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Pharmacist services in the enhancement of type 2 diabetes patients' therapeutic adherence

PhD thesis

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List of abbreviations

2-h PG	2-hours plasma glucose
BMQ	Brief Medication Questionnaire
CINAHL	Cumulative Index to Nursing and Allied Health literature database
DMAS	Diabetes Medication Assistance Service
DM	Diabetes Mellitus
DPP-4	Dipeptidyl Peptidase-4
DSR	Days Supply Remaining
FBG	Fasting Blood Glucose
GLP-1Ras	Glucagon-like peptide-1 receptor agonist
HbA1c	The A1C test also known as the hemoglobin A1C or HbA1c test
IDF	International Diabetes Federation
IFG	Impaired Fasting Glycaemia
IGT	Impaired Glucose Tolerance
MARS	Medication Adherence Rating Scale
MEMS	Medication Event Monitoring Scale
MI	Motivational Interview
MINORS	Methodological Index for Non-Randomized Trails
MMS-8	Morisky Medication Scale
MoH	Ministry of Health
MPR	Medication Possession Ratio
MRA	Medication Refill Adherence
MTM	Medication Therapy Management
MUR	Medication Use Review
NCD	Non-Communicable Disease
NCDs	Non-Communicable Diseases
OGTT	Oral Glucose Tolerance Test
OHA	Oral Hypoglycemic Agents
OTC	Over The Counter Drugs
PC	Pharmaceutical Care
PCNE	Pharmaceutical Care Network Europe
PDC	Proportion of Days Covered
PICO	Population, Intervention, Comparison, and Outcomes

PMC	PubMed Center
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
QOL	Quality Of Life
RCT	Randomized Controlled Trail
RoB2	Risk of Bias tool for Randomized Controlled Trails
ROBINS-I	Risk of Bias tool for Non-Randomized Trails
RPG	Random Plasma Glucose
NRCT	Non-Randomized Controlled Trail
SGLT2	Sodium-glucose co-transporter 2 inhibitors
SMSI	Self-Management Support Interventions
SPA	Syrian Pharmacist Association
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
UHC	Universal Health Coverage
VAS	Visual Analogue Scale
NGOs	Non-Governmental Organizations
WHO	World Health Organization

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List of important definitions

Adherent patients:	Patients who consistently and faithfully follow their prescribed treatment plan, including taking medications, adhering to dietary recommendations and maintain to the recommended lifestyle changes as advised by their healthcare provider
Non- adherent patients:	Patients who do not consistently follow their prescribed treatment plan. This may involve missing doses of medication, not following dietary guidelines, or failing to adhere to recommended lifestyle modifications
Intended- non- adherence:	Patients who stop their medications for a reason
Non- intended non-adherence:	Patients who ceased taking their medicines due to forgetfulness

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1. Introduction

1.1. Brief discreption of geographic, demographics in Syria

This section aims to present a geographical information about Syria in the context of a dissertation focusing on the satisfaction and perception of individuals with type 2 diabetes mellitus regarding local community pharmacy services in Latakia Governorate, Syria. It is crucial to provide the reader with an understanding of Syria's location and demographic profile, because the prevalence of diabetes among the Syrian population is considered high. Additionally, we will discuss key aspects of the Syrian healthcare system, providing the necessary background for comprehending the research.

1.1.1. Geographic profile of Syria (Latakia Governorate)

Syria is situated in the Middle East and forms part of Southwestern Asia. Since 2018, the World Bank has classified it as a low-income country. The country shares borders with Lebanon, Israel, Jordan, and Iraq, and it has a coastline along the eastern Mediterranean Sea adjacent to Turkey. Syria is divided into 14 Governorates, which are further subdivided into sixty districts. Each Governorate is led by a governor appointed by the president, who oversees various administrative functions, including healthcare, social services, education, tourism, public works, transportation, domestic trade, agriculture, industry, civil defense, and law enforcement (1). According to the latest data from the United Nations, the estimated population of Syria is 18,772,092.

Latakia, the primary port city located on the Mediterranean coast, has historical references as Laodicea in Syria or Laodicea ad Mare. The city's population is estimated to be around 709,000 as of 2023. The population growth in Latakia can be attributed to the ongoing Syrian civil war, which has led to the arrival of internally displaced persons from rebel-held areas. Latakia ranks as the fourth-largest city in Syria, following Aleppo, Damascus, and Homs (2).

Figure 1 displays the geographic location of Governorates of Syria as depicted by the WorldAtlas updated 2023.

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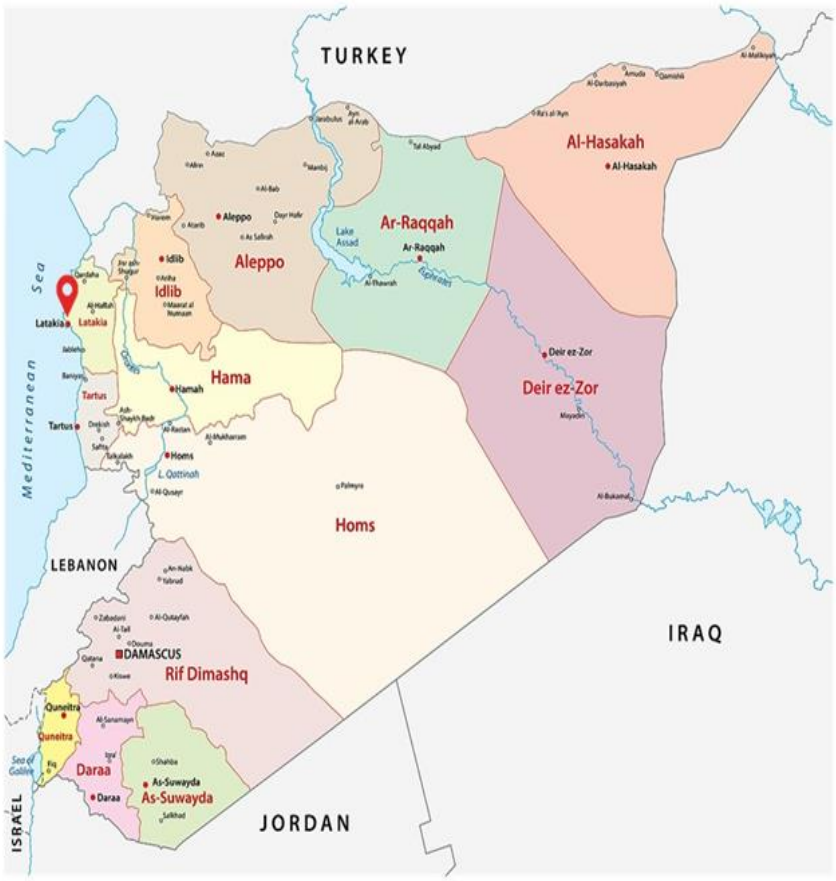

Figure 1: Geographical location of Syria. Governorates of Syria Map copied from this the electronic source https://www.worldatlas.com/maps/syrian-arab-republic

1.1.2. Diabetes care in Syria

Diabetes care is a crucial aspect of healthcare in Syria, and it is primarily delivered by the Ministry of Health through a network of healthcare facilities. These facilities include primary health centers, specialized diabetes centers, public clinics, general and specialist hospitals, as well as private clinics and hospitals. However, in situations of crises and other challenging circumstances, the availability and accessibility of these services may be affected, creating barriers to receiving proper diabetes care. The incidence of diabetes in Syria has been on the rise in recent years. In 2017, there were 705,700 reported cases of adult diabetes in Syria. However, during times of conflict, individuals with diabetes face numerous challenges, including food insecurity, limited access to medications and testing supplies (3). The conflict has disrupted healthcare infrastructure, making it difficult for individuals with diabetes to access appropriate medical care. Many

healthcare facilities have been damaged or destroyed, and there is a shortage of healthcare professionals, including diabetes specialists .

Morover, there are concerns regarding the availability and affordability of diabetes medications in Syria. Shortages and high costs of antidiabetic drugs, distributing glucometers, limited access to specialized diabetes care programs low adherence to guidelines, and insufficient utilization of available resources make it challenging for individuals to consistently access the medications they need for diabetes management (4).

The conflict has led to economic hardships, making it difficult for individuals to afford necessary medications, regular check-ups, and healthy food options.

Access to insulin becomes a major concern, especially for those with T1DM, as any disruption in the insulin supply can result in a medical emergency. As a result, a large number of diabetics in Syria rely entirely on external organizations, particularly the World Health Organization (WHO), to provide them with the vital medications they need. In 2021, WHO supported the Ministry of Health (MOH) and Non-Governmental Organizations (NGOs) with non-communicable disease (NCD) medicines, including 232,948 insulin vials and 37 NCD kits with an estimated 100,000 treatment courses (5). This situation highlights the crucial role played by these external entities in ensuring the well-being of hundreds of thousands of individuals affected by diabetes in Syria. However, ongoing conflict and limited resources continue to pose significant obstacles to comprehensive diabetes care in the country.

1.2. Definition, types of diabetes mellitus, and the prevalence of diabetes mellitus

Diabetes Mellitus (DM) is a chronic metabolic disorder characterized by high blood glucose levels over a prolonged period (6). It occurs when the body either does not produce enough insulin or is unable to effectively utilize the insulin it produces. There are many types of DM. Type 1 Diabetes (T1DM) previously known as insulin-dependent diabetes. It typically develops in childhood or early adulthood. In this form of diabetes, the immune system mistakenly attacks and destroys the insulin-producing cells in the pancreas. Type 2 diabetes (T2DM) is the most common form of diabetes, accounting for around 90% of all cases. It typically occurs in adulthood (7).

In T2DM, the body becomes resistant to the effects of insulin, and the pancreas may not produce enough insulin to compensate. This type of diabetes is often associated with

lifestyle factors such as obesity, physical inactivity, and poor dietary habits. Initially, T2DM can often be managed with lifestyle modifications, oral medications, or injectable medications (8).

In 2021, diabetes and its complications resulted in over 6.7 million deaths (9).

The prevalence of diabetes has rapidly increased worldwide over the past few decades and ranks among the top ten diseases leading to death in high-income and lower-middle-income countries (10, 11).

According to statistics in 2017, about 425 million people worldwide had diabetes (4). This number increased to 463 million people based on 2019 data from the International Diabetes Federation and by the year 2045, 783 million individuals worldwide are expected to be affected by this illness (12). In Syria, in particular the prevalence of diabetes is expected to reach 16.4% by 2045 (9).

The increased prevalence of diabetes in these populations poses risks for illness and places a burden on healthcare systems and their countries. Therefore, specific efforts should be directed toward addressing the diabetes burden in Syrian and similar societies (13).

1.2.1. Diabetes mellitus diagnoses and treatment

Diabetes can be diagnosed based on fasting blood glucose levels and long-term levels of glycated hemoglobin (14). The diagnosis of diabetes mellitus can be readily confirmed when a patient exhibits typical signs of high blood sugar levels such as increased thirst, frequent urination, weight loss, and blurred vision, alongside a random blood glucose measurement of 200 mg/dl (11.1 mmol/l) or higher.

In the case of T1DM, the majority of patients experience symptoms and display plasma glucose levels significantly surpassing the threshold of ≥200 mg/dl. Similarly, certain individuals with T2DM may also demonstrate symptomatic hyperglycemia and blood glucose levels equal to or exceeding 200 mg/dl (15).

Diabetes may be diagnosed based on plasma glucose criteria, either the fasting plasma glucose (FPG) value or the 2-h plasma glucose (2-h PG) value during a 75-g oral glucose tolerance test (OGTT) or HbA1c criteria (16).

The diagnostic criteria for diabetes are highlighted in Table1.

Table 1: Diagnostic criteria of prediabetes and diabetes (17).

	Prediabetes	Diabetes
A1C	5.7-6.4% (39-47 mmol/mol)	≥ 6.5% (48mmol/mol)
Fasting plasma glucose (FPG)	100-125 mg/dl (5.6-6.9 mmol/l)	≥ 126 mg/dl (7.0 mmol/l)
Oral glucose tolerance test (OGTT)	140-199 mg/dl (7.8-11.0 mmol/l)	≥ 200 mg/dl (11.1 mmol/l)
Random plasma glucose (RPG)		≥ 200 mg/dl (11.1 mmol/l)

Generally, FPG, 2-h PG during 75-g OGTT, and HbA1c are equally appropriate for diagnostic screening. It should be noted that detection rates of different screening tests vary in both populations and individuals. Moreover, the efficacy of interventions for primary prevention of T2DM has mainly been demonstrated among individuals who have impaired glucose tolerance (IGT) with or without elevated fasting glucose, not for individuals with isolated impaired fasting glucose (IFG) or for those with prediabetes defined by HbA1c criteria (17).

HbA1c has several advantages compared with FPG and OGTT, including greater convenience (fasting not required), greater pre analytical stability, and fewer day-to-day perturbations during stress, changes in nutrition, or illness. However, these advantages may be offset by the lower sensitivity of HbA1c at the designated cut point, greater cost, limited availability of HbA1c testing in certain regions of the developing world, and the imperfect correlation between HbA1c and average glucose in certain individuals (17).

At earlier stages, a healthy diet, exercise, and lifestyle management can help prevent the progression of T2DM to a certain extent (18). However, as T2DM develops, most patients require medication, such as oral hypoglycemic agents (OHAs), and later-stage diabetes may necessitate insulin therapy. There are two types of OHAs: those that improve tissue sensitivity to insulin, such as metformin and thiazolidinediones (19), and those that stimulate increased insulin secretion from the pancreas, such as sulfonylureas

and meglitinides (20). In recent years, incretin based therapies, including DPP-4 inhibitors and GLP-1 receptor agonists, have been developed and used as T2DM medications.

DPP-4 inhibitors function by blocking the activity of the enzyme responsible for breaking down incretin hormones in the body. As a result, these medications help to maintain the levels of GLP-1 (glucagon-like peptide-1) within the body at a natural and physiological level. On the other hand, GLP-1 receptor agonists operate at higher-than-normal concentrations, leading to a more robust impact on glycemic control and causing weight loss. This effect is achieved through delayed gastric emptying and increased central satiety, contributing to their therapeutic efficacy in managing diabetes (21, 22). SGLT2 inhibitors, the newest diabetes agents on the market, work by reducing glucose absorption in the leading to glucose excretion through urine (23).

1.3. Pharmaceutical care

1.3.1. Pharmaceutical care in general

Pharmaceutical care has gained significant recognition and adoption worldwide, following its introduction in the United States around 20 years ago (24). Pharmacists across the globe have embraced pharmaceutical care as their primary approach to optimize the benefits of pharmacological treatments for patients. The concept of pharmaceutical care has evolved, with the current definition by Pharmaceutical Care Network Europe (PCNE) stating that it is the pharmacist's contribution to optimizing medicine use and improving health outcomes (25, 26).

The focus of pharmaceutical care has shifted from merely the production and distribution of medications to patient-centered care and counseling. Pharmacists now evaluate the necessity, efficacy, and safety of patients' prescriptions, ensure their understanding of the treatment, and monitor any changes in their condition (24). The framework of pharmaceutical care comprises three main components: management of medication therapy, collaboration with physicians, and patient education. Its scope has expanded to include promoting healthy lifestyles, rational medication use, and enhancing clinical outcomes (27, 28).

