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

PhD thesis

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1.   Introduction

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

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.

2.   Objective

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?

3. Method

3.1. Literature search

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. The process of study selection and data extraction adhered to the guidelines set forth in the Cochrane Handbook.

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.

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

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.

Study selection was completed by reviewing the title, abstract, and full-text contents, in accordance with the pre-defined inclusion and exclusion criteria.

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.

For quality assessment, a risk of bias assessment accompanied each included study, using Cochrane guidelines ROB2 for randomized controlled trails, for non-randomized controlled trails, opened labelled intervention, case control studies I used ROBINS-I tool. In addition, MINORS tool was used for quasi-experimental studies.

3.2.   Questionnaire analysis

This study was conducted as the second part of a Ph.D. dissertation focused on investigating the perceptions of Syrian T2DM patients regarding community pharmacy

services. An online survey questionnaire was conducted over 8 months from April to November 2022 in the Diabetes Center in Latakia Governorate, Syria. The ethical committee of Al Manara University approved the study (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 Kind 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).

Inclusion criteria

Patients were informed that participation was entirely optional and the survey data would only be used for scientific research. All of their responses were recorded anonymously. On the other hand, during the filling of the survey, answers to every question were obligatory. 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. We exclude patients who take insulin and pregnant women.

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 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 mean and percentages, were used to summarize and analyze the data. Categorical variables were presented as percentages or represented using graphs for visual representation. To determine the response rate, the number of newly registered patients and the number of participants who took part in the survey were considered. The response rate was calculated as a percentage. In terms of adherence, intended non-adherence was calculated based on the responses to four specific questions ("Have you stopped taking your diabetes medicine(s) because you are suspected of feeling ill from taking this medicine(s)?"; "Have you stopped or discontinued your diabetes medication(s) because your condition has not improved and you are discouraged from taking the medication(s)?"; "When you feel that your diabetes is in balance, do you stop taking the medicine(s) for your diabetes?"; "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. Overall adherence was also calculated using a similar approach, but the question "Do you often forget to take your medication?" was additionally considered.

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.

Survey

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) and the Medication Adherence

6

Rating Scale (MARS) and then translated into Arabic. 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.

4. Results

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

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.

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.

Table 1 illustrates the results of literature search.

Table 1: The summary of pharmacist' interventions in diabetes care (**Al Assaf S**, 2022).

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)
Patient-oriented-drug related intervention	Medication use review (MUR)	Pharmacists actively tackled concerns related to medication optimization and adherence, thereby improving the effectiveness of drug therapy for patients.	Medication Therapy Management (MTM), Organizing drug-taking schedules, engaging in discussions, and evaluating medication regimens, as well as implementing dose up-titrations according to pre-established protocols	(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)

Strategies	Intervention category	Discerption of the intervention	Examples	References
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. Results of the questionnaire analysis

Based on the survey findings, it can be inferred that participants had positive opinions about community pharmacists and the services provided by pharmacies. The level of patient satisfaction was found to be influenced by various factors, including the age and educational background of the patients. 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.

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.

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.

Regarding satisfaction with community-pharmacy services in my 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 1.
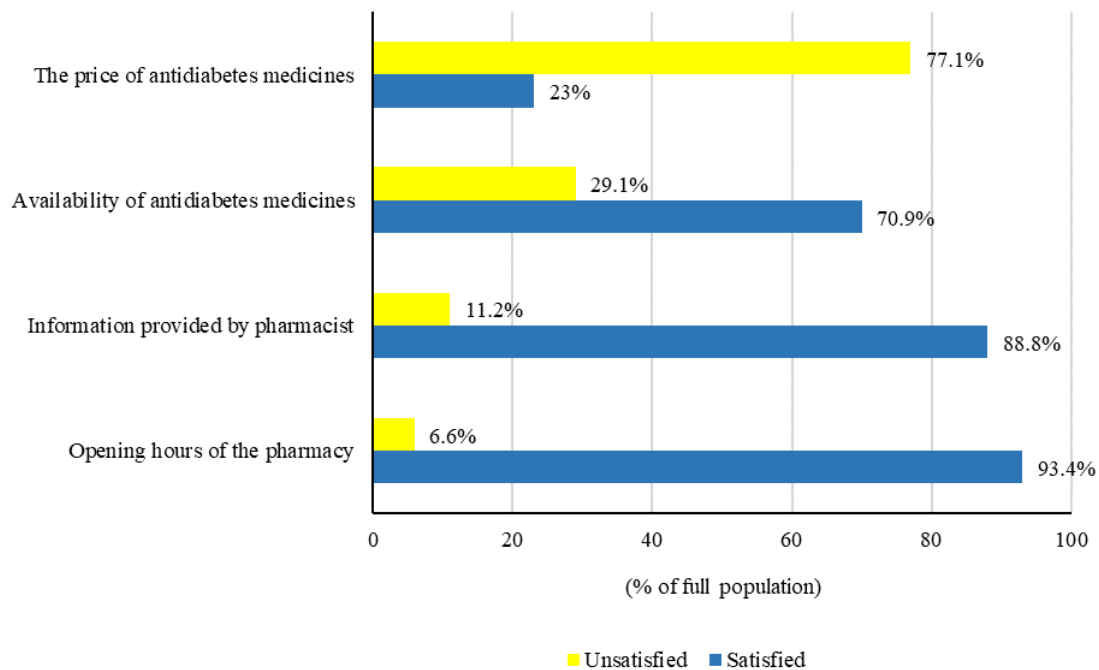

Figure 1: Percentage of satisfied & unsatisfied patients regarding pharmacy service (**Al Assaf S**, 2023).

