

TITLE: Perceptions and experiences of taking oral medications for the treatment of type 2 diabetes mellitus: A systematic review and meta-synthesis of qualitative studies

RUNNING HEAD: Taking oral medications for type 2 diabetes: Review of qualitative studies

AUTHORS: J. Mc Sharry^{1,2}, L. McGowan², A.J. Farmer³ & D.P. French²

1 Health Behaviour Change Research Group, School of Psychology, National University of Ireland, Galway, Ireland

2 Manchester Centre for Health Psychology, University of Manchester, Manchester, UK

3 Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

CORRESPONDING AUTHOR: Jennifer Mc Sharry (jenny.msharry@nuigalway.ie)

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ABSTRACT

Aims

To explore patients' perceptions and experiences of taking oral medications for the pharmacological management of Type 2 Diabetes Mellitus (Type2DM).

Methods

Cinahl, EMBASE, Medline and PsycINFO databases were searched in 2014 to identify qualitative studies exploring patients' perceptions or experiences of taking medications for the management of Type2DM. Key concepts and themes were extracted and synthesised using meta-ethnography.

Results

Eight studies were included. Primary study findings were synthesised to develop three higher order constructs that moved beyond the results of individual studies. The first construct, *Medications for diabetes: A necessary evil* outlines how patients' negative perceptions of medication risks co-exist with a resounding view that medications are beneficial. *Passive Patients but Active Experimenters* highlights the contrast between patients' passive acceptance of medication prescriptions and the urge to actively experiment and adjust doses to optimise medication use in daily life. Finally, *Taking oral medication for Type2DM: A unique context* describes features specific to the Type2DM medication experience, including lack of symptoms and the perceived relationship between medication and diet, which may impact on adherence.

Conclusions

Medication taking for Type2DM is a unique adherence context, which requires the development of condition-specific interventions. Our findings indicate patients understand the need for medications but adjust dosage and timing in their daily lives. Our review suggests providers should acknowledge patient preferences in the development of management strategies and highlights an opportunity to direct the motivation evident in patients' experimentation towards potentially more beneficial medication taking behaviours.

INTRODUCTION

Poor adherence to treatment with medication by patients with Type 2 diabetes mellitus (Type2DM) is associated with poorer glycaemic control (1), increased mortality and hospitalization (2), and higher healthcare costs (3). Despite the association between Type2DM medication taking and outcome, adherence remains sub-optimal. A recent systematic review of studies of adherence to oral Type2DM medications found that only six out of 27 studies (22.2%) reported adherence of $\geq 80\%$ among their study populations (4).

Understanding non-adherence to Type2DM medication has been of clinical and research interest for many years. Despite the time and effort invested, predicting non-adherence remains a challenge with only depression and medication cost consistently shown to be associated with non-adherence (4). The complexity of diabetes medication taking behaviour is reflected in the limited success of attempts to intervene; a recent review of 52 interventions concluded that no single strategy has consistently improve adherence (5). The findings in Type2DM echo the chronic condition literature more broadly; a recent Cochrane review concluded that current interventions for improving adherence in long-term conditions are not very effective (6).

Developing effective interventions requires a better understanding of medication taking behaviour in Type2DM. Qualitative research can help understand complex behaviours in context by emphasising the perceptions and experiences of participants (7). Although individual qualitative studies offer valuable insights, synthesising a body of qualitative literature can facilitate the development of overarching insights or frameworks that go beyond individual study findings. The qualitative meta-synthesis method is becoming more common in health research and is increasingly recognised as important for evidence-based healthcare and health policy (8). In Type2DM, qualitative meta-synthesis has been used to explore lay understandings of diabetes and diabetes care (9) and perceptions of diabetes self-management strategies over time (10). To date, the qualitative literature of experiences of taking oral medication for Type2DM has not been reviewed or synthesised.

The aim of this study was to explore patients' perceptions and experiences of taking oral medications for the pharmacological management of Type2DM by carrying out a systematic review and qualitative meta-synthesis of published qualitative studies. For the purpose of this review, we use the term adherence to describe the process by which patients take their medications as prescribed, with non-adherence describing the process of not taking medications as prescribed, in line with a published taxonomy (11).

