QATAR UNIVERSITY

COLLEGE OF PHARMACY

MEDICATION-RELATED BURDEN AMONG PATIENTS WITH CHRONIC DISEASE CONDITIONS: PERSPECTIVES OF PATIENTS ATTENDING NON-COMMUNICABLE DISEASE CLINICS IN A PRIMARY HEALTHCARE SETTING IN QATAR

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ABSTRACT

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Title: Medication-Related Burden among Patients with Chronic Disease Conditions: Perspective of Patients attending Non-Communicable Disease Clinics in a Primary Healthcare Setting in Qatar

This study aimed to adapt a medication-related burden instrument, the Living with Medicines Questionnaire (LMQ), into the Arabic context, report the psychometric properties of the Arabic version, and assess the burden resulting from the treatment of chronic conditions in Qatar.

The research included two phases. In Phase 1; cultural adaptation was conducted to generate an Arabic version of LMQ (LMQ-AR). In Phase 2, the LMQ-AR was used in a cross-sectional study among patients with chronic conditions in Qatar. Data obtained were used to assess the psychometric properties of the LMQ-AR, as well as to report medication-related burden perceived by patients. Construct validity of the LMQ-AR was evaluated by associating the LMQ-AR score with adherence, measured by the Adherence to Refills and Medications Scale (ARMS), and with global burden assessed by Visual Analogue Scale (VAS). Internal consistency was assessed using Cronbach's Alpha.

A total of 293 patients with diabetes, from different ethnicities, age groups, and educational levels completed the study forms. Of the total sample, 138 patients used the Arabic versions. The domains of LMQ-AR showed acceptable internal consistency with Cronbach's α ranging from 0.59 to 0.80. The overall LMQ-AR score was positively correlated with ARMS score (r_s=0.400, P<0.0001), and VAS (r_s=0.335, P<0.0001). Majority of the patients (n = 253) reported the existence of minimum (66.6%) to moderate (24.1%) medication-related burden. There was a moderate positive correlation between the scores of LMQ and ARMS, rs(251) =0.317, p < 0.0005. Diagnosis duration of diabetes ($\beta = 0.203$, $p < 0.05$), adherence score ($\beta = 0.342$, $p < 0.05$), marital status ($\beta = 0.161$, $p < 0.05$), employment status ($\beta = -0.191$, $p < 0.05$), and the presence of hypertension ($\beta = -0.131$, $p < 0.05$) were significant predictors of overall medication burden.

The Arabic version of the LMQ is a reliable and valid instrument that can be used to assess medication-related burden among patients with chronic conditions in the Arabic context. A considerable proportion of patients suffer from medication-related burden, which could be affected by many factors.

DEDICATION

To my precious and loving family,

My mother, father, sister, brothers, husband, and lovely son.

They have always been by my side, supporting, and encouraging me to achieve my goals. Without you I wouldn’t have been here.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ARMS	Adherence to Refills and Medications Scale
DM	Diabetes Mellitus
HTN	Hypertension
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
LMQ	The Living with Medicines Questionnaire
LMQ-AR	The Living with Medicines Questionnaire - Arabic version
NCD	Non-Communicable Diseases
PC	Pharmaceutical Care
PROMPT-QoL	Patient-reported Outcomes Measure of Pharmaceutical Therapy for Quality of Life
PROMs	Patient-Reported Outcome Measures
PROs	Patient-reported outcomes
TBQ	Treatment Burden Questionnaire
UN	United Nations
VAS	Visual Analogue Scale
WHO	World Health Organization

Chapter 1: INTRODUCTION AND LITERATURE REVIEW

1.1 The Burden of Non-Communicable Diseases

Chronic, non-communicable diseases (NCDs), are those illnesses that are non-infectious, non-transferable from one patient to another, and are most likely of lifelong duration with slow progression (1). Although most of the incidences of NCDs are preventable or manageable, NCDs are responsible for the global burden and increasing prevalence of morbidity and mortality (2). According to the World Health Organization (WHO)'s estimation in 2015, NCDs are responsible for 38 million deaths annually, a number that is higher than that from all other causes of deaths when combined (1). The majority of these deaths are considered premature (occur at less than 70 years of age) (1). The four major chronic diseases that cause 82% of the NCD deaths are cardiovascular diseases, cancers, respiratory diseases, and diabetes (1).

Generally, many risk factors such as smoking, excessive alcohol consumption, unhealthy diet, and physical inactivity contribute to the incidence and increasing prevalence of NCD conditions (1). There have been concerted global efforts aimed to reduce the burden of these diseases (1, 3, 4). For example, the United Nations (UN) has declared commitment to prevention and control of NCDs during the UN General Assembly in 2011 (4). Moreover, the WHO has designed and announced the Global Action Plan for the Prevention and Control of NCDs 2013-2020 that was endorsed by the 66th World Health Assembly in 2013 (3). This action plan contained nine voluntary global targets, to which the Head of State members declared commitment, to reach a relative reduction of the top four NCDs related premature deaths by 25% by the year 2025 (3). The nine targets concentrated on reducing the risk factors associated with the NCDs (4). The plan also offers a roadmap for collaboration between the member states of the WHO, the private sector, and other organizations to achieve the mortality reduction target (3). The global efforts against NCDs also highlighted the importance of the primary care in early detection and management of the chronic diseases (1, 3). Despite all these efforts, the main focus of healthcare systems and clinical practice guidelines in general is to maintain clinical therapeutic goals for single conditions when managing chronic illnesses (5-7). This type of fragmented care approach would lead to diminished quality of life among people with multimorbidities (7)

1.1.1 Multimorbidity and Polypharmacy

Despite the increasing number of patients with multi-morbidity (the co-existence of two or more chronic diseases in one patient), healthcare systems, research, and usual practice focus heavily on the management of individual chronic diseases separately (7, 8). Many studies have shown that multi-morbidity is becoming progressively prevalent among patients with chronic conditions (8-10). In a retrospective study that used the medical records of 1,751,841 patients, Barnett et al. showed that multimorbidity does not only occur in older patients, but also those who were younger than 65 years (8). The literature also demonstrated that patients with multiple chronic diseases utilize healthcare services more than patients with a single disease condition (11). Furthermore, multimorbidity has been associated with lower quality of life and worse prognosis (12). It has therefore been suggested that more effective ways for the management of multiple NCDs are needed, not only to improve the quality of life of the population, but also to reduce the economic pressures resulting from the emergence of new cases that place additional financial burden on the healthcare systems and the patients (9, 13).

Furthermore, the achievement of intended clinical endpoints regarding each individual disease, requires complex treatment regimens and multiple medications, consequently subjecting patients to unneeded treatments (14). Developing effective and well-established strategies to address such situations requires careful attention to the balance between the desired therapeutic goals and the potential risks of such therapies (10). Bower et al. have qualitatively explored the perceptions of general practitioners (GPs) and nurses regarding the management and impact of multimorbidity (10). Their study revealed discrepancy between meeting clinical targets and patients' expectations. This manifested mainly among patients attending multiple appointments to receive care focused on individual diseases. The investigators highlighted the challenges in the management of patients with multimorbidities due to lack of consultation time, which made patients overwhelmed by self-coordination of their care. (10). In concert with this, the recommendations in the literature are directed towards delivering patient-centered care, a model in which patients should be increasingly involved in the decision-making, and in coordination of their treatments (13).

The most common approach of the long-term management of chronic diseases is medication use (15). In fact, it is estimated that the use of medications in many countries represents a substantial portion of the healthcare expenditure regarding the management of NCDs (16, 17). The benefits of medications use in preventing premature deaths and the adverse consequences of NCDs, as well as managing associated symptoms, are indisputable (15).

Polypharmacy, which is the use of four or more medications simultaneously by the same patient (13), could be perceived as an unavoidable evil of the advancement in the treatment strategies of today's aging population (10, 13, 18). It is estimated that polypharmacy occurs in one out of every five patients taking regular medications, and in one out of every six patients who are 65 years or older (13). Several medications are prescribed for reasons other than treating the chronic conditions experienced by the patient only. Among other things, they might be prescribed but to prevent disease, promoting health, or to address other adverse consequences of the chronic diseases (18). Paradoxically, polypharmacy has also been associated with increased morbidity and mortality, hospitalizations, and demand for nursing home care (19, 20). Furthermore, polypharmacy has been shown to be the leading cause medication wastage (21, 22). In a study published in 2013, Krska et al. interviewed 21 patients attending primary care general practices in North West England regarding chronic medical conditions. The investigators reported patients' concerns about the level of medication regimen complexity, and the difficulty in coping with the prolonged medication use. Their study also reported the negative impact of medication therapy on the patients' well-being (18). Polypharmacy can also result in drug-related problems (DRPs), such as non-adherence to medications, adverse drug reactions, and unnecessary drug therapy (18, 23-25). For these reasons, medication use related to the control or management of the NCDs is considered burdensome (16, 18, 25-27).

The purpose of Pharmaceutical Care (PC), as described by Hepler and Strand, is to provide drug therapy for the purpose of achieving definite outcomes that improve the patient's quality of life (28). This description that places the patient at the center of care, considers the identification, prevention and resolution of DRPs as the main responsibilities of a PC provider (28). Consequently, an effective PC practice, with its patient-centered philosophy and outcome-oriented tenets, should at least hypothetically, concentrate on enabling strategies that help the patients cope with their treatment plans, hence reduce the burden of therapy.

1.1.2 Patients' Experiences with Non-Communicable Diseases and Treatment

Advanced medical intervention and technology has led to an increase in the number of patients suffering from chronic diseases and living longer with disability. This entails that more attention should be given to the patient's role in their treatment plans (13, 29, 30).

There have been several studies that evaluated the appropriateness of drug use process including; prescribing – intake – management (31-34). However, most of them have focused on the clinical outcomes as a measure for medication appropriateness (33, 35). On the other hand, many studies have also highlighted the importance of evaluating the treatment outcomes from the patient's perspective (36, 37). Given that patients' perspectives on issues related to the use of medicines are arguably different from those of healthcare providers, more attention has been drawn towards the appropriateness of drug therapy from the perspective of the patient in recent years (6, 18, 25). In their analysis of how NCDs are managed, May et al. argued that clinicians lack both the ability to identify and the strategies to manage the patient's perceptions of barriers and problems associated with drug treatment. (30). Moreover, in a recently published book by Duncan and Blythe, there was a comprehensive explanation about multimorbidity and polypharmacy (13). The authors have shown that treatment burden can result from the traditional passive role of patients when utilizing health care where patients need to visit many healthcare providers to follow up their diseases individually. As an alternative to this model, they proposed the patient-centered care model, in which the patient needs to visit one experienced practitioner to manage his/ her multimorbidities (13).

The traditional focus of clinical practice guidelines on individual diseases, the increasing coexistence of multiple comorbid conditions, and the lack of structured strategies to manage problems associated with the consequences of treatments meant that patients have to deal with extremely complex instructions and tasks associated with medications for the rest of their lives (38). Coping with adverse consequences of medications and having to tailor life activities according to the demands of the therapeutic regimens result in putting extra burden on patients (6, 14, 39). For example, the quality of life of patients with diabetes can be affected by the estimated daily average time they spend on treatment and monitoring of their health. This effect was expressed by type 2 diabetes patients as equal to the suffering from nephropathy or neuropathy (6).

The effect or burden of therapy can also be perceived differently by patients and healthcare providers (25). In 2002, Bernard et al. evaluated the credibility of the patients' self-assessment of the adverse consequences of chemotherapy as compared to evaluation of the same consequences by the physicians, and the results emphasized the importance of putting much more weight on the evaluation from the patients' perspective (40).

1.1.3 Patient-Reported Outcome Measures

Patient-reported outcome measures (PROMs) are those measures used to evaluate the health outcomes by the patients themselves (41). These measures are important in understanding and measuring the types of outcomes that affect the treatment regimens, as well as the life of the patients (42, 43). As the burden resulting from drug therapy is perceived by patients and cannot be quantified objectively, using an appropriate PROM is one of the best approaches given that these measures indicate the judgement of the patients about their treatment (15, 44). For this reason, there is an increased global interest in developing PROMs to determine the perceived burden of therapy among patients with chronic conditions in practice and research settings (6, 15, 25, 39, 45). Examples of these PROMS include the Treatment Burden Questionnaire (TBQ), the Patient-reported Outcomes Measure of Pharmaceutical Therapy for Quality of Life (ProQoL), and the Living with Medicines Questionnaire (LMQ).

1.1.3.1 Development of Patient-Reported Outcome Measures

Approaches used for the development and validation of PROMs are well-established and well-documented in the literature (46). The development process is usually iterative and of multiple steps (46, 47). The process starts with conceptualization of the overall objective using literature review of the subject matter, exploration of the views of the target population utilizing qualitative methodology, and formulation of a pool of items from which different domains are formed (44, 47). Synthesis and piloting of the scale is usually performed using expert opinions and a sample drawn from the target population (47).

1.1.3.2 Validation of Patient-Reported Outcome Measures

Validation, or assessment of the psychometric properties of newly developed measures, is an essential step that provides evidence for the validity and reliability of the new tool (or questionnaire)(46). As PROMs are subjective measures, and their results are therefore subject to bias, performing validation exercises prior to their formal utilization in research is of paramount importance. The three main psychometric tests typically performed in new measures are validity, reliability, and responsiveness.

Validity is generally a measure of the ability of the tool to measure what it is intended to measure. There are many types of validity, the most important being: (1) content validity, (2) construct validity and, (3) criterion validity (48, 49).

Content validity is the degree to which the tool contains all the items and components representing the topic of interest. This is usually part of the initial development and validation of PROMs, and is assessed by gauging opinions of individuals with expertise in the area addressed by the measure (expert judges) (50).

Construct validity examines whether the health measure relates to other measures in ways consistent with a plausible hypothesis (49). Data from measures of other variables and from the measure being validated are analyzed for trends or patterns of hypothesized relationships, to determine if these hypotheses could be empirically confirmed (48). Construct validity is achieved if the trends are consistent with the hypotheses. Variables often used to test the pattern of relationships are health services utilization, clinical or objective measures, scores from another valid PROM, and medication use. Factor analysis is another strategy for assessing construct validity, and it is performed as part of testing a new tool to examine if a set of items in it are clustered in the same domain and the weight or bearing of items in different domains.

Criterion validity, or predictive validity, refers to the empirical relationship between the measure and a reliable criterion with established construct validity, or with an individual or a group of individuals with an established characteristic such as medical diagnosis (51).

Reliability is the ability of the tool to produce consistent results. There are two main types of reliability testing: (1) test-retest reliability and, (2) internal consistency reliability. Test-retest reliability is the correlation of the results of the same questionnaire administered on the same respondents twice over time period. Typically, a reliable questionnaire would produce almost the same results. Conversely, internal consistency reliability, usually reported by Cronbach's alpha, is a measure of the degree to which the items of a questionnaire underlying the same construct or domain, produce similar results (52).

Responsiveness refers to the ability of the measure to indicate the change occurring to the target group of participants. This is usually assessed in longitudinal studies following patients over time and testing the change happening due to multiple reasons (intervention could be one of them) (53).

Psychometric analysis is not restricted only to the development stages of a questionnaire or measure. Questionnaires are usually developed and validated among specific populations, and it is not uncommon for the new instrument to be used among different populations (39, 54-57). The instruments adapted from one population into another with different characteristics, should be further tested (54, 56). These tests include cultural adaptation, cognitive debriefing, and, if necessary, validation exercises (39, 54, 58).

The development, adaptation, and validation of the TBQ can be represented as an example of the aforementioned processes. The TBQ was developed in French, using literature review and qualitative work. The psychometric properties of the tool were then tested using factor analysis, construct validity (association with adherence, satisfaction measuring questionnaire, and complexity of regimen), and test-retest reliability (6). The validated TBQ was then translated and validated in English using internationally accepted procedures (39).

1.2 Perceived Burden of Treatment

The experience of utilizing health care, especially for long durations, is perceived differently among patients, and worth studying as a potentially critical threat to the success of treatment regimens (30, 59). This experience presents as “treatment burden” or “medication-related burden”, a concept that was defined only recently (14, 27, 45, 59, 60). Treatment burden can be defined as *“the overall workload imposed on the patients resulting from all aspects of utilizing healthcare, which has multiple negative effects on the patients’ wellbeing and quality of life”* (14, 39). Treatment burden was reported to present a barrier to achieving the desired outcome of therapy (6, 25, 27). Like in the cases of polypharmacy and the associated complexity of treatment regimens, patients are at risk of the burden that accompanies the treatment of specific disease (40, 61-63). This burden has been reported as non-adherence to prescribed medications (64), experiencing adverse effects of the medications (65), economic burden (66), impact on health-related quality of life (67, 68), and time spent on utilizing the treatment (68).

In 2009, May and his colleagues proposed the term ‘Minimally Disruptive Medicine’ to represent a healthcare model that is about the effective use of health services designed to achieve the therapeutic goals with respect to the patients’ capacity (30). They explained that being a patient means suffering from not only the illness and its consequences, but also from the effects of healthcare utilization and its consequences (30). They argued that patients are often exposed to a fragmented healthcare system, and they try to cope with multiple recommendations and complex drug therapy regimens (especially if they have multimorbities). The investigators suggested that patients try to adjust their lives according to the requirements of their treatment plan. All that workload imposed on the patients, in addition to the economic burden of utilizing healthcare in some instances, constitute what they termed “Treatment Burden” (30).

1.2.1 Terms Associated with Perceived Burden

Although the term “treatment burden” describes the overall burden the patient experiences from utilizing health care (6, 45, 59, 62), in earlier works, this term was used to describe the adverse clinical outcomes of different treatments (40), satisfaction with therapy (69), poor adherence to drug therapy as measured by pill counts (70), or impact on quality of life (67, 68). The published literature described the burden perceived by patients mainly from using medications as “medication burden”, or “medication-related burden” (15, 18, 25, 60). Literature also described the term “patients’ lived experience with medicines” to describe individuals’ experience of this burden and its impact on beliefs, behaviors, and wellbeing. However, a closer look at the literature that described these terms, showed that medication burden frameworks also contained similar aspects as explained by treatment burden. In recent systematic reviews investigating medication-related burden, the literature describing treatment burden were all included in the analyses (15, 60). Hence, the terms “treatment burden”, “medication burden”, and “patients’ lived experiences with medicines” are used among scholars interchangeably to describe almost the same aspects of the perceived burden. In this thesis, “medication-related burden” is used to describe the perceived burden resulting from the overall treatment process (including therapies and other aspects associated with managing chronic health conditions).

