QATAR UNIVERSITY

COLLEGE OF PHARMACY

BARRIERS TO MEDICATION ADHERENCE IN PATIENTS WITH

UNCONTROLLED DIABETES IN A PRIMARY HEALTHCARE SETTING IN

QATAR: A MIXED METHOD TRIANGULATION STUDY

BY

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ABSTRACT

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Title: Barriers to Medication Adherence in Patients with Uncontrolled Diabetes in a

Primary Healthcare Setting in Qatar: A Mixed Method Triangulation Study

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Background: In Qatar, 86% of patients with diabetes are uncontrolled. Given that nonadherence to oral drug therapy and psychological insulin resistance are a common phenomenon, one could postulate that patients may not be taking their medications as prescribed. Therefore, the primary aim of this study was to explore the barriers to medication adherence among patients with uncontrolled diabetes in a primary healthcare setting from the perspectives of the patients and their healthcare providers.

Methodology: This study was divided into two phases: patients' perspective using a mixed-method approach, and healthcare providers' perspective on the issue using qualitative approach. Patients with uncontrolled diabetes responded to a questionnaire followed by one-to-one in-depth interviews. On the other hand, healthcare providers directly involved in the care of patients with diabetes participated in semi-structured one-to-one interviews. Descriptive and inferential analyses were used for quantitative data, while thematic analysis was used for qualitative data. Finally, data from the two phases were triangulated in interpretation.

Results: Overall, 74% of the sample was nonadherent to diabetes medications. The quantitative results indicated that sociodemographic characteristics did not significantly influence medication adherence, except living with family. The majority of pre-determined barriers to medication adherence were reported by nonadherent patients and the most commonly reported barrier was forgetfulness. In addition, significantly higher levels of nonadherence were found among patients who were younger than 65 years and those who were illiterate. Qualitative data revealed five different themes from both patients' and healthcare providers' perspectives: (1) patient-related aspects, such as patient's characteristics, perceptions, attitude and knowledge; (2) patient-provider interaction, which involved communication and interaction time; (3) appointment system and follow up, which was highly varied among patients despite their similar needs; (4) influence of other individuals including family support and social stigma and; (5) traveling and the use of traditional medicine by the patient in home country in an effort to cure the disease.

Conclusion: Despite the different perspectives related to medication nonadherence, similar themes emerged from patients and their respective healthcare providers. The identified barriers warrant concerted efforts and series of interventions which should be initiated in a step-wise approach in order to improve medication adherence and overall healthcare outcomes.

DEDICATION

This thesis is dedicated to all those who left a mark on my life and filled it with joy and happiness. This work could not have been done without your support and continuous encouragement.

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CHAPTER 1: INTRODUCTION

1.1. Introduction

Diabetes mellitus (DM) is considered a burdensome disease globally. The global burden of illness attributed to DM is high and it is projected to continue to rise. In 2015, there were about 415 million people diagnosed with DM worldwide, a number that is expected to rise to 642 million by 2040 (1-3). The International Diabetes Federation (IDF) indicated that 1 out of every 11 people is diagnosed with diabetes with a new case identified every 10 seconds (3). Not only does diabetes affect patients with the disease, but it also adds to the healthcare expenditure and increase burden to the society. In 2015, it was estimated that diabetes accounted for 12% of the total healthcare expenditure globally (3). In addition, around $673 billion was spent on diabetes in 2015 alone, a number that is expected to increase to $802 billion by 2040 (1, 3).

Currently, the Middle East and North Africa (MENA) region ranks the second highest in the prevalence of diabetes after North America and Caribbean region (10.7% vs. 11.5%, respectively) (3). Countries forming the Gulf Cooperation Council (GCC) – comprising of Bahrain, Kuwait, Oman, Qatar, Kingdom of Saudi Arabia (KSA), and the United Arab Emirates (UAE) – are amongst those with the highest diabetes prevalence within the MENA region (1, 4, 5). For instance, Kuwait and KSA both have a comparative prevalence of 20%, followed by Bahrain (19.6%) and UAE (19.3%) (3).

Qatar, a country with a reported population of slightly more than two million people, has a comparative diabetes prevalence of 20%, a current national prevalence rate of 13.5%, and is expected to maintain its high prevalence rank up to the year 2035 (3, 4, 6). The number of diabetes-related deaths in the country was reported as 553 in 2015, making it the fifth leading cause of death in Qatar (1, 7, 8).

DM is associated with many complications and severe consequences if left untreated or uncontrolled; thus, it is burdensome for patients as well as their caregivers to manage. Through the decades, numerous studies and reports have been published about the consequences of uncontrolled diabetes ranging from micro- and macro-vascular complications to possible hospitalizations and premature mortality (2, 8-11). Apart from cardiovascular diseases, a patient with diabetes has a 25-fold higher risk of amputations than a person without diabetes (10). It is also estimated that about one-third of patients with diabetes will have diabetes-related eye damage if left uncontrolled (10).

Despite the recent advances and improvements in the therapeutics and management of diabetes, hospitalizations and premature mortality commonly occur due to the disease. In 2015 alone, 5 million diabetes-related deaths occurred globally (3). Several studies related to DM were conducted in Qatar; reporting the prevalence of diabetes complications including nephropathy, retinopathy, and neuropathy to range from 9.7-12.4%, 12.5-18.4%, and 9.5-12.6%, respectively. These complications are highly linked to poor adherence (11, 12).

Due to the high burden of the disease, Qatar has placed diabetes as a top priority in its national healthcare agenda, in an effort to control its prevalence and reduce the direct and indirect costs associated with its management which constitute a serious drain on the healthcare budget (13). The current documented average cost per person with diabetes in Qatar is USD $2,868 which is the highest among the neighboring GCC countries (3). Within the National Health Strategy 2011 – 2016, one of the projects (Project 1.7) is to create a diabetes management program (13). For such intervention programs to be efficient and population-specific in Qatar, it is crucial to utilize current studies investigating the problems associated with uncontrolled diabetes, particularly medication nonadherence.

Medication adherence is an intricate, multi-dimensional issue which highly contributes to treatment success. It plays a vital role particularly in chronic diseases where medications are a necessity to maintain disease control and prevent complications and mortality. The World Health Organization (WHO) defines adherence as "the extent to which a person's behavior – taking medications, following a diet and/or executing lifestyle changes – corresponds, with agreed recommendations from healthcare providers" (14). The WHO also emphasizes that having a better intervention to manage medication nonadherence may have a far better outcome on the patients' health than developing new medicine (14).

Nonadherence to medications in patients with diabetes presents a major barrier to treatment success (15-17). The reported rate of adherence to oral antidiabetic medications ranged from 36-93% (16, 17). In Qatar, researchers reported that about 17-22% of patients with diabetes stopped taking their medications when feeling better and without notifying

their physicians (12). Despite this, the factors influencing such decisions have not yet been investigated in Qatar.

Studies have investigated the factors associated with intentional nonadherence in patients with diabetes worldwide (14, 18-21). For instance, a qualitative study found that lifestyle adjustments such as the ability to integrate medications and instructions into work-life were the main challenges to compliance with treatment (14). Another study found loss of motivation, medications side effects, and lack of knowledge about glycemic level targets as factors that played a major role in medication nonadherence (20). Additionally, the patient-provider relationship was found to influence medication adherence; a good rapport was associated with good adherence (22, 23).

Furthermore, most studies in the literature reported reasons for medication nonadherence from the patient's perspective, but few studies have looked at the healthcare provider's perspective (21, 24, 25). It is important to note that healthcare providers' perspectives and views are important in the delivery of healthcare to the patients. Thus, understanding what they believe and perceive as barriers to medication adherence, can contribute to better patient care and improve adherence to drug therapy. This is particularly important for Qatar since not only the patients are multicultural, but also the healthcare providers are of diverse background and come from different countries and different cultures. All of these may influence the healthcare providers' perceptions and attitudes towards medication nonadherence in patients with diabetes.

1.2. Study Rationale

Although medical services and medications are largely covered by the public health insurance for all residents in Qatar, the management and control of diabetes remain to be issues of serious concern. An unpublished study conducted among patients with diabetes in a primary health center in Qatar found that the majority of the patients had uncontrolled diabetes regardless of the regimen they were taking. The mean HbA1c among the cohort studied was 8%, and surprisingly patients who were taking oral monotherapy had better control of diabetes than those who were taking multiple medications including insulin. This strongly suggests that prescribing multiple medications may not necessarily translate into better therapeutic outcomes and that there could be several factors underpinning this lack of adequate diabetes control beyond treatment optimization. Given that nonadherence to oral drug therapy and psychological insulin resistance are a common phenomenon among patients with diabetes, one could postulate that patients with diabetes may not be taking their medications as prescribed (22, 25-27). Therefore, clinicians may be attempting to optimize drug therapy towards improving clinical outcomes without adequate considerations to medication nonadherence.

Factors influencing medication adherence in diabetes and possible solutions to overcome the barriers to nonadherence have not been previously investigated in a multi-cultural population such as in Qatar and rarely did the previous investigations involve the perspectives of healthcare providers regarding this topic. Given that nonadherence is a complex issue, it becomes apparent to understand the influencing factors from the different perspectives (in this case, patients' and healthcare providers' perspectives). This is

especially important in vulnerable patients with uncontrolled diabetes.

In addition, many interventions were conducted across the globe to improve medication adherence in patients with diabetes (28-31). Most of these interventions have two main limitations within their methodologies; they did consider individualized patient characteristics regarding specific barriers to adherence, and they mainly targeted type 2 diabetes (28-31). This not only limits the population and generalizability of the results, but can also reflect upon the magnitude of the effect observed which in many instances is either modest in size or is observed for a short duration of time. Consequently, it is very crucial to understand what barriers and what contributing factors exist in a multicultural population such as the one in Qatar in order to achieve better patient-centered and population-specific adherence improvement strategies. This would result in designing population-specific interventions that will be of more value and potentially yield better health outcomes.

1.3. Study Objectives

1.3.1. *General objective*

The overall aim of the present study is to identify and explore barriers to medication adherence among patients with uncontrolled diabetes in primary healthcare settings from the perspectives of the patients and their healthcare providers.

To achieve this general objective, the project is split into two phases: Phase I is directed towards the patients, while Phase II focuses on healthcare providers to achieve the below specific objectives.

1.3.2. Specific objectives for Phase I

   i.   To determine the level of medication adherence among patients with uncontrolled diabetes using a self-reported measure.

  ii.   To identify the characteristics, risk factors associated with, and barriers to medication adherence from the patients' perspective.

 iii.   To explore possible strategies for improving medication adherence in patients with uncontrolled diabetes in Qatar from the patients' perspective.

 iv.   To compare the characteristics, identified barriers and solutions, between patients with good medication adherence and patients with poor medication adherence.

1.3.3. Specific objectives for Phase II

   i.   To determine the barriers to medication adherence in patients with uncontrolled diabetes from healthcare providers' perspective.

  ii.   To explore possible strategies for improving medication adherence in patients with uncontrolled diabetes in Qatar from a healthcare providers' perspective.

1.4. Study Significance

(a) There is a lack of data about barriers to medication adherence among patients with diabetes in Qatar necessitating the need for this study. This study will provide healthcare providers with information regarding the factors associated with medication non-adherence and thus ultimately improve patient care and outcome.

(b) Patient counseling in current practice does not reflect upon the different cultures and diversities of patients in the country. This study will thus reveal whether cultural differences act as an influencing factor on medication adherence. Thus, this study will identify the needed information to make counseling more patient specific.

(c) Non-adherence to diabetes medications results in complications that necessitate the patient's increased use of the healthcare resources which is funded by the government. This study will potentially help reduce the economic burden of diabetes through providing a patient-specific counseling, and interventions therefore, decreasing morbidity and diabetes-related complications.

(d) This project targets a national priority in Qatar as it is in alignment with Qatar National Vision 2030 and National Health Strategy 2011-2016, where providing a patient-centered care in diabetes is very important (32, 33).

(e) This research will also involve healthcare providers from different disciplines (medicine, pharmacy, nursing, and nutrition). Therefore, it will promote and foster multidisciplinary research collaboration and capacity building.

CHAPTER 2: LITERATURE REVIEW

This chapter will provide an overview of the literary work relating to medication adherence in general and later tailored to medication adherence in diabetes. First, the term 'medication adherence' is defined and brought into perspective. This is followed by discussions on the methods for measuring medication adherence. Second, existing conceptual framework models that covered the barriers to medication adherence will be described through a systematic review of systematic reviews. The Chapter ends with a proposed holistic conceptual framework model derived from all of the evidence described and which will be used as a reference model throughout this study.

2.1. Definition of Adherence

The term adherence stems from the concept of 'drug utilization'. This concept covers multiple aspects and is connected to many terms relating to the medication-taking behavior (Figure 1). Initially most reporting literature used the term 'adherence' only as a synonym to 'compliance' (34). The origin of the term compliance comes from the old French word *compli* which means to accomplish or to fulfill, and from the Latin word *complere* which means to fill up and satisfy (35). However, the term 'compliance' has become less used in the past couple of years since it indicates that the patient is passively following instructions from the healthcare provider without a prior agreement or discussions (36, 37). The terms 'persistence' and 'concordance' were also used as synonys for 'adherence' or 'compliance' (34).
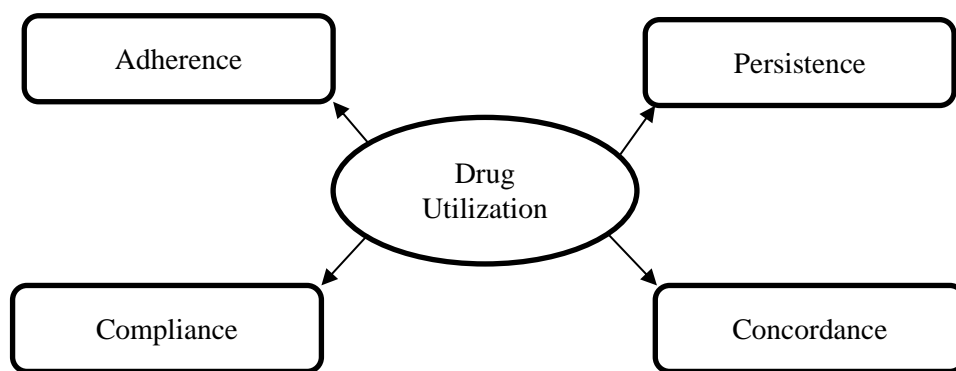
Figure 1: Terms commonly used with drug utilization

Cramer used both terms, 'compliance' and 'adherence' in 2008, as synonyms to each other and defined them as "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen." This definition is similar to the earlier definition by *Osterberg* in 2005, who defined adherence as "the extent to which patients take their medications as prescribed by their healthcare providers"(36). These definitions were then modified and termed 'adherence'. The new definition became "the extent to which the patient's behavior matches agreed on recommendations from the prescriber" (37). This definition indicates that there is a prior discussion and an agreement between the healthcare provider and the patient, a factor which was not initially indicated in the previous definitions.

Medication 'persistence' on the other hand, is defined as "the duration of time from initiation to discontinuation of therapy." This term was in some instances considered as a bigger umbrella for adherence (38). With this definition comes the concept of "permissible gap": a gap in the time allowed between refills based on the pharmacological properties of the drug (34, 38).

Another less commonly used term is "concordance" which is a wider concept incorporating adherence in addition to the communication and support provided by the healthcare provider to the patient in an effort to help them take their medications appropriately (37). This term not only incorporates the patient, and their relationship with the healthcare provider, but also looks at the outcome of the treatment (37). Despite this broader definition, the *National Coordinating Center for NHS Service Delivery and Organization* (NCCSDO) recommends the use of the term 'adherence' instead of all the other terms to describe the patient's medication-taking behavior (37).

Medication nonadherence can be split into two subcategories: primary nonadherence and secondary nonadherence. Primary nonadherence refers to the patient not filling the initial prescription after the physician provided it. Conversely, secondary nonadherence relates to the failure of either following the instructions or refilling the medications or both. Another categorization is unintentional nonadherence and intentional nonadherence (39). The unintentional nonadherence is the random inappropriate medication taking or the random cessation of taking the drug. This could be due to factors such as forgetfulness. On the other hand, intentional nonadherence is the purposeful decision in stopping or changing a medication regimen by the patient (39).

2.2. Measurement of Medication Adherence

Several methods are used to measure drug adherence, but all could be broadly classified into direct and indirect methods by *Osterberg* and *Blaschke* (36, 40). The direct methods involve objectively observing therapy using procedures such as biological biomarkers or having a directly supervised dosing. These direct methods may not always be practical and may not reflect upon patients' behavior. Therefore, they are not routinely conducted in real-world practice (40). On the other hand, the indirect methods take into consideration patient factors and are much easier to conduct than the direct methods. Adherence is reported by the patient through questionnaires and can also be indicated by the rate of prescription refills (40). Nonetheless, the indirect methods have their limitations such as patient recall and social desirability biases, but they give information about modifiable behavior which can ultimately be targeted and corrected, thus improving adherence.

There is no gold standard method for evaluating medication adherence (41). Each method has its own limitations. Choosing the best method will depend on its applicability in the healthcare setting. *Fairman* and *Motheral* summarized the methods used to measure medication adherence along with their advantages and disadvantages (41). These methods are summarized and briefly described in Table 1.

Table 1: Methods used to measure medication adherence

Method	How it is measured	Advantages/Disadvantages
Biological biomarkers measurement	Usually blood tests, but could also involve other bodily fluids	**Advantages:** Reliable and accurate **Disadvantages:** Requires availability of the patient in the health setting such as inpatients, labor-intensive, costly, may not work with drugs of short half-lives, affected by patient's metabolism
Direct observation of therapy	A dedicated person observes the patient taking the medication at each dose	**Advantages:** Reliable and accurate **Disadvantages:** Very much labor-intensive
Pill count	Counting medication pills after a specified duration	**Advantages:** Easy to conduct **Disadvantages:** Cannot determine if drug was taken on schedule or not
Electronic monitoring system	An electronic chip is attached to the medication bottle which can record how many times the medication box was opened and at what time	**Advantages:** Easy to conduct, more accurate than pill counts **Disadvantages:** Very costly
Patient self-reported measure	Questionnaires or patient diaries	**Advantages:** Easy to conduct, provides patient perspective **Disadvantages:** Subject to bias
Prescription claims	Checking pharmacy records	**Advantages:** Inexpensive and accessible data **Disadvantages:** Depends on reliability, comprehensiveness, and accuracy of existing records, can only be used for chronic medications

Note: Contents of this table were derived from Fairman and Motheral (2000)

2.3. Existing Conceptual Framework Models on Medication Adherence

Barriers to medication adherence have largely been studied and documented in the literature (18, 19, 42-47). Thus, multiple conceptual models have been developed to illustrate the complex relationship between the different factors relating to medication nonadherence (42, 48-50). One proposed model by *Gellad et al.* is demonstrated in Figure 2 (42). This model illustrates the different factors that are thought to influence medication adherence. Also, it highlights the network of interactions between the factors that influence the medication-taking behavior of patients with chronic health conditions. The factors illustrated in Figure 2. are briefly described below:
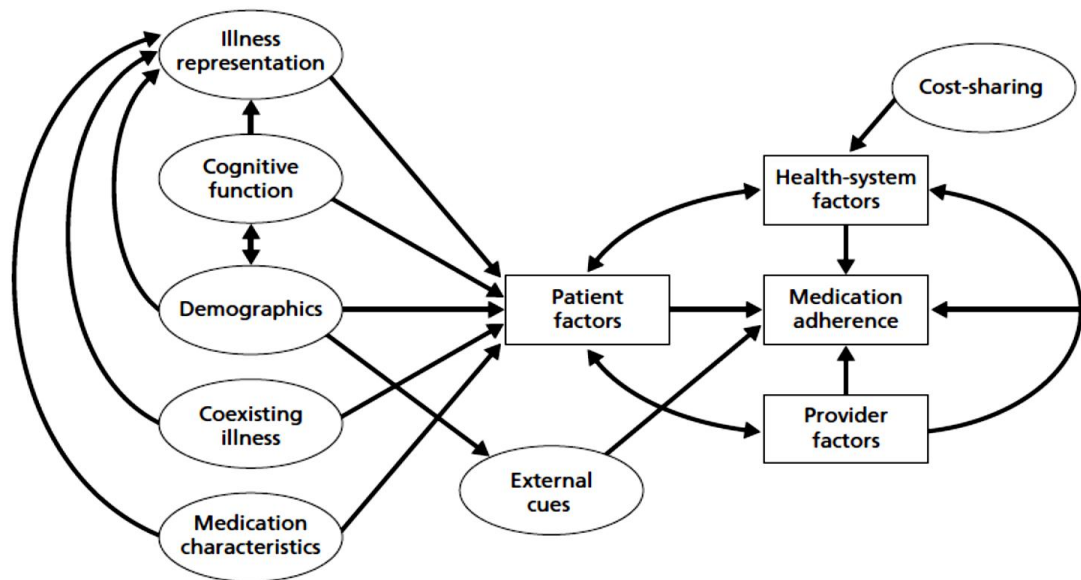
Figure 2: Conceptual framework model for medication adherence

Source: Gellad (2009)

Patient factors: This is a domain influenced by many components: 1) illness representation, which reflects the patient's knowledge about the illness and beliefs about the medications ; 2) the cognitive function, which is represented by the patient's ability to comprehend and recall information related to the illness and medications; 3) patients demographics, such as marital status; 4) coexisting illnesses whether physical or psychological and; 5) medication characteristics which represent the regimen complexity as well as side effects.

Health system factors: This includes formulary-related issues, fragmentation of care as well as access to care. It is also influenced by cost-sharing which may, in turn, affect patient's adherence.

Provider factors: This includes patient-provider relationship and interaction.

This model also reflects upon the different interactions which can exist between the various components and factors. Although this model is simple, yet it is not disease-specific, and at the same time it is not detailed for each category of factors. For instance, what specific demographics are mostly influencing medication adherence? What patient-provider aspects are most important? Also, what do external cues represent?

Another conceptual model exists for understanding medication adherence in older adults (Figure 3). This model was developed as a guiding map for an ongoing project - at the time - on heart failure patients who were above 50 years of age. The model focuses on the associations between environmental-related factors, patient-related factors, and medication adherence. The concepts were mainly developed based on behavioral

healthcare utilization model (48). The components of the model are briefly described below:
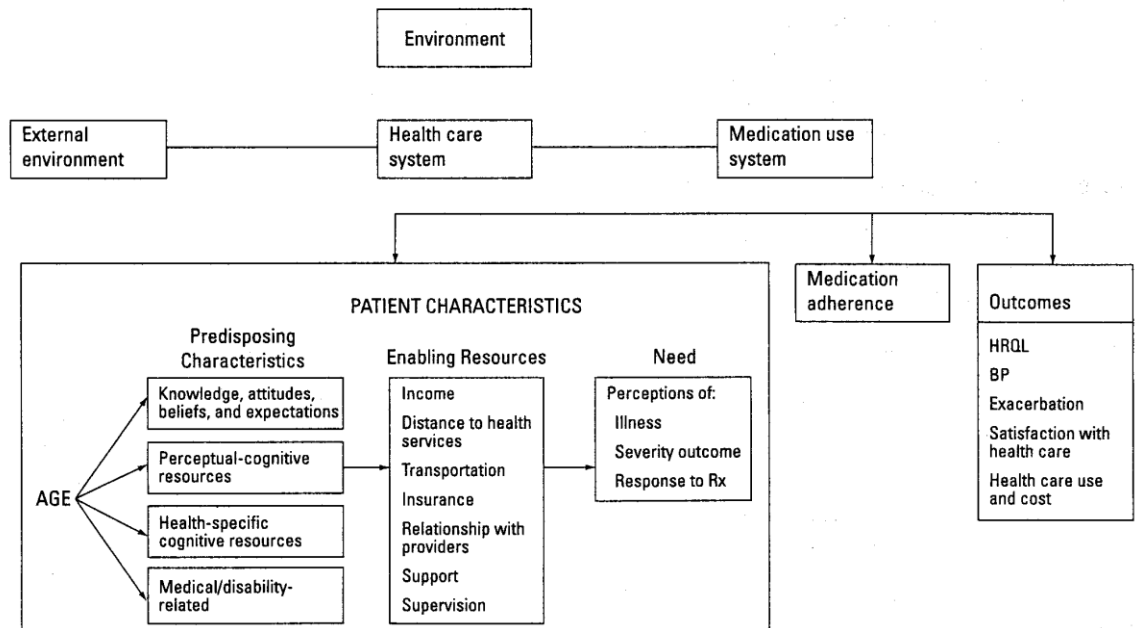
Figure 3: Conceptual framework model for medication adherence in older adults

Source: Murray (2014)

Environment: This includes patient's community, social support, stress, and environmental conditions which may influence the patient's ability to obtain medications.

Healthcare system: This includes the regulations, resources, and finances which would allow the medications to be available, accessible and affordable.

Medication use system: This stands for interventions which would work on improving medication adherence.

Patient characteristics: This reflects the features that the intervention should be tailored to, and are divided into three different categories: 1) Predisposing characteristics:

features that are predicting medication adherence but may not change by the intervention; 2) Enabling resources: these are supporting resources that can improve medication adherence; 3) Need: This reflects on the patient's perceived need for adhering to medications.

Although this model includes the intervention to improve adherence and reflects on focusing them on patient's characteristics, its major drawback is that it does not identify possible interactions between the different barriers and does not identify all the potential barriers and influencing factors that can contribute to medication nonadherence. Moreover, the model was created for developing an intervention specific to patients with heart failure and as such may not be useful in other diseases. Therefore, to understand the complexity and the influencing factors to medication adherence in diabetes, a new conceptual model is warranted. In order to gain a broader insight of the factors associated with medication adherence to guide the development of a conceptual framework model that is specific for diabetes, a review of systematic reviews was conducted.

2.4. Evaluation of Existing Evidence on Medication Adherence in Diabetes

Several systematic reviews have been conducted about medication adherence in diabetes. Nonetheless, they mainly focused on type 2 diabetes or multiple chronic disease conditions, neglecting type 1 diabetes (21, 45, 47, 51, 52). Another major limitation of the existing systematic reviews is the lack of risk of bias assessment of included studies, making them highly prone to misguided judgments (18, 25, 45, 51, 53). Furthermore, the methodological qualities of the published systematic reviews have not been previously

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evaluated. These reviews report a remarkably diverse complex network of barriers to medication adherence, making it challenging to develop holistic, evidence-based interventions.

The availability of multiple systematic reviews on the topic necessitates evidence appraisal to answer the question: What are the barriers to medication adherence in patients with diabetes and what is the quality of the evidence reporting those? Hence, a review of systematic reviews will bring together and appraise the existing evidence (54). This work will benefit healthcare providers in identifying the most reliable evidence to apply in practice and at the same time provide insight for researchers about the limitations of the existing studies to avoid in similar research in the future.

A comprehensive systematic literature search was conducted to identify existing systematic reviews addressing influencing factors and barriers to medication adherence in patients with diabetes. The search was performed on the following databases: PubMed, Cochrane Library, Campbell Library, Database of Abstracts of Reviews of Effects (DARE), Academic Search Complete, EMBASE, Evidence-Based Practice Center Program (EPC), SCOPUS, Health System Evidence, ProQuest, ScienceDirect, Global Health Database, Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports, and Google Scholar. The process also included manual searches of the bibliographies of the articles identified electronically as well as gray literature including abstracts of thesis and documents published by academic institutions as well as conference proceedings.

The search terms used were divided into four categories. Category A was adherence-related (adher*, compliance, comply*, nonadher*, noncompliance, refuse, refusal); category B was condition-related (diabetes, type 1 diabetes, type 2 diabetes, diabetes mellitus); category C was barrier-related (barrier, factor, facilitator, predictor, challenge, determinant); while category D was related to study design (review, systematic review, meta-analysis, scoping review, systematized, mixed method review, mixed studies review, integrative, narrative). Terms were combined differently from categories A, B, C, and D using Boolean operators (AND/OR) in such a way that all relevant reviews would be retrieved. Medical subject heading (MeSH) terms and limits were used in corresponding databases as appropriate.

Included articles were systematic reviews published in English language addressing barriers to medication adherence in patients with diabetes. Studies focusing on substance abusers, patients with mental disorders, tuberculosis, HIV, and gestational diabetes were excluded since each of these population groups has its circumstances that affect medication adherence. However, systematic reviews that looked at a combination of diseases were included if they analyzed barriers to medication adherence in diabetes separately. Moreover, narrative reviews not following systematic literature search, reviews reporting rates of medication adherence only, reviews looking at the impact of interventions as well as comparative reviews were also excluded since they are beyond the scope of this review.

AMSTAR (A Measuring Tool to Assess Systematic Reviews), a quality assessment tool for systematic reviews, was used for evaluating the methodological quality of the included reviews (55). Items 9 and 10 were not considered in the evaluation since they

were not applicable to the types of systematic reviews included. These items are directed to the assessment of meta-analysis and relate to the evaluation of heterogeneity and publication bias, respectively. All the elements of the AMSTAR tool were weighted equally with a quantitative score of 1 for each item. Final grading of the methodological quality was based on the following arbitrary criteria: $0 - 3$, $4 - 6$ and $7 - 9$ corresponding to "low quality", "moderate quality" and "high quality", respectively.

Data were extracted using a tool developed and pretested for this review. The elements extracted included: title, authors, year of publication, primary objective(s) of the review, inclusion and exclusion criteria, article sources including databases, search strategy, bias and quality assessment methodology for included studies, number of included articles, study design of included articles, key findings, conclusion, limitations, sources of funding, and quality level. In cases where a review included multiple disease conditions, only diabetes-related information was extracted.

The main outcome measures were factors associated with and barriers to medication adherence. Based on the extracted data, textual summaries and summary tables were developed. From these, emerging categories relating to factors influencing medication adherence were identified. Thematic content analysis was used to further categorize some of the emerged categories into subcategories. Specific factors and barriers were assigned to each of the categories and sub-categories. No software was utilized for the data synthesis and analysis.

Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were used in reporting the findings. Through searching and after removal of duplicates, 11,684 different references were found of which 26 reviews were potentially relevant based on screening of titles and abstracts. After full-text evaluation of the 26 reviews, nine were excluded. Two of the potentially relevant reviews were presented as conference abstracts, and their full-text were not available; therefore, they were excluded from the study (56, 57). Other studies were excluded for one or more reasons including not systematic reviews or did not use systematic search strategy (58, 59), not related to medication adherence in diabetes (60, 61), or presented rates of adherence only without investigating barriers (18, 25, 62) (Figure 4). Finally, 17 systematic review articles were eligible for inclusion in the review.
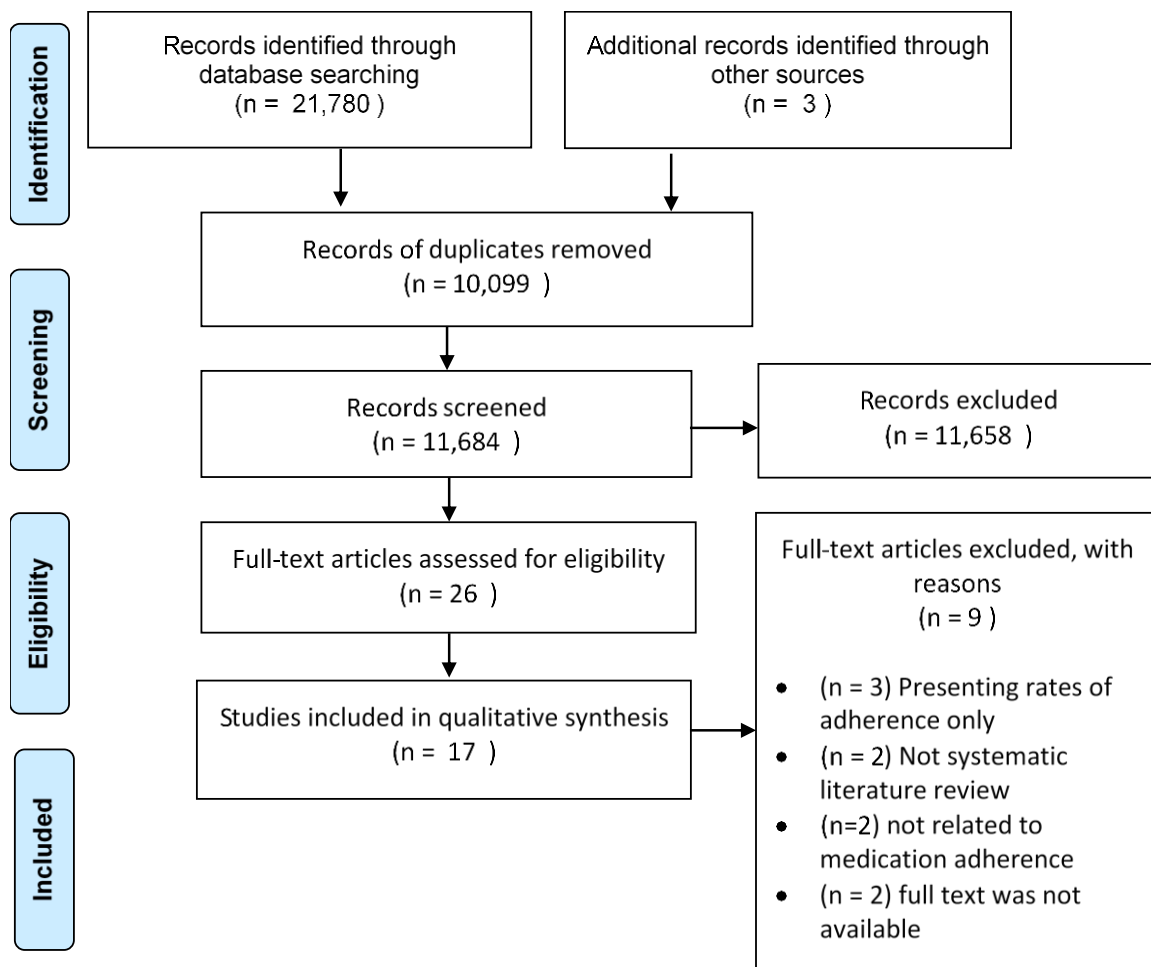
Figure 4: Articles selection flow diagram (Evaluating existing evidence)

All of the included systematic reviews were published in English from 1990 – 2016 covering primary studies published from 1967 – 2016. All the reviews included the details of the primary studies, most of which were conducted in the United States (U.S.) and United Kingdom (U.K.), with a wide representation of studies from other countries across the globe (Table 2). The total number of original investigations (i.e. primary studies) included in the 17 reviews was 542, with an average of 32 studies per review (range 6 – 98).

The AMSTAR score for the included systematic reviews ranged from $1 - 6$ (Table 3). Nine of the 17 articles were rated as 'moderate quality', while the rest were of 'low quality'. Overall, the evaluated systematic reviews shared common methodological pitfalls. For instance, none of the reviews had reported a conflict of interest related to the primary studies they included, and only three reported searching the gray literature. Furthermore, the majority of the reviews (11 of 17) did not report assessing the methodological quality of the primary studies, but those that assessed quality did it appropriately.

Table 2: Characteristics of the included systematic reviews

Reference/year of publication	Population	Number of studies included	Location of primary studies	Factors influencing medication adherence
Capoccia K. et al. (2016) (63)	Adults with Type 1 or Type 2 diabetes	98	Not indicated	• Patient-related factors: demographics, physiological status, health literacy, adapting to changes • Medication-related factors • Provider-related factors • Societal-related factors • Health system-related factors
Tiktin M. et al. (2016) (64)	Adults with Type 2 diabetes	30	U.S., England, Netherlands, Mexico, Korea, Denmark, Belgium	• Patient-related factors: demographics, physiological status • Medication-related factors • Disease-related factors • Provider-related factors
Brundisini F. et al. (2015) (65)	Adults with Type 2 diabetes	86	U.S., England, Canada, Netherlands, Australia, Norway, Sweden, Belgium, Croatia, Germany, Romania	• Patient-related factors: physiological status, health literacy, emotions, perceptions, adapting to changes • Medication-related factors • Disease-related factors • Provider-related factors • Societal-related factors
Krass I. et al. (2015) (21)	Adults with Type 2 diabetes	27	U.S., Iran, Netherlands, Malaysia, France, Korean, Sweden, Japan, Germany, Palestine, Egypt, Nigeria	• Patient-related factors: demographics, physiological status • Medication-related factors • Disease-related factors • Healthcare system-related factors

Table 2: *Cont.* Characteristics of included systematic reviews

Reference/year of publication	Population	Number of studies included	Location of primary studies	Factors influencing medication adherence
Sohal T. et al. (2015) (47)	Adults with Type 2 diabetes	20	U.S., England, Scotland, India, Norway	• Patient-related factors: health literacy, perceptions, adapting to changes • Medication-related factors • Societal-related factors
Al Hamid A. et al. (2014) (66)	Adults with cardiovascular diseases or diabetes	21 (15 diabetes related)	England, Scotland, Canada, Australia, Malaysia, Spain, South Africa, Taiwan, Croatia, Cameron, Brazil, Ireland	• Patient-related factors: physiological status, health literacy, perceptions, adapting to changes • Medication-related factors
Davies MJ. et al. (2013) (67)	Adults with Type 1 or Type 2 diabetes	17	England, Scotland, Mexico, New Zealand, South Africa	• Patient-related factors: demographics, health literacy, perceptions • Medication-related factors • Disease-related factors • Healthcare system-related factors
Polinski J. et al. (2013) (51)	Adults with Type 2 diabetes	10	Africa, Middle East, Asia, Eastern Europe, Latin America, Canada, Germany, Japan, Spain, Turkey, U.K., U.S., Spain	• Patient-related factors: emotions, fear, perceptions. • Medication-related factors • Disease-related factors • Societal-related factors • Provider-related factors • Healthcare system-related factors
Sarayani A. et al. (2013) (68)	Adults with cardiovascular disease or diabetes	14 (6 diabetes related)	Iran	• Patient-related factors: emotions, fear, adapting to changes • Medication-related factors • Societal-related factors • Healthcare system-related factors
Peeters B. et al. (2011) (52)	Adults with Type 2 diabetes	12	U.S., New Zealand, South Africa	• Patient-related factors: demographics, physiological status, perceptions, adapting to changes • Healthcare system-related factors
Gherman A. et al. (2011) (69)	Adults with Type 1 or Type 2 or gestational diabetes	48	U.S., Australia, India, Mexico, New Zealand, Turkey, Taiwan, Japan, China	• Patient-related factors: perceptions • Provider-related factors
Nam S. et al. (2011) (45)	Adults with Type 2 diabetes	80	Not indicated	• Patient-related factors: demographics, physiological status, health literacy, emotions, fear, perceptions, adapting to changes • Medication-related factors • Provider-related factors • Societal-related factors • Healthcare system-related factors
Fu AZ. et al. (2009) (70)	Adults with Type 1 or Type 2 diabetes	6	U.S., England, Netherlands	• Patient-related factors: fear

Table 2: *Cont*. Characteristics of the included systematic reviews

Reference/year of publication	Population	Number of studies included	Location of primary studies	Factors influencing medication adherence
Pun S. et al. (2009) (71)	Adults with Type 2 diabetes and healthcare providers	16	U.S., England, Mexico	• Patient-related factors: physiological status, health literacy, emotions, perceptions • Medication-related factors • Disease-related factors • Provider-related factors • Societal-related factors • Healthcare system-related factors
Gonzalez JS. et al. (2008) (72)	Adolescents, or adults with Type 1 or Type 2 diabetes	47 (18 studies related to diabetes medications)	Japan, U.S., New Zealand, Mexico, Germany, Canada, Croatia, Korea, England, Netherlands	• Patient-related factors: physiological status
Lee WC. et al. (2006) (73)	Adults with Type 2 diabetes	27	U.S., Scotland, France, Switzerland	• Patient-related factors: physiological status • Medication-related factors • Healthcare system-related factors
Nagasawa M. et al. (1990) (74)	Adolescents, or adults with Type 1 or Type 2 diabetes	26	Not indicated Not indicated	• Patient-related factors: demographics, health literacy, emotions, perceptions • Societal-related factors

Table 3: Quality assessment of the included systematic reviews as per the AMSTAR criteria

Reference /year of publication	Provides an "*a priori* design"	Duplicate data extraction	Searched 2 or more databases plus another source	Gray literature	Includes a list of included and excluded studies	Reports characteristics of each included study	Assesses and documents scientific quality of included studies	Used scientific quality of the studies appropriately	Includes conflict of interest statement	Overall rating of quality
Capoccia K. et al. (2016) (63)	No	Yes	Yes	No	No	Yes	Yes	Yes	No	Moderate
Tiktin M. et al. (2016) (64)	No	No	No	No	No	Yes	No	No	No	Low
Brundisini F. et al. (2015) (65)	Yes	Yes	Yes	No	Yes	Yes	No	No	No	Moderate
Krass I. et al. (2015) (21)	No	Yes	Yes	No	No	Yes	No	No	No	Low
Sohal T. et al. (2015) (47)	No	No	Yes	No	No	Yes	Yes	Yes	No	Moderate
Al Hamid A. et al. (2014) (66)	No	No	Yes	No	No	Yes	Yes	Yes	No	Moderate
Davies MJ. et al. (2013) (67)	No	No	Yes	No	Yes	Yes	Yes	Yes	No	Moderate
Polinski J. et al. (2013) (51)	No	Yes	Yes	No	Yes	Yes	No	No	No	Moderate
Sarayani A. et al. (2013) (68)	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Moderate
Peeters B. et al. (2011) (52)	No	Yes	Yes	No	No	Yes	No	No	No	Moderate

**Table 3: *Cont.* ** Quality assessment of the included systematic reviews as per AMSTAR criteria

Reference /year of publication	Provides an "*a priori* design"	Duplicate data extraction	Searched 2 or more databases plus another source	Gray literature	Includes a list of included and excluded studies	Reports characteristics of each included study	Assesses and documents scientific quality of included studies	Used scientific quality of the studies appropriately	Includes conflict of interest statement	Overall rating of quality
Gherman A. et al. (2011) (69)	No	No	No	No	No	Yes	Yes	Yes	No	Low
Nam S. et al. (2011) (45)	No	No	Yes	No	No	Yes	No	No	No	Low
Fu AZ. et al. (2009) (70)	No	No	Yes	No	No	Yes	No	No	No	Low
Pun S. et al. (2009) (71)	No	No	Yes	No	No	Yes	No	No	No	Low
Gonzalez JS. et al. (2008) (72)	No	Yes	Yes	Yes	No	Yes	No	No	No	Moderate
Lee WC. et al. (2006) (73)	No	No	No	Yes	No	Yes	No	No	No	Low
Nagasawa M. et al. (1990) (74)	No	No	Yes	No	No	Yes	No	No	No	Low

The reviewed systematic reviews indicate that barriers to medication adherence are multi-factorial with remarkably consistent findings across the reviews. Barriers to or factors associated with medication adherence derived from the included reviews were categorized into the following: patient–, medication–, disease–, care provider–, healthcare system–, and societal–related factors. Given the considerable variation in patient–related factors and its major subtypes across the reviews, it was further classified using thematic content analysis into several sub-categories: demographics, physiological status, health literacy, emotions, fear, perceptions, and adaptation to changes (Table 4).

The most predominantly reported patient–related factors included age, depression, and health literacy level. On the other hand, side effects and frequency of dosing were the most commonly reported medication–related factors. Disease–related factors such as duration of diabetes, disease complexity, and complications were rarely addressed. Societal–related factors commonly identified by the reviews were social stigma, cultural barriers, and lack of support. Moreover, within the healthcare system-related factors, issues surrounding insurance coverage and cost of medicines were the most frequently identified barriers to medication adherence in the reviewed studies.

Table 4: Factors influencing medication adherence in diabetes

Factors	References
Patient-related factors	
Demographics (age, gender, ethnicity, financial status and level of income, marital status, and level of education)	(21, 45, 52, 63-65, 67, 74, 75)
Physiological status (comorbidities, depression, smoking)	(21, 45, 52, 63-66, 71, 72)
Health literacy (lack of understanding about the disease and treatment, difficulty reading prescription)	(45, 47, 63, 65-67, 71, 72, 74)
Emotions (blame, guilt, shock and helplessness, frustration, negative attitude, stress, and anxiety)	(45, 51, 65, 66, 68, 71, 74)
Fears (injection, blood phobia, and fear of pain)	(45, 51, 65, 68, 70)
Perceptions of (need of medicine, barriers to following medication, benefit from treatment, misconception about medicines, and self-efficacy)	(21, 45, 47, 51, 52, 65-67, 69, 71, 74)
Adaptation to change (traveling overseas, alterations in daily schedule, change or lack of routine in managing treatment, and diet adjustments)	(47, 63, 65-68)
Medication-related factors	
Frequency of dose or injection	(21, 45, 63, 64, 67, 75)
Length of therapy	(75)
Number of medications and polypharmacy	(21, 52, 64, 66)
Timing of dosing	(63)
Changing of treatment	(67)
Fluctuating response to medications	(71)
Side effects	(21, 47, 51, 52, 63, 65, 66, 68, 71)
Complexity of regimen	(51, 63, 65, 66)
Drug class/type	(21, 45, 52, 64, 75)
Method of drug administration	(51, 64-66)
Traditional medicine and phytotherapy	(47, 65, 66)
Disease-related factors	
Diabetes duration	(21, 64)
Disease complexity	(65, 71)
Lower HbA1c	(51, 67)
Complications	(21)
Provider-related factors	
Support from healthcare providers	(63, 64)
Lack of patient involvement in decision-making process	(63, 65)
Duration of counseling and lack of time	(51, 64, 65)
Relationship with care provider	(45, 69)
Assumptions by providers about the patients' knowledge	(45, 51, 65)
Providing ambiguous or incomplete information	(45, 65)
Provider's lack of experience	(51)
Language and communication barrier	(21, 45, 65, 71, 74)

Table 4: *Cont.* Factors influencing medication adherence in diabetes

Factors	References
Societal-related factors	
Support from family	(45, 63)
Lack of support	(45, 65, 71)
Cultural barriers	(45, 65, 71)
Social stigma	(47, 51, 65, 68)
Healthcare system-related factors	
Insurance coverage	(21, 52, 63, 67, 68, 75)
Lack of guidelines for optimal treatment	(51, 71)
Cost of medicine	(21, 45, 65, 75)
Co-payment amount	(63, 75)
Convenience of obtaining medications	(63, 64)
Continuity of care	(63)
Other: Forgetfulness	(18, 63, 64, 66-68, 71)

Systematic reviews and meta-analysis are considered the highest in the hierarchy of evidence-based information. Nevertheless, the value of these evidence-based resources depends highly on their scientific quality (76). Therefore, it is essential for the reader to critically appraise the methodologic quality using appropriate instruments. The AMSTAR tool which we utilized is a reliable and widely used tool for the assessment of systematic reviews (55).

One item of the AMSTAR tool refers to disclosing conflict of interest for the systematic review itself as well as for all the individually included primary studies, which none of the reviews did. This appears to be similar across similarly conducted systematic reviews, were looking at the conflict of interest remains to be underestimated (77).

It is noteworthy that in this review all the AMSTAR items were given equal weight during scoring. However, items relating to the quality assessment of the primary studies as well as the comprehensiveness of search applied in the systematic review may be

considered the most essential elements for systematic reviews and should, therefore, be given greater weights. It is worthwhile to note that a new AMSTAR tool which can be used for non-randomized studies is under development taking into consideration the suggestions and feedback from users. Therefore, the overall scoring of the included reviews may differ accordingly (76).

It is evident that the included reviews have fallen into the common pitfalls of published reviews as recently described by *MacLure et al*. (76). The lack of detailed published protocol in most reviews presents a risk of bias in these reviews. In view of the duplicate data extraction item of the AMSTAR - having more than one researcher doing the extraction - it may reflect on lack of team experience and independent involvement in the methodological process of the reviews which is another issue presented in more than half of the reviews included in this study. One major pitfall is the absence of quality assessment of primary studies which can be considered as a major source of bias (76). These issues can easily be overcome and avoided with the use of focused and detailed protocol based on existing guidelines in addition to learning from the experience of other researchers.

There are some inherent limitations in the methodology employed in this review. This review relies on information presented by reviews of poor to moderate methodological quality which may undermine the quality of this review. Other limitations include duplicates of the primary studies within the reviews were not checked. It may, therefore, be that some evidence were counted more than once. The main purpose of this review was to assess the quality of the existing evidence. As expected, the quality of this review

depends on the quality of the primary studies within the included reviews. Not all reviews have assessed the quality of their included studies. Thus, the summary of influencing factors may not be as well-founded.

Our search indicates that the topic of medication adherence in patients with diabetes has been extensively studied and published in the literature. The findings of the review suggest that influencing factors and barriers to medication adherence are multifaceted with remarkably consistent findings across the existing systematic reviews; yet, the reviews were judged to be of low to moderate quality. Further comprehensive and well-designed systematic reviews as well as primary studies on this topic shall be conducted taking into considerations the pitfalls of the existing ones.

2.5. A Proposed Conceptual Framework Model on Medication Adherence in Diabetes

Multiple conceptual models for medication adherence have been published, yet they are not disease-specific (42, 43, 48). To have an effective intervention, an understanding of the complex network of barriers and factors influencing medication adherence in patients with diabetes is highly needed. An earlier review was conducted summarizing all these factors, yet their interactions and complexity have not been fully demonstrated by the primary studies and the reviews. Therefore, the aim of this section was to develop and create a model summarizing the complex network of influencing factors to be used as a reference for this thesis project and potentially for interventions targeting medication adherence in patients with diabetes in the future.

In brief, fourteen databases and gray literature sources were systematically searched through April 2016. Systematic reviews reporting barriers to medication adherence in patients with diabetes were selected based on predetermined criteria. Data were extracted using a pre-tested data extraction tool. Articles were also appraised for quality using the AMSTAR tool. ***Refer to section 2.4. for details and the synthesis of the review.*** Seventeen systematic reviews were initially identified. However, another unpublished systematic review was added as it was conducted later bringing the total to 18 systematic reviews.

From these reviews, a thematic approach was utilized to sort out the barriers and the factors into the matrix of the framework. Each barrier and factor was initially coded, then clustered into larger categories. Connections between different factors were extensively identified. Any emerging category was verified by checking and rechecking as well as comparing the categories to each other. Once all the reviews were analyzed separately, the factors were regrouped again to create the overall conceptual framework model. The overall methodology used to finalize the model utilized the Delphi technique (among the MSc student and three supervisors) until a final model was agreed upon.

A comprehensive list of themes was initially identified from the included systematic reviews: (1) patient-related factors; (2) diabetes-related factors; (3) medication-related factors; (4) healthcare provider-related factors; (5) healthcare system-related factors and; (6) societal-related factors. Figure 5 presents the core of the proposed conceptual framework model for medication adherence in diabetes. It summarizes the main categories and subcategories. This is followed by several extensions that detail the factors identified in the core model (Figures 6-11).
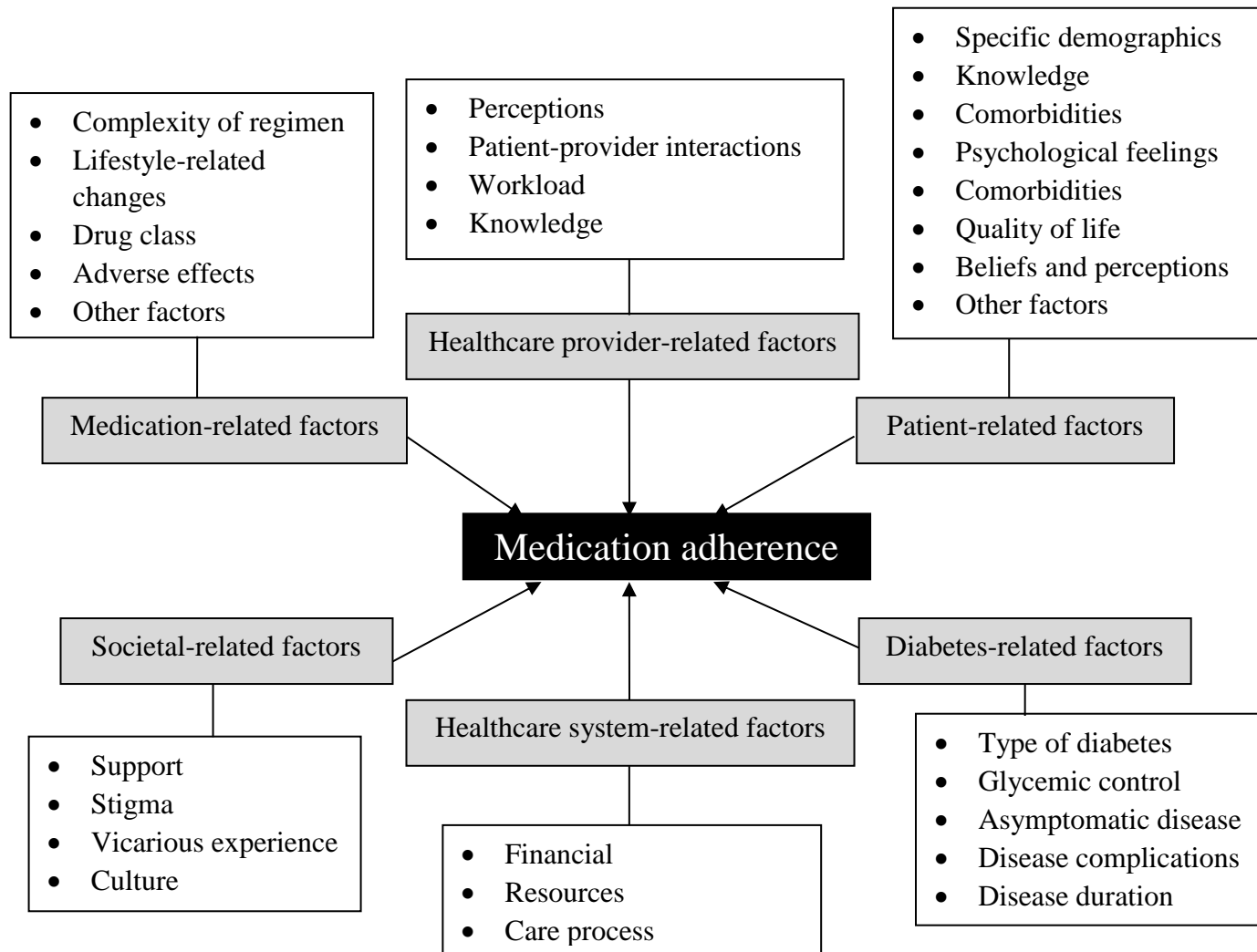
Figure 5: A core conceptual framework on factors associated with medication adherence in diabetes

Patient-related factors: Most studies investigated patient-related factors, particularly the association of patients' demographics and medication adherence. It was noted that most interactions were observed within this category as well as between the sub-categories. This complex network of interactions between patient-related factors is illustrated in Figure 6. Notably, demographics, perceptions and beliefs, and knowledge are associated with many other factors. For instance, studies indicated that an education level below elementary level was associated with patients' beliefs, while advanced age was related to comorbidities as well as the disease complications. All of these factors were in turn associated with medication adherence. Lack of knowledge about the disease and its medications was associated with poor patient's motivation, perception, as well as self-esteem (Figure 6).

Diabetes-related factors: Within this category, it was noted that the type of diabetes is associated with medication adherence, whereby patients with type 2 diabetes demonstrated lower adherence than those with type 1. An inverse relationship was noted between medication adherence and disease duration, while the levels of HbA1c were also associated with medication adherence. More details on diabetes-related factors and identified interactions are further illustrated in Figure 7.

Medication-related factors: This category included regimen-related factors such as its complexity, drug class, and adverse effects. In addition, polypharmacy, the number of injections, treatment duration and method of administration were associated with other factors that influence medication adherence. Figure 8 presents the medication-related factors and their interactions with other factors. It was noted that patients taking metformin

and short acting insulin had poorer adherence than those taking sulfonylureas and long-acting insulin, respectively. Lifestyle-related changes include changes in medication dose based on diet and cessation of medicines when exercising, all of which affect adherence (Figure 8).

Specific Demographic

- Gender: Female
- Ethnicity: African American, Latinos , Filipinos
- Marital status: Single
- Education:
  - Less than elementary level of education ➔ Beliefs
  - Higher levels of education
- Age:
  - Advanced age ➔ Comorbidities, disease complications
  - Less than 65 years old ➔ Routine in medication taking
- Socio-economic status: Financial status ➔ Medication cost, transportation to healthcare system
- Employment: Students

Psychological Feelings

- Stress ➔ Smoking
- Anxiety
- Injection phobia
- Blood phobia
- Pain phobia
- Fear from condition and complications
- Frustration with medications
- Fear of chemical nature ➔ Perceived benefit: Effectiveness of medication
- Self-esteem ➔ Depression
- Motivation

Knowledge

- Knowledge about medications (how they worked) ➔ Motivation, self-esteem, perceptions about medication
- Knowledge about the disease ➔ Fear from condition and its complications, motivation, self esteem
- Ability to read medication label
- Training
- Knowledge about glycemic target and glucose levels

Perceptions and Beliefs

- Perceptions ➔ Knowledge about disease
- **Perceived severity:**
  - Seriousness of disease
  - Perception of wellness
- **Perceived barriers:**
  - Life restrictions ➔ Insulin
- **Perceived benefits:**
  - Effectiveness of medications ➔ Use of alternative therapy
  - Need for medication
  - Medications worsen disease ➔ Insulin
  - Long term medication use is harmful ➔ Use alternative therapy
- **Self-efficacy** ➔ Frustration, anxiety, Depression
- **Others:**
  - Religious beliefs (higher power controls the condition)
  - Skeptical beliefs
  - Fatalistic beliefs
  - Punishment ➔ Insulin
  - Insulin means you are more sick

Quality of life

- Social status
- Psychological status
- Physical status
- Mental status
- Health status

Other factors

- Alterations in daily schedule due to holidays and weekends
- Routine in medication taking
- Forgetfulness
- Running out of medications
- Housing condition ➔ Stress
- Traveling oversees
- Newly treated
- Fasting
- Using other methods to control disease than medications

Comorbidities

- Comorbidities ➔ Polypharmacy, stress
- Depression
- Smoking
- Vision problems ➔ Ability to read medication label

Medication adherence ← Patient-related factors

Figure 6: Patient-related factors associated with medication adherence

Figure 7: Diabetes-related factors affecting medication adherence

Figure 8: Medication-related factors associated with medication adherence

Healthcare provider-related factors: This category included the patient-provider related aspects, care providers' knowledge, their attitude and beliefs, and others. It was noted that poor patient-provider communication and education skills were associated with poor medication adherence. Also, the lack of shared decision making among the different healthcare providers was also identified to have a negative influence on medication adherence. The only interaction observed within this category is the lack of awareness of the healthcare provider about diabetes-related guidelines which reflects on their poor self-efficacy and in turn associated with patients' medication nonadherence (Figure 9).
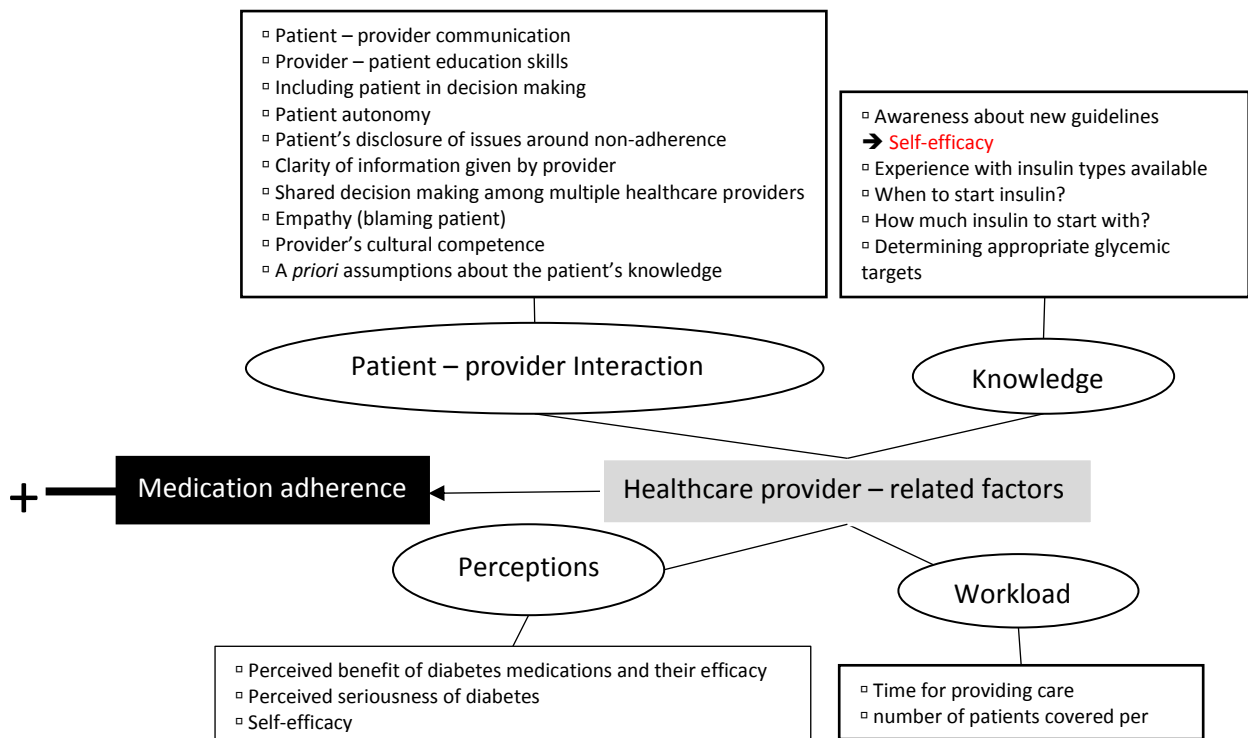
Figure 9: Healthcare provider-related factors associated with medication adherence