In Syria, the practice of pharmacy has a rich history. However, the increasing number of pharmacy graduates has resulted in a strained job market, especially as many graduates

seek careers in retail pharmacy (29). To practice pharmacy in Syria, individuals must graduate from a recognized pharmacy school, either in Syria or abroad, and subsequently register with the Ministry of Health (MoH), the Syrian Pharmacists Association (SPA), and the provincial Pharmacists' Association, depending on their practice location.

Pharmaceutical care is a legally mandated professional activity in Syria, exclusively performed by pharmacists in community or branch pharmacies, as well as hospital pharmacy units selling medications directly to the public. It is the responsibility of all pharmacists to provide basic pharmaceutical care to patients visiting the pharmacy without a medical diagnosis or with a prescription. This includes dispensing prescription and over-the-counter drugs (OTC) as well as other items like dietary supplements (30).

When a patient visits the pharmacy without a medical diagnosis, the pharmacist's obligations include providing expert assistance in assessing symptoms and, if necessary, referring the patient to a physician. They also recommend pain relief therapies, both non-pharmacological methods and OTC medications. Moreover, pharmacists provide information on the use of OTC medicines and other products, educate patients on identifying drug-related problems (DRPs), and advise on therapy suspension or discontinuation.

If a patient presents a prescription to a community pharmacy, the pharmacist is responsible for identifying and resolving any existing DRPs related to drug dispensing and prescription validation. This is especially crucial for specific populations with specific diseases and conditions, such as infants, pregnant or lactating women, geriatric patients, and individuals with liver or kidney diseases or drug allergies.

These guidelines and responsibilities outline the role of pharmacists in providing pharmaceutical care in Syria, ensuring safe and effective medication-use, and promoting optimal health outcomes for patients.

1.3.2. The changing role of the pharmacist

In the past, the primary focus of pharmacists was on the provision and dispensing of medications. Literature suggests that doctors often viewed the pharmacist's role as primarily being medication-focused rather than actively participating in patient care (31). However, there has been a transformation in the role of pharmacists, shifting towards patient-centered care (32, 33).

Pharmacists are encouraged to expand their knowledge and skills to actively contribute to patient management and follow-up, without intending to replace doctors (34).

The development of the pharmacist's role may differ between low- and middle-income countries and high-income countries. In low- and middle-income countries, the utilization of pharmacists in healthcare services beyond medication dispensing is often limited, whereas, in many high-income countries, pharmacists already play significant roles in patient care (35). Pharmacists work in various healthcare settings such as hospitals, clinics, and community pharmacies, making them highly accessible healthcare providers. This accessibility allows pharmacists to assume new responsibilities in patient care, particularly in managing chronic diseases (36, 37). This accessibility allows pharmacists to assume new responsibilities in patient care, particularly in managing chronic diseases (38-44).

The long-term use of medications that require regular monitoring is virtually invariably associated with chronic conditions. The monitoring of prescription use, lowering the risk the adverse drug reactions, and offering advice when there is a problem with the medication are all potential roles that pharmacists may play. Due to their frequent interactions with patients, pharmacists are able to produce the necessary clinical effect (38, 42, 44, 45).

The other potential benefit of regular contact with patients is that pharmacists can identify patients who may not be taking their medication regularly, find the reason, and provide necessary interventions through education or consultation (46). This potential benefit can be significant in monitoring medication use and adherence among patients with diabetes.

The expanded role of pharmacists in patient care is crucial, especially in areas where there is a shortage of healthcare professionals, such as primary care physicians. Physicians often lack the time to provide all the services related to preventive and chronic care that patients require. Pharmacists can help alleviate the physician's burden, especially in matters related to medication use (47-49). By actively participating in patient care, pharmacists can contribute to optimizing healthcare delivery, particularly in settings with high patient loads and limited medical staff (50).

In Syria medication non-adherence is an issue that requires specific attention from healthcare professional in diabetes care (51, 52).

Healthcare providers, including pharmacists, have a role in assisting patients in changing their non-adherence behaviors and promoting medication adherence.

Overall, the evolving role of pharmacists in patient care has the potential to improve healthcare outcomes, particularly in managing chronic diseases and addressing medication non-adherence. By working collaboratively with other healthcare

professionals, pharmacists can contribute to providing comprehensive and optimal care to patients.

1.4. Therapeutic adherence

1.4.1. Definition, reasons of non-adherence, and the importance of therapeutic adherence in diabetes care

According to WHO, the definition of adherence is the extent to which a person's behavior taking medication, following a diet, and or lifestyle changes that correspond to the recommendations agreed with a health service provider (53). In essence, adherent patients are characterized by their commitment to following their prescribed treatment regimen, as advised by their healthcare professionals. Conversely, non-adherent patients are those who discontinue their treatment and do not adhere to their prescribed therapy.

Non-adherence can be caused by behavioral factors (social support, thinking, and personal beliefs) as well as specific obstacles (complexity of the drug, various suppliers, or cost) (54). Medication compliance is crucial to reaching and sustaining goals in diabetes management (55).

Early detection, appropriate therapy selection, achievement of the target glycemic goal, and medication adherence are all-essential for the successful management and treatment of diabetes. Medication adherence in chronic disease patients can be affected by therapy management factors (complexity of the treatment, length of the therapy, medication side effects, time spent on treatment each day, and healthcare system factors), as well as factors specific to the patient and their immediate family, demographic and socioeconomic factors, and disease-related factors (56, 57).

Patients with chronic conditions, like diabetes, find it difficult to follow their medication regimens. According to two systematic review studies, the prevalence of prescription non-adherence worldwide is significant, ranging from 36-93%, particularly in diabetes (55, 58). The variation in the prevalence range is caused by the characteristic of the population being studied, medication use by patients, and tools, used to measure medication adherence. More frequent administration and a high number of medications are related to low adherence (59). These studies show that non-adherence to medication is a barrier to achieving optimal treatment outcomes for T2DM patients (55, 56, 60-62).

In general, few diabetes studies have been carried out in Syria. The majority of them were quantitative studies. For example, Albach et al. stated that because Syria has experienced a significant change in dietary habits and lifestyle over the last few decades, the prevalence of obesity was 35%, indicating that obesity was contributing to the rising incidence of diabetes. Furthermore, the high occurrence of complications in Syria may be attributable to a lack of effective diabetes control, as well as insufficient patient monitoring and follow-up (63).

Poor and insufficient glycemic control among T2DM patients is a serious public health issue and is a major risk factor for acquiring secondary complications (64).

Thus, controlling diabetes demands complex therapies and long-term lifestyle adjustments protecting body organs from damage and avoiding other complications. As a result, there is an urgent need to undertake studies on diabetes control experiences in developing nations. Unfortunately, there is little information available about the experiences of Syrian T2DM patients. However, to develop supportive and culturally relevant interventions for illness management, researchers must first understand the experiences from a Syrian viewpoint.

Medication adherence can affect the treatment outcomes and cost of care, as shown in other studies on the correlation between non-adherence and adverse clinical outcomes among patients with chronic diseases (65, 66). Another consequence of non-adherence behavior is increased health expenditures due to complications (64, 66-70).

Due to the impact of medication adherence on health expenditure, the Syrian government could anticipate increases in health expenditures, particularly after the war. To control and ensure the effective use of the national budget for the health sector and minimize unnecessary budget allocations, more knowledge and insight into non-adherence is necessary. The increasing number of patients with diabetes with non-adherence behavior puts them at a high risk of reallocating funding unnecessarily from other sectors to the healthcare system.

1.5. The scope of dissertation

Non-communicable diseases (NCDs) are the leading causes of death globally, with approximately 80% of premature deaths attributed to them. These diseases, including diabetes, cancer, chronic respiratory illnesses, and cardiovascular conditions, pose a

significant mortality risk, particularly in low- and middle-income countries where around 71% of NCD-related deaths occur (71).

In Syria, NCDs are a major health concern, and diabetes is one of the leading causes of death (72). Effective management of diabetes requires long-term medication adherence to achieve blood glucose control and reduce complications (73).

However, patients with diabetes face challenges in obtaining and maintaining medication compliance, especially in low- and middle-income countries like Syria. Factors contributing to medication non-adherence include insufficient education and knowledge about the condition or medications, patients' beliefs about medication, low income, limited drug availability, high costs, and compromised quality of life.

Adequate glycemic control is crucial for reducing the risk of diabetic complications and mortality, and it depends on patients' self-management, adherence to prescribed medications, and appropriate use of available anti-diabetic regimens. However, limited research has been conducted on diabetes in Syria. Therefore, this dissertation focuses on the pharmacist's involvement in diabetes care and the impact of their role in the enhancement of therapeutic adherence for T2DM patients in Latakia, Governorate, Syria.

Non-adherence to medication can have significant health implications, particularly in terms of increased treatment costs for diabetes-related complications. This not only affects the financial burden on individuals with diabetes but also impacts the healthcare system in Syria, particularly the healthcare budget of the national health insurance system that aims to achieve universal health care. The health and economic burden of diabetes are manifested through increased costs of treating complications and treatment failures.

In conclusion, addressing medication adherence in diabetes care is crucial for reducing the health and economic burden associated with the disease. My research focused on the role of pharmacists in diabetes care and the possibility to improve patient therapeutic adherence in Syria, which can contribute to enhancing treatment outcomes, reducing complications, and optimizing the utilization of healthcare resources.

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2. Objectives

The primary aim of my thesis was to enhance the health outcomes of patients diagnosed with T2DM and to recognize the valuable role that community pharmacists can play in optimizing diabetes care. Through a focused approach, the study aimed to gain a comprehensive understanding of the interventions carried out by pharmacists to improve medication adherence, specifically with an emphasis on controlling HbA1c levels, as outlined in a systematic review. Moreover, a unified survey was developed and implemented in a specific region of Syria, specifically Latakia Governorate, to evaluate the beliefs and perceptions of T2DM patients regarding pharmacy services and various aspects of adherence. This research endeavor sought to provide valuable insights that can contribute to the advancement of diabetes management and overall patient care within the healthcare system of Syria.

To achieve these goals, my work consisted of the following questions:

1. What are the current strategies employed by community pharmacists and how effective are they in improving patient adherence and glycosylated hemoglobin levels in individuals with T2DM?
2. How satisfied are T2DM patients with the services of community pharmacies, and what kind of association can be seen between these services and non-adherence, in Latakia Governorate, Syria?

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3. Method

3.1. Literature search and review protocol

In the present study, a comprehensive literature review was conducted to gain insights into the various interventions conducted by community pharmacists in the management of T2DM. A specific attention was given to examining the impact of community pharmacists' strategies on enhancing therapeutic adherence and reducing HbA1c levels. The findings of this review were synthesized and summarized in a systematic review, providing valuable insights into the effectiveness of community pharmacist-led interventions in improving patient outcomes related to medication adherence and glycemic control.

The systematic review followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 (67). The process of study selection and data extraction adhered to the guidelines set forth in the Cochrane Handbook (74).

To perform databases search I developed key questions using Population, Intervention, Comparison and Outcomes (PICO) tool.

The following 4 key questions

- What models of pharmacists' interventions exist in diabetes care?
- What beneficial outcomes of pharmacists' interventions for T2DM patients that reported in literature?
- Is there any association between the community pharmacists' interventions and reduction of HbA1c level?
- Is there any association between the community pharmacists' interventions and the patients' therapeutic adherence?

The references from all the electronic searches were downloaded into the EndNote X7 (Clarivate Analytics, Philadelphia, PA, USA) reference manager.

3.1.1. Search strategy

A cumulative search for studies was carried out in the following database:

PubMed / Medline, Web of Science, and CINAHL between 2010 and 2020. To ensure comprehensive and efficient database research, I categorized key words into three groups

and utilized various combinations of these keywords. This approach aimed to identify relevant studies that provided information related to the research questions.

- Pharmaceutical – pharmacist – pharmacists
- Type 2 diabetes mellitus – type 2 diabetes
- Therapeutic – therapeutic adherence –adherence

My search strategy in the electronic databases:

- PubMed/Medline: “type 2 diabetes mellitus” (MeSH Terms) OR (“type 2 diabetes” (All Fields) AND “mellitus” (All Fields)) OR “type 2 diabetes mellitus” (All Fields) AND “therapeutic adherence” (MeSH Terms) OR (“therapeutic” (All Fields) AND “adherence” (All Fields)) OR “therapeutic adherence” (All Fields)) AND (“pharmacists” OR “pharmaceutical” (MeSH Terms) OR “pharmacists” (All Fields) OR “pharmaceutical” (All Fields))
- Web of Science ((((ALL = (type 2 diabetes mellitus)) OR ALL = (type 2 diabetes)) AND ALL = (therapeutic adherence)) AND ALL = (pharmacists)) OR ALL = (pharmaceutical)
- CINAHL (“type 2 diabetes mellitus or type 2 diabetes” TX ALL TEXT) AND (‘therapeutic adherence” TX ALL TEXT) AND (“pharmacists or pharmaceutical” TX ALL TEXT)

3.1.2. Eligibility criteria

Inclusion in the study was based on the following criteria: (1) participants had to be diagnosed with T2DM, with no restrictions based on race or sex.
However, pregnant women and children were excluded from the study population, (2) the intervention was aimed at evaluating the effectiveness of interventions provided exclusively by community pharmacists and comparing it with usual care, (3) data on two primary outcome measures were required, namely patient adherence and HbA1c levels, (4) the study design had to be either a randomized controlled trial or a non-randomized controlled trial, (5) only full-text articles published in English were considered, (6) the studies included had to be original and published in peer-reviewed journals.

3.1.3. Study selection

All articles were imported into the reference management software EndNote X7 (Clarivate Analytics, Philadelphia, PA, USA). Following the removal of duplicates, I conducted the selection process based on the title, abstract, and full-text contents, in accordance with the pre-defined inclusion and exclusion criteria.

3.1.4. Data extraction

Data extraction from the included studies was conducted using Excel software (Microsoft Excel 2010, Microsoft Corporation, Washington, USA). The extracted data encompassed various elements, including the author's name, country where the study took a place, study design, duration of the study, pharmacists' interventions, methods employed to measure medication adherence, outcomes related to patient adherence, mean HbA1c levels, and reported results.

3.1.5. Quality assessment and data analysis

Based on our inclusion criteria, a risk of bias assessment accompanied each included study, using Cochrane guidelines ROB2 for randomized controlled trails (75), for non-randomized controlled trails, opened labelled intervention, case control studies I used ROBINS-I tool (76). In addition, MINORS tool was used for quasi experimental studies (77).

The risks were identified as 'high risk', 'low risk' and 'some concern'. Assortment, performance, detection, abrasion, and reporting biases were tested. The studies at "high risk" were discussed amongst the authors to certify suitability in the final review. Likewise, the studies were paralleled based on their study design, results, and the interventions assumed.

3.1.6. Ethics and dissemination

No ethical approval was necessary to obtain the data because this systematic review did not involve patient personal data.

3.2. Questionnaire design

This study represents the second phase of a Ph.D. dissertation, which primarily focused on examining the perceptions of Syrian T2DM patients concerning community pharmacy services. The research employed an online survey questionnaire, conducted over a span of eight months, from April to November 2022. This survey was administered at the Diabetes Center in Latakia Governorate, Syria.