METHODS

We followed the meta-ethnography model described by Noblit and Hare (12) and developed for healthcare research (13). Meta-ethnography involves identifying the key findings (metaphors) from participant quotes (first-order constructs) and author interpretations (second-order constructs) of included studies. Reviewers then iteratively develop key overall concepts (translations) across studies which are synthesised to develop overall interpretations or models (third-order constructs) that move beyond individual study findings (14). The seven-step method of meta-ethnography used in the current study is described in detail below. The terminology adopted throughout (e.g. metaphors, translations) is consistent with Noblit and Hare's meta-ethnographic method (12) and published examples of meta-ethnography (14).

Step 1 Getting Started

We specified the study aim and conducted preliminary scoping searches to estimate the number of relevant studies and to ensure a meta-ethnographic approach was feasible and appropriate. A review protocol was prepared and registered on PROSPERO (Registration number: CRD42014010339). The review team included a health psychologist and qualitative researcher (JMcS), a professor of general practice (AF), a professor of health psychology (DF), and a research assistant (LMcG).

Step 2 Deciding What's Relevant

Inclusion Criteria

Published studies using qualitative methods of data collection and analysis, with a primary focus on adult (>18 years) patients' perceptions and experiences of taking oral medication for the treatment of Type2DM were included. Studies not published in English, reviews, studies with mixed samples of patients with Type2DM and other conditions, and mixed methods studies where qualitative data were not reported separately were excluded. As taking oral medication differs from the experience of using insulin, studies that focused primarily on insulin use were excluded. Studies that included some patients that used insulin, but where the primary focus of the findings was on oral medication use, were eligible for inclusion.

Data Sources and Searches

EBSCO Cinahl (1937 onwards), Elsevier EMBASE (1947 onwards), OVID Medline (1946 onwards) and OVID PsycINFO (1806 onwards) databases were searched in June 2014. Type2DM search terms were combined with medication adherence and qualitative research terms. Search terms were based on

existing reviews, tested, and iteratively refined to ensure relevant studies were picked up. A sample search strategy for the Elsevier EMBASE database is shown in Appendix 1. Forward and backward citation searches were conducted on all included studies.

Screening

JMcS exported studies into an EndNote database and removed duplicates. LMcG screened titles and abstracts. A random sample of 10% of records were double screened by JMcS. Inter-reviewer agreement assessed by chance-corrected kappa was $k = 0.88$ indicating “almost perfect agreement” (15). LMcG and JMcS both conducted full-text screening; uncertainties were discussed and agreed with the full review team.

Step 3 Reading the Studies

Active reading was undertaken to become familiar with studies, to extract relevant data and to appraise study quality.

Data Extraction

LMcG extracted all text under Results/Findings, including participant quotes (first-order constructs) and author interpretations (second-order constructs) from each study. For one study which reported interviews with both patients and healthcare providers (16) only patient findings were extracted. For another study which reported on fasting and medication use during Ramadan (17), only findings related to medication use were extracted. Study details, including research question, country, sample, data collection and analysis conducted, were extracted by LMcG into a data extraction table.

Quality Assessment

LMcG and JMcS used the Critical Appraisal Skills Program (CASP) tool for qualitative research to assess study quality (18). The CASP tool consists of nine questions to assess if the results of the study are valid and a final question to assess if the results are of value. For our review, we modified the tenth question to assess the value of each study to the aims of the review using a rating of low, medium or high. Quality assessment was conducted by both LMcG and JMcS. Quality assessment was not used to exclude studies but provided information on the robustness and rigour of included studies that informed synthesis and write-up.

Step 4 Determining How the Studies are Related

LMcG prepared a table of key findings (metaphors) to facilitate exploration of how studies were related (19). The metaphors identified at this stage were: Knowledge/information about diabetes and medications; Negative perceptions and experiences of medications; Positive perceptions and experiences of medications; Adherence-related factors; Patient-physician relationship; Social/cultural/religious factors; and Self-monitoring/self-regulation. A group meeting was held to discuss relationships between metaphors across studies.

Step 5 Translating the Studies

Following discussion, JMcS identified one particularly relevant paper (20) as an index paper and entered the findings from this paper into the first row of a translation table. Additional papers were added to the table in chronological order of publication and similarities, differences or contradictions with preceding studies were assessed. First-order and second-order construct terminology from original papers were used to ensure translations remained faithful to the meanings generated in the original studies (13).