Healthcare system-related factor: This category mainly involved three aspects: financial issues, care process, and availability of resources. Financial aspects relate to the

systems use of insurance coverage, insurance type as well as the cost of medications and services. Care process includes visit duration, continuity of care, strict guidelines and lack of interpreters and translators which are reported to be associated with the poor patient-provider communication (Figure 10).
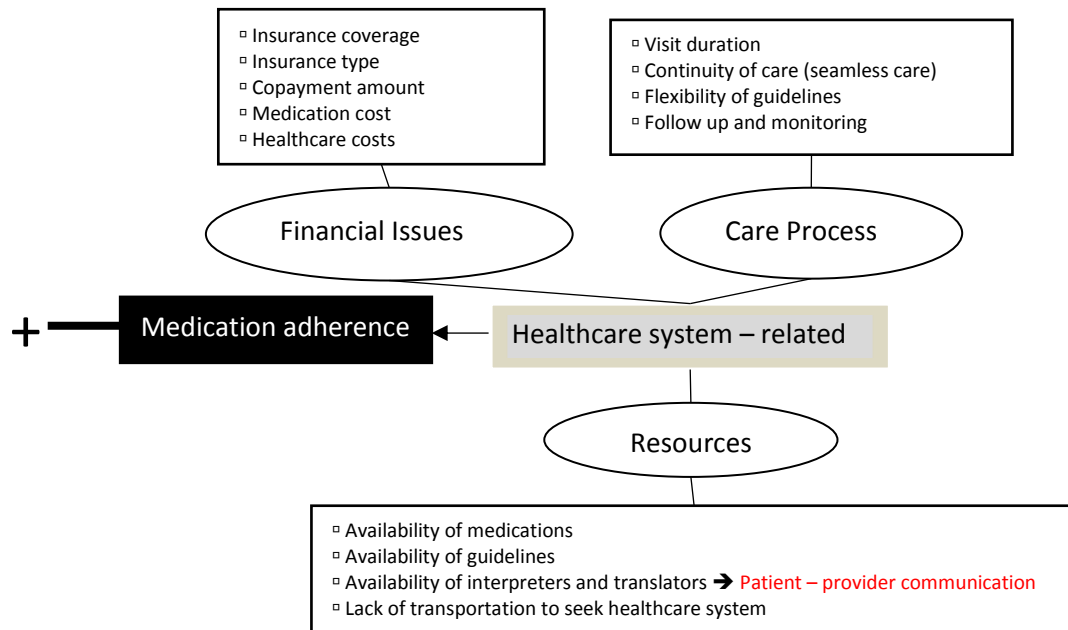
Figure 10: Healthcare system-related factors associated with medication adherence

Societal-related factors: Social stigma, social support, culture and vicarious experience were all reported to be associated with medication adherence. Vicarious experience was linked to the patients' fear of diabetes and its complications. In addition, culture was associated with perceptions and beliefs, and reflected on language which in turns was related to patient-provider communication (Figure 11).
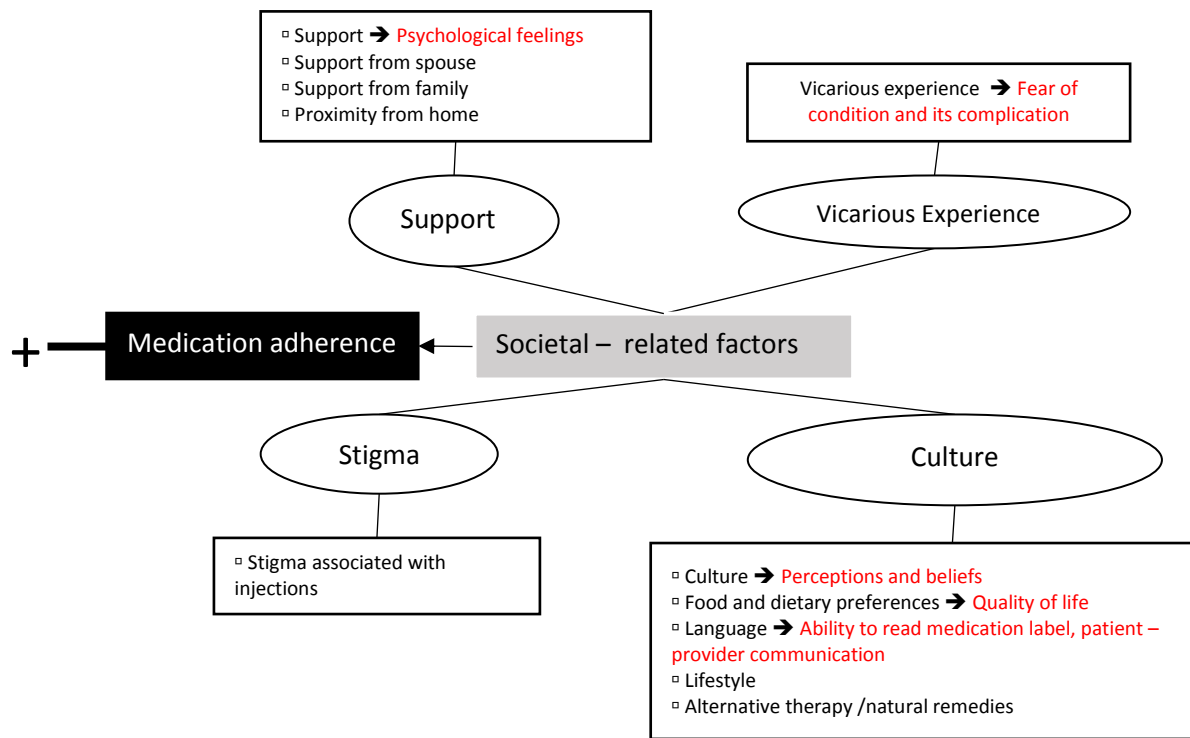
Figure 11: Societal-related factors associated with medication adherence

An enormous amount of research has targeted medication adherence in chronic diseases and particularly in diabetes. Nonetheless, a holistic conceptual framework which summarizes all the factors associated with adherence behavior among patients with diabetes has not been previously developed. To our knowledge, this is the first holistic conceptual framework model for medication adherence in patients with diabetes. All of the identified factors and barriers have been grouped together to allow for the development of more effective interventions towards improving medication adherence.

Although the framework lists all the identified factors that were associated with medication adherence and placed them into different categories, they can also be regrouped into modifiable and non-modifiable factors. This depends on the level of the intervention.

For example, a healthcare provider in a primary care setting may not be able to change the system-related factors, but should focus on the healthcare provider-related aspects. On the other hand, policymakers and administrators can look at the system-related and societal-related factors.

Healthcare providers should use the model as a guide to determine patients who are more likely to be non-adherent to their drug therapy, requiring greater attention than others. Consequently, patient-tailored interventions could be developed based on identified factors. We recognize that one-size-fits-all adherence intervention strategy may not be appropriate. Therefore, the model is not meant to develop a single action plan for all patients at risk of nonadherence, but should only be used as a guide to allow for more patient-specific interventions.

This model indicates that feeling stressed is associated with lack of control and both factors contribute to medication nonadherence. This suggests that a healthcare provider should determine the patient's level of stress before prescribing medications that the patient is less likely to take and that may also add to their stress resulting in wasting resources and continued deterioration of their health.

Patients' nonadherence to insulin, in particular, is linked to injection phobia, blood phobia, and pain. These fears can be addressed by allowing the patient to try insulin for the first time under the observation of the healthcare provider or be exposed to someone who dealt with insulin before. This may likely reduce the patient's fear and increase the likelihood of medication adherence.

Many of the barriers associated with nonadherence can be addressed with proper

counseling and education. These include fear, lack of education, beliefs, perceptions, quality of life, managing comorbidities, polypharmacy, and many others. A single session of counseling and education the first time the patient receives the medication(s) may not be adequate. Multi-faceted educational sessions have shown to be effective (78-80). Therefore, determining the patient's needs and specific barriers would allow for more targeted interventions. A healthcare provider can use this framework to identify which of these factors apply to the patient – perhaps through creating a checklist – before providing counseling and education.

This framework is not limitation-free. The methodologies used in the primary studies to identify the barriers and factors were mainly questionnaire-based surveys and qualitative interviews which bring bias related issues into perspective. In particular, social desirability and recall bias can undermine the quality of the data. However, these methodologies are the best ones to obtain reasons for nonadherence and influencing factors from the patients' perspectives. In addition, systematic reviews were the basis of this framework and not the primary studies, each of which carries its limitations. Finally, this framework served as the basis for this project and was accordingly used to draft the research protocol (questionnaire and interview guide).

CHAPTER 3: METHODOLOGY

3.1. Phase I: Identifying Barriers to Medication Adherence in Diabetes from Patients' Perspective

3.1.1. *Study design:*

This was a mixed method triangulation study design where qualitative and quantitative data were collected to increase the validity and comprehensiveness of the research results (81, 82). This approach provides an expanded understanding through the comparison between qualitative and quantitative data (81, 83). The specific model used was the "convergence model" in which the quantitative and the qualitative data were collected and analyzed separately, and then merged together during the interpretation of results (Figure 12) (81). The quantitative part of the study identified the level of adherence in patients with uncontrolled diabetes and determined the common barriers to medication adherence. On the other hand, the qualitative aspect allowed for an in-depth understanding of the problem, since participants would freely express their opinions. Therefore, the researcher had a better opportunity to explore reasons and barriers to medication adherence. Put together; these two approaches provide sound information which can then be targeted for future interventions.
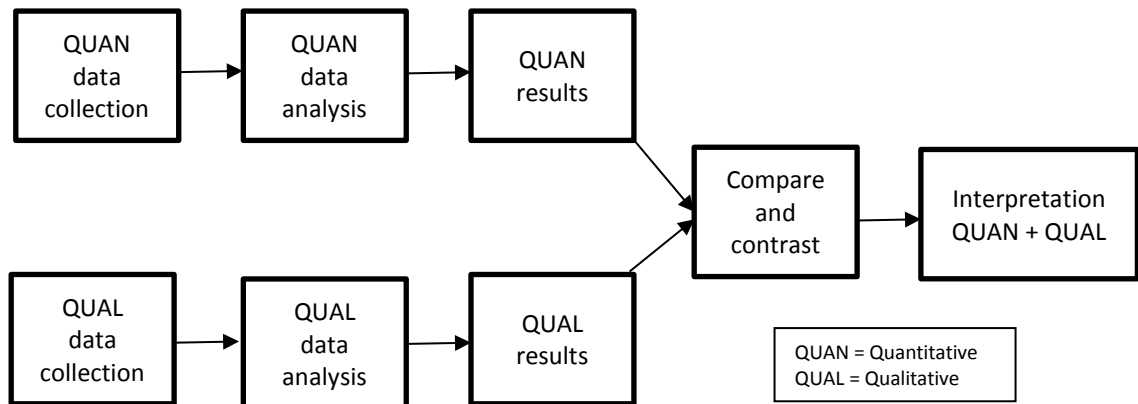
Figure 12: Triangulation design - Convergent model

Source: Creswell et al. (2006)

The study was conducted in the primary healthcare setting in Qatar. The Primary Health Care Corporation (PHCC) is under governmental support and comprises of 21 different primary health centers distributed across the country (84). The centers provide a broad range of services including outpatient management, immunization, health education, and antenatal care. Some clinics are specialized such as cardiology clinics, family medicine clinics, dental clinics, dietician clinics, non-communicable disease (NCD) clinics, and others (84). Health awareness campaigns also take place for different health conditions that are of priority to the country such as asthma, diabetes, hypertension, obesity, and cancer (84). Moreover, the centers receive a vast number of patients with different health conditions on a daily basis who are managed, treated and followed as outpatients or referred to hospitals as necessary. Recently, some centers received the platinum level status from Accreditation Canada International (ACI) for achieving high-quality standards (85). The study was conducted in the two approved centers: Airport Health Center and West Bay Health Center.

3.1.3. Target population:

The target population is patients with uncontrolled diabetes (type 1 or type 2) living in Qatar. Currently, the number of patients with a confirmed diagnosis of diabetes in Qatar is 239,100 as per the latest IDF report in 2015, representing 13.5% of the population (3). On the other hand, the percentage of uncontrolled diabetes was extrapolated from an unpublished study conducted in a primary health center in Qatar which revealed that 86% of patients with diabetes were uncontrolled.

3.1.4. Inclusion/exclusion criteria:

Participants were included in the study if they were:

- 18 years old or above

- diagnosed with diabetes for a minimum of one year

- attending primary health centers

- living in Qatar for the past 12 months at the time of recruitment

- having records of blood glucose levels and HbA1c monitoring within the past 12 months in the center's database

- judged as having uncontrolled diabetes (glycosylated hemoglobin A1c (HbA1c) values above 7%, or a fasting blood glucose above 130 mg/dL (>7.2 mmol/L) (86))

- able to speak English and/or Arabic language

Patients who did not satisfy the inclusion criteria above were excluded from the study. Moreover, pregnant women, patients with gestational diabetes, psychosis, HIV/AIDS, cancer, Alzheimer's, and patients on dialysis were also excluded from the

study due to the circumstances associated with these conditions which may influence medication adherence. Moreover, patients sending their drivers or housemaids to collect their medications were also excluded.

3.1.5. *Quantitative data*

3.1.5.1. Sample size determination

The sample size calculation was based on cross-sectional studies of qualitative variables (87). The following equation was used to determine the sample size needed for the study:

$$sample\ size = \frac{{Z_{1-a/2}}^2\ p(1-p)}{d^2}$$

$Z_{1-\frac{a}{2}} = standard\ normal\ variate$

$p = expexted\ poportion\ in\ population$

$d = absolute\ error$

- *Z* represents the *Z* statistic for a level of confidence chosen to present the results with a 95% confidence interval (CI). The *Z* value for 95% CI equals to 1.96.

- *p* is the expected prevalence or proportion of uncontrolled diabetes in Qatar. Based on unpublished data from a primary healthcare setting in Qatar, the reported rate of uncontrolled diabetes was 86%. The prevalence of diabetes in Qatar was 13.5% (1, 6, 10). Based on these findings, it was assumed that around 12% of the entire population would be patients with uncontrolled diabetes. Therefore, the value of *p* was 0.12.

- *d* represents the absolute error or precision which is usually estimated to be 5% to give the width of 95% CI; so the *d* value equals to 0.05.

$$sample\ size = \frac{1.96^2\ 0.12(1-0.12)}{0.05^2} = 163$$

The minimum effective sample size determined based on the above assumptions was 163. In order to account for missing or unusable data, the sample size was increased by 20% to reach a goal of 196 patients.

3.1.5.2. Sampling

A convenient sample of the adult population was recruited from the primary health centers while waiting to collect their medications at the pharmacy. Potential participants were identified through the administrative and clinical database at the pharmacy. A convenient sample was used because a sampling frame was non-existent at the centers.

3.1.5.3. Recruitment and data collection process

The recruitment and data collection processes are summarized in Figure13 below:
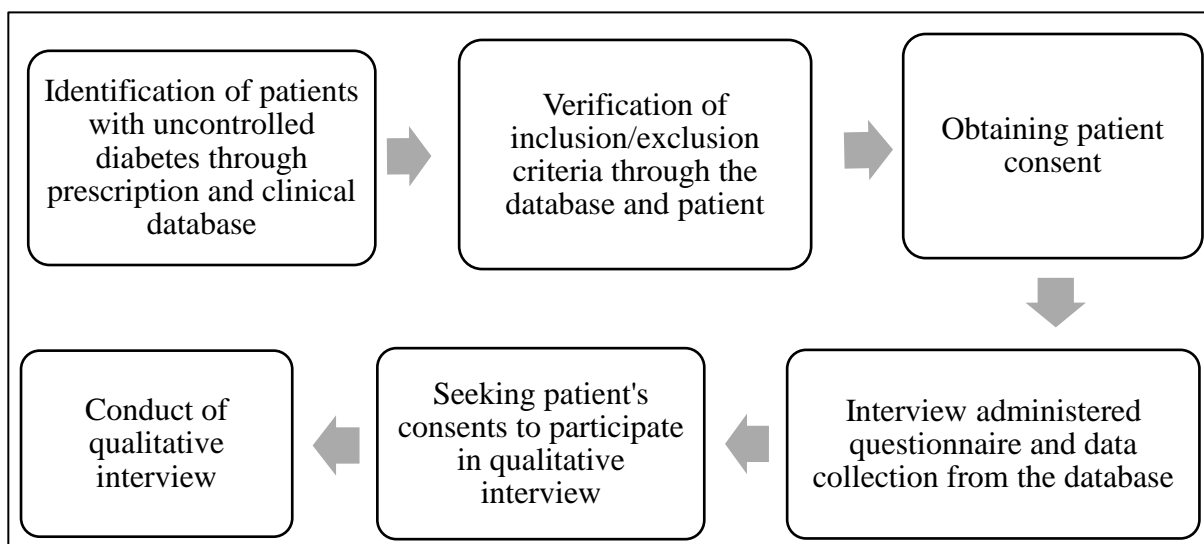
Figure 13: Recruitment process for the patients

3.1.5.4. Study instrument

The study instrument comprised of three sections: 1) Baseline demographic and clinical characteristics; 2) Adherence to Refills and Medication Scale for Diabetes (ARMS-D); 3) A questionnaire to determine barriers to medication adherence. The instrument started with sociodemographic and clinical data which were obtained from the patient's database and then largely verified with the patient. This section was followed by the ARMS-D questionnaire (88, 89), a validated 11-item scale used to measure adherence level in patients with diabetes (88). This questionnaire has two subscales: 7 items for medication taking and 4 items for refills. The final section was developed to identify barriers to medication adherence based on the conceptual framework model for factors influencing medication adherence in diabetes. ***Refer to section 2.5.*** Twenty-five items representing the most commonly reported medication adherence barriers were listed in which the participant would indicate for each item whether or not it represents a barrier to them (using a

dichotomous scale of Yes/No) (Appendix A). The complete study instrument was translated into Arabic and five most commonly spoken languages in Qatar (Tamil, Urdu, Malayalam, Hindi and Nepali) through the use of a translation agency

3.1.5.5. Questionnaire validation

The English and Arabic versions of the full questionnaire were pretested and piloted on four potential participants (two with type 1 diabetes, and two with type 2 diabetes) to check content validity. Comprehensiveness and clarity of the questionnaire were checked, and modifications were applied based on the participants' feedback. The published psychometric properties of ARMS-D indicate that it has a good internal consistency reliability (Cronbach α=0.86) and a good construct validity of the subscales (average factor loading of 0.75 and 0.77 for the 7 items relating to medication taking and for the 4 items relating to refills, respectively) (88).

3.1.5.6. Data analysis

Data were analyzed using IBM Statistical Package for Social Sciences (IBM SPSS$^{®}$ Statistics for Windows, Version 22.0; IBM Corp, Armonk, NY, USA). Descriptive and inferential statistics were used for the data analyses. Normality was checked through Kolmogorov-Smirnov test which indicated that the assumption of normality was violated for all continuous variables, except for age. Therefore, demographic and clinical characteristics, as well as adherence scores, were presented descriptively as median (IQR) for continuous variables (except for age which was presented as mean $\pm$ SD) and as frequencies and percentages for categorical variables. Mann-Whitney U-test was used

whenever comparing two groups while Kruskal-Wallis was used whenever comparing more than two groups. Associations between different variables and adherence score were tested using Spearman Rho test - if variables are continuous or ordinal) - or using Chi Square test whenever the variables are categorical. For all statistical tests, an alpha level of 0.05 was used to determine statistical significance.

3.1.6. Qualitative data

3.1.6.1. Sampling

A purposive sample of patients who participated in the quantitative phase of the study (**Refer to section 3.1.4.)** was invited to take part in the semi-structured interviews. Patients were selected from diverse ethnic and cultural backgrounds and from both genders in order to broaden the perspectives on the topic. The process of recruitment and interview continued until saturation was achieved. Saturation, as defined by *Strauss* and *Corbin,* is "a point in which further data collection becomes redundant and fails to further contribute to the study's dimensions and categories development" (90).

3.1.6.2. Sample size

The number of participants interviewed was based on the concept of saturation. Therefore, a total of fourteen patients were interviewed.

3.1.6.3. Interview structure

The semi-structured in-depth interview focused on barriers to and factors associated with medication adherence. The interview guide was derived from the conceptual

framework model (***Refer to section 2.5***). During the interviews, open-ended questions were used to allow for participants' expression of their own views and perceptions. The introductory section was about the patient's experience with diabetes followed by discussing the barriers and factors that affect their medication adherence. Then the interview transitioned into the patient's identified solutions based on their own identified barriers. The interview was conducted in either English or Arabic based on the participant's preference. New entrants were interviewed until saturation point was reached. The interview guide is available in Appendix B.

3.1.6.4. Validation of interview guide

After developing the interview guide, it was reviewed and validated by researchers in the field of diabetes with relevant expertise in qualitative and mixed methodology research to ensure the coverage and comprehensiveness of the interview. This was then followed by piloting the interview guide on two patients to assess for validity, feasibility and burden. Since there were no changes to the interview structure, the piloted interviews were included in the analysis.

3.1.6.5. Transcribing

The interviews were audio-taped to allow for transcribing of responses and analysis. Interviews that were conducted in Arabic language were translated into English language directly and as they were transcribed. The translation and transcription of each session took place on the same day directly after the session by the same researcher to ensure the meaning was kept intact. Translation accuracy and quality were validated by

another research team member than the one who did the translation.

3.1.6.6. Data analysis

A thematic approach to data analysis was used. Transcripts were read by the researcher for familiarizations, then coded for common phrases that discussed the same idea or meaning. Comparisons of codes were conducted, and phrases of similar idea were clustered together in the same category. Irrelevant codes were discarded, and similar category codes were placed under respective themes. This process was conducted by two researchers in order to ensure consistency and reliability of coding and themes generated. Consensus and opinions of all research team members were used to finalize the themes.

3.1.7. Data interpretation

Qualitative and quantitative data were analyzed separately. However, the findings were combined in interpretation and presentation. Barriers to medication adherence in diabetes were organized and categorized based on the frequency of reporting; then they were discussed individually bringing evidence from both the qualitative and the quantitative data collected.

3.2. Phase II: Identifying Barriers to Medication Adherence in Diabetes from Healthcare Providers' Perspective

3.2.1 Study design

A qualitative semi-structured interview methodology was used in this phase. This methodology was chosen in lieu of focus group discussions due to the logistic difficulties

of bringing different healthcare providers for focus groups. Therefore, we opted for qualitative one-to-one interviews which would allow for the exploration of the perceptions and beliefs of healthcare providers about the factors associated with and barriers to medication adherence in patients with diabetes.

3.2.2. Study setting

Healthcare providers' interviews were conducted at the same primary health centers in Qatar from which the patients were selected during Phase 1 of the study. The interviews were carried out in individual participant's offices or clinical rooms during working hours.

3.2.3. Study population and selection

Participants were healthcare providers directly involved in the care of patients with diabetes. These included physicians, pharmacists, nurses, dietitians and other health professionals involved in diabetes management at the health centers. Participants were purposively selected from their respective health centers, and this approach was supplemented by using the snowballing technique to identify additional healthcare providers interested to participate (91).

3.2.4. Inclusion/exclusion criteria

Healthcare providers were included in the study if they were: 1) practicing in Qatar for at least one year; 2) working at the primary health center and; 3) involved in providing care for patients with diabetes. Those who did not fulfill these criteria were not included in the study.

3.2.5. Interview structure

The semi-structured in-depth interviews were conducted in English or Arabic language based on participant's preference. The number of interviews conducted was based on the concept of saturation; thus, the study continued until there were no new emerging themes and ideas identified. A set of questions were developed for each of the study objectives in this phase to help guide the discussion and avoid drifting away from the study's focus. The probing questions were identified from the conceptual model developed for this study (***Refer to section 2.5***). Each session started with a brief introduction to the study, then probing the discussion to the barriers to and factors associated with nonadherence in patients with diabetes, then moving into what possible interventions can be applied to address the identified factors and barriers. The sessions were audio-taped for transcribing purposes. The healthcare provider interview guide can be found in Appendix C.

3.2.6. Transcribing

The audio-taped sessions were transcribed verbatim in a similar manner to **Section 3.1.6.5.**

3.2.7. Data analysis and interpretation

A thematic approach to data analysis was used. Transcripts were read by researchers for familiarizations, then coded for common phrases that discussed the same ideas or meaning. Comparison of codes was conducted, and similar idea phrases were

clustered together in the same category. Irrelevant codes were discarded, and similar category codes were placed under respective themes. Consensus and opinions of all research team members were required to finalize the themes. A deeper interpretation of Phase I and Phase II was conducted through the comparison of the results obtained from the different perspectives (patients' vs. healthcare providers') in terms of barriers as well as identified strategies for improvements.

3.3. Ethical Considerations

Ethics approval for the study was granted from the PHCC ethics committee prior to the conduct of the study (Research Section, Clinical Affairs, PHCC – Approval Number PHCC/IEC/16/04/013). A written informed consent form was developed and provided to the participants prior to recruitment in the study and after having informed them about the purpose of the research. Information sheet about the objectives of the investigation and researcher's contact information was provided to all participants. Letter of approval is available in Appendix D.

A summary of the methodology used to address the study objectives is presented in Table 5 below.

Table 5: Summary of study objectives and method used

Objective	Method
Phase I	
To determine the level of medication adherence among patients with uncontrolled diabetes using a self-reported tool	Questionnaire: ARMS-D Descriptive statistics
To identify the characteristics, risk factors associated with, and barriers to medication adherence from patients' perspective.	Questionnaire and interviews Inferential statistics and thematic analysis
To explore possible strategies for improving medication adherence in patients with uncontrolled diabetes in Qatar from patients' perspective.	Interviews Thematic analysis
To compare the characteristics, identified barriers and solutions, between patients with good medication adherence and patients with poor medication adherence.	Questionnaire and interviews Inferential statistics and thematic analysis
Phase II	
To determine the barriers to medication adherence in patients with uncontrolled diabetes from healthcare providers' perspective.	Interviews Thematic analysis
To explore possible strategies for improving medication adherence in patients with uncontrolled diabetes in Qatar from a healthcare providers' perspective	Interviews Thematic analysis

CHAPTER 4: RESULTS

This chapter presents the results pertaining to the overall aim of this project which is to identify the barriers to medication adherence in patients with uncontrolled diabetes from both patients' and healthcare providers' perspectives in a primary care setting. The study was split into two phases: Phase I – Patients' perspective, and Phase II – Healthcare providers' perspective on this topic. The results of quantitative data from Phase I are presented followed by qualitative data from both Phase I and Phase II.

4.1. Quantitative Data

4.1.1. Sociodemographic characteristics

Over a period of three months (October 1, 2016 to January 1, 2017), a total of 260 patients with uncontrolled diabetes (55.8% male) participated in the quantitative phase of the study through answering the study questionnaire. Other relevant clinical data of the patients were obtained from the electronic medical records at the study centers. The mean ± SD age of the patients was 56.1±10.40 years, and the majority (83.5%) were non-Qatari. Moreover, about half (51.5%) of the patients were Arabs, 76.9% reported living with family, and over two-thirds (69.2%) were employed at the time of data collection. The sociodemographic characteristics did not significantly differ between adherent and nonadherent patients, except in terms of living status, where 25.7% of the nonadherent group lived without their family as compared to 15.9% of those who were adherent (*p=0.047*). The sociodemographic characteristics of the study patients are provided in Table 6.

Table 6: Sociodemographic characteristics of Phase I patients

Variable	Total (N = 260)	Adherent (n = 69)	Nonadherent (n =191)	P value*
	n (%)			
Gender				0.325
Male	145 (55.8)	35 (50.7)	110 (57.6)	
Female	115 (44.2)	34 (49.3)	81 (42.4)	
Age category (years)				0.330
≥ 65	50 (19.2)	16 (23.2)	34 (17.8)	
< 65	210 (80.8)	53 (76.8)	157 (82.2)	
Nationality				0.197
Qatari	43 (16.5)	8 (11.6)	35 (18.3)	
Non-Qatari	217 (83.5)	61 (88.4)	156 (81.7)	
Ethnicity				0.742**
Arab	134 (51.5)	35 (50.7)	99 (51.8)	
Asian	110 (42.3)	28 (40.6)	82 (42.9)	
Persian	14 (5.4)	5 (7.2)	9 (4.7)	
Other	2 (0.8)	1 (1.4)	1 (0.5)	
Religion				0.381
Islam	208 (80.0)	55 (79.7)	153 (80.1)	
Christianity	24 (9.2)	5 (7.2)	19 (9.9)	
Hinduism	20 (7.7)	8 (11.6)	12 (6.3)	
Buddhism	8 (3.1)	1 (1.4)	7 (3.7)	
Living status				**0.047**
With family	200 (76.9)	58 (84.1)	142 (74.3)	
Without family	60 (23.1)	11 (15.9)	49 (25.7)	
Employment status				0.188**
Employed	180 (69.2)	44 (63.8)	136 (71.2)	
Unemployed	49 (18.8)	13 (18.8)	36 (18.8)	
Retired	30 (11.5)	11 (15.9)	19 (9.9)	
Student	1 (0.4)	1 (1.4)	0 (0)	

* p-value was computed using Chi Square test to compare between adherent and nonadherent groups
** Fisher exact test was used to calculate the p-value
*** Missing values

Table 6: *Cont.* Sociodemographic characteristics of Phase I patients

Variable	Total (N = 260)	Adherent (n = 69)	Nonadherent (n =191)	P value*
	n (%)			
Education level				0.616**
Primary	26 (10.0)	5 (7.2)	21 (11.0)	
Secondary	37 (14.2)	7 (10.1)	30 (15.7)	
High school	60 (23.1)	14 (20.3)	46 (24.1)	
Diploma	10 (3.8)	3 (4.3)	7 (3.7)	
University	103 (39.6)	34 (49.3)	69 (36.1)	
None, but literate	6 (2.3)	1 (1.4)	5 (2.6)	
Illiterate	18 (6.9)	5 (7.2)	13 (6.8)	
Monthly income (QR)*				0.665
Not receiving any income	29 (15.5)	7 (14.3)	22 (15.9)	
Less than 3,000	59 (31.6)	13 (26.5)	46 (33.3)	
3,000 to less than 7,000	30 (16.0)	8 (16.3)	22 (15.9)	
7,000 to less than 15,000	33 (17.6)	12 (24.5)	21 (15.2)	
More than 15,000	36 (19.3)	9 (18.4)	27 (19.6)	
Monthly medication costs (QR)*				0.443**
0 – 100	171 (75.3)	43 (71.7)	128 (76.6)	
101 – 300	56 (24.7)	17 (28.3)	39 (23.4)	

* p-value was computed using Chi Square test to compare between adherent and nonadherent groups
** Fisher exact test was used to calculate the p-value
*** Missing values

4.1.2. Clinical characteristics

Almost all (98.5%) of the patients were diagnosed with type 2 diabetes and the median (IQR) HbA1c of the studied cohort was 7.9% (1.4). In addition, the majority of the patients (72.3%) were on oral antidiabetic medications, and 91.5% were taking metformin as part of the treatment regimen. Regarding comorbidities, 75.0% had hypertension, and 69.2% had dyslipidemia. The most frequently reported diabetes complication was neuropathy followed by retinopathy (29.6% and 21.9%, respectively).

