: 2012/2013-04

The amendments to you above proposal have been considered be the Chair of the Faculty Research Ethics Committee and we can confirm that your proposal has been approved.

Please could you ensure that any further amendments to wither the protocol or documents submitted are notified to us in advanced and also that any adverse events which occur during your project are reported to the Committee. Please could you also arrange to send us a report once your project is completed.

The Committee would like to wish you good luck with your project.

Yours sincerely

Yvonne Kirkham
Project Officer

Appendix 5.2 Example of ‘recruitment poster’ used in participant consultation exercise

Finding out the difficulties of taking medicines: An invitation to participate in a focus group study

University of East Anglia

Researchers from the School of Pharmacy at the University of East Anglia are looking for volunteers to help with an important part of their study.

Who are we looking for?

We need people who are:

- Prescribed any medicines to prevent heart disease; this includes low dose aspirin, blood pressure medicines and 'statins' to reduce cholesterol
- Aged over 18 years of age
- Able to read and speak English
- Not taking medicines for the treatment of addiction or mental health problems

If you know anybody who matches these criteria and who you think may like to join the study, please let them know of the study and pass on the researchers contact details.

What would you have to do if you participate?

If selected, you will be invited to attend an informal meeting between two researchers and 6-8 other members of the public. The group will be asked for their thoughts on some written statements concerning why people may not take their medicines as prescribed.

The meeting will last two hours and will most likely be held at the UEA. Participants will be given a **£10 high street shopping voucher** as a thank you for their time.

Who should I contact if I'm interested in participating?

If you're interested in participating in this study (or you know somebody else who is) please contact the lead researcher **Claire Easthall on c.easthall@uea.ac.uk or 01603 591973** with your contact details. An information pack containing a consent form and full details of the study will be sent to you, with instructions for what to do if you would like to participate.

Appendix 5.3 Participant information leaflet for consultation exercise

with the consent form. The survey will provide information to ensure we have a good mix of different people in each focus group

Whilst most of the questions in the survey are fairly 'routine' such as your name, address, age and gender, others may seem a little strange. We need to know how many medicines you take and whether you pay for your prescription as this might influence your thoughts on the difficulties of taking medicines as prescribed. We also need to have an idea of how easy or difficult you find reading certain materials such as doctors' letters. This is because we need to be sure that our questionnaire is suitable for people who sometimes find reading things a bit tricky. The information given on the survey is strictly confidential and will only be seen by the research team at the UEA.

If you change your mind, you are free to withdraw from the study at any time, without giving a reason.

What happens after the focus groups?

The focus groups will help to confirm what the final questionnaire looks like. This will be posted to you for your feedback to make sure you think that it is OK. Information on the findings of the focus group and how the questionnaire was developed will be published, but this will not include any names or personal details that would make the focus group participants identifiable.

Who is doing this research?

This research is being carried out by the University of East Anglia.

What if there is a problem or I would like more information?

In the first instance, please contact the lead researcher Claire Easthall:

Address: School of Pharmacy,
University of East Anglia,
Norwich, Norfolk, NR4 7TJ

Telephone: 01603 591973
e-mail: c.easthall@uea.ac.uk

If your concern is about the lead researcher or you are not satisfied that your concern has been addressed, the lead researcher's supervisor, Debi Bhattacharya, can be contacted on the address given above or via telephone on 01603 593391 or e-mail at d.bhattacharya@uea.ac.uk

In circumstances where you would like to make a compliant about the study, independently of the research team, your complaint can be directed towards Mark Searcey who is the Head of the School of Pharmacy at UEA. Mark can be contacted on 01603 592026 or at m.searcey@uea.ac.uk. His contact address is the same as the UEA address provided above.

Participant information leaflet vs2 Oct. '12

Finding out the difficulties of taking medicines

University of East Anglia

An invitation to participate in a focus group study

What is this study about?

This study is about finding out what might get in the way of someone taking their medicines as prescribed.

We're developing a questionnaire for patients to tell us their main reasons for not taking their medicines as prescribed. We will use this information to then give them the right support to take their medicines as prescribed.

For the questionnaire to work, it is important that we ask the right questions and that they are easily understood. So we are asking members of the public to give us their views on the questionnaire in a focus group discussion.

What is a focus group?

A focus group is a meeting between 6 and 8 people, brought together to discuss a topic. In this focus group, participants will chat about their thoughts on the difficulties of

taking medicines and the questionnaire that we've developed.

What will the focus group involve?

Two researchers from the UEA will be at the focus group to structure the discussions. The focus group will last around two hours and we'll stop for a short break halfway through. There will be light refreshments provided. As a thank-you for taking part, we will also give you a £10 retail gift voucher.

The questionnaire will have several 'statements' about difficulties with taking medicines. During the focus group, the researcher will show the group these statements one-by-one and then ask the group whether the statement:

- makes sense
- could be better worded or improved
- represents something that causes genuine difficulty with taking medicines.

Similar statements will be grouped together. Once all of the statements in a group have been discussed the researcher will ask:

- which statements seem to be most important
- whether there are any difficulties with taking medicines that have been missed.

The focus group will be tape recorded so that we don't miss anything said.

Am I suitable for participation?

This information leaflet has been sent to you because you were interested in participating. We're looking for certain people to take part.

To be suitable you must:

- be prescribed a medicine for the prevention of heart disease, this includes any medicines from the following list:
  - low dose aspirin (75mg)
  - Statins (for lowering cholesterol)
  - blood pressure medicines
- be aged over 18 years and be able to sign the informed consent form enclosed

It doesn't matter whether you always take your medicines as prescribed or whether you sometimes miss doses for any reason; we're interested in your thoughts either way.

Whilst we'd like to welcome everybody into this study, some people are not suitable:

- people who cannot read or speak English – as they will need to read and discuss the questionnaire statements
- people who are taking medicines for the treatment of addiction or mental health problems – as these patients often have very specific barriers to medication adherence.

If you're unsure whether you are suitable, please feel free to telephone Claire Easthall at the UEA on 01603 591973.

How will my opinion be heard?

The group will be supported to discuss the topics openly so that everyone is able to speak freely and comfortably.

Are there any disadvantages to taking part?

We don't think that there are any

disadvantages to taking part in this study, only the time that we ask you to give up.

What happens if I agree to take part?

We would like the opinions of a wide range of people and so may not need everybody that agrees to take part. If you agree to take part, we will let you know by letter or telephone whether or not we need you, within 4 weeks of receiving your consent form.

If you are invited to attend a focus group it will most likely take place at the university and we will offer you a choice of dates and times to attend.

What about confidentiality?

Only the researchers in the room for the focus group will be able to identify you. Nothing that can identify you will be published in any way. The recording will be kept in a secure location at the UEA. The information that you share with us will only be used for this research study. It will not be shared with your GP or anybody else.

What should I do if I've decided to take part?

If you'd like to take part in this study please complete the consent form that came with this leaflet and return it to us in the pre-paid envelope.

If you're based at UEA you can also return the documents in the internal mail. We'd also like you to fill in a brief survey and return this

Appendix 5.4 Consent form for participant consultation exercise

Finding out the difficulties of taking medicines: focus group consent form

Thank you for taking an interest in this study. If you would like to take part in the focus groups, please complete this consent form by initialling the boxes below and filling in the details at the bottom of the form. Once completed, please return this form, together with the brief survey, to the University of East Anglia (UEA), by post, using the pre-paid envelope provided. Alternatively if you are based at UEA, the forms can be returned to Claire Easthall in the School of Pharmacy via the internal mail system.

Focus group consent form

1. I confirm that I have read and understand the information sheet dated Oct. 2012 (version 2) for the above study. ☐

2. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

3. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

4. I am willing to allow the discussion within the focus group to be audio-taped for the purposes of analysing the conversations that take place. ☐

5. I understand that the research team will use the information that I give on the brief survey to decide whether I am suitable for the focus group and that they will contact me accordingly with further details. ☐

6. I understand that the research team will contact me again after the focus group to ask my thoughts on the questionnaire that they have developed. ☐

7. I agree to take part in the above study. ☐

Family name: _____ First name: _____

Signature: _____ Date: _____

Appendix 5.5 Brief survey for consultation exercise recruitment

Finding out the difficulties of taking medicines: focus group participation survey

University of East Anglia

Thank you for taking an interest in this study. If, having read the enclosed information leaflet, you would like to take part in the focus groups, please complete this survey. The survey has three sections and should take about five minutes. Once completed, please return this **survey** and the **consent form**, to the University of East Anglia, using the enclosed pre-paid envelope.

Section one: Details about yourself

Please answer the questions below in the spaces provided.

Name: _____ Telephone number: _____

Address: _____

_____

Age: _____ Gender: _____ Number of medicines that you regularly take: _____

Do you pay for your prescriptions? YES/NO (please delete as appropriate)

Section two: How easy do you find written material to read?

Please answer the question below by ticking (☑) the response you think best represents you:

How often do you need to have somebody help you when you read instructions, pamphlets or other written material from your doctor or pharmacy?

Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Always ☐

Section three: Your preferences for attending a focus group

For each of the suggested times below, please select from options A-D to indicate what time would be most convenient for you to attend a focus group.

A. This would be my first choice, this time would suit me well
B. This time is fine for me, I'd be happy to attend then
C. I could probably attend at this time but it wouldn't be my first choice
D. This time would be really tricky for me, I don't think I could attend a focus group at this time

Weekday morning: _____ Weekday afternoon: _____ Weekday evening:_____

Saturday morning: _____ Saturday afternoon: _____

Appendix 5.6 Summary of study characteristics of studies included in literature review of medication adherence barriers

Author and date	Full text used?	Disease area	Population	Barrier identification method	No. of participants/studies
Alqasem *et al.* 2010[2]	No – conference abstract	Hypertension	Patients from the United Arab Emirates receiving anti-hypertensives	Semi-structured interviews	20 hypertensive patients recruited from cardiology outpatient clinic
Amico *et al.* 2007[3]	Yes	HIV	HIV positive patients in the deep south of America	Patient interviews	72 HIV+ patients confessing self-reported non-adherence
Biadgilign *et al.* 2009[4]	No- full text not available	HIV	Paediatric HIV+ patients in Ethiopia	Qualitative study – no specific details	12 caregivers and 14 key informants from 5 hospitals
Bregnballe *et al.* 2011[5]	Yes	Cystic Fibrosis (CF)	Danish adolescents and young adults with CF	Questionnaire based survey	88 adolescents and 161 parents
Buchanan *et al.* 2012[6]	Yes	HIV	USA based HIV infected children and youth	Questionnaire regarding potential barriers	120 patients
Campbell *et al.* 2012[7]	No – conference abstract	Chronic conditions	Cognitively impaired older adults	Systematic review	10 observational studies
Cedillo-Galindo & Gracida 2011[8]	Yes	Immunosuppressive therapy – renal transplant	Renal transplant recipients in Mexico	Patient surveys	177 patients
Compton *et al.* 2010[9]	Yes	Chronic conditions	US based Latino patients who had failed to collect a repeat prescription from the pharmacy	Patient survey over telephone	38 patients
Constantiner & Cukor 2011[10]	No – could not access	Immunosuppressive therapy – renal transplant	US based renal transplant patients	Patient questionnaires	94 patients
Dahab *et al.* 2008[11]	Yes	HIV	South African HIV+ patients	Qualitative interviews	6 Patients on ART therapy and 6 healthcare providers

Table A5.6 Summary of studies included in literature review of adherence barriers

Author and date	Full text used?	Disease area	Population	Barrier identification method	No. of participants/studies
Dennis *et al.* 2011[12]	Yes	Hypertension	Indian based patients with hypertension	Patient questionnaire	608 patients
Dziuban *et al.* 2010[13]	Yes	Cystic fibrosis (CF)	US based adolescents with CF	Patient questionnaire	60 patients
Ellis *et al.* 2011[14]	Yes	Dermatology	Caregivers of US based children with skin problems e.g. eczema	Caregiver survey	101 caregivers of children attending dermatology outpatient clinic
Farsaei *et al.* 2010[15]	No – conference abstract	Type two diabetes	Iranian patients taking oral anti-diabetic drugs	Open ended questions	248 patients
Fetzer *et al*. 2011[16]	No – could not access	HIV	Paediatric patients in a sub-Saharan setting	In depth qualitative interviews	24 HIV positive children and their caregivers
Fields *et al*. 2012[17]	No – conference abstract	HIV	Adolescents with HIV (country unknown)	Semi-structured interviews	30 patients
Gadkari *et al.* 2011[18]	No – conference abstract	General chronic conditions	General populations	Systematic review	117 studies included
Gellad *et al.* 2011[19]	Yes	Chronic conditions -elderly	USA based elderly patients	Systematic review	9 studies included (cost and regimen complexity excluded)
Gidman *et al.* 2011[20]	No – conference abstract	Chronic diseases	Adolescent school children in UK	Semi-structured focus groups	23 school children
Gordon *et al.* 2009[21]	Yes	Immunosuppressive therapy	US based renal transplant patients	Semi-structured interviews	82 patients
Greenley *et al.* 2010[22]	Yes	Inflammatory bowel disease	Adolescents with IBD – US based	Self-report questionnaires	64 adolescents and 86 parents
Ibrahim *et al.* 2011[23]	No- full text not available	Chronic diseases – diabetes, hypertension or hyperlipidaemia	Patients in the United Arab Emirates	Patient questionnaire	240 patients
Ingerski *et al.* 2010[24]	Yes	Inflammatory bowel disease (IBD)	US based adolescents with IBD	Questionnaires and semi-structured interviews	174 adolescents and their carers

Table A5.6 (continued) Summary of studies included in literature review of adherence barriers

Author and date	Full text used?	Disease area	Population	Barrier identification method	No. of participants/studies
Joglekar *et al.* 2011[25]	Yes	HIV	Indian patients with HIV	Patient interviews	32 patients
Kennedy *et al.* 2008[26]	Yes	Chronic illnesses	US based medicare patients	Patient survey	664 patients
Konkle-Parker *et al.* 2008[27]	Yes	HIV	Minority populations in southern US states	3 focus groups	20 patients with HIV
Kripalani *et al.* 2008[28]	Yes	Cardiovascular (acute coronary syndrome(ACS))	US based patients recently discharged from hospital following an admission for ACS	Telephone interviews	84 patients
Kulchaitanaroaj *et al.* 2010[29]	No – conference abstract	HIV	HIV+ patients living in rural states of USA	Patient survey	202 patients
Kumarasamy *et al.* 2005[30]	Yes	HIV	HIV+ Indian patients	In-depth patient interviews	60 patients
Lacey *et al.* 2009[31]	Yes	Glaucoma	UK based patients with glaucoma	Focus groups and semi-structured interviews	24 patients
Marhefka *et al.* 2008[32]	Yes	HIV	US based paediatric HIV patients	Caregiver interviews	Caregivers of 127 HIV positive children
Mills *et al.* 2006[33]	Yes	HIV	Multi-national including both developed and developing nations	Systematic review and meta-analysis of patient reported barriers	84 studies including both qualitative and quantitative work
Morales *et al.* 2012[34]	Yes	Immunosuppressive therapy	Spanish liver and renal transplant patients	Patient questionnaire	1983 renal transplant and 1479 liver transplant patients
Murray *et al.* 2009[35]	Yes	HIV	Urban Zambian women with HIV	Qualitative techniques – free listing and key informant interviews	47 patients

Table A5.6 (continued) Summary of studies included in literature review of adherence barriers

Author and date	Full text used?	Disease area	Population	Barrier identification method	No. of participants/studies
Nair *et al.* 2011[36]	Yes	Hypertension	US based non-adherent hypertensive patients	Telephone survey	2451 patients
Odegard and Gray 2008[37]	No – could not access	Type two diabetes	US based patients with poorly controlled type 2 diabetes	Questionnaire	77 patients
Pallares *et al.* 2009[38]	Yes	Cardiovascular	US based patients taking clopidogrel post stent placement	Telephone interviews	257 patients
Peyrot *et al*. 2012[39]	Yes	Diabetes	Insulin dependent diabetics from China, France, Japan, Germany, USA and UK	Internet survey of patients and healthcare providers	1250 healthcare providers and 1530 patients
Senkomago *et al.* 2011[40]	Yes	HIV	Rural HIV population in Uganda	Self-reported questionnaire	140 patients
Silva *et al.* 2009[41]	No – conference abstract	Hypertension	Portuguese patients with hypertension	Self-reported questionnaire	1005 patients
Simons *et al*. 2009[42]	Yes	Immunosuppressive therapy	US based adolescent transplant recipients	Interviews with patients and their caregivers	80 patients and their caregivers
Sleath *et al.* 2009[43]	Yes	Glaucoma	Indian patients with glaucoma	Patient survey	243 patients
Talati *et al.* 2010[44]	No- conference abstract	Asthma	Inner city African American adolescents with asthma	Focus groups	4 patients
Toh *et al.* 2010[45]	Yes	Heart failure	Australian patients with chronic heart failure	Observational study	66 patients
Turner *et al.* 2009[46]	Yes	Hypertension	Racially diverse group of elderly patients in USA with hypertension	Telephone survey	202 patients
Van der Loock *et al.* 2011[47]	No – conference abstract	Immunosuppressive therapy – transplant	Renal, liver and heart transplant recipients – unknown country	Novel questionnaire to identify barriers	440 transplant recipients
Vawter *et al.* 2008[48]	Yes	Hypertension (HT)	US based – adults with hypertension	Data from larger 'health styles' survey	1432 survey respondents receiving medicines for HT

Table A5.6 (continued) Summary of studies included in literature review of adherence barriers

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Appendix 5.7 Preliminary adherence barriers statements

Whilst positively and negatively phrased statements were created, only one option for each statement is shown.