Step 6 Synthesising the Translations

A line of argument approach was taken to develop third-order constructs that synthesised findings across studies in an original way (12). Third-order constructs were initially identified by JMcS who then engaged in active re-reading of all included studies to verify the appropriateness of the synthesis. A written summary of the synthesis with comments and queries was then prepared by JMcS, circulated to the review team, discussed and modified.

Step 7 Expressing the Synthesis

The current paper is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; 21) and the ENhancing Transparency in REporting the synthesis of Qualitative research (ENTREQ; 8) statements. The language used to describe synthesis findings is predominantly our own. A limited number of first-order and second-order constructs are included when author's or participant's own words provided a particularly useful illustration. Bold text indicates translations identified in the synthesis, italics indicate words used by authors in the original studies and quotations marks indicate participant quotes from the included studies.

RESULTS

Fig. 1 shows details of studies screened, excluded and included. Database searches identified 805 unique citations. Seven met the inclusion criteria (16, 17, 20, 22-25) and an eighth study (26) was

identified from forward searching of included studies. Some studies were excluded at full-text stage that met most of the inclusion criteria but which we judged did not have a primary focus on the experience of taking oral medication (e.g. 27, 28, 29).

Study perspectives

Key features of included studies are summarised in Table 1. Four studies focused on the general experience of taking medications (16, 20, 24, 26), one study explored medication taking concerns (25), one study explored factors related to high and low adherence (23) and one study focused on medication taking during Ramadan (17). One paper had a broader focus and aimed to explore patients' experience and knowledge about diabetes alongside a more specific exploration of experiences of medication and factors that contribute to adherence in Malaysia (22). The experiences of particular groups were explored in four studies and included people of Pakistani and Indian origin living in Scotland (24), Muslims of Pakistani origin living in Denmark (17), American Samoan adults (16), and people of Turkish origin living in Belgium (26).

Quality assessment

The studies generally met the CASP tool criteria in terms of clarity of research aims, appropriateness of design, recruitment, data collection, analysis and reporting of findings. Insufficient detail was provided to answer some questions; the consideration of the relationship between the researcher and participants which was not described in any of the included studies. The value of the included studies to the aims of the review ranged from good (20, 23-26) to medium (16, 22) to low (17). The study rated of low value described experiences of Ramadan in Type2DM more broadly, with only limited findings of relevance. However, as perspectives of medication in relation to fasting experiences were found useful for the purposes of the synthesis, this study was still included.

Synthesis findings

Twelve overall translations were identified across studies, which were used to develop three third-order constructs. Table 2 shows these third-order constructs identified, the translations encompassed by each of these constructs and the studies that included each translation.

1. Medication for diabetes: A necessary evil

The title of the first third-order construct **"a necessary evil"** was taken from the paper by Tija et al. (25). This phrase aptly described the complex nature of patient perceptions of taking medications for Type2DM but was not identified as a stand-alone theme in any other study.

As described by Lawton and colleagues (20), there was *a resounding view that drugs were beneficial*. Patients appreciated the need for medication (22), felt lucky to have it (24, 25) and perceived short and long-term benefits of medications (26). Specific benefits of oral medications included to control blood glucose, prevent complications and stay healthy and increase physical well-being (22, 26)

Disadvantages and risks of medications was also a common theme across studies and included a dislike of drugs and long-term effects (24-26), dislike of non-natural treatments (16, 20) perceived inefficacy of long-term medication (25, 26) and medication cost (16). Anticipated and *unanticipated and unpleasant side effects* were frequently described (20, 25, 26) although one study reported most participants did not suffer adverse medication effects (22). **Dislike of multiple medications** was also common (20, 24, 26). Patients worried about interactions between medications, and wanted to avoid feeling “like you’re rattling because I’m taking the whole blooming chemist” (20). Uncertainty about diabetes medication was linked to an overall dislike of Western medicines by people of Pakistani and Indian origin in one study (24).

The negative aspects of the medication taking experience in Type2DM contributed to the active non-adherence described below, with patients more likely to take medications if perceived advantages outweighed disadvantages (26).

2. The Passive Patient as Active Experimenter

We developed the second third-order construct from a contrast between patients’ role as passive acceptors of medication prescription within the healthcare system, and their active approach to taking medications in their daily lives. This contrast was evident both between and within studies but was not drawn out as a finding in any of the included studies. One study did make reference to active and passive categories of adherence (26) but used this distinction to differentiate between patients rather than to describe within-patient differences across healthcare and every-day life settings.