1.2.2 Classification of Literary Works of Medication–Related Burden

The work by May et al. in 2009 triggered discussions among researchers trying to agree on a better understanding of this term as it was critical for the delivery of tailored interventions (30). Qualitative studies and systematic reviews were performed to better understand the views of patients as well as the impact and the predisposing factors of this burden (60). There are also published studies about developing tools to measure burden related to therapy from the patient perspective (6, 25, 39, 71). In addition, the literature suggests that prolonged medications use constitutes a major challenge that impacts on patients' coping ability with treatment regimens, and hence worsens medication burden (15, 18, 25)

The following is a summary of the literary works that explained, and facilitated, the measurement of medication-related burden:

1.2.2.1 Qualitative Studies

- Montori and colleagues published a qualitative study, in which they investigated the treatment burden as a subject of discussion between patients and physicians during diabetes follow up visits. They found that less than half of the monitored visits contained discussions about treatment burden, with only 30% of them precisely mentioning treatment burden. Those discussions demonstrated some aspects of treatment burden like access to treatment, administrative burden, treatment consequences, and monitoring of the process (72).
- In order to build a framework to inform measurement of treatment burden, Eton et al. conducted two qualitative studies. First, they conducted semi-structured interviews among patients with at least one chronic condition and who had complex regimens to follow. Data resulting from these interviews were used to formulate a framework and themes describing treatment burden. These themes included: (a) the workload imposed on patients, (b) the strategies needed to self-care, and (c) the factors that magnify the perceived burden, and these themes were further detailed into six subthemes. Later in 2015, Eton's research team published an article about refining their framework using

semi-structured interviews with their previous study sample, in addition to new cases from different health institution to account for differences in utilization of different healthcare services. They also used four focus groups in this study in order to confirm the structure of the emerging framework. The final framework contained a sub-theme of barriers to self-care under the main theme “factors that exacerbate treatment burden”. Moreover, the “impact of treatment burden” main theme was added to quantify the exhaustion patients experience as a result of treatment burden (45).

- Through a qualitative study that used interviews with patients taking more than four medications regularly, and aimed to identify issues related to prolonged medication intake, Krska et al. highlighted eight themes representing aspects of medication burden: “relationships with health professionals”, “practicalities in using medications”, “information about medications”, “efficacy of their medications”, “side effects”, “attitudes”, “impact of the perceived burden” and “control or autonomy” (18).
- Sav et al. published results of an in-depth analysis of the qualitative data collected from a large sample of patients (n= 97) with chronic conditions or their carers regarding treatment burden. They found out that treatment burden is a multidimensional concept of cyclic nature that contains subjective and objective elements. The elements that emerged from this study were: “financial burden”, “time and travel burden”, “medication burden” and “healthcare access burden”. These elements were considered predisposing factors that can cause treatment burden, and as consequences resulting from that perceived burden (27).

- Sav et al. also published a qualitative study that explored the patients' treatment burden from the perspective of the Australian consumer health organizations. Those organizations are responsible for representing and providing help for patients with chronic diseases or their carers (26). During the interviews with key informants in these organizations, the investigators explored main factors of treatment burden. Medication-related burden was the main factor, followed by the burden perceived by the carers, time spent on treatment, financial burden among the low income people, and the burden resulting from fragmented healthcare system (26).

1.2.2.2 Quantitative Studies

There is paucity of quantitative studies with the main focus of evaluating perceived overall treatment or medication-related burden. The following is a brief description of some quantitative studies highlighting burden from the perspective of the patients:

- There have been studies that assessed burden of therapy as part of quality of life measures among patients with specific chronic diseases. For example, the cystic fibrosis questionnaire (a disease-specific quality of life measure) contains a domain that measures perceived treatment burden. This was subsequently used in many studies to assess perceived burden as part of quality of life (67, 73, 74).

- Treatment burden was also reported as part of assessing psychological distress resulting from diabetes management. This was reported as diabetes distress (75, 76), quality of life (77), signs of depression (75), or emotional burden(78).

- Moreover, time to treat side effects of chemotherapy, and loss of working days were measured and reported as treatment burden among cancer patients (61).

- In 2016, a study with the main focus of measuring the overall treatment burden from the perspective of patients with chronic conditions in Australia, was published. This work indicated that a considerable proportion of patients in Australia suffers from burden resulting from treatment regimens. It also showed that age, the existence of carer, and having endocrine health conditions (like diabetes) are considered predictors of treatment burden (79).

1.2.2.3 Systematic Reviews

- In 2013, Eton et al. published a systematic review of the PROMs used to evaluate treatment burden of three chronic diseases (diabetes, nephropathy, and heart failure) in order to inform the development of generic measure for chronic conditions (44). They identified 57 PROMs, majority of them (82%) were assessing burden resulting from diabetes care, and only 15 PROMs were developed using patients' perspectives. The common domains across all the measures were 12 accounting for all aspects of treatment or medication burden: 1) Distress resulting from regimen, 2) Scheduling flexibility, 3) Family conflict, 4) Side effects of medications, 5) Appropriateness of treatment, 6) Dietary burden, 7) Self-care convenience, 8) Overall treatment burden, 9) Monitoring/workload burden, 10) Device use burden, 11) Lifestyle changes or activity restrictions, 12) Economic burden (44).

- Mair et al. published a systematic review of the qualitative research that investigated the perceived burden resulting from treatment of stroke (38). As a result of this work, they formulated a framework of the components of the treatment burden associated with stroke management (38). Their findings, although restricted to stroke, were, as hypothesized by the investigators, in line with the elements of the concept of treatment burden.
- Sav et al. published a systematic literature review to analyze the concept of treatment burden (16). In their study, and in an effort to reduce the treatment burden, they demonstrated that the main consequences of treatment burden are failure of treatment plans leading to poor health outcomes and imposing burden on others. The predisposing factors they highlighted in the study were comorbidities, age, gender, and family circumstances of the patients (16).
- Recently, in 2016, Katusiime et al. published a systematic review, in which they summarized the evidence from the literature regarding the developed PROMs measuring medication burden, and their psychometric properties (15). They concluded that there was no specific tool that measures all the aspects of treatment or medication burden. Among the 15 tools identified, nine were multidimensional (covering many aspects of medication burden), and six were unidimensional. These measures varied in development and validation approaches. The overall domains covered by the questionnaires were

treatment related quality of life, availability and accessibility of medicines, self confidence in using medicines, control of treatment regimen, treatment and/or medication related burden, issues related to adherence or follow up, beliefs, perceptions, attitudes, general satisfaction, impact on the life of patients, relationship with healthcare providers, effectiveness, management, and knowledge of using medicines (15).

- Similarly, in 2016, Chen et al. published a systematic review and metasynthesis which used the published qualitative studies investigating treatment burden, medication burden, or patients' lived experiences with treatments; regardless of the specific cases or chronicity of the diseases (n=34). They used this pool of data to formulate a model, that could be used later to develop a comprehensive tool for the measurement of medication-related burden (60). This model contained three domains that explained the problems related to medication use: "Medication-related problems", "Medication-related beliefs", and "Medication taking practices". Within the 13 subdomains, the authors explained the relationship between the three domains as the first two domains affect each other, and subsequently affect the third one (practices of medication intake) leading to the ultimate effect on the success or failure of the therapy (60).

1.2.2.4 Questionnaires Developed and Validated and/or Adapted

Below is a description of the developed tools with a focus on medication and/or treatment burden.

- In 2012, the Treatment Burden Questionnaire (TBQ), a tool that measures the treatment resulting from therapy regardless of the health condition being managed, was developed and validated in France. The development was based on literature review and expert opinions. In their article, the researchers described the psychometric properties of the TBQ determined through factor analysis and construct validity (6). This tool was then adapted into the English language and subjected to validation testing, demonstrating similar psychometric properties to the original tool (39).
- Sakthong et al. published a study about the development and validation work of an instrument measuring medication management. Their multidimensional tool, Patient-reported Outcomes Measure of Pharmaceutical Therapy for Quality of Life (PROMPT-QoL), was intended as a health-related quality of life measure. The instrument contained 10 domains measuring many aspects of medication burden besides the overall QoL (71).
- Finally, the Living with Medicines Questionnaire (LMQ) was developed and validated in English to measure the burden resulting from prolonged use of medicines among patients with chronic diseases. The tool includes eight domains covering wide range of issues regarding the impact of medicines' use on the lives of the patients. The authors demonstrated the novelty of their work as the tool's statements were derived entirely from patients' perspective (25).

1.2.3 The Relationship between Perceived Burden and Treatment Plans

A plethora of literature has described treatment or medication burden, and highlighted the association of this burden with adherence to medication therapy (6, 14, 25, 60). As nonadherence is considered a critical issue affecting outcomes that matter to patients, the effect and magnitude of treatment burden on adherence is worth further assessment.

The level of adherence to drug therapy among patients with specific health conditions could be affected by the magnitude of treatment burden (80). Some aspects of treatment burden (economic, administrative burden, knowledge) were described as barriers to proper self-management of multimorbidity (81).

In reviews aiming to describe the factors that complicate patient care, non-adherence was considered a possible negative outcome associated with excessive workload imposed on the patients (82). Systematic reviews and metasynthesis of qualitative studies, or concept analysis, also focused on the association between non-adherence and perceived treatment burden (16, 38, 60). Pill count or prescription burden was also found to be associated with adherence and clinical variables of the disease (40, 63, 70, 83).

Further, the impact of treatment burden on patients' lives was well demonstrated in several qualitative studies. These studies explained that patients' commitment to treatment regimens and quality of life were hindered by suffering from aspects of utilizing healthcare (14, 27, 45, 59, 67, 72).

The literature also reported that validation studies measuring treatment burden provided evidence that burden was indeed associated with adherence scores. In the validation of both the French and English versions of TBQ, high treatment burden was found to be associated with low adherence to prescribed medications (6, 39).

Although the concept of treatment burden is attracting greater attention from various research groups, studies with main focus of associating treatment burden with adherence to therapy are scarce, mainly qualitative, and are investigating specific diseases (83, 84).

1.3 Non-Communicable Diseases Prevalence and Management in Qatar

The growing prevalence of NCD is affecting all countries around the world. The proportion of people living with NCDs is increasing in the developed countries, with the increase in risk factors for these illnesses like poor diet and inactive lifestyle (85). Moreover, although the prevalence of NCDs is higher in low and medium income countries (1), wealth can also be associated with increasing risk factors for NCDs (85). According to the World Bank classification, Qatar is considered as a high-income country (86). In 2014, NCDs were estimated to cause 69% of the deaths in Qatar (87). Of these, cardiovascular diseases were responsible for the highest proportion of the deaths (24%), followed by diabetes (19%), and cancers (18%) (87). These three NCDs forming a health priority in Qatar, share similar risk factors including tobacco use, obesity, inactive lifestyle and poor diet (88). NCDs are also associated with significant economic burden in Qatar. Knowing that the total direct and indirect cost associated with cardiovascular diseases, mental disorders, cancer, respiratory diseases, and diabetes management was $36.2

billion in 2013 in the Gulf Cooperation Council; it was estimated that spending per head of the population in Qatar will reach about $2,778 by 2022 (85).

To the best of our knowledge, there are no available estimates of the multimorbidity or polypharmacy associated with chronic NCDs in Qatar. However, as these are usually associated with increasing prevalence of patients with NCDs (8, 13), one can assume their presence among patients with NCDs in Qatar.

The major primary health care provider in Qatar is Primary Health Care Corporation (PHCC). This corporation includes 21 primary health centers that are distributed throughout the State of Qatar to maintain the population's health and prevent diseases. The health services provided by PHCC include the management of NCDs, through dedicated NCD clinic(s) in each health center (89). According to PHCC annual statistics, in 2014, the total number of registered NCD visits was 17318, with 78% of these visits due to diabetes (90).

1.3.1 Health Care Services Provided by Primary Health Care Corporation in Qatar

The global recommendations regarding the management of chronic multimorbidities highlight the need to establish primary care clinics where patients can visit regularly a GP to follow up their multiple conditions (13).

The Qatar's National Health Strategy, designed and published by the Supreme Council of Health (now the Ministry of Public Health), declared the establishment of a world-class healthcare system among its priority goals. The aim is to provide a comprehensive primary care model that puts the patient at the center of care (91). Further, the Qatar National Primary Healthcare Strategy aimed to provide high quality care, reduce barriers, and maximize the efficiency of provided services (92). Moreover, the management of the NCDs among the PHCC clinics was established using the evidence-based Chronic Care Model, which empowers the role of the patient in the success of treatment regimens (89, 93). NCD clinics that provide usual management and follow up for patients with chronic diseases in Qatar are distributed across the country (89). Providing the health services in these centers; which include follow up, laboratory tests, and supply of medications at an affordable costs; is part of the Social Health Insurance Scheme offered for all people in Qatar (94). This Scheme aimed to provide basic healthcare services to citizens and residents in the country (94). The aim and strategies of the primary care services provided for the NCD patients in Qatar resemble the recommended transition in health care globally, as well as the plans and strategies that are aimed at reducing the mortality and burden related to the NCDs.

1.3.2 Rationale of the Study

It has been shown that measuring medication-related burden as perceived by the patients is important as a key step to designing and delivering minimally disruptive medicine to NCD patients (30). Polypharmacy, non-adherence to treatments, and the consequences of failures of treatment plans not only affect the life of patients, but also lead to increased economic and social burden on the society as a whole (13).

As Qatar’s healthcare system is aimed at providing world-class services, it is important to identify any existing or potential barriers to the achievement of its target goals and primary mission. Hence, assessment of the medication-related burden, from the patient perspective is an important endeavor to inform the National Health Strategy of any barriers that may hinder the optimum use of health services at the primary health care level.

In recent years, PROMs have been developed and validated to measure medication-related burden (25, 39, 71). Given that the development and validation of these tools were done in environments that differ from Qatar (15), it is pertinent to adapt, and to determine the psychometric properties of any tool before its use in Qatar’s population.

Moreover, previous studies have reported the association between perceived medication-related burden and the patients’ well-being as well as adherence to therapy. To our knowledge, this association has not yet been measured quantitatively among patients with NCDs.

1.3.3 Aim and Objectives of the Study

The aim of this study was to assess the burden resulting from the treatment of chronic NCD conditions in Qatar and its impact on medication adherence. To achieve this aim, the following specific objectives of the study were set:

1. To identify a tool that measures medication-related burden from patients' perspective and to adapt it into the Arabic context.
2. To determine the psychometric properties of the tool adapted into Arabic.
3. To assess the burden of medication therapy from the perspective of patients with chronic NCD conditions in Qatar.
4. To investigate the magnitude of the association between medication-related burden and the self-reported adherence to prescribed medications.

CHAPTER 2: METHODS

The research was performed in two phases. In Phase 1, a literature search was performed to select a tool that measures medication-related burden, followed by cultural adaptation to generate an Arabic version of the tool. In Phase 2, the adapted tool was then used in a cross-sectional study among patients taking multiple medications for chronic NCD conditions in Qatar. Data obtained from this study were used to assess the psychometric properties of the adapted Arabic version of the medication-related burden questionnaire. Medication-related burden perceived by patients and the impact of this burden on adherence to drug therapy among the cohort of patients was reported. The study also looked into the patient-related variables that could have bearing on the medication-related burden.

2.1 Phase 1: Selection and Adaptation of a Medication-Related Burden Questionnaire

2.1.1 Selection of a Medication-Related Burden Questionnaire

Only a few self-administered questionnaires have been found in the literature, which were developed to measure patients' perceived medication-related burden (6, 25, 71). For this research, the following criteria were considered as a guide to selecting an appropriate tool to be used among our cohort of patients:

a. Comprehensiveness: The questionnaire must be comprehensive and should include a wide range of areas associated with burden expressed by patients through well-conducted research. The burden must be related to the problems that may face patients receiving primary healthcare in NCD clinics.

b. Development process: The questionnaire must have been developed utilizing best practices and evidence-based processes.

c. Psychometric properties: The questionnaire has to document an evidence of appropriate psychometric properties generated through robust validation studies.

Based on the above criteria, three questionnaires that were developed for the purpose of assessing perceived burden were identified through the literature search and examined to assess their suitability for use in this research. The original developers of the three questionnaires were contacted by the researchers who explained the objectives of the present study and requested access and permission to adapt and use the full questionnaires.

Description and characteristics of the identified tools are summarized in table 1 below.

Table 1. *Characteristics of the Identified Tools Measuring Treatment or Medication-Related Burden*

	TBQ*	**ProQoL****	**LMQ*****
Country and language	France - French (6)	Thailand – Thai (71)	United Kingdom – English (25)
Other languages	English (39)	-	-
Structure of items and response choices	The English version contains 15 items for which the respondents indicate their rating of the items being a problem using a numbered scale (from 0 indicating not a problem, to 10 indicating a big problem). Global score is the sum of the items' scores. The tool measures the patients' difficulties regarding medication management, follow-up, lifestyle changes, administrative tasks and regular healthcare (6, 39).	Contains 9 domains measuring aspects of medication management, medication use, and its consequences, besides the overall quality of life, with 43 items, each having 4-5 response choices (71).	Constituting 8 domains, the tool contains 41 statements to which the respondents indicate their level of agreement using a five-point Likert-type scale (from strongly agree, to strongly disagree). In addition, there is a free text (open-ended) question allowing the patient the freedom to add any other relevant issues. LMQ also contains a visual analogue scale (VAS), through which the respondents provide an overall evaluation of perceived medication-related burden using a scale of 0 (no burden at all) to 10 (extremely burdensome) (25).