The duration of diabetes was higher in nonadherent as compared to adherent patients, this difference however, was not statistically significant [6 (8) vs. 7(11) (*p=0.373*)]. On the other hand, statistically significant differences were observed in HbA1c and fasting blood glucose, both of which were significantly higher in the nonadherent group compared to the adherent group (*p=0.002* and *p=0.*004 respectively) (Table 7). Similarly, a significantly higher level of diabetes complications was observed in the nonadherent group as compared to the adherent group (*p=0.003).* The complications potentially driving this difference were hyperosmolar hyperglycemic state, neuropathy, nephropathy, and diabetes-related emergency visits (*p<0.05* each*).* In addition, 43.5% of nonadherent patients were taking sitagliptin as compared to 29.0% in the adherent group (*p=0.035).* Similarly, the majority of patients taking insulin were nonadherent (84.0%, *p=0.014)* (Table 7).

Table 7: Clinical characteristics of Phase I patients

Variable	Total (N = 260)		Adherent (n = 69)		Nonadherent (n = 191)		P value*
	n (%)	Median (IQR)	n (%)	Median (IQR)	n (%)	Median (IQR)	
BMI (kg/m²)		28.9 (8.2)		28.1 (7.4)		28.8 (8.3)	0.931***
BMI category****							0.982**
Underweight <18.5	1 (0.4)		0 (0)		1 (0.6)		
Normal weight 18.5 – 24.9	44 (20.1)		12 (21.1)		32 (19.8)		
Overweight 25 – 29.9	83 (37.9)		22 (38.6)		61 (37.7)		
Obese 30 – 39.9	76 (34.7)		20 (35.1)		56 (34.6)		
Morbidly obese >40	15 (6.8)		3 (5.3)		12 (7.4)		
Type of diabetes							1.00**
Type 1	4 (1.5)		1 (1.4)		3 (1.6)		
Type 2	256 (98.5)		68 (98.6)		188 (98.4)		
Diabetes duration (years)		7 (10)		6 (8)		7 (11)	0.373***
Latest HbA1c (%)		7.9 (1.4)		7.8 (0.9)		8 (1.8)	**0.002***
Latest fasting blood glucose (mmol/L)		8.65 (3)		8.3 (2.3)		8.9 (3.6)	**0.004***
Number of diabetes medications		2 (1)		2 (1)		2 (2)	**0.006***
Type of diabetes treatment							0.155
Oral	188 (72.3)		56 (81.2)		132 (69.1)		
Injections	7 (2.7)		1 (1.4)		6 (3.1)		
Oral and injections	65 (25.0)		12 (17.4)		53 (27.7)		

* p-value was computed using Chi Square test
** Fisher exact test was used to calculate the p-value
*** Mann-Whitney U test was used to calculate the p-value
**** Missing values

Table 7: *Cont.* Clinical characteristics of Phase I patients

Variable	Total (N = 260)		Adherent (n = 69)		Nonadherent (n = 191)		P value[*]
	n (%)	Median (IQR)	n (%)	Median (IQR)	n (%)	Median (IQR)	
Medication regimen							0.099
Single (oral)	49 (18.9)		18 (26.1)		31 (16.2)		
Single (insulin)	7 (2.7)		1 (1.4)		6 (3.1)		
Double (oral and insulin)	30 (11.5)		5 (7.2)		25 (13.1)		
Double (two oral)	74 (28.5)		27 (39.1)		47 (24.6)		
Triple (oral)	56 (21.5)		11 (15.9)		45 (23.6)		
Triple (two oral and insulin)	27 (10.38)		5 (7.2)		22 (11.5)		
Quadruple (oral)	6 (2.3)		1 (1.4)		5 (2.6)		
Quadruple (3 oral and insulin)	11 (4.2)		1 (1.4)		10 (5.2)		
Diabetes medications[$]							
Metformin	238 (91.5)		66 (95.7)		172 (90.1)		0.152
Repaglinide	3 (1.2)		1 (1.4)		2 (1.0)		1.00[**]
Sitagliptin	103 (39.6)		20 (29.0)		83 (43.5)		**0.035**
Vildagliptin	9 (3.5)		1 (1.4)		8 (4.2)		0.452
Gliclazide	90 (34.6)		24 (34.8)		66 (34.6)		0.973
Glimiperide	40 (15.4)		10 (14.5)		30 (15.7)		0.811
Glibenclamide	1 (0.4)		0 (0)		1 (0.5)		1.00[**]
Pioglitazone	21 (8.1)		4 (5.8)		17 (8.9)		0.417
Liraglutide	2 (0.8)		0 (0)		2 (1.0)		1.00[**]
Exenatide	1 (0.4)		1 (1.4)		0 (0)		0.265[**]
Insulin	75 (28.8)		12 (17.4)		63 (33.0)		**0.014**[***]

* p-value was computed using Chi Square test
** Fisher exact test was used to calculate the p-value
*** Mann-Whitney U test was used to calculate the p-value
\$ Items are not mutually exclusive

Table 7: *Cont.* Clinical characteristics of Phase I patients

Variable	Total (N = 260)		Adherent (n = 69)		Nonadherent (n = 191)		P value[*]
	n (%)	Median (IQR)	n (%)	Median (IQR)	n (%)	Median (IQR)	
Number of pills per day		8 (4)		(8) 4		8 (4)	0.486[***]
Number of injections per day		0 (1)		0 (0)		0 (1)	**0.040**[***]
Number of all medications		8 (3)		7 (4)		8 (3)	0.375[***]
Number of comorbidities		2 (2)		2 (2)		2 (2)	0.981[***]
Comorbidities[$]							
Cardiac disease	33 (12.7)		7 (10.1)		26 (13.6)		0.458
Hypertension	195 (75.0)		53 (76.8)		142 (74.3)		0.685
Dyslipidemia	180 (69.2)		47 (68.1)		133 (69.6)		0.815
Vitamin D deficiency	41 (15.8)		18 (26.1)		23 (12.0)		**0.006**
Gastroesophageal reflux disorder	16 (6.2)		4 (5.8)		12 (6.3)		1.00[**]
Hypothyroidism	22 (8.5)		4 (5.8)		18 (9.4)		0.353
Others	64 (24.6)		17 (24.6)		47 (24.6)		0.996
Number of diabetes complications		1 (2)		0 (1)		1 (2)	**0.003**[***]

* p-value was computed using Chi Square
** Fisher exact test was used to calculate the p-value
*** Mann-Whitney U test was used to calculate the p-value
$ Items are not mutually exclusive

Table 7: *Cont.* Clinical characteristics of Phase I patients

Variable	Total (N = 260)		Adherent (n = 69)		Nonadherent (n =191)		P value[*]
	n (%)	Median (IQR)	n (%)	Median (IQR)	n (%)	Median (IQR)	
Diabetes complications[$]							
Diabetic ketoacidosis	2 (0.8)		1 (1.4)		1 (0.5)		0.461[**]
Hyperosmolar hyperglycemic state	14 (5.4)		0 (0)		14 (7.3)		**0.024[**]**
Retinopathy	57 (21.9)		13 (18.8)		44 (23.0)		0.470
Neuropathy	77 (29.6)		14 (20.3)		63 (33.0)		**0.048**
Nephropathy	38 (14.6)		5 (7.2)		33 (17.3)		**0.043**
Foot complications	30 (11.5)		7 (10.1)		23 (12.0)		0.672
Diabetes-related emergency visits in past year	27 (10.4)		2 (2.9)		25 (13.1)		**0.017**
Diabetes-related hospitalization in past year	4 (1.5)		0 (0)		4 (2.1)		0.226[**]
ARMS-D score		15 (7)		11(0)		17 (5)	**<0.001[***]**

* p-value was computed using Chi Square test
** Fisher exact test was used to calculate the p-value
*** Mann-Whitney test was used to calculate the p-value
$ Items are not mutually exclusive

4.1.3. ARMS-D items responses

Adherence levels were calculated using the ARMS-D questionnaire, whereby a score of 11 corresponded to "adherent" and higher values (12 to 44) indicated "nonadherence". Accordingly, a total of 191 patients (73.5% of the sample) were nonadherent to antidiabetic medications as measured by the ARMS-D. The median (IQR) ARMS-D score among the patients was 15 (7). The most frequently reported item to be problematic was forgetting to take antidiabetic medication (46.2%) of which 8.1% reported that they forget all the time. This was followed by planning ahead and refilling the medicine before they ran out (44.2%), and forgetting to take the medicine when it is more than once a day (35.1%). Table 8 presents the responses to the ARMS-D questionnaire.

Table 8: Patients' responses to the items of ARMS-D questionnaire (n=260)

ARMS-D Items	None of the time	Some of the time	Most of the time	All of the time
	n (%)			
Forget to take diabetes medicine	140 (53.8)	65 (25.0)	34 (13.1)	21 (8.1)
Decide not to take your diabetes medicine	210 (80.8)	26 (10.0)	15 (5.8)	9 (3.5)
Forget to get your prescription filled	215 (82.7)	25 (9.6)	15 (5.8)	5 (1.9)
Run out of diabetes medicine	171 (65.8)	54 (20.8)	20 (7.7)	15 (5.8)
Skip a dose of diabetes medicine before you go to the doctor	175 (67.3)	23 (8.8)	19 (7.3)	43 (16.5)
Miss taking your diabetes medicine when you feel better	206 (79.2)	26 (10.0)	19 (7.3)	9 (3.5)
Miss taking your diabetes medicine when you feel sick	233 (89.6)	15 (5.8)	9 (3.5)	3 (1.2)
Miss taking your diabetes medicine when you are careless	238 (91.5)	16 (6.2)	4 (1.5)	2 (0.8)

Table 8: *Cont*. Patients' responses to the items of ARMS-D questionnaire (n=260)

ARMS-D Items	None of the time	Some of the time	Most of the time	All of the time
	n (%)			
Forget to take you diabetes medicine when you are supposed to take it more than once a day	169 (65.0)	55 (21.2)	27 (10.4)	9 (3.5)
Put off refilling your diabetes medicine because they cost too much money	236 (90.8)	11 (4.2)	7 (2.7)	6 (2.3)
Plan ahead and refill your medicines before they run out	15 (5.8)	33 (12.7)	67 (25.8)	145 (55.8)

4.1.4. *Barriers to medication adherence*

The median (IQR) number of barriers reported by the patients was 3 (4). The most frequently reported barriers to medication adherence in the questionnaire were forgetfulness (41.5%), followed by inconvenience, and the use of traditional medicine (36.5% each), while the only barrier that was not reported by the sample was "taking medications is against my culture." Table 9 and Figure 14 indicate the response rates to the barriers to medication adherence. More barriers to medication adherence were reported in those who were nonadherent than those who were adherent (median [IQR] 4 (4) vs. 1(1)] respectively, *p<0.001*). Table 9 compares between adherent and nonadherent groups in terms of the reported barriers.

Table 9: Reported barriers to medication adherence from quantitative data

Barrier	Total (N = 260)	Adherent (n = 69)	Non adherent (n =191)	p value*
	n (%)			
Time or schedule problems	58 (22.3)	4 (6.9)	54 (93.1)	**<0.001**
Inconvenience	95 (36.5)	17 (17.9)	78 (82.1)	**0.017**
Side effects of the medicine	66 (25.4)	5 (7.6)	61 (92.4)	**<0.001**
Forget to take the medicine	108 (41.5)	3 (2.8)	105 (97.2)	**<0.001**
Health problems	24 (9.2)	2 (8.3)	22 (91.7)	**0.034**
Too painful to administer the medicine	16 (6.2)	1 (6.3)	15 (93.8)	**0.077****
Too costly to buy the medicine	41 (15.8)	8 (19.5)	33 (80.5)	0.267
Special occasions	42 (16.2)	6 (14.3)	36 (85.7)	**0.050**
Feeling depressed or other negative emotions	81 (31.2)	8 (9.9)	73 (90.1)	**<0.001**
Believe that the medication prescribed is not helpful	29 (11.2)	1 (3.4)	28 (96.6)	**0.003**
Interferes with you daily activities	19 (7.3)	3 (15.8)	16 (84.2)	0.270
Having multiple diseases	19 (7.3)	2 (10.5)	17 (89.5)	**0.101**
Taking many medications	34 (13.1)	4 (11.8)	30 (88.2)	**0.038**
Regimen is too complicated to follow	22 (8.5)	1 (4.5)	21 (95.5)	**0.015**
Taking the medicine multiple times a day	65 (25.0)	6 (9.2)	59 (90.8)	**0.001**
Use of traditional medicine	95 (36.5)	21 (22.1)	74 (77.9)	0.219
Long diabetes duration	28 (10.8)	7 (25.0)	21 (75.0)	0.845
Time or schedule problems	58 (22.3)	4 (6.9)	54 (93.1)	**<0.001**
Diabetes is too complicated to manage	35 (13.5)	8 (22.9)	27 (77.1)	0.596
Healthcare provider is not very supportive	16 (6.2)	3 (18.8)	13 (81.3)	0.571**
I don't know why I am on diabetes medications	11 (4.2)	1 (9.1)	10 (90.9)	0.297**
Healthcare provider does not give me enough information	29 (11.2)	4 (13.8)	25 (86.2)	0.099

* p-value was computed using Chi Square test
** Fisher exact test was used to calculate the p-value

Table 9: *Cont.* Reported barriers to medication adherence from quantitative data

Barriers	Total (N = 260)	Adherent (n = 69)	Non adherent (n =191)	p value[*]
	n (%)			
Not understanding what the healthcare provider is telling me about the medicines	25 (9.6)	6 (24.0)	19 (76.0)	0.762
Family is not very supportive	23 (8.8)	6 (26.1)	17 (73.9)	0.959
Taking these medications is against my culture	0	0	0	-
Having health insurance	12 (4.6)	2 (16.7)	10 (83.3)	0.738[**]

* p-value was computed using Chi Square test
** Fisher exact test was used to calculate the p-value
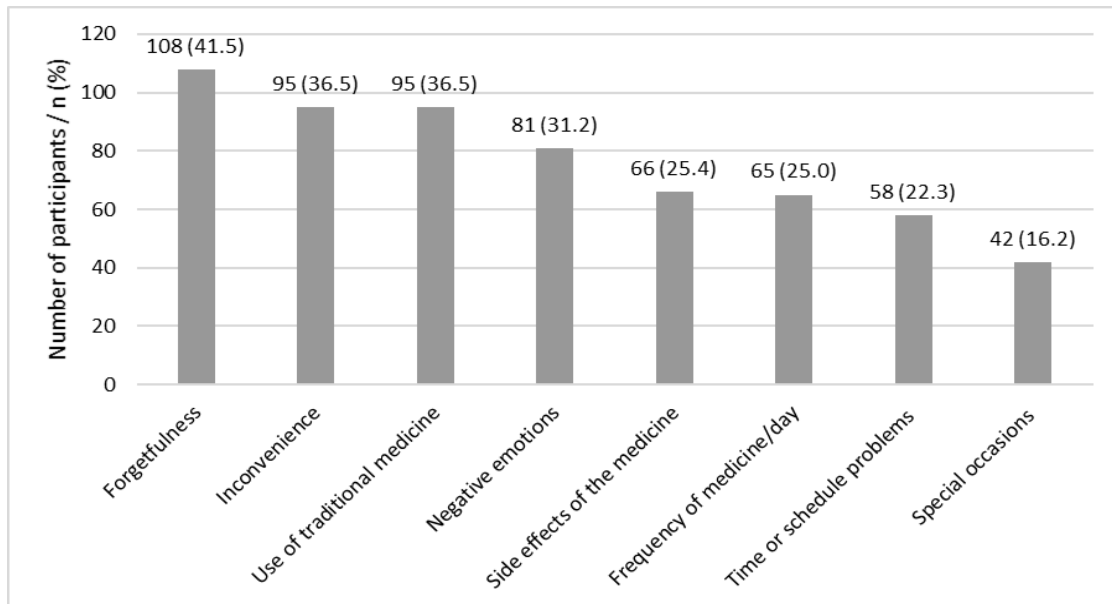
Figure 14: Top eight reported barriers to medication adherence

4.1.5. *Difference of adherence score across different patients' characteristics*

Tables 10-12 represent the differences of adherence scores across patients'
characteristics, while Table 13 indicates the correlations between patients' characteristics
and adherence scores. Patients below 65 years of age had significantly higher adherence
score than those who were 65 years of age or older (*p=0.039*) (Table 10). This difference
is further emphasized with the weak negative correlation observed between age and
adherence score (r = - 0.175, *p=0.005*). Moreover, patients living with family had lower
adherence scores as compared to those living without family [median (IQR) 14 (6), 17 (5),
respectively, *p=0.004*]. In addition, the highest adherence score was amongst those with
no formal education when compared with other educational levels [23(0), *p=0.042*] (Table
10). On the other hand, the lowest adherence score was observed to be in patients taking
single oral therapy followed by dual oral therapy as compared to other types of regimens
(12 (5) and 13.5 (7), *p=0.005*) (Table 11).

Differences in adherence score across different barriers to medication adherence
are presented in Table 12. Overall, patients who indicated any item as a barrier always had
higher adherence score compared to those who did not indicate the same item as a barrier.
However, for seven items the difference between the two groups was not statistically
significant (Table 12). The top five barriers based on mean adherence score are presented
in Figure 15 which indicates that the highest adherence score was amongst patients who
believed that the prescribed medication was not useful, followed by those who reported
that it was painful to administer the medicine (21.31 ± 6.27 and 19.93 ± 6.17, respectively).

When testing the correlations between different factors and adherence score,
significant but weak correlations were noted with the number of diabetes complications
(r=0.195, *p=0.002*), the number of diabetes drugs (r=0.202, *p=0.001*), and latest HbA1c

level (r=0.353, *p<0.001*). Furthermore, a moderate positive correlation was noted between

adherence score and the total number of barriers reported (r=0.503, *p<0.001*) (Table 13).

Table 10: Differences in adherence score across different sociodemographic characteristics

Variable	Adherence score Median (IQR)	*p value*[*]
Gender		0.059
Male	16 (7)	
Female	14 (6.5)	
Age category (years)		**0.039**
≥ 65	13 (5)	
< 65	15 (7.5)	
Nationality		0.965
Qatari	14 (5.5)	
Non-Qatari	15 (7)	
Ethnicity		0.595[**]
Arab	14 (6)	
Asian	15.5 (7)	
Persian	13 (7.25)	
Other	14.5 (7)	
Religion		0.813[**]
Islam	15 (6)	
Christianity	12 (7)	
Hinduism	12 (8.5)	
Buddhism	17 (3.8)	
Living status		**0.004**[**]
With family	14 (6)	
Without family	17 (5)	

* p-value was computed using Mann-Whitney U test
** Kruskal-Wallis test was used to calculate the p-value

Table 10: *Cont.* Differences in adherence score across different sociodemographic characteristics

Variable	Adherence score Median (IQR)	p value[*]
Employment status		0.223[**]
Employed	15 (6.3)	
Unemployed	15 (7)	
Retired	12.5 (5.5)	
Student	11 (0)	
Education level		**0.042[**]**
Primary	16 (7)	
Secondary	17 (3.8)	
High school	15 (8)	
Diploma	15 (9.8)	
University	14.5 (7)	
None, but literate	23 (0)	
Illiterate	13.5 (7.5)	
Monthly income (QR)*		0.667[**]
Not receiving any income	15 (6.5)	
Less than 3,000	16 (7)	
3,000 to less than 7,000	15 (7)	
7,000 to less than 15,000	13 (6.5)	
More than 15,000	14 (6)	
Monthly medication costs (QR)*		0.626
0 – 100	15 (8)	
101 – 300	15 (6.75)	

* p-value was computed using Mann-Whitney U test
** Kruskal-Wallis test was used to calculate the p-value

Table 11: Differences in adherence score across different clinical characteristics

Variable	Adherence score Median (IQR)	p value[*]
BMI category (kg/m^2)		0.842[**]
Underweight <18.5	16 (0)	
Normal weight 18.5 – 24.9	16 (8)	
Overweight 25 – 29.9	15 (8)	
Obese 30 – 39.9	15 (4)	
Morbidly obese >40	15.5 (11.8)	
Type of diabetes treatment		0.095[**]
Oral	14.5 (7)	
Injections	15 (4.8)	
Oral and injections	17 (7)	
Medication regiment		**0.005[**]**
Single (oral)	12 (5)	
Single (insulin)	15 (4.8)	
Double (oral and insulin)	17 (5.5)	
Double (two oral)	13.5 (7)	
Triple (oral)	16 (5)	
Triple (two oral and insulin)	16 (7)	
Quadruple (oral)	27 (0)	
Quadruple (3 oral and insulin)	17 (0)	
Diabetes medications		
Patients on Metformin		0.181
Yes	15 (7)	
No	15 (5.5)	
Patients on Repaglinide		0.512
Yes	14 (0)	
No	15 (7)	
Patients on Sitagliptin		**0.042**
Yes	16 (5.8)	
No	14 (7)	
Patients on Vildagliptin		0.088
Yes	18.5 (7)	
No	15 (7)	

* p-value was computed using Mann-Whitney U test
** Kruskal-Wallis test was used to calculate the p-value

Table 11: *Cont.* Differences in adherence score across different clinical characteristics

Variable	Adherence score Median (IQR)	p value[*]
Patients on Gliclazide		0.450
Yes	16 (7)	
No	15 (7)	
Patients on Glimiperide		0.640
Yes	15 (7.25)	
No	15 (7)	
Patients on Pioglitazone		**0.020**
Yes	16.5 (9.25)	
No	15 (7)	
Patients on Liraglutide		0.196
Yes	23 (0)	
No	15 (7)	
Patients on Insulin		**0.025**
Yes	16 (6)	
No	15 (7)	
Comorbidities		
Cardiac disease		0.533
Yes	16 (6)	
No	15 (7)	
Hypertension		0.734
Yes	15 (7)	
No	15 (7)	
Dyslipidemia		0.481
Yes	15 (7.5)	
No	14 (7)	
Vitamin D deficiency		0.104
Yes	14.5 (7.25)	
No	15 (6)	
Gastroesophageal reflux disorder		0.677
Yes	15 (7.25)	
No	15 (7)	
Hypothyroidism		0.473
Yes	16 (5)	
No	15 (7)	

* p-value was computed using Mann-Whitney U test
** Kruskal-Wallis test was used to calculate the p-value

Table 11: *Cont.* Differences in adherence score across different clinical characteristics

Variable	Adherence score Median (IQR)	p value*
Diabetes complications		
Diabetic ketoacidosis		0.654
Yes	14 (0)	
No	15 (7)	
Hyperosmolar hyperglycemic state		**0.004**
Yes	18 (10)	
No	15 (7)	
Retinopathy		0.640
Yes	15 (8)	
No	15 (7)	
Neuropathy		0.472
Yes	15 (7)	
No	15 (7)	
Nephropathy		**0.040**
Yes	16 (5.75)	
No	15 (7)	
Foot complications		0.082
Yes	17 (6.25)	
No	15 (7)	
Diabetes-related emergency visits in past year		**0.002**
Yes	17 (5)	
No	15 (7)	
Diabetes-related hospitalization in past year		0.173
Yes	20.5 (17)	
No	15 (7)	

* p-value was computed using Mann-Whitney U test
** Kruskal-Wallis test was used to calculate the p-value

Table 12: Differences in adherence score across different barriers to medication adherence

Variable	Adherence score Median (IQR)	p value[*]
Time or schedule problems		**<0.001**
Yes	17 (9)	
No	15 (6)	
Inconvenience		**<0.001**
Yes	16 (7.75)	
No	14 (6)	
Side effects of the medicine		**<0.001**
Yes	11 (6)	
No	14 (6)	
Forget to take the medicine		**<0.001**
Yes	17 (5)	
No	13 (5)	
Health problems		**0.026**
Yes	17 (5.5)	
No	15 (7)	
Too painful to administer the medicine		**0.001**
Yes	18 (7)	
No	15 (7)	
Too costly to buy the medicine		**0.030**
Yes	17 (4.5)	
No	14.5 (7)	
Special occasions		**0.020**
Yes	16.5 (5.75)	
No	15 (7)	
Feeling depressed or other negative emotions		**<0.001**
Yes	17 (5)	
No	14 (6)	
Believe that the medication prescribed is not helpful		**<0.001**
Yes	19 (10.5)	
No	14 (6.5)	
Interferes with you daily activities		**0.021**
Yes	18 (13.25)	
No	15 (7)	

* p-value was calculated using Mann-Whitney U test

Table 12: *Cont.* Differences in adherence score across different barriers to medication adherence

Variable	Adherence score Median (IQR)	*p value*[*]
Having multiple diseases		**0.016**
Yes	17 (10)	
No	15 (7)	
Taking many medications		**0.019**
Yes	16 (9)	
No	15 (7)	
Regimen is too complicated to follow		**0.005**
Yes	17 (4)	
No	15 (7)	
Taking the medicine multiple times a day		**<0.001**
Yes	19 (9)	
No	14 (6)	
Use of traditional medicine		0.125
Yes	16 (7)	
No	15 (7)	
Long diabetes duration		0.307
Yes	15 (12.25)	
No	15 (7)	
Diabetes is too complicated to manage		**0.011**
Yes	17 (11.5)	
No	15 (7)	
Healthcare provider is not very supportive		0.727
Yes	14.5 (7.5)	
No	15 (7)	
I don't know why I am on diabetes medications		0.213
Yes	17.5 (7.5)	
No	15 (7)	
Healthcare provider does not give me enough information		**0.009**
Yes	18 (7.5)	
No	15 (7)	
Not understanding what the healthcare provider is telling me about the medicines		0.165
Yes	16.5 (7.75)	
No	15 (7)	

* p-value was calculated using Mann-Whitney U test

Table 12: *Cont.* Differences in adherence score across different barriers to medication adherence

Variable	Adherence score Median (IQR)	p value[*]
Family is not very supportive		0.663
Yes	15 (6.25)	
No	15 (7)	
Having health insurance		0.384
Yes	16.5 (6)	
No	15 (7)	

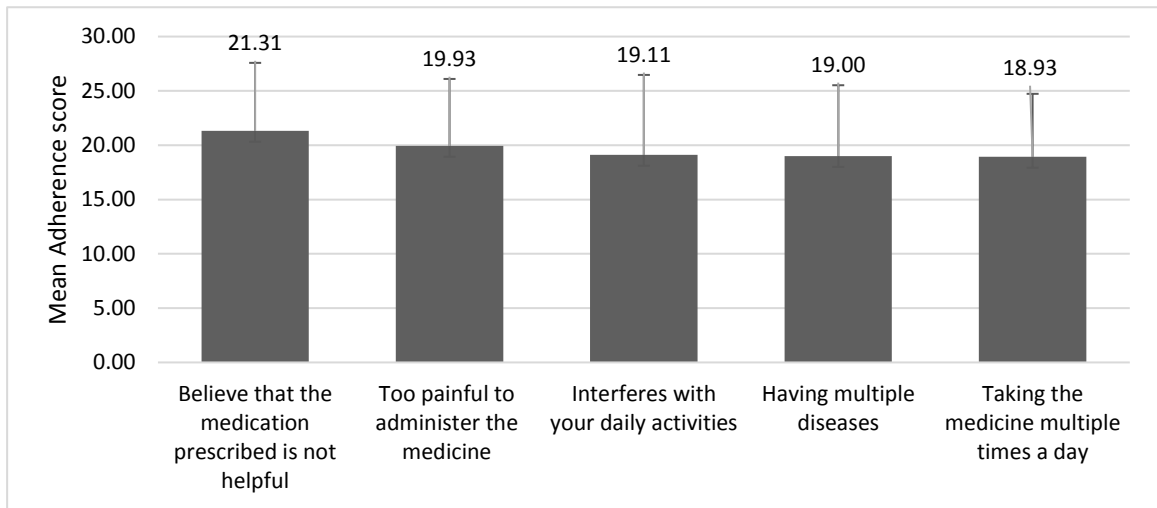* p-value was calculated using Mann-Whitney U test

Figure 15: Top five barriers based on adherence score

Table 13: Correlations of patients' characteristics and adherence score

Variables	Correlation with adherence score	
	R	*p-value*[*]
Age (years)	-0.175	**0.005**[**]
Level of education	-0.191	**0.002**
Level of income	-0.118	0.108
BMI (kg/m^2)	-0.030	0.661
Diabetes duration (years)	0.001	0.984
Number of comorbidities	0.019	0.764
Number of diabetes complications	0.195	**0.002**
Number of diabetes drugs	0.202	**0.001**
Number of all medications	0.005	0.930
Latest HbA1c (%)	0.353	**<0.001**
Latest fasting blood glucose (mmol/L)	0.236	**<0.001**
Total number of pills	-0.05	0.423
Total number of injections	0.110	**0.078**
Total number of barriers to adherence	0.503	**<0.001**

* p value was calculated using Spearman Rank test
**p value was calculated using Pearson Correlation test

4.1.6. *Summary of quantitative data*

Overall, 74% of the studied population (i.e. patients with uncontrolled diabetes) was nonadherent to diabetes medications. It was found that the median ARMS-D score was 15 (7). The quantitative results indicated that sociodemographic characteristics did not influence medication adherence, except living with family. However, several clinical characteristics were found to influence the medication adherence. Notably, HbA1c, fasting blood glucose, and diabetes complications were significantly higher among nonadherent patients compared to their counterparts who were adherent to drug therapy. The majority of barriers to medication adherence were reported by nonadherent patients and the most commonly reported barrier was forgetfulness. Higher levels of nonadherence (i.e. higher adherence scores) were reported among patients who were younger than 65 years old and

illiterate. Patients who believed that medications are not useful as a barrier had the highest adherence score among all the barriers.