The study's participants included individuals between the ages of 18 to 70, who were registered with the diabetes center and had been diagnosed with T2DM. These patients, who were receiving oral anti-diabetes drugs, were provided with guidance by the head of the diabetes center to complete the questionnaire, taking into account their age as a criterion.

It is essential to emphasize that all responses collected from the patients were handled with complete anonymity. Furthermore, participation in the survey was entirely voluntary, and participants were reassured that the survey data would be used exclusively for scientific research purposes. Notably, respondents were obligated to respond to all questions as part of the survey's established protocol.

The ethical committee of Al Manara University approved this study, as indicated by the (approval protocol code 5245-2022).

I initially created the questionnaire survey in English. To ensure the accuracy and appropriateness of the information, (R.Z) the head of pharmacy administration, reviewed the questionnaire. Afterward, the questionnaire was translated into Arabic, and Kinda Darwish (K.D.) a subject-matter specialist in the clinical pharmacy department who possesses expertise in the area of the present study, and examined it.

Before conducting the actual survey, a pilot study involving 13 patients was conducted to test the comprehensibility of the questionnaire. This pilot study aimed to ensure that the survey forms were clear and understandable to the participants. The feedback received from the pilot study helped in refining and improving the questionnaire for the final phase, when data was collected.

The survey itself took an average of 10 minutes to complete and was designed to be distributed online via Google Form (Google LLC, Mountain View, CA, USA).

3.2.1. Inclusion criteria

We included only T2DM patients who take oral antidiabetic drugs. No racial or gender restrictions were made. In terms of age, we only included adults between 18-70 years old. The study's sample size was estimated by referencing similar research (78-84).

3.2.2. Exclusion criteria

We exclude patients who take insulin and pregnant women.

3.2.3. Evaluation / statistical method

Since there was no probability sampling in this study, basic statistics, raw numbers, and percentage were calculated to provide an overview of the survey data.

Only descriptive statistics were performed. The statistical software support for the analysis was provided by Dénes klierner (D.K) Semmelweis University, Budapest. The statistical calculations were performed using SPSS 27 (IBM, Armonk, USA) and Microsoft Office Excel 2016 (Microsoft Corp, Redmond, USA).

Descriptive statistics, such as means and percentages, were employed to summarize and analyze the data. For categorical variables, we presented percentages and utilized graphs for visual representation. To calculate the response rate, we considered both the number of newly registered patients and the number of participants who took part in the survey, expressing it as a percentage.

In terms of medication adherence, we categorized participants into two primary groups: adherent and non-adherent patients.

Within the non-adherent group, we further divided patients into two subgroups: those with intended non-adherence (defined as patients who stopped taking their medicines for specific reasons) and those with non-intended non-adherence (defined as patients who ceased taking their medicines due to forgetfulness).

To determine intended non-adherence, we evaluated responses to four specific questions:

1. "Have you stopped taking your diabetes medicine(s) because you suspected feeling ill from taking this medicine(s)?"
2. "Have you stopped or discontinued your diabetes medication(s) because your condition has not improved, and you are discouraged from taking the medication(s)?"

3. "Do you stop taking the medicine(s) for your diabetes when you feel that your diabetes is in balance?"
4. "Do you stop taking your diabetes medicine(s) if your friend/relative/neighbor is taking the same medicines as you and has experienced any side effects?"

If a patient answered "yes" to any of these questions, they were classified as non-adherent. Additionally, we calculated overall adherence in a similar manner, incorporating the question: "Do you often forget to take your medication?" into our analysis.

This approach allowed us to comprehensively assess medication adherence among the study participants.

3.2.4. Ethical Approval

The study was conducted following the Declaration of Helsinki and approved by the Ethics Committee of Al Manara University (protocol code 5245-2022). All participants included in the study gave informed consent.

3.2.5. Survey

A comprehensive literature search was conducted before the development of a self-administered questionnaire (38, 78-82). The survey consisted of four components which can be found in the Appendix. Part 1 of the survey included questions about demographic information such as age, gender, place of residence, and education. Part 2 consisted of questions regarding patients' therapeutic behavior, including issues with daily medication intake, frequency of forgetting to take medications, and the number of prescribed drugs. To assess therapeutic adherence, questions were adapted and modified from established scales like the Morisky Medication Scale (MMS-8) (85), and the Medication Adherence Rating Scale (MARS) and then translated into Arabic (86). Part 3 of the questionnaire focused on diabetes health status, including the duration of diabetes, family history of diabetes, and the presence of diabetes complications. Part 4 explored the perceptions of T2DM patients regarding the capabilities of community pharmacists.

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4. Results

4.1. Results of literature analysis – Models and outcomes of pharmacists' interventions in diabetes care

The primary outcome measures were the effectiveness of pharmacists' interventions on patient adherence levels and HbA1c levels.

The initial search phase of the systematic review yielded 8,362 papers (Figure 1). After screening titles and abstracts, 103 papers met the predefined inclusion criteria.

Among these, 20 did not involve interventions delivered by community pharmacists, 14 did not utilize validated self-reported tools to assess patients' adherence, 13 papers did not include clinical measurement of HbA1c, 8 employed unclear adherence measurement tools, 12-lacked information on patients' adherence measurement, and 15 were not relevant to type 2 diabetes. Ultimately, 21 studies were deemed eligible based on the inclusion criteria and were included in the systematic review.

The study selection process for the literature research is illustrated in PRISMA flowchart (Figure 2) (38).

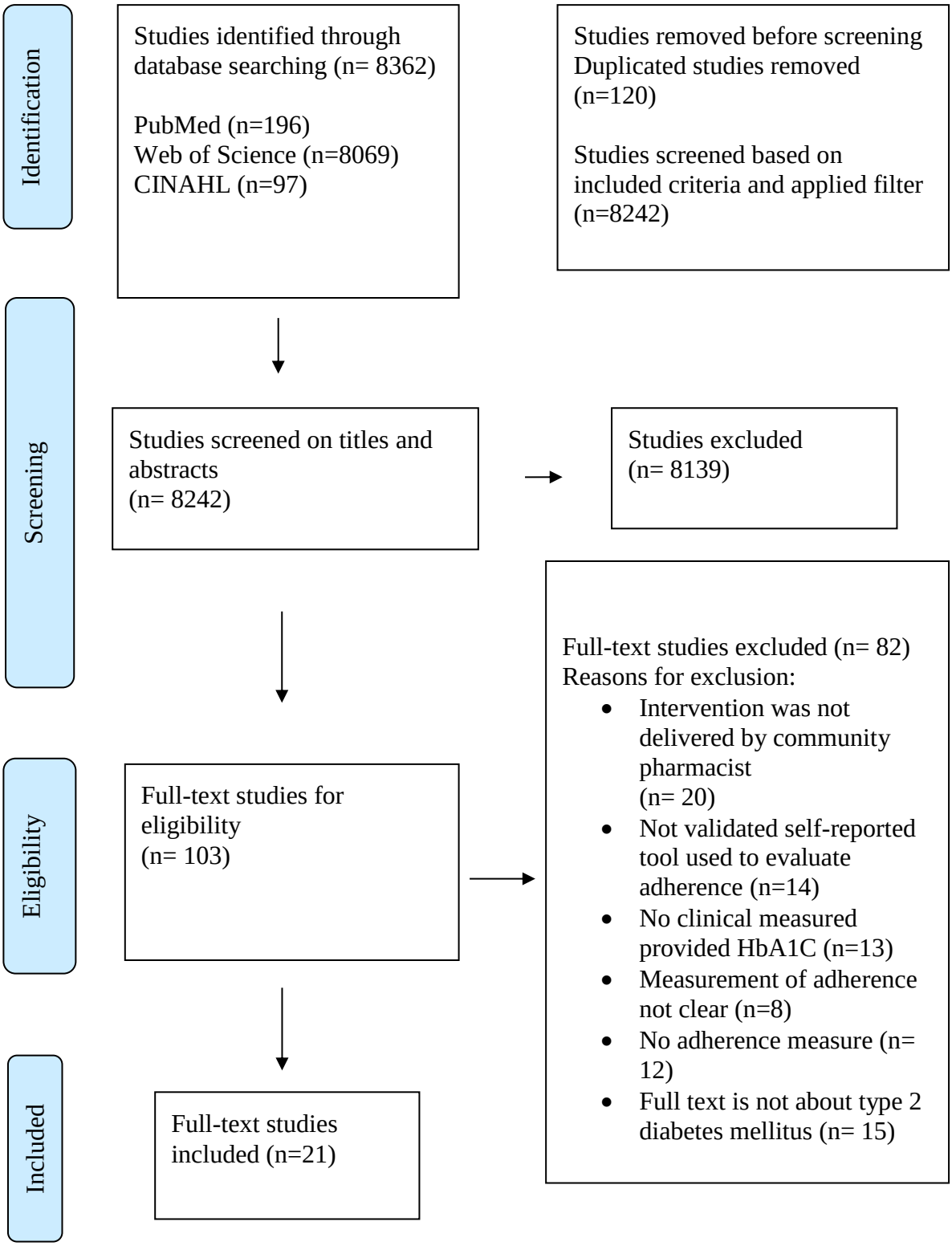

Figure 2: PRISMA-2020 flowchart, which shows the relevant articles in this Systematic Review (38).

4.1.1. Study characteristics

The 21 studies included in this systematic review were conducted in various countries worldwide. Two studies were conducted in Europe, specifically in the United Kingdom and France (87, 88). Three studies were conducted in the USA (89-91), one in Australia (92), two in Brazil (93, 94), and one in New Zealand (95). Additionally, twelve studies were conducted in the Middle East and Asia, including Malaysia, Iran, Pakistan, India, Ethiopia, South Thailand, Cyprus, and Jordan (96-107).

The majority of the studies included in the review were randomized controlled trials. Each study assessed patient adherence and HbA1c levels as outcomes. Furthermore, most of the studies were conducted in primary diabetic care clinics or centers.

Table 2: Provides a summary of the characteristics of the studies included in the review (38).

Author name/ year	Study design	Study duration	Country	Sample size	Pharmacist Intervention	Adherence tool	Impact on Adherence	Reduction of HbA1c	Reference
Michiels.Y et al. 2019	Cluster- RCT	6-month follow-up	France	377	Education	Medication Possession Ratio (MPR)	Did not significantly improve the already high adherence rates	Significant decreases in HbA1c ($P < 0.01$)	(88)
Sankar.V et al. 2019	Open labelled interventional study	9-month Follow-up	India	55	Education	Validated questionnaire	Adherence significantly improved ($P< 0.05$)	Statistically significant reduction ($P< 0.05$)	(104)
Rashid Nazir.SU et al. 2020	Non -RCT	3-month follow-up	Pakistan	392	Education	Morisky Medication Adherence Scale (MMS-8)	Adherence significantly improved ($P< 0.05$)	Statistically significant reduction ($P< 0.05$)	(101)
Aguiar.PM et al. 2018	RCT	21-month follow-up	Brazil	73	Pharmacist-physician collaboration model	4-item Morisky–Green test	Adherence significantly improved ($P< 0.001$)	Greater reduction in HbA1c ($P< 0.05$)	(93)
Kharjul.M et al. 2018	Records analysis	48- month follow-up	New Zealand	115	Follow up by pharmacist	Medicines Use Review (MUR) Service	Adherence significantly improved ($P< 0.05$)	Greater Significant reduction ($P< 0.05$)	(95)
Samtia.AM et al. 2013	Case-control study	5-month follow-up	Pakistan	500	Counselling by pharmacist	Self-reporting approach	Significantly improved ($P= 0.003$)	Significant reduced ($P< 0.001$)	(100)

Author name/ year	Study design	Study duration	Country	Sample size	Pharmacist Intervention	Adherence tool	Impact on Adherence	Reduction of HbA1c	Reference
Goruntla.N et al. 2019	Prospective, open-labelled-RCT	3 month 6 month Follow-up	India	330	Counselling by pharmacist combined with message reminder	A pill count and (VAS) methods	Adherence significantly improved (P< 0.001)	Significantly reduced in Intervention group (P< 0.01)	(103)
Withidpanyan.U et al. 2019	RCT	9-month follow-up	Thailand	196	Family support led by pharmacist	Self-reported Morisky Medication Adherence Scale (MMAS)	Adherence significantly improved (P< 0.05)	Significant reduction in HbA1c (P< 0.001)	(105)
Ekong.G et al. 2020	Quasi-experimental intervention with a single-group design	6-month follow-up	USA	28	Motivational interview-strategy led by pharmacist	Self-reported diabetes medication adherence	Adherence significantly improved (P= 0.010)	Statistically significant reduction. HbA1c (P= 0.090)	(89)
Mitchell. B et al. 2011	RCT	6-month Follow-up	Australia	387	Diabetes Medication Assistance Service (DMAS)	Brief Medication Questionnaire (BMQ)	Significant improved (P< 0.05)	Significantly decreased (P< 0.001)	(92)
Ayele.TA et al. 2019	RCT	12-month follow-up	USA	1,400	Impact of a telephone-based patient-cantered intervention	Proportion of days covered (PDC)	“slightly difference but not significant”	Not significant in patients with poorly controlled diabetes	(90)

Author name/ year	Study design	Study duration	Country	Sample size	Pharmacist Intervention	Adherence tool	Impact on Adherence	Reduction of HbA1c	Reference
Lyons.I et al. 2016	RCT	6 -month follow-up	United Kingdom	612	Telephone consultations with a pharmacist	Self-reported adherence to medication Diagnostic Adherence to Medication Scale (DAMS) + medication possession ratio (MPR)	Adherence significantly improved (P= 0.010)	Statistical significance reduction (P= 0.061)	(87)
Sarayani.A et al. 2018	RCT	9-month follow-up	Iran	88	A telephone-based intervention led by pharmacist	Morisky Medication Adherence questionnaire (8 items)	Adherence significantly improved (P< 0.05)	HbA1c significantly improved (P< 0.05)	(99)
Skinner.JS et al. 2015	Retrospective case-control study	12-month follow-up.	USA	100	Medication therapy management (MTM)	Anti-diabetes prescription refill	Adherence significant improved (P< 0.001)	Significantly improved (P< 0.001)	(91)
Ayele.AA et al. 2019	Cross-sectional study	2-month follow-up	Ethiopia	275	Simplicity of complex medication regimes	Morisky Medication Adherence for Sub-Saharan counties (MMAS)	Low diabetes MRCI→significantly increased adherence (P< 0.001)	High diabetes MRCI →poor glycaemic control	(102)

Author name/ year	Study design	Study duration	Country	Sample size	Pharmacist Intervention	Adherence tool	Impact on Adherence	Reduction of HbA1c	Reference
Borges.AP et al. 2010	Prospective and experimental study	12-month follow-up	Brazil	71	Pharmaceutical care intervention (PC)	Morisky–Green test	Adherence significantly improved (P< 0.05)	A significant reduction HbA1c (P< 0.05)	(94)
Chung.WW et al. 2014	RCT	12-month follow-up	Malaysia	241	Pharmaceutical care intervention (PC)	Malaysian Medication Adherence Scale (MMAS)	Adherence significantly improved (P= 0.007)	A significant reduction of HbA1c (P< 0.001)	(96)
Wishah.RA et al. 2015	RCT	6- month follow-up	Jordan	106	Pharmaceutical care intervention (PC)	Self-reported medication adherence (Morisky Scale)	Adherence significantly improved (P< 0.05)	HbA1c decreased significantly (P< 0.05)	(107)
Jahangard-Rafsanjani.Z et al. 2015	RCT	5-month follow up	Iran	85	Pharmaceutical care intervention (PC)	Morisky Medication Adherence Scale (MMAS)	Adherence significantly improved (P< 0.05)	HbA1c Significantly decreased (P= 0.0001)	(98)
Butt.M et al. 2018	RCT	6-month follow-up	Malaysia	73	Pharmaceutical care (PC)	Morisky scores	Significantly increased (P=0.02)	Significantly decreased (P= 0.001)	(97)
Korcege. EI et al. 2017	RCT	12-month follow- up	Northern Cyprus	152 participants	Pharmaceutical care intervention (PC)	Self-reported medication adherence (Morisky-Green test)	Adherence significantly increase (P= 0.013)	A greater reduction in HbA1c (P< 0.001)	(106)

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4.1.2. Studies risk of bias

The The risk of bias varied among the included 21 studies (see Figure 3). The risk of bias in each study was assessed regarding the following criteria: randomization process , timing of identification or recruitment of participants, deviations from intended interventions, missing outcome data, measurement of outcome data, selection of the reported result, and overall bias. Each item assessing the risk of bias was categorized as "low risk" if the likelihood of bias significantly impacting the results was minimal, "unclear" if bias may introduce some uncertainty in the results, or "high risk" if bias could substantially alter the results.