Psychometric properties	The psychometric properties of the tool were evaluated among 610 patients with chronic conditions, and included; factor analysis, reliability analysis (Cronbach α of 0.90), and construct validity (correlation with clinical variables, adherence to medications measured by Morisky's Medication Adherence Scale, quality of life assessed by PatientLikeMe Quality of Life Scale, and patients confidence in their knowledge of conditions and treatments) (39).	The psychometric properties were evaluated among patients with chronic conditions in Thailand, and included practicality (i.e., administration time, missing data, and floor/ceiling effects), reliability (i.e., internal consistency and test-retest), and validity (confirmatory factor analysis and known-groups, convergent, and criterion validity) (71).	Explanatory factor analysis (EFA) and confirmatory factor analysis (CFA) were performed among patients in the UK and Australia. The CFA (with discriminant and convergent validity) suggested that the items gave a reasonable fit to data. The testing of the subscales also resulted in reasonable psychometric properties with the domains affected by pharmaceutical care interventions (95).
Consensus of the research team regarding the selection of a tool	The research team found that this unidimensional tool would not be sufficient to capture existing burden among our cohort of patients. Since the services provided by NCD clinics are provided free of charge or at minimal cost, and are aimed for all	After closely studying the English version provided by the developers, the research team judged that the English translation had serious issues that interfere with understanding of the intended meaning of the tool's items; some	The LMQ is a valid tool, and covers many aspects of the burden that patients with chronic conditions may face. It needed to be adapted into our context before its use (Appendix A).

	the population without complicated fragmentation in utilizing the care, administrative and practical issues measured by TBQ would not reflect the burden patients in our study my suffer from (89).	questions were two tailed, and the leading question of some items misleads the respondents. There were also no studies in its English version that contain linguistic issues which may prohibit its ability to assess burden in our setting.

[*] Treatment Burden Questionnaire

[**] Patient-reported Outcomes Measure of Pharmaceutical Therapy for Quality of Life

[***] The Living with Medicines Questionnaire

From the three tools identified, the Living with Medicines Questionnaire (LMQ) was selected based on the above mentioned criteria. The LMQ contains 41 statements with which respondents are required to indicate their level of agreement using a five-point Likert-type scale (from strongly agree, to strongly disagree). In addition, a free text (open-ended) question accord the respondent the opportunity to add any other relevant issues that were not covered in the questionnaire. The tool comprised of eight domains: Relationships with health professionals, Practicalities, Information, Efficacy, Side effects, Attitudes, Impact, and Control. A visual analogue scale (VAS) that allowed the respondent to express his/her overall perceived medication burden on a scale of 0 (no burden at all) to 10 (extremely burdensome) was also included.

2.1.2 The Translation and Cultural Adaptation Process of LMQ

The guidelines developed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) for adaptation, validation, and translation of questionnaires related to measurement of patient-reported outcomes (PROs) were utilized in this study (56). Figure 1 provides a flow diagram summarizing the multistep process and outcomes of each stage in the development of the Arabic version of the LMQ.

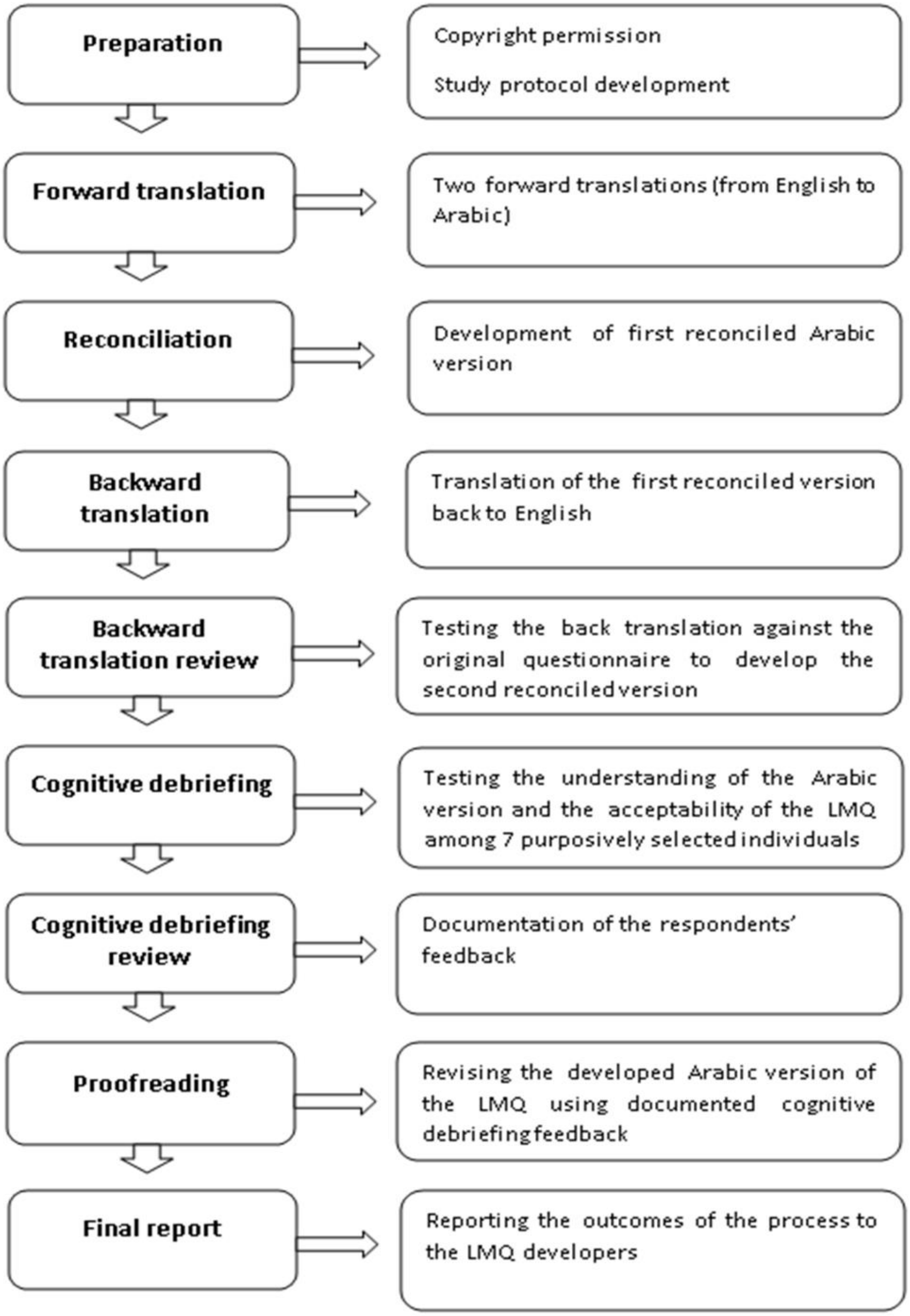

Figure 1. Flow diagram of the process followed in developing the Arabic version of LMQ

Preparation: Permission to use the LMQ was obtained from the original developers of the questionnaire. A comprehensive study protocol, which contained detailed information about the design, methods, and expected results of the project was developed and shared with the developers. The developers provided details and explanations as needed throughout the process of the Arabic questionnaire adaptation.

Forward translation: Two translations of the LMQ from English to Arabic were conducted by two independent, bilingual, and qualified translators. The translators, who were experienced in translating PROs, were not informed about the content of the tool prior to the translation process.

Reconciliation: A panel comprising three study investigators (two of whom are fluent in English and Arabic) and the translators was convened on several occasions to develop a single Arabic version of the LMQ translations. This was done to eliminate any discrepancies in translation, and to ensure cultural equivalence of the tool between the original and target populations. This generated the first reconciled Arabic version of LMQ.

Back translation and review: The first reconciled Arabic version of LMQ was back translated to English by a third independent, bilingual and qualified translator who was not familiar with the original English version of LMQ. This new English translation was compared to the original LMQ by the study investigators to test the quality of the translation and to ensure that the intended meanings of all items were maintained. A review of the outcome of this step led to further refinement of the Arabic questionnaire and to the second reconciled Arabic version. According to the ISPOR guidelines, this step should be followed by a step of ’harmonization’. Harmonization is recommended when the tool of interest is translated into more than one language, in which different versions are compared to ensure equivalence between them. However, this was not the case in the current work.

Cognitive debriefing and review: A group of seven people was purposively selected for cognitive debriefing. These Arabic speaking participants were selected to obtain representation of a balanced gender, age, educational level, and nationality. While the purpose of this step is to ensure that the developed Arabic version is comprehensible to the general population, the majority of the selected participants had at least one chronic condition. Through one-to-one interviews, they provided feedback on the second reconciled LMQ Arabic version in areas related to comprehension, time burden, and acceptability. Discussions during review of the cognitive debriefing process resulted in refining the changes made in the previous steps pertaining to cultural and linguistic issues. The cognitive debriefing process also allowed investigators to assess the acceptability of the content of the original LMQ, and to communicate this to the developers of the original version.

Proofreading and final report: The Arabic version of the LMQ was revised carefully by the study investigators to produce the final translation (called LMQ-AR) (Appendix B). A final report regarding the original LMQ and the Arabic translation, the methods used to generate the translated version and the findings arising during the linguistic validation process was generated and shared with the LMQ developers.

2.2 Phase 2: Measurement of Medication-Related Burden among Patients with Non-Communicable Diseases

2.2.1 Ethical Considerations and Approval

Ethical approval to conduct the study was granted by the Research Section (Clinical Affairs) of the PHCC (approval no. RC Ref. PHCC/RC/15/10/015). Ethical considerations and principles in line with the requirements of research involving human subjects were followed. An informed consent was obtained from each patient prior to enrolment into the study and confidentiality of the patients' information was guaranteed by the research personnel.

2.2.2 Study Design

A cross-sectional quantitative study using a self-administered, and adapted questionnaire was conducted to measure perceived medication-related burden and medication adherence among patients with chronic NCD conditions in Qatar.

2.2.3 Study Setting

Primary health care services in Qatar are provided by the PHCC through 21 primary health centers that are intended to cover almost all of the population as part of the National Health Strategy (91). PHCC, through the NCD clinics of the health centers, offers disease management and regular follow up for the largest number of patients with chronic disease conditions in Qatar. In 2014, the number of visits to PHCC clinics was 5.2 million (89). For this research, three centers (Mesaimeer, Airport, and Omar Bin Al-Khattab Primary Health Centers) were selected. The selection of the clinics was based on the ethical approval conditions and the approximate similarity in demographic distribution of patients’ visits across the health centers and based on the fact that all the three centers provide NCD services (89).

2.2.4 Study Population

Medication-related burden is extensively reported in the literature to be an issue among patients with chronic disease conditions, which leads to a negative impact on adherence to treatment plans (60). For this reason, the target population was patients with chronic disease conditions attending NCD clinics at PHCC centers for regular follow up. Although the perceived burden is expected to be associated with seeking treatment for any chronic illness (60), patients in this study were recruited if they have diabetes mellitus (DM), with or without comorbidities (other NCDs). DM can be considered a representative example of patients living with chronic conditions, and an NCD of priority in Qatar due to its high prevalence. Other chronic disease conditions usually co-exist with DM and may affect the success of its management. These common comorbidities include, but are not limited to, obesity, hypertension, dyslipidemia, other cardiovascular diseases, chronic kidney disease, depression, and sleep disorders (96). According to the statistics report published by PHCC, 78% of the visits to the NCD clinics in Qatar in 2014, were by patients with diabetes (90).

2.2.5. Participants and Eligibility Criteria

Patients were eligible for enrollment in the study if they were at least 18 years of age, diagnosed with diabetes for at least 6 months prior to the study (with or without comorbidities), and able to communicate in English and/or Arabic. Patients were excluded from the study if any of the following criteria was met: inability to communicate in English or Arabic, documented mental disabilities, having any speech impairment, or pregnant women.

2.2.6 Sample Size

Sample size was aimed to be representative of the target population (i.e. patients with diabetes in Qatar). It was calculated using the following equation (97):

$$\text{Sample size} = \frac{(Z_{1-a/2})^2 \, P \, (1 - P)}{d^2}$$

Where $Z_{1-a/2}$ is standard normal variate, which is 1.96 at 5% level of confidence and P is the expected proportion in the population. In the current study, P is the proportion of the patients with diabetes, who suffer from medication-related burden in Qatar. According to the International Diabetes Federation, 13.5% of the population in Qatar has diabetes (98). As the proportion of the patients with diabetes who suffer from medication-related burden is not known, we assumed that burden could be perceived by all patients. For this reason, the P of this equation was estimated as 0.135 (expected proportion of the diabetes patients in Qatar i.e 100% of the 13.5%) to calculate the sample size of this study. Assuming an absolute error (d) to be 0.05, the minimum sample size required for this study was 180 patients. This number increased by 30% to account for missing data. Hence, a total of 234 patients was the target for this study.

2.2.7 Sampling Technique

Although random sampling technique is warranted in such a study in order to draw an unbiased sample (99), this was not feasible in the setting of the current study. NCD patients are given scheduled 20 minutes follow up appointments with physicians. As each of them arrives consecutively for their appointments, it was not feasible to have all of them screened together (obtaining a sampling frame of eligible patients), and to draw a random sample among them. For this reason, convenient sampling was used, in which patients were screened for eligibility upon their arrival to the clinic using electronic medical records. Eligible patients were then approached to participate in the study. Those who consented to participate were enrolled in the study.

2.2.8 Outcome Measures

The primary outcome measure was the self-reported medication-related burden (including LMQ score and the VAS score). Self-reported adherence was assessed as a secondary outcome measure. Additionally, the data collected using the designed data collection form were used as variables to be associated with the main outcome measures. Medication-related burden was measured using the LMQ, while self-reported adherence was measured using the Adherence to Refills and Medications Scale (ARMS) (100).

2.2.9 Study Instruments

The following were the instruments used in the study:

1. The Living with Medicines Questionnaire (LMQ), validated in English (95), and adapted into the Arabic context during Phase 1 of this research (101). Both the Arabic and the English versions were used in this research, as applicable (Appendixes A&B).

2. The 12-item Adherence to Refills and Medication Scale (ARMS) (100), validated in English, and translated into the Arabic context by the research team and in coordination with the original developers of the tool. ARMS was developed to measure adherence to drug therapy and was validated among patients prescribed long-term therapy for coronary heart diseases. The scale demonstrated a high internal consistency reliability (Cronbach's $\alpha=0.814$) and a significant correlation with Morisky Adherence Scale (Spearman's rho $=-0.651$, $P < 0.01$) (100). Both the Arabic and the English versions were used in this research, as appropriate (Appendixes C&D).

3. A data collection form was also designed and piloted for use in this research. The variables collected included: demographic information (age, gender, country of origin, marital status, and education level), smoking history, and clinical information (diagnosis of DM, disease duration, comorbidities, prescribed medications, BMI, lifestyle changes, and clinical indicators of the disease). This information was elucidated through patients' interviews and/or from electronic medical records.

2.2.10 Data Collection Procedures

Eligible patients were met during their regular follow up visits to the NCD clinics at the health centers. The researcher approached the patient to introduce herself, provided information about the study, and obtained informed consent to participate in the study. The questionnaires were then self- or interviewer-administered depending on the patient's preference or literacy level. Other patient-related information were then obtained from the electronic medical records as needed using the data collection form that was specifically designed for this project.

2.2.11 Data Analysis

Phase 2 of the study (the cross-sectional quantitative study) resulted in data, for which the analysis plan was designed as follows.

2.2.11.1 Study Variables

Table 2 illustrates the variables collected from the medical records and from the patients for the purpose of data analysis. Selection of the variables (socio-demographic, and clinical) was based on previous studies indicating possible association of each variable with perceived medication-related burden.

Table 2. *The Variables Used in the Data Analysis of Phase 2*

Variable	**Measurement type**	**Variable expressed as**	**Source of data**
Socio-demographic variables			
Age	Continuous	Years	Medical records
	Categorical	- Up to 65 years - Over 65 years	
Gender	Categorical	- Male - Female	Medical records
Country of origin	Categorical	- Qatari - Non-Qatari	Medical records
Ethnicity	Categorical	- Arab (Qatari) - Arab (Non-Qatari) - Asian (Indian Subcontinent) - Asian (Philippines) - Others	Medical records
Marital status	Categorical	- Married - Single -Divorcee -Widowed	Patient
Education level	Categorical	- Less than primary school - Primary school -Middle school - High/ or secondary school - Technical college - University degree - Post graduate degree	Patient
Lifestyle changes	Categorical	- None - Exercise - Healthy diet	Patient

		- Heathy diet and exercise	
Employment	Categorical	- Employed - Unemployed - Retired - Full-time student	Patient
Smoking history			
Cigarette smoking	Categorical	- Current smoker - Former smoker - Never smoker	Patient
Shisha smoking	Categorical	- Usual shisha smoker - Social shisha smoker - Former shisha smoker - Never shisha smoker	Patient
Clinical variables and medications			
Diagnosis duration	Continuous	Years	Patient
HbA1c	Continuous	Percentage	Medical records
Control of DM	Categorical	- Uncontrolled DM (HbA1c $> 7\%$) - Controlled DM (HbA1c $\leq 7\%$)	Medical records
Number of prescribed medications	Continuous	Each prescribed medication was counted	Medical records
Doses frequency	Continuous	Total number of daily doses	Medical records
Presence of co-morbidities	Categorical	- No - Yes	Medical records
Number of co-morbidities	Categorical	- None - One - Two - Three or more	Medical records
BMI[*]	Continuous	BMI in Kg/m^2	Medical records

Outcome measures			
LMQ Score	Continuous Ordinal	The overall score of the items or the score in categories: - (41 – 73): No burden at all - (74 – 106): Minimum burden - (107–139): Moderate burden - (140 – 172): High burden - (173 – 205): Extremely high burden	LMQ tool
LMQ VAS Score	Continuous	A score from 0 to 10	LMQ tool
ARMS Score	Continuous Dichotomous	A score from 12 to 48 - A score of 12: Adherent - Over 12: Non-adherent	ARMS tool

*Body Mass Index

2.2.11.2. Normality Distribution

Continuous variables of this research, including age, duration of diagnosis, number of prescribed medications, LMQ score, VAS score, ARMS score, and BMI, were tested for normality. The tests were performed using SPSS, and included Shapiro-Wilk test as well as Kolmogorov-Smirnov (K-S) tests (102). These tests were done to inform the selection of the statistical tests of medication-related burden assessment.