4.2. Qualitative Data

In-depth interviews were conducted with both patients and healthcare providers to gain an insight of the barriers to medication adherence in uncontrolled diabetes. This section will cover the themes that emerged from both perspectives.

4.2.1. Patients' interviews

Fourteen patients with uncontrolled diabetes of varied gender, age, educational level, and nationality consented to be interviewed. Their characteristics are presented in Table 14. The average duration of the interviews was 33.86 ± 16.25 minutes with a range of 11-63 minutes. The average age of the interviewees was 58.29 ± 8.06 years (range: 46 to 68 years old), while the average diabetes duration was 11.36 ± 6.22 years (range: 1 to 20 years). The mean ± SD of HbA1c was 9.91 ± 1.43. All the interviewees were taking metformin as part of their diabetes treatment regimen, and five were taking insulin concomitantly. Six patients had neuropathy, three had nephropathy, and two had retinopathy. Other diabetes complications experienced by the included patients included foot complications (infection), increased hospitalization in the past year and amputation (of little toe).

Table 14: General characteristics of patients who participated in interviews (n=14)

Patient No.	Nationality	Gender	Religion	Education level	DM meds	DM complication
Pt. 1	Indian	Male	Hindu	University	1	1
Pt. 2	Sudan	Male	Muslim	University	2	2
Pt. 3	Indian	Female	Hindu	High school	3	0
Pt. 4	Sri Lankan	Male	Buddhism	Primary school	2	1
Pt. 5	Yemeni	Male	Muslim	University	2	0
Pt. 6	Sudan	Male	Muslim	Primary school	5	4
Pt. 7	Egyptian	Female	Muslim	Secondary school	2	2
Pt. 8	Iranian	Male	Muslim	Primary school	2	0
Pt. 9	Qatari	Male	Muslim	Illiterate	3	2
Pt. 10	Sri Lankan	Female	Buddhism	Diploma	2	2
Pt. 11	Indian	Male	Hindu	University	2	0
Pt. 12	Egyptian	Female	Muslim	High school	3	2
Pt. 13	Pakistani	Male	Muslim	High school	3	0
Pt. 14	Palestinian	Male	Muslim	University	4	0

Patient No.: Patient interview number; Pt.: Patient; DM meds: Diabetes medications.

4.2.2. *Healthcare providers' interviews*

A total of 16 healthcare providers of diverse characteristics (profession, gender, nationality, and experience) were interviewed with an average interview time of 46.50 ± 15.30 minutes (range: 21 to 129 minutes). The average duration of practice experience of the participating healthcare providers was 7.53 ± 5.93 years. The characteristics of the healthcare providers who participated in the interviews are summarized in Table 15.

Table 15: General characteristics of healthcare providers who participated in interviews (n=16)

HCP No.	Gender	Profession
HCP. 1	Male	Pharmacist
HCP. 2	Female	Pharmacist
HCP. 3	Female	Pharmacist
HCP. 4	Male	Pharmacist
HCP. 5	Male	pharmacist
HCP. 6	Female	pharmacist
HCP. 7	Female	Health Educator
HCP. 8	Female	Nurse
HCP. 9	Female	Social worker
HCP. 10	Female	Dietician
HCP. 11	Female	Nurse
HCP. 12	Male	Physician
HCP. 13	Male	Physician
HCP. 14	Male	Physician
HCP. 15	Female	Physician
HCP. 16	Male	Physician

HCP No.: Healthcare provider interview number

4.2.3. *Barriers to medication adherence*

Despite the different perspectives of patients and healthcare providers, similar themes in relation to medication adherence emerged from the two groups. Since the themes retrieved from the perspectives of patients and healthcare providers were similar in context, the results provided a triangulation that enhances the validity of the results and are presented together to give an overall understanding of the barriers to medication adherence. All quotes from healthcare providers are denoted as HCPI followed by the interview number, while patients' quotes are designated as PI followed by the interview number. A total of 5 themes emerged from healthcare providers' and patients' interviews. Table 16 represents all the identified themes and subthemes that emerged from the interviews.

Table 16: Themes and subthemes related to barriers to medication adherence

Theme: Patient-related aspects (HCPI, PI)

       Patient's characteristics (HCPI, PI)

       Patient's perceptions, attitude and behavior (HCPI, PI)

       Patient's knowledge and source of information (HCPI, PI)

Theme: Patient-provider interaction (HCPI, PI)

       Patient-provider communication (HCPI)

       Patient involvement in the decision-making process (HCPI, PI)

       Patient-provider interaction time (HCPI)

       Seeing more than one physician/care provider (HCPI)

Theme: The appointment system and patient's follow up (HCPI, PI)

Theme: The influence of other people on patients with diabetes (HCPI, PI)

Theme: Traveling and use of traditional medicine (HCPI, PI)

HCPI: Theme or subtheme was identified from healthcare providers' interviews
PI: Theme or subtheme was identified from patients' interviews

4.2.3.1. Theme: Patient-related aspects

Due to the diversity of codes and categories identified within this theme, three subthemes were generated. This includes patient's characteristics; patient's perceptions, attitude and behavior; and finally, patient's knowledge and source of information.

- Patient's characteristics

Patient's age: Some healthcare providers perceived that older individuals or elderly patients tend to have lower adherence than younger adults due to being more forgetful, having many medications and are less independent than younger people.

> *"The age yea .. the age .. as he gets older, he would forget .. because it's also with older age there would be other medications. it's not only diabetic*

medications; there is antihypertensives, medications for cholesterol. Things

would be crowded" HCPI 4.

Conversely, some providers believe that younger patients are more prone to to medication nonadherence compared to older patients.

"On the contrary, I find that older people are more careful and they come

to their appointments .. and the young ones too most of them but the older

people they are.. they come, and they are caring.. they come with their

family or by themselves so that they take care" HCPI 7.

Patients level of education: The level of education can contribute to the patient's ability to comprehend and understand the instructions given by the healthcare provider. It was mostly perceived that those who are more educated are more likely to be adherent than those who are less or not educated.

"Of course if the patient is highly educated he would be able to receive the

information and stick to the information that he received and everything

will go smoothly and also it will reflect on the case itself like he would be

mostly stable. But if someone who is not educated or not highly educated,

you find that there is difficulty at least in the beginning like the first few

months until things go smoothly and he knows how to control himself like

how to make things, and he doesn't have problems" HCPI 5.

When medications are dispensed, the patients are provided with verbal instructions as well as written labels on each medication box. There is, however, a general assumption that the patient will be able to read these labels and remember the instructions provided.

One of the interviewed patients was completely illiterate and therefore, depends on others to help him understand how to take his medications correctly.

> *"I am uneducated .. illiterate. I cannot read or write. Now it's been a while so I know them all.. If there is a new medication .. it would be written on it, so my wife would read it and tell me" PI 9.*

Patient's socioeconomic status: Most of the participants (both patients and healthcare providers) indicated that the cost of medications is not a barrier to medication adherence since the amount paid by the non-Qatari nationals is only 20% of the total medication(s) cost, while for Qatari nationals it is provided for free. Therefore, for the majority of patients, this constitutes a minor proportion of their living expenses.

> *"It's absolutely very, very reasonably subsidized .. for the same medicine you pay a lot outside. It's absolute.. It's a rare kind service you don't get anywhere in the world .. This kind of subsidized service, nowhere else. State people should feel happy that they are paying one-third or not even one-fourth of the outside .. even if it's increased because of economic issue .. The government is giving us more options .. People should not be upset .. People should be happy to pay" PI 11.*

On the other hand, there were patients with low-income levels or even with no fixed income and even the 20% of the total cost was considered expensive based on its proportion to the rest of their expenses.

> *"Medication is expensive because I am jobless .. I pay like 170 and also my wife .. Medicine is more than four to five hundred per month. It's very*

expensive .. anyhow .. we took before free of charge .. You see all these, still Crestor I didn't take, because it's costly.., so medicine 400 to 500 per month for me. There is also Asthma.. myself also seratide .. I have Seratide with me .. so monthly I have for me only 150, 160 .. my wife also she took .. my son also .. Singular .. like this .. medicine expensive for us .. But we cannot purchase outside.. never .. Thank God" PI 13.

"These [poor patients] are also few ..very small in number. You are talking about something [barriers], and this is one of the things that we face, but this is very small number, because as you can see the medication is not expensive and is available, but despite this there are some who can't afford so we send them to the social worker. So these are few, like for example in a couple of months you find one only. So not big number, the government here provides everything thank God. We pray it stays like this. Sometimes there are some people who cannot get the medications. He can't, he is a laborer, he can't buy it. Money wise he can't afford the medications, so he takes one tablet and stops one tablet [alternating].. like this" HCPI 7.

Patient's working conditions: At many instances, the patient's working conditions appeared to affect medication adherence. This was noted from both patients' and healthcare providers' perspectives.

"I observed those patients who are busy and working and have stress also sometimes they are not compliant with the medicine .. I just observed..

Because they just come here 'oh I'm tired' .. 'I'm busy in my work'.. like this. If they are working under pressure .. sometimes .. they are tense .. they forgot their medicine" HCPI 8.

"My work involves traveling a lot … this is actually one of the problems .. too much moving. Because once I went to Libya and there were problems, the medication finished and with the political tension I was out of medications for about ten days I did not take any medication .. But I also was controlling my diet .. until I get back" PI 2.

Work conditions do not only affect the patient's ability to take the medications correctly, but also influence their ability to go to the healthcare center, hence, late collection of medications.

"Some people it's a problem of coming to the health center you know .. They don't get time off to come here. They don't manage to get time off work, like you know, because they are working very long hours. Its specific people like housemaids, like drivers, security guards." HCPI 13.

Religious aspects: Qatar is a multicultural country, bringing people from different religions and cultures. Religious rituals and beliefs may differ from one religion to another. Fasting, however, is one ritual which is not limited to Muslims only, but is practiced by other religions as well. One patient who was Hindu indicated that he fasts for a specific duration of time, and during this period he only eats vegetables but does not take his medications.

"There is one-month fasting but not complete; we can use vegetable, not non-vegetable. Light food and I don't use insulin, no, because the food is very light food, so I don't take it. Only vegetable, so I don't think this will increase my sugar" PI 1.

It was noted that Hinduism has many affiliations and not all the affiliations have a dedicated fasting period as mentioned above, while in Buddhism, the patients indicated that they do not have fasting period. On the other hand, Muslim patients are asked to come before Ramadan to fix their doses and assess the ability to fast. Yet some patients use their own experiences to adjust the medications dosing during this holy period.

"I change the dose in Ramadan by myself .. It's two times.. morning and evening same.." PI 13.

- Patient's perceptions, attitude and behavior

Patient's perceptions and attitude about diabetes and their health: One healthcare provider noted that some patients do not care much about their health status or about their disease control; and some become careless because of the realization that diabetes is a life-long chronic disease condition. They realize that they will be taking medications for the rest of their lives, so they just give up trying to make it controlled.

"They are not very happy with the fact that it's a lifetime disease .. This is one of the reasons. Also they feel that it should be for their lifetime.. this doesn't make them happy .. So they feel okay I can take it [medications] all my life so maybe one day yes one day no" HCPI 2

Laziness to re-fill medication was perceived a sign of lack of motivation by some healthcare providers and patients alike. One of the participating healthcare practitioners noted.

> *"and some when their medication is finished already they are like lazy or tired to go to collect their medicine like that"* HCPI 8.

> *"Honestly I was very careless in taking the medication on time and they [healthcare providers] just told me now that I have to take it at this time, then it must be on the same time, I was taking it anytime, when I remember I would take it, so of course, they told me this is wrong and so, things were messy in this regard, and I try to fix it"* PI 8.

> *"Thank God .. I am taking my medications, but sometimes someone would just get lazy about taking the medicine .. so .. like Januvia it's been two days it's finished and I was lazy to come here, so today they found my sugar 11"* PI 11.

Data generated pointed out that many patients with diabetes may present without symptoms. Some of the participants indicated that such patients have a hard time accepting the disease, and therefore, they do not take the medications as instructed.

> *"The patient is unconvinced about the disease. There are patients who deny they are sick and they are not convinced they need all these medications especially in the elderly… I see this"* HCPI 3.

"This is more common in type 2 diabetes because of type 2 diabetes. Here in particular, they are lucky that they are diagnosed early before complications. They tell you or for example they go to do a surgery and says if you do anything in Hamad they will tell you that you have diabetes 'I went for surgery and ended up with diabetes', 'I don't feel any complications' 'there are no symptoms for diabetes, I don't feel thirsty, or frequently go to the toilet'" HCPI 10.

On the other hand, some patients realize the seriousness of the disease after the occurrence of a serious complication or after witnessing the death of someone they care for due to complications associated with diabetes. Such trauma creates a motivation for the patient to care more about their health to avoid going through the same path as others.

"I got an abscess in my foot, so they amputated my little toe, so that you know, it affected me a lot. Now I care more, especially about my feet. So when you see it [the disease] hitting you even if it's a little toe you start being more protective of himself, because sometimes these things make you realize that diabetes is very important to control" PI 2.

"If you don't take care of diabetes, ultimately diabetes will make you suffer, because I know in my family there is a history. People are dying because of diabetes. I have seen, I am seeing, my mother died because of diabetes. From diabetes she developed complications and then she died, my own father, everyone was diabetes, they did not take care of the things. My own

brother who is younger than me by one and a half years, very serious disease, he is diabetic. His kidneys are damaged, he is on dialysis every day. He is younger than me. He did not bother about his food habits. He did not bother about his things. During his engagement he knows he is diabetic. So what's happening? It has a direct effect. It kills you slowly. It doesn't kill you fast, it kills you slowly" PI 11.

Patients' refusal and fear of medications: Results from interviews revealed that patients fear medications particularly insulin since it is an injection. Some of the interviewed patients expressed fear of needles and apprehension to self-inject while others were afraid of side effects. Many regarded insulin as a final or late treatment, and can cause more harm than benefit

"Once you start insulin, means you have to continue… you cannot stop it, your body will get used to it, and that's it, no escape" PI 3.

"Insulin, yeah there is a total fear from it because it's a needle prick every time so yes. There are many patients that say I will not take insulin let me get tablets and I will manage with the sugar even if its high a little, I will manage, but I will not take insulin. insulin is something which is scary and the procedure itself people are afraid of the needle prick and everything" HCPI 2.

"yes that is the biggest barrier: starting patients in insulin. I have like a problem with two or three patients, I tried my best to convince them to start insulin ok; first it's the needle phobia, they don't like this every day needle; second it's the understanding, like this [insulin] means there is no hope, this is bad thing gone very bad; so I think it affects their whole lifestyle. That's what I have noted" HCPI 13.

"and fear from hypoglycemia .. they hear that this person was taking insulin got hypoglycemia and died, so they completely refuse it because of fear from dangerous side effects" HCPI 15.

Part of this fear is due to what others say about insulin, the stigma associated with its use, and also the misconception that insulin is addictive. Consequently, even when the patient fulfills the criteria of insulin initiation, they tend to refuse to take it.

"I took insulin for a short time and then I stopped it. I didn't like to take it in front of people; it's just they look at you like you have something very bad. I stopped it because people told me I should never start insulin and I should stay on tablets only. They told me that it could damage the body. Actually, they told me to stop all medications. So I stopped insulin and the doctor tried to convince me, but I don't want to take it" PI 14.

"Yes that is the biggest barrier starting patients on insulin. I have like a problem with two or three patients, you know, I tried my best to convince them to start insulin ok. First, it's the needle phobia; they don't like this

every day needle. Second, is still the understanding, you know, like this

means there is no hope. This is bad thing, gone very bad and the third thing

is they think once they got insulin there is no, like, it will affect their jobs,

and you know things like that. So that's what I have noted" HCPI 13.

Although health care providers try their best to convince patients about the importance of insulin in managing their diabetes, patients exhibit resistance to taking insulin. Therefore, providers end up adding more oral medications in an effort to reduce the high blood sugar and risk of complications as noted by one of the healthcare providers. He commented":

"People have a fear from insulin, and at many times they really refuse to

take it, so you see a doctor going for Quadramed [four different diabetes

medications] which is really weird because it's not recommended by any

guideline, but it's done because the patient does not want insulin at all. I

DON'T want to start anyone on insulin because insulin here is killer... People

can die because of insulin." HCPI 12.

Patient's perceptions about the effectiveness of medications: Many patients stop taking their medications because they did not see any improvements in their sugar levels.

"I used all the tablets there is, but, from my opinion, these tablets are

useless. So I tried Daonil, Amaryl, Diamicron, and whatever... All of these

did not control my sugar, except for insulin. Tablets they are very slow. They

should stop it! It doesn't have any effectiveness. I tell them; the people who

use tablets: you must be on diet control and must have exercise on daily

basis. They ask me why, I tell them these tablets are slow and insulin is much

faster, but since you are taking tablets and stuff, you must control your diet

and do exercise on daily bases" PI 2.

One patient considered that all chronic medications are ineffective, because pharmaceutical companies do not really want to cure these diseases as they are a source of profit to them.

"Look, you see all these medications, they are useless! Companies lie to us.

I read once they get over 100 billion from diabetes medications. They don't

want to help people, because keeping them as they are means yearly profit

of billions and billions of dollars on yearly basis. If they cure you, they lose

all this money. So they make useless medications that barely affect your

sugar, so you take more and more of it." PI 14.

On the other hand, there are patients who do not believe that insulin pens are as effective as vials. Therefore, they do not take the pens when prescribed for them and ask for the vials instead.

"The second thing is the injection itself, before there was the vial, now there

is the pen. Some people are complaining about the pen, and they ask for

the vial. Imagine! I have three, four patients, they tell me they don't want

the pen. I don't know, my dear this pen is painless, but these are very few

like in all my patients just three or four. No, he feels that the pen is not

controlling his sugar. "He feels". Okay but the blood tests are the ones that

would inform and he can't understand that the vial is the same as the pen. There is no difference between Novomix and Mixtard, it's the same" HCPI 16.

"I had a bit of perception on the pen and on the regular insulin injection the bottle. One time I have taken the pen, I felt that my sugar level is not controlled with the pen, because I felt that the insulin is not going inside, so I have changed. Then I asked the doctor. Psychologically you should be happy taking this new medicine. I told him very clearly that I am not happy by taking the pen; I would like to switch over to my injection, my syringe." PI 11.

Patient-initiated changes in medication regimen: In many instances, patients intentionally change the prescribed dose of medications. This happens at the discretion of the patient based on the blood sugar level or based on their diet. If they notice their glucose readings are high they tend to take more of the medication and vice versa. These changes are not limited to insulin, but to the oral medications alike.

"Sometimes they [the patients] want to take the medication according to their convenience, "this one is ok .. ah .. this I don't like", sometimes the patients are like that" HCPI 8.

"Sometimes you get a patient who takes Januvia twice, and there is no added benefit from taking this twice, so you see for example he is taking it

like this by himself like he felt he is uncontrolled, so he decided to take

Januvia twice" HCPI 3.

"Sometime, this Amaryl, it's supposed to be three tablets in the morning,

but I take 2 tablets. Sometimes when I see that the meal has no rice, like

this" PI 13.

Patients on insulin are generally educated about adjusting their dose based on their diet. This is very common with type 1 diabetes. However, all the patients who were interviewed had type 2 diabetes and most of them were taking insulin glargine, a long acting insulin usually taken in the evening. Nonetheless, patients would adjust the dosing of the medication based on what they perceive appropriate and without a standard procedure or actual calculations.

"When my blood sugar is high. I would take higher dose, I just do it myself,

I estimate and I just take it when my sugar is high. Like yesterday, I didn't

eat or anything, and I don't know why my blood sugar was high. For the

first time I found it 300, so for 300 the only thing that works is insulin dose.

When I took it, unfortunately I got hypoglycemia at night. When I get

hypoglycemia I am not the type that can sleep; I can't sleep. There are

people who can get diabetes-related coma. I just feel that I can't sleep.

When I feel this I would get up and measure my blood sugar and I find it

low, so I feel this is what make me unable to sleep" PI 7.

Taking medications is a burden on its own, yet sometimes the healthcare provider does not take this into consideration when prescribing medications. Some patients would be prescribed more than one tablet of the same medication, and the patient would not administer them all at once in an effort to reduce the burden.

> *"I don't take them [tablets] all at once. In the morning after breakfast I take half of them, the controller [Glucophage] and sometimes the aspirin, and at night I take the rest of them. It's too much tablets to take together" PI 14.*

On the other hand, providers indicated that some patients stop the medications once they are stable. This is because of the wrong belief that diabetes is a short-term acute disease that is curable.

> *"As soon as he [the patient] notices stability.. Look there is a belief in some people that yeah .. they tend to convince themselves that if they are better, they can stop the medication, so he tends to do this or believes that this is something minor and it would go away, and he sees himself stable once, twice, and three times that's it; the disease went away, so he starts to get worse again. This keeps happening until he is convinced" HCPI 5.*

However, sometimes the patient tends to unintentionally forget to take the medication due to house chores for example and would take it at an incorrect timing.

> *"Sometimes I would be cooking and so, I forget to take the injection before … Like I set the table and we start eating, and I would forget. I could be eating, and in the middle, I would remember, but sometimes I forget, and I*

feel .. I remember after that, and I find the sugar really high, and sometimes

I feel that my arm hurts and I remember that I did not take the injection.

Because when I don't take it I feel that my arm is numb, and it would hurt,

I feel it's heavy, so I remember that I didn't take the injection, so I take it

and thank God it gets fixed. Most of the time I don't take it, but thank God

when I forget I would end up taking it after food" PI 7.

Some patients would combine medication doses when they missed a dose, which predisposes them to possible adverse effects.

"Sometimes I don't take it [mediation tablet], I forget. Some medications I

am taking one in the morning and the other medication in the evening, so

if I forget the morning medication, I will have it combined with the evening"

PI 10.

Patients always try to incorporate their medications in their daily routine; however, sometimes the routine is changed because of a special occasion which results in them forgetting to take the medications. These special occasions usually happen during the weekend which by itself is a different routine than weekdays.

"Weekends it is distorted. Simply distorted because of any other thing. It

[the routine] is never distorted other than the weekend. Sometimes I go for

dinner. Sometimes some friends call us. We just go there and at 11:30 or

12:00 we come back. Ok 12 o'clock you don't take medicine. You are

supposed to take medicine at 9 o'clock, so at night you skip it. Next day

again you start." PI 11.

Experiencing side effects is one common reason expressed by the patients for stopping or changing the dose of medications. Most commonly discussed side effects were gastrointestinal-related side effects mainly with metformin and hypoglycemia with insulin.

"I stopped taking insulin long time ago because one time I fell down in my office because my sugar was very low, was very low, it's very bad feeling when you can't move" PI 5.

"For me Glucophage causes me disturbance, always disturbance. This is one reason why I prefer not to take it. Like sometimes I remember it's time for the dose, but I don't want to take it because of the disturbance it causes me" PI 8.

- Patient's knowledge and source of information

Many patients gain knowledge about diabetes and its management from family members who have the diseases. This prior knowledge seems to help the patient be more adherent than those who never had an experience with the disease through someone they know. The majority of patients, however, receive the education from the healthcare provider. Nevertheless, there were a couple of patients who did not know what diabetes is. This could be because they were not initially diagnosed at the primary care center.

"Yeah the nurse told me, because of its model of care, you know. Why do you become diabetic? What is pancreas? How does it work and how does it not work? What are you supposed to do etc. and why are you given insulin,

and how are you compensating with insulin, so all this I know from here [center]" PI 11.

"Researcher: You know when you have the disease someone will explain what is the disease, how does it happen, what is the treatment, did anyone explain this to you?

P: Never, never, no. No one explained, because for them it's ten years I have diabetes" PI 13.

As for medications, all interviewed patients know the correct instructions for their medications. However, when asked about their knowledge of how medications help in diabetes, many could not answer. The patients who do not receive education or information about the disease and the medication, usually will seek the information from other sources such as the Internet, or from other people.

"I saw on YouTube what is diabetes, yeah. Anything you want; YouTube is there just type that only" PI 3.

"No I refer to the Internet also, and I am getting educated by the Internet also, and most of my friends also are having the same medical condition so by them also I learned" PI 10.

"It's [education] from the physician yes. But they [patients] have you know

may be from other people or other friends or those who have experience"

HCPI 2.

Many patients indicated that they did not know their HbA1c levels or the goal they should achieve. Healthcare providers justify this by saying that they do not tell the patient if the levels are within normal range, but would only indicate if it is good or not.

"Maybe they don't know the levels because the doctor told them and they

forgot, or they don't know what HbA1c is, or it could be that we have seen

it normal so why bother the patient and tell him you are 6 point something.

But if there is something major, like for me I always tell them, their HbA1c

is good, this is good" HCPI 15.

Generally, patients gain information and expand their knowledge about the disease and medication from the healthcare providers especially through medication reconciliation. Medication reconciliation which involves educating the patient about his/her medications is highly underutilized. This service is provided by the pharmacist in a dedicated room within the pharmacy, but is only used upon physician referral.

"May be for the physician if he noticed that the patient is uncontrolled and

he did not know how to use his medications and the purpose of taking the

medications.. Maybe he (the physician) can ask for medication

reconciliation so the pharmacist can sit personally with the patient to

educate him about it. This happened in the last three years two or three

times only" HCPI 1.

Unfortunately, pharmacists are not allowed to bring the patients from the dispensing window to the medication reconciliation room even if they identify that the patient is confused about their medications or lacks certain medication- or disease-related knowledge. This can only be done upon the physician's referral.

> *"This year no we didn't do medication reconciliation, last year I did .. This year I didn't get the chance.. It was maybe 2 to 3 times last year. Surprised right! .. We don't have medication reconciliation regularly .. They are not sending too many patients.. Very less. That's what this is.. Depending on the physician themselves .. He has to refer to the pharmacist" HCPI 2.*

4.2.3.2. Theme: Patient-provider interaction

Several aspects are involved in the patient-provider interaction. These include communication, patient's involvement in decision making, time of the interaction and the involvement of many physicians in the patient care.

- Patient- provider communication

Patient-provider interaction, particularly communication, plays a vital role in the care of the patient. Although the main languages spoken are Arabic and English, healthcare providers often see patients who are unable to speak either Arabic or English, and some find it difficult to communicate.

> *"The language barrier is a huge problem .. For example here we have two to three Indian sisters with us here, but unfortunately not in all the areas .. Sometimes I have my colleague and I working on shifts, she has some days,*

and I have some other days. Ok, if I found that it is difficult to deal with the

patient because of the language .. like if I had a patient and he is Indian I

tell him to go and take the appointment on date x, the date where she is

available because she knows Indian and sometimes I request one nurse, and

from reception there are boys, and they can come and interpret" HCPI 10.

Sometimes the patient is able to speak the same language as the provider. However, the provider would use medical jargons which the patient is not familiar with.

"Language is one barrier also sometimes they [other providers] use medical

terms and the patient doesn't understand what is meant. So the patient

comes and asks me, and I explain to them" HCPI 2.

The magnitude of this barrier could not be adequately investigated from the patient's side as those who can speak either English or Arabic were selected to participate in the interviews.

- Patient's involvement in the decision-making process

Another feature of the interaction between the patient and the healthcare provider appears to be the involvement of the patient in the decision-making process. Some providers indicated that there is no patient autonomy in the decision-making process.

"Generally, no - the patient does not know what medications were

prescribed to him ... He [the physician] just writes the order, and the patient

comes to the pharmacy, and we tell him this is the medication prescribed

for you by the doctor .. We ask did the doctor tell you he will add a new

medication "yes" that's all .. did he tell you how to use it "yes" but that's

all" HCPI 3.

"... some medications they [healthcare providers] change.. I am not aware

of this plan.. .. But I showed these medications in my country and they told

me these are the best medicines" PI 10.

- Patient-provider interaction time

There is a continuous increase in the number of patients attending primary health centers, while resources and number of providers remain to be limited. This has a direct influence on patient management and the quality of care provided which ultimately affects the patient's adherence to medications. Therefore, interviews pointed out that the time of the interaction between the patient and the physician could be another perceived barrier to medication adherence.

"There is not really enough time, actually there is never enough time, but

you also can't do it all in one visit. You educate the patient about the

condition the first time and then ask them to come back a week later to

carry on from where you left off .. You have a total of 15 minutes with the

patient of which only 7.5 minutes go to educating the patient about what

they have, the symptoms, and how to manage with the diet and exercise,

and their medications, and side effects… Time is inadequate especially if the

patient comes late or misses an appointment and we don't know what

happens" HCPI 12.

"I don't know if he [the patient] is taking his medications because I don't

ask .. I don't ask if you take the medications or not. I just dispense here, and

that's it .. There is no time to even deal with him much with the pressure

here in this center .. And the number of patients lining up, it's impossible to

take more time with the patient" HCPI 4.

- Seeing more than one physician/care provider

Some participants indicated that seeing more than one care provider for the same issue (i.e. diabetes) can create unnecessary confusion and complications in the care management plan. When the patient seeks care from different providers, he/she often receives different information from each, a situation that can lead to confusion.

"Some patients they are like doctor shopping, so they go and see all the

doctors because they are not convinced by one physician .. These are always

having poor adherence … His physician has changed, so he didn't like to

continue .. or he came to a different doctor and the doctor gave him

information different from the first physician .. So these could be some

reasons for not taking the medications" HCPI 15.

Sometimes the patient gets an appointment with different physicians, but not intentionally as it is not ideally set in the appointment system itself.

"I saw so many doctors here .. I once told my friend.. I told him in Hamad, it's like the United Nations .. one day it's Indian, one day it's Egyptian, one day it's Sudanese, one day it's Jordanian, and each has his own way of doing things" PI 2.

Other times, the patients seek different providers from different health settings and even different countries if they have the opportunity to do so, such as having private insurance.

"I'm following up with another physician outside in Doha Clinic .. and I follow up with him .. because I have private insurance as well" PI 2.

Patients who seek different providers in different locations are much more difficult to manage, particularly that the patient records are incomplete and split in multiple locations. This clearly reflects on the patient's treatment plan and medications. Each provider would change the treatment plan according to what they deem appropriate.

"I change the doctor, then now he changed the medicine .. Before.. actually first, I used two [medications] for a month .. then I go to another hospital .. and then they do nice medicine, and everything is good .. then after suddenly they changed medicine.. then I went to three. four pharmacies .. each doctor, is changing the medicine" PI 3.

"There was a patient … one physician told him there is no need to take this medication while another tells him no you should take it ..We have many like this and on the system you can note the conflict of opinions between

the doctors.. Of course when you change the physician or when you change the opinion between physicians in Hamad and physicians in PHCC this can affect medication adherence" HCPI 3.