The Passive Patient

Discussion of medication concerns with providers was the specific focus of only one study (25) but a feature of many others. With the exception of a minority of younger educated patients described as **engaging in a kind of collaboration**, authors described prescribing decisions made by providers without negotiation and accepted without question (20, 25, 26). Peeters et al. (26) described both active and passive interactions with providers but characterised the doctor-patient relationship as mostly hierarchical; decision power rested with the provider. Although Tija and colleagues (25)

found most patients did discuss medications with their provider, Borgsteede et al. (23) reported that the passive patient would never question the authority of the prescribing physician. Al-Qazaz et al. (22) identified a conflict between patient satisfaction with healthcare interactions and the limited provision of information. Lawton and colleagues (20) suggested participants needed non-judgemental guidance on missed doses but felt unable to discuss adherence choices with providers. The acceptance of provider instructions was linked to cultural beliefs in one study as evidenced by an American Samoan patient's view that "What the doctor tells us is the same as what the Bible tells us, 'No to this' and 'Yes to this' and 'No to that'—it's the same thing." (16).

Active Experimentation

The philosophy of "**obey the doctor and you will live longer**" (16) was at odds with actual adherence behaviour. Across studies, authors characterised **full adherence to medication regimes as rare** with the timing of dose particularly likely to be modified (20, 22, 24, 26). As described by Borgsteede et al. (23), trust in providers did not translate into full adherence with prescribed regimens. Tija et al. (25) found while patients do discuss concerns, only one participant discussed their plans to reduce medication intake with their doctor.

The specific phrase, **deliberate and routine adjustments**, was used in two studies to describe this particular form of non-adherence (22, 24). Lawton et al. (24) provided an illuminating participant quote evidencing deliberate adjustment: "Sometimes I will take two when I don't spread too much jam on my toast or even sometimes I don't spread any. If I feel like a bit of pleasure then I will put some on and take the extra tablets".

Alongside meal size and content (22, 24, 26) other reasons for dose adjustments included: to reduce unpleasant side-effects (16, 23, 24); **dislike of taking multiple medications** (24, 26); self-monitoring of blood glucose, with tablets used only when blood glucose was perceived to be high (24); a belief that medications provide symptomatic relief and are not needed when feeling well (24); preference for traditional treatments (16); lack of trust in providers (26); and to fit with personal understanding of the body's needs (22). Reducing medication in line with fasting during Ramadan was mentioned in three studies (17, 22, 26) and could lead to a belief that medication intake could be reduced on other occasions (20, 22).

The active experimenter engaged in **personal experiments to search for proof** that medications were working; symptom reduction and blood glucose or HBA1c readings were used to evidence the impact of medication (24, 26). Patients also continued to take medications if negative effects were experienced when medications were discontinued (20, 23). Lawton et al. (20) provided some of the

strongest evidence of personal experiments under their theme *evidencing the impact*, and described that without obtaining their own proof, patients may be sceptical about the benefits of medication.

The active nature of adherence was also evident in the **personal responsibility** for medication described across studies; participants described personal guilt and concern about health consequences if non-adherent (20, 22). Although support from family and friends was described in two studies (22, 23), adherence was chiefly regarded as the patient's own responsibility. (20, 22, 23). Medication adherence was described as “down to me” (20), patients were described as self-dependant (22) and medication taking during Ramadan was described as a private issue in one study (17). Gender differences in taking a more active role in adherence were described by Peeters et al. (26), with male patients described as engaging in more active medication management.

A potential contradiction to the actively experimenting patient concept came from the discussion of **forgetting** or lack of knowledge as a major cause of non-adherence, with broken routines a frequently described cause of forgetting (20, 22, 23, 26). However, strategies used by patients to improve adherence, including **developing routines** and the use of prompts and reminders (20, 23), suggested that the impact of forgetting on adherence could be minimised when patients were truly motivated. This issue was openly addressed by Al-Qazaz and colleagues (22), who argued that although forgetting has traditionally been classified as non-intentional non-adherence, it can also be understood as an indication of limited belief in medication necessity.

