Abstract

Objectives: To identify barriers to medication adherence in patients prescribed medicines for the prevention of cardiovascular disease and map these to the Theoretical Domains Framework (TDF), to produce a conceptual framework for developing a questionnaire-based medication adherence tool.

Methods: A scoping review of barriers to medication adherence in long-term conditions was conducted to generate an initial pool of barriers. After preliminary mapping to the TDF, these barriers were presented to two focus groups of patients prescribed medicines for the prevention of cardiovascular disease (n=14) to stimulate discussion. The group discussions enabled the patients' interpretations of the adherence barriers to be determined, provided validity from the patient perspective, and identified additional barriers unrepresented in the scoping review.

Key findings: The preliminary pool of adherence barriers was identified from 47 studies across a range of long-term conditions. The majority of TDF domains were represented by these literature-identified barriers except 'social/professional role and identity' and 'behavioural regulation'. Barrier mapping was largely endorsed by focus group participants, who also contributed additional barriers, including those relating to not having a 'system' in place for managing their medicines and the negative emotions evoked by medicine taking.

Conclusion: The TDF enabled full exploration of adherence barriers including those relating to emotions which have received limited attention in the literature. This work has provided a conceptual framework for developing a questionnaire to identify an individual's adherence barriers which may then be coupled with appropriate behaviour change techniques to deliver a theory-based intervention tailored for individual need.

Keywords: Scoping review, Theoretical Domains Framework (TDF), focus group, questionnaire, IMAB-Q

Introduction

An estimated 30 to 50% of patients with long-term conditions (LTCs) are non-adherent to their prescribed medicines.[1] A large-scale meta-analysis, estimated adherence to medicines for the prevention of cardiovascular disease (CVD) to be 57% (95% CI 50-64%).[2] These medicines are prescribed for a range of LTCs including hypertension, dyslipidaemia and angina and are amongst the most commonly prescribed medicines in the UK.[2]

Medication adherence is a complex health behaviour, influenced by a plethora of factors.[3] Non-adherence can diminish treatment effects leading to increased morbidity and mortality[4] plus wasted healthcare resources.[3] Evidence suggests that a greater understanding of the barriers to adherence is needed to improve the effectiveness of adherence interventions.[5] A plethora of theoretical models have been developed to explain the complexities of medication adherence, including those focused on the balance between patient perceived necessity and concerns about medicines[6] and those focused on the importance of practitioner consultation style[7]. Though these models highlight important considerations for medication adherence research, the most recent Cochrane review highlights that meaningful progress with adherence research is still sub-optimal. [5] Theoretical models such as Social Cognitive Theory, the Health Belief Model and Self-regulation model have been applied to medication adherence interventions.[8] However, a systematic review of theory-based interventions to improve medication adherence identified that none have successfully guided the development of an effective adherence intervention applicable to all long-term medications[8].

Psychology-based behaviour change techniques, such as motivational interviewing, show promise as effective adherence interventions.[9] However, core training of the existing healthcare workforce is not designed to equip practitioners in selecting the most appropriate

behaviour change techniques (BCT) for improving adherence, according to identified individual adherence barriers.[10,11,12,]

Developing an adherence tool which identifies a patient's barriers to adherence and guides the practitioner to work with the patient to select the most appropriate BCTs may enable the healthcare workforce to respond to the call for theory and evidence guided, individualised interventions, [13, 14,] which identify potential barriers to behaviour change. [8, 155,]

The Theoretical Domains Framework (TDF)[16, 17] is a composite of health psychology theory which offers a structured approach for exploring the determinants of individual behaviour.[18] The domains of the TDF have been linked to evidence-based BCTs,[19,20] leading to successful use of the TDF to guide the intervention development for behaviour change.[21] The TDF may therefore be suitable for mapping adherence barriers and creating a conceptual framework.

Literature describing application of the TDF to medication adherence[22-25] represents notable advancements in the field. However, each study focusses on medication adherence in a specific disease rather than multiple LTCs. Most patients have multiple diseases for which they are prescribed multiple medicines; routine practice consultations such as medication reviews are therefore not focused on medication adherence in one specific disease state. Intervention implementation is supported by compatibility with routine practice,[26] thus, an adherence support tool applicable across a range of LTCs is a stronger candidate for effective implementation into routine practice.[27] Exploration of barriers to adherence in medicines prescribed for the prevention of CVD (which covers multiple LTCs) is therefore an intuitive opportunity to broaden TDF-based adherence research towards multiple LTCs, whilst minimising the confounding factors that could be introduced by considering all LTCs collectively.