2.2.11.3 Statistical Tests

Below is a description of the statistical tests used to answer the objectives of Phase 2 of the study. Tables 3 and 4 contain the details of the statistical tests used.

2.2.11.3.1 Psychometric validation of the Arabic version of LMQ

It is recommended to report the psychometric properties of the adapted tools among populations that differ from the populations in which they were developed (39, 54, 57). The data produced from this research was used to measure: (1) the internal consistency reliability of the items in the Arabic version of the LMQ using Cronbach alpha and, (2) the construct validity of the Arabic version of the LMQ through correlations of the LMQ score with the VAS indicating global burden, clinical variables, and ARMS score representing adherence to medications.

(1) Internal consistency reliability

The internal consistency reliability (measured by Cronbach alpha) is a measure of reliability to assess if the scale’s items are measuring the underlying dimension or theme (103). This test was used to determine the internal consistency of each of the eight dimensions of the LMQ (Arabic version).

(2) Construct validity

Construct validity gives an insight about the ability of the instrument to measure the constructs it is supposed to measure, and it is preferred when there is no gold standard criterion available for the test of interest (48). As medication burden is assumed to be affected by treatment regimen and its consequences, the adapted LMQ’s construct validity was tested using associations of the LMQ score with the ARMS score, prescribed medications and regimen, and each of the afore-mentioned clinical variables.

Table 3. *Summary of the statistical tests used to validate the Arabic version of the LMQ*

Category	**Variable measurement's type**	**Comparison**	**Statistical test**
Internal consistency	Continuous	8 dimensions	Cronbach Alpha
Construct validity	Continuous Ordinal	Correlation of LMQ scores with adherence score/ VAS: global burden/ Specific dimensions	Spearman's correlation

2.2.11.3.2 Assessment of medication-related burden

1. Description of the sample: Descriptions and comparisons using frequencies and percentages were used to describe all the variables of the sample, and to express the perceived medication-related burden among the patients. (Table 4)

2. Inferential statistics (univariate analysis) were also used to determine and compare the medication-related burden scores across different demographic and clinical characteristics. (Table 4)

2.2.11.3.3 Association between medication-related burden and self-reported medication adherence

In order to demonstrate the relationship between the perceived medication-related burden and adherence to medication therapy, correlation analyses were applied (104). As reported in the literature, perceived medication-related burden was assumed to be correlated with medication adherence (25, 60). Given the cyclic nature of perceived burden (60), the direction of this association was not hypothesized in this study. In order to further explain the score of the medication burden after accounting for the measured variables altogether, regression analysis was used. (Table 4)

Table 4. *Summar*

y of the Statistical Tests Used to Assess Medication Burden and Associate it with Adherence

Statistical purpose	**Variables/ measurement type**	**Comparison**	**Statistical tests**
Description	Continuous/ordinal	Descriptions of the study sample	Frequencies and percentages
Differences	Dependent variable: LMQ score, ARMS score, and VAS score: continuous variables	Difference of the distributions of medication burden, and adherence scores among the categories of patients	Mann-Whitney and Kruskal-Wallis
Associations	Continuous/ordinal	Global scores of burden and adherence	Spearman correlation co-efficient
Predictions	Burden score as dependent variable: continuous	More than one independent variables to explain the dependent variable	Multiple regression

CHAPTER 3: RESULTS

3.1 Phase 1: Translation and Cultural Adaptation of LMQ into the Arabic Context

3.1.1 Translation and Cultural Adaptation of LMQ

3.1.1.1 Title and Instructions

The instrument's title and the instructions were translated with no need for changes. Questions about demographics, which were at the end of the original LMQ, were moved to the first page to avoid missing important demographic data. The question about the ethnic group of the respondent was replaced by a question about nationality. The research team felt that nationality rather than ethnicity categorizes participants within a mostly similar ethnic group.

3.1.1.2 Items of LMQ

The 41 items contained in the instrument were evaluated carefully by the study investigators at the semantic, conceptual, and cultural levels. In this respect, some words were changed to retain the intended meaning and direction of the statement, and to suit the Arabic context (Table 5).

An example of re-wording to reflect the Arabic context is as follows; within the items that contained the phrase "my doctor(s)"; we kept it as "doctor" since in Arabic mentioning both the plural and singular forms of the word would be lengthy and unnecessary to the sentence. In the Arabic Language, this translates to any number of doctors the patient is dealing with.

The backward translation review revealed no major issues in the translation. Only a few statements were rearranged to be easier and closer to the Arabic respondents' understanding, while maintaining the intended meaning of the original statements. Details of the issues raised were reported to and discussed with the LMQ developers. Issues arising during the process of translation and cultural adaptation are summarized in Table 5.

Table 5. *Major Issues Resolved in the Translation and Cultural Adaptation of the LMQ into Arabic*

No.	**Statement**	**Translation issue**	**Action**
4	*"I am comfortable with the times I should take my medicines"*	When back-translated into English, the term "comfortable" became "relieved" which would change the meaning and the direction of the item.	The word "*comfortable*" was translated into a word in Arabic that means "accept".
11	*"I can vary the dose of the medicines I take"*	Literal translation may change the direction of the item and may give the meaning that the patient will change the dose regardless of the need.	It was translated to express the confidence that respondent would have to tailor the dose as per their needs, which is the intended meaning of the item.
17	*"I am concerned that my medicines interact with alcohol"*	Cultural adaptation were performed to ensure acceptance of the respondents to answer such an item since alcohol consumption, while not uncommon, is not a norm in the Arabic culture.	This was translated into Arabic in what means "*I am concerned that my medicines interact with my nutritional habits (other foods, alcohol drinks)*".
41	*"My life revolves around using my medicines"*	If translated literally, it would be hard to understand and would deliver a different meaning and direction of the item.	This item was translated into a sentence that means using medicines takes a major part of the life of the patient.

3.1.2 The Visual Analogue Scale

A decision was made, through discussions among the research investigators, to change the scale to one with discrete, graduation between 0 (no burden at all) and 10 (extremely burdensome) (Figure 2). This proposed change was communicated to (and approved by) the original instrument developers. The rationale for adding the discrete scores to the VAS was to help in providing a global self-assessment of the burden of medicine use and to allow measuring associations with the overall LMQ score and with each of its domains.

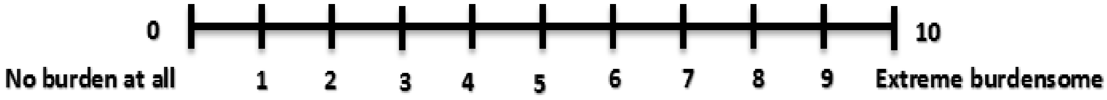

Figure 2. Visual analogue scale representing global burden

3.1.3 Cognitive Debriefing

The characteristics of the individuals who participated in the cognitive debriefing interviews are summarized in Table 6. The interviews conducted revealed an overall good understanding of most of the questionnaire's statements and their Arabic translation. Almost all of the interviewed individuals commented on the length of the questionnaire (41 items) and the presence of some items that cluster around similar meaning. For example, item 3 "*I am satisfied with the effectiveness of my medicines*", and item 25 "*My* *medicines live up to my expectations*” were, to some respondents, measuring the effectiveness of their medications. However, no changes were suggested regarding these items, because these closely-related questions have subtle differences between them. Respondents’ suggestions and comments regarding not only the Arabic, but also the original version were reported to the LMQ developers in details.

Table 6. *Characteristics of Cognitive Debriefing Participants*

Participant	**Gender**	**Nationality**	**Age**	**Occupation**	**Interview place**	**Interview duration**
P1	Female	Syrian	26	Physical therapist	Home	60 min
P2	Female	Qatari	35	Red crescent volunteer	Coffee shop	50 min
P3	Male	Lebanese	57	Manager	Participant’s office	60 min
P4	Female	Syrian	23	University student	Researcher’s office	75 min
P5	Female	Libyan	28	University student	Researcher’s office	45 min
P6	Male	Qatari	58	Real estate expert	Participant’s office	40 min
P7	Male	Egyptian	45	Laborer	Construction work site	45 min

3.2 Phase 2: Measurement of Medication-Related Burden among Patients with Non-Communicable Diseases

Of the 500 eligible patients approached in the four heath centers, 307 were consented to participate in the study. After excluding forms with incomplete, or invalid data (i.e. the participant responded to only one questionnaire, or responded with neutral to all the items of the LMQ), a total of 293 patients were included in the analysis. The responses of these patients, in Arabic or English, were used to answer the remaining objectives of the research (LMQ-AR validation, medication-related burden assessment, and relationship between medication-related burden and adherence).

3.2.1 Validation of the Arabic Version of the LMQ

A subset of the patients who participated in the study completed the Arabic versions of the LMQ and ARMS (n = 138), during their regular visits to NCD clinics in Qatar. The median (IQR) age of this subset was 55.0 (16.0) years. Patients were mainly male (63.8%), non-Qatari Arabs (60.9%), married (92.8%), and educated (50% with university degree or higher). The median (IQR) duration of DM diagnosis was 10.0 (10.0) years, while the median (IQR) number of prescribed medications was 5.0 (3.0). Most of the patients (65.2%) had two or more co-morbidities (Table 7).

Table 7. *Description of the Patients Who Responded to the LMQ Arabic Version (N =138)*

Variable	Median (IQR)	Frequency (%)
Age	55.0 (16.0)	
Gender		
Male		88 (63.8)
Female		50 (36.2)
Country of origin/ ethnicity		
Qatar		37 (26.8)
Arab countries (excluding Qatar)		84 (60.9)
Indian subcontinent		14 (10.1)
Others		3 (2.2)
Education Level		
Less than primary school		3 (2.2)
Primary or middle school		29 (21.0)
Secondary school		28 (20.3)
Technical college		9 (6.5)
University degree		61 (44.2)
Postgraduate degree		8 (5.8)
Marital status		
Married		128 (92.8)
Single		4 (2.9)
Divorcee		3 (2.2)
Widowed		3 (2.2)
Duration of DM diagnosis	10.0 (10.0)	
Number of prescribed medications	5.0 (3.0)	
Number of co-morbidities		
None		10 (7.2)
One		38 (27.5)
Two		54 (39.1)
Three or more		36 (26.1)

The completion rate for the whole items in the questionnaire was 87%. The LMQ score was the sum of the response choices' scores to all the 41 items, and ranged from 41 to 205. All of the items were correlated with the overall score (r_s ranged from 0.123 to 0.685).

3.2.1.1 Internal Consistency Reliability

The Cronbach's α coefficient of each of the eight domains (themes) of the LMQ-AR, showed accepted to good internal consistency reliability (range 0.583 to 0.808). Tables 8 and 9 illustrate the internal consistency reliability and item analysis of the eight LMQ domains.

Table 8. *Internal Consistency Reliability of the LMQ Arabic Version*

Theme/Domain	**No. of items**	**Cronbach's α**
Relationships with healthcare providers	5	0.674
Practical difficulties in using medicines	7	0.588
Cost-related burden	3	0.704
Side effects of medicines	4	0.781
Effectiveness of medicines	6	0.616
Attitudes/ concerns about using medicines	7	0.760
Impact/ Interference to day-to-day life	6	0.808
Control/ Autonomy of varying the regimen	3	0.583

Table 9. *Item Analysis of the LMQ Arabic Version*

No.	Items	Median (IQR)	Item-total correlation co-efficient	Cronbach's α if item is deleted
Theme 1: Relationships with healthcare providers				
7	I trust the judgement of my doctor(s) in choosing medicines for me.	2.0 (1.0)	0.083	0.748
14	My doctor(s) listen to my opinions about my medicines.	2.0 (2.0)	0.528	0.572
20	My doctor(s) takes my concerns about side effects seriously.	2.0 (2.0)	0.638	0.512
24	I get enough information about my medicines from my doctor(s).	2.0 (1.0)	0.498	0.589
34	The health professionals providing my care know enough about me and my medicines	2.0 (1.0)	0.419	0.629
Theme 2: Practical difficulties in using medicines				
1	I find getting my prescriptions from the doctor difficult*	2.0 (1.0)	0.400	0.516
2	I find getting my medicines from the pharmacist difficult*	2.0 (1.0)	0.437	0.500
4	I am comfortable with the times I should take my medicines	2.0 (1.0)	0.232	0.580
10	I am concerned that I may forget to take my medicines*	4.0 (2.0)	0.389	0.519
23	I have to put a lot of planning and thought into taking my medicines*	2.0 (2.0)	0.471	0.487
27	It is easy to keep to my medicines routine	2.0 (0.0)	-0.042	0.655
29	I find using my medicines difficult*	2.0 (2.0)	0.286	0.557
Theme 3: Cost-related burden				
5	I worry about paying for my medicines*	2.0 (3.0)	0.416	0.736

31	I sometimes have to choose between buying basic essentials or medicines*	2.0 (2.0)	0.576	0.532
33	I have to pay more than I can afford for my medicines*	2.0 (3.0)	0.559	0.542
Theme 4: Side effects of medicines				
21	The side effects I get are sometimes worse than the problem for which I take medicines*	3.0 (2.0)	0.627	0.707
22	The side effects I get from my medicines interfere with my day-to-day life (e.g. work, housework, sleep)*	4.0 (2.0)	0.566	0.738
30	The side effects I get from my medicines are bothersome*	2.0 (2.0)	0.646	0.698
38	The side effects I get from my medicines adversely affect my well-being*	2.0 (2.0)	0.511	0.766
Theme 5: Effectiveness of medicines				
3	I am satisfied with the effectiveness of my medicines	2.0 (1.0)	0.260	0.564
15	My medicines prevent my condition getting worse	2.0 (1.0)	0.357	0.515
25	My medicines live up to my expectations	2.0 (0.0)	0.380	0.512
32	My medicines allow me to live my life as I want to	2.0 (1.0)	0.141	0.627
39	My medicines are working	2.0 (1.0)	0.414	0.505
40	The side effects are worth it for the benefits I get from my medicines	2.0 (1.0)	0.472	0.480
Theme 6: Attitudes/Concerns about using medicines				
6	I worry that I have to take several medicines at the same time*	2.0 (2.0)	0.518	0.722
8	I would like more say in the brands of medicines I use*	2.0 (1.0)	0.337	0.757
9	I feel I need more information about my medicines*	4.0 (2.0)	0.452	0.737

12	I am concerned about possible damaging long term effects of taking medicines*	4.0 (3.0)	0.524	0.721
16	I am concerned that I am too reliant on my medicines*	4.0 (2.0)	0.473	0.732
17	I am concerned that my medicines interact with my nutritional habits (other foods - alcohol drinks)*	2.0 (2.0)	0.511	0.724
18	I worry that my medicines may interact with each other*	3.0 (2.0)	0.524	0.721
Theme 7: Impact/Interference to day-to-day life				
19	My medicines interfere with my social or leisure activities*	2.0 (2.0)	0.691	0.747
28	Taking medicines affects my driving*	2.0 (1.0)	0.555	0.781
35	My medicines interfere with my social relationships*	2.0 (4.0)	0.665	0.758
36	Taking medicines causes me problems with daily tasks (such as work, housework, hobbies) *	2.0 (1.0)	0.651	0.758
37	My medicines interfere with my sexual life*	2.0 (1.0)	0.439	0.805
41	My life revolves around using my medicines*	4.0 (2.0)	0.420	0.811
Theme 8: Control/ autonomy of varying regimen				
11	I can vary the dose of the medicines I take	4.0 (2.0)	0.442	0.402
13	I can choose whether or not to take my medicines	4.0 (2.0)	0.347	0.545
26	I can vary the times I take my medicines	4.0 (2.0)	0.392	0.482

*Item was reverse coded

3.2.1.2 Construct Validity

The results showed a significant moderate correlation between the overall LMQ score and ARMS score (r_s=0.400). Similarly, there was a significant moderate correlation between the LMQ score and the global burden; VAS (r_s=0.335). There were also significant associations between the scores of the domains (themes) of the LMQ and overall LMQ score, adherence score (ARMS), and global burden (VAS). Tables 10 and 11 illustrate these correlations.

Table 10. *LMQ-AR Correlations with Global Burden and Adherence Scores*

Spearman's rho		**LMQ**	**N**	**P value**
	VAS: Global burden	0.400	119	<0.0001
	ARMS	0.335	120	<0.0001

Table 11. *Correlations of the LMQ Domains with the Scores of LMQ, Adherence, and VAS: Global Burden (N = 138)*

Spearman's rho	**LMQ domains**	**LMQ Score**	**VAS: global burden**	**ARMS Score**
	Relationships with healthcare providers	0.544	0.172	0.099
	P value	<0.0005	0.05	0.628
	Practical difficulties in using medicines	0.727	0.287	0.303
	P value	<0.0005	0.001	<0.0005
	Cost-related burden	0.536	0.145	0.337
	P value	<0.0005	0.095	<0.0005
	Side effects of medicines	0.821	0.464	0.279
	P value	< 0.0005	< 0.0005	0.001
	Effectiveness of medicines	0.521	0.218	0.725
	P value	<0.0005	0.012	<0.0005
	Attitudes/Concerns about using medicines	0.756	0.357	0.388
	P value	<0.0005	<0.0005	0.002
	Impact	0.806	0.382	0.271
	P value	<0.0005	<0.0005	0.002
	Control/Autonomy of varying regimen	- 0.331	- 0.225	- 0.268
	P value	< 0.0005	0.009	<0.0005

3.2.2 Description of the Overall Sample

Tables 12 and 13 contain the sociodemographic, clinical and other characteristics of the study participants. Most of the patients were young to middle age adults (78.4%), male (71%), non-Qataris (non-Qatari Arabs 41.6%), married (94.9%), educated (54.3% with university degree or higher), and employed (70.4%). The majority of the patients

(66.6%) reported that they were not following any lifestyle changes recommended by their healthcare providers. Smoking history (cigarette and shisha) revealed that the majority of the study cohort was never smoker.