For RCTs I used Rob 2 tool to assess the risk of bias. From Figure 3 it is visible that around (81%) of the studies, randomization process was adequetly made. There was some concerns not clear described regarding the deviations from intended interventions in more than 70% of the studies. Half of the studies performed missing outcome data. Measurment of the outcome was clearly discribed in (85.7%) of the studies. Around (50%) of the studies had high risk other overall sources of bias.

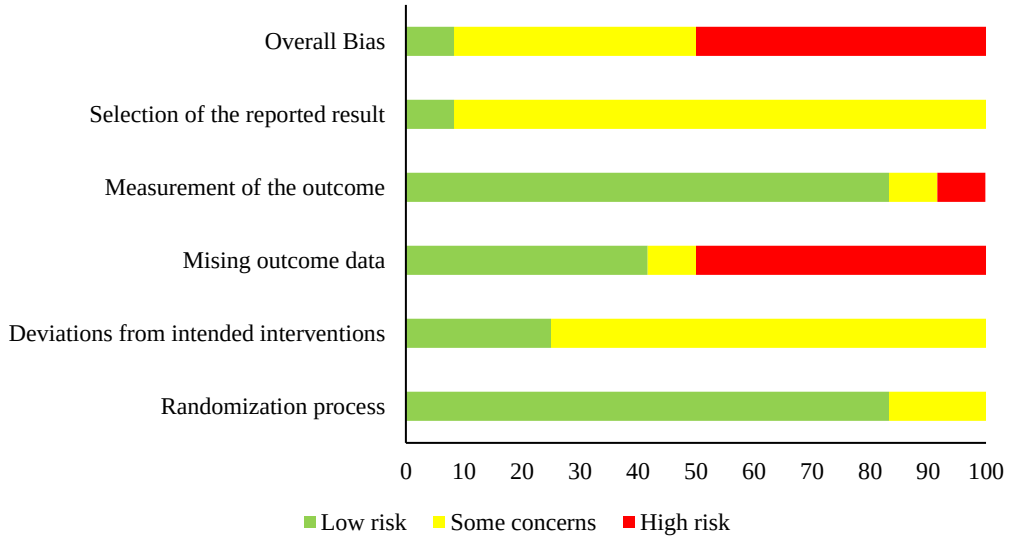

Figure 3: Risk of Bias analysis of randomized controlled studies (12) by RoB2.0 (38).

In the analysis of the remaining nine studies, the risk of bias assessment was conducted for eight of them using the ROBINS-I tool. Among these, five studies were found to have a moderate risk of bias, three studies had a low risk of bias, and one study was identified as having a serious risk of bias.

As for the quasi-experimental study, the assessment of bias was performed using the MINORS tool, which indicated a high risk of bias in this study.
Based on the my systematic review, i categorized the pharmacist interventions into four categories that focus on patient satisfaction and positive health outcomes.

4.1.3. Pharmacists' interventions categories

4.1.3.1. Patient oriented-verbal interventions

4.1.3.1.1. Education and counceling by pharmacist

This strategy emphasizes the importance of enhancing diabetic patients' knowledge regarding their treatment, including drug side effects such as hypoglycemia, proper dosage administration, and addressing any concerns or beliefs, they may have about therapy.
Educational methods have been widely recognized as a primary approach employed by pharmacists to meet the needs of patients. This approach has proven effective in eliciting recommendations from patients on how to improve their adherence to diabetes medications.
Two studies in this systematic review have demonstrated that patient education delivered by pharmacists leads to a significant improvement in therapeutic adherence (101, 104).
Moreover, pharmacy-counseling services play a crucial role in helping patients understand their medications. Several studies in the literature have demonstrated the significant positive impact of pharmacists' counseling on T2DM patients (93).
For instance, face-to-face counseling sessions considered by pharmacist, focusing on diabetes knowledge, self-monitoring of blood glucose, regular checkups, and non-pharmacological management strategies like diet control, exercise therapy, and early identification of hypoglycemia symptoms, have been shown to positively influence therapeutic adherence and lead to a measurable reduction in HbA1c levels. Pharmacists also provide education on antidiabetic medications and their indications ensuring that patients are well-informed about their treatment options.
Furthermore, pharmacists tailor medication administration time and dosage to meet the individual needs of patients, as demonstrated by Goruntla et al. (84). this persolized approch to medication management contributes to improved adherence.

Similarly, the study conducted by Samtia et al. highlighted the crucial role of pharmacist counseling in enhancing glycemic control among diabetic patients (100).
These findings emphasize the importance of pharmacist counseling in diabetes management, promoting medication adherence, and improving overall glycemic control.

4.1.3.1.2. Motivational Interview (MI), and telephone-led intervention by pharmacist

MI is widely recognized as an effective method for improving long-term medication adherence in patients. A study investigating the impact of MI on medication adherence demonstrated a positive and significant effect on adherence rates. However, this intervention did not show a significant improvement in HbA1c levels, which reflects long-term glucose control (89).
Telephone-led interventions by pharmacists have also been explored in several randomized controlled trials (RCTs). Among the three studies conducted, two showed a positive effect on improving patient adherence to medication. However, these interventions did not result in a significant improvement in HbA1c levels (87). In contrast, the third RCT, which involved trained pharmacists leading the telephone intervention, demonstrated a positive and significant change in both HbA1c levels and patient adherence (99).

4.1.3.2. Patient oriented-drug related intervention

4.1.3.2.1. Medicine use review service (MUR)

This strategy emphasizes the role of trained community pharmacists who carry out interventions by reviewing the patient's medication regimen and providing customized tutoring and training on the proper methods to take their medications. Many experiences had a positive impact, increasing patients' adherence and refining glycemic control levels (94, 96, 107). Indeed, pharmacist-led care programs have been shown to help patients with diabetes succeed in achieving treatment goals and improving outcomes. In this review, five studies displayed a favorable significant impact of pharmacist-led diabetes programs and these programs were associated with improved patient adherence to medication, and reduction in HbA1c (97, 98, 106).

4.1.3.2.2. Simplifying of complex medication regimes

Patients with T2DM often face challenges related to the complexity of their medication regimens, as measured by the Medication Regimen Complexity Index (MRCI). One study thet included in this review showed a significant number of patients with T2DM have been found to have high MRCI scores. Moreover, it has been observed that high diabetes-specific medication regimen complexity is linked to poor glycemic control (102). This highlights the importance of simplifying complex medication regimens for patients with diabetes. By working collaboratively, physicians and pharmacists can play a crucial role in seeking ways to simplify these regimens. Doing so can lead to improved medication adherence, subsequently resulting in better glycemic control.

4.1.3.3. Physician-oriented collaborative intervention

Improved communication and collaboration between pharmacists and physicians have been found to be effective in enhancing medication management and patient outcomes in the management of T2DM (108).

A study conducted by Mouhtadi et al. demonstrated the success of a collaborative care model involving physicians and pharmacists in reducing fasting blood glucose levels and improving patient satisfaction. By working together, physicians and pharmacists can optimize medication regimens and provide comprehensive care that addresses both clinical and patient-centered needs (109).

Additionally, Aguiar et al. found that the collaborative care model was not only feasible but also more effective than usual care in reducing HbA1c levels in patients with uncontrolled T2DM (93).

This collaborative approach allows for shared decision-making, regular monitoring of patient's progress, medication adjustments, and patient education, resulting in improved glycemic control. These findings highlight the significance of collaborative care models involving pharmacists and physicians in achieving better outcomes for patients with T2DM. By combining their expertise and working closely together, healthcare professionals can provide comprehensive and patient-centered care that leads to improved diabetes management and overall health.

4.1.3.4. Interpersonal-oriented intervention

Family involvement in diabetes management has been recognized as a valuable intervention strategy. Involving family members in the care and support of individuals with diabetes can have positive effects on glycemic control and medication adherence. A randomized controlled trail that included in my review demonstrated the effectiveness of family involvement intervention in improving diabetes management outcomes. This intervention led to a greater reduction in HbA1c levels, which is an important indicator of long-term glucose control in individuals with diabetes. Additionally, significant improvements in medication adherence were observed (105).

4.1.3.4.1. Self-management support intervention led by community pharmacy

This strategy highlight the efficacy of programs that are offered by community pharmacists to help the patient self-manage aspects of their diabetes effectively, including motivation to lose weight, knowledge of correct medication use, diet, and regular exercise. This intervention was observed in an RCT study that resulted in a greater reduction in HbA1c level, and a significant improvement in patient adherence (92). Table 3 provides a descriptive of the different categories of interventions led by pharmacists in the care of diabetic patients.

Table 3: The summary of pharmacist' interventions in diabetes care (38).

Strategies	**Intervention category**	**Discerption of the intervention**	**Examples**	**References**
Patient-oriented verbal intervention	Education	Provide patients with comprehensive information about diabetes, equipping them with the necessary knowledge and skills to effectively manage their medical condition and adopt a healthy lifestyle	Face-to-face, group teaching session, live educational session, Motivational interview (MI), Patient Education by Pharmacist Program (PEPP)	(88, 89, 96-100, 104-107)
Patient-oriented verbal intervention	Counseling	Assists patients in understanding their medications and emphasizes the significance of adhering to prescribed drug regimens	Pill counts, reviewing medication diaries, examining pill boxes, and utilizing pill reminder apps, message reminder services	(87, 93, 95-97, 103, 107)

Strategies	Intervention category	Discerption of the intervention	Examples	References
Patient-oriented-drug related intervention	Medication use review (MUR)	tackled concerns related to medication optimization and adherence	Medication Therapy Management (MTM)	(90, 91, 94, 96, 110)
Patient-oriented verbal intervention	Self-care support program led by pharmacist	Strategies led by pharmacist to manage and prevent diabetes complications through self-blood glucose monitoring	Diabetes Medication Assistance Service (DMAS), behavior change strategies	(92, 97, 98, 100)
Interpersonal-oriented intervention	Family support led by pharmacist	Strategies that provide both emotional and psychological support	Family members, friends, and other sources of social support in the intervention program	(105)
Physician-oriented intervention	Simplifying of complex medication regimes	Physician-pharmacist collaborative approach to streamlining and making the process of developing and implementing drug-related plans more straightforward and easier to understand	Assess the effectiveness of the current medication regimen, and make any necessary changes or modifications	(93, 102)

4.2. Result of the questionnaire

At the National diabetes center in Latakia Governorate, Syria an online questionnaire was distributed to T2DM patients who were registered at the center. These patients were chosen as the target population for the survey. After collecting the responses, a total of 196 questionnaires were considered evaluable for data analysis and inclusion in the study. The data obtained from these questionnaires formed the basis for the statistical evaluation and analysis of T2DM patients' perceptions and preferences regarding community pharmacy services and therapeutic adherence.

4.2.1. Study characteristics

In this present study, 196 patients agreed to participate, resulting in a response rate of 24.4% based on the total number of newly registered cases, which was 803 during the

specified timeframe. This number of registered patients was provided from the National Diabetes center. Among the participants, (55.6%) were male. The age distribution of the respondents showed that 44.4% fell into the 46-60 age group.

The participants had varying levels of education, with 50% being intermediate education holders. In terms of diabetes health status, the majority of participants (89%) had been diagnosed with diabetes for more than 6 months, and (73.5%) had a family member with diabetes. More than half of the respondents (62.2%) had a combination of health problems that led to diabetes complications. Among these complications, hypertension was the most prevalent, affecting 52.6% of the participants, followed by high cholesterol levels at 36.7%. A detailed overview of the demographic and patient characteristics can be found in Table 4.

Table 4: characteristics of patients (111).

Demographic part questions	**Type 2 diabetes respondents**	**Number (%)**
Gender	Male Female	109 (55.6%) 87 (44.4%)
Age	18-30 31-45 46-60 61-70	3 (1.5%) 30 (15.3%) 86 (43.9%) 77 (39.9%)
Place of residence	Country side City center Village	30(15.3%) 147(75%) 19 (9.7%)
Level of education	Elementary High school (intermediate) College or higher	36 (18.4%) 98 (50%) 62 (31.6%)
Duration of diabetes disease	Less than 6 months More than 6 month	22 (11.2%) 174 (88.8%)
Family member had diabetes	Yes No	144 (73.5%) 52 (26.5%)
Any complications of diabetes	Yes No	122 (62.2%) 74 (37.8%)

4.2.2. Evaluation of patients' adherence to prescribed medications

When asked about the daily medication routine, 125 respondents (63.8%) reported that it was not a problem for them, while 71 respondents (31.9%) felt that taking medicines every day is a problem for them. Majority of respondents (99.5%, n = 195) agreed that they received sufficient recommendations from their general practitioners (GPs) regarding their diabetes treatment. The relationship between the patients and healthcare providers in our study appears to be positive, as more than (90%) of participants reported having no difficulties in asking their GP or pharmacist about their diabetes treatment in any situation, as shown in Table 5.

One-quarter of the participants (25.0%) admitted to occasionally forgetting to take their medication. Furthermore, (21.9%) of respondents stated that they would stop or discontinue their treatment if they felt their diabetes was under control, and (18.9%) would cease treatment if their condition did not improve. A small proportion of participants (17.9%) indicated that they would discontinue their treatment if someone around them would have a suspected toxicity from the same drug, and 12.8% reported that they would not take their medication if they believed they were experiencing side effects. Detailed data can be found in Table 5.

Table 5: Patients' adherence to prescribed medicines (111).