The current article presents the developmental work which underpinned the Identification of Medication Adherence Barriers Questionnaire (IMAB-Q); [28] a TDF-based questionnaire to support practitioners in identifying non-adherent patient's and elucidating their individual reasons for non-adherence. It comprises a scoping review of barriers to adherence in LTCs, the initial mapping of these barriers to the TDF and the qualitative exploration of these barriers in patients prescribed medicines for the prevention of CVD, in order to develop a conceptual framework to inform questionnaire development.

Existing literature syntheses (e.g.[29,30]) report quantitative findings from intervention studies and non-modifiable adherence determinants such as age, gender and socioeconomic status. Modifiable determinants of adherence, relating to psychosocial and environmental barriers are often overlooked. These reviews also consider non-adherence in all conditions, yet important differences in adherence determinants exist between acute and LTCs.[3] A broader evidence synthesis, narratively combining both quantitative and qualitative studies may therefore provide a better foundation for exploring adherence barriers. Scoping reviews are an appropriate method to 'map' relevant literature and address broad topics where differing study designs are available.[31]

Correct mapping of adherence barriers to a theoretical framework requires deep understanding which cannot always be elucidated from the literature. Qualitative exploration to supplement a literature review can provide this depth of understanding,[32] enhance the utility of a scoping review and ensure meaningful mapping.

Methods

The programme of work included four phases:

1. Scoping review of barriers to medication adherence in LTCs

2. Preliminary mapping of literature-identified barriers to the TDF
3. Focus groups with patients prescribed medicines for the prevention of CVD
4. Refinement of adherence barriers mapping

Phase 1 Scoping review

This phase aimed to generate a preliminary repository of barriers to medication adherence in LTCs, for stimulating focus group discussions.

Search strategy

The Embase, Medline and PsychINFO databases were accessed via the Ovid interface on 18th September 2012, to undertake the search detailed in supplementary file 1. The search was restricted to articles written in English and since 2005, as scoping searches indicated that prior to this, psychosocial determinants of adherence were seldom explored. Abstracts were screened against pre-defined inclusion and exclusion criteria.

Inclusion and exclusion criteria

Abstracts of any study design, reporting medication adherence barriers in LTCs were eligible for inclusion. LTCs beyond those covered by 'CVD prevention' were included to ensure breadth of the preliminary pool of adherence barriers before later refinement.

Abstracts were excluded if they:

- Included participants with drug addiction or mental health problems (the nature of non-adherence in this population is condition-specific)

Data collection and synthesis (charting)

Full texts were accessed where possible, but when unavailable, adherence barriers were extracted from abstracts. Adherence barriers were initially recorded using the exact terminology in the article. Once all barriers had been extracted, barriers with the same underpinning characteristic but presented differently due to specifics of context or variations in language were grouped, for example 'forgetting to take medicines' and 'not remembering doses' were grouped as one barrier related to forgetting medicines.

Phase 2 Mapping of adherence barriers to the TDF

Adherence barriers were mapped to one of the 12 domains of the original TDF.[16] . Existing literature[16, 17, 33] were utilised to interpret each of the TDF domains in the context of barriers to medication adherence. Preliminary mapping was discussed by the authors until consensus was achieved about which barriers belonged to each domain.

Phase 3 Focus groups with patients prescribed medicines for the prevention of CVD

Focus groups with patients prescribed medication for CVD prevention were undertaken to:

1. Identify additional adherence barriers not elicited from the scoping review
2. Optimise the research team's understanding of identified barriers
3. Ensure appropriate mapping of barriers to the TDF

Participants and recruitment

Recruitment commenced post ethical approval from the University of East Anglia Faculty of Health ethics committee (reference number 2012/2013-04). The large pool of employees and students at the university were used as potential participants and gatekeepers to the wider non-university community for recruitment. Recruitment was via posters placed across campus, a weekly e-bulletin emailed to all staff and students, and university social media.