***** In barrier column represents a barrier added in from background knowledge and NOT something identified through literature search

***** In adherence barrier statement column represents a negatively phrased statement that will be reverse scored in the questionnaire

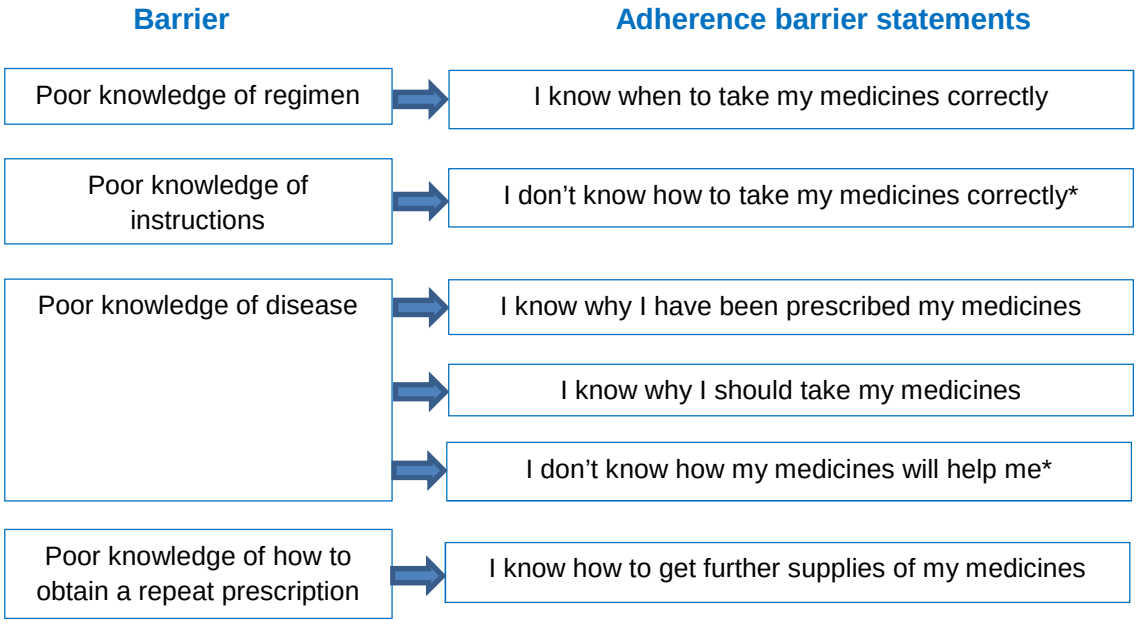


Figure A5.7.1 **Adherence barriers and proposed statements for the 'knowledge' behavioural domain**

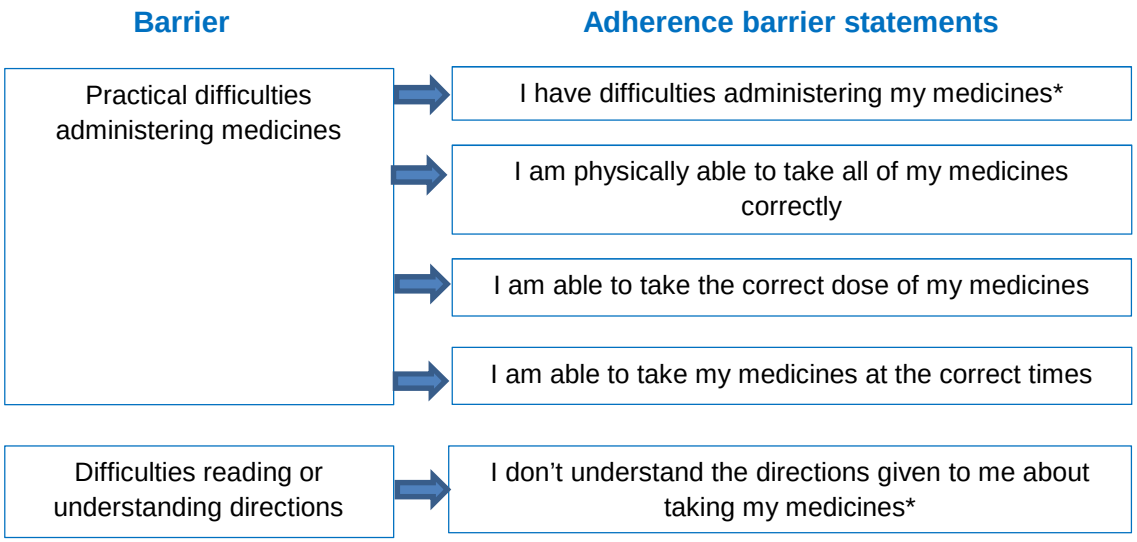


Figure A5.7.2 **Adherence barriers and proposed statements for the 'skills' behavioural domain**

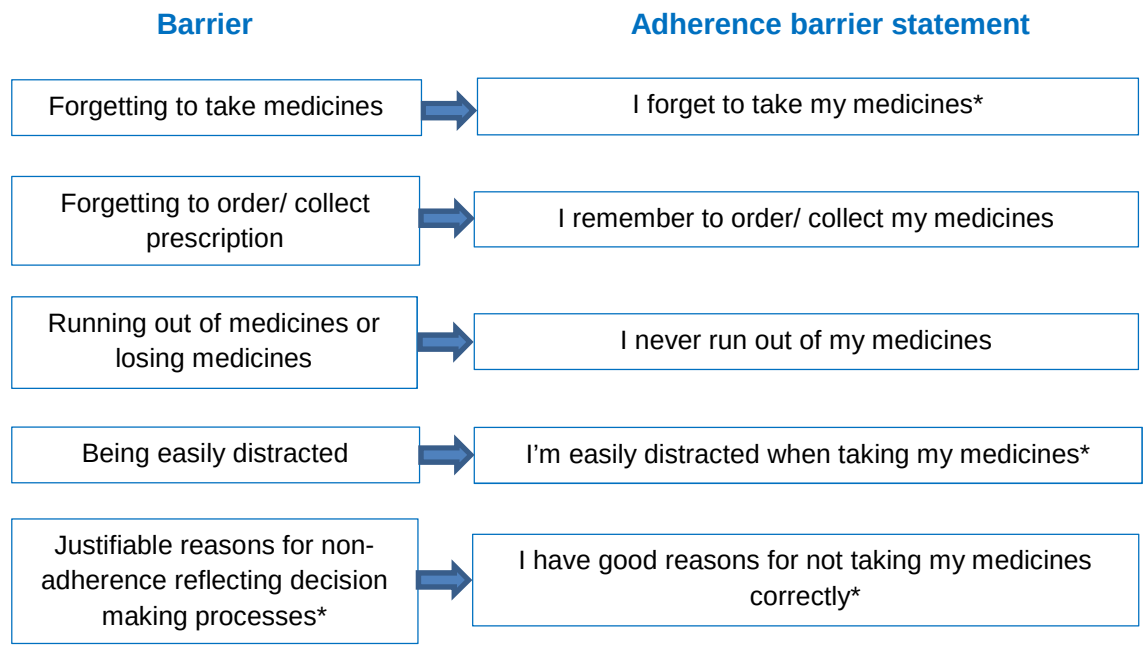


Figure A5.7.3 **Adherence barriers and proposed statements for the 'memory, attention and decision making processes' behavioural domain**

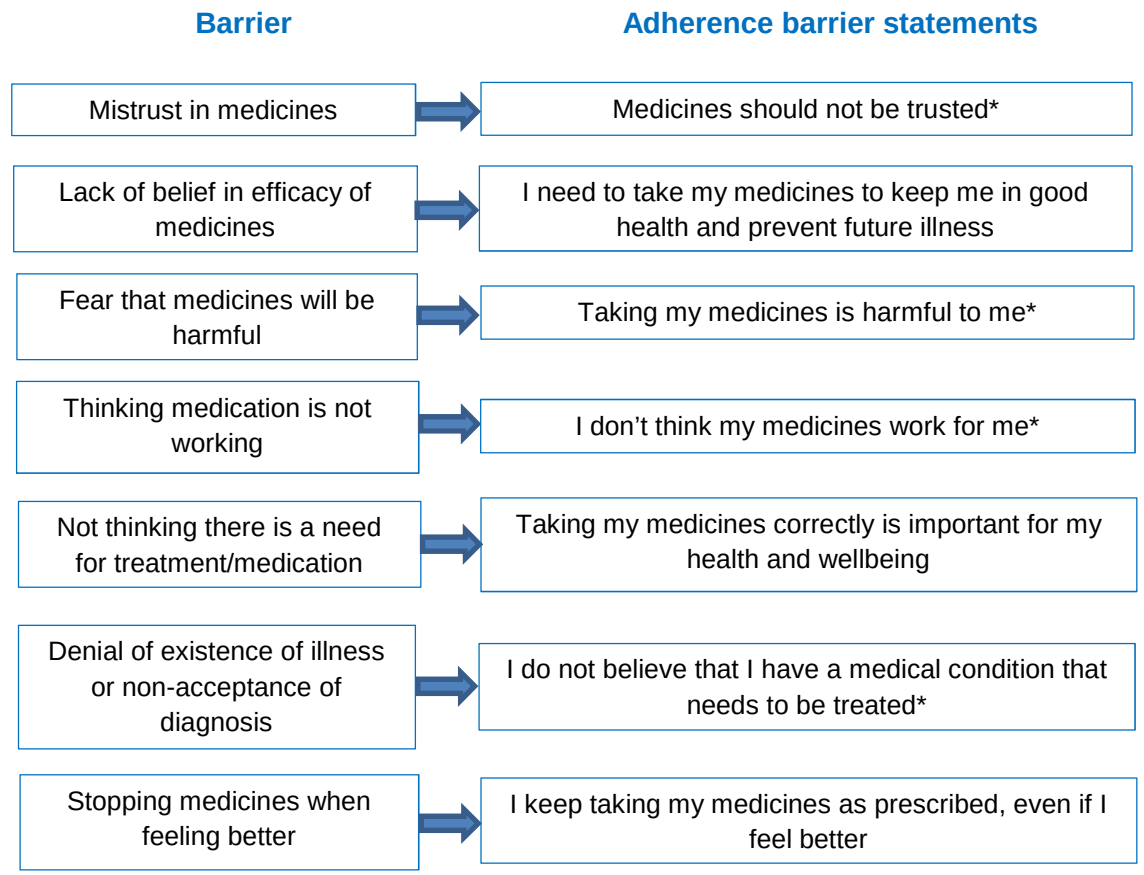


Figure A5.7.4 **Adherence barriers and proposed statements for the 'beliefs about consequences' behavioural domain**

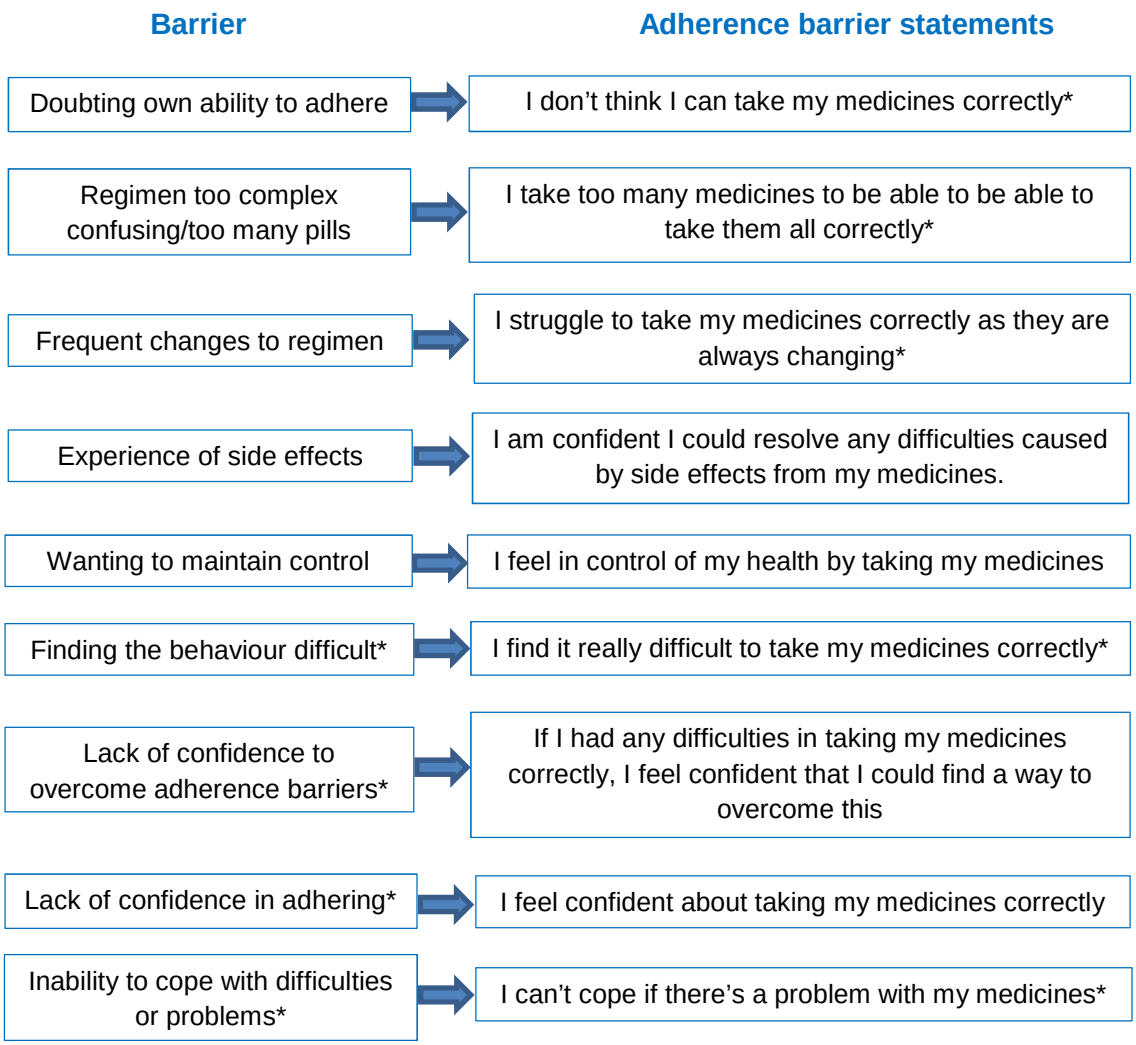


Figure A5.7.5 **Adherence barriers and proposed statements for the 'beliefs about capabilities' behavioural domain**

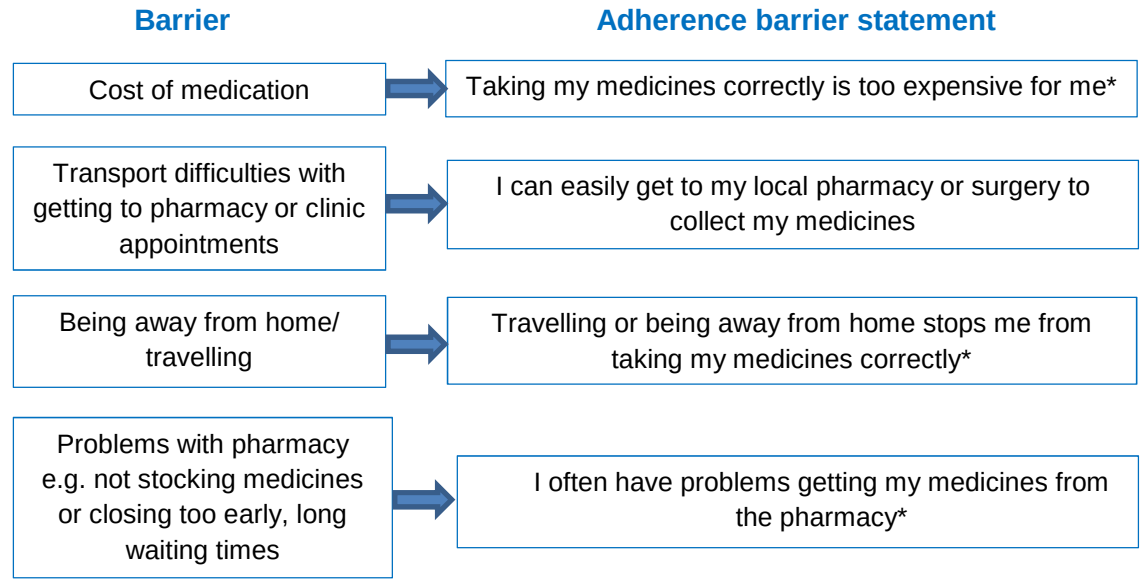


Figure A5.7.6 **Adherence barriers and proposed statements for the 'environmental constraints' behavioural domain**

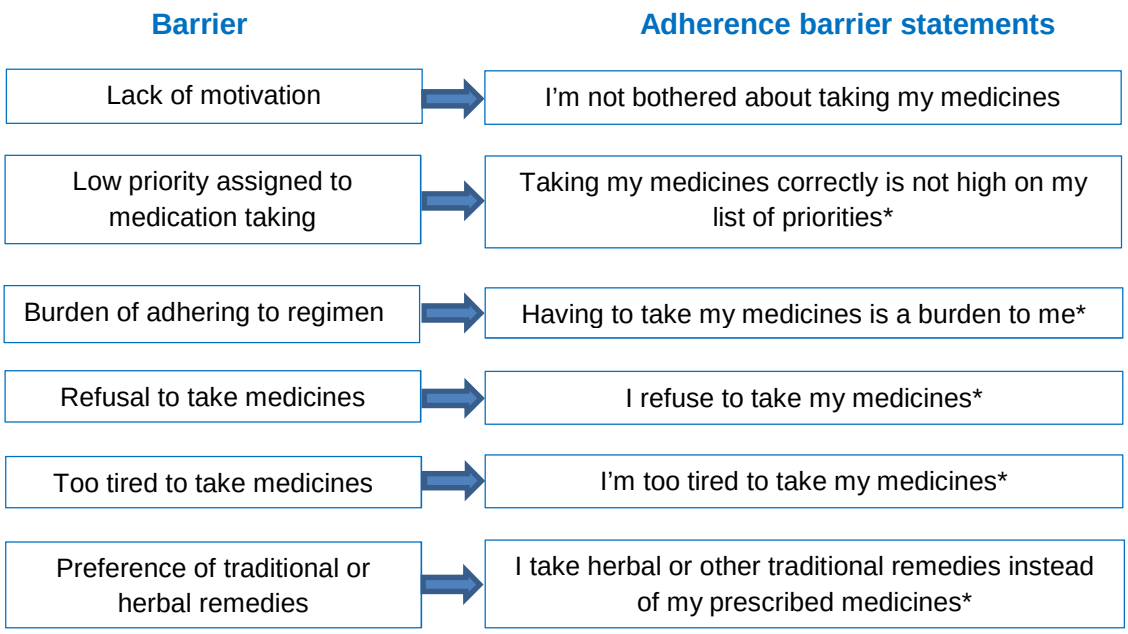


Figure A5.7.7 **Adherence barriers and proposed statements for the 'Motivation and goals' behavioural domain**

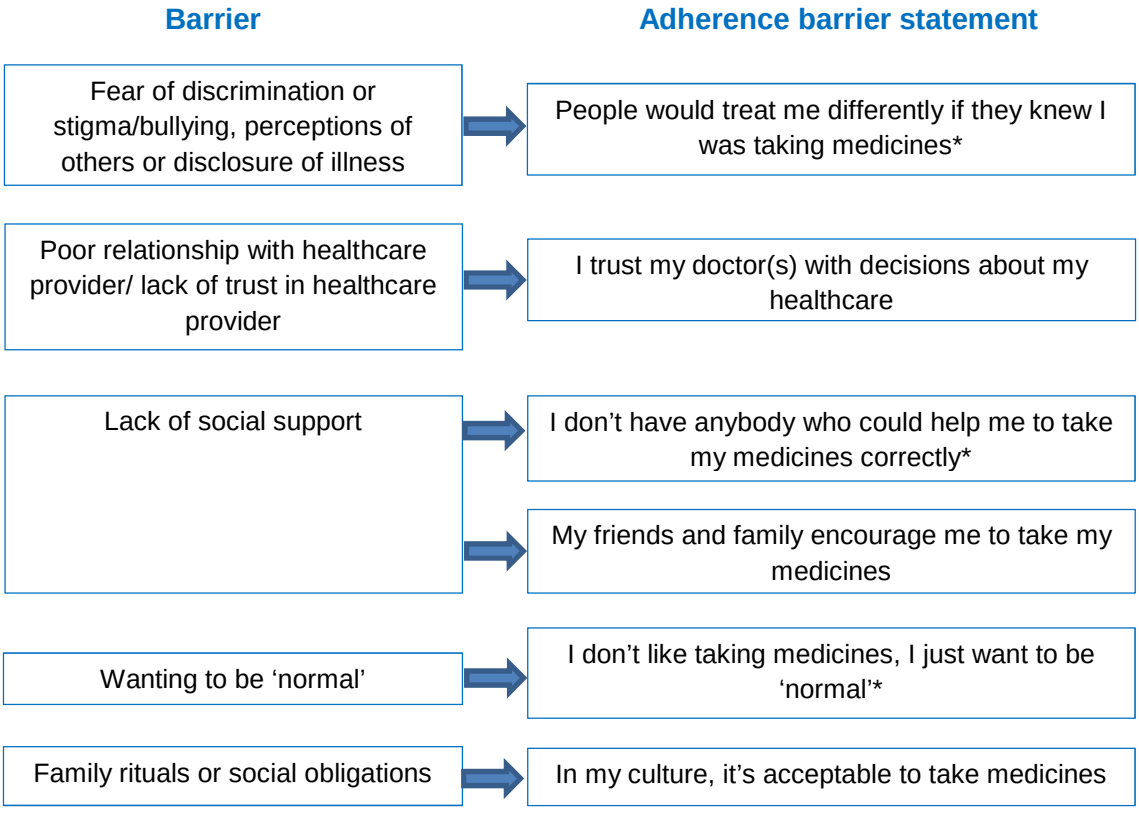


Figure A5.7.8 **Adherence barriers and proposed statements for the 'social influences' behavioural domain**