When such changes occur, the patient may get confused and end up taking all the prescribed medications from the different prescribers which only adds to the complexity of the regimens, leading serious adverse effects and nonadherence to therapy.

"Look I know in general the attitude of the geriatric in general like they have a problem in sometimes trusting the medication or trust in the physicians themselves for example or conflict of opinion between the doctors and the rapid change in medications for them.. The patient becomes confused, he doesn't know should I take this or that.. and sometimes he takes all together" HCPI 3.

4.2.3.3. Theme: The appointment system and patient's follow up

The late appointment is a barrier noted in many interviews from both patients' and providers' perspectives alike. Participants indicated that over three months appointments (mostly six months) are not good as a follow-up timeframe. During this time, it is unknown whether complications occurred, or whether the patient faced any problem with the medications.

"Six months for diabetic patients is a lot .. especially if they start on new medications, and you ask them to come back in six months .. If there is a

start of complication like in kidney .. If there is proteinuria .. he will come

back with high creatinine the next time" HCPI 10.

"Medication adherence is a major problem for a number of reasons. First,

in general, follow-up is poor. Six months follow-up will not really help the

patient. The patient comes every six months and gets medications in three

batches every two months as refill.. You don't know what is going on within

this period if they are attending for refills or not.. and you just have no idea

about what is going on… and when the patient comes after six months it's

all a waste to the clinic.. It's a problem and all what the doctors do is repeat

the medications" HCPI 12.

Even patients find the appointment schedules problematic for them and perceive these as very long especially if they are facing problems with the medications or their condition.

"Now look .. to be honest with you .. here in the center if you want to meet

the physician for diabetes, it's as if you are meeting the Prime Minister ..

They give you appointments you know after 3 months.. four months .. very

long … and sometimes when they give you after three months and four

months.. you find yourself without an appointment" PI 2.

However, some providers indicated that the late appointment schedule is not fixed for all patients, yet it was not clear if there is a set of standards or criteria identifying which patients would be scheduled for two months appointment for instance compared to those

scheduled for six months appointments. There were obvious inconsistencies between providers in terms of follow up duration.

> *"I think the six months NCD is not fixed .. Like if the patient's compliance is good .. the blood test is generally ok .. we give them a six months appointment .. but if we feel that their HbA1c is not good .. or they need slightly more .. we also give them three or four months appointment as well .. But because NCD clinics are quiet overbooked .. we tend to give them six months if they are you know .. reasonable .. but if their control is very poor, we have the ability to give an early appointment as well … I tend to give them 2 to 3 months appointment to see them extra if things are not very good .. I try to bring them to the general clinic"* HCPI 13.

4.2.3.4. Theme: The influence of other people on patients with diabetes

Social stigma is a factor which highly influences treatment success especially if the disease is perceived negatively by individuals close to the patient or the society in general. If the patient needs to hide the condition from the surrounding people, he/she surely would not be taking the medication as he should.

> *"I had one patient with type 1 diabetes, and she got married and pregnant, and she did not tell her husband she is diabetic, and she came, and I didn't know this information. So we started talking about diet, and she would say its gestational diabetes .. because her husband was with her .. So I went to the doctor and told him is she type 1 diabetes and he explained the situation to me .. So we started to deal with her that this is temporary .. it came*

during your pregnancy and we gave you insulin for it .. We did this and moved on because of patient privacy.. and also because it is something that could create a problem for her which could possibly lead to a divorce because she did not tell her husband about it before." HCPI 10.

Patients also indicated that it is difficult to take injections in the presence of other people as injections are associated with addiction.

"Honestly, I intentionally sometimes not take it in front of people .. I remember I was once taking insulin and someone got up .. and from far he screamed .. hey heroine! .. I told him does it make sense for someone to take it like that! .. So since then I intentionally don't take it in front of people" PI 2.

Patients are highly influenced by what the surrounding individuals say and talk about. Sometimes they share information about the disease and the medications, and they advise each other on the best treatment according to their experience.

"Honestly I asked him [the physician] to prescribe it [sitagliptin] for me .. because my siblings in Egypt they are taking it .. and they are doing well on it .. So I told him my siblings are taking this .. so he told me okay we stop the glucophage and we take this" PI 12.

"Sometimes patients are inviting each other over medications ..like he [the patient] has high blood sugar and is taking a specific medication and he happened to be a guest at someone or at his friend's house, so he [the host]

gives him a tablet of medication "and this will fix it for you" … sometimes it

could be completely wrong" HCPI 5.

The majority of interviewed patients indicated that they receive family support through reminding them to take the medication on time or through helping them in diet management. However, one patient indicated that family support is lacking which influences how she manages her health.

"That one [family support] really we need .. someone will take care ..

someone .. something .. Here it's a routine .. My husband will go off .. he

will go for ten days .. one week. Then he will come .. I am alone in my house

only .. children I have to care about I have to pick ..I have to drop, I have to

go to health center .. This is my life.. so minimal support" PI 3.

Many patients are being cared for by housemaids and individuals other than their close relatives. It is very important to determine who is taking care of the patient and to educate them as well about the patient management.

"There was once a housemaid and there was a Qatari woman on a

wheelchair and I was asking her [the maid] who gives the medications to

the patient? .. She said I give her .. So I said ok come on how do you give her

the insulin .. and it's all wrong ..all her answers were wrong!! And there was

another pharmacist .. I told him come and see .. the patient is sitting over

there on the wheelchair and the maid is giving her, her medications and I

ask her about each medication and each is given wrong there wasn't one

medication correct answer.. All were wrong" HCPI 6.

4.2.3.5. Theme: Traveling and use of traditional medicine

More than 60% of the Qatar's population are non-nationals and majority of them would travel back to their home countries for vacations and on special occasions. There was a consensus among all the interviewed providers that traveling is a big barrier to medication adherence. Patients generally go back to their home countries and change in their medications, believing that their levels will automatically be improved once there.

> *"He [patient] has an idea that when traveling to his home country, he will get better and his health will improve, he will get better. These two things are very common, so that's why he would reduce the dose by himself. It may have a right aspect to it, because when he goes to his family, he will psychologically improve. Also, in his country, he doesn't use cars, and so he walks. He also considers that the food there is healthier, etc. So anyone who travels and comes back from travel, I automatically consider him noncompliant." HCPI 14.*

> *"When I go to Egypt, I think my sugar can be controlled without insulin, because I move; I go around and up and down. So there is always movement, but here I can't move; I just stay at home" PI 7.*

Another provider considered nonadherence during the travel period to be acceptable as it is difficult to be controlled all the time.

"In Christmas, in Eid, Ramadan, these are seasons patients get messed up. Holidays; they go travel back to their families, they eat, and I don't insist on the patient. To win the patient over, I don't scare him. I tell him it's okay once in a year its fine, because he is human at the end, for sure he will be invited and for sure he will go. It's a vacation!" HCPI 15.

The general policy at the primary healthcare centers is the provision of medications for a maximum of two months for non-Qatari patients and three months for Qatari patients. There are no exceptions to this rule, therefore, patients who travel for a longer time (e.g. exceeding two months) are not given enough supply. This is considered problematic from patient's perspective, while providers consider this to be acceptable.

"Sometimes, because they give only two months and sometimes the medicine finishes before, so I buy from outside. I don't know why they do this. I think they don't believe I travel or maybe they think I take medicine for other people, because here it's cheap yes. I don't know .. Can you tell them this is bad" PI 8.

It is well known that certain items are not allowed on the aircraft, one of which is sharp objects such as needles. One patient indicated that it is very difficult to take his dose of insulin when traveling because of this factor.

"I am here in the gulf area for the last 30 years. I have seen each security man in the airport, so as a patient you don't take it [to the airplane] because you are afraid why, because they will remove it and throw it away. They will not do anything but throw it away. So you don't take the insulin on that

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day. Traveling you take 5 to 6 hours to reach home, then what happens is,

you are traveling from seven you are supposed to take your dose at 8 you

don't take it" PI 11.

Moreover, there are patients who start using traditional and complementary medicines or natural products that are common in their home countries and difficult to obtain in Qatar. This is not limited to one culture over the other, but was noted in many patients from different cultures and ethnicities.

"I take Sri Lankan medicine, but it's very time consuming and you have to,

when you are taking that, you have to continue it. You should not do lots

of things, you should not eat some kind of food .. There are lots of

instructions, and it takes lots of time and the thing is in this country you

can't do it because I have to go to Sri Lanka and do it. it's not easy. When I

am in Sri Lanka, I think of doing it, because it is more effective and fewer

side effects" PI 4.

"I am living here for the past 14 years here, so I can't take except these

medications, but when I go for vacation I use them [traditional medicine]...

Yes they are useful, because they are more useful and are safe. Our

grandparents they teach us these are good and they come from nature, so

they are good" PI 10.

Nonetheless, there are patients who use some herbs and spices which are easily found in Qatar to help reduce the blood sugar; this includes okra, cinnamon, and many others.

> *"Yes so many [use herbal and traditional medicine]. The garlic tablets, cinnamon ginger, whatever. And these things they take it a lot; Roselle, a lot. Its everyone; people from the gulf countries, from Qatar, from outside. On the contrary, not only Indians for example, they have a lot of beliefs in herbs" HCPI 13.*

One provider indicated that people tend to use these products in an effort to completely cure themselves of diabetes.

> *"To be honest, I have noticed that mostly the people between 30 to 40 middle aged as we call them; those are the ones mostly they experiment a lot, you know they will go to India as they heard about this herbal medicine. They say if you take it for six months, you know. So mostly drivers, house workers, low socioeconomic, they tend to try in the initial phase alternative medications as well. Its more cultural, because in India there is historical tradition of going to the natural path and most of these people you know, they are from villages or small cities in which still there is strong culture of trying natural remedies first. So this population they will start taking it, but they will just disappear and come after few months, with very bad HbA1c and everything is all over the place and when you ask them what happened, you know, they will say I have been taking this medicine from India because*

I don't want to take this medicine for whole of my life. So I was just trying

that to be cured completely" HCP 13.

4.2.4. Strategies and interventions to tackle medication nonadherence

Interventions to improve medication adherence are widely reported in the literature. However, the interventions are usually planned and tested from researchers' perspective. Long-term benefits of interventions and their sustainability can possibly be achieved if the stakeholders (patients and healthcare providers) were both involved in identifying the best interventions that work for the patients and are applicable in the primary healthcare setting.

4.2.4.1. Theme: Patient-related interventions

Multiple intervention strategies to tackle the problem of medication nonadherence were proposed by both patients and healthcare providers.

Providing more patient education was the most prominent strategy stressed upon by the interviewees. Other suggested interventions include the use of mobile phone applications and pillbox for medications.

- Providing more patient education

Many of the identified barriers can be overcome with the provision of more education. Even patients who have diabetes for a long time were asking for more education and more emphasis on the information.

"Now I have had diabetes for twelve thirteen years, so I know now how to

control, but there should be education and awareness more than this" PI 2.

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One provider suggested the use of demonstration of complications as a means of convincing the patient about the seriousness of the disease. One interesting suggestion was the use of a video which can demonstrate the journey of a nonadherent patient.

"For me because I am a visual person, so maybe a video clip every time they would show to them [the patients] may be some situations we can show to them. So if there is a video clip that would show what would happen if you are not compliant to the medicine, could also create an impact. But the problem is may be the language ..if the patient is not speaking that language may be can't understand, but if it's moving, it could relate. So maybe during the visit it will take time also for each patient fifteen minutes" HCPI 8.

Another suggested educational material was the use of brief, easy-to-read patient information leaflets (PILs) which can be provided in more than one language. Leaflets should describe the disease and its management and avoid complicated terms and instructions.

"I used to have leaflets in Urdu for patient and give them out, but I ran out. They included information about the disease, but I never had any in Arabic. Arabic leaflets would be really helpful" HCPI 12.

"For example leaflets that have brief information in Arabic, in simple English. What is the medication? How it works? Not the medication leaflet, this would confuse the patients and give the things that are rare sadly, they

write rare things. It should tell them simple things like if you had this, do

that. If this happens, this is expected. This would help a lot" HCPI 15.

Patients group discussions and meeting was also another suggestion by a healthcare provider. The idea is to bring a number of patients for an educational session and providing them with information as a group rather than one at a time.

"First we need like, especially for the new patients, we need proper diabetes

education program. May be we have once a week something like we call all

the newly diagnosed and bring them together. Like if we are diagnosing 2,

3, 5 patients, they have the opportunity to, you know, meet with the

diabetes educator, like a formal meeting in which she has lots of time; may

be half an hour or something .. as a group .. to educate them. That's one

thing in which she will explain what is the illness, how insulin would affect,

you know,   depending on what they do" HCPI 13.

- Mobile phone application and SMS reminders

The use of technology and mobile phones in addressing medication adherence was recommended by one patient. He suggested that mobile reminders and SMS text messages would help him remember to take his medications and would solve the problem of forgetfulness.

"The best way, cheapest, through the SMS services. Everyone has got a

mobile. If an SMS comes to the diabetic patient saying that please time for

your medicine, time for your insulin. It's just a reminder; time for insulin.

You tend, the moment the mobile bleeps, everyone in this world right from

the age of 8 to 80 they have the habit to check what is this message. The

message for a diabetic patient will help. You need to develop an application

as a reminder. The technology is so much advanced now so the healthcare

system should develop a system. Its heaven, I am telling you, it's going to

help with anything" PI 11.

On the other hand, one healthcare provider indicated that the mobile phone use for reminding the patient to take the medication will be annoying and not practical to implement.

"It [mobile reminders] will be annoying .. no, no, no it's not practical. First

it could be that his hearing is a bit impaired, he has to have it [mobile] at all

times and it will keep ringing. There are patients taking so many

medications. It will be annoying to the people around him, annoying to him

and it's not practical." HCPI 7.

- Use of medication pillbox

Pillbox, a simple medication divider unit can help the patient remember his/her doses. Many providers indicate that it can be useful if applied and used for patients medications.

"A pillbox filled by the day and the month, so you just empty the

medications, so that even if the patient is traveling or even if he is an elderly

he knows this is the dose for today, for tomorrow and for morning and

evening. I have seen this pillbox in a private pharmacy and I got it for my

mother in-law. It will help a lot for the patient, because for me, my mother

in-law is old so she takes a lot of medications, so I empty them in the pillbox

and the box has the days. The pillbox will act like an alarm especially for

older age is a good idea I would try to implement it here" HCPI 4.

4.2.4.2. Theme: Healthcare system-related interventions

The majority of the interventions suggested within this theme were identified by the healthcare providers themselves. These included adjusting the appointment system, hiring more healthcare providers, increasing the use of medication reconciliation, introducing Arabic induction courses, and simplifying medication regimens.

- More frequent appointments and less refill orders

The late appointment system is, as previously indicated, a barrier that was mentioned in almost all the interviews. One suggested solution is to improve the appointment system and allow the patients to see their healthcare provider more frequently. At the same time reduce the number of refill orders and allow the patient to do more frequent check-ups. Moreover, the appointments should be set in a way to allow the patient to see the same healthcare provider and avoid unnecessary barriers mentioned before.

> *"The only thing I am having is the time period of visiting the doctor only*
>
> *after six months, so I prefer to visit them more frequently that's all" P10*

> *"The receptionist should take into account which doctor referred the*
>
> *patient to the NCD and to give the patient the booking with the same*
>
> *doctor. This will not only save the problem of continuity of care, but will also*

be very important for the language barrier so the patient that speak English

can be booked with those who speak English and this will solve the

communication issue and the language barrier" HCPI 12.

- Hiring more healthcare providers

More education is needed; therefore, more time is needed with the patients to address their needs. This ultimately requires more staff. Many healthcare providers indicated the need for more providers to help reduce the workload and improve the quality of care.

"They should reduce the number of patients seen by the physician per day

especially for the chronic patients" HCPI 1.

"Increase the number of physicians so that the allocated time for the

patient is enough for him to talk and get information and ask whatever he

wants" HCPI 5.

"They should recruit more doctors or more clinics that are available in the

morning and the evening so that the patient gets his rights to be able to see

the doctor every month" HCPI 6.

One care provider indicated the cost saving and the benefits of hiring more staff.

"You have to increase the staff in the clinic, because the cost of disease and

the cost of complications is much higher than the cost of salaries for new

staff. Recruit new staff, because if the patient received a good education and good service; first you reduce the medications, you reduce complications, you reduce time of production because when the patient comes a lot to the clinic, these are patients excuses from work. So he will stop the work for some time. Also for a productive person, unfortunately you find the diabetes complications present in younger age, for example in 40s and 30s. These are the people working and if you are wasting time in the clinics and started renal failure for example, three times a week, just think about the cost of dialysis is how much, the cost of the medications, the cost of things is how much, in addition he is also leaving his work for medical excuse. All these are costs, it's a huge, huge cost. Diabetes burden is very high. There are lots of studies on this. So if you come and increase the staff, how much would this cost? You will reduce the complications, reduce the medications, that's a huge benefit. HCPI 10.

The role of pharmacists in Qatar is continuously evolving. Clinical pharmacists were introduced into the hospitals (secondary and tertiary care levels), but not yet in the primary healthcare setting. Many providers indicated that having a clinical pharmacist in the NCD clinic would improve patient's adherence to medications.

"Each clinic dealing with diabetes should have a pharmacist in this clinic. The pharmacist is really important and the benefit for the patient will be much higher so that's a perfect solution, but until now they [administration] don't see it as practical" HCPI 5.

Medication reconciliation is an important highly underused service. This service requires some attention to make it more efficient and useful for the patients. Providers indicated that pharmacist should be identifying patients needing reconciliation in addition to physicians' referrals.

> *"It's pharmacists who can increase the adherence of the patients and do reconciliation with the patients. It should not be for all patients, but they should get the chance to do the reconciliation and review the patients medications with no referrals" HCPI 6.*

- Learn Arabic courses

Although language did not appear to be a major barrier, some providers struggle when encountering patients who do not speak the same language. Some providers can speak only English, while the majority can speak both Arabic and English. One English speaking provider suggested Arabic courses during the training or induction period.

> *"For us doctors when we come, we have to do three months training which is basically doing nothing; they should give the non-Arabic speaking doctors like myself an Arabic course which would be really useful" HCPI 12.*

- Simplify medication regimens

Complex medication regimens can be simplified and be made patient-specific. One physician suggested the use of combination tablets or long acting medications in order to reduce the burden of medications. In addition, another provider suggested the slow initiation of medications to not overwhelm the patient.

"There is now the combinations. That's why in order to reduce this issue [burden] we try to give combination tablets. Like if the patient is taking Januvia and Glucophage, so we give Janumet. The combination therapy improves and fixes the issue of compliance or nonadherence. Now there are also the medications that are sustained-release; once per day better than twice or three times per day. This improves adherence" HCPI 14.

"Gradual initiation, like you don't see a patient who is scared of insulin and we give him basal and three rapid insulin injections! We do it gradually" HCPI 16

Table 17 provides a summary of the solutions proposed by the patients and the healthcare providers detailed above.

Table 17: Themes and subthemes related to interventions to tackle medication nonadherence from the interviewees perspective

Theme: Patient-related interventions (HCPI, PI)
Providing more patient education (HCPI, PI)
Mobile phone application and SMS reminders (HCPI, PI)
Use of medication pillbox (HCPI)
Theme: Healthcare system-related interventions (HCPI, PI)
More frequent appointments and less refill orders (HCPI, PI)
Hiring more healthcare providers (HCPI)
Learning Arabic courses (HCPI)
Simplify medication regimens (HCPI)

HCPI: theme or subtheme was identified from healthcare providers' interviews
PI: theme or subtheme was identified from patients' interviews

4.2.5. *Other relevant factors that require attention*

Despite the focus of this research on barriers to medication adherence and the possible interventions, interesting findings were captured within the interviews in relation to the primary healthcare setting in general. Although these issues may not directly affect medication adherence, they do indirectly influence it and generally affect the patient care outcomes. Therefore, such emerging issues require serious attention and intervention.

- Lack of role clarification

The findings indicated that there is a lack of understanding of other professions' roles and scope of practice which is further illustrated in the minimal referrals done to other professions. This means that a patient may not get all the necessary education about his disease and its management including medication use.

> *"There is one nurse in the NCD clinic, but I don't know what they are telling the patients, if they are checking what the patient is taking and if they enquire about the disease management. I'm not sure if there is a standardized practice that goes to all patients because sometimes the nurse would document useful things like the labs and the missing vaccines and ophthalmologist visits but it's more of a tick box (✔) exercise like do you take your meds? Check (✔). Did you take your vaccine? Check (✔), Did you do, etc., etc. they are more of a reminder for the physician and the patient, but I don't know what education they give. But there is a need for role awareness" HCPI 12.*

"What makes me upset, I found many doctors they are not recognizing

what a dietician is and what is the role of health educator .. What is the role

of diabetic educators .. and there is overlap between our jobs and as you

know .. diet management is being done by everybody.. except a dietician!"

HCPI 10.

Although there is a specified dietician for the NCD clinic who has clinical expertise

in managing diabetes, some providers were not aware of her role and her expertise.

Therefore, patients were not referred to her on a regular basis.

"There is a nutritionist, but she is not specific .. If specific then the patient

would go to her a lot .. But she [nutritionist] is mostly with children and

antenatal and things like that obese and all but not specific for diabetes"

HCPI 7.

"I have diabetes since 15 years. I have been referred to nutritionist ..yes..

but once or twice I have seen her only.. since a long time" PI 11.

Many providers do not know each other's roles and scope of practice. Accordingly,

many providers suggested conducting sessions or workshops on role clarification which

would identify each person's role. Another solution was to apply the roles in case

discussions and regular meetings. This will address many issues at once; first, role

clarification and communication among providers and second, improve patient care

through providing a plan developed through teamwork.

"I'm thinking we should have lectures for all the paramedics .. for all the team to tell them this is the role of this and this is the role of this .. and the difference between us and educator" HCPI 10.

"We should have group discussions. There should be group meetings. The group discussion when the patients' cases are set and each is talking about his experience especially in newly diagnosed, You could see two patients with the same history of diabetes, same age of diabetes, but different complications, one controlled and the other one with problems and complications. So you start really to see" HCPI 10.

"and we should have some sort of multidisciplinary cases at which all the physicians who are doing this NCD clinic would show the difficulties, they should discuss at least once or twice a month along with dietician and others they should sit together. They should discuss all those cases … and make like a uniform approach, and that would help us understand each other as well, clarify the role of each other" HCPI 13

There is a clear hierarchy in the organizational structure which reflects upon the duties done by each profession. Almost all healthcare providers including physicians themselves indicated that the physician is the key player in patient care.

"Look sorry, the control all happens from the physician, and if he starts to follow correctly, you will see that things are going the right way" HCPI 5.

When asking which profession should be involved in educating the patient about their medication and the disease, one interviewee indicated that patient management should be solely by the physician.

> *"It should be the doctors full stop. They are the ones who know the patients and the diagnosis and they are the ones following up with the patient and communicating with them their diagnosis, give them choices of therapy, increase their awareness of the disease and follow up" HCPI 12.*

- Duration of care process

The process of care which the patient has to go through within the primary healthcare setting is sometimes perceived as a long one from both the provider and patients' perspectives alike.

> *"So the process here if he [patient] came to the center, he needs to take an appointment first over the phone, or he has to come to the reception to take an appointment, then he will come to take the vital signs and then wait to see the physician. Then, he will take an order for the laboratory to take a blood sample, then he will have to wait for the results and then come back to the physician to make an order for the pharmacy. Then, he will come to the pharmacy and then wait for his turn and wait for maybe 30 minutes to one hour to collect his medications .. it's a very long process so if I were the patient I would not even bother to come" HCPI 1.*

Due to the time required to go through the entire process of care; some patients would skip seeing the care providers and go directly to collect the medications. Therefore, may not receive the necessary education of treatment plan.

> *"There are patients who come here and say that I don't want any blood tests. I just want you to write me the medications" HCPI 7.*

Some patients would seek care from the private sector such as hospitals and clinic due to the long waiting time. This mainly happens in patients who have private insurance. This can indirectly influence medication adherence.

> *"Health center coming waiting like that .. I go private hospital ..I feel private hospitals you go and finish very fast .." PI 3.*

- The use of treatment guidelines in managing diabetes

Guidelines for managing diabetes are accessible for healthcare providers through the intranet of the center. In addition, continuing education sessions and documents as well as guidelines updates are sent via email followed by multiple choice questions. Despite the availability of these resources, not all healthcare providers are following the same guidelines in managing diabetes. Although this factor may not directly result in patient's nonadherence; it reflects on the differences in treatment regimens observed from one patient to the other.

> *"The guideline is available on the system .. But most of the physicians don't check it .. They don't see it .. When to give statin, when to give aspirin .. There are differences in perspectives" HCPI 16.*

"You have a varying degree of practice and experience. Some doctors are not competent in diagnosing diabetes and not informed about guidelines, and some don't even follow guidelines in managing their patients. You can become deskilled quickly if you are not following the right approaches. The thing is that patient comes asymptomatic, and they ask for a full checkup, and the doctors diagnose them with diabetes based on one test only, when guidelines recommend two tests for asymptomatic patients and one test if the patient presents with symptoms.. You don't know from which guidelines they are doing this. When doctors diagnose based on one test, they ruined it for the patient because you need a second test to confirm and if the patient is already on medication that's it, the HbA1c levels will be useless. Adherence to guidelines is a problem" HCPI 12.

Some providers rely on their experience which was originally based on guidelines. However, they perceive that the current guidelines are not specific to the population in Qatar and that is why they do not rely on it but use their personal judgement.

"These guidelines were made for Caucasian people and not people who eat rice three times a day and bread and whatever…all these are killers for diabetes… You see strange things here like patients having HbA1c of 16. And when they start managing their diet it drops significantly in just a few months.. The guidelines don't have such values at all.. the guidelines tell you that medications would lower the levels by fractions! Not from 16 to 8" HCPI 12.

"Let me tell you, scientifically there are no guidelines in diabetes .. In the management of diabetes .. because of the good .. the very good guideline in diabetes .. tailor your guideline on your patient so no fixed guideline in diabetes" HCPI 14.

- Documentation of patient information

There is a clear variation in the quality of documenting information between one provider and the other. The system itself does not indicate mandatory fields for the provider to fill and is open for the reporter's convenience. This problem highly affects the patient management from one provider to the other. In addition to poor documentation, some providers believe that whatever is being documented is not actually read by others, but rather done for the purpose of just documenting and following the policy.

"Documentation is also an issue .. For me, I don't document everything, but I document what is relevant in the clinic.. The plan needs to be there, so we know what was done and what the doctor wants to do.. This is really a shame because I have seen patients whom I'm sure they have cancer and you know I order labs and all, but on their next visit they are only prescribed things like iron because apparently, the patient has anemia. Doctors don't check what others have written to know what is really the plan and at the same time I cannot step on anybody's toes and ask them to document and read" HCPI 12.

"I think documentation side is very poor here, to be honest .. People don't document the full story .. which needs a lot of improvement especially in changing the medications .. with the chronic disease why they change from one medication to another one .. was it a patient problem? .. Like you know the patient did not like it? having side effect? or it was physician choice to try this one? .. and most of the time the notes are blank .." HCPI 13.

- Feedback system within the healthcare center

The healthcare providers are the ones directly involved in managing the patients care and the ones applying the policies and regulations stipulated by the management of the primary healthcare setting. These providers come from various countries and have diverse experiences which can add value to the practice in the primary care. It is of paramount importance to understand their views on how to improve the system further, and also to identify the problems they face in their practice in order to improve. Despite this, a good feedback system which would allow the providers to speak freely and comfortably is lacking in this setting.

"Another thing is that no one here is allowed to give any input into the system which is a shame, because we are the ones seeing the patients and we come from different backgrounds and different educational systems so at an organizational level things need to be fixed… There are these occasional meetings that they do here which I stopped attending because it's in Arabic and I can't speak the language, and at the same time things

turn out really intense, and people are not comfortable with each other"

HCPI 12.

4.2.6. *Summary of qualitative findings*

Figure 16 summarizes the different factors that can contribute to medication nonadherence.
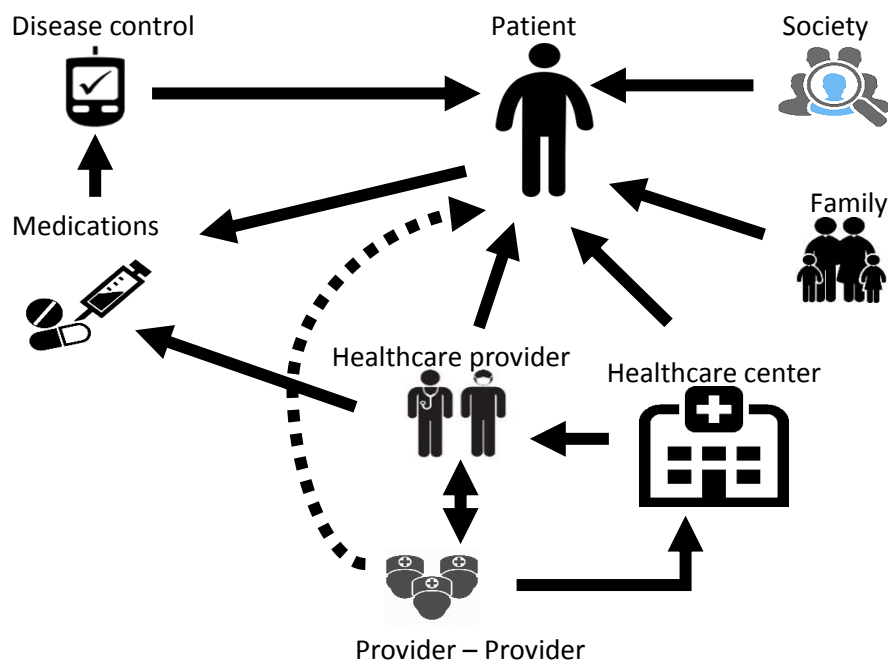

Figure 16: Barriers to medication adherence identified in uncontrolled diabetes in primary healthcare centers in Qatar – patients' and providers' perspectives

CHAPTER 5: DISCUSSION AND CONCLUSION

5.1. Introduction

Medication adherence is an important determinant of treatment success for any disease condition. The literature has unequivocally documented poor adherence to medications in chronic diseases including diabetes (36, 92). Diabetes and its complications are highly burdensome (1, 3). Therefore, it is very important to keep the blood glucose under control. Previous unpublished studies conducted in Qatar have found high prevalence of uncontrolled diabetes in the primary care setting. The general assumption and reason for uncontrolled diabetes has always been that patients may not be taking their medications as prescribed. To improve medication-taking behavior, it is important to understand why nonadherence occurs. It is therefore imperative to investigate medication adherence and its associated barriers among patients with uncontrolled diabetes. Nevertheless, barriers to medication adherence identified in one country or region may not necessarily be the same as those in another country or region due to environmental, socio-economic, and cultural differences across countries. This project was therefore conducted to gain a better understanding of the barriers to medication adherence in patients with uncontrolled diabetes from the context of Qatar. To date, this is the first mixed-method study conducted in Qatar and within the MENA region, to investigate barriers to medication adherence in uncontrolled diabetes from both patients' and healthcare providers' perspectives. The project was accordingly designed to address the following primary question: What are the barriers to medication adherence in patients with uncontrolled diabetes attending primary healthcare centers in Qatar?