Advertisements were worded to extend recruitment beyond university students and staff, to include their friends and family, thus increasing the likelihood of recruiting a diverse population. Participants were offered a £10 high street shopping voucher for participation.

Inclusion and exclusion criteria

Adults (individuals aged 18 years or older) able to provide informed consent were eligible if prescribed medication for the prevention of CVD as defined in the literature.[2] Those who were unable to read or speak English, or receiving medication for the treatment of addiction or mental illness were excluded.

Procedures

Eligible members of the public expressing interest in participation were posted a study information leaflet, consent form and brief questionnaire to collect demographic information, plus the number of medicines prescribed and prescription charge exemption status. Returned consent forms and questionnaires were used to assign participants to one of two focus groups. Two focus groups, each with six to eight participants was deemed to be appropriate for generating sufficient data for the exploratory nature of this stage, whilst not over-burdening members of the public. Recruitment continued until each focus group had between six and eight participants representing a range of demographic characteristics.

Focus groups

Each focus group was audio-recorded, approximately two hours long, transcribed verbatim and moderated by the lead author with co-facilitation. The TDF-domains deemed applicable to medication adherence barriers (established in phase one) were divided across the two focus groups. Adherence barriers mapped to differing behavioural domains were considered in each

focus group but the 'emotions' domain was duplicated to investigate consistency of interpretation between participants of the two focus groups. This domain was selected for duplication across both focus groups as it was considered to be the domain most likely influenced by differing personal experience; we therefore aimed to explore how these personal experiences differed across the largest possible number of participants.

Each behavioural domain was described to participants in turn, before discussing the literature-identified adherence barriers mapped to the domain. The initial mapping of barriers to each domain of the TDF is provided in supplementary file 4; this mapping therefore served as the topic guide for the focus groups. Participants were encouraged to share their experiences and thoughts, using the adherence barriers presented as prompts for discussion. For each behavioural domain, participants were asked if there were any additional adherence barriers that were not represented.

Data analysis

Primary data analysis was undertaken by the lead author then validated by the co-authors as recommended in the literature.[34] Data were analysed using a framework approach,[35]based upon the domains of the TDF.

Phase 4 Refinement of adherence barriers mapped to the TDF and summary

Data from the focus groups were used to refine the mapping of adherence barriers, according to the participants' understanding of their meaning and relevance. Any additional barriers generated during the consultation exercises were also considered.

Results

Phase 1 Scoping review

Forty-seven eligible studies (representing a range of LTCs) were identified, from which the preliminary pool of adherence barriers were extracted. Similar barriers were initially grouped into 17 themes, (as summarised in supplementary file 2) which included beliefs, cognitive and memory associated factors, knowledge-related factors and administration problems.

Phase 2 Mapping of adherence barriers to the TDF

The agreed interpretations of how each behavioural domain of the TDF relates to medication adherence barriers are provided in supplementary file 3. All adherence barriers were considered carefully, though some required a deeper level of consideration and discussion. An interesting example here is the adherence barrier 'experience of side effects' which was ultimately mapped to the 'beliefs about capabilities' domain of the TDF. This decision was reflective of the recognition that it is not the side effects per se that influence medication adherence, but more an individual's ability to appropriately cope with the medication side effect that determines their behaviour. The 'skills' domain was considered to encompass both physical skills, (e.g. medicines administration) and cognitive skills (e.g. processing and understanding instructions). A number of barriers such as 'being too busy' and 'having a chaotic lifestyle' related to competing goals; these barriers did not intuitively map onto any of the existing behavioural domains of the TDF. Guided by relevant literature,[33] an additional behavioural domain termed 'goal conflicts' was created. The behavioural domains termed 'social/professional role and identity' and 'behavioural regulation' were excluded as no literature identified adherence barriers were mapped to these domains. The constructs associated with the 'behavioural regulation' domain are barriers and facilitators to behaviour[16]; as the study was focused on barriers to medication adherence, the 'behavioural regulation' domain was redundant. The 'nature of the behaviour' domain was also excluded; Michie *et al*[16] explain that this domain is accorded to a different order as it describes the

dependent variable, in this case, taking medicines as prescribed.[36] It is therefore not treated as a domain of behaviour change, but its constructs such as habits, were considered throughout the mapping task. Of the original 12 domain TDF, the three domains of 'social/professional role and identity', 'behavioural regulation' and 'nature of the behaviour' were not therefore active in the context of medication adherence barriers and an additional 'goal conflicts domain' was generated yielding 10 active domains in the present study.