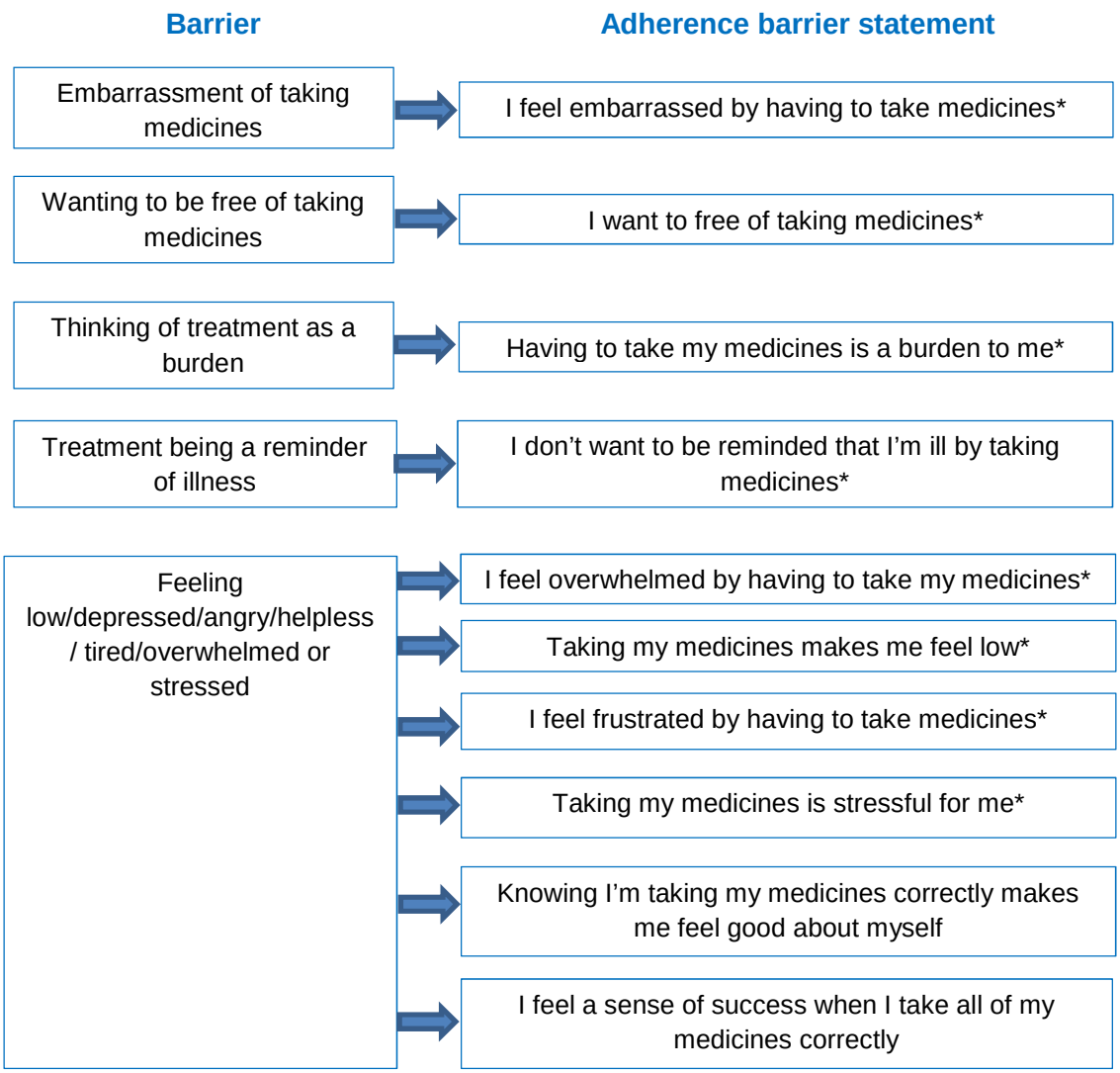


Figure A5.7.9 **Adherence barriers and proposed statements for the 'emotions' behavioural domain**

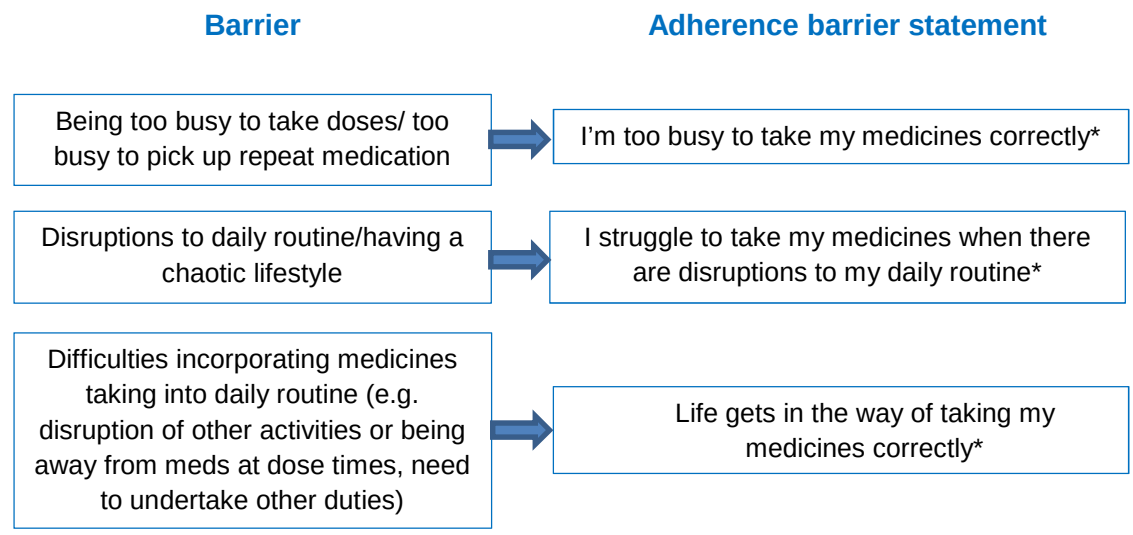


Figure A5.7.10 **Adherence barriers and proposed statements for the 'goal conflicts' behavioural domain**

Appendix 5.8 Topics discussed in first participant consultation exercise

Knowledge

The first topic discussed related to medicines packaging and specifically how receipt of medicines in different packaging each month can be confusing. One participant raised this issue, stating that the frequent changes in packaging made it difficult to know how to identify his tablets and suggested that this could be another barrier. The participant expressed strong feelings on this topic and felt that standardisation of packaging was an important issue to support medicines taking, especially for older patients. Other participants expressed agreement.

In addition to changes in tablet packaging, one participant raised the issue of accessing her medicines out of the blister packs, commenting on the difficulties of getting her thumb behind the foil seal and then dropping the tablets on the floor. This raised notable agreement from other participants, indicating that this may be a common barrier to adherence.

When discussing the specific barriers displayed, one participant suggested that knowing 'how' and 'when' to take medicines were unlikely to pose barriers to adherence as these were printed on the box. When probed further by the moderator and asked what would happen if these instructions were not clear, she agreed this was something that she'd not thought of and another participant added that in that situation he would go back to the doctors surgery. This respondent elaborated to say that this had never happened to him personally, but that he would know to go back to the surgery if his medicines instructions were not clear.

The moderator asked the participants for their thoughts on 'knowing why medicines had been prescribed' and whether this was important; one participant instantly commented that it was important to him. Another participant commented that knowing why the medicine had been prescribed was important when experience of side effects can create reluctance to take the medicine. The participant described an occasion where he had felt notable conflict between his prescriber's recommendation to continue taking a medicine because 'it was good for him' and his desire to stop the medicine because of side effects. It was agreed amongst the group that in addition to knowing why the medicine had been prescribed, it was also important to know what to expect from a medicine and how likely side effects may be. A different participant commented that he had experienced a similar problem regarding his statin:

"I got the impression from the GP that unless the side effect is serious, you should continue taking the statin because it's good for you, they kind of ignored anything else I said".

This anecdote sparked a discussion about weighing up the risks and benefits of taking medicines and the group agreed that 'knowledge' was important to enable informed decision making about medicines taking. One participant commented that the information about likely side effects and medicine indication are contained within the Patient Information Leaflet (PIL) and that this is a very useful document. The participant went on to state that when a new medicine is prescribed he always reads the PIL and for every box of medicine he always keeps the PIL until all of the tablets are used in case there is a side effect. When asked by the moderator if he found the information in the PIL worrying or frightening he replied that he did not and another participant stated that she found it interesting not frightening. In contrast, another participant confessed that she had never read the PIL and discarded the leaflet as soon as she opened the box of tablets.

When the moderator asked the participants to rank the barriers in order of importance, this proved to be difficult. However, useful comments about the barriers were yielded; participants felt ranking was difficult as many of the barriers were very similar. Upon displaying the questionnaire statements for the 'knowledge' behavioural domain, participants agreed that on the whole, the statements were clear and made sense. Participants understood the concept of completing the questionnaire the need to only tick one box for each statement.

In relation to specific statements, one participant commented that statements four and five looked to be very similar. Another participant took interest in statement six and suggested that this was a separate topic from the others in this group. With probing, the participant went on to describe that the process of ordering prescriptions is lengthy and complex, often taking a full day. One participant expressed agreement and another commented that it can be difficult unless the prescription can be collected from the pharmacy at the same time as going to the doctor's surgery. This comment sparked debate regarding discrepancies in the services that participants had access to, with some participants collecting their prescriptions from pharmacies attached to their GP surgery and other having to make separate journeys. It was agreed that difficulties in getting to the pharmacy can be a notable problem for many people, especially the elderly or those living in remote rural communities without access to transport.

Input from the moderator regarding mechanisms for easing difficulties in the prescription ordering and collection process such as prescription collection and delivery services facilitated further discussion on the topic. It was agreed that 'knowing' that these services are available is an important aspect. One participant

added that he felt the process of how to get further prescriptions was not well explained and went on to describe that he only recently found out that his pharmacy will order and collect his prescription from the GP surgery for him. This service had transformed the participant's experience of ordering and collecting his prescription into a streamlined and far more straightforward process that had really helped him.

The topic of ordering and collecting prescriptions was also described by a participant who used an online ordering system at her GP surgery. Her prescription then went straight to her local pharmacy for collection and her surgery sent her e-mail reminders to say when her next prescription should be ordered. Other participants commented on how impressive this service was and how much easier it must be. The participant using the service commented that with two young children and working full time, without the service she would really struggle. In discussion of different ways to order prescriptions, one participant commented that he always telephoned his order so that he could order exactly what was needed as he sometimes used up a backlog of tablets rather than ordering every month. It was agreed that knowing different ways to order prescriptions and that it's possible to order individual items rather than everything on the repeat list are important factors.

Skills

As the barriers were introduced, the participant who had previously commented on difficulties with accessing medicines from the packaging became active, suggesting that this point perhaps fitted better here. On discussing difficulties with accessing medicines from their packaging, one participant added that their tablets often 'jump out' of the packet and fall on the floor, adding that it's then even harder to identify a dropped tablet if the shape and packaging regularly change.

One participant also commented on a current batch of medicines that appeared to break into pieces when being pushed through the packaging. The participant commented that not only was this frustrating, it had also made him 'run short' on this particular medicine. This prompted discussion on the importance of 'having a system' for ordering medicines to ensure ample supplies are always available. 'Forward planning' was considered to be an important skill for managing medicines.

In relation to difficulties reading and understanding directions, the participant who had previously spoken about the usefulness of PILs reiterated this again, detailing an occasion where he was unsure of how to take his medicine and had used the PIL to assist. This raised some discussion on the 'skill' of knowing how to cope when there is a problem or difficulty. Another participant commented that the print on PILs is very

small so patients who have difficulties reading medicines labels, would unlikely be able to cope with the small print on PILs.

Prioritisation of the barriers was not deemed necessary as the moderator felt the discussions had been sufficient.

The potential questionnaire statements were displayed and read in turn. One patient commented that there was overlap between statements four and five as one could not really be done without the other. However, one participant disagreed and suggested they were better as separate statements as although he understood the directions on his medicines, he often forgot to take them at the correct time.

The thought of taking medicines at the correct time of the day prompted one participant to mention the difficulties of receiving medicines at the correct time when staying in hospital:

"You do your best for yourself at home but when you go into hospital you get them when they're ready not when you want them"

The participant added that for some patients, changes to medicines and routines whilst in hospital can be very confusing and make the transition back to home even harder. Strong feelings regarding changes to medicines were evoked:

"It's when they muck about with them that's the trouble, that's when the fun really begins"

In relation to statement two, one participant mused upon the future and whether he would continue to be able to take all of his medicines. The participant said that it wasn't a worry for him and it wouldn't prevent him for being able to complete the questionnaire but that it was more just something that he was mindful of. Two other participants agreed that this is something they'd considered too. The moderator asked if the phrase 'administer my medicines' in statement one was appropriate and it was noted that this may confuse some patients. One participant suggested changing the wording to, 'take' rather than 'administer' and participants agreed this might be better. Another participant suggested 'use' as an alternative that would cover other dosage forms such as creams or inhalers and it was agreed that this was the best suggestion

Memory, attention and decision making processes'

The introduction to the topic prompted one participant to share his experiences of practicing yoga to reduce his blood pressure and cholesterol levels. The participant

explained the yoga techniques and their benefit at length, describing the conflict that occurred in his mind when the doctor advised that he no longer needed his cholesterol tablets as his cholesterol levels had reduced. The participant related his preference for yoga, cycling and eating certain foods as a decision making process that had affected his medicine taking, but noted that it had been a confusing and difficult decision to make. The participant elaborated that he had intended undertake these preferences as an addition to his medicines, so then felt a sense of dilemma when the doctor advised stopping the medication. The participant also linked this back to the knowledge section as he felt not knowing about alternatives to medicines could be a barrier.

In relation to 'forgetting to take medicines', the group agreed that it can be hard to always remember every dose of medicine. One participant commented that his lunchtime doses were the most difficult to remember as he was not always at home or doing the same thing at that time. A variable routine therefore made remembering more difficult. One participant added that she sometimes forgot to take her medicines in the morning due to the distraction of getting her two young children ready for school.

The participant who had previously mentioned ordering their prescription online commented that without the e-mail reminder she would forget to order and collect her prescription, and so could identify with this particular barrier. Other participants agreed that it can be easy to forget about collecting or ordering your prescriptions. In discussion on this topic, one participant suggested that because the ordering and collecting of prescriptions is so difficult for her, she doesn't forget because it's at the forefront of her mind. It was agreed that for some people, if the process was very easy it might be easier to forget about it. For other participants, an easy ordering system was pertinent to be able to collect the medicines.

As with the other sections, formal prioritisation of the barriers was not necessary as it was agreed that 'being distracted', 'forgetting to take' and 'forgetting to order or collect' were the most important barriers and that 'losing medicines' was less important.

Participants agreed that they would be able to complete the questionnaire for the statements shown. One participant suggested that statement one could perhaps be improved by using the phrase 'I usually remember…' and other participants agreed that this might be helpful.

Strategies for remembering to take medicines were discussed, as well as the necessity of knowing how to manage medicines. One participant commented that he had not taken his 'water tablet' before coming out as he did not wish to disturb the meeting by needing frequent toilet visits. However, through having a strategy and knowing what to do, he had planned to take the tablet as soon as he got home so that he did not miss it. Strategies for remembering and managing medicines included the use of daily pill boxes, which were used by two participants and described as 'a god send'. One of the participants using daily pill boxes commented that preparing his boxes in advance helped him to remember to order his prescriptions in plenty of time. In relation to this, it was discussed whether medicines taking is a 'priority' as the older participants stated that they didn't forget their prescriptions as it's such an important part of their lives. Conversely, the younger patient with two young children confessed that taking her medicines was not a priority for her. This prompted consideration of statement four and the participant suggested that re-phrasing to 'I can be easily distracted' might be useful, as this better reflects something that doesn't happen every day.

It was suggested that statement three may be superfluous as it related directly to statement two. Statement five also attracted comments as it was suggested that the wording 'good' should be removed as personal reasons are not necessarily good reasons. The moderator also identified that 'correctly' should be altered to 'as prescribed'. It was agreed that phrasing this statement as 'I have my reasons for not taking my medicines as prescribed' reflected the best option.

Social influences

Participants indicated that they had not personally felt any sense of discrimination or stigma relating to their medicines taking and suggested that these factors, especially the fear of being bullied were more likely relevant to school children and teenagers. One participant commented that he could see how it could be an issue for younger people, but that older people are far more accepting and just discuss it. It was agreed that for older people, medicines taking was seen as 'normal'.

The adherence barrier 'lack of trust in healthcare provider' prompted comment from the participant who had previously discussed his dilemma of being told to stop his statin after his yoga proved to be successful:

"In all honesty, in the beginning I didn't trust my doctor"

The participant described how he had felt when the doctor had doubted his blood pressure readings that had been taken through self-monitoring, commenting that trust has to operate in both directions. A different patient commented that doctors can be very persistent and not 'take no for an answer' which can adversely affect relationships.

On the topic of poor relationships with healthcare providers, one participant commented that relationships with surgery receptionists are known to be particularly fraught. The participant went on to describe the difficulties that many people have in getting access to their GP as they are 'protected from being bothered' by the receptionists. With further questioning the participant agreed that hostile reception staff at surgeries could lead to negative feeling about medicines:

"Some people wouldn't want to face what they consider to be hostility from the receptionists"

Poor relationships with surgery staff were therefore considered to be a barrier to adherence. In discussing 'family rituals or social obligations', the participant who had previously mentioned her young children, agreed that her family obligations were sometimes a barrier to adherence. Another participant commented that religions and faiths could act as barriers, citing the Islamic faith as an example where medicines containing alcohol would need to be avoided.

One participant commented that 'lack of social support' could be addressed by the many support groups that exist, expressing his sentiment that such groups were very important for sharing experiences and talking through the troubles of medicines taking, especially for carers who can have tremendous worries about medicines.

For the questionnaire barrier statements, one participant suggested amending statement six to 'my faith and religion' and another participant suggested 'my beliefs'. These suggests prompted further contributions from other participants regarding Chinese medicines, superstitions and other religions such as Jehovah Witnesses' refusing blood transfusions. It was agreed that phrasing this statement as 'my faith or culture' was the best option for capturing these different potential barriers

Environmental context and resources

The adherence barrier 'cost of medicines' sparked notable discussion, with participants who were exempt from prescription charges expressing genuine shock at the current levy. Participants were largely knowledgeable about the prescription pre-payment card, but commented that it was still an expense that may be difficult for

many people. 'Cost of medicines' was therefore agreed to be an important barrier to adherence.

Previously discussed topics such as difficulties with getting to the pharmacy and frequent changes to the boxes medicines are supplied in were revisited in relation to the barrier 'problems with the pharmacy'. Further consideration was also given to pharmacy opening hours and the participant with two young children commented on how reliant she was on her pharmacy opening on a Saturday morning.

In relation to the barrier 'being away from home/travelling' the participant who had previously mentioned struggling to remember his lunchtime doses conveyed the importance of preparation and forward planning for travelling to ensure adequate medicine supplies are taken. Again, the participant made reference to his medicines being 'a way of life' for him and high on his list of priorities.

As the questionnaire statements were read, participants nodded in agreement, which suggests the statements were acceptable. When asked about the interpretation of statement four, one participant said they would take this to mean the medicines were not in stock and wouldn't consider this statement to cover wider issues or other problems with the pharmacy such as its opening hours. Other participants expressed their agreement.