5.2. Adherence Level

Diabetes management involves three main components: medications, diet, and physical activity (66, 93). Nonadherence to these components can lead to high or uncontrolled blood glucose levels. This study focused only on one aspect which was medication nonadherence. Medication nonadherence represents a failure in transferring the benefits of the medications to the individual's health improvement (37). The findings of this study revealed that around 74% of patients with uncontrolled diabetes were nonadherent to drug therapy. On the other hand, an unpublished study conducted in Qatar indicated that 86% of patients with diabetes are uncontrolled, therefore, it can be postulated that 64% of all patients with diabetes are nonadherent. The remaining 26% of patients with uncontrolled diabetes who reported adherence to drug therapy can have other factors such as dietary indiscretion or lack of treatment optimization contributing to their uncontrolled blood glucose levels (66, 93). The very high percentage of nonadherence found in this study further emphasizes the magnitude of the problem, especially that significantly more diabetes complications were observed in the nonadherent group as compared to the adherent group. It has already been demonstrated in the literature that medication nonadherence leads to uncontrolled diabetes and contributes to diabetes-related complications (2, 8-12). The nonadherence rate found in this study is much higher than that reported from neighboring countries such as Saudi Arabia and the United Arab Emirates which indicated nonadherence rates of 43% and 40%, respectively (94, 95). The lower adherence rate in these countries can be explained by the inclusion of all patients with diabetes regardless of disease control (i.e. both controlled and uncontrolled patients).

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5.3. Barriers to Medication Adherence

Several important barriers to medication adherence were identified from the qualitative and quantitative analyses in this study. Studies investigating medication adherence generally identified many patient-related aspects and linked some sociodemographic characteristics to nonadherence (15, 18, 19, 42-47, 92). Similarly, certain sociodemographic characteristics were identified to play a role in medication nonadherence among this cohort of patients with uncontrolled diabetes. Age as a variable did not differ between adherent and nonadherent patients. However, a significantly higher level of nonadherence (higher adherence score) was noted among patients who were less than 65 years old. This finding was interestingly different from what was found in the qualitative interviews whereby healthcare providers indicated that older patients as compared to the younger ones are less adherent to drug therapy due to forgetfulness and polypharmacy. The qualitative findings are consistent with *Rolnick et al.* who conducted a study examining patients' characteristics and their influence on medication adherence and found the odds of being nonadherent increasing with older age (96). Nonetheless, one provider indicated that younger patients are more likely to experiment in terms of using traditional medicine. Moreover, the younger individuals represent the working force; therefore, the influence of working conditions may be the factor influencing their adherence rather than the age itself. Hence, this is a case of interaction between the age and busy working condition. It is worthwhile to note that the majority of studies conducted within the MENA region did not find any significant influence of age as a variable on medication adherence (97-104).

The majority of the reported literature investigated employment status and linked it to medication adherence (52, 63, 66, 68, 95, 98, 100, 102, 105-107). Although in the present study, employment status did not statistically differ between the adherent and the nonadherent patients quantitatively, qualitative interviews indicated that working conditions, rather than status, can highly contribute to the appropriate use of medications. Working conditions such as traveling and prolonged working hours, in particular, were mentioned to be problematic. This finding emphasizes the importance of enquiring about the working conditions of patients with diabetes and identifies how it can contribute to medication adherence rather than just associating employment status alone to medication adherence.

When talking about work or occupation, income and expenses come into perspective. It is well known that patients who cannot afford the medications will less likely be adherent (15, 63, 92, 95, 108). Although the majority of participants indicated that medications are quite affordable, particularly that health insurance is provided to almost all residents in Qatar, there were few patients who still found medications to be expensive due to their small income. Those patients noted that the cost of medications represents a high proportion of their living expenses. The cost of medications and health services was noted as a barrier to medication adherence in studies conducted in Egypt and the United Arab Emirates, both of which indicated a negative influence of cost on medication adherence (95, 108). Nonetheless, the availability of social support within the primary healthcare setting in Qatar that primarily targets those who cannot afford the medications can help in reducing the burden of this barrier.

Many of the adherent patients were living with family as compared to nonadherent

patients suggesting that family support can positively contribute to patient's adherence to therapy. Several studies indicated that family support can positively contribute to medication adherence in diabetes, one of which is a study published by the American Diabetes Association (109). This study indicated that patient's perception of family members performing diabetes-related supportive behavior was associated with better medication adherence (109). This corroborates with the qualitative interviews in which many patients indicated that family members would remind them of their dose, give them the medication doses themselves, and take care of their diet management. Nonetheless, an interesting notion in patients with diabetes, particularly those on insulin, was that they were willing to conceal their disease from their loved ones for fear of being stigmatized. Hiding such information means the patient is not taking the medication in front of the family members, therefore, not taking the medications as prescribed. In fact, no previous study has reported that patients with diabetes would withhold their diabetes diagnosis from their spouses as found in the present study. This further emphasizes the importance of family support and the need for family involvement in the management and care of the patient with diabetes.

The fear of being rejected or stigmatized - by family members or the public - stems from the society's misconceptions about and stereotyping of diabetes. Patients indicated that they do not like to take medications in public because they are worried about being discriminated, a behavior that is common among patients taking insulin (46, 110). Therefore, patients resort to taking their medications while hiding away from other people or, in some instances, not taking them at all. This behavior is also reflected in quantitative data where "inconvenience" as a barrier was reported higher in the nonadherent group.

The study findings showed that the majority of the patients were not on insulin despite their uncontrolled diabetes. Healthcare providers progressively added medications to patients with uncontrolled diabetes. Both triple and quadruple therapies were commonly provided to the patients, while they still remained uncontrolled. This can be explained by the high rate of psychological insulin resistance (i.e. reluctance of patients to accept insulin) observed in many patients and attested by healthcare providers in this study (111). *Brod et al.* and *Snoek* both indicated that social stigma and the misconceptions about insulin can highly affect patients' acceptance of the medication as well (112, 113). Qualitative data revealed that insulin is quite problematic for the patients to accept due to the social stigma and fear associated with side effects and self-injection. Similar findings have been reported by other studies (47, 66, 111, 113, 114). This reemphasizes the need for educating the society and not only the patients about insulin. Recently, the US Food and Drug Administration (FDA) approved insulin inhalation which is not yet available in the primary healthcare centers in Qatar (115). It is however unclear whether this new route of administration will mitigate the fear of insulin injection and psychological insulin resistance in general. Further studies are needed to investigate the impact of this new insulin product on adherence and the psychological resistance.

The society, culture, and beliefs direct patients towards the use of traditional and complementary medicine or natural remedies (15, 47). Surprisingly, this factor was not restricted to certain cultures or ethnicities as expected, but was found to be a common phenomenon in patients from different countries including Qatari nationals. Participants in this study tried numerous products such as cinnamon, dried okra, herbs from Thailand, natural products from Sudan, Sri Lanka and others. A study conducted in Saudi Arabia

indicated that 24.6% of diabetic patients use herbal products as well (116). While in the quantitative phase of this study, 36.5% indicated that they use traditional medicines in managing diabetes. These high percentages indicate the need for real assessment of patients' beliefs and behaviors in relation to the use of traditional medicine. Patients seek these products in belief of their ancestors and in the hope of being completely cured of diabetes (47). At the same time, some patients believe that these traditional remedies are more effective and have fewer side effects than modern or orthodox medicines (15, 47). Nonetheless, the literature indicated that the effectiveness of Ayurveda herbs in diabetes control is inconclusive and most of them are ineffective (117, 118).

It was intriguing to find that patients with diabetes can invite their counterparts with the same disease to share their medications with the belief that theirs is more effective in managing diabetes. To our knowledge, this finding is unique since no previous studies have reported similar findings about medications sharing in diabetic patients. It is well known that diabetes is a chronic condition which requires lifelong management and medications to maintain glucose levels within an acceptable range. Qualitative data reflected an interesting perception with regards to the effectiveness of medications whereby patients believe that the pharmaceutical industry is not making efforts to cure diabetes, but rather makes the medications a necessity to sustain life, and a source for making profit by the manufacturers. Such beliefs and perceptions are highly emphasized by the media which always reflects on the pharmaceutical profit gained from chronic disease medications such as those used for diabetes (119, 120). This notion is somewhat reflected in the quantitative data where the item "believe that the medication prescribed is not helpful" was the most frequently reported barrier by those with the highest nonadherence level and appears to be

consistent with findings from Palestine and United Arab Emirates (103, 121-123).

Although studies reflected on the improvement in adherence, patient satisfaction and convenience with the use of insulin pen (124, 125), some patients perceive that this "new" insulin delivery device is ineffective as compared to the traditional insulin vials. Such patients request the prescription of vials instead of pens, which is surprising especially given the ease of administration and convenience of the pens as compared to the vials (124, 125). However, healthcare providers indicated that these patients are very few in number as compared to those using insulin pen.

Another interesting finding was that a significant proportion of patients taking sitagliptin were nonadherent. This finding is not consistent with a previous study which reports that patients are more adherent to sitagliptin than they are to sulfonylureas (126). Qualitative data, however, reflected what is found in the literature and showed that patients usually discontinue metformin due to gastrointestinal side effects and stop insulin due to hypoglycemia (12, 99, 101, 108, 123). Therefore, the significant difference observed in quantitative data for sitagliptin deserves further investigations to identify the reasons behind it.

Unlike other studies (95, 102, 104, 107, 121, 122, 127), the number of pills per day or polypharmacy did not significantly influence medication adherence in the present study. However, it was interesting to note that patients would try to reduce the burden of medications through splitting their medication doses throughout the day. Some medications like glimepiride are available in a strength of 2mg in the primary health centers; therefore, when the doctor prescribes 6mg or 8mg, the patient will be asked to take three or four tablets at once. The increased pill burden causes the patient to take half the

dose in the morning and the rest in the evening. Consequently, the desired therapeutic concentration of the drug is not achieved, and the patient would remain uncontrolled.

Although changing the dose of medications based on diet is sometimes considered appropriate in diabetes, it is usually recommended in patients with type 1 diabetes who are on rapid acting insulin and not usually in patients with type 2 diabetes who are on oral medications with or without long-acting insulin (128). At the same time, the patients changed their medication doses according to what they deem appropriate and in some instances reported experiencing adverse drug events such as hypoglycemia. This could be due to lack of education and counseling in regards to dose adjustments. Also, patients do not commonly inform their healthcare providers about these changes which can highly influence treatment success. One reason for concealing information is the patient-provider relationship and trust (15, 129). At the same time patients are passively receiving information rather than being part of the decision making process (129). Moreover, the limited patient-provider interaction time can also contribute to lack of disclosing information as time is not enough to examine the patient, provide information and listen to their illness story (15).

When the patient does not have adequate information about the disease and its management, they will likely not be as adherent as they should be, particularly if they do not know the risks and benefits of being on the medications (46, 95, 97, 130). Quantitative data showed that 11% of the patients were not provided with adequate information by the healthcare providers. This concurs with the qualitative data whereby many patients were not aware of what diabetes is and how their medications could help them maintain glucose levels within normal range. One major factor contributing to patients' lack of information

is the limited use of medication reconciliation. Several studies have demonstrated the positive influence of pharmacist in improving medication adherence (78-80, 131). Yet, the medication reconciliation service which is done by the pharmacists in the healthcare centers is highly underutilized.

The American Diabetes Association periodically publishes standards of medical care in diabetes which recommend performing HbA1c testing twice a year for patients with controlled levels of HbA1c, while patients who are uncontrolled must be monitored more frequency (every 3 months) (132). One major barrier identified in this study was the poor follow-up in the primary healthcare centers. Many of the patients interviewed were visiting the centers for refilling their medications, while their records clearly indicated uncontrolled blood glucose. The usual practice in this setting is that patients are scheduled for follow-up appointment every four to six months, and if they experience any issue with their medications in between the appointments, it may not be addressed until their next follow-up appointment. *Odegard et al*. indicated that inadequate follow-up could highly contribute to medication nonadherence (18). It is highly risky to delay follow-up visits especially knowing that persistence to medications drops dramatically within the first six months of therapy (36). At the same time, these patients are at high risk of experiencing complications since they are uncontrolled. Healthcare providers indicated that the prolonged follow-up schedule is also a problem and a potential barrier to medication adherence. This barrier highly contributes to medication nonadherence, especially that patients would seek care elsewhere during the waiting period as reported by some of the participating patients in this study. Seeing different physicians for diabetes in different settings could mean that the

patient's medical record is split, and so is the care plan, which again, can contribute to patient's confusion and nonadherence to therapy.

Factors such as interprofessional collaboration between the healthcare providers, appropriate use of guidelines, proper documentation of care, and workload could indirectly influence patients' management and ultimately medication adherence (15, 133, 134). Therefore, it is imperative to address these factors and consider them when developing intervention strategies. Figure 17 summarizes how different organizational factors and patient's lack of information can contribute to medication nonadherence.
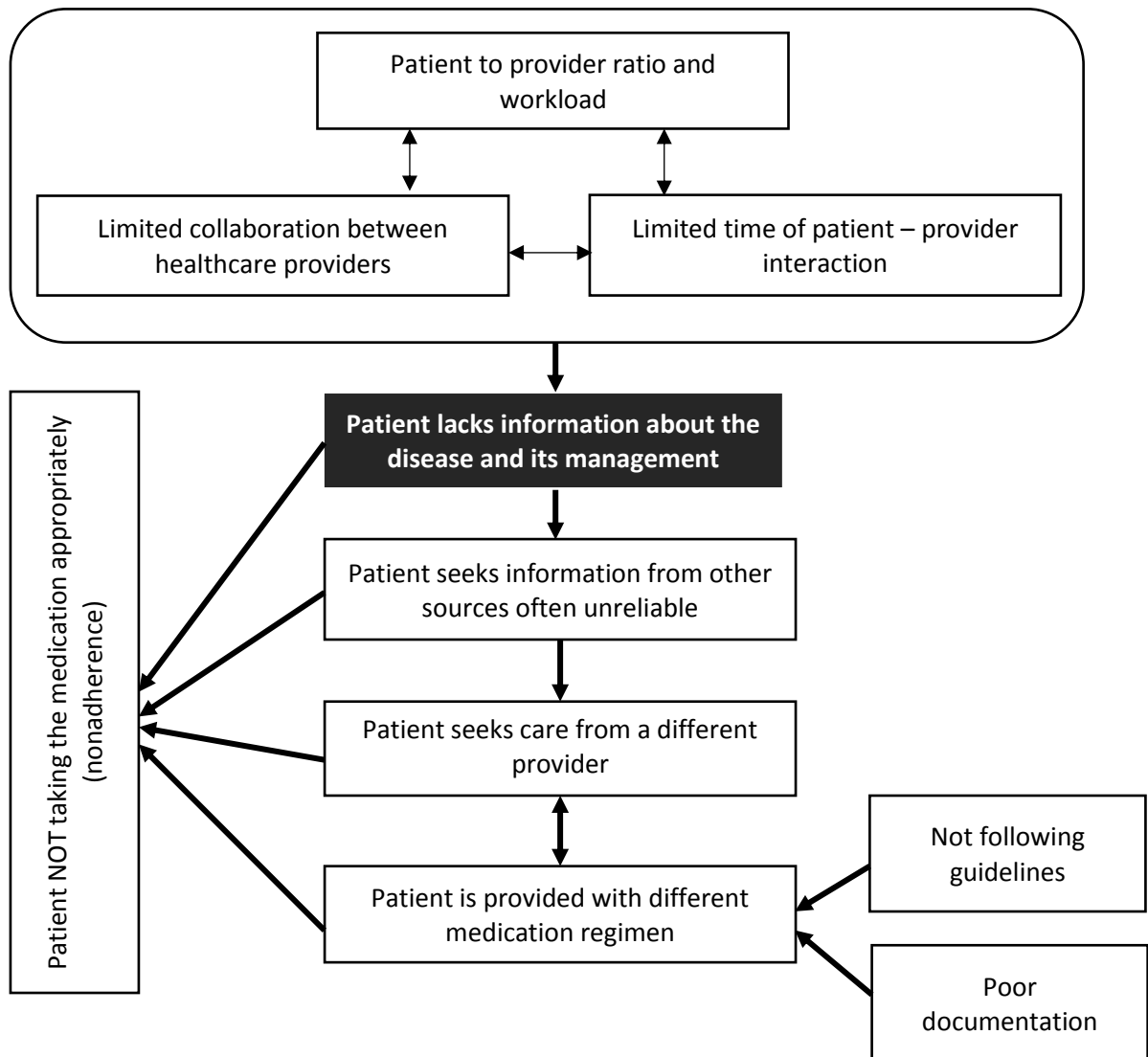
Figure 17: Organizational factors and their influence on medication adherence

5.4. Matching the Barriers to Medication Adherence with the Conceptual Framework Model

Section 2.5. of this thesis covered the development of the conceptual framework model for medication adherence in diabetes. The barriers to medication adherence identified within this project were matched with the conceptual framework model as presented in Figure 18.

Barriers that are highlighted in red within the model above are ones which were not initially identified from the literature review. In terms of patient-related factors, working conditions rather than working status appeared to influence medication adherence, while for medication-related factors, taking sitagliptin as compared to other diabetes medications such as metformin was more common in nonadherent patients. This factor was not justifiable within the scope of this project and requires further studies to confirm and understand why nonadherence was significantly higher among those on sitagliptin.

Investigating healthcare provider-related factors revealed that provider-provider interaction can also indirectly influence medication adherence. This is in terms of interprofessional collaboration and role clarification, as well as the provision of care to the same patient by more than one physician.

On the other hand, system-related factors indicated that documentation, guidelines use and availability, as well as process duration all influence medication adherence indirectly. In general, having a feedback system is also important for continuous improvement and addressing any barriers to medication adherence and patient care outcomes.
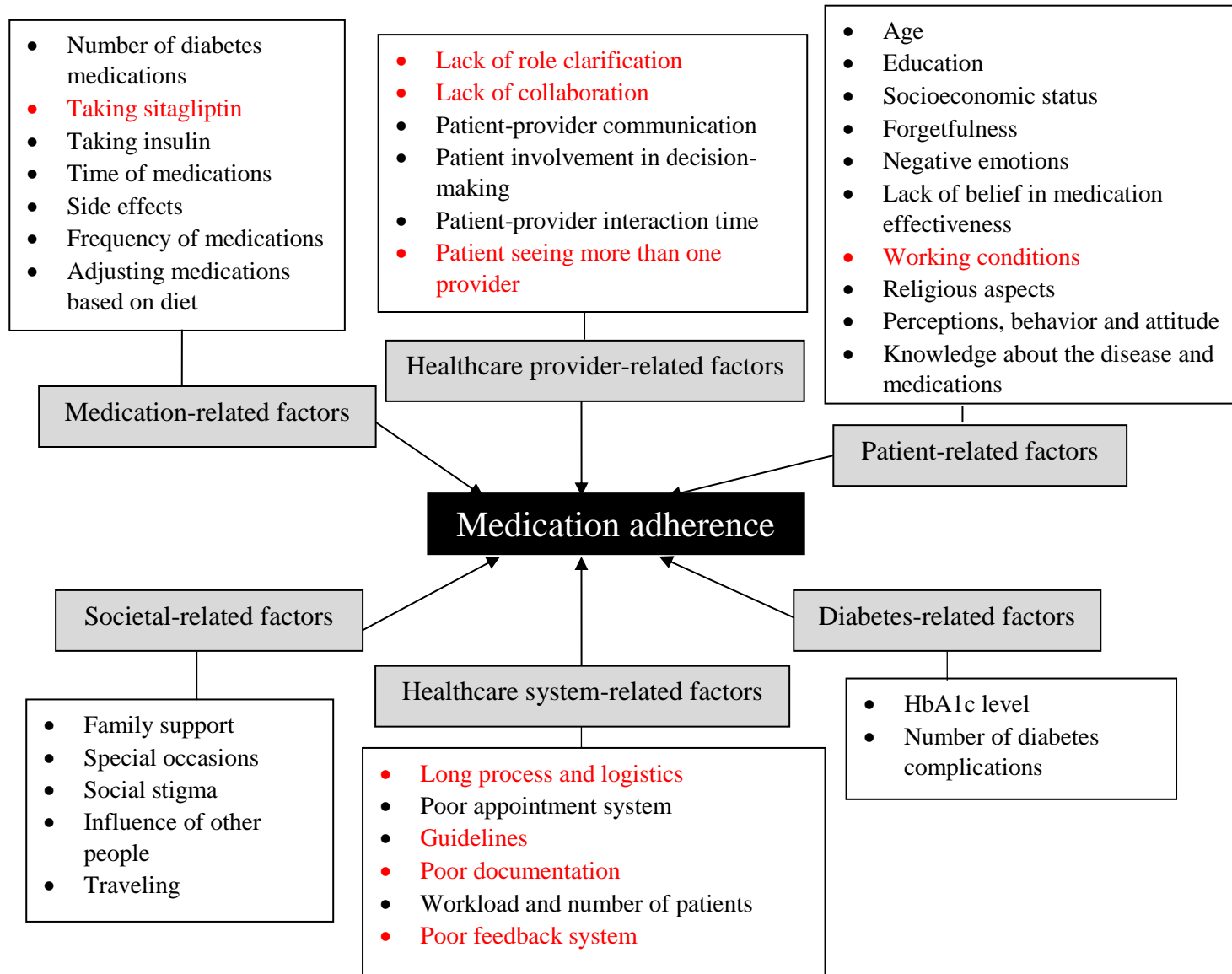
Figure 18: Matching the barriers to medication adherence with the conceptual model

5.5. Recommendations to Improve Medication Adherence

The identification of the barriers to medication adherence alone is insufficient in addressing the problem. On the other hand, there is no solution or strategy to overcome all the barriers medication adherence at once. Although numerous strategies and interventions aiming at improving medication adherence have been published, the best interventions are yet to be determined (31, 131). It was interesting to identify some potential solutions from the participant's perspective through this research. Many of the participant-identified interventions in this study have previously been reported in the literature (31, 78, 79, 131, 135-139). This section covers the suggested interventions by the participants in addition to the researchers' perspective and ends with a summary of all barriers and possible interventions.

As previously highlighted, pharmacists play an important role in addressing medication adherence (78-80, 131). Many patients were not referred to the pharmacist for medication reconciliation despite the clear need for it. Therefore, guidelines and criteria on patient referral for medication reconciliation should be developed. In addition, the scope of practice and the role of pharmacist should expand to allow them to perform medication reconciliation without the need for physician's referral. A reconciliation session should be structured and focused on patient's perceptions and fears that were identified in this study as well as the patient-initiated changes such as adjusting the medications according to their diet. One interesting suggestion was the use of videos for educating patients (e.g. to show the negative consequences of diabetes such as complications). Such videos can include information about what is diabetes, what are the medications and how they help patients

achieve positive outcomes, and what would happen if diabetes is uncontrolled. Such imagery will reinforce the patient's information (140). Surprisingly, no recent studies have investigated the use of interactive videos in educating patients with diabetes and its influence on patient's understanding of the disease and treatment plan; indicating the need for such studies.

Healthcare providers need to be aware of the needs to tailor health information to the level of patient's understanding and health literacy level, given the varying levels of education or literacy, and languages among patients (15, 141). Diabetes is a complex chronic disease condition that requires a high level of patient involvement including reading, understanding, and acting on complex health information and medication regimens as well as consenting to invasive investigations and monitoring of outcomes (142). In the studied sample, about 7% was completely illiterate and much higher proportion may have limited or poor health literacy. These individuals may not be able to read medication labels and other health information. Therefore, visual instructions and other strategies to enhance communication such as pictograms and teach-back method should be used for those individuals (143). Pictograms have demonstrated a positive influence on medication adherence (143, 144). Nonetheless, pictograms must be tested in the targeted population (i.e. user testing) prior to their application in practice, to ensure they are correctly comprehended by the patients (145).

The two main languages spoken in Qatar are Arabic and English. Nevertheless, many expatriate healthcare providers can only speak English. One provider suggested introducing Arabic courses during the orientation period of new hires which will

significantly help them when managing patients who speak Arabic. Moreover, a significant portion of the immigrant workforce in Qatar is from India, Nepal, Bangladesh, Sri Lanka and others (146). Many of these workers may neither speak English nor Arabic which significantly impacts patient-provider interactions and communication. Therefore, the use of voice-to-voice translation software, which is now readily available, can considerably reduce the problem of language barrier (147).

The appointment system in the primary healthcare setting needs significant attention as well. The follow-up visits need to be convenient and efficient in order to improve medication adherence and ultimately healthcare outcomes (36). Criteria needs to be set for which patients should be scheduled later and which should be scheduled earlier. At the same time, patient should be advised about the means of reaching the healthcare provider if the need to do so arises. One good intervention is creating interactive online platforms for the patients where they can receive answers to their inquiries in a timely manner and at the same time from a reliable source. In fact, previous studies have shown that online platforms and electronic health tools have a promising outcome in terms of improving medication adherence, patients' knowledge and satisfaction (148-150). Therefore, such a platform can be designed and used in Qatar for patients with diabetes. This can be in the form of informal care technology using cloud-based systems.

Similar to what is well-documented in the literature (63, 66-68, 71), the most commonly reported barrier to medication adherence was forgetfulness. Interventions targeting this barrier are numerous such as mobile phone application reminders, SMS text messages, and incorporating the medication into daily routine (135, 136). Many mobile

applications are available for free and can easily be set up by the patients to remind them of their medication doses (151).

As indicated by some providers, there is a clear need to upscale the health workforce in primary care setting in Qatar by recruiting more healthcare providers. Currently, the primary healthcare centers are increasing in number in response to increasing population and increasing demand for healthcare services (84). Nonetheless, increasing the number of providers within each center is highly needed and will significantly help in reducing the burden and costs associated with diabetes management.

The use of clinical practice guidelines is another problem highlighted by the healthcare providers, where they pointed that the diabetes guidelines available and used in their setting are not specific to the population of Qatar. Therefore, creating evidence-based population-specific guidelines is warranted. These guidelines should include a section about the process of care for patients who refuse taking insulin, thereby creating a standard of care amongst all the providers across primary care centers. This will also minimize the problem of huge treatment discrepancies when the patient seeks care from different healthcare providers.

Another factor that indirectly influences adherence is poor documentation of care. For example, the documentation system requires improvement by making certain fields mandatory to fill (such as the provider's plan for the patient and the patient's adherence level). Some practitioners tend to repeat general patient information such as age, gender, and past medical history, most of which are already available in the system. Therefore, documentation should focus on what is really needed rather than being repetitive. Some

new fields need to be introduced in the electronic health record system such as the patient's socioeconomic status which could guide the selection of medications for a particular patient. Similarly, the patient's religious, spiritual, or cultural obligations such as dietary restrictions or fasting obligations should also be documented in the system. This will remind the provider to adjust a patient's treatment plan and make it more individualized and patient-centered. Table 18 summarizes the identified and suggested interventions that can address the identified barriers.

Table 18: Suggested interventions to tackle the identified barriers to medication adherence among patients with diabetes in primary care setting in Qatar

Barrier	Intervention
Illiterate patients	• Validated pictograms • Teach-back method
Poor socioeconomic status of patients	• Documenting patient's socioeconomic status • Selecting cheaper alternative medications
Religious rituals of patients	• Documentation in the patient profile • Adjusting treatment plan accordingly
Patient forgetfulness	• Using pillbox • Reconciliation point: incorporating the medication into daily routine • Mobile phone applications
Social stigma	• Educating the general public to demystify stigma and misconceptions • Platform for the public to access information about diabetes and its management
Use of traditional medicine by the patient	• Reconciliation point: educating the patient about the importance of the medications and the risks of traditional medicines
Patient's beliefs and perceptions	• Medication reconciliation and therapy management
Patient's confusion about medications	• Using medication chart • Using pillbox
Lack of roles clarifications among providers	• Developing clear policies about the roles and duties of each profession • Role clarification through case discussions
Lack of referrals to other providers	• Role clarification through case discussions • Audit system • Setting criteria for patients referrals

Limited medication reconciliations	• Setting criteria for patient referrals • Allowing pharmacists to do reconciliation without physician's referral • Introducing clinical pharmacist in the NCD clinic
Long process duration	• Use of the waiting time for more education • Hiring more healthcare providers
Late appointments	• Setting criteria for late vs. early appointments • Hiring more healthcare providers
Lack of population-specific clinical practice guidelines	• Developing evidence-based population-specific guidelines
Nonadherence to clinical practice guidelines	• Conducting audits to check compliance with guidelines
Poor documentation of care	• Performing audits to check the quality of documentation • Setting mandatory fields in the system for the providers to fill
High workload and large number of patients	• Expanding workforce through employing more healthcare providers
Poor feedback system	• Allowing an efficient feedback system for continuous improvement
Language	• Introducing Arabic course during orientation periods of new recruits • Using translation software • Hiring interpreters
Caretaker	• Involving caretaker during patient counseling and education
Careless/lack of motivation	• Reconciliation point: emphasizing the importance of medications • Use of videos to show-case the complications of disease if left uncontrolled
Patient refusal of medications	• Medication reconciliation • Correcting misconceptions through public campaigns • Developing guidelines for managing patients who refuse injections or have injection phobia
Patient self-adjust their dosing	• Medication reconciliation
Number of pills	• Using fixed-dose combination medications • Using long-acting medications
Side effects	• Medication reconciliation
Patient's lack of information	• Medication reconciliation • Online platform/website • Brochures
Traveling to other/home countries	• Medication reconciliation

5.6. Strengths and Limitations of the Study

To our knowledge, this is the first study which addresses medication adherence in uncontrolled diabetes using a mixed-method approach. The findings of this study highlight the complexity of medication adherence and the influencing factors that contribute to nonadherence. One of the main strengths of this study is the robustness of the methodology used which allowed addressing the study objectives comprehensively.

The two methods (quantitative and qualitative) were complementary to each other which reflected on the breadth of the barriers identified. The quantitative data allowed for understanding the characteristics of patients with uncontrolled diabetes and the comparison between adherent and non-adherent groups, while the qualitative data provided an in-depth understanding of the patients' and healthcare providers' experiences.

To our knowledge, this is also the first study in the MENA region to involve healthcare providers' perspective on the subject of medication adherence. The interviews with the healthcare professionals who provide care to patients with diabetes further reaffirm and stress the fact that adherence is a multi-faceted problem.