The adherence barriers initially grouped to each TDF domain are detailed in supplementary file 4. Barriers were well distributed across the 10 relevant domains, though the beliefs about capabilities, beliefs about consequences and social influences domains had the broadest range of adherence barriers. Some barriers, for example 'no medical insurance' were excluded as they were not relevant to the UK healthcare system.

Phase 3 Focus groups with medicine-taking members of the public

Interest in focus group participation was expressed by 32 members of the public; signed consent forms and demographic questionnaires were returned by 17 (54.8%) respondents, of whom, 14 (82.4%) were able to attend one of the two focus groups. Table 1 summarises the participant's descriptive characteristics. Across all participants, there was a relatively even gender split and a median (IQR) age of 62.0 (51.5, 75.5) years. The majority of participants were exempt from prescription charges and most were prescribed multiple medicines; the median (IQR) number was 3 (1.5, 6). Only three participants (21.4%) were students or employees of the university.

[Table 1 about here]

Participant discussions demonstrated an understanding of the TDF and agreement with the mapping process.. Participants discussed adherence barriers known through personal

experience as well as offering opinion on potential adherence barriers that others may experience.

Focus group one

A summary of topics discussed is provided in supplementary file 5. Topics were discussed across all six TDF domains presented in this focus group. Three adherence barriers, undetected by the scoping review were discussed:

- Not knowing about medicine delivery and repeat ordering systems – mapped to the knowledge domain
- Difficulties with identifying medicines, especially when the brands and packaging regularly change – mapped to the skills domain
- Hostility from GP receptionists which can prohibit medicine access – mapped to the social influences domain

Focus group two

A summary of the topics of participant discussion is provided in supplementary file 6. Topics were discussed across all five behavioural domains presented but the beliefs about consequences domain was particularly stimulating of discussion. Adherence barriers discussed by participants undetected by the scoping review were:

- Negative emotions caused by feelings of getting a 'raw deal' with regards to medicines supply, e.g. only getting one month's worth of medicines when others get three months' – mapped to the emotions domain
- Reduced motivation to adhere caused by questioning whether medicines represent 'good value for money' – mapped to the motivation and goals domain

- ‘Annoyance’ about medicines taking when medicines have to be declared on insurance forms – mapped to the emotions domain.

The emotions domain was discussed in both focus groups, whilst there were similarities in the discussions on this topic between the two focus groups, differing personal experiences meant that in the second focus group, emotions related to ‘annoyance’ and ‘getting a raw deal’ were discussed which were not raised within the first focus group.

Phase 4 Refinement of adherence barriers mapped to the TDF

A summary of the re-mapping of adherence barriers from one TDF domain to another due to the additional perspectives identified from the focus groups is provided in supplementary file 7. Seventeen adherence barriers were re-mapped at this stage. Some barriers, for example knowing how to identify tablets or access them from packaging were moved from the knowledge domain to the skills domain. Additional understanding gained from the patients’ perspective meant that these behaviours could be understood as an ability that can be acquired through practice (skill), rather than direct knowledge. Similarly, barriers such as feeling negative about medicines taking or burdened by this were originally conceived to relate to motivation and goals but understanding from the patient perspective enabled an appreciation of the genuine emotive aspects of these barriers.

Table 2 summarises the adherence barriers mapped to the domains of the TDF[16] highlighting the wide range of adherence barriers captured.

[Table 2 near here]

Discussion

Use of the TDF[16] to both organise literature-identified barriers to adherence and structure focus group discussions has facilitated their detailed analysis. It has identified ten active domains, each incorporating a range of determinants of medication adherence, such as those relating to emotions, which have previously received less attention in literature.[29]

It is acknowledged that further relevant literature may have emerged since the conduct of the scoping review, however, its function was to act as a vehicle for prompting discussion in the focus groups. Given that the scoping review was designed to be supplemented by qualitative work and not intended to quantify the importance or prevalence of different barriers to adherence a full systematic review was inappropriate. The new adherence barriers and changes in mapping arising from the focus groups indicate that the methodological approach was appropriate for initiating and structuring the discussions.