Table 12. *Sociodemographic Characteristics of the Patients who Participated in the Study (N = 293)*

Variable	**Frequency (%)**
Age (years)	
Up to 65	256 (87.4)
Above 65	37 (12.6)
Gender	
Male	208 (71.0)
Female	85 (29.0)
Country of origin/ ethnicity	
Qatar	41 (14.0)
Arab countries (excluding Qatar)*	122 (41.6)
Indian subcontinent**	107 (36.5)
Philippines	14 (4.8)
Others***	9 (3.1)
Education Level	
Less than primary school	3 (1.0)
Primary or middle school	47 (16.0)
Secondary school	52 (17.7)
Technical college	32 (10.9)
University degree	145 (49.5)
Postgraduate degree	14 (4.8)
Marital status	
Married	278 (94.9)
Single	7 (2.4)
Divorcee	5 (1.7)
Widowed	3 (1.0)
Lifestyle changes	
None	184 (62.8)
Exercise	103 (35.2)
Exercise & healthy diet	6 (2)
Cigarette smoking	
Current smoker	32 (10.9)

Former smoker	42 (14.3)
Never smoker	219 (74.7)
Shisha smoking	
Current daily smoker	8 (2.7)
Current social smoker	11 (3.8)
Former smoker	16 (5.5)
Never smoker	258 (88.1)
Employment	
Employed	205 (70.4)[****]
Unemployed	68 (23.4) [****]
Retired	17 (5.8) [****]
Full-time student	1 (0.3) [****]

[*] Arabs countries include: Egypt, Jordan, Lebanon, Palestine, Sudan, Syria, Yemen, Iraq, Tunisia, and Morocco.

[**] Indian subcontinent include: India, Pakistan, Sri Lanka, and Bangladesh.

[***] Others include: Eretria, Hungary, Iran, Germany, Canada, Kenya, Brazil, and Britain

[****] Percentages total may not be 100% due to some missing responses.

All of the participants had DM with or without other comorbidities. The median (IQR) duration of DM diagnosis was 8.0 (8.0) years, with majority (66.6%) diagnosed from 6 months to 10 years ago. Most of the patients (90.1%) had comorbidities, with 77.1% having up to three comorbidities. The most commonly reported comorbidities were; hypertension (55.3%), dyslipidemia (55.3%), and obesity (48.1%). Patients were prescribed with median (IQR) of 5.0 (3.0) medications, and 6.0 (3.0) daily doses. In addition, approximately 29% of the patients were prescribed more than five medications. Nearly 70% of the patients reported receiving help with their medicines. The diabetes control status of the patients was determined using the most recently available HbA1c value in the medical records. The median (IQR) HbA1c value was 7.80% (2.3), and 66.2% of the patients had uncontrolled DM (HbA1c greater than 7%). In addition, the median (IQR) BMI of the study participants was 29.98 (6.68) kg/m^2.

Table 13. *Clinical Characteristics of the Study Participants (N = 293)*

Variable	Median (IQR)	Frequency (%)
Duration of DM diagnosis	8.0 (8.0)	
6 months to 10 years		167 (66.5)*
More than 10 years		84 (33.5) *
Presence of co-morbidities		264 (90.1)
Number of co-morbidities		
One		93 (31.7)
Two		104 (35.5)
Three or more		67 (22.9)
Hypertension		162 (55.3)
Dyslipidemia		162 (55.3)
Vitamin D deficiency		18 (6.1)
Thyroid dysfunction		10 (3.4)
Obesity		141 (48.1)
Asthma		6 (2)
Others*		19 (6.5)
Number of prescribed medications	5.0 (3.0)	
Up to 5 medications daily		208 (71)
More than 5 medications daily		85 (29)
Medication type		
Tablet/ capsules		211 (72)
Any other type		82 (28)
Help with medicines		88 (30.4)*
HbA1c	7.80% (2.3)	
DM control status		
Controlled		85 (29)*
Uncontrolled		194 (66.2)*
BMI (Kg/m^2)**	29.98 (6.68)	

*Percentages total may not be 100% due to some missing responses.

**Body Mass Index

3.2.3 Medication-Related Burden Assessment

3.2.3.1 Overall Perceived Medication-Related Burden

Perceived medication-related burden was measured among the patients using the LMQ. The overall LMQ score was the sum of the scores of all the 41 items in the questionnaire, and ranged from 41 to 205, with higher scores indicating higher burden. The questionnaire also contained a VAS, through which respondents provided a global assessment of the overall burden they experience (0 to 10 points, with higher scores representing higher perceived burden). The median (IQR) LMQ score and VAS score were 95.00 (22) and 3.00 (4), respectively. The findings showed that the majority of the patients suffer from minimum (66.6%) to moderate (24.1%) degrees of burden (Table 14).

Table 14. *Perceived Medication-Related Burden Measured Using LMQ in Patients Attending NCD Clinics in Qatar (N = 293)*

Variable	**Range**	**Mean (SD)**	**Median (IQR)**	**Frequency (%)**
LMQ overall score[*]	(41–205)	97.5 (18.6)	95.0 (22)	
No burden at all	(41–73)			18 (7.1)
Minimum burden	(74 –106)			169 (66.8)
Moderate degree of burden	(107–139)			61 (24.1)
High burden	(140–172)			5 (2)
Extremely high burden	(173–205)			-
Theme 1: Relationships with healthcare professionals about medicines	(5–25)	9.74 (3.12)	9.0 (4.0)	
Theme2: Practical difficulties	(7–35)	15.19 (4.0)	15 (5.0)	
Theme 3: Cost-related burden	(3–15)	6.75 (2.80)	6.0 (4.0)	
Theme 4: Side effects of prescribed Medications	(4 – 20)	9.65 (3.72)	8.0 (5.0)	
Theme 5: Effectiveness of medicines	(6 – 30)	11.36 (2.9)	12.0 (3.0)	
Theme 6: Attitudes/concerns about medicines use	(7 – 35)	20.35 (5.3)	20.0 (9.0)	
Theme 7: Impact/Interference to day to-day life	(6 – 30)	14.31 (4.4)	13.0 (6.0)	
Theme 8: Control/ Autonomy to vary Regimen	(3 – 15)	10.17 (2.6)	10.0 (4.0)	
VAS: global burden	(0 – 10)	3.17 (2.5)	3.0 (4)	

[*] Total of LMQ with complete responses is 253 due to some missing responses

3.2.3.2 Perceived Medication-Related Burden by Domains and Items

Items measuring the themes (domains) of relationships with health care providers showed that 89.4% of the patients trusted the judgment of their physicians, 76.4% of them agreed that their physicians listen to their opinions about their medicines, 78.9% agreed that physicians take their concerns about side effects seriously, 78.5% get enough information from their physicians, and 83.6% agreed that the healthcare providers know enough about their conditions and medications (Table 15).

Table 15. *LMQ - Theme 1: Relationships with Healthcare Providers (N=293)*

Statement	**Strongly agree**	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
			Frequency (%)*		
7. I trust the judgement of my doctor(s) in choosing medicines for me	139 (47.4)	123 (42)	13 (4.4)	11 (3.8)	6 (2)
14. My doctor(s) listen to my opinions about my medicines	93 (31.7)	131 (44.7)	22 (7.5)	33 (11.3)	13 (4.4)
20. My doctor(s) takes my concerns about side effects seriously	89 (30.4)	142 (48.5)	28 (9.6)	23 (7.8)	11 (3.8)
24. I get enough information about my medicines from my doctor(s)	82 (28)	148 (50.5)	22 (7.5)	31 (10.6)	8 (2.7)
34. The health professionals providing my care know enough about me and my medicines	104 (35.5)	141 (48.1)	28 (9.6)	15 (5.1)	3 (1)

**Percentages total may not be 100% due to some missing responses.

Items evaluating practical difficulties in the experience of using medicines indicated that the majority of the patients did not find difficulties in getting prescribed medications from the physician (88.4%), or the pharmacist (84.9%), or to keep their medicines' routines (82.2%). The participants were mostly comfortable with the times of taking their medicines (91.8%), did not have to put a lot of planning in taking medicines (57.3%), with a substantial proportion of the respondents concerned about forgetting their medicines (41.3%) (Table 16).

Table 16. *LMQ - Theme 2: Practical Difficulties in Using Medicines (N=293)*

Statement	**Strongly agree**	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
			Frequency (%)[*]		
1. I find getting my prescriptions from the doctor difficult	14 (4.8)	14 (4.8)	6 (2)	145 (49.5)	114 (38.9)
2. I find getting my medicines from the pharmacist difficult	12 (4.1)	21 (7.2)	11 (3.8)	140 (47.9)	108 (37)
4. I am comfortable with the times I should take my medicines	111 (37.9)	158 (53.9)	5 (1.7)	10 (3.4)	8 (2.7)
10. I am concerned that I may forget to take my medicines	26 (8.9)	95 (32.4)	44 (15)	99 (33.8)	29 (9.9)
23. I have to put a lot of planning and thought into taking my medicines	14 (4.8)	60 (20.5)	48 (16.4)	129 (44)	39 (13.3)
27. It is easy to keep to my medicines routine	59 (20.1)	182 (62.1)	25 (8.5)	21 (7.2)	5 (1.7)
29. I find using my medicines difficult	11 (3.8)	25 (8.5)	17 (5.8)	140 (47.9)	99 (33.9)

[*] Percentages total may not be 100% due to some missing responses.

The theme underlying cost-related burden showed that the majority of patients did not worry about paying for medicines (61.7%), did not have to choose between buying essentials or medicines (70.2%), and did not agree that medicines' cost exceeded what they could afford (61.8%). (Table 17)

Table 17. *LMQ - Theme 3: Cost-Related Burden (N=293)*

Statement	**Strongly agree**	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
			Frequency (%)*		
5. I worry about paying for my medicines.	22 (7.6)	40 (13.8)	49 (16.9)	90 (31)	89 (30.7)
31. I sometimes have to choose between buying basic essentials or medicines.	11 (3.8)	36 (12.3)	40 (13.7)	99 (33.9)	106 (36.3)
33. I have to pay more than I can afford for my medicines.	11 (3.8)	63 (21.5)	38 (13)	99 (33.8)	82 (28)

*Percentages total may not be 100% due to some missing responses.

The domain measuring burden related to side effects showed that a considerable proportion of patients were facing side effects: worse than the condition (24.6%), interfering with their daily lives (19.2%), bothersome (18.5%), or adversely affecting their well-being (24.4%) (Table 18).

Table 18. *LMQ-Theme 4: Side Effects of Medicines (N=293)*

Statement	**Strongly agree**	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
			Frequency (%)[*]		
21. The side effects I get are sometimes worse than the problem for which I take medicines.	22 (7.6)	49 (17)	37 (12.8)	134 (46.4)	47 (16.3)
22. The side effects I get from my medicines interfere with my day-to-day life (e.g. work, housework, sleep).	19 (6.5)	37 (12.7)	41 (14.1)	138 (48.4)	56 (19.2)
30. The side effects I get from my medicines are bothersome.	14 (4.8)	40 (13.7)	41 (14.1)	127 (43.6)	69 (32.7)
38. The side effects I get from my medicines adversely affect my well-being.	13 (4.5)	58 (19.9)	32 (11)	117 (40.2)	71 (24.4)

[*] Percentages total may not be 100% due to some missing responses.

Furthermore, items measuring the effectiveness of medicines indicated that most of the patients agreed that they were satisfied with their medicines (89.7%), their medicines were working (94.5%), lived up to their expectations (88.7%), prevented their condition from getting worse (86.5%), allowed them to live as they want (80.5%), and worth the side effects they were facing (80%) (Table 19).

Table 19. *LMQ - Theme 5: Effectiveness of prescribed medications (n=293)*

Statement	**Strongly agree**	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
		Frequency (%)*			
3. I am satisfied with the effectiveness of my medicines.	112 (38.5)	149 (51.2)	13 (4.5)	11 (3.8)	6 (2.1)
15. My medicines prevent my condition getting worse.	103 (35.5)	148 (51)	17 (5.9)	16 (5.5)	6 (2.1)
25. My medicines live up to my expectations.	80 (27.4)	179 (61.3)	15 (5.1)	15 (5.1)	3 (1)
32. My medicines allow me to live my life as I want to.	81 (27.6)	155 (52.9)	22 (7.5)	27 (9.2)	8 (2.7)
39. My medicines are working.	104 (35.9)	170 (58.6)	10 (3.4)	4 (1.4)	2 (0.7)
40. ***The side effects are worth it for the benefits I get from my medicines.***	84 (29.1)	147 (50.9)	33 (11.4)	16 (5.5)	9 (3.1)

*Percentages total may not be 100% due to some missing responses

Regarding concerns about using medicines, items responses showed that patients mostly did not worry about taking several medicines (53.9%), were concerned about possible damaging effects of the medicines on the long-term (56.6%), were concerned that they were reliant on their medicines (47.1%), and were not worried about interaction between medicines and diet (63.2%), or between each other (59%). Furthermore, 46.8% of the patients did not prefer to have more say in the brands of medicines they use, and 47.4% needed more information (Table 20).

Table 20. *LMQ - Theme 6: Concerns about Medicines Use (N=293)*

Statement	**Strongly agree**	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
			Frequency (%)*		
6. I worry that I have to take several medicines at the same time.	29 (10)	76 (26.1)	29 (10)	115 (39.5)	42 (14.4)
8. I would like more say in the brands of medicines I use.	21 (7.2)	57 (19.5)	76 (25.9)	101 (34.5)	36 (12.3)
9. I feel I need more information about my medicines.	51 (17.4)	88 (30)	37 (12.6)	96 (32.8)	21 (7.2)
12. I am concerned about possible damaging long term effects of taking medicines.	61 (20.8)	105 (35.8)	45 (15.4)	66 (22.5)	15 (5.1)
16. I am concerned that I am too reliant on my medicines.	41 (14)	97 (33.1)	59 (20.1)	75 (25.6)	20 (6.8)
17. I am concerned that my medicines interact with my nutritional habits (other foods - alcohol drinks).	27 (9.2)	55 (18.8)	25 (8.5)	113 (38.6)	72 (24.6)
18. I worry that my medicines may interact with each other.	33 (11.3)	59 (20.1)	27 (9.1)	121 (41.3)	52 (17.7)

*Percentages total may not be 100% due to some missing responses.

The theme assessing the impact of the medicines on day-to-day life, indicated that the patients noticeably disagreed that their medicines interfered with social activities (69.1%), social life (80%), daily tasks (77.9%), driving (76.1%), or with sexual life (70.2%).

They also indicated mostly their agreement that their lives revolved around using medicines (51.9%) (Table 21).

Table 21. *LMQ -Theme 7: Impact of Using Medicines on Daily Life (N=293)*

Statement	**Strongly agree**	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
			Frequency (%)*		
19. My medicines interfere with my social or leisure activities.	17 (5.8)	44 (15.1)	29 (10)	142 (48.8)	59 (20.3)
28. Taking medicines affects my driving.	9 (3.1)	25 (8.7)	35 (12.2)	120 (41.7)	99 (34.4)
35. My medicines interfere with my social relationships.	11 (3.8)	23 (7.9)	24 (8.3)	168 (57.9)	64 (22.1)
36. Taking medicines causes me problems with daily tasks (such as work, housework, hobbies).	11 (3.8)	37 (12.8)	16 (5.5)	158 (54.5)	68 (23.4)
37. My medicines interfere with my sexual life.	15 (5.1)	27 (9.2)	45 (15.4)	110 (37.7)	95 (32.5)
41. ***My life revolves around using my medicines***	57 (19.5)	95 (32.4)	79 (27)	47 (16)	12 (4.1)

*Percentages total may not be 100% due to some missing responses.

Lastly, items measuring autonomy to vary regimen showed patients' disagreement to their ability to vary the dose of their medicines (59.5%), choose whether or not to take medicines (73.7%), or to vary the times of taking medicines (48.4%) (Table 22).

Table 22. *LMQ -Theme 8: Autonomy to Vary Regimen (N=293)*

Statement	**Strongly agree**	**Agree**	**Neutral**	**Disagree**	**Strongly disagree**
			Frequency (%)[*]		
11. I can vary the dose of the medicines I take.	27 (9.2)	70 (24)	21 (7.2)	133 (45.5)	41 (14)
13. I can choose whether or not to take my medicines.	11 (4)	54 (19.5)	8 (2.9)	150 (54.2)	54 (19.5)
26. I can vary the times I take my medicines.	22 (7.5)	111 (37.9)	16 (5.5)	117 (39.9)	25 (8.5)

[*] Percentages total may not be 100% due to some missing responses.

3.2.3.3 Open-Ended Question

Only 14 patients responded to the open-ended question regarding their views about how medication-related burden affected their lives. Ten issues emerged from their comments. These issues are summarized in Table 23.

Table 23. *Additional Issues Contributing to Medication Burden Identified by the Study Participants (N=14)*

No.	Issues identified in the comment
1	Travel time to utilize healthcare
2	Side effects of the medicines
3	Technical issues of medicines' refill system
4	Long waiting periods before seeing the physician
5	Seeing different physician for each follow-up appointment
6	Lack of information and instructions to live with their health conditions
7	Worry about taking several medicines at the same time, and about side effects of medicines
8	Worry about the long-term effects of the chronic condition on the body organs
9	Lack of information regarding the side-effects of the medicines, and their effect on the body
10	Feeling that follow-up appointments are not enough

3.2.3.4 Self-Reported Adherence

Adherence was measured using ARMS, and the results showed that 84% of the patients were non-adherent to their prescribed medications (Table 24). Table 25 contains the results of the responses to the individual ARMS items.