Questions	Yes (%)	No (%)
Daily medications is a problem for many. Is this a problem for you in your everyday life?	71 (36.2%)	125 (63.8%)
Do you often forget to take your medicines?	49 (25%)	147 (75%)
Is your doctor advised you to take antidiabetic medicines for your diabetes?	195 (99.5%)	1 (0.5%)
Have you stopped taking your diabetes medicine (s) because you are suspected to feel ill from taking this medicine (s)?	25 (12.8%)	171 (87.7%)
Have you stopped or discontinued your diabetes medicine (s) because your condition has not improved and you are discouraged from taking this medicine (s)?	37 (18.9%)	159 (81.1%)
When you feel that your diabetes is in balance, do you stop taking the medicine (s) for your diabetes?	43 (21.9%)	153 (78.1%)
Do you stop taking your diabetes medicine (s) if your friend / relative / neighbor is taking the same medicine as and has experienced any side effect?	35 (17.9%)	161 (82.1%)
Is it a problem to ask GP about the drug therapy of diabetes?	9 (4.6%)	187 (96.9%)
Is it a problem to ask the pharmacist about the drug therapy of diabetes?	19 (9.7%)	177 (90.3%)

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4.2.3. Percentage of non-adherent patients depends on educational level

Based on the data presented in Figure 4, there appears to be an association between the participants' educational level and their rates of overall non-adherence and intended non-adherence. Among the participants with an elementary educational level, the highest overall non-adherence rate was observed, with 23 out of 36 patients (63.9%) being non-adherent. On the other hand, the college or higher educational group had the lowest overall non-adherence rate, with 23 out of 62 patients (37.1%) being non-adherent. In the case of intermediate education, 56 out of 98 patients (57.1%) were non-adherent in the overall setting. Interestingly, the highest level of intended non-adherence was observed in this education group too, with 44 out of 98 patients (44.9%). In comparison, only 15 patients in the elementary education group and 20 patients in the higher education group showed features of intended non-adherence. All in all the data indicate that the rate of overall non-adherence was 52%, and the rate of intended non-adherence was 40.3% among the entire group of respondents. These findings suggest a potential relationship between educational level and non-adherence behavior. Details are shown in Figure 4.

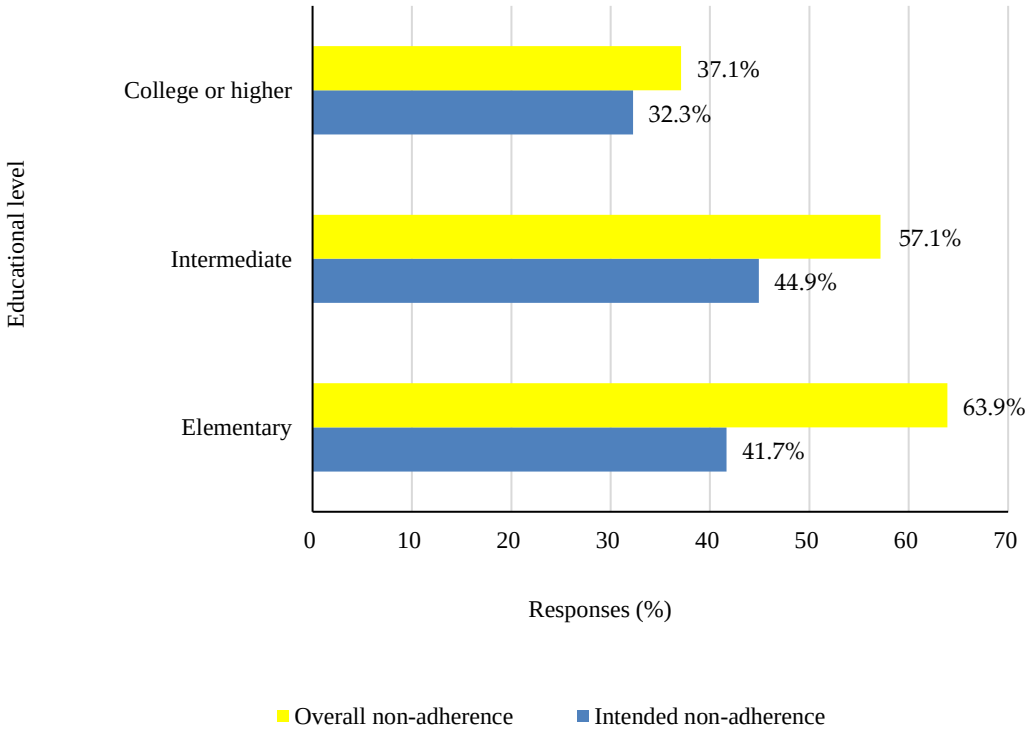

Figure 4: Percentage of non-adherent patients based on educational level (111).

4.2.4. Reasons for not taking the medications as recommended by a health provider

The participants were questioned regarding their main justifications for not following their healthcare provider's recommended course of treatment.

In Figure 5, it is visible, that most of the respondents' fear of side effects (32.7%), hence it is a common reason that could make them stop their treatment. The second most common reason is that the medicine affected their meals (23.0%). This question with various options give us a good insight, into why T2DM patients would stop their medications, therefore helping us to tackle this problem, and encourage the patients to be adherent for better health and wellbeing.

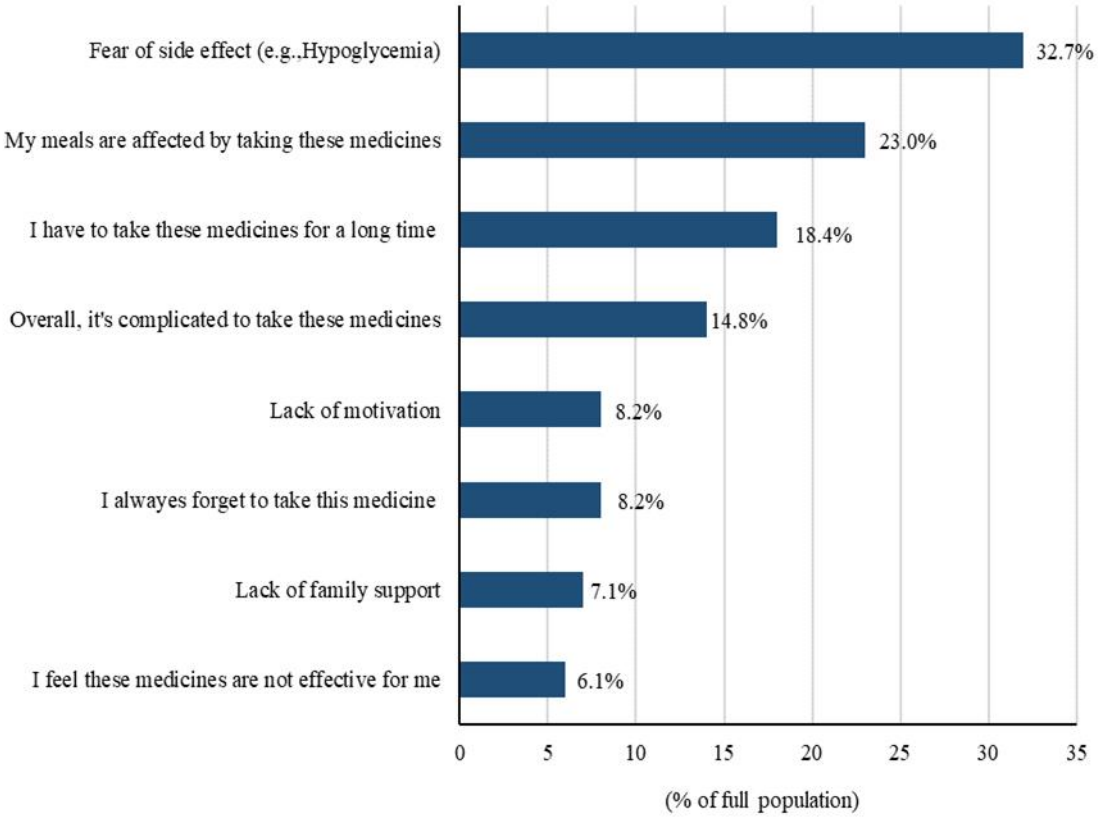

Figure 5: Common reasons that make patients stop their treatment (111).

4.2.5. Evaluation of patients' knowledge about diabetes

To evaluate the patient's knowledge about diabetes, we asked the participants about the solution they could make if they feel their health situation is getting worse. More than half of participating patients (52.6%) reported that they prefer to go to GP.

On the other hand, less than 1% were reported to control their weight (0.5%) and reduce their high-fat content food (0.5%). Details of data are presented in Figure 6.

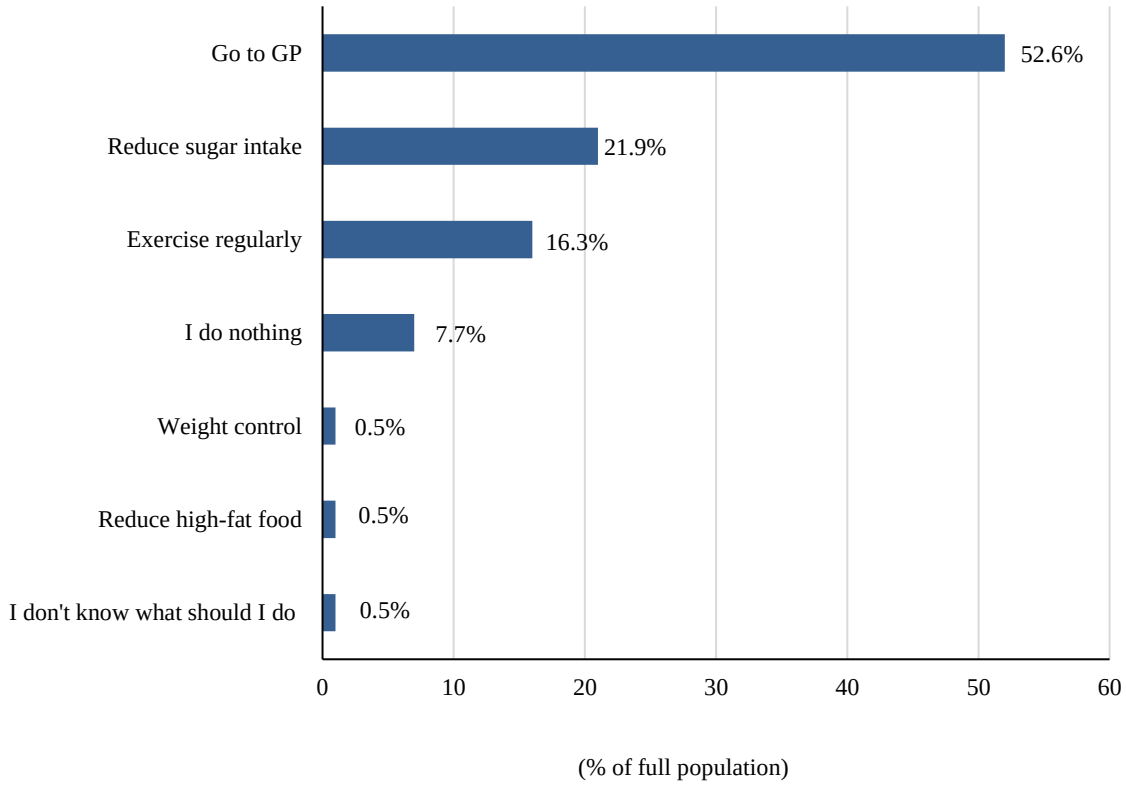

Figure 6: Patients' behavior towards health conditions (GP: General Practitioner) (111).

4.2.6. Percentage of non-adherent in certain complications

Based on the data presented in Figure 7, we can note that among the overall non-adherent participants, the most commonly reported diabetes complication was high blood pressure, with (27.0%) of respondents indicating its presence. Another frequently reported complication among the overall non-adherent participants was high cholesterol levels, with (15.8%) of respondents indicating its presence. In terms of specific diabetes-related complications, eye damage or vision problems were reported by (11.2%) of participants, while a few participants reported nerve damage or numbness in the limbs with (8.7%). When comparing the intended non-adherence group to the overall non-

adherence group, it is notable that a higher percentage of respondents in the intended non-adherence group reported nerve damage or numbness in the limbs (46.2%).

On the other hand, among the overall non-adherence group, a higher percentage of respondents reported eye damage or vision problems (66.7%).

This difference suggests that different diabetes complications may have varying impacts on treatment adherence, with patients experiencing specific complications potentially being more prone to intentional or unintentional non-adherence.

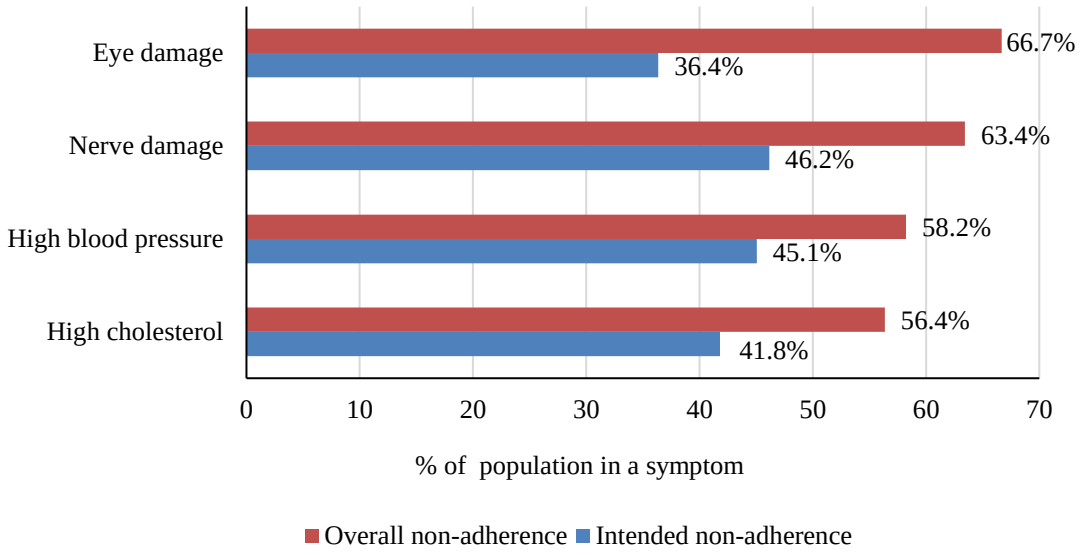

Figure 7: Percentage of non-adherent patients in certain complications of diabetes (111).

4.2.7. Views of patients regarding the accessibility and skills of services provided by local pharmacist

As can be seen in Figure 8, most respondents (64.4%) emphasized that community pharmacists are available to provide information related to treatments in the pharmacy, and (69%) said the pharmacist who offers a measure blood test sample to monitor glucose level. Moreover, (41%) said the pharmacist took sufficient time with them and gave them some sensible advice, such as a diet recommendation and over-the-counter medications, but also 28% said the pharmacist seemed to be ready to provide them clear answers to

their questions and had shown them how to use the blood-glucose meter device with guidelines. Whereas, only 1% of participants said that the delivery of various materials related to diabetes, such as brochures or up-to-date publications is available in Latakian pharmacies.