Recruitment through university advertisements for the focus groups may have introduced biases. However, participants represented a wide range of ages and medication regimen complexities. Furthermore, only three participants were university students or employees, of which only one was an academic. Whilst anecdotal evidence gathered from the focus group discussions means that we are confident that a wide range of educational and professional backgrounds were covered in our sample of focus group participants, characterisation of participants through formal data collection about educational level may have added further rigour. Additional information regarding whether adherence barriers suggested by focus group participants were based upon personal experience or supposition, may have been beneficial and provided readers with further contextual information.

No relevant adherence barriers were identified for three of the TDF domains and a new domain termed ‘goal conflicts’ was added to capture adherence barriers that were not

reflected by the 2005 version of the TDF. The appropriateness of the adaptation is confirmed by the updated version of the TDF,[17] which now incorporates goal conflicts.

Contrary to the present paper which mapped adherence barriers to all bar three of the TDF domains, Presseau *et al.*[22] report that fewer TDF domains were relevant and did not map adherence barriers to the skills, beliefs about capabilities, motivation and goals, environmental context or emotions domains. Differing methodological approaches may account for this as Presseau and colleagues sought to identify the most relevant domains whereas the present article sought to explore the breadth of determinants. The latter approach has allowed exploration of adherence barriers which are often overlooked. A further difference is that Presseau and colleagues included the social/professional role and identity domain which was excluded from the present paper. Crayton *et al.*[23] also report redundancy of this domain when exploring adherence determinants in stroke survivors, as do Voshaar *et al.*[24] with regards to adherence barriers and facilitators for disease-modifying anti rheumatic drugs. In the present paper the social norms domain was used for barriers associated with not identifying oneself as a medicines taker. These minor differences in mapping highlight that despite robustly employed methods, there is still inherent subjectivity in TDF interpretation. The inherent subjectivity of the TDF mapping process means that a different theoretical map could have been produced by other researchers, as highlighted by the work reported by Presseau et al.[22] The mapping decision being undertaken by a research team with expertise in behavioural science and medication adherence plus refinement of this mapping based on patient input provides some confidence in the final map. However, further validation of the mapping decisions by an independent peer with expertise in these fields may have added further rigour.

Crayton *et al.*[23] highlight that 'emotions', 'beliefs about consequences' and 'knowledge' appeared to be most influential TDF domains when mapping adherence determinants in stroke survivors. This finding is consistent with the qualitative explorations reported in this present paper. Voshaar *et al.*[24] also report mapping of adherence barriers across the range of TDF domains, with notable consistency in mapping compared to the work presented in the present paper. Both studies therefore support applicability of the work presented in the current article, beyond CVD prevention.

The studies reporting mapping of adherence barriers to the TDF[22-24] provide useful contextualisation of the present work and highlight the similarities of adherence barriers across a range of LTCs. However, the utility of each of these studies for adoption as routine practice is limited by their focus on specific diseases. The present paper presents the first TDF-based conceptual framework of medication adherence barriers across multiple LTCs, and is also the first paper to develop a framework based on both literature-identified and qualitatively explored adherence barriers.

The focus groups in the present study, added richness to the data and, despite a large body of existing literature regarding adherence barriers, new barriers were identified spanning a range of TDF domains. An awareness of barriers such as a lack of knowledge about repeat prescription ordering services may be useful in supporting patients who wish to adhere but struggle with the management of their medicines. Likewise, the information yielded about the range of negative emotions associated with medicines taking, adds to our knowledge of the factors that may influence a patient's decisions to not adhere. Emotions, such as feelings of frustration and being 'short-changed', may represent modifiable determinants of adherence worthy of further investigation as these are often overlooked[29,37]. Practitioners seeking to

resolve non-adherence should be aware of the diverse plethora of factors that may influence adherence and mindful of the emotional components of medicines-taking behaviour.

The present work creates an evidence-based platform for developing novel, theory guided interventions to improve medication adherence. Whilst other theoretically informed adherence interventions have not always yielded improved outcomes,[15,37] this may be influenced by the lack of guidance regarding how these theories should be used for intervention design. The structured approach offered by the TDF and availability of work linking TDF domains to evidence based BCTs may address this difficulty. A programme of work to develop a novel adherence intervention, based on this conceptual framework will follow. Whilst theory guided litertaure[20] can be utilised to match BCTS to the domains of the TDF, much work is needed in understanding how these BCTs are appliacable to medicines-related consultations. Moreover, notable implementation work is necessary to explore how these BCTs are best delivered, from where and by whom.