3. Taking oral medication for Type2DM: A unique context

The final third-order construct describes the features of medication taking which are specific to Type2DM. A contrast between experiences of taking Type2DM medications and other medications was not a specific theme identified in any of the included studies. The development of this third-order construct was informed by considering identified translations in relation to the review team's knowledge of, and engagement with, the medication taking literature more broadly.

Medication taking in diabetes forms part of a management pathway that typically begins with control by diet alone. Findings related to **oral medication initiation** was described in the two studies by Lawton and colleagues (20, 24). Most participants described negative reactions to initiation, felt uneasy about medication use and wanted to stay diet controlled for as long as possible. Initiation of oral medication was described as “a slippery slope” of increasing medication, which would eventually lead to insulin (20). Lawton and colleagues also linked initiation to identity change as “if you start taking them, you become a patient” (24). Initiation could also be perceived as personal failure, indicating that the patient had been unable to manage diabetes themselves (20). Conversely,

medication initiation could also be seen as inevitable or framed as facilitating understanding of diabetes as a serious progressive illness (20). Control by diet alone could result in patients questioning if they really had diabetes and taking medication led patients to better understand the nature of the condition. The progressive chronic nature of Type2DM also results in medication taking acting as **a dynamic process** with can change with disease progression and over time (20, 26).

Two particular features of Type2DM appeared to impact on taking medication: the asymptomatic nature of diabetes and the perceived relationship between medication, diet and glucose control. The asymptomatic nature of diabetes, resulting in the condition not being “at the forefront of your mind” (20), was identified as a reason for non-adherence in three studies (20, 22, 26). Patients were described as having a high awareness of the relationship between food intake and medication (22) and deliberate and routine dose adjustment often went hand in hand with dietary choices. This link with diet resulted in patterns of non-adherence particular to the diabetes context, with patients taking extra tablets following a heavy meal or skipping a tablet if a meal was missed.

DISCUSSION

From eight included studies we identified three higher order constructs that add to our understanding of adherence behaviour in Type2DM. While clearly viewed as beneficial, oral medications are not seen as exclusively positive but as “a necessary evil” (25). Concerns about side effects and a dislike of medications, particularly when taking multiple medications, were common. Patients’ passive acceptance of healthcare providers’ prescriptions contrasted to deliberate dose adjustments and the active search for proof that medications are working. Accordingly, full adherence to medication regimes was rare. Finally, taking oral medication for Type2DM operates as a unique context, characterised by a lack of symptoms and a perceived relationship between medication and diet, which appears specific to the Type2DM experience.

The present study is the first systematic review of qualitative studies exploring the complex reality of Type2DM medication adherence. The methods were transparent rigorous and reported according to published guidelines. Examining medications for a specific condition allowed more in depth insight across a diverse range of countries and cultures. A previous systematic review of quantitative studies reported little is known about factors associated with T2DM medication adherence in ethnic groups (30). Our review included four studies conducted with ethnic groups and throughout the synthesis process, we discussed if developing constructs specific to different groups was a better way to synthesise findings. Overall, we believe the findings to be applicable to different ethnic groups, even though the way these constructs manifest may vary for different populations, for example dose adjustments during Ramadan.

We acknowledge limitations of our review. We excluded studies which did not aim to explore patients' perceptions and experiences of taking oral medication for the treatment of Type2DM whose findings may have provided interesting additional insights. As with primary qualitative analysis, we acknowledge that the findings of the synthesis reflect the background and experience of the reviewers and may have differed if conducted by another review team. Our review also inevitably reflects the limitations of the included studies. The included study populations cannot be claimed as representative and participants who chose to take part in research may have a greater interest and understanding of their health than the general diabetes population.

Our findings complement recent quantitative reviews of medication adherence. The frequent observation in included primary studies that full adherence to medication regimes is rare is in keeping with recent quantitative reviews (4). Reports of sub-optimal adherence in the existing literature do not adequately convey an important point identified in our review; most patients with Type2DM do understand the importance of taking medication and are aware that drugs are beneficial. Our findings also suggest that while patients appreciate the health benefits of taking medications, the importance of following dose and time instructions has not been as effectively communicated and could be a target of future interventions.

The current review also provides new evidence as to possible reasons for low adherence and suggests future avenues of research. Personal experiments to guide adherence behaviour can be problematic; the dose of oral glucose lowering medications is not intended to be titrated against symptoms or blood glucose levels and can be harmful rather than beneficial. However, recognising the proactive approach underpinning the desire to actively adjust dose, in particular when taken alongside the clear awareness of medication benefit, suggests potential for intervention, although the complexity of beliefs about treatment in this area need to be considered.