Table 24. *Self-Reported Adherence of Patients with Chronic Conditions Attending NCD Clinics in Qatar Measured By ARMS (N = 293)*

Variable	Mean (SD)	Median (IQR)	Frequency (%)
ARMS overall score	17.4 (4.8)	16.0 (7)	
Adherent			47 (16)
Non-adherent			246 (84)

Table 25. *Self-Reported Adherence of Patients Attending NCD Clinics in Qatar Measured By ARMS Items (N = 293)*

tem	**None of the time**	**Some of the time**	**Most of the time**	**All of the time**
		Frequency (%)		
1.”*How often do you forget to take your medicine?”*	169 (57.7)	118 (40.3)	5 (1.7)	1 (0.3)
2. “How often do you decide not to take your medicine?”	212 (72.4)	72 (24.6)	5 (1.7)	4 (1.4)
3. “*How often do you forget to get prescriptions filled?”*	218 (74.4)	57 (19.5)	16 (5.5)	2 (0.7)
4. “How often do you run out of medicine?”	189 (64.5)	83 (28.3)	20 (6.8)	1 (0.3)
5. “*How often do you skip a dose of your medicine before you go to the doctor?”*	195 (66.6)	74 (25.3)	17 (5.8)	7 (2.4)
6. “*How often do you miss taking your medicine when you feel better?”*	199 (67.9)	75 (25.6)	11 (3.8)	8 (2.7)
7. “How often do you miss taking your medicine when you feel sick?”	219 (74.47)	56 (29.1)	13 (4.4)	5 (1.7)
8. “*How often do you miss taking your medicine when you are careless?”*	202 (68.9)	73 (24.9)	9 (3.1)	9 (3.1)
9. “How often do you change the dose of your medicines to suit your needs (like when you take more or less pills than you’re supposed to)?”	196 (66.9)	76 (25.9)	16 (5.5)	5 (1.7)
10. “How often do you forget to take your medicine when you are supposed to take it more than once a day?”	162 (55.3)	113 (38.6)	14 (4.8)	4 (1.4)
11. “How often do you put off refilling your medicines because they cost too much money?”	224 (76.5)	43 (14.7)	11 (3.8)	15 (5.1)
12. “How often do you plan ahead and refill your medicines before they run out?”	136 (46.4)	73 (24.9)	49 (16.7)	35 (11.9)

3.2.3.5 Influence of Patients' Demographic and Clinical Characteristics on Medication Burden

Mann-Whitney *U* and Kruskal-Wallis tests were used to determine the influence of sociodemographic and clinical characteristics of participants on perceived medication burden. Table 26 describes the details of the findings of these tests.

Median LMQ score for Qataris was significantly higher, representing worse experience worse medication-related burden, than that for non-Qataris, (p = 0.011). Patients who had spouses showed significantly lower LMQ scores than patients who did not have spouses (p = 0.002).

Statistically significant differences were also found between median scores of LMQ of different categories of employment status (p = 0.036). Subsequently, pairwise comparisons were performed using Dunn's (1964) procedure with a Bonferroni correction for multiple comparisons. This revealed statistically significant differences in median LMQ scores between the employed and non-employed patients, (p = 0.044).

Furthermore, patients diagnosed with DM for more than 10 years showed statistically significantly higher median LMQ score than that of patients who had the diagnosis for less than 10 years (p = 0.007).

According to VAS scores representing global burden, patients with uncontrolled DM reported significantly higher global burden than patients with controlled DM (p = 0.018). Furthermore, median VAS score for patients diagnosed with DM for more than 10 years was significantly higher than that for patients diagnosed with DM for less than 10 years (p = 0.043).

Table 26. *The Influence of Sociodemographic and Clinical Characteristics on LMQ and VAS Scores among Patients Attending NCD Clinics in Qatar (N=293)*

Variable	**LMQ score**	**VAS**
	Median (IQR)	
Gender		
Male	93.00 (20)	3.00 (4)
Female	101.50 (34)	3.00 (5)
P value	0.053	0.736
Age		
Up to 65years	96 (19)	2.46 (4)
Over 65 years	93 (34)	2.56 (3.5)
P value	0.984	0.406
Country of origin		
Qatari	103.00 (24)	4.00 (5)
Non-Qatari	94.00 (20)	3.00 (4)
P value	0.011	0.256
Marital status		
Spouse	94.00 (21)	3.000 (4)
No spouse	114.00 (24)	2.000 (7)
P value	0.002	0.394
Education Level		
Less than primary school	103.00	0.00
Primary or middle school	97.00 (25)	2.00 (5)
Secondary school	97.00 (16)	3.00 (4)

Technical college	80.00 (29)	3.00 (4)
University degree	93.00 (21)	3.00 (4)
Postgraduate degree	106.00 (28)	3.50 (2.8)
P value	0.157	0.354
Comorbidities		
No	101.00 (25)	2.00 (3.8)
Yes	95.00 (21)	3.00 (4.0)
P value	0.537	0.723
No of co morbidities		
None	101.00 (25)	2.00 (3.8)
One	92.00 (22)	3.00 (3.8)
Two	97.00 (22)	3.00 (5.0)
Three or more	95.50 (20)	3.00 (4.0)
P value	0.255	0.925
DM diagnosis duration		
6 months to 10 years	93.00 (19)	3.00 (4.0)
Over 10 years	100.00 (32)	3.25 (5.0)
P value	0.007	0.043
Prescribed medications		
Up to 5 daily medications	95.00 (23)	3.00 (4.0)
Over 5 daily medications	96.00 (18)	2.75 (4.0)
P value	0.324	
Medication type		
Tablet/ capsules	94.00 (19)	3.00 (4.0)
Any other type	97.00 (26)	3.00 (4.0)
P value	0.210	0.026
Help with medicines		
No	96.00 (22)	3.00 (4.0)
Yes	94.00 (20)	3.00 (3.0)
P value	0.216	0.520
DM Control status		
Controlled	94.50 (17)	2.00 (4.1)

Uncontrolled	96.00 (22)	3.00 (4.0)
P value	0.458	0.018
Cigarette Smoking		
Current smoker	100.00 (20)	3.00 (3.0)
Former smoker	93.00 (20)	3.00 (4.0)
Never smoker	96.00 (21)	3.00 (4.0)
P value	0.628	0.627
Shisha Smoking		
Current daily smoker	101.00 (6.0)	3.50 (7.0)
Current social smoker	92.00 (38)	2.00 (4.0)
Former smoker	92.00 (44)	3.50 (2.3)
Never smoker	95.00 (22)	3.00 (4.0)
P value	0.716	0.660
Lifestyle changes		
None	96.00 (21)	3.00 (4)
Exercise	94.50 (20)	3.00 (4)
Exercise & healthy diet	77.00	1.50
P value	0.720	0.751
Employment		
Employed	93.00 (19)	3.00 (4)
Non-employed	103.00 (33)	3.00 (4.9)
Retired	95.00 (36)	3.00 (4)
Full-time student	114.00	1.50
P value	0.036	0.874

3.2.3.6 Relationship between Medication Burden and Adherence

A Spearman's rank-order correlation was used to assess the relationship between perceived burden (LMQ and VAS scores) and adherence to prescribed medications (ARMS score) among the study population. Preliminary analysis showed the relationship to be monotonic, as assessed by visual inspection of a scatterplot (Figure 3). As shown in Table 27, there was a moderate positive correlation between LMQ score and ARMS score, $r_s(251) = 0.317$, $p < 0.0005$. This correlation implies that the more medication-related burden, the lower adherence level. There was also a moderate positive correlation between the VAS scores and ARMS score, $r_s(284) = 0.325$, $p < 0.0005$. This indicates also that the more perceived burden, the lower the adherence level.

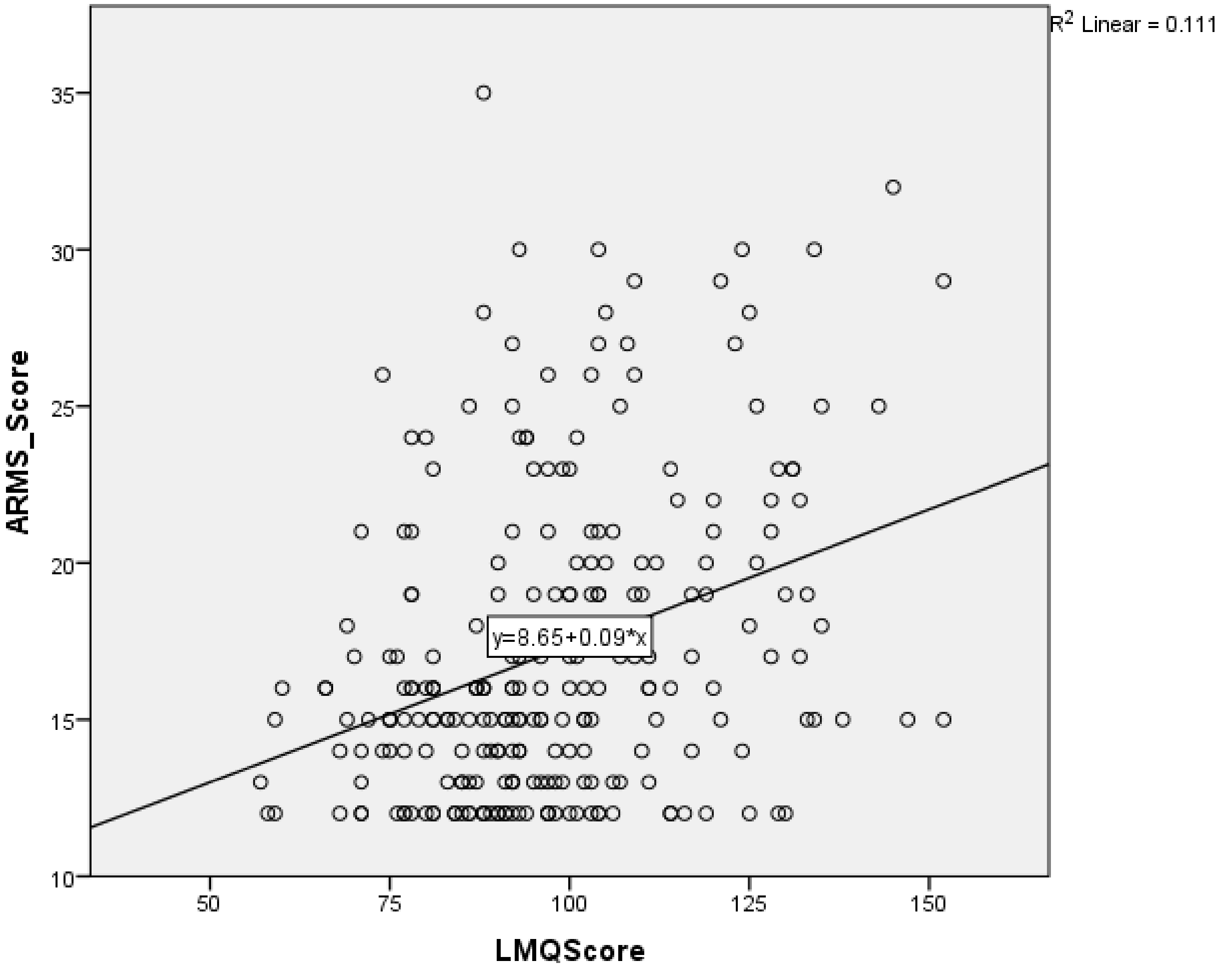

Figure 3. Relationship between the scores of LMQ and ARMS (n=293)

Table 27. *Correlation between Medication-Related Burden (LMQ and VAS Scores), and Adherence (ARMS Score)*

	LMQ Score	**VAS: global burden**
	Spearmen's rho (P value)	
ARMS Score	0.317	0.325
P value	<0.0005	<0.0005

Spearman's rank-order correlations were also conducted to evaluate the relationship between each of the eight domains (themes) of LMQ and ARMS scores as well as VAS. Practical difficulties, cost, side effects, attitudes, and impact of using medicines, showed significant positive correlation with adherence score ($p < 0.05$). On the other hand, autonomy of varying regimen showed significant negative correlation with ARMS ($p < 0.05$). However, relationships with healthcare providers and effectiveness of medicines domains were not significantly associated with adherence. Regarding the VAS, which represents global burden, it showed statistically significant correlation with all of the domains, except the cost domain. Table 28 summarizes these correlations.

Table 28. *Correlations of LMQ Domains with VAS and ARMS Scores*

LMQ domains	**LMQ Score**	**VAS: global burden**	**ARMS Score**
	Spearman's rho		
Relationships with healthcare providers	0.680^{*}	0.245^{*}	0.099^{****}
Practical Difficulties in using medicines	0.748^{*}	0.292^{*}	0.291^{*}
Cost- related burden	0.360^{*}	0.078^{****}	0.226^{*}
Side effects of medicines	0.818^{*}	0.370^{*}	0.240^{*}
Effectiveness of medicines	0.585^{*}	0.218^{*}	0.081^{****}
Attitudes/ concerns about medicines use	0.760^{*}	0.370^{*}	0.329^{*}
Impact on day-to-day life	0.838^{*}	0.329^{*}	0.248^{*}
Control/Autonomy of varying the regimen	-0.177^{**}	$-.161^{***}$	-0.214^{*}

$^{*}P < 0.0005$, $^{**}P = 0.005$, $^{***}P = 0.009$, $^{****}P > 0.005$

To further understand the effect of the ARMS score (adherence) on the LMQ score (medication-related burden), a simple linear regression was performed. Linearity was evaluated through visual inspection of the scatterplot between the two scores with superimposed regression line (Figure 3). There was homoscedasticity and normality of the residuals. Two participants were outliers with LMQ scores of 152 and 147. These were removed from the analysis due to not representing the target population. The prediction equation was: LMQ score = 74. 509 + 1.317*ARMS score. Average ARMS score significantly predicted LMQ score, *F* (1, 249) = 35.85, *p* < .0005, accounting for 12.6% of the variation in burden score with adjusted R^2=0.122, a medium effect size according to Cohen (1988). An extra one score of ARMS representing non-adherence leads to 1.317 increase in medication burden (95% CI, 0.884 to 1.751).

A stepwise multiple linear regression was conducted to determine if the addition of the other collected variables improve the explained variance and prediction of LMQ score. The multiple regression model significantly predicted LMQ score, F (5, 204) = 13.212, $p < .0005$, adj. $R^2 = 0.226$. The variables that added statistically significant changes to the prediction, $p < .05$ were ARMS score, DM diagnosis duration, marital status, employment status, and presence of hypertension (HTN). Regression coefficients and standard errors can be found in Table 29.

Table 29. *Coefficients and Standard Errors of Multiple Regression Analysis Predicting Medication Burden Score*

Variable	**B***	**SE**$_B$**	**Beta** ***
Intercept	98.113	4.361	
ARMS score	1.297	0.232	0.342****
Employment	-7.526	2.452	-0.191****
DM diagnosis duration	7.697	2.410	0.203****
Marital status	-13.578	5.180	0.161****
HTN	-4.768	2.290	-0.131****

* B = unstandardized regression coefficient

**SE$_B$ = standard error

*** Beta = Standardized coefficient

****P < 0.05

CHAPTER 4: DISCUSSION

4.1 Phase 1: Translation and Cultural Adaptation of LMQ into the Arabic Context

The development of the LMQ aimed to introduce an instrument that assesses the burden related to the use of medicines from a patient’s perspective (25). This work emphasizes the view that medication intake is perceived differently by patients when compared to healthcare providers (105).

While studies focusing on culturally adapting measures may vary in their methodologies, we committed to follow best practices provided by ISPOR to ensure credible outcomes. Current recommendations in the literature propose adopting already existing tools for use in different study environments and setting (54, 55, 57). However, achieving cultural equivalence of measurement tools in practice is important to enhance the comparability of results generated from the use of these tools in different cultures (55). The use of questionnaires among societies with different cultures should only be performed after generating data that supports the validity of these measures within the target environment (54).

Different approaches had been used to conduct translation and cultural adaptation processes (39, 54, 106). For example, Santo et al. have adapted the Brazilian-Portuguese version of a self-report measure for dry eye from the US English version. Within their nine-step approach in cultural adaptation, they performed the back-translation on the final adapted version after it has been tested for comprehension. On the other hand, prior to conducting the translation of the French Treatment Burden

Questionnaire into English, Tran et al. characterized the concept which the tool of interest measures among the target population (English-speaking). This diversity is due to the enormous differences in languages, cultures, and settings where these studies have been conducted, in addition to the diversity of the types of the tools adapted.

As the statements of the LMQ were derived from earlier qualitative investigations among patients diagnosed with chronic morbidities (25), they were found to be clear and easy to understand by participants of different backgrounds. Our study revealed no major challenges during the translation process. This may be due to the fact that guidelines were carefully followed in order to maintain the cultural equivalence besides the questionnaire's intended meaning.

Decisions regarding the addition, elimination, or re-wording items of instruments to maintain the cultural equivalence in questionnaire translation and validation processes have been described in the literature (39, 58). In the current study, several issues emerged; most notably was a question among the demographic information page where participants are asked about their ethnic group. A decision was made to replace the ethnic group with the nationality as a better identifier among the Arabic-speaking people. Also an item where respondents were asked about concerns related to interactions between alcohol and other medications raised some concerns related to culture sensitivities. We proposed changing or re-wording the question because, despite the fact that consuming alcohol is not uncommon, it is still considered socially unacceptable in the Arabic culture and therefore seemed out of place in its original format in the questionnaire. The point was that including alcohol consumption as the main focus within an item in the questionnaire seemed inappropriate. It was not totally deleted; but the item was paraphrased such that alcohol consumption remained within an item that covered other dietary items and their potential interactions with medications.

Discussion was raised with the developers regarding the inclusion of a non-graduated VAS which was added at the end of the LMQ. The investigators of this study proposed the use of VAS with scores ranging from 0 to 10; this was to help in the interpretation of the findings resulting from using this tool, a suggestion that was approved by the developers.