Conclusion

This work provides the foundations for developing a patient questionnaire, grounded in the adherence barriers mapped to the TDF which will enable identification of an individual's barriers to adherence. As the focus groups were undertaken in the context of medicines prescribed for the prevention of CVD, it is intuitive to develop and trial a questionnaire in the same population. However, as the literature-identified barriers discussed in these focus groups were sourced from a variety of LTCs, it is likely that the adherence barriers will also be applicable to medication non-adherence in other LTCs. Further work is necessary to confirm this and to establish how adherence barriers vary for acute conditions.

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Table 1: Summary of participant characteristics for consultation exercises

Participant characteristics	Measure	Consultation exercise one (n = 5)	Consultation exercise two (n=9)
Male gender	Number (%)	3 (60%)	5 (55.5%)
Age (years)	Median (IQR)	70.0 (45.5, 76.5)	62.0 (54.0, 75.5)
Exempt from prescription charges	Number (%)	3 (60%)	6 (66.7%)
Number of regularly prescribed medicines	Median, (IQR)	3 (1, 5)	2 (2, 6)
Employed by the university	Number (%)	2 (40%)	1 (11.1%)

Table 2: Summary of adherence barriers mapped to each domain of the original TDF

TDF Domain	Adherence barriers mapped to this domain
Knowledge	• Not knowing how to order prescriptions or about services that facilitate this process • Not knowing how to collect prescriptions or about services that facilitate this process • Having insufficient information about medicines e.g. how they work, why they were prescribed, side effects and benefits • Not knowing how (and when) to take medicines as prescribed
Skills	• Physical inability to take medicines as prescribed e.g. swallowing difficulties and problems accessing medicines from packaging • Cognitive inability to take medicines as prescribed e.g. inability to read and/or understand instructions • Inability to identify and differentiate between different medicines • Lack of organisational and forward planning skills (not having a system in place to help manage medicines)
Beliefs about capabilities	• Lack of confidence in ability to adhere and manage medicines e.g. feeling regimen is too complex • Lack of confidence to overcome difficulties with medicines taking e.g. experience of side effects • Perceived inability to cope with medicines related changes
Beliefs about consequences	• Fear that medicines will be (are) harmful • Belief that medicines cannot be trusted

	• Doubting the efficacy of medicines • Not believing that there is a need for treatment • Denial of illness or non-acceptance of diagnosis • Decision making process justified belief about consequences (or lack of consideration of consequences) e.g. preference for alternative remedies
Motivation and Goals	• Not perceiving medicines taking as a priority • Lack of intention to adhere • Lack of motivation to adhere
Goal Conflicts*	• Cost of medicines (having to choose between paying for a prescription and something else) • Having a busy lifestyle (e.g. work and travel) and other priorities (e.g. family commitments or meal times) which impede medicines taking at specific times • Being too busy to order and collect prescriptions/having other priorities which impede ordering and collecting medicines
Memory, attention & decision processes	• Forgetting to take medicines • Forgetting to order/collect medicines from pharmacy • Lack of attention in medicines taking e.g. making errors or forgetting due to distractions
Environmental context and resources	• Problems with pharmacy/GP surgery e.g. not stocking medicines, lost prescriptions, failed orders etc. • Difficulties getting to pharmacy/GP surgery to collect prescriptions • Changes to environment or daily routine which impede medicines taking
Social influences	• Fear of judgement, discrimination or social stigma • Cultural and religious norms and expectations • Lack of trust in prescriber • Lack of social support
Emotion	• Experience of negative emotions associated with medicines taking e.g. frustration or embarrassment • Perceiving medicines taking as a negative reminder of illness/condition • Perceiving medicines taking as a burden
Social/professional role & identity	*No adherence barriers mapped to this domain*
Behavioural regulation	*No adherence barriers mapped to this domain*
Nature of the behaviour	*No adherence barriers mapped to this domain*

* A newly created domain to reflect adherence barriers that did otherwise not fit