Our findings also speak to the results of a previous qualitative meta-synthesis exploring medication-taking across a range of conditions (31). Pound et al. (2005) identified findings related to concerns and lay practice of testing medicines similar to our review. By contrast, Pound et al.'s identification of different categories of adherence (passive and active accepters, rejecters and modifiers) does not fit as clearly with the findings of our synthesis, where active experimentation appeared to be the norm. Our identification of diabetes as a unique medication context might explain this difference, with perceived links between diet, medication and blood glucose control in Type2DM facilitating greater experimentation.

Our review suggests that patients with Type2DM can be motivated consumers of medication and highlights a need to engage patients in active discussion on the role of diabetes medication in their own lives. Patients appear to modify their medication taking in line with their own experimentation; healthcare providers could acknowledge patient preferences and develop diabetes management strategies that combine immediate medication taking preferences with long-term medical outcomes. Adherence support strategies do not always appear to be generalizable across patients; reminders or dose organizers, for example, may not be appropriate for the actively experimenting patients identified in our review. The findings highlight the importance of engaging with patients, and the need for qualitative work in intervention development, to ensure interventions are targeted to the actual reasons for non-adherence.

Our review provides evidence to support the argument in a recent editorial that “patients who are not adhering to prescribed medication regimens are, in most cases, trying to make the healthiest choice they can”(32). The potential to capitalise on motivation and to work with patients to direct energy towards more beneficial behaviours is also worth considering. For those previously controlled by diet alone, the initiation of medication may also be used as a teachable moment (33) to facilitate a more open discussion of self-management behaviours.

Clear, evidenced based communication around medicines delivered consistently may be helpful. Identifying those with concerns about medications or unconvinced about their worth, particularly when starting a new treatment, may offer a point at which any difficulties can be addressed. The challenge for healthcare providers and researchers is to establish how best to interact with patients and develop interventions that allow the issue of poor adherence to be openly discussed and resolved collaboratively.

Table 1: Characteristics of Included Studies

Reference	Research Question	Country	Setting	Participants	Data Collection	Analysis
Lawton et al. 2005 (24)	To explore British Pakistani and British Indian patients' perceptions and experiences of taking oral hypoglycaemic agents.	Scotland	Primary care and community	N = 32 (17 F) Age: 30-50: 6 51-60: 10 61-70: 13 ≥71: 3 23 Pakistani 9 Indian	In-depth interviews	Grounded theory
Lawton et al. 2008 (20)	To examine Type2DM patients' expectations, perceptions and experiences of oral glucose-lowering agents including their reasons for taking/ not taking drugs as prescribed.	Scotland	Primary care and hospital	N = 20 (9 F) Mean age: 60.8 20 White	Repeat in-depth interviews	Thematic analysis
Tija et al. 2008 (25)	To explore the concerns of older adults with diabetes about the complexity of their drug regimens and to determine whether they discussed medication-related concerns with their physician.	US	Outpatient geriatric medicine practice	N = 22 (16 F) Mean age: 75.0 16 African American 3 White 1 Asian/Pacific Islander/ Hawaiian 1 American Indian/ Alaskan Native 1 Other	In-depth semi-structured interviews	Thematic analysis
Al-Qazaz et al. 2011 (22)	To explore Type2DM patients' experience and knowledge about diabetes. To explore the experiences of diabetic patients in terms of their medication. To understand the factors contributing to medication adherence in Malaysia.	Malaysia	Health clinic	N=12 (4 F) Mean age: 54.0 8 Malay 2 Indian 2 Chinese	Semi-structured interviews	Thematic content analysis