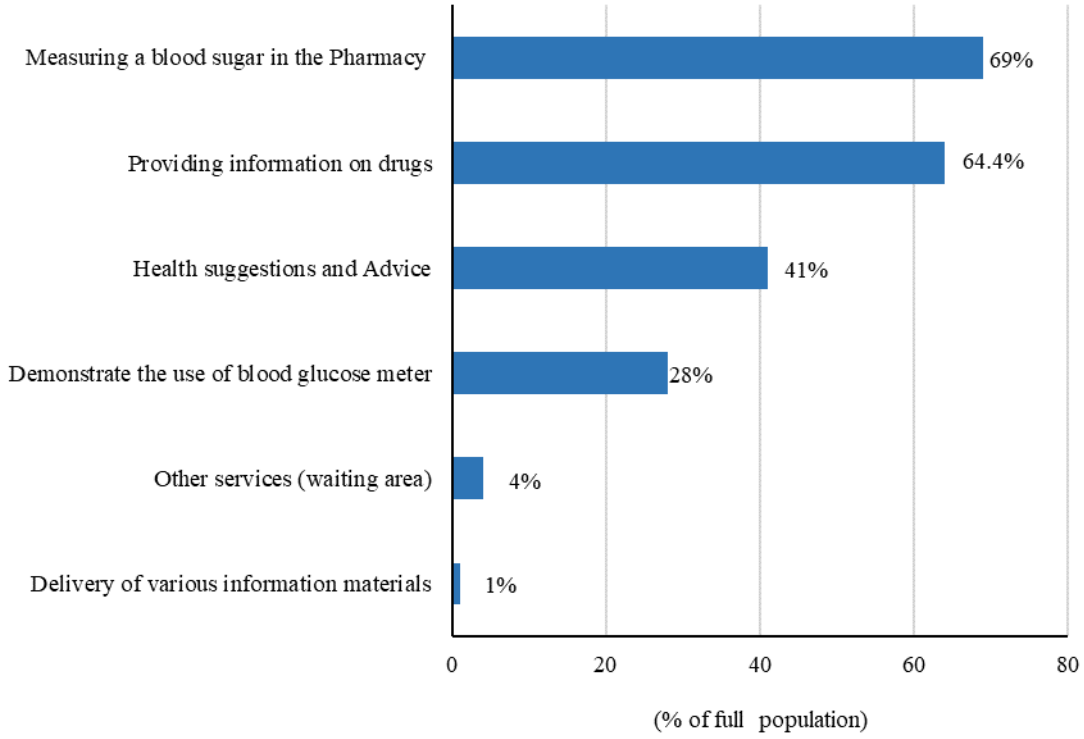

Figure 8: Percentage of patients' satisfaction towards the availability of pharmacy services (111).

4.2.8. Percentage of the full population's satisfaction with the services provided by their local pharmacy

In the healthcare and pharmacy sectors, patient satisfaction is considered a gauge of service quality. We observed that the patient's responses to questions about the cost and accessibility of their medications were inconsistent, as shown in Figure 9. Around three 71% of respondents are pleased with the availability of diabetes medications in pharmacies. In addition, 88.8% of them said that they had received clear instructions from pharmacists on how to utilize their drugs. Approximately all are delighted with the pharmacy's opening times (93.4%). Considering diabetic drug prices, (77.1%) of patients are unsatisfied, particularly in the current conflict in Syria. (Figure 9).

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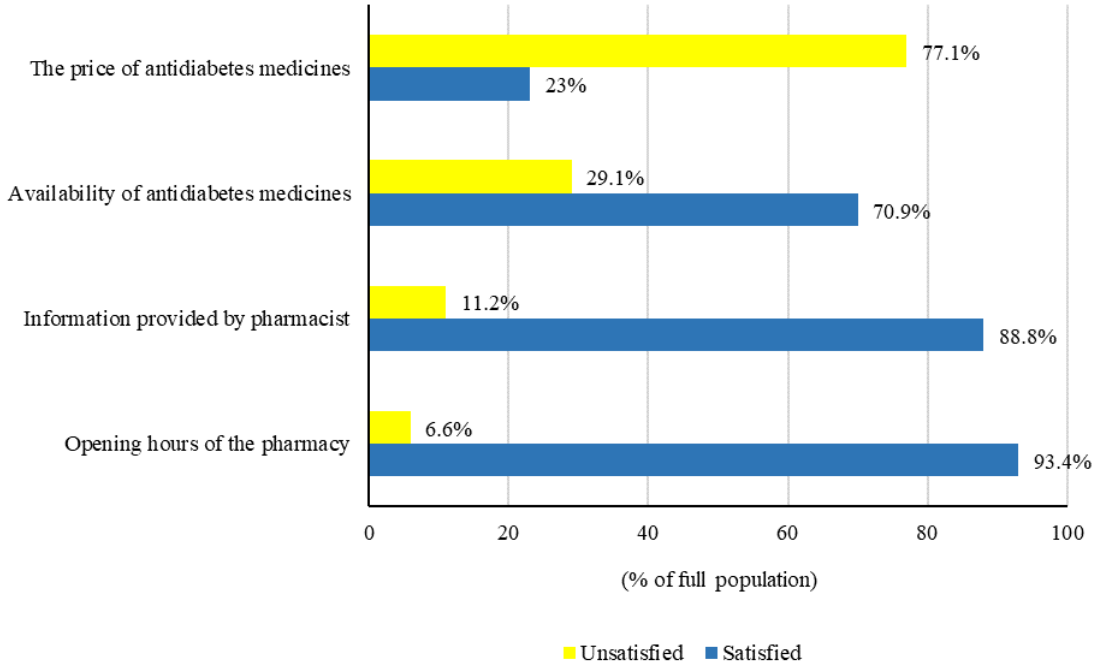

Figure 9: Percentage of satisfied & unsatisfied patients regarding pharmacy service (111)

4.2.9. Percentage of non-adherent patients' satisfaction with the services provided by the pharmacist

Among patients with diabetes who classified in the overall non-adherent group 44.4% of respondents showed interest and satisfaction with the information on the drugs provided by a pharmacist in a community pharmacy, while only 6.1% answered satisfied with the price of the antidiabetics' drugs. Similar pattern was seen in the intended non-adherent group (Figure 10).

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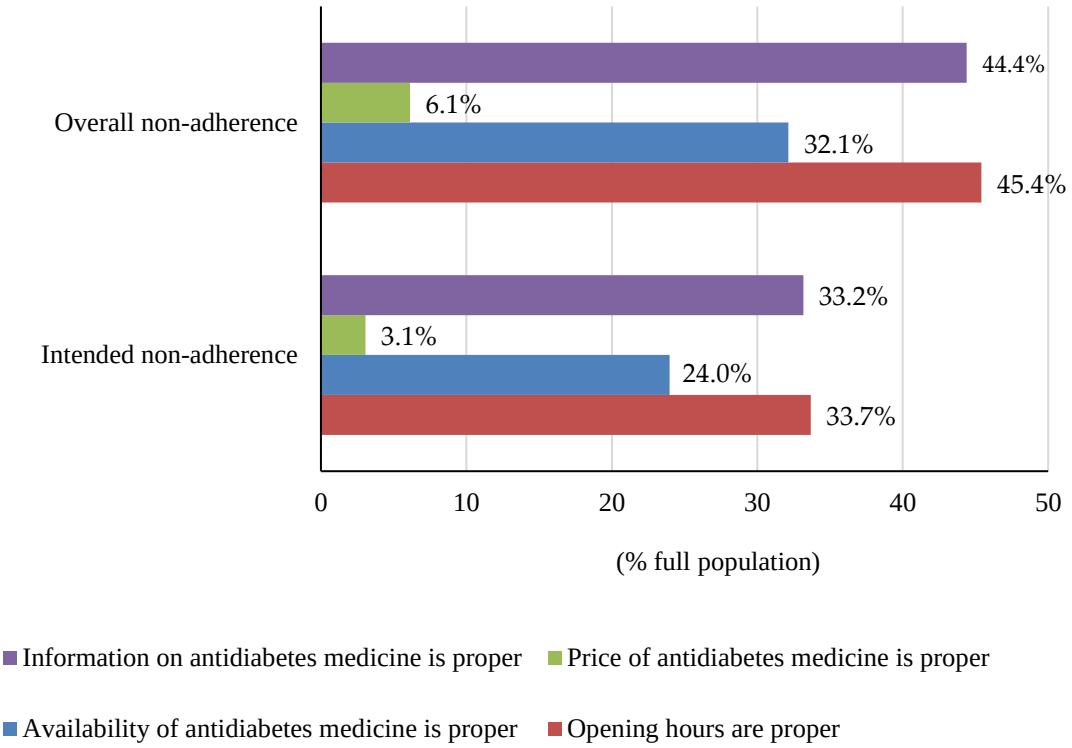

Figure 10: Percentage of non-adherent patients (% full population) (111).

4.2.10. The relationship between the complexity of the treatment and patients' adherence

As the survey showed, the rate of therapeutic non-adherence for patients in both intended and overall non-adherent groups especially those who take one, two, or even three tablets per day is increased. Whereas increased the number of pills > 4 led to a decrease in the rate of the patient's non-adherence in both groups (Figure 11).

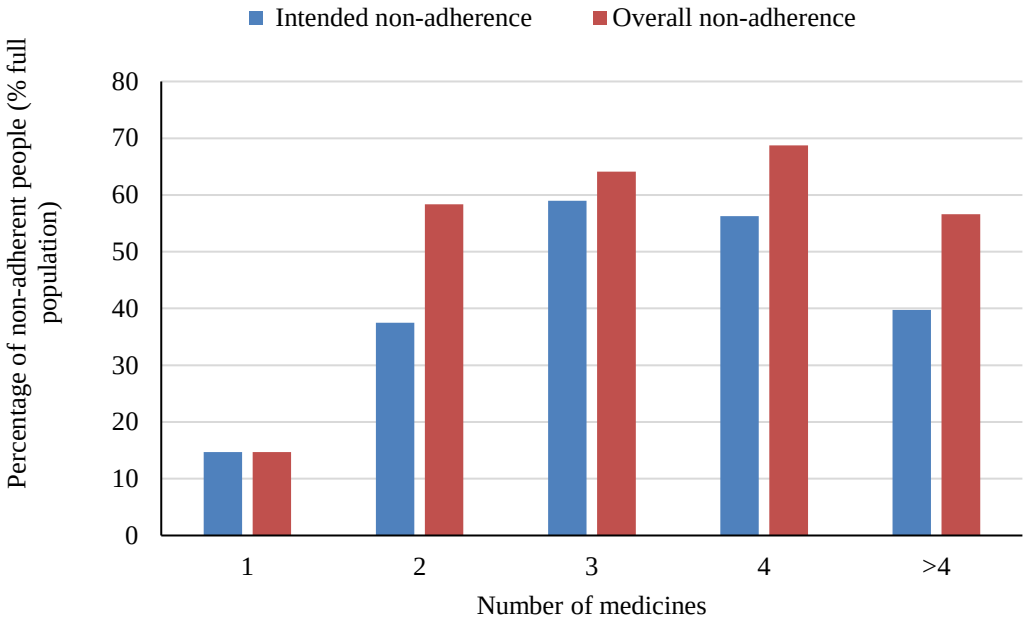

Figure 11: The relationship between the number of medicines that patient take and the patient adherence (111).

4.3. Summary of the results based on patients' need

Based on the systematic review results and patient's answers from our survey it can be said that the first line choice to tackle the adherence problem is to address the patient-oriented drugs related medication interventions, since majority of non-adherent patients have problems with the price of the drugs and their availability. An approach in community pharmacies to simplify medications or detect unintended duplications could decrease the need of medication and may result in lower amount of unavailable drugs. From Figure 8 it is also visible, that patient-oriented verbal interventions seem to be more effective, than increasing family support. Meanwhile Syria struggle with the lack of physicians, therefore it is not feasible to increase physician-oriented collaborative interventions, like patient support programs, as they seem to be already overwhelmed. Figure 12 illustrated the primary and lately goals in the enhancement therapeutic adherence.

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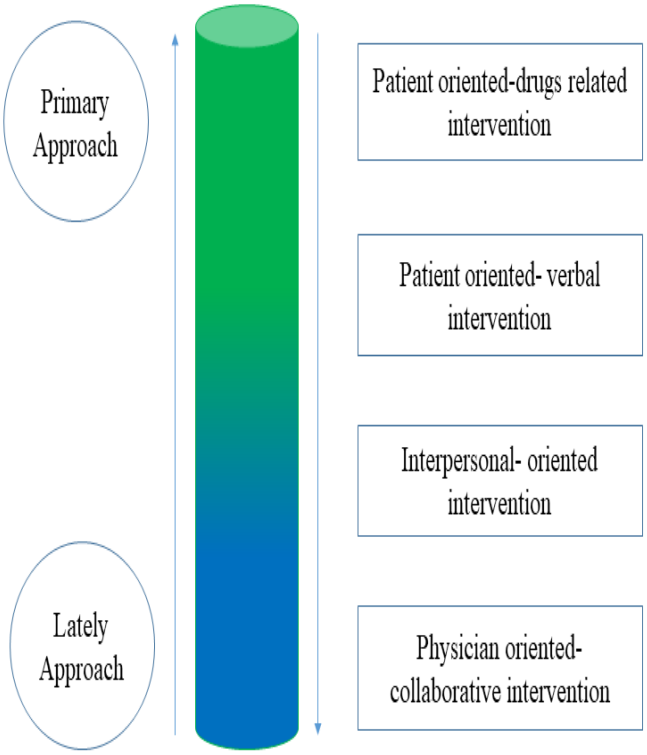

Figure 12: Primary and lately goals of the enhancement therapeutic adherence process

5. Discussion

5.1. Clarification and critical analysis of the findings

5.1.1. Critical analysis of the literature research

Literature research was performed with the objective of the current strategies employed by community pharmacists, and how effective are they in improving patient adherence and HbA1c levels in individuals with T2DM. In summary, many existing pharmaceutical care approaches seem efficacious and beneficial to increase patients' adherence, control glycemic levels, and improve knowledge about diabetes. The study findings show that majority of the included studies in reported a significant impact of the pharmacists' interventions on patients' therapeutic adherence. Some studies showed a positive impact of pharmacists in enhancing therapeutic adherence and glycemic control in the intervention group. These studies included several interventions, such as face-to-face interviewing (89), pharmaceutical consultation (100), community pharmacists' services (92), educational sessions (104), diabetes programs led by pharmacists (97), and remote telephone support (99).

Unsurprisingly, there are more reported beneficial outcomes associated with HbA1c levels. The total achievement level of improvement in glycemic levels due to pharmacist intervention was described as 68.75% for counseling interventions, 69% for education, and 61% for medication management and telephone-based interventions, which reminded patients about refilling prescriptions on time.

The most effective interventions to improve patients' adherence and glycemic levels include a combination of components, such as education, counseling, face-to-face interviewing, simplification of treatment regimens, and follow-ups (97, 98).

In summary, I catigrized the interventions led by pharmacists in diabetes care into four groups: patient-oriented verbal intervention, patient-oriented drug-related medication intervention, physician collaborative-oriented intervention, and interpersonal-oriented interventions. These interventions focus on different aspects of patient-centered care, aiming to improve patient satisfaction, engagement, and overall health outcomes.

Patient-oriented verbal interventions, such as education, counseling, and motivational interviewing (MI), prioritize effective communication and interaction with the patient.

These approaches are interconnected and emphasize tailoring the communication to the patient's specific needs, concerns, and understanding of their condition and treatment.

Patient-oriented drug-related interventions refer to the strategies and services provided by community pharmacists to optimize medication use and improve patient outcomes. These interventions focus on ensuring that patients receive the most appropriate and effective medications for their condition, understand how to take them correctly, and are supported in managing any associated side effects or concerns.