Another important strength of the study is the identification of possible interventions and solutions from the participants' and not only from the researchers' perspectives which would reflect on the applicability of the interventions in real-world practice in Qatar.

The focus of the study on "patients with uncontrolled diabetes" is another strength of the study, since these are the patients at higher risk of developing complications and

therefore requiring more attention. Moreover, Qatar is currently investing in improving the care management in the primary healthcare sector. In fact, the Qatar Primary Healthcare Strategy was recently published emphasizing the importance of transforming care in this setting (152). Therefore, this project is in concert with the Primary Health Strategy goals and plays a significant role in supporting it.

The development of a holistic conceptual framework model adds so much value to the current knowledge about medication adherence in diabetes, as it summarizes all the evidence on the topic. This is a useful tool that can be used as the ground bases for diabetes medication adherence-related studies.

Despite these strengths, there are some important limitations that need to be acknowledged. First, the sample size was calculated based on the assumption that all patients with uncontrolled diabetes were non-adherent to their medications. However, the effect of such assumption on the study was minimized since there was 60% increase in recruitment over the required sample size. Nonetheless, there is still a limited generalizability of the quantitative results with this sample size and limited stings requiring the need for a larger scale study taking into consideration multiple primary healthcare centers and their population.

Second, the adherence measurement tool used in the study (ARMS-D) was translated into five most commonly spoken languages in the country, yet the psychometrics of the translated instrument were not determine due to time constraints. However, throughout the study, only the Arabic and English versions were used as the sample who consented to participate in the study could speak either or both languages.

Third, the method used to assess adherence level in patients was the self-reported questionnaire (ARMS-D), which subject the responses to social desirability bias. However, published literature has reported appreciable validity and reliability of this questionnaire as an adherence measurement tool (88). Unfortunately, other objective methods of assessing medication adherence such as proportion of days covered (PDC) and medication possession ratio (MPR) were not applied as the healthcare system does not clearly and reliably reflect the medication refill times.

Fourth, the quantitative results of the study can only be generalized to patients with diabetes who are uncontrolled and attending the specifically mentioned primary healthcare and not necessarily to those attending other settings such as secondary or tertiary level hospitals. Two healthcare centers may not be reflective of the entire population which has many expat laborers and people of low socioeconomic status.

Moreover, the study was conducted in Qatar; an oil-rich country, with reasonably advanced and far-reaching health services that does not represent most of the health environments world-wide. For example, medicines are available and affordable to most patients, and healthcare providers are accessible compared to what we find in many other countries worldwide. On the other hand, qualitative data are not usually generalizable, but provide a wealth of information that help in better conceptualizing the area studied and provides an insight into all the possible barriers to medication adherence.

The validity of the transcripts could not be checked with the participants for multiple reasons including time constraint, and at the same time, the contact information

of the participants were not sought. However, the coding process was conducted by two researchers to ensure reliability of the generated themes.

Finally, selection bias might have occurred as it was possible that those who turned up to refill their medications and follow-up appointments and agreed to participate in the current study are those who are more likely to be adherent to their medications. Additionally, patients who could neither speak English nor Arabic were excluded from participating in the qualitative interviews even if they fulfilled the other inclusion criteria. Patients who did not attend to their appointments and those who could not speak either languages might have important barriers and experiences which were not captured in this research.

5.7. Future Work and Recommendations

Section 5.4 has covered aspects of future work in relation to medication nonadherence in diabetes, particularly the interventions and strategies that can be applied in the primary healthcare setting to improve medication adherence among patients with diabetes. However, policymakers and managers shall take into consideration their population's characteristics. Over three-quarters of the patients in the current study were taking two or more medications for diabetes management; therefore, the researchers caution against the initiation of several adherence-improving-interventions at once as this will likely cause a significant increase in the incidences of hypoglycemia and other adverse events. If a patient is non-adherent while being prescribed three medications and suddenly starts taking all three together, they are more likely to experience adverse events.

Therefore, the researchers highly recommend that the interventions suggested in section 5.4. need to be prioritized based on the resources available and initiated in a stepwise approach with monitoring of potential adverse events at the same time.

In addition to the interventions listed in section 5.4., the researchers also recommend a larger scale study taking into consideration different healthcare settings (e.g. private sector, public sector, secondary care, and tertiary care) and including patients who cannot speak English or Arabic. Moreover, including the perspective of family members will add value to the current knowledge particularly that it is very common in the MENA region for family members to take care of their relatives and help them administer medications.

Finally, this study looked at only one aspect of patient-self management which is medication adherence. Therefore, future research should investigate other aspects such as diet management and physical activity, and the barriers associated with them. This would allow a better understanding of patients with uncontrolled diabetes in general.

5.8. Conclusion

This study contributed to the existing body of knowledge through an in-depth understanding of the barriers to medication adherence in patients with uncontrolled diabetes in Qatar. The study revealed that over 70% of the patients with uncontrolled diabetes were non-adherent to their medications. Barriers to medication adherence are very complex, multifactorial in nature, and require a lot of attention in order to be adequately

addressed. Results from this study indicate that there are six main players in the patient's behavior towards medications: the patients themselves, healthcare providers, healthcare system, the society, the disease, and medications. Many of the barriers identified in this study were directly related to patient's information and knowledge about the disease and its management. However, there were also barriers related to the society such as social stigma and lack of support. On the other hand, healthcare providers indicated some barriers relating to the patient-provider interaction as well as the provider-provider interaction all of which ultimately influence patient's medication adherence.

In relation to interventions, one main intervention that would address multiple barriers is the expansion of pharmacist role and the increase use of medication reconciliation services. Reconciliation and therapy management should focus on the gaps in patient's knowledge identified within this study. Generally, interventions addressing medication nonadherence are costly in terms of human and other resource requirements. Therefore, having specific interventions targeting pre-determined barriers and factors associated with medication nonadherence would result in the best use of resources and more efficient interventions. In addition to use of medication reconciliation, several interventions should be implemented to tackle medication nonadherence. However, interventions must be initiated in a stepwise approach to avoid risks of adverse drug events.

Finally, the findings of this study can potentially help reduce the economic burden of diabetes through providing a patient-specific counseling and interventions, thereby decreasing the morbidity and complications associated with diabetes. Moreover, future

research should target other aspects relating to uncontrolled diabetes such as diet management and identify the barriers associated with it.

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APPENDIX A

Questionnaire

Part A: Personal Characteristics

Instructions: Please answer all questions and put a check mark (✓) on the most appropriate answer.

Age: _____	Gender: ☐ Male ☐ Female
Nationality: ☐ Qatari ☐ Indian ☐ Nepali ☐ Filipino ☐ Egyptian ☐ Bangladeshi ☐ Sri Lankan ☐ Pakistani ☐ Sudanese ☐ Jordanian ☐ Palestinian ☐ Indonesian ☐ Iranian ☐ Other, specify: _____	Insurance: ☐ Governmental ☐ Private ☐ None ☐ Other, specify:_____
	Religion: ☐ Islam ☐ Christianity ☐ Buddhism ☐ Hindu ☐ Others, specify: _____
Weight:_____	Level of education: ☐ Primary education ☐ Secondary education ☐ High school education ☐ University level ☐ None, but can read and write ☐ None, cannot read and write
Height:_____	
Living situation: ☐ Alone ☐ With a family member(s) ☐ With other(s), please specify:	Employment status: ☐ Student ☐ Unemployed ☐ Retired ☐ Employed, specify job type: _____

Average medical cost per month (QR):	Average income per month:
☐ QR 0 – 100 ☐ QR 101 – 300 ☐ QR 301 – 500 ☐ QR 501 – 1,000 ☐ QR 1,001 – 2,000 ☐ QR 2,001 – 3,000 ☐ More than QR 3,000	☐ Not receiving any income ☐ Less than QR 1,000 ☐ QR 1,000 – 2,999 ☐ QR 3,000 – 4,999 ☐ QR 5,000 – 6,999 ☐ QR 7,000 – 9,999 ☐ QR 10,000 – 14,999 ☐ QR 15,000 – 19,999 ☐ QR 20,000 or more

Part B: Clinical Data

Instructions: Please answer the following questions based on your health condition and put a check mark (✓) on the most appropriate answer for each question.

Type of diabetes:
   ☐ Type 1
   ☐ Type 2
   ☐ Other:
_____

Number of all medications (including diabetes and other chronic diseases):
   ☐ 1
   ☐ 2
   ☐ 3
   ☐ 4
   ☐ 5
   ☐ Other, specify: _____

Treatment type:
   ☐ Pills
   ☐ Injection (e.g. Insulin)
   ☐ Pills + injection

Comorbidities (check all that apply):
   ☐ Cardiac disease
   ☐ Hypertension
   ☐ Hypercholesterolemia
   ☐ Lung disease
   ☐ Cancer
   ☐ Alzheimer
   ☐ Other, specify:
_____

Duration of diabetes (in years):

Number of diabetes medications:
   ☐ 1
   ☐ 2
   ☐ 3
   ☐ 4
   ☐ 5
   ☐ Other, specify: _____

Diabetes-related complications (check all that apply):
   ☐ High sugar readings (> 250mg/dl or 13.9mmol/L) in past 12 months
   ☐ Very high sugar readings (> 600mg/dl or 33.0mmol/L) in past 12 months
   ☐ Eye damage
   ☐ Nerve damage
   ☐ Kidney damage
   ☐ Foot complications
   ☐ Amputation(s)
   ☐ Emergency visit(s) within 12 months
   ☐ Hospitalization(s) within 12 months
   ☐ Other, specify: _____

Current **Diabetes** Medications

Name	Indication (why do you take this medication)	Strength (what is written on the medication box)	Dose (how much you take)	Frequency (how many times you have to take it)	Start Date
eg: Panadol	Knee pain	500mg	Half tablet	Three times	1/1/2016

Part C: Adherence to Refills and Medication Scale – Diabetes (ARMS – D)

It is common for patients with diabetes to report missing doses of their medicines or take less than the amount prescribed from time to time. Some people find it hard to take their medicines, either because of cost, or they decide to skip doses or reduce the amount to avoid side effects or for other reasons. We are most interested in what you are actually doing. Don't worry about telling us that you don't take your medicine, or don't take it all the time. We need to know what is really happening for you, not what you think we want to hear. Remember all your answers are confidential and won't be shared with your doctor.

Instructions: Now we ask you how often you actually miss taking your diabetes medicines. If you are taking more than one diabetes medicine, please answer the questions by thinking about your daily experiences, on average, with all of the diabetes medicines you take, not just a certain medicine. There are no right or wrong answers. On a scale of 1 to 4 (1 being none of the time to 4 being all the time), please answer in relation to time approximation

How often do you:	None of the time	Some of the time	Most of the time	All the time
forget to take your diabetes medicine(s)?	1	2	3	4
decide not to take your diabetes medicine(s)?	1	2	3	4
forget to get your diabetes prescription(s) filled?	1	2	3	4
run out of your diabetes medicine(s)?	1	2	3	4
skip a dose of diabetes medicine(s) before you go to the doctor?	1	2	3	4

miss taking your diabetes medicine when you feel better?	1	2	3	4
miss taking your diabetes medicine when you feel sick?	1	2	3	4
miss taking your diabetes medicine(s) when you are careless?	1	2	3	4
forget to take your diabetes medicine(s) when you are supposed to take it more than once a day?	1	2	3	4
put off refilling your diabetes medicine(s) because they cost too much money?	1	2	3	4
plan ahead and refill your medicines before they run out?	1	2	3	4

Part D: Barriers to Diabetes Medication Adherence

Instructions: This section assesses factors associated with or barriers to medication adherence. Here we list some possible barriers to medication adherence. Please choose all the factors that can keep you from taking your diabetes medications as you should.
 (Choose all that apply)

☐ Time or schedule problems (e.g. taking your medicine(s) during work)

☐ Inconveniences (e.g. carrying medicine(s) with you, finding a place to take the medicine)

☐ Side effects of the medicine(s)

☐ Forget to take the medicine(s)

☐ Health problems (e.g. trouble seeing, shaky hands)

☐ Too painful to administer the medicine

☐ Too costly to buy the medicine

☐ Special occasions (e.g. on your birthday)

☐ Feeling depressed or other negative emotions (e.g. anger, frustration, denial)

☐ Do not believe the medication prescribed is helpful

☐ Interferes with your daily activities

☐ Having multiple diseases

☐ Taking many medications

☐ The regimen is too complicated to follow

☐ Taking the medicating multiple times a day

☐ Use of traditional medicine(s) (eg: herbs)

☐ Long diabetes duration

☐ Diabetes is too complicated to manage

☐ Healthcare provider is not very supportive

☐ I don't know why I am on diabetes medications

☐ Healthcare provider does not give me enough information

☐ Not understanding what the healthcare provider is telling me about the medicines

☐ Family is not very supportive

☐ Taking these medicine(s) is against my culture

☐ Having health insurance

☐ Other, please specify:

For Researcher's Use Only (from Medical Records)	
Code:	Date:
Patient's Characteristics	
Date of birth d d – m m – y y y y	Gender:　　☐Male　　☐ Female
Nationality:	Insurance:　　☐Governmental
Religion:	☐Private
Weight:	☐None
Height:	☐Other, specify:
Living situation: 　　☐ Alone 　　☐ With a family member(s) 　　☐ With other(s), please specify:	Level of education: 　　☐ Primary education 　　☐ Secondary education 　　☐ High school education 　　☐ University level 　　☐ None, but can read and write 　　☐ None, cannot read and write
Employment status: 　　☐ Student 　　☐ Unemployed 　　☐ Employed, (specify job type):	
Clinical Data	
Type of diabetes: 　　☐ Type 1 　　☐ Type 2 　　☐ Other (exclude)	Duration of diabetes (in years):
	Number of current diabetes medications:
	Number of all medications (including DM and other chronic diseases):

Treatment type:	Diabetes-related complications (check all that apply)
☐ Diet only ☐ Oral drugs ☐ Injectable ☐ Oral + injectable drugs	☐ History of DKA (in past 12 months) ☐ History of HHS (in past 12 months) ☐ Retinopathy ☐ Neuropathy ☐ Nephropathy ☐ Foot complications ☐ Amputation ☐ Emergency visit(s) within 12 months ☐ Hospitalization(s) within 12 months ☐ Other, specify:
Comorbidities (check all that apply): ☐ Cardiac disease ☐ Hypertension ☐ Hypercholesterolemia ☐ Lung disease ☐ Cancer (exclude) ☐ Alzheimer (exclude) ☐ Other, specify:	

Most Current Glucose Readings

Date:	HbA1c:	FBG:	RBG:
Date:	HbA1c:	FBG:	RBG:

Current Diabetes Medications

Name	Strength	Dose	Frequency	Start Date

Other Medications

Name	Indication	Strength	Dose	Frequency	Start Date

APPENDIX B

Interviewer's guide (Patients with Diabetes in Qatar)

The following will be the focus of the discussion during the patient interviews. The thematic questions will be used as prompts and would allow free expression of opinion from the participant.

Start
Welcome: Interviewer will welcome the participant   **General introduction:** The interviewer will introduce him/herself.   **Example**   "Thank you for being here today. My name is ___, a research investigator at Qatar University. The main purpose of this interview is to identify barriers to medication adherence in patients with diabetes like yourself and to explore the strategies that you think should be used to improve medication taking-behavior and adherence. We are very interested to hear your opinions and learn from your experiences regarding medication-taking and adherence… The interview is a method of learning from experience both positive and negative. We are not trying to achieve consensus; we are just gathering information to help us have an in-depth understanding of the context…"
Ground Rules
1- **We want you to do the talking. Talk freely; there is no right or wrong answers.**   2- **Try to reflect on your experiences with the diabetes medications**   3- **Whatever is mentioned within the room, will stay within the room and will not be linked back to you**   4- **We will tape record the discussion to capture everything you have to say, but we will not identify anyone by name in our report, you will remain anonymous. This is to help us not to miss anything important that you say and so that we revisit the information during transcribing if necessary. Tape records will be deleted once transcribed.**   5- **You may refuse to answer any question or withdraw from the study at anytime**   6- **We would appreciate if you could please turn off your mobile phone to avoid distractions during the session.**   7- **The duration of this interview is about 45 – 60 minutes.**
Participant's introduction

Ask participants to introduce themselves, their work and how long they have been in Doha for.
 Example:
    1. Can you tell me the story of your diabetes? When did it start? How are your levels?
                    ,

Introductory questions

1. What medications are you taking for diabetes?
    2. When did you start these medications?
    3. Have you had any difficulties in taking your medications as prescribed by your doctor?
                    .

Barriers to medication adherence
1. What do you understand about the role of medicines in the management of DM?   a. Prompt: Did your doctor explain how medicines should be taken

  b. Prompt: Do you think that you completely understand how meds should be taken

2. What barriers do you encounter in taking your medications for diabetes?
3. What about these factors:
  i. **Patient – related factors:**
   a. Demographics (gender, age, education, marital status, ethnicities, financial status)
   b. Psychological status (Stress, fear, motivation)
   c. Knowledge
   d. Perceptions/Beliefs
   e. Comorbidities
   f. Other (fasting, traveling, weekend, forgetfulness)
  ii. **Medication – related factors:** frequency, duration of therapy, polypharmacy, timing, side effects, complexity of treatment etc
    1. Why do you think it is important to take medicines as prescribed by physicians
    2. What do you do when you experience any side effects.
    3. Does the fear of side effects influence your decision for taking or not taking medications?
  iii. **Disease – related factors:** disease duration, complexity, low HbA1c, complications
  iv. **Provider – related factors:** support, inclusion in decision making, relationship, language, assumptions
  v. **Healthcare system – related factors:** cost, lack of guidelines, continuity of care, convenience
  vi. **Societal – related factors:** Social support, cultural beliefs, stigma

Some patients start by being adherent to therapy and then they become non-adherent or vice versa, what do you think are the reasons behind such changes in medication-taking behavior?

Strategies to improve adherence
• Based on the problems you told me about, how do you think we can improve? • What solutions do you think would work for you?

Concluding
Mrs/Mr. X, Do you have any additional comments related to medication adherence in diabetes or in general that you would like to share with us? Mrs./Mr. X, we have come to the end of the interview. Thank you very much for your time today and for your honest opinion and fruitful discussions. We greatly appreciate your support.

APPENDIX C

Interviewer's guide (Healthcare Providers)

The following will be the focus of the discussion during the interview. The thematic questions will be used as prompts and allowing free expression from interviewees Questions asked will be open ended.

Start
Welcome: Interviewer will welcome participants **General introduction :** The interviewer will introduce him/herself. **Objective:** State the objective of the study, ensure privacy and freedom of discussion **Example** "Thank you for your interest in sharing your experience. My name is __, a research investigator at Qatar University. The main aim of this interview is to identify barriers to medication adherence in patients with diabetes from your perspective as a healthcare provider and to explore potential solutions for enhancing medication adherence in this patients population. We are very interested to hear your opinions as healthcare providers and learn from your experiences...
Ground Rules
8- **We would like you to do the talking. Please talk freely; there is no right or wrong answers** 9- **Try to reflect on your experiences with patients with diabetes in Qatar.** 10- **Whatever is mentioned within the room, will stay within the room and will not be linked back to you.** 11- **We will tape record the discussion to capture everything you have to say, but we will not identify anyone by name in our report, you will remain anonymous. Tape records will be deleted once transcribed.** 12- **You have the freedom to refuse to answer any question or stop the interview at anytime.** 13- **We would appreciate if you could please turn off your mobiles to avoid distractions during the session.** 14- **The duration of this interview is about 45 – 60 minutes.**
Participant introduction
Ask interviewee to introduce themselves, their work and how long they have been in Doha for **Example:** Can you please introduce yourself? How long have you been practicing ___ in Qatar?
General Introductory Questions
1. Can you tell me what the term "medication adherence" means to you? 2. How would you label your patients as non-adherent? 3. In your opinion is medication non-adherence a big problem among diabetic patients in Qatar? 4. Generally speaking, what percentage the patients you encounter in your practice would you say are adherent to their medications? 5. What are the questions generally asked by the patients about their mediations? And how do you respond?
Barriers to medication adherence

1. What do you think are the barriers to medication adherence in patients with diabetes that you see in your current practice in Qatar?
2. Why do you think these are barriers to medication adherence?
   a. Probing: How do you think ___(factor)___ affects medication adherence?
   b. Probing: Can you give example from your practice where you noticed barriers to medication adherence?
   - **Patient – related factors:**
     - Demographics (gender, age, education, marital status, ethnicities, financial status)
     - Psychological status (Stress, fear, motivation)
     - Knowledge
     - Perceptions/Beliefs
     - Comorbidities
     - Other (fasting, traveling, weekend, forgetfulness)
   - **Medication – related factors:** frequency, duration of therapy, polypharmacy, timing, side effects, complexity of treatment etc
   - **Disease – related factors:** disease duration, complexity, low HbA1c, complications
   - **Provider – related factors:** support, inclusion in decision making, relationship, language, assumptions
   - **Healthcare system – related factors:** cost, lack of guidelines, continuity of care, convenience
   - **Societal – related factors:** Social support, cultural beliefs, stigma
3. Some patients start by being adherent to therapy and then they become non-adherent or vice versa, what do you think are the reasons behind such changes in medication-taking behavior?

Strategies to improve adherence

4. How do you deal with nonadherence in your clinical practice?
5. From your experience what has worked/not worked?
6. Are there any strategies used to address medication adherence in patients with diabetes in your practice in Qatar? What are these strategies?
7. How effective do you think these strategies are?
8. What changes do you propose from your perspective that should be applied to improve these already existing strategies (if any)?
9. What other solutions do you propose for improving medication adherence in patients with diabetes in Qatar?

Concluding

1. Do you have any additional comments related to medication adherence in diabetes or in general that you would like to share?
2. Thank you very much for your time today and for your honest opinion and fruitful discussions. We greatly appreciate your support.

APPENDIX D

مؤسسة الرعاية الصحية الأولية
PRIMARY HEALTH CARE CORPORATION

Primary Health Care Corporation
Clinical Affairs
Research Section
researchsection@phcc.gov.qa
Form RS/AF1

Research/Project/Study
Approval Notice Form

Title of the Project:	Barriers to medication adherence in patients with uncontrolled diabetes in Primary Health Care setting in Qatar: A mixed method study	
Reference No:	**IEC: PHCC/IEC/16/04/013**	Date:09/06/2016
Principal Investigator:		
Name	Dr. Ahmed Awaisu	
Title	Principal Investigator	
Department/Organization	College of Pharmacy/ Qatar University	
Contact details	Tell: 6662 1268, Email: aawaisu@qu.edu.qa	

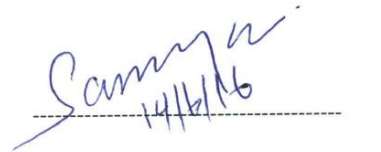| Required Information Checklist	Ref. No	Yes	No	N/A	Date
Research Proposal Submission Form signed and Completed		✓			
Research Proposal Supplementary Form Completed				✓	
HMC /WCMCQ IRB Approval Obtained, (or Previously HMC Research Committee Approval)				✓	
PHCC Research Committee Approval Obtained		✓			
Investigator agreement Form Signed		✓			
Other Ethics Committee Approval (Please specify) e.g. Qatar University		✓			
Informed Consent Form Copy Provided		✓			
Sponsors	none				

Dear Dr. Ahmed,

Having considered the ethical and logistical (site specific) issues relating to the above project, the PHCC Research Committee confirms that there are no objections to carrying out this project. Therefore the departments of Clinical Affairs and Operations give **approval** for it to commence. Please see the accompanying letter which sets out the **specific terms and conditions** of this approval that must be adhered to in carrying out the research.
We wish you every success in this endeavor.

Kind Regards,

on behalf
13/06/ 2016
Dr. Hanan Mujalli
Executive Director of Clinical Affairs

14/6/16
Dr. Samya Ahmad Al Abdulla
Executive Director of Operations

For more information: Researchsection@phcc.gov.qa

Our Ref: PHCC/IEC/16/04/013

9th June 2016

Dear Dr. Ahmed,

Final Opinion: Barriers to medication adherence in patients with uncontrolled diabetes in Primary Health Care setting in Qatar: A mixed method study

I write to confirm approval from the PHCC Research Committee at its last meeting on 30th May 2016 for you to carry out the above research study in PHCC Health Centers. This approval is granted under the terms for **Expedited from full research review** of the PHCC Research Committee which identifies that your request does not raise any material ethical issues (NMEI).
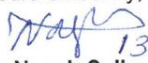
This Final Opinion follows further review by the Research Committee following your response to the Committee's request for further information and clarification. Approval is valid for the period: 9th June 2016 until 9th June 2017 subject to the following conditions: that

- You adhere to the principles of good research practice and ensure patient safety, privacy, confidentiality and data protection throughout the study
- You ensure the necessary logistical support is in place at the named Health Centres prior to commencement of the study.
- You ensure that participants are fully briefed on the nature and purpose of the study and what is expected of them, as part of the consent process
- You do not undertake other procedures and / or use patient materials or data outside of the scope of this present study, or for future use beyond this study.
- You agree to provide a progress report within **6 months** of the start and a final report at the end of the study or in the event that the study terminated early, an appropriate report.

This final opinion requires no further review as long as you fulfil all the requirements. However please note that this favourable opinion is applicable only in so far as you adhere to the terms of approval and the Committee reserves the right to revise its favourable opinion should this become necessary.

On behalf of the Research Committee, I wish you success in the conduct of this study and look forward to receiving your final report following its completion.

Yours Sincerely,

13-06-2016

Dr Nagah Selim

Chair, PHCC Research Committee
Consultant Community Medicine

APPENDIX E

MSc thesis-related scholarly output

❑ **Research article publication**

- Jaam M, Ibrahim MIM, Kheir N, Awaisu A. Factors associated with medication adherence among patients with diabetes in the Middle East and North Africa region: A systematic mixed studies review. Diabetes Res Clin Pract (2017). DOI: http://dx.doi.org/10.1016/j.diabres. 2017.04.015

- Jaam M, Awaisu A, Ibrahim MM, Kheir N. Factors influencing medication adherence in diabetes mellitus: Developing a holistic conceptual framework model. Res Social Admin Pharm (2017). DOI: http://dx.doi.org/10.1016/j.sapharm.2017.05.003

❑ **Abstract Publications in Peer-Reviewed Journals:**

- Jaam M, Awaisu A, Ibrahim MIM, Kheir N. Evaluating the evidence on barriers to medication adherence in patients with diabetes: A systematic review of systematic reviews. International Journal of Pharmacy Practice. 2016. 24(S3):91-92. doi: 10.1111/ijpp.12289.

- Jaam M, Ibrahim MIM, Kheir N, Awaisu A. A proposed holistic conceptual framework for barriers to medication adherence in diabetes. Value in Health. 2016. 19:7, A676-A677. doi: 10.1016/j.jval.2016.09.1897

- Awaisu A, Jaam M, Ibrahim MIM, Kheir N. Quality of the evidence on barriers to medication adherence in patients with diabetes mellitus: a systematic review of systematic reviews. Pharmacotherapy. 2016. e298-e299

❑ **Protocol Publications:**

- Jaam M, Awaisu A, Ibrahim MIM, Kheir N. Factors associated with medication non-adherence in patients with diabetes in the Middle East and North Africa region: a systematic mixed studies review. PROSPERO. 2016:CRD42016042474

❑ **Research Grants:**

- Awaisu A, Jaam M, Nadir K, Ibrahim MIM. Barriers to medication adherence in patients with uncontrolled diabetes. Qatar University Student Grant. Awarded May 2015. (QUST-CPH-SPR-15/16-19)

❑ **Poster Presentations (Outside Qatar University)**

- Jaam M; Awaisu A, Kheir N, Ibrahim MIM. Evaluating the evidence on barriers to medication adherence in patients with diabetes: A systematic review of systematic reviews. Royal Pharmaceutical Conference, Birmingham, UK. 5-6 Sep, 2016.

- Awaisu A, Jaam M, Ibrahim MIM, Kheir N. A proposed holistic conceptual framework for barriers to medication adherence in diabetes. 19th Annual European Congress. International Society for Pharmacoeconomics and Outcomes Research (ISPOR). Vienna, Austria. Oct 29 – November 2, 2016

- Jaam M, Ibrahim MIM, Kheir N, Awaisu A. Quality of the evidence on barriers to medication adherence in patients with diabetes mellitus: a systematic review of systematic reviews. (Poster). 2016 American College of Clinical Pharmacy (ACCP) Annual Meeting. Hollywood, Florida, USA. October 23 – 26, 2016

❑ **Poster Presentations (Inside Qatar University)**

- Jaam M, Ahmed A, Ibrahim MIM, Kheir N. Factors associated with medication nonadherence in patients with diabetes in the Middle East and north African Region: A systematic mixed studies review. (Poster). Qatar University Annual Research Forum. Doha, Qatar. 3-4th May 2-17.

- Jaam M, Awaisu A, Kheir N, Ibrahim MIM. Barriers to medication adherence in patients with uncontrolled diabetes in a primary healthcare setting: a mixed method study. (Podium). 7th Annual Research Forum, College of Pharmacy, Qatar University, Doha, Qatar. May 24th, 2017.

- Jaam M, Awaisu A, Kheir N, Ibrahim MIM. Understanding barriers to medication adherence in patients with uncontrolled diabetes: a qualitative study. (Podium and Poster). Second Annual Health Research Symposium at Qatar University, Doha, Qatar. 22nd April 2017.

- Jaam M, Awaisu A, Kheir N, Ibrahim MIM. Barriers to medication adherence in patients with unconrtrolled diabetes in a primary healthcare setting in Qatar: a mixed method triangulation study. (Oral). 3 MT competition. Doha, Qatar. 25th April 2017.

- Jaam M, Awaisu A, Kheir N, Ibrahim MIM. Evaluating the evidence on barriers to medication adherence in patients with diabetes: A systematic review of systematic reviews. (Poster). 6th Annual Research Forum, College of Pharmacy, Qatar University, Doha, Qatar. May 26th, 2016.

❑ **Publications Under Peer Review or Prepared:**

- Jaam M, Kheir N, Ibrahim MIM, Awaisu A. Evaluating the evidence on barriers to medication adherence in patients with diabetes: A systematic review of systematic reviews. BMJ Open.

- Jaam M, Kheir N, Ibrahim MIM, Hadi M, Diab M, Al-Abdulla S, Awaisu A. Exploring barriers to medication adherence in patients with uncontrolled diabetes from patients' and healthcare providers' perspectives: A qualitative study.

- Jaam M, Kheir N, Ibrahim MIM, Hadi M, Diab M, Al-Abdulla S, Awaisu A. Assessing prevalence of and barriers to medication adherence in patients with uncontrolled diabetes attending primary care clinics in Qatar: a cross sectional study.