The cognitive debriefing interviews were conducted to assess the comprehension and time burden of the questionnaire. The overall good level of comprehension of almost all the statements within the tool was predicted as the development of the LMQ was based on qualitative explorations of patients' perspectives on medication-related issues. The respondents' comments about the length of the questionnaire and the redundancy of some items could be explained by the fact that this tool was designed to identify almost all possible issues related to medicine intake. This is not unusual, where in previous studies criticism of the original instrument occurred and changes that could affect its central construct were proposed as a result of testing the tool in different populations (39, 54, 106).

Most of the guidelines regarding translation and cultural adaptation of patient-reported outcome measures recommend that the back translation is carried out by a native speaker of the original language who is also fluent in the target language. Finding a person with such characteristics in our setting was difficult (English native speaker who is also fluent in Arabic). The back translation in our study was performed by a qualified bi-lingual translator whose mother language was Arabic, and who was familiar with the western culture. While cultural adaptation was rigorous, and research usually use versions of scales emerging from such studies (79), further research was warranted to determine the psychometric properties of the produced Arabic version (LMQ-AR) among Arabic-speaking populations. Specifically, the construct validity and internal consistency reliability that needed to be measured.

4.2 Phase 2: Measurement of Medication-Related Burden among Patients with Non-Communicable Diseases

This study was the first to measure medication-related burden from the perspective of patients living with chronic health diseases, attending NCD clinics at PHCC in Qatar. As majority of the patients visiting NCD were suffering from diabetes, we deliberately investigated medication –related burden among patients with diabetes as the main NCD disease focus.

The Living with Medicines Questionnaire was used to measure aspects of medication –related burden experienced by the NCD patients. Although almost all of the patients interviewed found this measure extremely relevant, the majority of them commented on the length of it. For this reason, 86.3% of the cohort of patients provided complete responses to all of the items of the LMQ and the remaining minority of patients provided comments in the open-ended question at the end of the questionnaire. This might be due to questionnaire filling fatigue experienced by the participants.

Our cohort of patients resembled the population in Qatar (107), with the majority of them were males, and from different nationalities. As expected, and similar to previous studies (9, 79), most of our patients suffered several comorbidities, had been prescribed several medications, non-adherent with their therapy, with uncontrolled diabetes, and adopted an inactive life style.

4.2.1 Validation of the Arabic Version of LMQ

The data generated from this study allowed us to measure the psychometric properties of the LMQ-AR. To validate any PROM, data should be generated through a study that uses the scale of interest (39, 52, 54), and this was the case in our study (phase 2). As the Arabic version of the LMQ was adapted from the original English tool, best practice requires the assessment of its construct validity and internal consistency among patients representing the new target population.

The validation work of LMQ-AR utilized data generated from 138 Arabic-speaking patients with chronic conditions (mainly diabetes). As indicated by validation study of the original tool, the LMQ contained 8 themes (domains), with several items clustering under each of them. Our internal consistency results provided evidence supporting this clustering. As hypothesized, perceived medication-related burden was significantly associated with adherence to medications as well as to the VAS indicating global burden. This study is one of few studies that investigated these associations as independent of the context of the disease and its treatment (39). In the validation of the TBQ in English (another tool to measure treatment burden), Tran et al have also found significant association between perceived burden and self-reported adherence (39). These results were expected due to the presence of qualitative studies highlighting the relationship between perceived burden and adherence (45, 59, 60). Finally, our results provided evidence supporting the validity of the original tool (95).

4.2.2 Medication–Related Burden Assessment

As the interest in conceptualizing and measuring medication-related burden is relatively new, there are currently only few studies to compare our results to. To our knowledge, this is one of the first studies to assess medication-related burden among patients with NCDs from the perspective of the patients as independent measure from the disease or medication context (79). Our study indicated that a considerable proportion of the patients (90%) were suffering from varying degrees of burden related to their medication and overall treatment. As expected, this burden was minimum to moderate, given the high quality services provided to NCD patients in Qatar at minimal cost, and in one clinical setting. Previous studies indicated that 44.6% of patients with diabetes were suffering from the consequences of treatment (namely, diabetes distress) (108). However, that findings were derived as part of quality of life measure, which was related to the characteristics of a specific condition (108). The results of the current study can best be compared to the results of a recent study conducted in Australia, which assessed overall treatment burden among patients with chronic conditions (79). Although in that study, Sav. et al used a different tool (TBQ), the main focus of their measurement was still close to that of our study. They have also found that, independently from the ailment itself, treatment burden affected considerable proportion of patients with chronic diseases. Similar to our study, they have further highlighted the effects of patients' characteristics on the perceived burden (79).

Moreover, patients of Qatari nationality, females, patients without spouses, unemployed patients, patients diagnosed with DM for more than 10 years, patients with uncontrolled DM demonstrated significantly higher scores of medication burden, and those who are prescribed with medication types other than tablets or capsules. Cultural differences between Qatari nationals and non-Qatari residents could translate into different levels of perceiving burden resulting from therapy. As indicated in other studies, females tended to show higher levels of burden than males (16, 27). These findings also indicate that having someone to provide support, and having a job could reduce the burden perceived by the patient. Our results also highlights the importance of the controlled status of the chronic condition in living with less burden. As expected, living longer with the disease, or being prescribed with any other dosage form other than pills, could translate into suffering more with the treatment and its consequences.

As pointed out, only few patients (n = 14) responded to the open-ended question that asks respondents to raise any issues related to medication intake. These respondents raised 10 issues, which they consider burdensome. Among the raised issues, only five were not covered in the LMQ. These are travel time to utilize treatment, waiting time, issues related to the refill system, having to meet different physician in each appointment, and lack of sufficient number of follow-up appointments. Those highlighted burdensome issues were discussed in other studies focusing on overall treatment burden (16, 27, 60).

Adherence has been reported in literature to be a factor that can affect or be affected by the perceived burden (70). However, measuring this effect quantitatively is lacking. To the best of our knowledge, this is one of the first studies to measure adherence and investigate its association with burden. We have found significant positive association between the scores of medication burden and self-reported adherence. This finding supports the qualitative studies suggesting lack of adherence among patients who suffer from medication burden (18, 27). In a study used to validate TBQ among patients with chronic conditions from many English-speaking countries, Tran et al. found higher perceived burden among patients with lower levels of adherence (39).

The current study has also provided evidence regarding the correlation of LMQ domains with global burden (VAS), LMQ score, and adherence. Impact of using medicines and side effects showed the strongest correlation with LMQ score, followed by attitudes/ concerns about medicines. Whereas the domains; effectiveness of medicines, relationships with healthcare providers, cost-related burden, and control of varying the regimen, showed moderate to weak associations with LMQ score. This suggests the contribution of each domain to the overall perceived medication-related burden among the studied population. This implies that the "impact on daily life", "side effects", "concerns about medicines", and "practicalities", respectively, were the strongest contributors in perceived medication-related burden among patients receiving care in NCD clinics. On the other hand, the cost-related burden and the control of varying regimens showed the weakest correlation with the LMQ score, suggesting their minimal contribution to the perceived burden.

Similarly, global burden represented by VAS was not significantly associated with cost-related burden. This can be explained by the affordable prices patients pay for their regular medications and follow up at PHCC in Qatar. Interestingly, autonomy with varying regimen was negatively associated with global burden as well as LMQ score. This means that less control is associated with less burden, and this contradicts the magnitude of association between this domain and the total LMQ score (of the original version). However, this contradiction could be explained by culture differences between the population among whom the tool was developed, and those where the adapted tool was applied. For example, the concept of patients' autonomy in making therapeutic decisions as one of the patients' rights is applied and well understood in societies where the LMQ was developed. For this reason, more control of medication regimens is translated into less burden. On the other hand, in Arab countries there are still barriers to a well-established system in which patients will be fully involved in the control of their treatments (109, 110). Subsequently, less control was associated with less burden in our setting.

Moreover, adherence was associated with all themes of burden except the relationship with healthcare providers and effectiveness of medicines. This suggests that adherence in not related to these two aspects of medication burden.

As adherence alone explained only 12% of medication-related burden, we have further incorporated all the possible confounding factors in regression model as an attempt to investigate the factors that can explain or predict the perceived medication burden. Regression results suggest that the mean medication burden for participants with diabetes alone for less than 10 years, without spouse, and not employed, will be 98.113 (minimum burden) (standard error 4.361), out of possible score 205. The presence of hypertension surprisingly reduces the burden score by -4.768 (standard error 2.290). This could be due to the fact that an additional diagnosis of hypertension (one more NCD) could create more awareness of risk factors, and hence less perceived burden by the treatment. This finding contradicts the finding by Sav. et al who highlighted that having extra chronic condition would lead to increase treatment burden (79). Furthermore, the presence of spouse as well as having a job were associated with reduced medication burden score by 7.526, 13.578, respectively. This is expected, since the evidence from literature suggests that having familial support in the life of the patients with chronic disease (79), as well as a steady job reduces the perceived burden. Finally, exceeding 10 years of living with the chronic condition (diabetes in our case) increased burden score by 7.697 (standard error 2.410). Although one would assume that living more with the disease could mean learning more about it, getting used to its management, and hence feeling less burden; our results suggest that this was not the case in our sample. This could be explained by the possibility that the longer someone suffers a health condition and uses treatment for it, the more h/she experience multiple issues related to long-term adverse treatment effects.

4.3 Limitations and Future Studies

This study has several limitations that warrant mention to benefit future research. First, as a cross-sectional study, it meant that we could not capture all factors that might have affected medication-related burden over time. Longitudinal studies would be better capable to investigate the effect of those factors on perceived burden over time. Second, some of the variables (for example diagnosis duration, lifestyle changes) were obtained from the patients, and this could be subject to recall bias. Third, it is true that self-reported adherence is still considered the most feasible, user-friendly, and simple way of adherence measurement(111), but combination of subjective and objective methods of measuring adherence is recommended (112). The research team initially aimed to measure adherence using the ARMS tool as well as the formula of Proportion of Days Covered (PDC) (113). However, after piloting of the procedure of phase 2 of this research, calculation PDC was not feasible given the scarce data that was kept at the pharmacy. Fourth, this study was restricted to patients who were able to communicate in English or Arabic. Hence, results cannot be generalized to people coming from different cultures constituting a considerable proportion of the population in Qatar. In fact, perceived burden could be affected by factors related to the differences in beliefs about medications (60); and such differences can also be related to culture. Future studies investigating these factors are recommended.

Fifth, although stratified or systematic sampling techniques would have been the most suitable for this study to produce generalizable results, but convenience sampling was utilized for two reasons: (1) limited access to three health centers as per ethical approval conditions, and (2) formulating a sampling frame of eligible patients was not feasible due to the nature of patients' visits to the NCD clinics. Although our sample demographic information resembles those of the population in Qatar, it may not be representative of it due to the limitation of sampling technique. Moreover, in spite of the use of comparisons in analyses, the sample size calculation was for descriptive study. This is because the main focus of the study was to measure medication-related burden for the first time. However, we approached more patients than the estimated sample size to account for this issue.

Finally, regarding data collection, questionnaires were self- or interviewer-administered. This can be considered a limitation due to possible positive or social desirability in case of the interviewer based administration. Furthermore, the use of two methods, could compromise the reliability of the results obtained from the study instruments. However, during the interviews, the researcher made sure to restrict her role to objectively read the tools' items in order to limit the influence on patient's responses.

Furthermore, as much as this study is important in highlighting the presence of medication-related burden as a possible barrier to achieve the maximum benefits of health care services provided to patients in Qatar, the critical role of the healthcare providers (e.g. pharmacists) in reducing medication-related was not investigated in this study. This, however, warrants further research specifically designed to investigate the role of healthcare practitioners in reducing medication-related burden.

Finally, we have attempted to investigate the effect of confounding factors on the perceived medication burden. The results of this investigation could be considered preliminary, as the main focus of the study was not about investigating this effect, and the sample size was not calculated based on regression. For example, beliefs about medications, which play a considerable role in perceived burden, was not assessed in this study. Future studies (qualitative and quantitative) with the aim of understanding the characteristics of the patients struggling with burden are needed.

4.4 Conclusion

This research has produced an Arabic version of the Living with Medicines Questionnaire (LMQ-AR), adapted it into the Arabic context, and demonstrated the psychometric properties of it. The study further used this adapted tool in measuring medication-related burden among patients with chronic diseases attending primary care clinics in Qatar. A considerable proportion of those patients suffer from medication burden, which could be affected by many factors including adherence to drug therapy, duration of the diagnosis, control of the disease, being employed, or receiving support from family. Our study findings suggest that healthcare professionals should be aware of the impact of treatment plans on the lives of patients who live with chronic conditions. In addition, factors affecting medication-related burden should be taken into consideration when designing tailored interventions to reduce this burden.

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Appendix A: The Living with Medicines Questionnaire: English version (LMQ)

LMQ
Living with Medicines Questionnaire

Medicines and Your Day-to-Day Life

Health Center code:
Patient Code:
Date:

This questionnaire seeks your views and opinions about the prescribed medicines you use and how they affect your life.

Medicines include tablets, creams, inhalers, liquids, injections and so on.

You may be using more than one medicine, please think about ALL your medicines when completing this questionnaire.

LMQ© Version 3 2015

Please answer a few questions **ABOUT YOU AND YOUR MEDICINES**

1. How many prescription medicines do you use regularly?

Please write the TOTAL number of medicines here: ____________________

Medicines include tablets, capsules, creams, inhalers, inhalers, liquids, eye drops and so on. Count each different prescription as one medicine.

2. Which type of medicines do you use regularly? You may tick one or both options

☐ **Tablets/Capsules** ☐ **Any other type**

3. How often do you use your medicine(s)? *You may tick one or more options*

☐ **Once per day** ☐ **Twice per day** ☐ **Three times per day**

☐ **More than three times per day** ☐ **Other, please specify……………………………………………**

4. Do you pay for your prescriptions? ☐ **Yes** ☐ **No**

5. Does someone help you with using your medicines? ☐ **Yes** ☐ **No**

If you answered yes, who helps you?

6. Are you: ☐ **Male** ☐ **Female**

7. What is your age? *Please write it here in years* ☐

8. What is your nationality?

Qatar	Egypt	Jordan	Palestine	Lebanon	Sudan	Yemen	Syria	Philippines	India	Pakistan	Other, please indicate

9. What is the highest level of education you have completed?

☐ **School** ☐ **Technical College/Apprenticeship** ☐ **University** ☐ **Other**

10. What is your employment status?

☐ **Employed** ☐ **Unemployed** ☐ **Retired** ☐ **Full-time student**

The following statements cover different aspects of using medicines.

Please read each statement carefully and tick the response box that is closest to your personal opinion.

Please tick **only one** box for each statement.

	Strongly agree	**Agree**	**Neutral opinion**	**Disagree**	**Strongly disagree**
1. I find getting my **prescriptions** from the doctor difficult.	☐	☐	☐	☐	☐
2. I find getting my **medicines** from the pharmacist difficult.	☐	☐	☐	☐	☐
3. I am satisfied with the effectiveness of my medicines.	☐	☐	☐	☐	☐
4. I am **comfortable** with the times I should take my medicines.	☐	☐	☐	☐	☐
5. I worry about **paying** for my medicines.	☐	☐	☐	☐	☐

	Strongly agree	**Agree**	**Neutral opinion**	**Disagree**	**Strongly disagree**
6. I worry that I have to take **several** medicines at the same time.	☐	☐	☐	☐	☐
7. I **trust** the judgement of my doctor(s) in choosing medicines for me.	☐	☐	☐	☐	☐
8. I would like **more say** in the brands of medicines I use.	☐	☐	☐	☐	☐
9. I feel I need **more information** about my medicines.	☐	☐	☐	☐	☐
10. I am concerned that I may **forget** to take my medicines.	☐	☐	☐	☐	☐

	Strongly agree	**Agree**	**Neutral opinion**	**Disagree**	**Strongly disagree**
11. I can **vary the dose** of the medicines I take.	☐	☐	☐	☐	☐
12. I am concerned about possible damaging **long term effects** of taking medicines.	☐	☐	☐	☐	☐

	Strongly agree	**Agree**	**Neutral opinion**	**Disagree**	**Strongly disagree**
13. I can **choose** whether or not to take my medicines.					
14. My doctor(s) **listen** to my opinions about my medicines.	☐	☐	☐	☐	☐
15. My medicines **prevent** my condition getting worse.	☐	☐	☐	☐	☐
16. I am concerned that I am **too reliant** on my medicines.	☐	☐	☐	☐	☐
17. I am concerned that my medicines **interact** with my **nutritional habits (other foods - alcohol drinks)**.	☐	☐	☐	☐	☐
18. I worry that my medicines may **interact** with **each other**.	☐	☐	☐	☐	☐
19. My medicines interfere with my **social or leisure activities.**	☐	☐	☐	☐	☐

	Strongly agree	**Agree**	**Neutral opinion**	**Disagree**	**Strongly disagree**
20. My doctor(s) takes my **concerns** about side effects seriously.	☐	☐	☐	☐	☐
21. The **side effects** I get are sometimes worse than the problem for which I take medicines.	☐	☐	☐	☐	☐
22. The **side effects** I get from my medicines interfere with my day-to-day life (e.g. work, housework, sleep).	☐	☐	☐	☐	☐
23. I have to put a lot of **planning and thought** into taking my medicines.	☐	☐	☐	☐	☐
24. I get **enough information** about my medicines from my doctor(s).	☐	☐	☐	☐	☐

	Strongly agree	**Agree**	**Neutral opinion**	**Disagree**	**Strongly disagree**
25. My medicines live up to **my expectations**.	☐	☐	☐	☐	☐
26. I can **vary the times** I take my medicines.	☐	☐	☐	☐	☐
27. It is **easy** to keep to my medicines routine.	☐	☐	☐	☐	☐
28. Taking medicines affects my **driving**.	☐	☐	☐	☐	☐
29. I find **using** my medicines difficult.	☐	☐	☐	☐	☐
30. The side effects I get from my medicines are **bothersome**.	☐	☐	☐	☐	☐

31. I sometimes have to **choose** between buying basic essentials or medicines.	☐	☐	☐	☐	☐

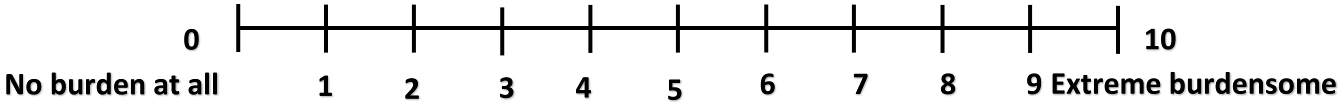
	Strongly agree	**Agree**	**Neutral opinion**	**Disagree**	**Strongly disagree**
32. My medicines allow me to **live my life** as I want to.	☐	☐	☐	☐	☐
33. I have to **pay** more than I can afford for my medicines.	☐	☐	☐	☐	☐
34. The health professionals providing my care **know enough** about me and my medicines.	☐	☐	☐	☐	☐
35. My medicines interfere with my **social relationships**.	☐	☐	☐	☐	☐
36. Taking medicines causes me problems with **daily tasks** (such as work, housework, hobbies).	☐	☐	☐	☐	☐

	Strongly agree	**Agree**	**Neutral opinion**	**Disagree**	**Strongly disagree**
37. My medicines interfere with my **sexual life**.	☐	☐	☐	☐	☐
38. The **side effects** I get from my medicines adversely affect my well-being.	☐	☐	☐	☐	☐
39. My medicines are **working**.	☐	☐	☐	☐	☐
40. The **side effects** are worth it for the benefits I get from my medicines.	☐	☐	☐	☐	☐
41. My **life** revolves around using my medicines	☐	☐	☐	☐	☐

The question below seeks your OVERALL OPINION about ALL your prescribed medicines.