Emotions

The final group to be discussed in the first consultation exercise was 'emotions'. As time was running short this section was not discussed in as much depth as previous sections, but this was not considered to be problematic as this section was also be discussed in the second focus group.

When asked if taking tablets was a reminder of illness, one participant commented that he did not feel this was so and that he just 'lived with it'. It was agreed that maybe this depended on the condition and medicines taken, for example taking medicines for cancer could be an unwelcome reminder of a terminal illness. One participant said that if taking medicines was a reminder of illness, the negative thoughts evoked could make the condition worse and stop the tablets from working. The participant described a friend who has been 'OK' until he started taking medicines and who had then become very depressed as they kept focussing on their illness. In agreement, another participant added that being reminded of an illness could trigger any of the negative emotions listed. This also prompted some discussion on acceptance of the condition and need for medication, one participant commented:

"You accept it after a while; it might be a shock at first but then you just accept it"

One participant commented that all of the 'negative' emotions listed as barriers such as feeling low, angry or stressed could actually be caused as a side effect of medicines. Another participant added that she felt worse if she didn't take her medicines and could notice a difference after a few days; experience of negative feelings was therefore an adherence promoter for this participant.

For the questionnaire statements, one participant proposed that statements three and seven were very similar as thinking of medicines as a burden would likely evoke feelings of frustration. The moderator asked if several of the similar statements could be combined into more general terms such as 'taking my medicines makes me feel negative feelings'. It was agreed that this may be possible, but that the statements would need to be carefully worded; 'mood changes' was suggested as wording by one participant.

In concluding the session, participants agreed that it had been an enjoyable and informative meeting and that there were not any points that they had wished to raise but had not had an opportunity to. One participant concluded:

"It's been fascinating".

Appendix 5.9 Topics discussed in the second participant consultation exercise

Motivation and goals

In relation to being too tired to take medicines, one participant commented that it was not being too tired that caused a problem but more that in the evening forgetfulness can prevail. Once all of the barriers had been displayed, one participant commented that motivation was very important and the single most important factor in taking medication:

"For me, the motivation is very strong and that alone would be thing that makes me take it, some of the things like being too tired might impinge on it, but my motivation is very high"

The issue of side effects was also raised during this section, generating marked discussion and demonstrating a clear topic of interest. One participant commented that experience of side effects had affected his medicines taking in the past. In agreement, one participant commented that he could relate to almost all of the barriers presented due to his previous experience of a severe side effect from one of his medicines which had effectively caused a stroke. When asked if his previous experience of side effects had made him reluctant to take medicines, he replied that it had put him off taking the problem causing medicine and elaborated that he would be reluctant to take newly prescribed medicines until he had 'researched' them, as he is now very cautious with which medicines he will take.

Incapacity to take medicines was also commented upon, with one respondent noting that even when motivation is very strong, forgetting or not being able to cope with taking medicines can be a problem. Following on from this, the moderator explained that incapacity could relate to other factors such as difficulties with getting the medicines out of their packaging which sparked numerous comments, once again indicating that this was barrier of note. One participant described tablets 'flicking out' of the packaging and being lost down the sink plughole and another reported having to pick their tablets up off of the floor after they had 'popped out and gone everywhere'.

Discussing the difficulties of accessing medicines from their packaging prompted one participant to reflect upon the fact that she now received one of her medicines in a pot rather than blister pack. The participant commented that this was because she chose to buy it herself rather than getting a prescription as she knew it would save NHS money. For this participant, the cost of medicines was not an adherence barrier. The concept of the cost of medicines sparked an interesting discussion regarding the perceived value of medicines. One participant explained that his daughter was

studying pharmacy and had told him how much his medications cost to the NHS and that he realised this is less than the prescription charge that he paid. The participant described how this had made him question whether he was getting value for money and the best possible treatment that could be afforded. When asked whether this had affected his medicines taking, the participant described an intrinsic link between the known monetary value of a medicine and its perceived quality and that this had initially affected his perception of the medicine. The participant added that he had later been able to rationalise this therefore not been affected in his medicines taking.

Consideration of medication costs generated discussion regarding variations in the quantities of medications prescribed, as some participants received two or three months' worth of medication at a time whereas others only received one months supply. The inconvenience and unfairness of this was discussed and participants said that only receiving a month's worth of medication rather than two made a difference to them, especially for those who pay for their medication. Participants agreed that negative feelings towards medicines could be evoked by knowing other people were getting more medicines at a time, leading to a sense of being given a 'raw deal'.

The topic of Patient Information Leaflets (PILs) was raised by one participant and this also generated discussion. In raising the topic, the participant described PILs as "one of the most terrifying things about taking medicines". When asked whether reading the PIL had made him reluctant to take the medicines he replied that it had not as he trusted his doctor but recognised that reading the PIL could unnerve some patients. One participant had brought their PILs to the meeting to ask what 'he was missing' and confessed that he always threw them straight in the bin. Another participant added that he thought most people start reading the PILs and then wished they hadn't as they are quite off putting.

In reference to the specific barriers, one participant commented that 'refusal to take medicines' was very strong and that 'reluctance' may be more appropriate. When asked if they could prioritise the barriers in order of their perceived importance, the group struggled and one participant commented that he felt it was quite a personal thing to do and that it would also depend on the circumstances. When asked if the prioritisation would also depend on which specific medicine was considered, the participant agreed.

When asked if they could prioritise the barriers in order of their perceived importance, the group struggled and one participant commented that he felt it was quite a personal thing to do and that it would also depend on the circumstances. When asked if the

prioritisation would also depend on which specific medicine was considered, the participant agreed.

With regard to questionnaire statements, Participants agreed that they understood they layout of the questionnaire and how they would need to fill it in. However, when asked if they would be able to complete it, whilst most nodded or agreed that they would, one participant commented that they wouldn't be able to fill it in because it would be different for each medicine that he took.

One participant expressed concern with the questionnaire design as they considered themselves to be somebody that would tend to tick at the polar ends rather than in the middle and that the alternating positive and negative statements could cause confusion and 'ticking the wrong box'. The 'strong wording' of the statements was also discussed and one respondent felt this would make it hard to know whether to say 'agree' or 'strongly agree'. Another respondent added that he found himself having to re-read the statements two or three times to check they he had understood them correctly. In response to this, another participant posed that having to re-read the statements to check understanding wasn't necessarily a bad thing. In further discussion and with explanation from the moderator, participants appeared to agree with the rationale for using a mixture of positive and negative statements.

One participant suggested that his responses would be considered as 'a spoilt paper' because he would give conflicting responses. Another participant thought that providing the option of 'neither agree nor disagree' was a bit 'negative' because this would not provide an indication of the respondent's real views.

In relation to the specific statements, one participant expressed dissatisfaction with the first statement, and suggested that the term 'bothered' was ambiguous as it could also mean worried, several respondents agreed that they would interpret it as 'worried' rather than 'not motivated'. One respondent suggested phrasing the statement as 'I don't care' instead of 'I'm not bothered'. Statement number six was discussed with the suggestion that the word 'sometimes' could be added to read 'I'm sometimes too tired to take my medicines'. The participant felt this would be useful as he could not imagine any patient would always miss their medicines because of being too tired. Agreement on this was not achieved as another participant disagreed and noted that 'sometimes' could be added to every statement.

Goal conflicts

The first barrier selected for discussion was 'being too busy to collect or order prescriptions', generating several participant comments. One participant related back

to the previously discussed topic of having to order and collect your prescription every month compared to those who only have to collect every three months and reflected that it's far harder for the patients who only get one month's worth. The same participant commented that he would be more than willing to pay somebody to deliver his prescription and post it through the letter box which sparked a discussion on prescription delivery services.

Opening hours of pharmacies and getting there at a particular time was also raised as an issue as were the benefits of using automated or online ordering systems. This prompted reflection upon the different experiences people may have depending upon which surgery and pharmacy they use. One participant commented that the hardest thing about their medicines was the collection as they lived quite a distance from their GP surgery. One participant also talked about the need to be 'disciplined' and 'having a system' in order to stay on top of managing your medicines.

The issue of forgetting to pack medicines when being away from home or travelling was raised by one participant in response to the 'change in routine' barrier and a fellow participant agreed that he felt everyone had most likely forgotten to take their medicines away with them at some point. Further comments were added that when travelling away, running out of medicines would be possible if insufficient supplies had been packed. Discussions also took place on the matter of twice daily dosing being convenient as it fitted into daily routines of being at home morning and evening.

Beliefs about consequences

In relation to 'mistrust in medicines' and 'fear that medicines will harmful' the participant who had previously described a serious side effect from one of his medicines commented that he could strongly identify with these barriers, but not with the others. The moderator used an example of a prescription for antibiotics in discussing 'stopping medicines when feeling better' and one participant stated that it is the prescribers job to explain why the full course must be taken. One participant noted that he could relate all of the displayed barriers to a character in a popular soap who had a brain tumour but was in denial of this.

The concept of misunderstanding was raised by one participant, who questioned whether a misunderstanding of how medicines worked or why they were prescribed could be an adherence barrier, if the relevant information was not explained properly. When asked if he felt whether knowing what a medicine was for and why it had been prescribed were important, he agreed and commented 'it's what drives confidence and motivation'. General agreement was expressed. One participant commented

that this information should be ‘every part of the explanation’ and one participant added that the patient should ask for it.

‘Non-acceptance of the diagnosis’ prompted discussion, as one participant felt this wasn’t necessarily accurate and that mistrust in their prescriber’s proficiency may be more pertinent:

“I accept the diagnosis, I just don’t accept that the guy necessarily knows what he’s doing”

Dose changes were raised as an issue which could spark mistrust, as one participant described a friend who had recently been switched to a different medicine of different strength and that this prompted consideration of whether the previous dose was correct. Adding to this, one participant reporting having their dose of one medication reduced to avoid side effects and that he was now uncertain as to whether the medicine would still be effective.

The asymptomatic nature of conditions such as hypertension was considered by one participant, who posed that feeling well and not having any symptoms could prompt doubting of the diagnosis and need for medication. In relation to ‘fear that medicines might be harmful’ one participant commented on the uncertainty of long term effects. The participant agreed that the long term effects were a worry to her, but that it did not impose a barrier to her adherence because her motivation was sufficient to overcome her worries; her motivation was driven by her father’s history of hypertension and subsequent stroke. Following on from this, one participant suggested that the ‘fear that medicines will be harmful’ was likely the most important barrier as it was more quantifiable. Another participant agreed with this and suggested that this fear is augmented when multiple medicines are prescribed as information regarding interactions is often difficult to obtain.

Non-acceptance, denial and thinking there is no need for treatment were considered to be phases that people might go through when they are first diagnosed with a condition. The participant raising this suggested that with time, these thoughts pass and acceptance prevails. With consideration to this, the participant suggested that it was therefore the remaining barriers which were perhaps most important and agreement in this thought was expressed by other participants.

In response to the questionnaire statements, statement one evoked a reaction from one participant who felt that it was very emotive and ‘too far’. The moderator suggested that emotive statements were useful for eliciting polar responses rather

than those which fall into the middle and one participant agreed with this. Statement two also elicited a negative response from the same participant and another participant commented that it was completely untrue. This participant went on to suggest that it must be the diagnosis that was doubted not the medicine and felt that the statement was 'nonsense' posing that if somebody didn't trust their medicine then there was no way they could trust the person giving it to them. When asked by the moderator whether he would be able to respond to this question as patient, he commented that he would easily tick 'strongly disagree' and two other participants showed agreement

The third statement also prompted discussion with one participant commenting that she would be uncertain in answering this statement and therefore unable to offer her usual polar responses. Another participant added that medicines can be correctly prescribed, even if they're not safe. Statement four was considered to be more personal and the terminology 'work for me' was found to be ambiguous. Alternative wording of 'have an effect' was suggested but another participant noted that this could include having a side effect. Another participant suggested wording as 'beneficial' and this was more popular. In further relation to this statement, one participant asked if we were considering whether the medicines were working or whether the correct medicines had been prescribed and it was agreed that these were two different matters. Another participant mentioned 'benefit balances' of weighing up benefits and risks and several participants agreed that this was important.

The moderator asked if the term 'medical conditions' in statement six was clear and one participant suggested that it perhaps meant something temporary rather than a disease. With explanation form the moderator, participants agreed that 'disease' was not a useful term and one participant suggested leaving the word 'medical' out to simply say 'I have a condition'. Participants agreed that this was an improvement.

Statement seven was also discussed, with one participant commenting that he continues to take his medicines as it reduces his risk of further problems, irrespective of how he 'feels'. Another participant added that he would be fearful of stopping his medicines as although he might feel well for a time, his symptoms might return. It was also noted that the term 'feel better' might be confusing in the context of preventative medicines such as those for cardiovascular disease. It was agreed that separate questionnaires, one for active treatments and one for preventative treatments may be necessary. Altering the phrasing of this statement to 'even if I feel well' was also suggested and other participants agreed with this recommendation.

Beliefs about capabilities

This group proved to be quite challenging for participants to understand and the majority of participants stated that they could not relate to the barriers presented from their personal experiences. One participant posed that perhaps the central concept of 'beliefs about capabilities' was incorrectly phrased.

Whilst participants struggled to relate to the barriers based on their own experiences, anecdotes of friends and family member's experiences were shared in trying to further understand the barriers. One participant described a friend, whose elderly parents were unable to cope with their medicines or any difficulties that arose. The moderator suggested that this represented a genuine barrier rather than perceived inability or belief and participants agreed with this and suggested that this barrier may be better suited to a different group.

One participant reflected on his own experiences when faced with caring for his father who was unable to manage his medicines following a stroke and the difficulties that arose from this. The participant identified with the 'wanting to maintain control' barrier as his father refused his medication for this reason. Another participant added that to her, wanting to maintain control was a promoter of adherence as she felt that by taking her medicines, she maintained control of her illness. It was agreed that the phrasing of this barrier was in the questionnaire would be pertinent as it could be a barrier to some people and promoter to others depending upon interpretation. A further comment was also made relating to wanting to maintain control, with a participant suggesting that this though would most likely be a barrier to adherence in the early stages of being prescribed a medicine, before there had been time to adjust.

One participant provided an example of lack of confidence in managing medicines by relating this to his brain damaged son, and explaining that his son took many medicines and lacked confidence in taking them correctly and sticking to the regime. The participant's son had found the use of a weekly pill organiser very useful in overcoming the deficit in confidence.

In relation to the questionnaire statements for this section, It was agreed that statements four and six were verbose and may need refinement. With specific relation to statement four, one participant commented that the 'I' element of the statement was confusing as resolution of side effects is unlikely to be something that would be undertaken alone. The participant suggested that 'we' may be better as this would reflect inclusion of the patient's GP in the process. It was agreed that the

phrasing of this statement needed some refinements, and that reluctance to take medicines as prescribed due to side effects was the pertinent barrier for inclusion.

Statement eight was described as ‘an adventurous statement’ by one participant who commented that this statement did not make sense. Another participant added that the statements phrasing implied that a patient could cope on their own without seeking advice and it was agreed that this was not accurate. One participant suggested altering the phrasing to ‘I know what to do if there is a problem with my medicines’ and it was agreed that this represented a good starting point for an improved statement, which would covered multiple barriers.

One participant commented that he could identify with the third statement as his warfarin dose regularly changed, but commented that for him, it was the dose that changed not the medicine. It was agreed that .the phrasing of this statement should perhaps be altered to better reflect this. Another participant expressed agreement that changes to doses or medicines was confusing and made adherence more difficult.

Emotions

Contrary to the first session, one participant could identify with ‘embarrassment of taking medicines’, describing an occasion where she had collected three large carrier bags full of medicines from the pharmacy and had tried to hide them in her coat as she had felt embarrassed and concerned about what other people might think. Another participant described himself as ‘the black sheep’ of his family and felt embarrassed by having to take medicines when the rest of his family were ‘super’ healthy. He added that the embarrassment would however, not be an adherence barrier for him.

The barrier ‘thinking of treatment as a burden’ prompted one participant to ask if this meant a burden to the patient or a burden to other people such as caregivers and other helpers. It was agreed that either would be possible and one participant added that feelings of being a burden to others would be the stronger of the two emotions. One participant summarised many of the barriers as ‘mental health’ and commented that if a patient’s mental health was fragile, their ability to follow their prescribed regimen might be impaired. Another participant added that people may experience negative emotions by questioning why they have a condition and why they have to take medicines when other people around them do not. It was agreed that this may relate to the idea of ‘stages of change’ that had previously been mentioned by another participant.

One participant commented that the experience of negative emotions might be more likely in younger people, adding that he had only had to start taking medicines in his seventies and at this stage of life, he was grateful for medicines to prolong his health. The participant stated that if he had started taking medicines in his thirties, he suspected he would have been very depressed at the thought of having to take medicines for the rest of his life.

For one participant, 'treatments being a reminder of illness' was seen as a motivating factor rather than barrier. The participant explained that being reminded of her illness motivated her to keep taking her medicines due to a strong family history of heart disease. Another participant agreed with this and commented that she felt the same way about her medicines. However, this participant added that her daughter was embarrassed by her condition and hating taking her medicines at it reminded her of the illness she had. It was agreed that the emotion evoked by being reminded of an illness may well depend upon the illness in question and vary from one individual to another.

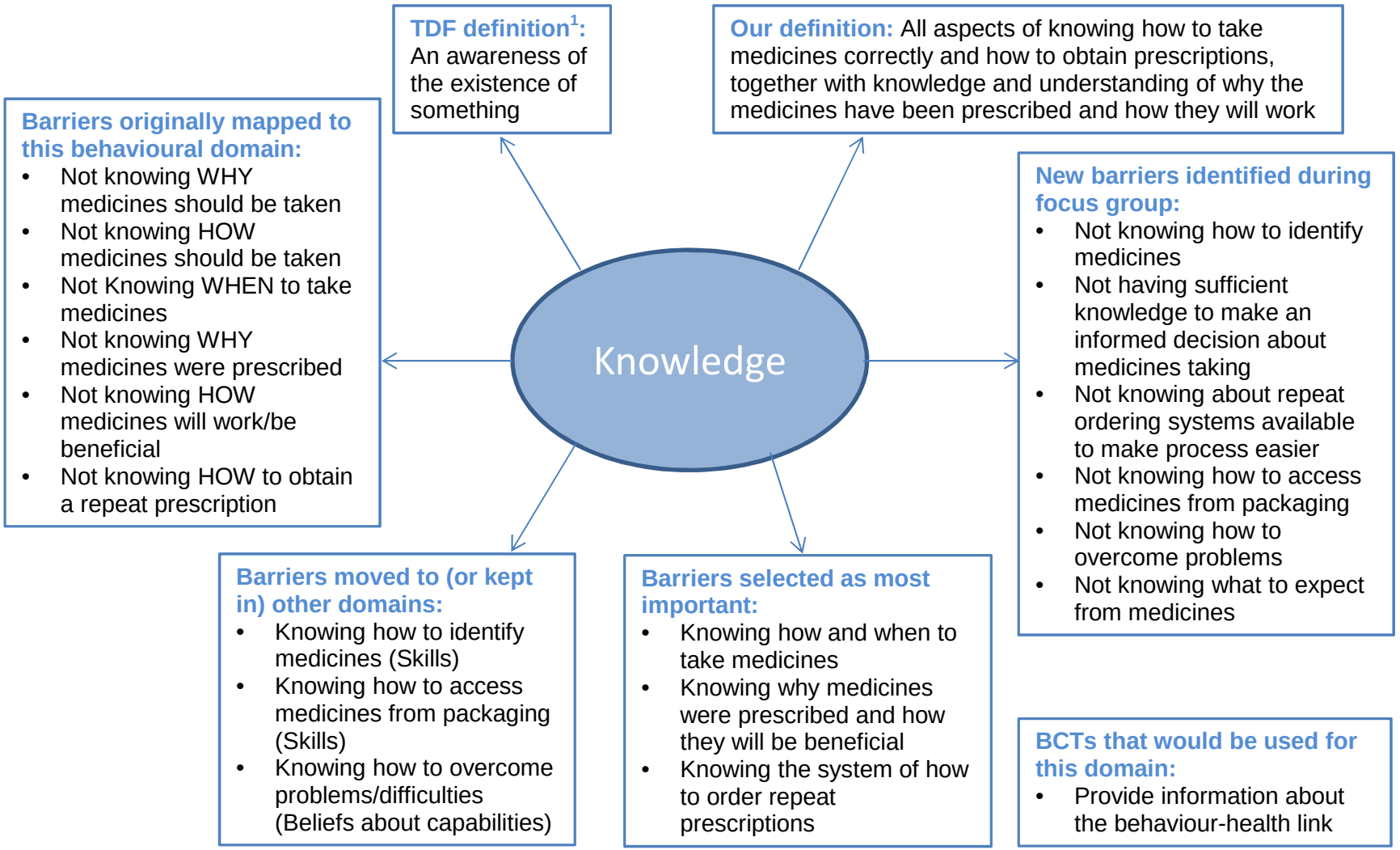
One participant suggested that 'annoyance about taking medicines' could be another emotion that could be evoked when insurance forms are completed and medicines have to be declared. Several other participants agreed with this and declaration of medicines taking was also mentioned for the DVLA. One participant added that for holiday insurance forms, taking multiple medicines can make a substantial difference to the cost of insurance. The participant went on to describe an occasion where he had persuaded his doctor to reduce the number of prescribed medicines and prescribe a combination product to keep the number below the threshold for an increase in insurance cost. Another participant commented that this must have been quite stressful, and also reflected on the stress of making sure you're adequately covered for insurance.