By adopting a patient-centered approach, community pharmacists can have a more comprehensive understanding of the effectiveness and potential benefits of their involvement in diabetes care. This approach recognizes the importance of addressing the unique needs and preferences of each patient, promoting effective communication, and fostering a collaborative relationship between the patient, pharmacist, and other healthcare professionals. These findings contribute to the growing body of evidence supporting the role of community pharmacists in diabetes care.

A previous systematic review conducted by Presley et al. provided evidence regarding the role of pharmacy in diabetes care worldwide, aiming to enhance and improve medication adherence and blood glucose levels among patients with diabetes. The review evaluated the effectiveness of pharmacy-related interventions by analyzing the overall and sub-analysis effect sizes for three types of outcome measures: medication adherence as stated by patients, HbA1c levels, and blood tests other than HbA1c (such as FPG, PPG, and RBG). The review specifically focused on randomized controlled trials (RCTs) and assessed the impact of pharmacist interventions on individuals with diabetes (112). However, my study differs from this review in terms of inclusion criteria and primary outcomes is the change of HbA1c value, providing a unique perspective on the topic.

In my study, I specifically focused on patients with T2DM only, and investigated the impact of community pharmacists in enhancing patient adherence. The primary clinical outcome measure of interest was the effect of these interventions on HbA1c levels only. Unlike the previous review, I did not restrict the study selection based on the type of study design. As a result, my study included a diverse range of study designs, including randomized controlled trials (RCTs), non-RCTs, quasi-experimental studies, case-control studies, cross-sectional studies, and record analyses. This broader approach allowed me to gather a comprehensive understanding of the topic and explore the effectiveness of community pharmacist interventions across different study types.

The findings from this systematic review align with the concept, as the interventions led by pharmacists positively influenced patient knowledge and satisfaction.

Either strategy used by pharmacists, including frequent contact with patients through phone calls or consultation, should be focused on in future studies. This unique approach has given an overall view of the existing literature regarding community pharmacists' interventions for T2DM, and has evaluated these interventions on both behavior and clinical outcomes (38).

5.1.1.1. Limitation

The limitations are related to the time frame and the relatively low number of patients involved in each study. The authors of the cited articles explained that some only had a short period of intervention, which is not enough for monitoring long-term adherence. Other studies justified these results by the tools they used for measuring medication adherence, which were considered not precise enough, such as self-report, and may give overestimations on medication adherence.

5.1.2. Critical analysis of questionnaire analysis

Pharmaceutical services in developing countries present unique challenges that differ from those experienced by pharmacists in developed nations. One of the predominant issues encountered in most developing countries is the inadequate availability of appropriate and high-quality medicines (37). As a result, it becomes crucial to conduct thorough searches and identify the specific needs of patients as an appropriate approach to enhance their quality of life.

This study aimed to enhance our understanding of the challenges faced by Syrian patients with (T2DM) in controlling their condition. The findings revealed three significant barriers that hindered therapeutic adherence among the participants. (i) The lack of antidiabetic drugs availability, (ii) Inadequate education and (iii) the cost of medications. To understanding of the barrier that T2DM patients had, a questionnaire survey was conducted to gather preliminary data regarding the perceptions of T2DM patients in Syria towards community-pharmacy services, focusing specifically on therapeutic adherence.

A total of 196 patients, comprising 87 females and 109 males, were included in the survey, and their opinions regarding community-pharmacy services and treatment behavior were assessed. The findings of our study indicate that diabetic patients in Latakia, Syria, expressed satisfaction with the services provided by community

pharmacies. However, the cost of medications emerged as the most frequently reported issue-affecting participants.

Similar investigations conducted globally have also explored the satisfaction and expectations of diabetic patients towards community-pharmacy services (79-81, 113, 114).

Maintaining pharmaceutical care is crucial for motivating patients to adhere to their treatment regimens and improving their quality of life.

The relationship between patient satisfaction with healthcare services and their commitment to therapy is a crucial and complex one. Understanding this relationship is vital for healthcare providers and policymakers as it can significantly impact patient outcomes and the overall quality of care.

A key aspect of patient satisfaction is effective communication between patients and healthcare providers. When patients feel heard, understood, and involved in decisions about their treatment, they are more likely to adhere to their prescribed therapy. Clear explanations about the importance of therapy, potential side effects, and the expected outcomes can motivate patients to stay committed to their treatment plan. Conversely, when patients experience dissatisfaction with healthcare services, it can lead to reduced commitment to therapy. Issues such as long waiting times, difficulty accessing medications, or poor communication can create barriers to adherence.

Based on the survey findings, it can be inferred that participants had positive opinions about community pharmacists and the services provided by pharmacies.

These findings highlight the importance of considering individual characteristics when assessing patient satisfaction with community pharmacy services. By understanding how different factors affects patient satisfaction, healthcare providers can tailor their services to meet the specific needs and expectations of each patient group. Comparable studies showed that the positioning of the community pharmacy, the punctuality of services, and the expertise of the pharmacist were all significant determinants of customer satisfaction with community-pharmacy services (79, 114, 115).

Regarding satisfaction with community-pharmacy services in our study, it was crucial to assess various aspects. Participants expressed satisfaction with the information provided by pharmacists and the convenient opening hours of the pharmacy, with satisfaction rates of (88.8%) and (93.4%) respectively. However, when it came to the availability of drugs, only (71%) of patients reported satisfaction. Surprisingly, the satisfaction rate regarding medicine prices was significantly lower, at just (23%) Figure 9. These findings highlight

the importance of addressing issues related to drug availability and affordability to further improve patient satisfaction with community-pharmacy services.

The level of patient adherence to treatments was found to be influenced by various factors, including the age and educational background of the patients. In order to evaluate patients' therapeutic behavior, our survey included inquiries about the factors contributing to non-adherence to treatment. Based on the responses, participants were categorized into two groups: adherent and non-adherent. To assess adherence, I have considered three key factors: educational level, patients' beliefs regarding treatments, and the perceived seriousness of the disease. Notably, there was a direct correlation observed between educational level and patients' commitment to treatments, as depicted in Figure 4. These findings emphasize the need for diabetes education to address specific knowledge gaps with greater precision. By targeting these areas of knowledge deficit, pharmacists can enhance patient understanding and promote better adherence to treatment regimens.

Regarding patients' beliefs about treatments, it is noteworthy that concerns related to adverse drug effects can lead to treatment discontinuation or non-adherence, as shown in Table 4. A similar effect was observed in a study conducted by Roborel de Climens et al. (116). Consequently, newly diagnosed patients with complex drug regimens may face challenges in maintaining consistent adherence to prescribed medications. In the survey findings, approximately (15%) of participants reported that the complexity of their treatments contributed to non-adherence. This finding aligns with a study by Jimmy et al., where they also observed that the complexity of drug regimens had a negative impact on medication adherence (53). It is evident that addressing these concerns and simplifying treatment regimens for patients could potentially improve overall adherence to medications and positively influence treatment outcomes.

However, adherence can be predicted by the patient’s disease state, and their awareness of its severity. Patients who are most severely ill with serious diseases may be at greatest risk for non-adherence to treatment, but this situation could make the patients more aware of the need to take their medicines in a proper way. In our survey, we made a comparison between non-adherent patients based on the number of pills that patient take (see Figure 11). DiMatteo et al. demonstrated that patients who had poorer health issues were more adherent to treatment (70).

The findings from the survey provide valuable insights into the potential factors contributing to patient non-adherence and suggest advices for improvement in healthcare delivery.

Moreover, based on the data depicted in Figure 7, several noteworthy observations can be made regarding the diabetes-related complications reported by the non-adherent participants.

Firstly, it is apparent that the most frequently reported diabetes complication among the non-adherent participants was high blood pressure, with 27.0% of respondents acknowledging its presence. Following closely, high cholesterol levels were also commonly reported, with 15.8% of participants indicating its occurrence. In terms of specific diabetes-related complications, 11.2% of respondents reported eye damage or vision problems, while a smaller proportion, 8.7%, mentioned experiencing nerve damage or numbness in their limbs.

Upon comparing the intended non-adherence group to the overall non-adherence group, a noteworthy disparity becomes evident. A higher percentage of respondents in the intended non-adherence group, specifically 46.2%, reported nerve damage or numbness in their limbs as a complication. Conversely, among the overall non-adherence group, a notably higher percentage, 66.7%, reported eye damage or vision problems.

This discrepancy suggests that different diabetes complications may exert varying influences on treatment adherence. Patients experiencing specific complications may be more susceptible to intentional or unintentional non-adherence, shedding light on the complex interplay between diabetes complications and adherence behavior.

Furthermore, a significant finding from our survey indicates that the most prevalent concern among respondents was the fear of experiencing side effects (32.7%). This fear emerged as a common reason that could potentially lead individuals to discontinue their treatment. The second most frequently cited reason was the impact of medications on their meals (23.0%). (See Figure 5).

Understanding how individuals perceive their disease is crucial for healthcare providers to support patients in preventing and managing their conditions effectively. To explore this aspect, I included a question in the survey that focused on the solutions patients would consider if their health deteriorated (see Figure 6). The results indicate that a significant proportion (52.6%) of participants prefer visiting a general practitioner (GP) when experiencing health deterioration. This may indicate a lack of awareness or understanding of the role of lifestyle modifications in managing diabetes. Healthcare

providers can play a vital role in educating patients about the importance of self-management strategies, including healthy eating habits and maintaining a healthy weight. By providing comprehensive education and guidance, healthcare professionals can empower patients to be more knowledgeable about their health and support better diabetes management outcomes.

To address these gaps, it is crucial to implement awareness campaigns and educational programs within the Syrian community. These initiatives should aim to educate the public about the roles and capabilities of community pharmacists in delivering patient-centered care and fostering meaningful interactions between patients and pharmacists. Emphasizing the importance of treatments, including lifestyle modifications such as adopting a better diet, without incurring additional costs, can have a particularly impactful effect.

Patients' perspectives on the accessibility of pharmacist services were a crucial aspect explored in our study, as illustrated in Figure 8. Overall, the majority of participants rated each factor as being available. However, approximately 60% of participants expressed a lack of general health advice, including self-management support programs, information about drug-food interactions, and guidance on maintaining a healthy lifestyle. Furthermore, nearly all patients reported a lack of access to various information materials related to diabetes, such as brochures, up-to-date publications, online resources, and leaflets. These findings underscore the need for awareness initiatives and informational campaigns within the Syrian community to educate patients about treatment adherence and enhance the community pharmacists' skills in delivering satisfactory diabetes care.

Research conducted by Caetano et al. supports the positive impact of interventions using leaflets distributed in basic healthcare settings, particularly among younger individuals with limited research exposure, in promoting medication adherence
(117). This highlights the potential of providing informative materials, such as brochures, to educate patients about their condition and treatment options.

Addressing the information gaps and enhancing the delivery of pharmacist services remain crucial in improving patient satisfaction and treatment adherence among individuals with diabetes in the Syrian community. By providing accurate and accessible information through brochures and combining them with oral discussions, healthcare providers can empower patients to make informed decisions about their health and improve their medication adherence.

It's important to recognize that individual patient factors also play a role. Patients have varying levels of commitment to therapy based on their beliefs, values, and personal circumstances. While satisfaction with healthcare services can influence commitment, it is not the sole determinant. There is a clear interplay between patient satisfaction with healthcare services and their commitment to therapy. A positive healthcare experience that prioritizes effective communication, trust, and patient-centered care can enhance commitment to treatment. Conversely, dissatisfaction with services can create hurdles to adherence. Healthcare providers should strive to create an environment where patient satisfaction and commitment to therapy are mutually reinforcing, ultimately leading to improved patient outcomes.

In summary, based on the systematic review and survey findings, a patient-oriented approach focusing on drug-related interventions is crucial for diabetic patients in Syria. Pharmacists can address the patients' needs related to drug availability and cost-effectiveness by providing counseling, conducting medical use reviews, and recommending alternative drugs that are readily available. Increasing patients' knowledge about their treatments and supporting self-care routines, including healthy lifestyle recommendations, is also important.

To further validate the importance of pharmacy services in diabetes care, future studies with larger sample sizes and longer durations are recommended. To improve patient satisfaction and enhance the professional image of the pharmacy, it is suggested to consider the appointment of dedicated pharmacists in each community pharmacy solely for consultations and medical-history reviews. This specialization can enhance the quality of care provided by community pharmacists and strengthen their role in diabetes management.

5.1.2.1. Limitation

Most importantly, probability sampling was not achieved; hence, not all types of Syrian patients may be covered well by the study. Furthermore, the response rate was also rather low, and only a small number of patients were considered which might hinder how far the results can be accepted as a general feature of Latakian diabetic patients. A future study examining community pharmacists’ viewpoints and experiences in improving diabetes therapeutic adherence would provide a more comprehensive review and

examine other pharmacist strategies in diabetes care. Because of these limitations, only basic statistics were provided, and further analysis was not conducted.

Finally, my literature research fills a significant gap in the literature by comprehensively examining pharmacists' interventions in relation to therapeutic adherence and HbA1c levels in diabetes care. By focusing on these specific criteria, I have provided valuable insights into the impact of pharmacist-led interventions on patient outcomes. This contributes to a deeper understanding of the role that community pharmacists can play in supporting T2DM patients and enhancing their adherence to treatment regimens (38). Furthermore, my questionnaire survey sheds light on the perceptions of T2DM patients in Syria regarding pharmacy services. This firsthand information from patients themselves provides invaluable insights into their needs, expectations, and satisfaction with the services provided by community pharmacists. By considering the perspectives of the patients, I have identified the most appropriate approach to improving patient quality of life in Syria (111).

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6. Conclusion

This dissertation underscores the importance of prioritizing human and technological resources to effectively combat the spread of T2DM. Specifically, it focuses on the preferences of T2DM patients in Latakia Governorate Syria, regarding community pharmacists' services as a means to increase medication adherence.

The research findings emphasize the need to carefully consider various aspects of pharmacist services, including service approach, types of services offered, privacy considerations, and respecting patients' autonomy in choosing services that align with their needs. By integrating patients' viewpoints, a comprehensive understanding of pharmacist services can be achieved, tailored to the specific medication requirements of patients.

Assessing the currently available services is crucial to fill the gap between identified preferences and the reality of pharmacist services. Most participants with T2DM did not encounter difficulties in seeking diabetes treatment information from pharmacists, indicating a favorable perception of pharmacists as healthcare providers. This presents an opportunity for pharmacists to expand their involvement in diabetes care and contribute to improved therapeutic adherence among patients.

The design of pharmacist services in Syria should prioritize a Medication Use Review (MUR). These findings underscore the significance of addressing concerns pertaining to drug availability and affordability in order to enhance patient satisfaction with community-pharmacy services. One potential strategy to tackle this issue is the implementation of MUR in Syrian pharmacies. MUR involve pharmacists reviewing patients' medications and, if necessary, recommending alternative drugs that exhibit similar efficacy to those that may not be available. By employing MUR, pharmacists can actively contribute to resolving medication availability challenges and ensuring patients receive appropriate and effective treatments. This approach holds promise in improving patient satisfaction and overall healthcare outcomes within the Syrian context.

The dissertation serves as a preliminary step toward establishing services that consider the perspectives of individuals with T2DM in Syria, with the aim of enhancing medication adherence in a cost-effective manner.

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7. Summary

The prevalence of T2DM is increasing at an alarming rate, making it a significant public health concern worldwide. Proper management of T2DM requires active participation from individuals, including adherence to therapy and self-care behaviors. However, national health systems face challenges in dealing with the expanding problem due to limited human and financial resources. This creates a growing gap between the increasing prevalence of T2DM and the resources available to manage it.