Borgsteede et al. 2011 (23)	To explore both factors related to high and lower levels of adherence that patients experienced in their medication use.	Netherlands	Primary care	N=20 (10 F) Mean age: 70	In-depth semi-structured interviews	Content analysis
Mygind et al. 2013 (17)	To explore patient perspectives on medicine use during Ramadan, reasons for fasting, and experiences with counselling on medicine use during Ramadan among people of Pakistani background with Type2DM and at least one other chronic condition.	Denmark	Community	N = 6 (5 F) Age: 42-69 6 Muslims of Pakistani background	Semi-structured interviews	Unclear
Stewart et al. 2013 (16)	To explore diabetes medication-taking experiences and knowledge and related cultural beliefs in American Samoan adults with diabetes and healthcare providers.	American Samoa	Community health centre	N = 39 (22 F) Age: 30-39: 3 40-49: 3 50-59: 12 60-69: 12 70-79: 8 80-89: 1	Focus groups	Unclear
Peeters et al. 2014 (26)	To explore perspectives of Turkish migrants with Type2DM on adherence to oral hypoglycaemic agents.	Belgium	Primary care and community	N = 21 (12 F) Age: 30-39 years: 2 40-49 years: 7 50-59 years: 6 60-69 years: 6 21 Muslim	In-depth interviews	Grounded theory

Table 2: Third-order constructs and identified translations

Third-order constructs	Identified translations	Studies including this translation
Medication for diabetes:	A necessary evil: Risks and benefits	(16, 22, 25, 26)
A necessary evil	Dislike of multiple medications	(20, 23-26)
The Passive Patient as Active Experimenter	Obey the doctor and you will live longer	(16, 20, 23-26)
	A kind of collaboration (for the minority)	(20, 23, 25, 26)
	Full adherence to medications rare	(20, 22, 24, 26)
	Deliberate and routine adjustments	(16, 17, 22-24, 26)
	Personal experiments to search for proof	(20, 23, 26)
	Personal responsibility	(17, 20, 22, 23)
	Forgetting	(20, 22, 23, 26)
	Developing routines	(20, 23)
Taking oral medication for Type2DM: A unique context	Oral medication initiation	(20, 23)
	A dynamic process	(20, 26)

1. Egede LE, Gebregziabher M, Echols C, Lynch CP. Longitudinal effects of medication nonadherence on glycemic control. *Annals of Pharmacotherapy*. 2014;48(5):562-70.
2. Ho PM, Rumsfeld JS, Masoudi FA, McClure DL, Plomondon ME, Steiner JF, et al. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Archives of internal medicine*. 2006;166(17):1836-41.
3. Egede LE, Gebregziabher M, Dismuke CE, Lynch CP, Axon RN, Zhao Y, et al. Medication Nonadherence in Diabetes Longitudinal effects on costs and potential cost savings from improvement. *Diabetes Care*. 2012;35(12):2533-9.
4. Krass I, Schieback P, Dhippayom T. Adherence to diabetes medication: a systematic review. *Diabetic Medicine*. 2015;32(6):725-37.
5. Sapkota S, Brien J-a, Greenfield J, Aslani P. A systematic review of interventions addressing adherence to anti-diabetic medications in patients with type 2 diabetes-impact on adherence. *PloS One*. 2015;10(2).
6. Nieuwlaat R, Wilczynski N, Navarro T, Hobson N, Jeffery R, Keenanasseril A, et al. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2014;11.
7. Pope C. Qualitative research: reaching the parts other methods can not reach: an introduction to qualitative methods. *British Medical Journal*. 1995;311:42-5.
8. Tong A, Flemming K, McInnes E, Oliver S, Craig J. Enhancing transparency in reporting the synthesis of qualitative research: ENTREQ. *BMC Medical Research Methodology*. 2012;12(1):181.
9. Campbell R, Pound P, Pope C, Britten N, Pill R, Morgan M, et al. Evaluating meta-ethnography: a synthesis of qualitative research on lay experiences of diabetes and diabetes care. *Social Science & Medicine*. 2003;56(4):671-84.
10. Frost J, Garside R, Cooper C, Britten N. A qualitative synthesis of diabetes self-management strategies for long term medical outcomes and quality of life in the UK. *BMC Health Services Research*. 2014;14(1):348.
11. Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppar T, et al. A new taxonomy for describing and defining adherence to medications. *British Journal of Clinical Pharmacology*. 2012;73(5):691-705.
12. Noblit GW, Hare RD. *Meta-ethnography: Synthesizing qualitative studies*: Sage; 1988.
13. Britten N, Campbell R, Pope C, Donovan J, Morgan M, Pill R. Using meta ethnography to synthesise qualitative research: a worked example. *Journal of Health Services Research & Policy*. 2002;7(4):209-15.
14. France EF, Ring N, Thomas R, Noyes J, Maxwell M, Jepson R. A methodological systematic review of what's wrong with meta-ethnography reporting. *BMC Medical Research Methodology*. 2014;14(1):119.
15. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. *Family Medicine*. 2005;37(5):360-3.
16. Stewart DW, DePue J, Rosen RK, Bereolos N, Goldstein MG, Tuitele J, et al. Medication-taking beliefs and diabetes in American Samoa: A qualitative inquiry. *Translational Behavioral Medicine*. 2013;3(1):30-8.
17. Mygind A, Kristiansen M, Wittrup I, Norgaard LS. Patient perspectives on type 2 diabetes and medicine use during Ramadan among Pakistanis in Denmark. *International Journal of Clinical Pharmacy*. 2013;35(2):281-8.
18. Critical Appraisal Skills Programme. CASP Qualitative Checklist Oxford 2014. Available from: <http://www.casp-uk.net/#!/checklists/cb36>.
19. Atkins S, Lewin S, Smith H, Engel M, Fretheim A, Volmink J. Conducting a meta-ethnography of qualitative literature: lessons learnt. *BMC Medical Research Methodology*. 2008;8(1):21.
20. Lawton J, Peel E, Parry O, Douglas M. Patients' perceptions and experiences of taking oral glucose-lowering agents: A longitudinal qualitative study. *Diabetic Medicine*. 2008;25(4):491-5.
21. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine*. 2009;151(4):264-9.