In response to the questionnaire statements, the second statement was the first to be commented upon, as one participant commented that surely everyone wants to be free of taking medicines. In relation to embarrassment, one participant commented that the only other person who saw him taking tablets was his wife and that he therefore wondered how common medicines taking in public was. Another participant replied that it might depend on what medicines were prescribed or how frequent the doses were. The notion of embarrassment was also related to travelling on holiday and the hotel cleaners seeing tablets laid out ready to take, one participant commented that he was conscious of what the cleaner might think.

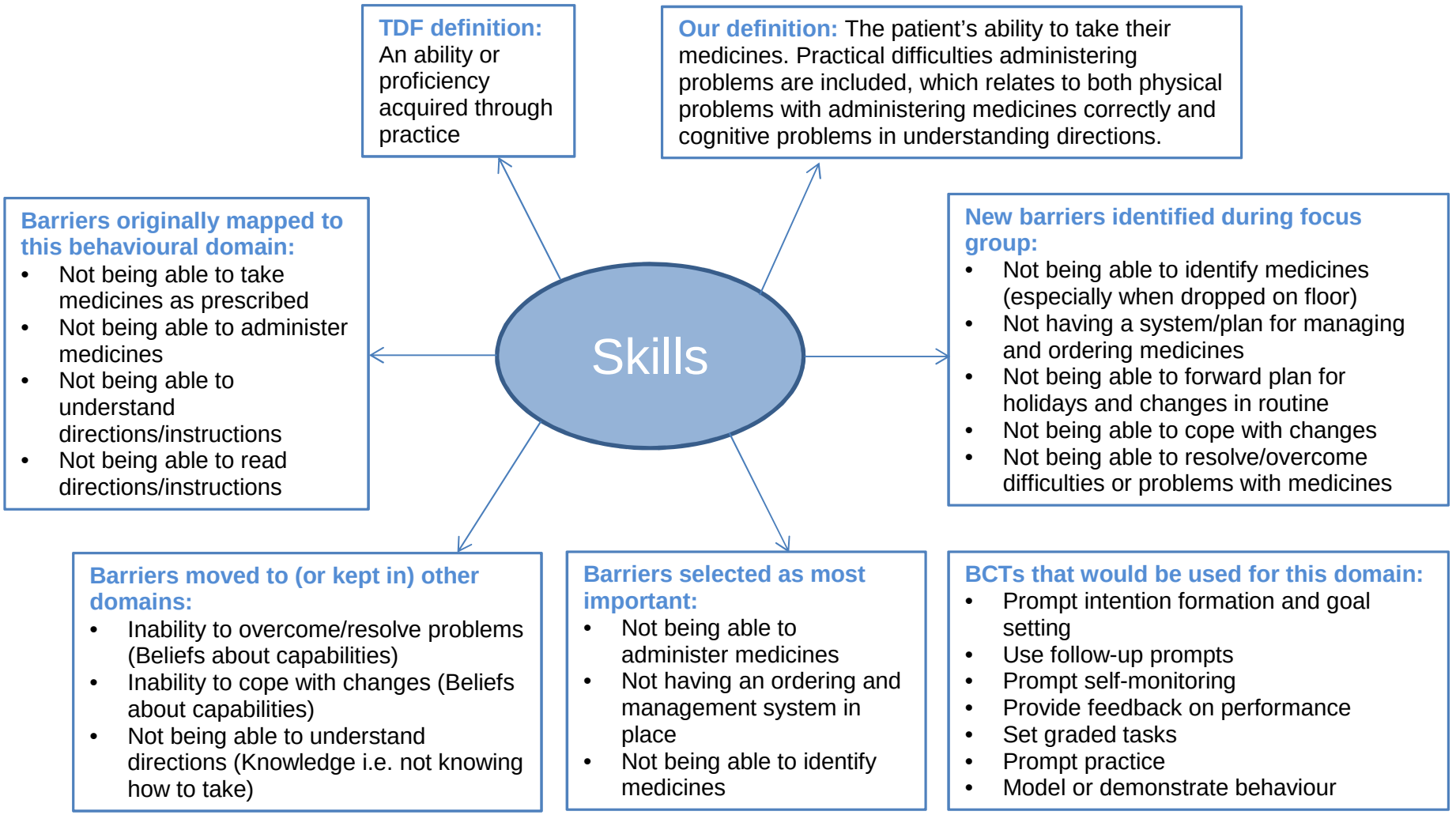
In relation to the sixth statement, one participant stated that rephrasing may be necessary as it's not the physical act of taking the tablet that might induce low mood, but more the reliance on having to take the tablet.

In summary, participants were thanked for their time and the future proceedings were explained. Participants commented that they had enjoyed the evening and that they had all had opportunity to raise all points that they had wished to and they did not think that there was anything that had been missed.

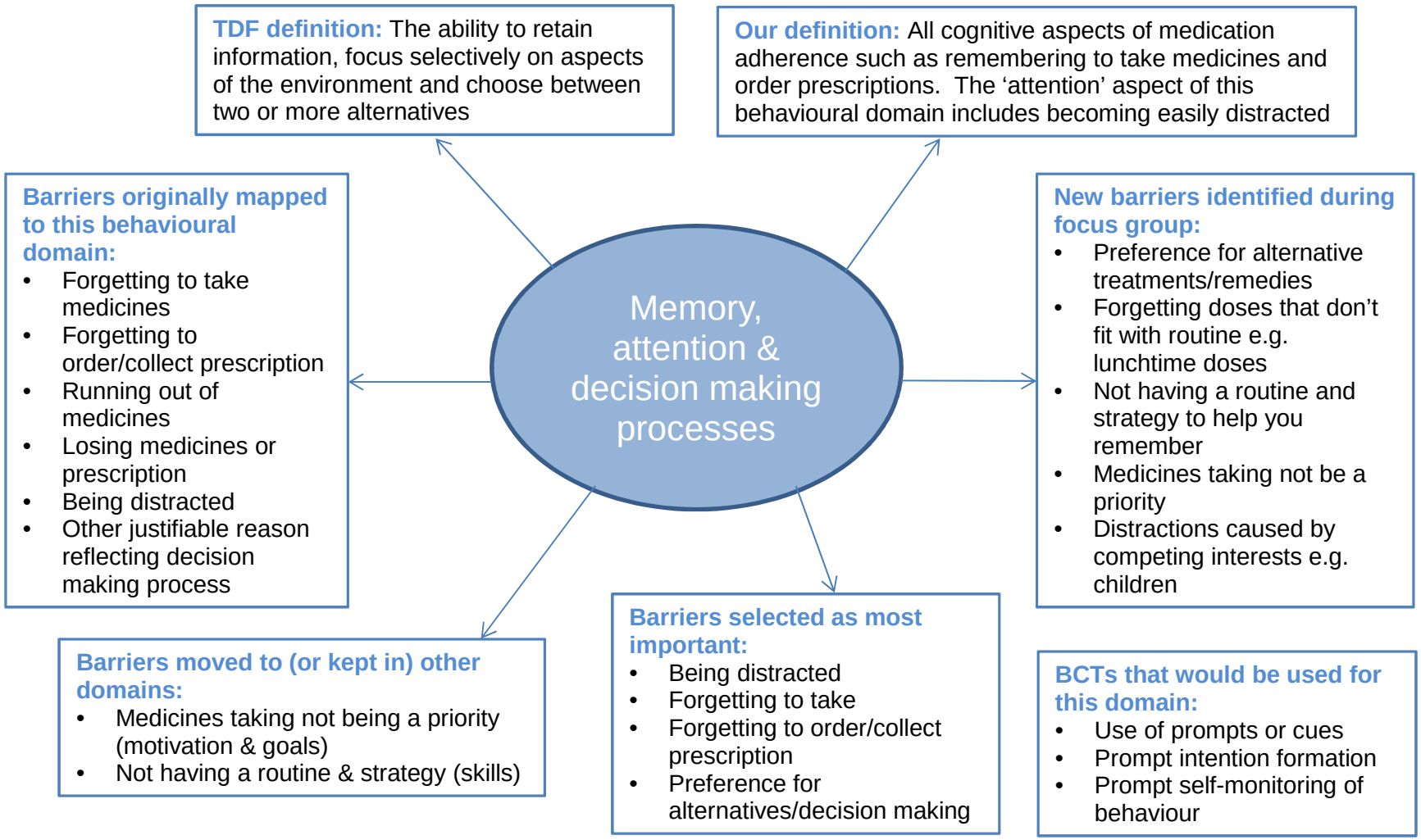
Appendix 5.10 Mind maps used in questionnaire refinement process



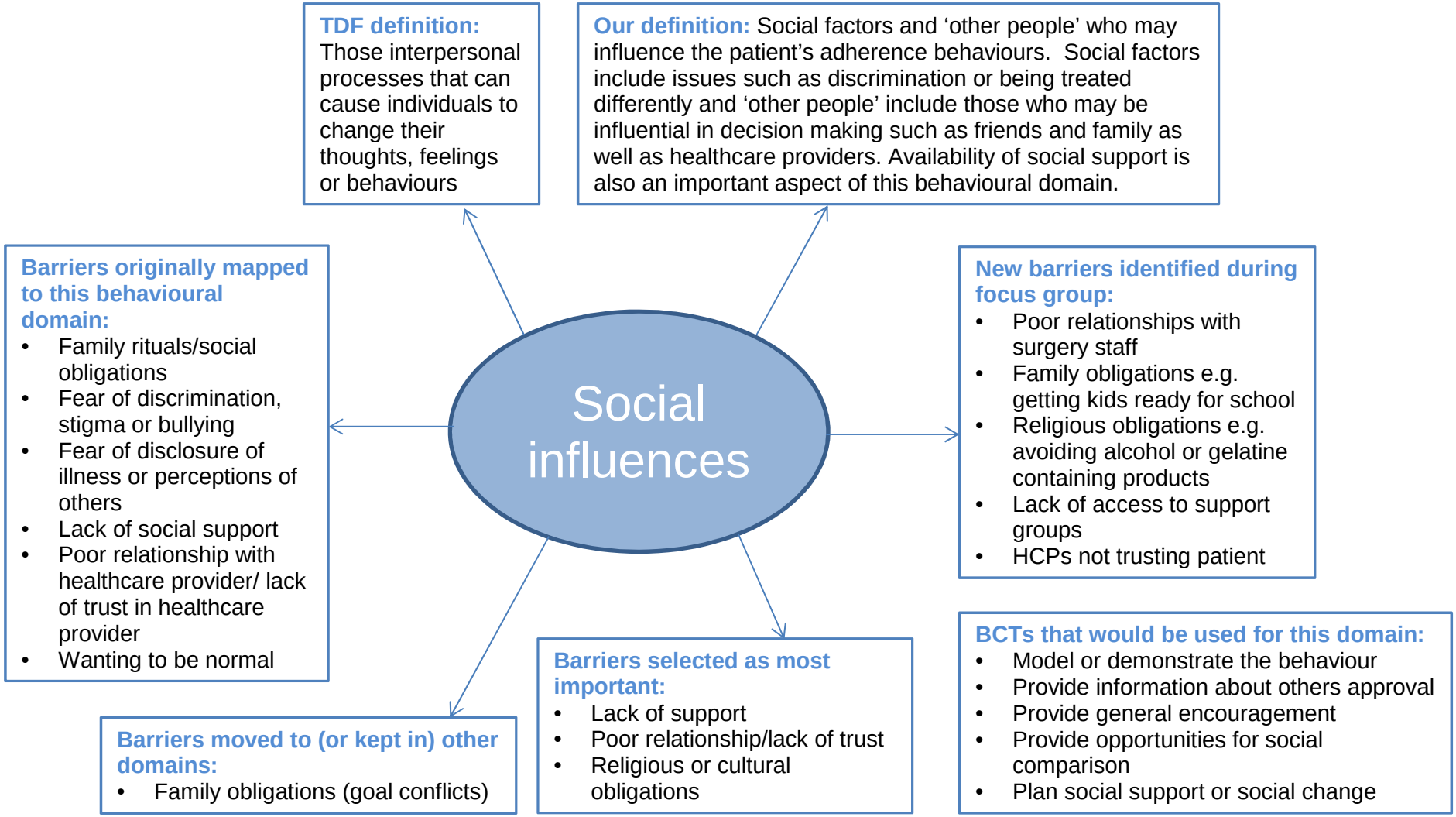
Appendix 5.10 **Mind map for 'knowledge' behavioural domain**



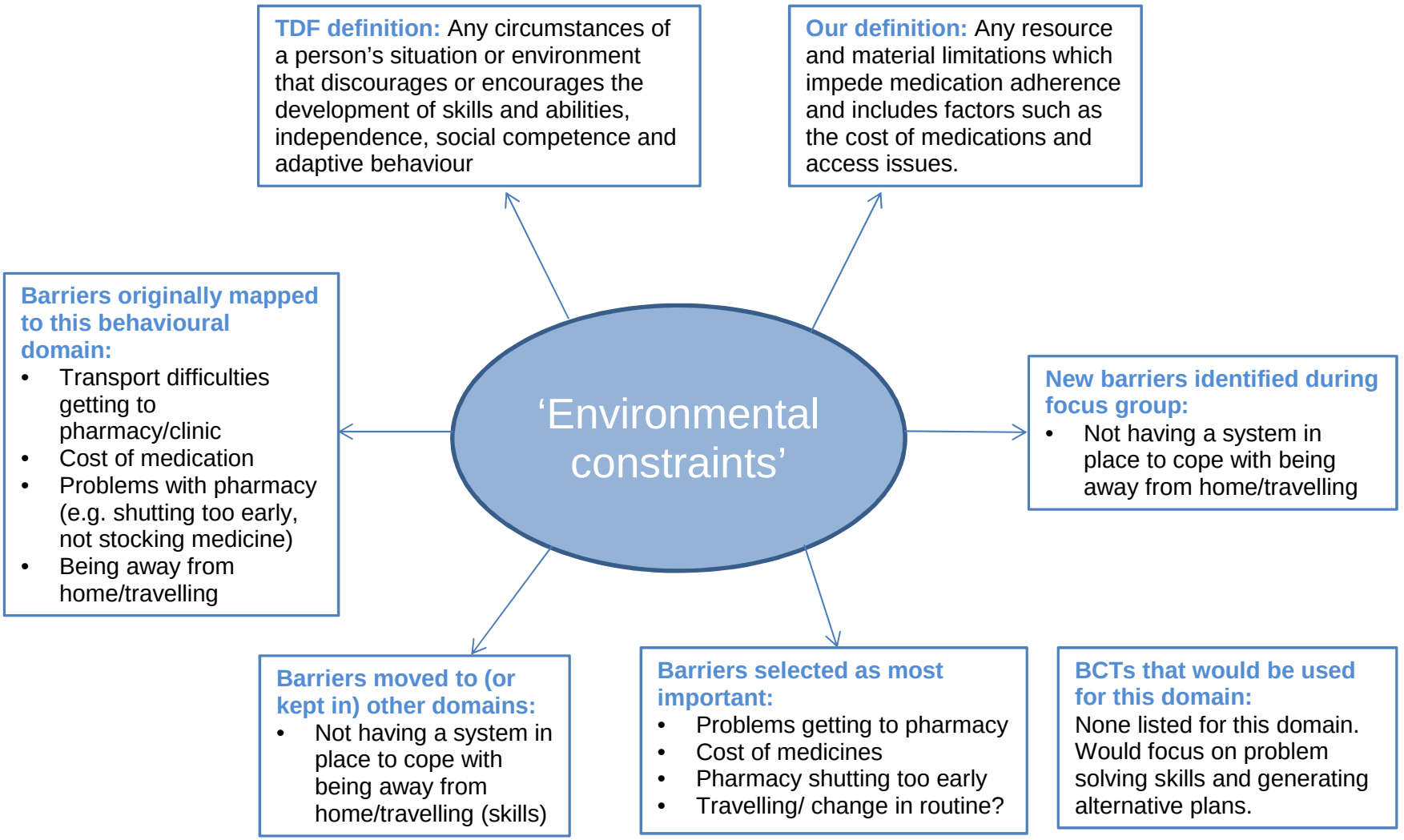
Appendix 5.10 Mind map for 'skills' behavioural domain



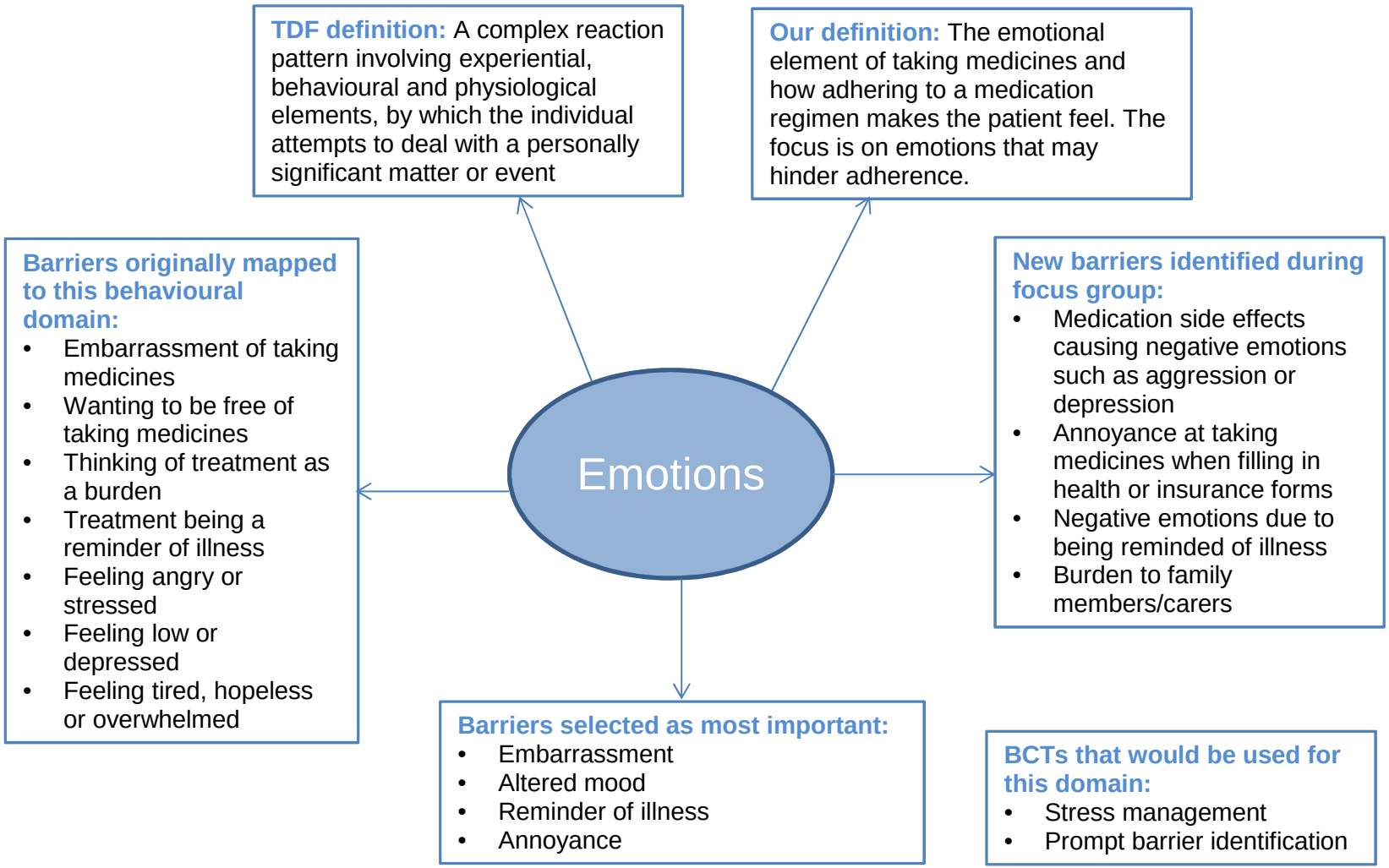
Appendix 5.10 **Mind map for 'memory, attention and decision making processes' behavioural domain**