I tried to explore if pharmacists can contribute to the containment of this escalating problem. In my research, I conducted a systematic review to analyse the scientific research on pharmaceutical interventions in diabetes care, with a focus on the role of community pharmacists in enhancing patients' therapeutic adherence and controlling HbA1c levels. This analysis allowed me to categorize existing approaches in the literature and gain an overview of current community pharmacy interventions for T2DM patients.

Furthermore, I investigated the perceptions of T2DM patients toward the use of community pharmacists in diabetes care. I developed a questionnaire and distributed it to T2DM patients at the national diabetes center in Latakia, Syria. Through the analysis of the survey responses, I obtained a positive image of pharmacist services among T2DM patients. This positive perception opens up opportunities for community pharmacists to expand their role in diabetes care and contribute to improving therapeutic adherence among patients. The findings also provided valuable insights into the essential requirements and expectations of pharmacists in the daily lives of diabetes patients. This further highlights the high demand and usefulness of community pharmacists in the management of diabetes.

My Ph.D. thesis represents a standard method by filling the gap between literature research and the reality of community pharmacists' contributions to diabetes care in Syria. The evaluation of this project covered the significant need for pharmaceutical support in diabetes management. It also emphasized the role of pharmacists in encouraging patients to adhere to their therapies. The results of my thesis should serve as a foundation for further investigations and the optimization of underutilized resources in national health systems.

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9. All publication related to the thesis

Al Assaf S, Zelko R, Hanko B. (2022) The Effect of Interventions Led by Community Pharmacists in Primary Care for Adults with Type 2 Diabetes Mellitus on Therapeutic Adherence and HbA1c Levels: A Systematic Review. International Journal of Environmental Research and Public Health, 19:6188.
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Al Assaf S, Kleiner D, Zelkó R, Hankó B. (2023) Type 2 Diabetes Patients' Views of Local Pharmacists and Fulfilment with Pharmaceutical Diabetes Care in Syria's Latakia Governorate: An Online Survey Research. Healthcare, 11:1720.
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11. Appendix

Survey: perceptions of T2DM patients towards community pharmacy services

Dear Ladies and Gentlemen,

My name is Sarah Al Assaf, a Ph.D. candidate in Pharmaceutical Science Doctoral School of Pharmacy Administration and drug development at the Semmelweis University in Hungary. I am conducting a study about the Effect of Community Pharmacy services in increasing the therapeutic adherence of T2DM patients in Latakia,Syria

We cordially invite you to take part in a survey on T2DM patients perceptions towards the community pharmacy services. Please only complete the questionnaire if you are diagnosed with T2DM and are taking any prescription medication (such as tablets or capsules). However, if you are already using insulin or other injectable medicines for your diabetes, and a pregnant woman please do not fill in the questionnaire. If you are taking other medicines for other illnesses, you can still fill the questionnaire!

The information obtained in this survey is just for scientific purposes only and the participants remains anonymous.

Your contribution is very important to achieve the study objectives.

Thank you for your cooperation!

If you have any questions about this study, feel free to contact me at sarah.assaf@phd.semmelweis.hu

سيداتي وسادتي،

اسمي الصيدلانية سارة العساف ، طالبة دكتوراه في قسم الصيدلة السريرية وتطوير الأدوية في كلية الصيدلة في جامعة سيميلويس, المجر. أقوم بإجراء دراسة حول تأثير خدمات الصيدلة المجتمعية على زيادة الالتزام العلاجي لمرضى السكري من النوع 2 في سوريا.

لطفا ادعوك (ي) للمشاركة في هذا الاستبيان لأخذ فكرة واضحة عن تصورات مرضى السكري من النوع الثاني اتجاه الخدمات المتوفرة في الصيدليات العامة . يرجى إكمال الاستبيان فقط إذا تم تشخيصك بمرض السكري وكنت تتناول دواءً موصوفًا (مثل حبة أو كبسولة) لعلاج مرض السكري.

إذا كنت تتناول بالفعل الأنسولين أو أدوية أخرى قابلة للحقن، فيرجى عدم ملء الاستبيان. إذا كنت تتناول أدوية أخرى لأمراض أخرى ، فلا يزال بإمكانك ملء الاستبيان!

المعلومات التي تم الحصول عليها في هذا الاستبيان هي للأغراض العلمية فقط وسيكون هذا الاستبيان على قدر من الخصوصية.

مساهمتك مهمة للغاية.

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شكرا جزيلا لتعاونكم!

إذا كان لديك أي أسئلة حول الدراسة ، فلا تتردد في الاتصال بي

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الجزء الأول: البيانات الشخصية Part 1: Demographic patients' characteristics		
1.Your gender (الجنس): □ Male (ذكر) □ Female (انثى)		
2.Your age (العمر): □ 18-30 □ 31-45 □ 46-60 □ 61-75		
3. our place of residence (مكان السكن) : □ country side (الريف) □ city center (وسط المدينة) □ village (قرية)		
4. Your highest level of education: (مستوى التعليم) □ elementary (تعليم ابتدائي) □ intermediate (تعليم متوسط) □ higher education (تعليم عالي)		
Part 2: Patient therapeutic behavior (سلوك المريض العلاجي)		
5. How many prescription drugs are you taking in total? كم عدد الأدوية الموصوفة التي تتناولها إجمالاً؟ □ 1 □ 2 □ 3 □ 4 □ > 4		
6. Daily medication is a problem for many. Is this a problem for you in your everyday life? هل هذه الأدوية اليومية مشكلة بالنسبة للكثيرين. مشكلة بالنسبة لك في حياتك اليومية؟	Yes (نعم)	No (كلا)
7. Do you often forget to take your medication? هل تنسى كثيرًا تناول أدويتك؟	Yes (نعم)	No (كلا)
8. How often is it difficult to remember to take your medicine (s)? كم مرة يكون من الصعب تذكر تناول الدواء (الأدوية) الخاص بك؟ □ Always دائما □ Often غالبا □ Sometimes احيانا		

□ Rarely نادرا □ Neverأبدا		
9. Is your doctor advising you to take your medicines for your diabetes? هل ينصحك طبيبك بتناول الأدوية المضادة لمرض السكر؟	Yes(نعم)	No(كلا)
10. Have you stopped or stopped taking your diabetes medicine (s) because you are suspected of feeling ill from taking this medicine (s)? هل توقفت عن تناول دواء (أدوية) السكري بسبب الاشتباه في شعورك بالمرض بسبب تناول هذا الدواء (الأدوية)؟	Yes (نعم)	No (كلا)
11. Have you stopped or discontinued your diabetes medication (s) because your condition has not improved and you are discouraged from taking this medication هل توقفت عن تناول دواء (أدوية) السكري لأن حالتك لم تتحسن ولايوجد احد يُشجعك على تناول هذا الدواء (الأدوية)؟	Yes (نعم)	No (كلا)
12. When you feel that your diabetes is in balance, do you stop taking the medicine (s) for your diabetes? عندما تشعر أن مرض السكري لديك في حالة توازن ، هل تتوقف عن تناول دواء (أدوية) ؟	Yes (نعم)	No (كلا)
1. Do you stop taking your diabetes medicine (s) if your friend / relative / neighbor is taking the same medicines as you and has experienced any side effects? هل تتوقف عن تناول دواء (أدوية) السكري إذا كان صديقك / قريبك / جارك يأخذ نفس الأدوية التي تتناولها وتعرض لأية آثار جانبية؟	Yes (نعم)	No (كلا)
14. Is it a problem for you to ask the GP about the drug therapy for their diabetes? هل تواجه مشكلة في سؤال الطبيب العام عن العلاج الدوائي لمرض السكري؟	Yes (نعم)	No (كلا)
15. Is it a problem for you to ask the pharmacist questions about the drug therapy for your diabetes? هل تواجه مشكلة في طرح أسئلة حول العلاج الدوائي لمرض السكري في الصيدلية؟	Yes (نعم)	No (كلا)

16. Please indicate the most common reasons why you may not be taking your diabetes medicine (s) as recommended by your doctor or pharmacist.
(You can enter more than one answer!)
يرجى الإشارة إلى الأسباب الأكثر شيوعًا التي قد تجعلك لا تتناول أدوية السكري الخاصة بك على النحو الموصى به من قبل طبيبك أو الصيدلي (يمكنك إختيار أكثر من إجابة واحدة !)

□ Overall, it is too complicated to take this (these) medicine (s) بشكل عام ، من الصعب جدًا تناول هذه الأدوية
□ Lack of family supportعدم وجود دعم الأسرة
□ Lack of any motivationعدم وجود أي دافع لتناول الدواء
□ I have been taking this medicine (s) for too many years لقد كنت أتناول هذا الدواء (الأدوية) لسنوات عديدة
□ My meals are affected by taking this medicine (s)تتأثر وجباتي بتناول هذا الدواء (الأدوية)
□ Fear of side effects (e.g. hypoglycemia)الخوف من الآثار الجانبية (مثل نقص السكر في الدم)
□ I always forget to take this medicine (s)أنسى دائمًا تناول هذا الدواء (الأدوية)
□ I feel this (these) drug (s) are not effective for meأشعر أن هذه الادوية ليست فعالة بالنسبة لي

17. In total, how many tablets or capsules should you take in just one day for your diabetes? (Whether from just one type of medicine, or even from several types of medicine combined!)
كم عدد الأقراص أو الكبسولات التي يجب أن تتناولها في يوم واحد فقط لمرض السكري لديك؟
(سواء من نوع واحد فقط من الأدوية ، أو حتى من عدة أنواع من الأدوية مجتمعة !)
□ only one
□ two kinds
□ three kinds
□ more than three kinds
□ I do not know

18. When should you only take medication for your diabetes in one day? متى يجب أن تتناول الدواء ؟

□ only in the morningصباحا فقط
□ only in the afternoonظهرا فقط
□ only in the evening في المساء
□ morning and eveningصباحا و مساء
□ morning, noon and eveningصباحا, ظهرا و مساء

Part 3: Diabetes knowledge الجزء الثالث: مرض السكري

19. When was it found that you were diabetic?؟منذ متى تم تشخيصك بمرض السكري
□ less than 6 monthsاقل من 6 اشهر
□ more than 6 monthsاكثر من 6 اشهر

20. Was there a diabetic family member in the family? هل يوجد فرد في الأسرة مصاب بمرض السكري؟	Yes (نعم)	No (كلا)
21. Do you have a complication of your diabetes?	Yes (نعم)	No (كلا)

هل لديك مضاعفات لمرض السكري الخاص بك؟ أي هل لديك شكوى، او مرض ظهر بعد تشخيص الاصابة بمرض السكري؟ سواء كان مع أو بدون تقرير طبي		

22. If you have a complication, what is it like? (Multiple answers possible!)
Only mark a complaint if it occurred after the onset of diabetes
اذا كانت لديك مضاعفات ، ماهي
هذه المضاعفات؟ ضع علامة على شكوى فقط إذا حدثت بعد التشخيص بالاصابة بمرض السكري (يمكن اختيار اكثرمن اجابة واحدة!)

□ Eye damage or vision problems تلف في العين أو مشاكل في الرؤية
□ Renal impairment or complaints القصور الكلوي
□ High blood pressure ارتفاع ضغط الدم
□ High cholesterol or triglyceride levels ارتفاع الكوليسترول أو الدهون الثلاثية
□ Feeling nerve damage or numbness in the limbs الشعور بتلف في الأعصاب أو تنميل في الأطراف
□ Diabetic foot القدم السكرية
□ Obesity or weight gain السمنة أو زيادة الوزن
□ I have no diabetes symptoms (other symptoms for example: headache) اعراض اخرى

23. What are you doing to ensure that you do not develop complications of diabetes in the future or that your current health condition worsens?
(Multiple answers available!)

ما الذي تفعله للتأكد من عدم تعرضك لمضاعفات مرض السكري في المستقبل أو أن حالتك الصحية الحالية تزداد سوءًا؟ (يمكن اختيار اكثرمن اجابة واحدة!)

□ I keep an eye on my weight مراقبة الوزن
□ Restricting and reducing high fat foods during my meals تقليل الأطعمة الغنية بالدهون
□ Restricting and reducing sugar intake during my meals تقليل تناول السكر
□ Regular exercise, physical activity ممارسة الرياضة بانتظام
□ I go to the doctor regularly أذهب إلى الطبيب بانتظام
□ I do nothing لا أفعل شيئًا
□ I don't know what I could do لا أعلم ما الذي يمكنني فعله

Part 4): Pharmacy services: الجزء الرابع: خدمات الصيدلية لمرضى السكري
Below, we are curious about your level of satisfaction with pharmacy services for your diabetes.
Next to the statements, check the option you agree with.

24. The opening hours of the pharmacy I visit most often ساعات عمل الصيدلية التي أزورها!	Satisfied (جيدة)	Unsatisfied (غير جيدة)
25. Availability of the drug (s) prescribe for me for my diabetes in the pharmacy توافر الأدوية الموصوفة لمرض السكري في الصيدلية	Satisfied (جيدة)	Unsatisfied (غير جيدة)
26. The price of my drug (s) for my diabetes	Satisfied(جيدة)	Unsatisfied (غير جيدة)

سعر الدواء (الأدوية) الخاصة بمرض السكري		
27. In general, information on the use of medications provided by pharmacy staff for my diabetes (e.g., dosage, side effects, expected efficacy) المعلومات عن كيفية استخدام الأدوية التي يقدمها طاقم الصيدلية لمرضى السكري (مثل الجرعة والآثار الجانبية والفعالية المتوقعة)	Satisfied(جيدة)	Unsatisfied(غير جيدة)

28. What kind of diabetes-related service have you ever encountered in public pharmacies?

ما نوع الخدمة المتعلقة بمرض السكري و المتوفرة في الصيدليات العامة

(Multiple answers available!)
(يمكنك اختيار اكثر من اجابة واحدة !)

- □ Information on how to take your medicine (s) for diabetes (e.g., what, why and how should I take it)?
  تقديم معلومات حول كيفية تناول الأدوية الخاصة بك (على سبيل المثال ، ماذا ولماذا وكيف يجب أن أتناوله؟)
- □ Health suggestions and advice on diabetes other than taking medication (e.g., diet, exercise, etc.)
  تقديم قتراحات ونصائح صحية حول مرض السكري بخلاف تناول الأدوية (مثل النظام الغذائي والتمارين الرياضية وما إلى ذلك)
- □ Measuring blood sugar in the pharmacy
  قياس سكر الدم بالصيدلية
- □ Demonstrate the use of the device when purchasing a blood glucose meter
  تقديم معلومات عن كيفية استخدام الجهاز عند شراء جهاز قياس السكر في الدم
- □ Delivery of various information materials related to diabetes (e.g., publications, online access, distribution of leaflets, etc.
  زيادة تثقيف المريض عن طريق تقديم مواد إعلامية متنوعة تتعلق بمرض السكري (مثل المطبوعات ، والوصول عبر الإنترنت ، وتوزيع المنشورات ، وما إلى ذلك)
- □ Other services (waiting area, counselling service)
  خدمات اخرى (الانتظار والاستشارة الدوائية)

Thank you for completing the questionnaire! Your cooperation means a lot to us!