22. Al-Qazaz HK, Hassali MA, Shafie AA, Syed Sulaiman SA, Sundram S. Perception and knowledge of patients with type 2 diabetes in Malaysia about their disease and medication: a qualitative study. *Research In Social & Administrative Pharmacy*. 2011;7(2):180-91.
23. Borgsteede SD, Westerman MJ, Kok IL, Meeuse JC, de Vries TP, Hugtenburg JG. Factors related to high and low levels of drug adherence according to patients with type 2 diabetes. *International Journal of Clinical Pharmacy*. 2011;33(5):779-87.
24. Lawton J, Ahmad N, Hallowell N, Hanna L, Douglas M. Perceptions and experiences of taking oral hypoglycaemic agents among people of Pakistani and Indian origin: Qualitative study. *British Medical Journal*. 2005;330(7502):1247-9.
25. Tjia J, Givens J, Karlawish J, Okoli-Umeweni A, Barg F. Beneath the surface: Discovering the unvoiced concerns of older adults with Type 2 diabetes mellitus. *Health Education Research*. 2008 Feb;23(1):40-52.
26. Peeters B, Van Tongelen I, Duran Z, Yüksel G, Mehuys E, Willems S, et al. Understanding medication adherence among patients of Turkish descent with type 2 diabetes: a qualitative study. *Ethnicity & Health*. 2015;20(1):87-105.
27. Nair KM, Levine MA, Lohfeld LH, Gerstein HC. "I take what I think works for me": a qualitative study to explore patient perception of diabetes treatment benefits and risks. *Canadian Journal of Clinical Pharmacology*. 2007;14(2):e251-9.
28. Vermeire E, Van Royen P, Coenen S, Wens J, Denekens J. The adherence of type 2 diabetes patients to their therapeutic regimens: A qualitative study from the patient's perspective. *Practical Diabetes International*. 2003;20(6):209-14.
29. Goering EM, Matthias MS. Coping with chronic illness: information use and treatment adherence among people with diabetes. *Community Medicine*. 2010;7(2):107-18.
30. Peeters B, Van Tongelen I, Boussery K, Mehuys E, Remon JP, Willems S. Factors associated with medication adherence to oral hypoglycaemic agents in different ethnic groups suffering from type 2 diabetes: a systematic literature review and suggestions for further research. *Diabetic Medicine*. 2011;28(3):262-75.
31. Pound P, Britten N, Morgan M, Yardley L, Pope C, Daker-White G, et al. Resisting medicines: a synthesis of qualitative studies of medicine taking. *Social Science & Medicine*. 2005;61(1):133-55.
32. Polonsky WH. Poor medication adherence in diabetes: what's the problem? *Journal of Diabetes*. 2015;7(6):777-778.
33. Lawson PJ, Flocke SA. Teachable moments for health behavior change: a concept analysis. *Patient education and counseling*. 2009;76(1):25-30.