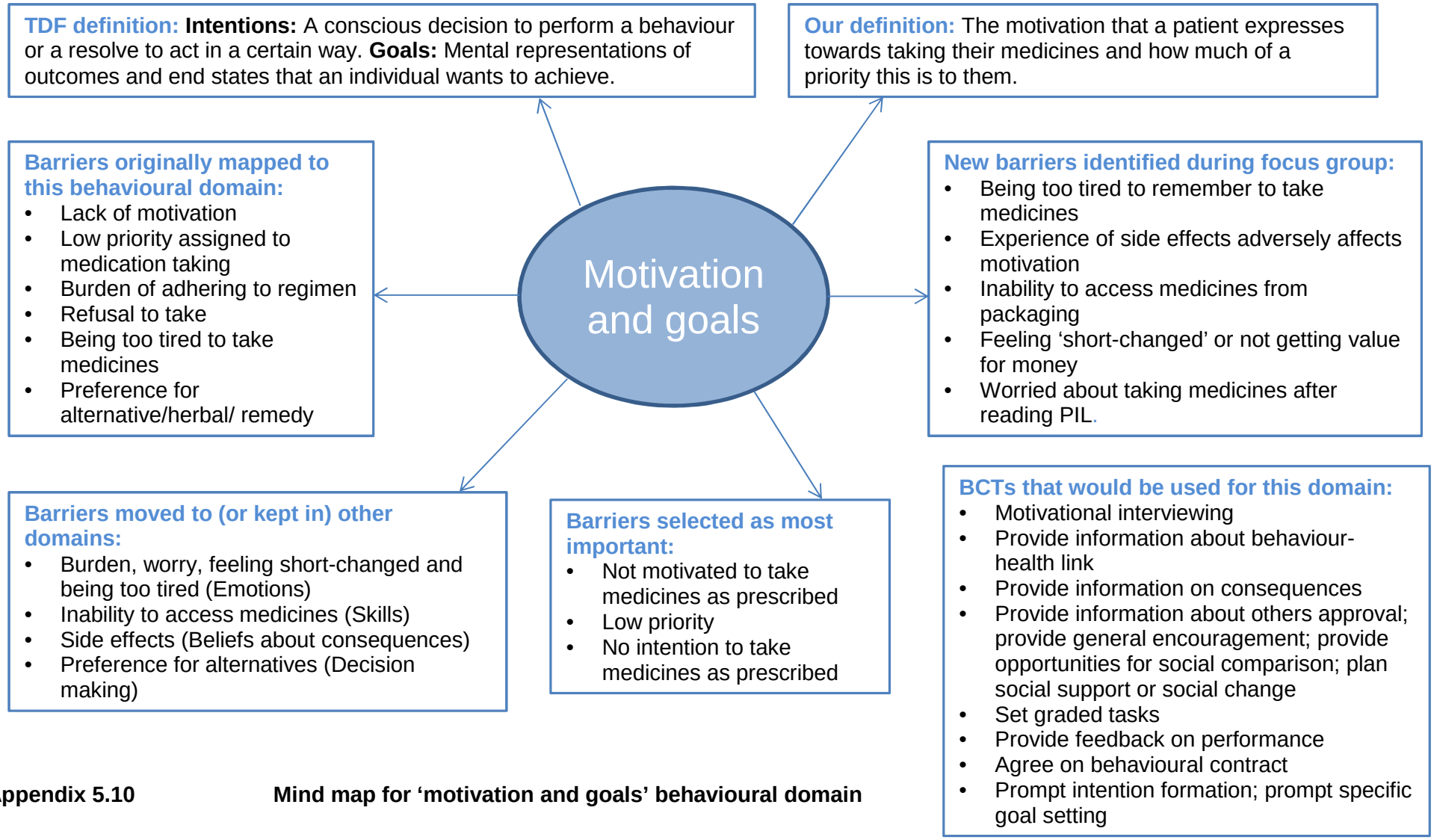
Appendix 5.10 Mind map for 'social influences' behavioural domain



Appendix 5.10 Mind map for 'environmental constraints' behavioural domain

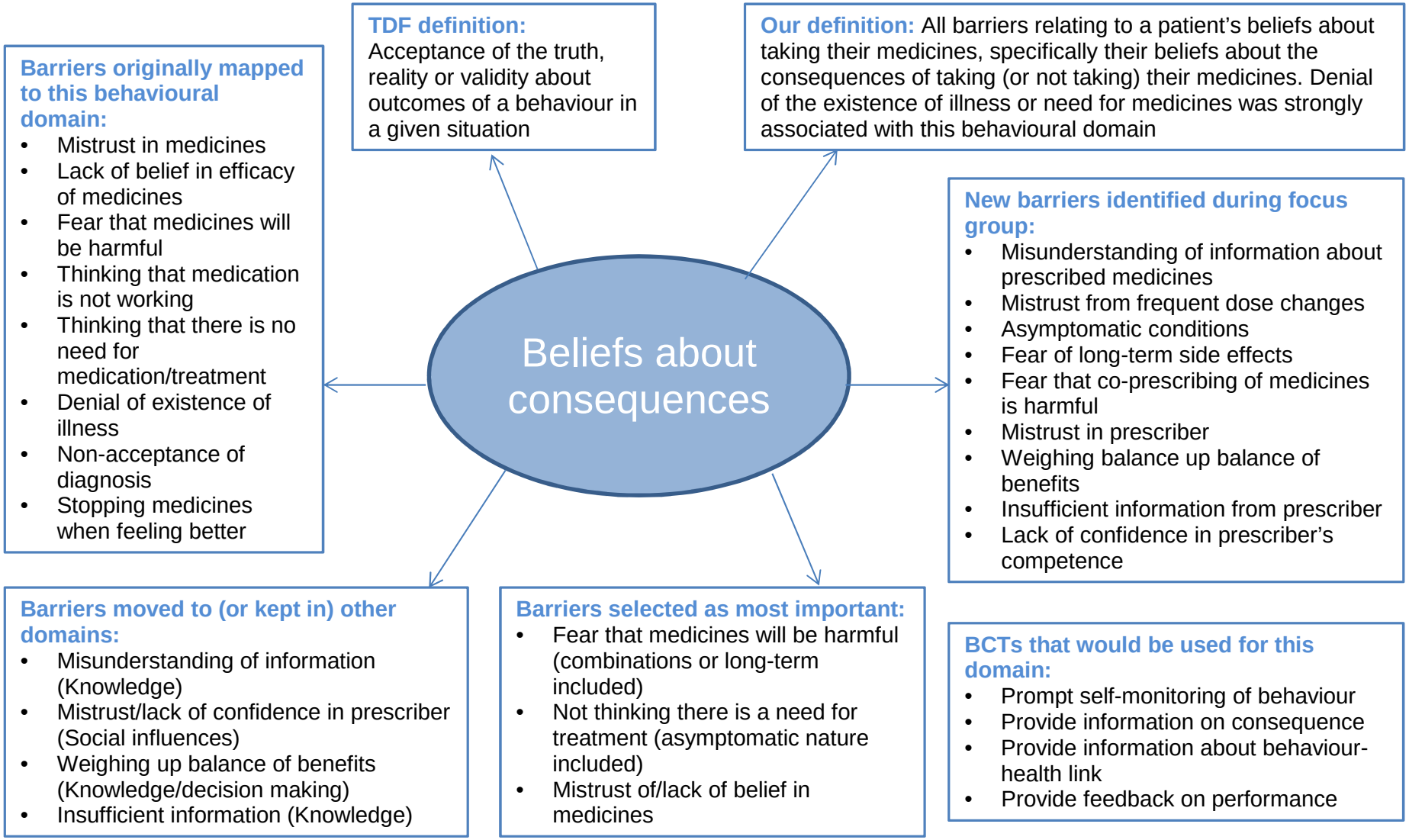


Appendix 5.10 **Mind map for 'emotions' behavioural domain**

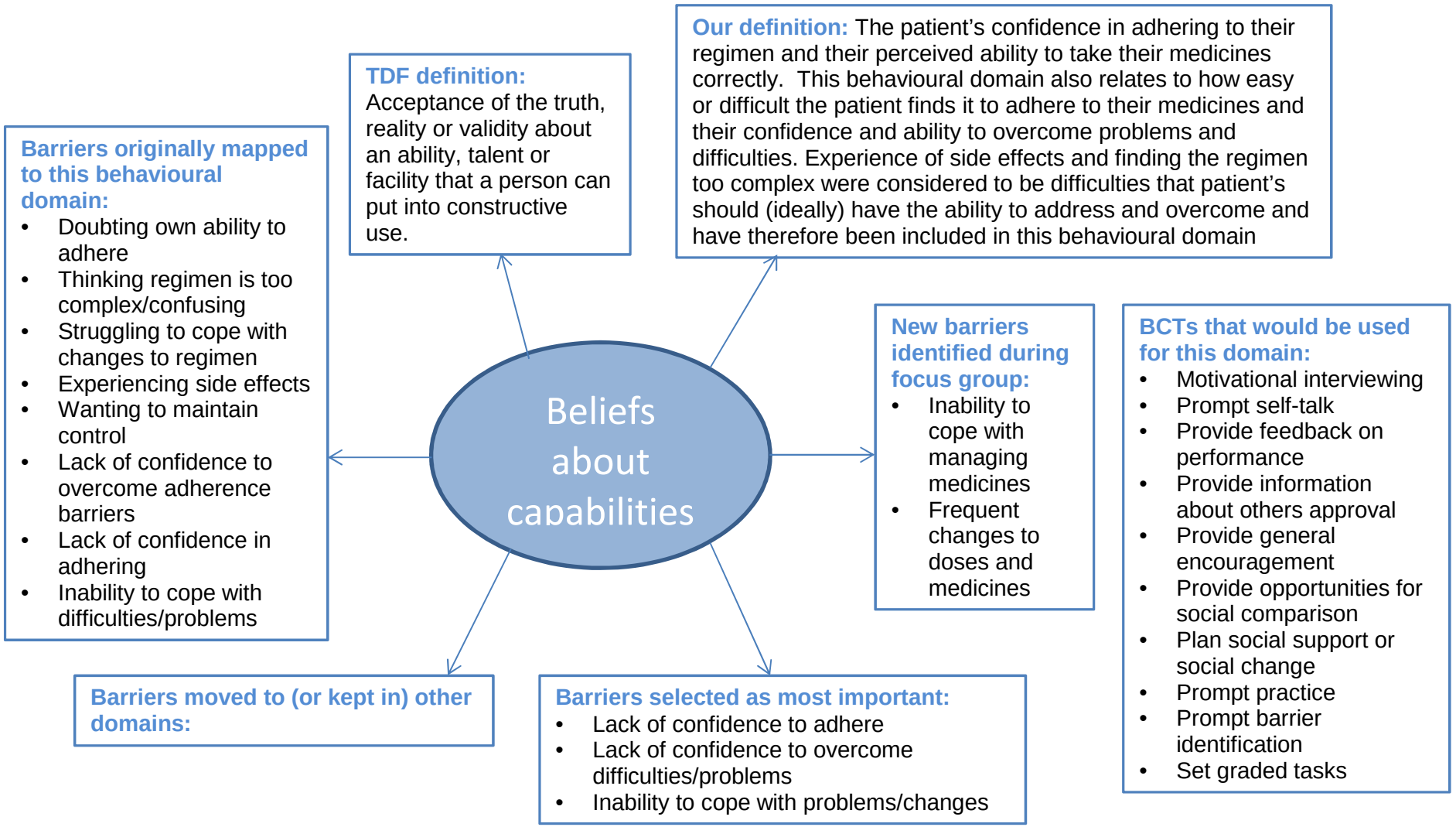


Appendix 5.10 **Mind map for 'motivation and goals' behavioural domain**

Appendix 5.10 **Mind map for 'goal conflicts' behavioural domain**



Appendix 5.10 Mind map for 'beliefs about consequences' behavioural domain



Appendix 5.10 **Mind map for 'beliefs about capabilities' behavioural domain**

Appendix 5.11 First prototype questionnaire

The Identification of Medication Adherence Barriers (IMAB) Questionnaire

- Thank you for taking the time to complete this questionnaire
- The questionnaire will help us to understand more about any difficulties that you may have with taking your medicines
- There are no right or wrong answers to the questions asked, we're interested in your honest views
- The questionnaire should not take any longer than15 minutes to complete

The identification of medication adherence barriers questionnaire

Many people who are prescribed medicines often struggle to take their medicines as prescribed. There can be many different reasons for not taking medicines as prescribed and we understand that lots of different things can 'get in the way' of following your doctors recommendations about taking your medicines.

This questionnaire lists 30 different statements about taking your medicines. For each of the statements below, please tick (✓) the box that best reflects your level of agreement with the statement. Please only tick ONE box per statement. Some of the statements may appear to be similar to others but please be sure to respond to each statement.

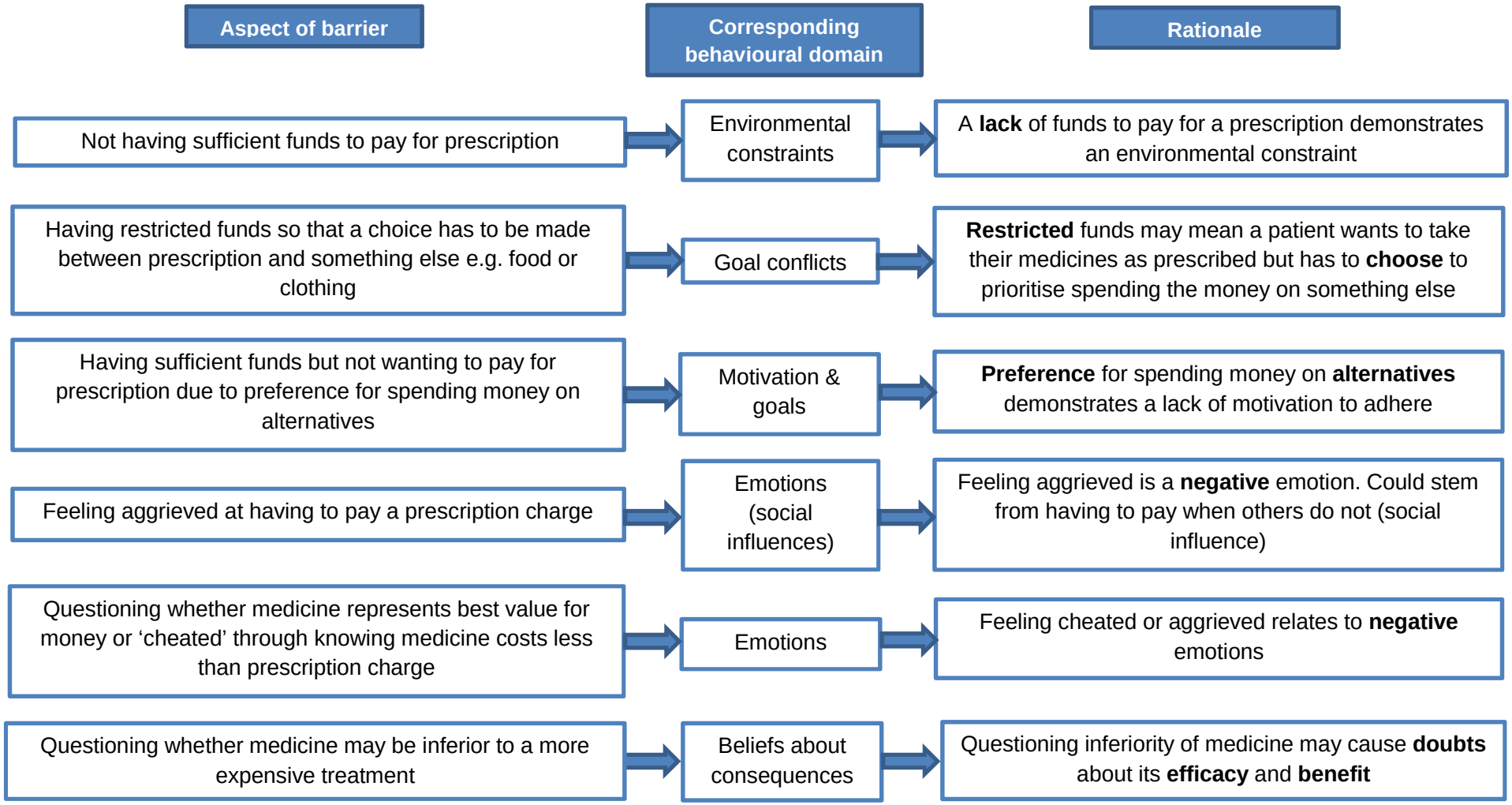
Statement	**Strongly agree**	**Agree**	**Neither agree nor disagree**	**Disagree**	**Strongly disagree**
I know how to take/use all of my medicines as prescribed					
I am able to take/use all of my medicines as prescribed					
I struggle to remember to order, collect AND/OR take my medicines as prescribed					
I trust my doctor(s) with decisions about my healthcare					
Taking all of my medicines as prescribed is not good value for money					
Having to take my medicines makes me feel negative emotions (e.g. frustration, anger, embarrassment)					
I am motivated to take my medicines as prescribed					
I'm too busy to order, collect AND/OR take my medicines.					

Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
I am confident about ordering, collecting AND/OR taking my medicines as prescribed					
Taking my medicines as prescribed is harmful to me					
I know enough about my medicines to decide whether to take them					
I am able to put a system in place to help me order, collect AND/OR take my medicines as prescribed					
I can easily be distracted from taking my medicines					
I have the support that I need from others to help me take my medicines as prescribed					
I can easily get to my local pharmacy or surgery to collect my medicines					
Taking my medicines as prescribed is an unwelcome reminder of my illness					
Taking my medicines as prescribed is high on my list of priorities					
Taking my medicines as prescribed does not fit with my daily routine					
If I experienced difficulties with my medicines I would know what to do to overcome these					

Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
If I don't take my medicines as prescribed my condition will get worse					
I know about the different ways to order and collect my repeat prescriptions					
I am able to identify each of my medicines from others					
I have my own reasons for not taking my medicines as prescribed					
I worry that other people will think badly of me if I take my medicines					
I struggle to take my medicines as prescribed when there are changes to my daily routine					
I feel positive about taking my medicines as prescribed					
I intend to take my medicines as prescribed					
Life gets in the way of me taking my medicines as prescribed					
I could easily overcome any difficulties that arise from side effects of my medicines					
I don't think my medicines will help me with my condition					

Thank you for your time

Appendix 5.12 Summary of ‘cost of medicines’ adherence barrier

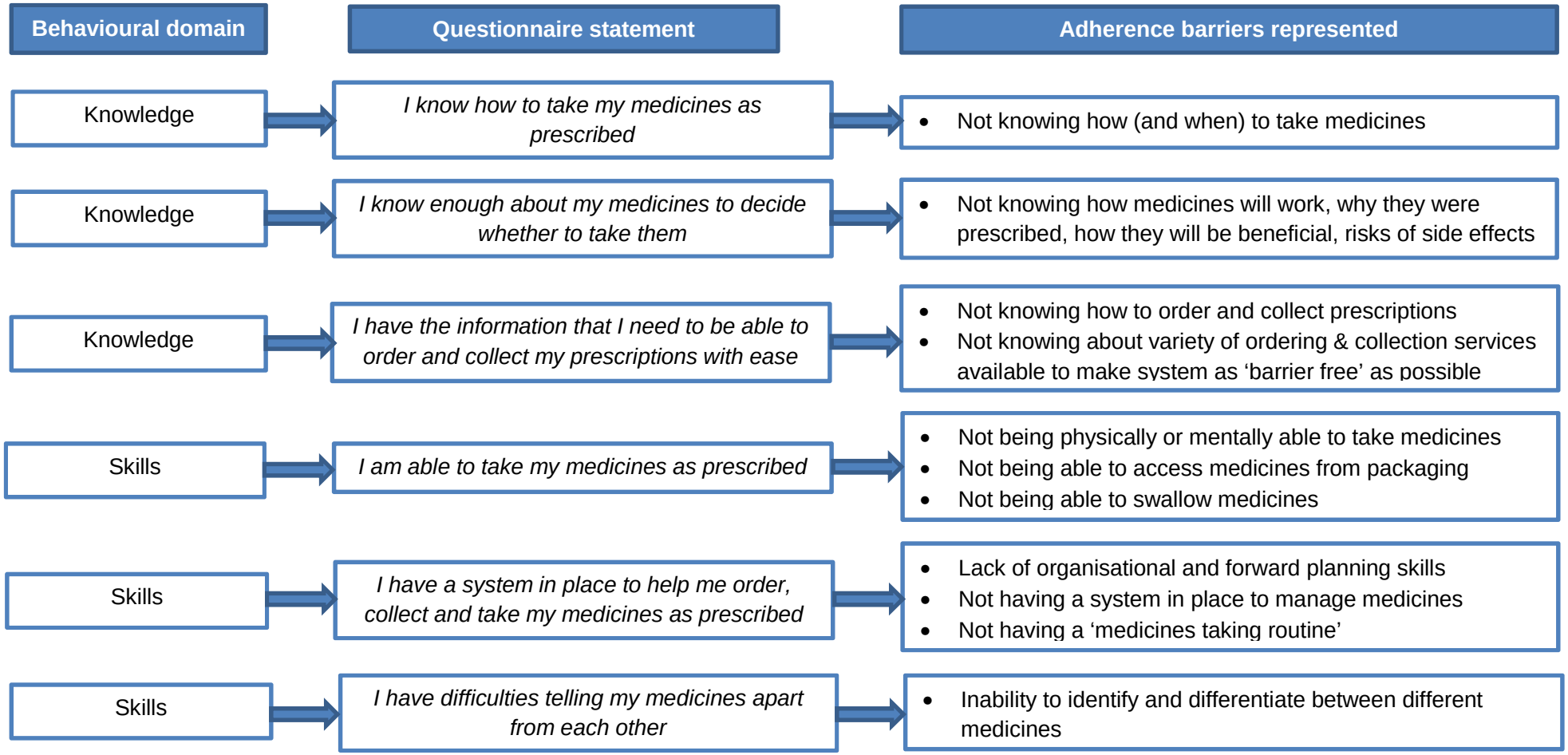


Appendix 5.12 Summary of the adherence barrier 'cost of medicines'

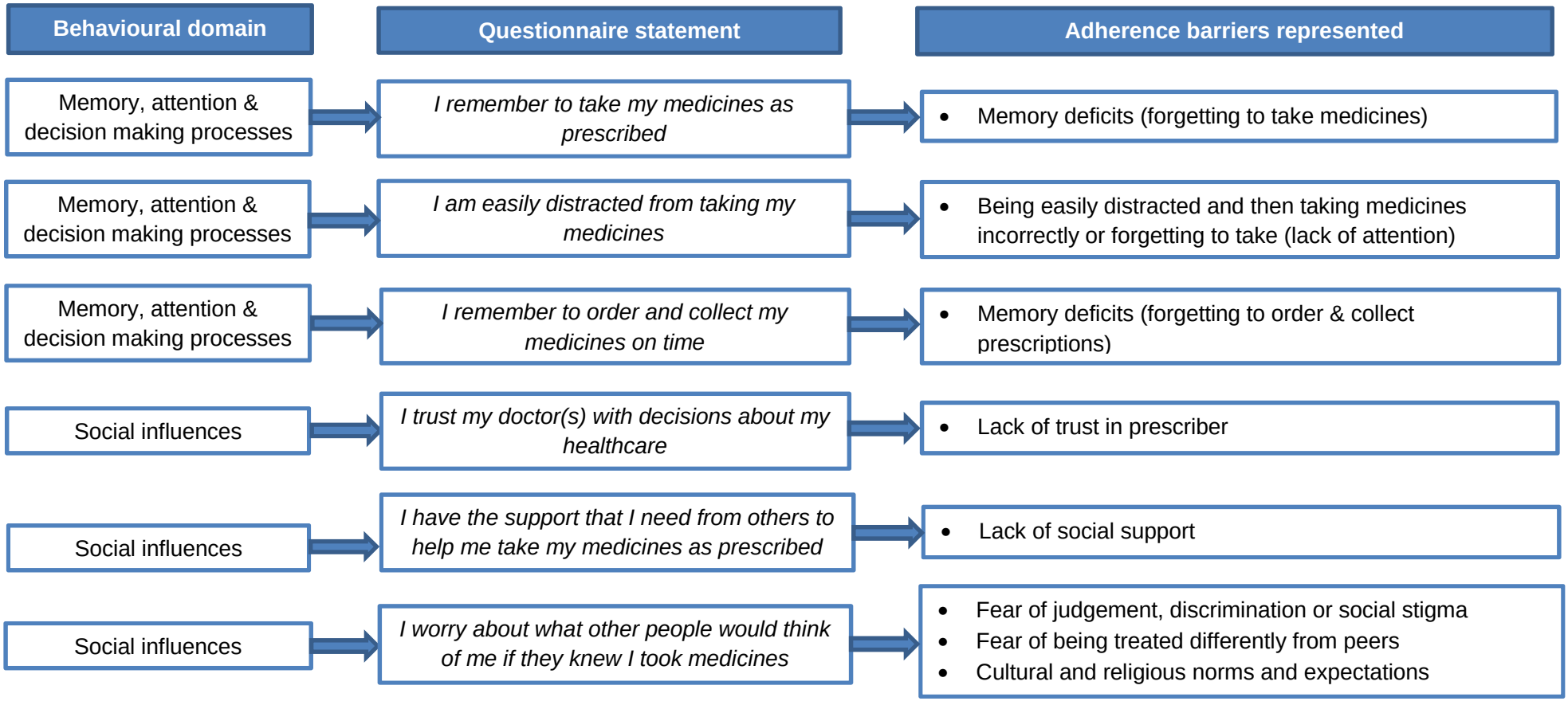
Aspect of 'cost of medicines' barrier	Strategy for incorporation into questionnaire
Not having sufficient funds to pay for prescription	Unlikely to represent genuine barrier for chronic condition such as cardiovascular disease in UK populations therefore not included
Having restricted funds so that a choice has to be made between prescription and something else e.g. food or clothing	New statement included in goal conflicts domain; 'I have to choose between paying for my prescription and paying for other things that are important to me'
Having sufficient funds but not wanting to pay for prescription due to preference for spending money on alternatives	Relates to 'motivation and goals' domain, as patient has resources to pay for medicines but would prefer not to (not motivated to). Covered by 'I am motivated…' and 'I intend to…' statements
Feeling aggrieved at having to pay a prescription charge	Covered by generic statement in 'emotions' domain relating to experience of negative emotions
Questioning whether medicine represents best value for money or through knowing medicine costs less than prescription charge	Covered by generic statement in 'emotions' domain relating to experience of negative emotions
Questioning whether medicine may be inferior to a more expensive treatment	Covered in 'belief about consequences' domain by statement relating to medicines being an effective treatment

Table A5.12 Incorporation of barrier aspects into questionnaire

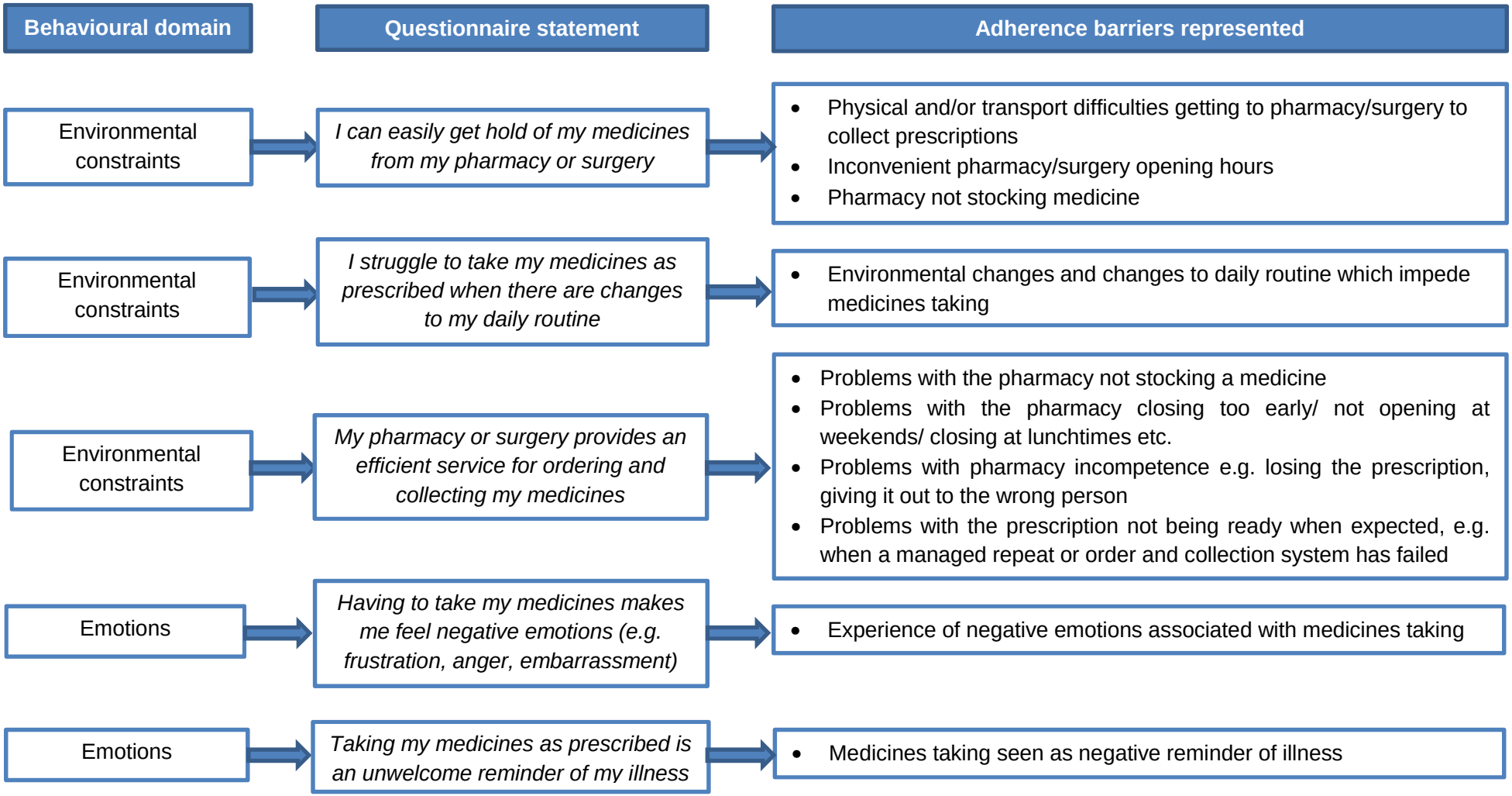
Appendix 5.13 Overall summary of refined questionnaire statements following research colleagues feedback



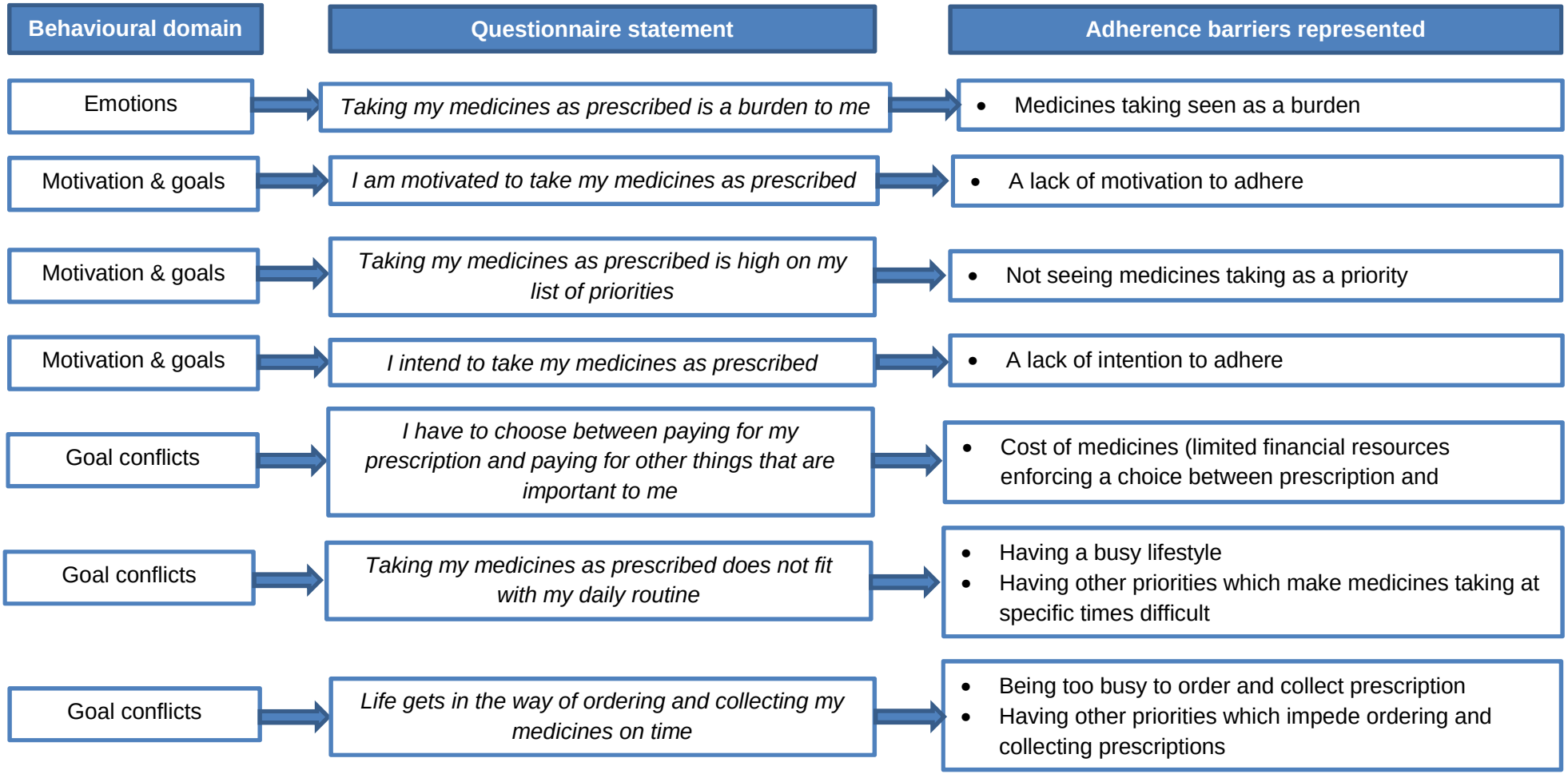
Appendix 5.13 Summary of changes to barrier statements following feedback from research colleagues



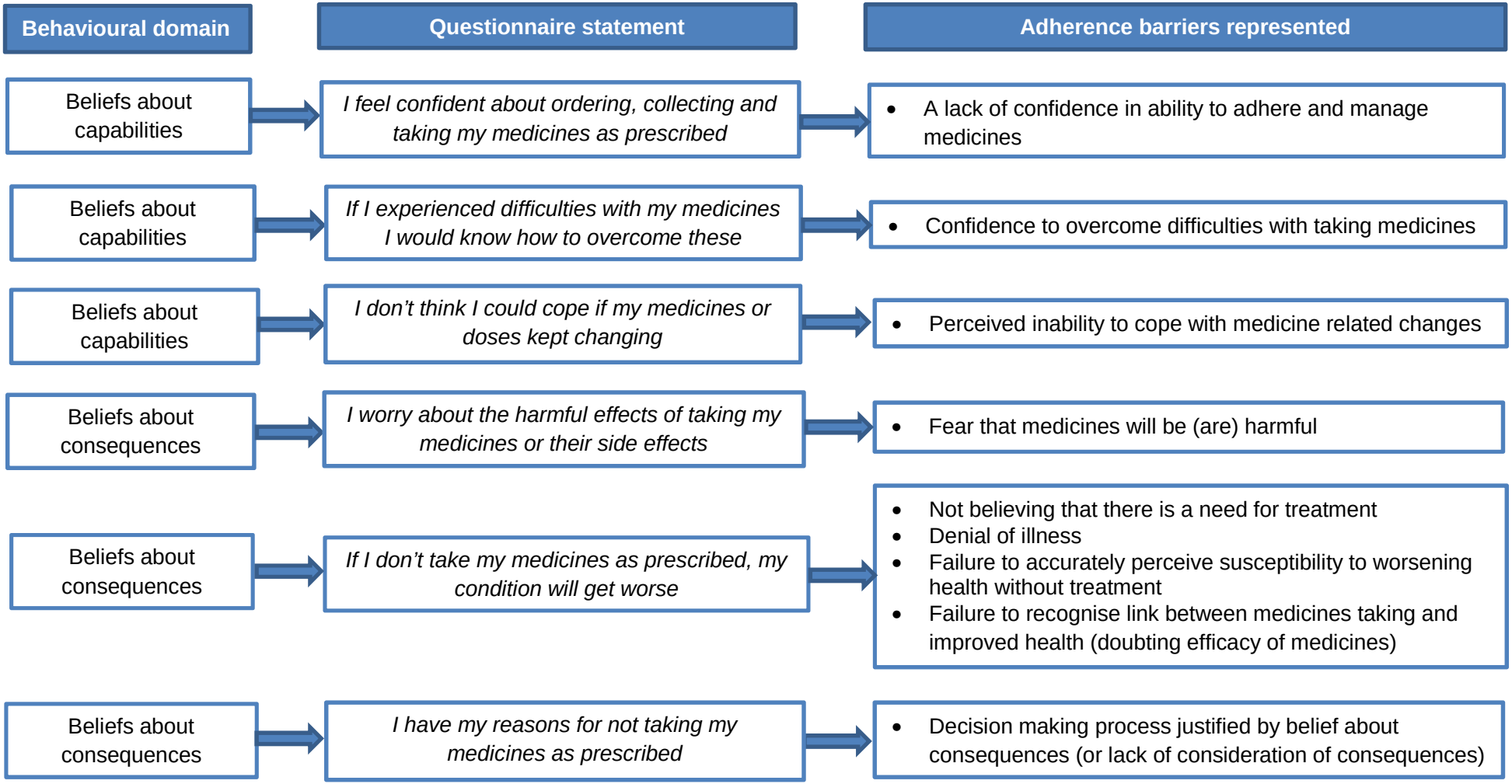
Appendix 5.13 (continued) **Summary of changes to barrier statements following feedback from research colleagues**