Please **<u>mark on the line with an ‘X’</u>** at the position that best reflects your opinion.

1. Overall, how much of a burden do you feel your medicines are to you?



2. If you have any other views about how your medicines affect your day-to-day life, please describe them here.

Appendix B: The Living with Medicines Questionnaire: Arabic version (LMQ-AR)

استبيان التعايش مع الأدوية **LMQ**

الأدوية وحياتك اليومية

Health Centre code:
Patient Code:
Date:

يهدف هذا الاستبيان للحصول على وجهات **نظرك** وآرائك حول الأدوية الموصوفة التي **تتناولها** وكيف تؤثر على **حياتك**.

وتشمل الأدوية الأقراص، والكريمات، وأجهزة الاستنشاق والسوائل، والحقن وخلافه.

ربما تستخدم أكثر من دواء، الرجاء التفكير **بكل أدويتك** وقت الإجابة على هذا الاستبيان.

الأدوية وحياتك اليومية- إستبيان التعايش مع الأدوية

بدايةً، يرجى منك الاجابة على بعض الأسئلة المتعلقة بك وبأدويتك

1- كم عدد الأدوية التي تتناولها بإنتظام ؟ الرجاء كتابة عدد الأدوية التي تتناولها هنا ☐

تشمل الأدوية الأقراص، والكبسولات، والكريمات، وأجهزة الاستنشاق والسوائل، والقطرات العينية وخلافه

<u>احسب كل وصفة دواء مختلفة كدواء واحد</u>

2- ما نوع الأدوية التي تتناولها بانتظام؟ يمكن اختيار واحد أو أوكثر من الخيارات التالية:

○ حبوب/ كبسولات ○ أي نوع آخر

3- كم مرة تتناول أدويتك يومياً؟ يمكن اختيار واحد أو أوكثر من الخيارات التالية:

○ **مرة في اليوم** ○ **مرتين في اليوم** ○ **ثلاث مرات في اليوم** ○ **أكثر من ثلاثة في اليوم**

أخرى، الرجاء كتابتها هنا ....

4- هل تدفع ثمن أدويتك الموصوفة؟ نعم ☐ **لا** ☐

5- هل يساعدك أحد في استخدام أدويتك؟ نعم ☐ **لا** ☐

إذا أجبت بنعم، فمن الذي يساعدك في استخدام أدويتك؟ زوج ☐ **أحد الأقارب** ☐ **موظف رعاية** ☐

آخرون ☐ **إذا أجبت ب(آخرون) ، يرجى كتابة من يساعدك هنا** ________________________________

6- هل أنت ؟ ذكر ☐ **أنثى** ☐

7- ما هو عمرك:؟ الرجاء كتابة عمرك بالسنوات هنا ________________

8- ما هي جنسيتك ؟

قطر	مصر	الأردن	فلسطين	لبنان	السودان	اليمن	سوريا	الفلبين	الهند	باكستان	أخرى، الرجاء كتابتها

9- ماهو أعلى مستوى تعليمي وصلت إليه؟

مدرسة ☐ كلية مهنية/تدريب مهني ☐ جامعة ☐ أخرى ☐

10- ما هو وضعك الوظيفي؟ أعمل ☐ **لا أعمل** ☐ **متقاعد** ☐ **طالب بدوام كامل** ☐

الأدوية وحياتك اليومية- إستبيان التعايش مع الأدوية

تغطي الجمل التالية الجوانب المختلفة لاستخدام الأدوية.

الرجاء قراءة كل جملة بعناية ، ووضع علامة في مربع الإجابة الأقرب إلى رأيك الشخصي. يرجى اختيار مربع واحد فقط لكل جملة.

	أوافق بشدة	أوافق	رأي محايد	لا أوافق	لا أوافق بشدة
1. أجد أن الحصول على **وصفات دوائي** من الطبيب صعبًا	☐	☐	☐	☐	☐
2. أجد أن الحصول على **أدويتي** من الصيدلي صعبًا	☐	☐	☐	☐	☐
3. **أنا راضٍ عن** فعالية أدويتي	☐	☐	☐	☐	☐
4. إنني **أتقبل** أن أتناول الأدوية في الأوقات المحددة لها	☐	☐	☐	☐	☐
5. يقلقني **أن أدفع** لقاء أدويتي	☐	☐	☐	☐	☐

	أوافق بشدة	أوافق	رأي محايد	لا أوافق	لا أوافق بشدة
6. يقلقني تناول **عدة أدوية** في نفس الوقت	☐	☐	☐	☐	☐
7. **أثق** برأي طبيبي في اختيار أدويتي	☐	☐	☐	☐	☐
8. أود أن يكون لي **دور أكبر** في اختيار الاسم التجاري للدواء الذي أستخدمه	☐	☐	☐	☐	☐
9. أشعر أحياناً بالحاجة للحصول على **معلومات أكثر** عن أدويتي	☐	☐	☐	☐	☐
10. ينتابني القلق من أنني قد **أنسى** تناول أدويتي	☐	☐	☐	☐	☐

	أوافق بشدة	أوافق	رأي محايد	لا أوافق	لا أوافق بشدة
11. يمكنني **تغيير جرعة** الأدوية التي أتناولها وفق حاجتي	☐	☐	☐	☐	☐
12. ينتابني القلق إزاء **الآثار الضارة المحتملة** من تناول الأدوية على المدى البعيد	☐	☐	☐	☐	☐
13. أستطيع **الاختيار** بين تناول أدويتي أوعدم تناولها	☐	☐	☐	☐	☐
14. **يستمع** طبيبي إلى آرائي بشأن أدويتي	☐	☐	☐	☐	☐
15. **تمنع** أدويتي حالتي الصحية من أن تسوء	☐	☐	☐	☐	☐
16. يقلقني **إعتمادي التام** على أدويتي	☐	☐	☐	☐	☐
17. يقلقني احتمال **تفاعل** ادويتي مع **عاداتي الغذائية (مشروبات كحولية، أطعمة أخرى)**	☐	☐	☐	☐	☐

الأدوية وحياتك اليومية- استبيان التعايش مع الأدوية

الرجاء وضع علامة في مربع الإجابة الأقرب إلى رأيك الشخصي

	أوافق بشدة	أوافق	رأي محايد	لا أوافق	لا أوافق بشدة
18. يقلقني أن **تتفاعل أدويتي مع بعضها البعض**	☐	☐	☐	☐	☐
19. تؤثر أدويتي على **نشاطاتي الاجتماعية أوالترفيهية**	☐	☐	☐	☐	☐
20. يهتم طبيبي **بما يقلقني** حول التأثيرات الجانبية للدواء	☐	☐	☐	☐	☐
21. **الآثار الجانبية** للدواء تكون أحياناً أسوأ من المشكلة الصحية التي أتناول الدواء من أجلها	☐	☐	☐	☐	☐
22. **الآثار الجانبية** الناتجة عن أدويتي تؤثر على حياتي اليومية (مثل: العمل، الأعمال المنزلية، النوم)	☐	☐	☐	☐	☐
23. يتطلب تناول أدويتي الكثير من **التخطيط والتفكير** مني	☐	☐	☐	☐	☐
24. أحصل على **معلومات كافية** من طبيبي عن أدويتي	☐	☐	☐	☐	☐

	أوافق بشدة	أوافق	رأي محايد	لا أوافق	لا أوافق بشدة
25. أدويتي تحقق **توقعاتي** منها	☐	☐	☐	☐	☐
26. أستطيع **تغيير مواعيد** تناول أدويتي إذا أردت ذلك	☐	☐	☐	☐	☐
27. من **السهل** الحفاظ على روتين تناول أدويتي	☐	☐	☐	☐	☐
28. تناول الأدوية يؤثر على قدرتي **على قيادة السيارة**	☐	☐	☐	☐	☐
29. أجد **استخدام** أدويتي أمراً صعباً	☐	☐	☐	☐	☐
30. الآثار الجانبية الناتجة عن أدويتي **مزعجة**	☐	☐	☐	☐	☐
31. علي **الاختيار** أحياناً بين شراء الحاجات الأساسية أو الأدوية	☐	☐	☐	☐	☐

	أوافق بشدة	أوافق	رأي محايد	لا أوافق	لا أوافق بشدة
32. أدويتي تسمح لي بأن **أعيش حياتي** كما أريد	☐	☐	☐	☐	☐
33. ما يتوجب علي **إنفاقه** على شراء الأدوية يفوق مقدرتي	☐	☐	☐	☐	☐
34. اختصاصيو الرعاية الصحية الذين يوفرون الرعاية لي **يعرفون ما يكفي** عني وعن أدويتي	☐	☐	☐	☐	☐
35. تؤثر أدويتي على **علاقاتي الاجتماعية**	☐	☐	☐	☐	☐
36. يسبب لي تناول الأدوية مشاكل مع **أنشطتي اليومية** (كالعمل، والاعمال المنزلية والهوايات)	☐	☐	☐	☐	☐

الأدوية وحياتك اليومية- استبيان التعايش مع الأدوية

الرجاء وضع علامة في مربع الإجابة الأقرب إلى رأيك الشخصي

	أوافق بشدة	أوافق	رأي محايد	لا أوافق	لا أوافق بشدة
37. أدويتي تؤثر على **حياتي الجنسية**	☐	☐	☐	☐	☐
38. **الآثار الجانبية** الناتجة عن أدويتي تؤثر سلباً على صحتي	☐	☐	☐	☐	☐
39. أدويتي **فعالة**	☐	☐	☐	☐	☐
40. الفوائد التي أحصل عليها من الدواء تفوق **الآثار الجانبية**	☐	☐	☐	☐	☐
41. أدويتي تشغل حيزاً كبيراً من **حياتي**	☐	☐	☐	☐	☐

يهدف السؤال التالي لمعرفة رأيك الإجمالي عن كل أدويتك الموصوفة.

الرجاء وضع علامة X في الموقع الأقرب الذي يدل على رأيك:

- بشكل عام، كيف تشعر بالعبء الذي تشكله أدويتك؟

0 — لا تشكل عبئاً

1 2 3 4 5 6 7 8 9

10 — تشكل عبئاً كبيراً

اذا كانت لديك أية آراء اخرى حول مدى تأثير أدويتك على حياتك اليومية، يرجى ذكرها هنا

Appendix C: Adherence to Refills and Medications Scale (ARMS) – English version

ADHERENCE TO REFILLS AND MEDICATIONS SCALE (ARMS)

I would like to ask you how often you actually miss taking your medicines. There are no right or wrong answers. For each question, please answer "none of the time," "some of the time," "most of the time," or "all of the time."

	None	**Some**	**Most**	**All**
1. How often do you forget to take your medicine?	1	2	3	4
2. How often do you decide not to take your medicine?	1	2	3	4
3. How often do you forget to get prescriptions filled?	1	2	3	4
4. How often do you run out of medicine?	1	2	3	4
5. How often do you skip a dose of your medicine before you go to the doctor?	1	2	3	4
6. How often do you miss taking your medicine when you feel better?	1	2	3	4
7. How often do you miss taking your medicine when you feel sick?	1	2	3	4
8. How often do you miss taking your medicine when you are careless?	1	2	3	4
9. How often do you change the dose of your medicines to suit your needs (like when you take more or less pills than you're supposed to)?	1	2	3	4
10. How often do you forget to take your medicine when you are supposed to take it more than once a day?	1	2	3	4
11. How often do you put off refilling your medicines because they cost too much money?	1	2	3	4
12. How often do you plan ahead and refill your medicines before they run out?	1	2	3	4

Appendix D: Adherence to Refills and Medications Scale (ARMS) – Arabic version

تقييم الالتزام بتناول الأدوية وإعادة صرفها

أود أن أسألك عن مدى تكرار عدم تناولك لأدويتك بالفعل. ليس هناك إجابة صحيحة أو خاطئة. الرجاء اختيار الإجابة من بين، "أبداً"، "بعض الأحيان"، "معظم الأحيان"، أو " دائماً".

	أبداً	بعض الأحيان	معظم الأحيان	دائماً
1. ماهو مدى تكرار نسيانك لأخذ أدويتك؟	**1**	**2**	**3**	**4**
2. ماهو مدى تكرار قرارك بعدم تناول دوائك؟	**1**	**2**	**3**	**4**
3. ماهو مدى تكرار نسيانك لصرف أدويتك؟	**1**	**2**	**3**	**4**
4. ماهو مدى تكرار نفاذ أدويتك التي بحوزتك؟	**1**	**2**	**3**	**4**
5. ماهو مدى تكرار تركك جرعة من دوائك قبل زيارة طبيبك؟	**1**	**2**	**3**	**4**
6. ماهو مدى تكرار تغاضيك عن تناول دوائك لشعورك بتحسن حالتك الصحية؟	**1**	**2**	**3**	**4**
7. ماهو مدى تكرار تغاضيك عن تناول دوائك لشعورك بسوء حالتك الصحية؟	**1**	**2**	**3**	**4**
8. ماهو مدى تكرار تغاضيك عن تناول أدويتك بسبب الإهمال؟	**1**	**2**	**3**	**4**
9. ماهو مدى تكرار تغييرك لجرعة الدواء لتناسب احتياجاتك؟ **(مثلا، عندما تتناول أقراص من الدواء أقل أو أكثر من المطلوب منك تناوله)**	**1**	**2**	**3**	**4**
10. ماهو مدى تكرار نسيانك لتناول أدويتك التي يفترض عليك تناولها أكثر من مرة يومياً؟	**1**	**2**	**3**	**4**
11. ماهو مدى تكرار تأجيل إعادة صرف أدويتك لأنها تكلف الكثير من المال؟	**1**	**2**	**3**	**4**
12. ماهو مدى تكرار تخطيطك مسبقاً لإعادة صرف أدويتك قبل نفاذها؟	**1**	**2**	**3**	**4**

Appendix E: Data collection form

Patient Data Form (to be filled from Medical Records and/or patients' interviews)

Patient HealthCare center Code:	
Patient research ID:	
Date of interview/ PHCC visit:	
Patient mobile:	
Patient email address if any:	

Inclusion Criteria (Must ALL be "Yes" to be included)	**Yes**	**No**
1. At least 18 years of age		
2. Communicates in English and/or Arabic		
3. Has a chronic condition for at least 6 months at the time of the interview		

Sociodemographic information

Marital status	☐ Married ☐ Single ☐ Divorcee ☐ Widowed
Education level	• Less than primary school • Primary or middle school • Secondary or high school only • Technical College/Apprenticeship • University degree • Post graduate University degree

Medical conditions

DM diagnosis duration	
Comorbidities (all that apply)	☐ Hypertension ☐ Dyslipidemia ☐ Hyperlipidemia ☐ Vit. D deficiency

	☐ Obesity ☐ Depression ☐ Other (Please specify):

Smoking History

Cigarette smoking	☐ Current smoker: ------------- cigarettes per day ☐ Former smoker ☐ Non-smoker
Shisha smoking	☐ Current daily shisha smoking ☐ Current social shisha smoking ☐ Former shisha smoker ☐ Non smoker

Medications Intake

Prescribed Medications	Medication list	Regimen	Date of last refill
lifestyle changes	☐ None ☐ Exercise ☐ Exercise and healthy diet		

Clinical indicators (last values)

HbA1c%	
BMI	

Appendix F: Publications

- Zidan A, Awaisu A, Kheir N. The Impact of Long-term Medicines Use: Validation of an Arabic version of the Living with Medicines Questionnaire. (Poster). 6th Kuwait international Pharmacy Conference (KIPC 2017), February, 2017.
- Zidan A, Awaisu A, Hasan S, Kheir N. (2016). The living with medicines questionnaire: translation and cultural adaptation into the Arabic context. Value in Health Regional Issues, 10, 36-40.
- Zidan A, Awaisu A, Hasan S, Kheir N. The Impact of Long-term Medicines Use: Linguistic Validation of the Living with Medicines Questionnaire. (Poster). Qatar Foundation Annual Research Conference, March 2016.
- Zidan A, Awaisu A, Hasan S, Kheir N. The living with medicines questionnaire: translation and cultural adaptation into the Arabic context. (Poster). GCC Pharmaceutical Congress, Dubai, UAE. October, 2015.
- Zidan A, Awaisu A, Hasan S, Kheir N. The living with medicines questionnaire: translation and cultural adaptation into the Arabic context. (Poster). College of Pharmacy 5th Annual Student Research Evening, Qatar University. Doha, Qatar. June 3, 2015.