Appendix 5.13 (continued) **Summary of changes to barrier statements following feedback from research colleagues**

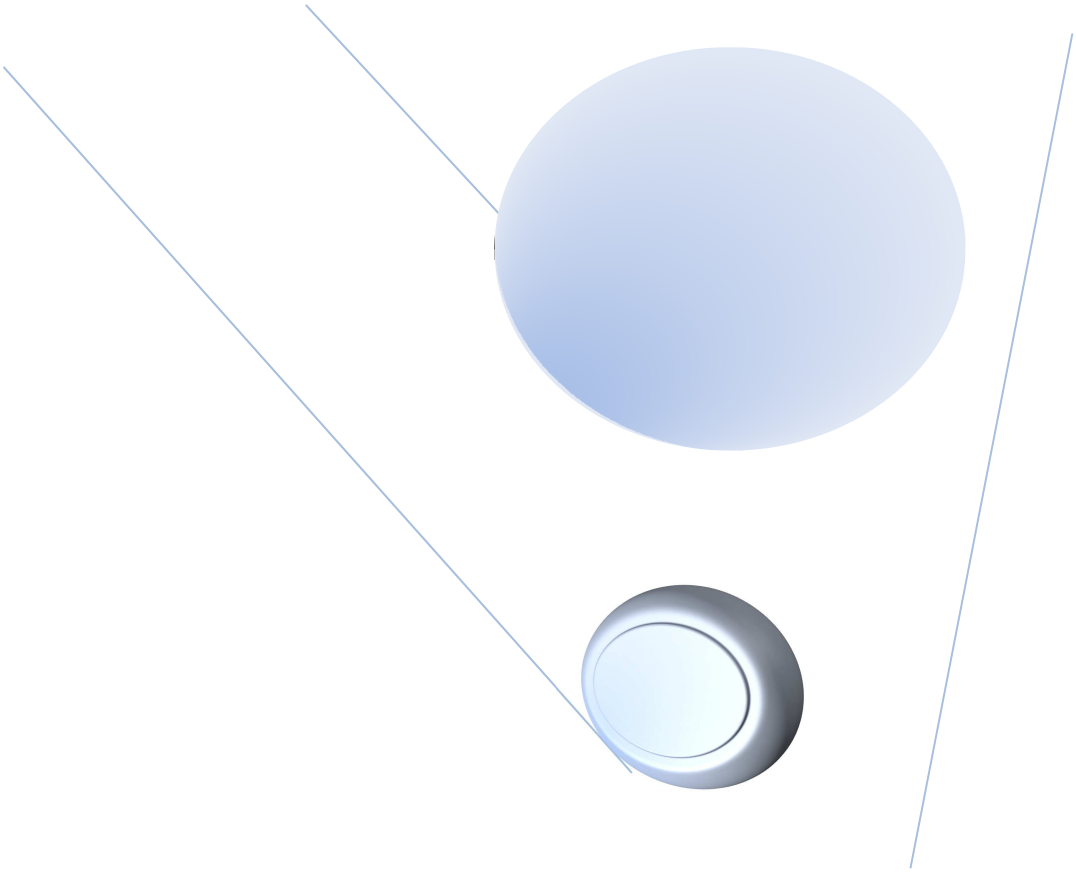


Appendix 5.13 (continued) **Summary of changes to barrier statements following feedback from research colleagues**



Appendix 5.13 (continued) **Summary of changes to barrier statements following feedback from research colleagues**

Appendix 5.14 Prototype questionnaire sent to consultation exercise participants for feedback



The Identification of Medication Adherence Barriers (IMAB) Questionnaire

- This questionnaire will help us to understand more about any difficulties that you may have with taking your medicines
- There are no right or wrong answers to the questions asked, we're interested in your honest views
- The questionnaire will take approximately 5-10 minutes to complete

The Identification of Medication Adherence Barriers (IMAB) Questionnaire

Many people often struggle to take their medicines as prescribed, for many different reasons. We understand that different things can 'get in the way' of following your doctors recommendations about taking your medicines.

This questionnaire lists 30 different statements about taking your medicines. For each of the statements below, please tick (✓) the box that best reflects your level of agreement with the statement. Please only tick ONE box per statement. Some of the statements may appear to be similar to others but please be sure to respond to each statement.

	Statement	**S. agree**	**A**	**Neither agree nor disagree**	**Disagree**	**S. disagree**
1	I know how to take my medicines as prescribed					
2	I am able to take my medicines as prescribed					
3	I remember to take my medicines as prescribed					
4	I trust my doctor(s) with decisions about my healthcare					
5	I can easily get hold of my medicines from my pharmacy or surgery					
6	Having to take my medicines makes me feel negative emotions (e.g. frustration, anger, embarrassment)					
7	I am motivated to take my medicines as prescribed					
8	I have to choose between paying for my prescriptions and paying for other things that are important to me					
9	I feel confident about ordering, collecting and taking my medicines as prescribed					
10	I worry about the harmful effects of taking my medicines or their side effects					

	Statement	S. agree	A	Neither agree nor disagree	Disagree	S. disagree
11	I know enough about my medicines to decide whether to take them					
12	I have a system in place to help me order, collect and take my medicines as prescribed					
13	I am easily distracted from taking my medicines					
14	I have the support that I need from others to help me take my medicines as prescribed					
15	I struggle to take my medicines as prescribed when there are changes to my daily routine					
16	Taking my medicines as prescribed is an unwelcome reminder of my illness					
17	Taking my medicines as prescribed is high on my list of priorities					
18	Taking my medicines as prescribed does not fit with my daily routine					
19	If I experienced difficulties with my medicines I would know how to overcome these					
20	If I don't take my medicines as prescribed I think my condition will get worse					
21	I have the information that I need to be able to order and collect my prescriptions with ease					
22	I have difficulties telling my medicines apart from each other					
23	I remember to order and collect my medicines on time					

	Statement	S. agree	A	Neither agree nor disagree	Disagree	S. disagree
24	I worry about what other people would think of me if they knew I took medicines					
25	My Pharmacy or surgery provides an efficient service for ordering and collecting my medicines					
26	Taking my medicines as prescribed is a burden to me					
27	I intend to take my medicines as prescribed					
28	Life gets in the way of me taking my medicines as prescribed					
29	I don't think I could cope if my medicines or doses kept changing					
30	I have my reasons for not taking my medicines as prescribed					

Thank you for your time

*Note abbreviations and smaller font have been used in this replication to enable production in thesis format

Appendix 5.15 Consultation exercise participants ‘feedback booklet’

Identification of Medication Adherence Barriers (IMAB) Questionnaire – Focus Group Participant Feedback Document

Section one – feedback on the questionnaire statements

- The thirty statements below are taken directly from the prototype questionnaire that you have been sent. They have been replicated on this form to provide you with the space to give any comments, concerns or feedback. Please feel free to provide as much detail as you wish as every piece of information that we gather will be really helpful for improving the questionnaire.

- As you read each statement, please think about how you would respond as a patient yourself, if you want to tick the boxes as if you were filling it for real, please feel free to do so. Please use the comments/feedback box to tell us what you thought as you read the statement. We're particularly interested to know if the statement was clear; did it make sense to you, did you know how to answer it and how easy or difficult was this? There's extra space at the end of this form to write any further comments if you haven't got enough room here.

	Statement	**Strongly agree**	**Agree**	**Neither agree nor disagree**	**Disagree**	**Strongly disagree**	**Comments/feedback**
1	I know how to take my medicines as prescribed						
2	I am able to take my medicines as prescribed						
3	I remember to take my medicines as prescribed						
4	I trust my doctor(s) with decisions about my healthcare						

	Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Comments/feedback
5	I can easily get hold of my medicines from my pharmacy or surgery						
6	Having to take my medicines makes me feel negative emotions (e.g. frustration, anger, embarrassment)						
7	I am motivated to take my medicines as prescribed						
8	I have to choose between paying for my prescriptions and paying for other things that are important to me						
9	I feel confident about ordering, collecting and taking my medicines as prescribed						
10	I worry about the harmful effects of taking my medicines or their side effects						
11	I know enough about my medicines to decide whether to take them						

	Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Comments/feedback
12	I have a system in place to help me order, collect and take my medicines as prescribed						
13	I am easily distracted from taking my medicines						
14	I have the support that I need from others to help me take my medicines as prescribed						
15	I struggle to take my medicines as prescribed when there are changes to my daily routine						
16	Taking my medicines as prescribed is an unwelcome reminder of my illness						
17	Taking my medicines as prescribed is high on my list of priorities						
18	Taking my medicines as prescribed does not fit with my daily routine						
19	If I experienced difficulties with my medicines I would know how to overcome these						

	Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Comments/feedback
20	If I don't take my medicines as prescribed I think my condition will get worse						
21	I have the information that I need to be able to order and collect my prescriptions with ease						
22	I have difficulties telling my medicines apart from each other						
23	I remember to order and collect my medicines on time						
24	I worry about what other people would think of me if they knew I took medicines						
25	My Pharmacy or surgery provides an efficient service for ordering and collecting my medicines						
26	Taking my medicines as prescribed is a burden to me						

	Statement	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Comments/feedback
27	I intend to take my medicines as prescribed						
28	Life gets in the way of me taking my medicines as prescribed						
29	I don’t think I could cope if my medicines or doses kept changing						
30	I have my reasons for not taking my medicines as prescribed						

Section two – general feedback on the questionnaire

- We're keen to be sure that the questionnaire has a professional feel but that the instructions are clear and easy to understand and that overall the questionnaire is as 'user-friendly' as possible. The questions below relate to these points, please provide as much detail as possible. All points are important, it doesn't matter if they may seem a small or silly point to you, we're really want to hear any thoughts that you may have, no matter how big or small they are.

1) Do you have any comments on the design or layout of the of the questionnaire? Is the front cover OK? Is the font size acceptable?

2) Do you have any comments on the instructions for completion? Is it clear what you are expected to do? Would a patient understand what the questionnaire is about? Do you think our estimate of 5-10 minutes for completion is accurate (if not what would be a more realistic time frame)?

3) Do you have any other comments about the questionnaire? Can you think of any ways to improve it?

Section three – specific questions

- Based on the feedback that we've already received from other researchers and some healthcare providers, there are a few specific points that we'd really value your feedback on.

1) Statement number 29 is 'I don't think I could cope if my medicines or doses kept changing'. Is the word 'doses' here OK? Is it clear and easily understood?

2) Statement number 2 is ‘I am able to take my medicines as prescribed’. We had hoped that this statement would cover factors such as problems with swallowing the tablets or getting them out of their packets (or dropping them!). If you were a patient experiencing these kinds of problem, would you think to disagree with this statement? What did you think this statement meant?

3) Statement number 8 is ‘I have to choose between paying for my prescriptions and paying for other things that are important to me’. How did you fill in this statement if you do not pay for your prescription? Did you find that this statement was really difficult for you complete, would a ‘not applicable’ option have made it easier if you do not pay?

4) Statement 4 mentions trust in your doctor(s) and similarly, we mention ‘following your doctor’s recommendations...’ in the introduction. Do you find the term ‘doctors’ acceptable or is it too specific? Imagine you had your medicines prescribed by a nurse rather than a doctor or your pharmacist had given you recommendations rather than the doctor, would this statement then be confusing to you? We wondered whether the term ‘prescriber’ or ‘healthcare provider’ would work instead of ‘doctor’. How do you find these terms, are they clear and understandable to you or do you think they would cause confusion?

Section four – overall summary

- Thank you for taking the time to provide this feedback, it will be invaluable in the questionnaire development. The findings from the focus group were also incredibly useful. In summary, we just wanted to ask if there were any other comments you wanted to provide, be it about the questionnaire, or the research project in general. If you have any further comments, please use the space below to record these:

Thank you so much for your time and feedback

Appendix 5.16 Covering letter sent with ‘feedback booklet’ to consultation exercise participants

<Participant name>
<Participant address 1>
<Participant address 2>
<Participant address 3>
<Participant address 4>

<Date>

Dear participant,

Thank you so much for agreeing to give your feedback on the prototype questionnaire that we've been working on. I'm so pleased to have your continued support with this important piece of research.

Since the focus groups that you participated in, we have been busy working through the recordings made and analysing the discussions that were held. The focus groups were a real success and a pivotal part of this research thanks to your views, opinions and honesty. Using the work from the focus groups we have been able to develop a prototype questionnaire, which we would now like to receive your feedback on.

As discussed, you will find enclosed a full colour copy of the questionnaire and an additional document titled 'focus group participant feedback form'. Once you have read through the questionnaire, please work through the feedback form where you will be guided through specific points that we would value your thoughts on.

I hope that the feedback form will be straightforward for you to complete but if there is anything that is not clear, or you feel it would be easier to discuss a matter with me directly rather than leave written feedback, then please do not hesitate to contact me. My contact details can be found at the end of this letter.

Thank you once again for your valued support,

With kindest regards and best wishes,

Claire Easthall MPharm, MRPharmS
Research Pharmacist & PhD Student
School of Pharmacy
University of East Anglia
Norwich Research Park
Norwich, Norfolk, NR4 7TJ
c.easthall@uea.ac.uk
01603 591973/07807 389493

Appendix 5.17 Summary of recommended changes to questionnaire following consultation exercise participant's feedback

Questionnaire statement	Participant suggested changes	Agreed changes	Rationale
1) I know how to take my medicines as prescribed	'I know how and when' might be better, as prescribed could be confusing	No changes necessary	As prescribed deemed appropriate and 'how and when' should be avoided due to 'double loading'
3) I remember to take my medicines as prescribed	Add 'always'	No changes necessary	5 point Likert scale allows for strength of frequency to be conveyed e.g. always remember = strongly agree, mostly remember = agree etc.
5) I can easily get hold of my medicines from my pharmacy or surgery	'Prescribed medicines'?	'I can easily get hold of my prescribed medicines from the pharmacy or surgery'	Specification of 'prescribed medicines' useful to differentiate from purchased over-the-counter medicines. Specificity of 'my' pharmacy or surgery is unnecessary as patients can choose to go to any pharmacy
6) Having to take my medicines makes me feel negative emotions (e.g. frustration, anger, embarrassment)	'Have' negative emotions not feel	I have negative emotions (e.g. frustration, anger, embarrassment) about taking my medicines as prescribed.	According to Scherer in 2005, a feeling is the subjective experience of emotional state once it has occurred[1]. Emotions are therefore something that are experienced (had) rather than felt. Wording chosen to ensure there is no inference of medicines causing negative emotions as side effects, as identified in consultation exercises
9) I feel confident about ordering, collecting and taking my medicines as prescribed	None	I feel confident about all aspects of managing (ordering, collecting and taking) my medicines	Research team agreed that 'AND' conjunction had the potential to be misleading and cause response difficulties. Statement rephrased to focus on confidence in managing medicines as this reflects the barrier and participant used terminology well.
10) I worry about the harmful effects of taking my medicines or their side effects	'I worry about taking my medicines or having side effects'	I worry about unwanted effects (e.g. harmful effects or side effects) from taking my medicines	'Worry about taking' could be quite ambiguous as this could include many components, plus worrying about harmful effects is important. Re-phrased to improve clarity

Table A5.16 Summary of changes made following feedback from consultation exercise participants

Questionnaire statement	Participant suggested changes	Agreed changes	Rationale
11) I know enough about my medicines to decide whether to take them	'I know enough about my medicines to decide whether to take them or not'	No changes necessary	The addition of 'or not' adds greater complexity to the sentence without any justifiable benefit and is therefore best avoided
13) I am easily distracted from taking my medicines	I wonder if you mean 'do you forget'.	No changes necessary	Forgetting and being easily distracted are similar but different constructs and should therefore remain distinct
14) I have the support that I need from others to help me take my medicines as prescribed	• Add a not applicable options as patients may not need support • Two separate statements may be necessary, whether they need any help and whether its available	'If I needed support from others to take my medicines as prescribed, I could get it'	Worded amended to facilitate completion for patients who do not need support. 'To help me' removed as considered unnecessary and removal facilitates easier readability.
15) I struggle to take my medicines as prescribed when there are changes to my daily routine	Difficult to answer if you haven't experienced this therefore might need to be changed	'Changes to my daily routine would not interfere with taking my medicines as prescribed'	This barrier relates to environment constraints and therefore needs to establish whether changes to routine acts as a barrier to adherence. Phrased to enable easier completion for patients who have not experienced changes to their routine
16) Taking my medicines as prescribed is an unwelcome reminder of my illness	'Taking my medicines as prescribed is an unwelcome reminder of my illness or condition'	'Taking my medicines as prescribed is an unwelcome reminder of my condition'	'Condition' and 'illness' are synonymous terms, but condition may be more appropriate for preventative medication as patients may not perceive themselves as having an illness
18) Taking my medicines as prescribed does not fit with my daily routine	'Taking my medicines as prescribed does not fit in with my daily routine'	No changes necessary	Recommended change relates to minor semantics which does not improve the statement but may reduce readability

Table A5.16 (continued) Summary of changes made following feedback from consultation exercise participants

Questionnaire statement	Participant suggested changes	Agreed changes	Rationale
19) If I experienced difficulties with my medicines I would know how to overcome these	'I know how to overcome difficulties with my medicines', as if-then statements can be difficult	'I am confident that I could find ways to solve any difficulties that I have with taking my medicines as prescribed'	Suggested change and original statement relate to knowledge not beliefs about capabilities and are therefore not appropriate. New statement worded to reflect belief about capability.
20) If I don't take my medicines as prescribed I think my condition will get worse	'My condition will get worse if I don't take my medicines as prescribed'; avoids if-then statements	No changes necessary	Whilst recommended change lessens impact of 'if-then' statement it does not resolve the issue. Moreover, recommended change detracts from emphasis on belief about consequences.
21) I have the information that I need to be able to order and collect my prescriptions with ease	'I have the information that I need to be able to easily order and collect my prescriptions'	'I have the information that I need to be able to easily order and collect my prescriptions'	Recommend change improves flow of sentence slightly and was therefore implemented
22) I have difficulties telling my medicines apart from each other	Needs amending as only applicable to patients who are taking more than one medicine	'Telling my medicines apart from each other would not be a problem for me'	Re-phrased to ease completion for patients who do not have more than one medicine
24) I worry about what other people would think of me if they knew I took medicines	'...took medicines for an illness or condition'	No changes necessary	Suggested change adds unnecessary complexity to statement
25) My Pharmacy or surgery provides an efficient service for ordering and collecting my medicines	'Pharmacy' should not have a capital 'P'	'My pharmacy or surgery provides an efficient service for ordering and collecting my medicines'	A well spotted genuine typographic error
26) Taking my medicines as prescribed is a burden to me	'Necessary burden'?	No change necessary	Inappropriate and unnecessary addition

Table A5.16 (continued) **Summary of changes made following feedback from consultation exercise participants**

References for table A5.19 1) Scherer, K. R. (2005). "What are emotions? And how can they be measured?" Social science information **44**(4): 695-729.