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 2. 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.
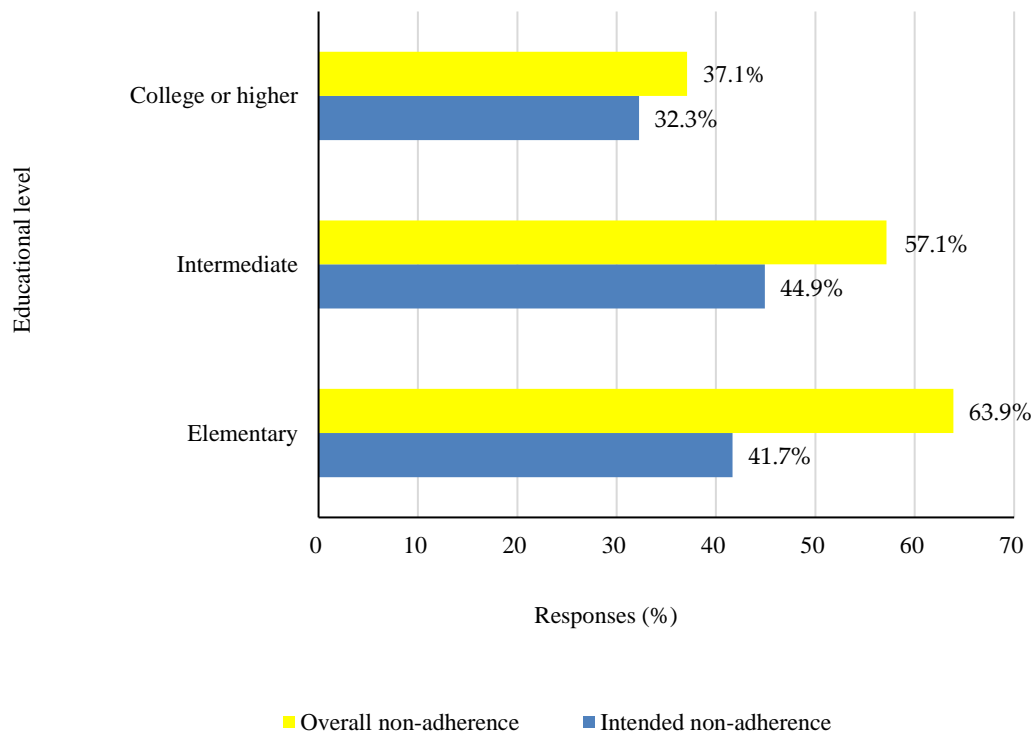

Figure 2: Percentage of non-adherent patients based on educational level (**Al Assaf S**, 2023).

Regarding the seriousness of the disease, 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%).

12

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
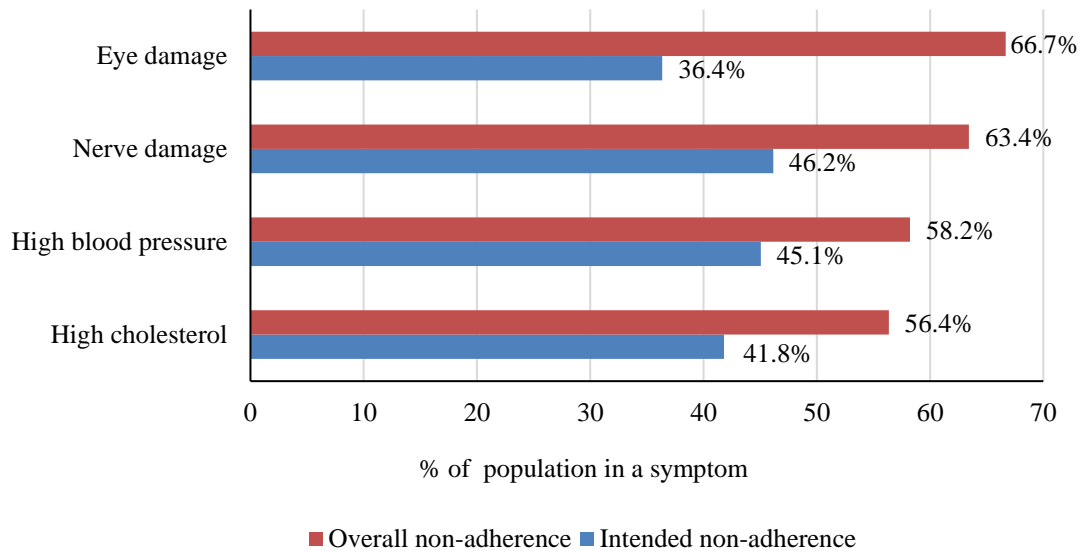

Figure 3: Percentage of non-adherent patients in certain complications of diabetes (**Al Assaf S**, 2023).

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 3).

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.
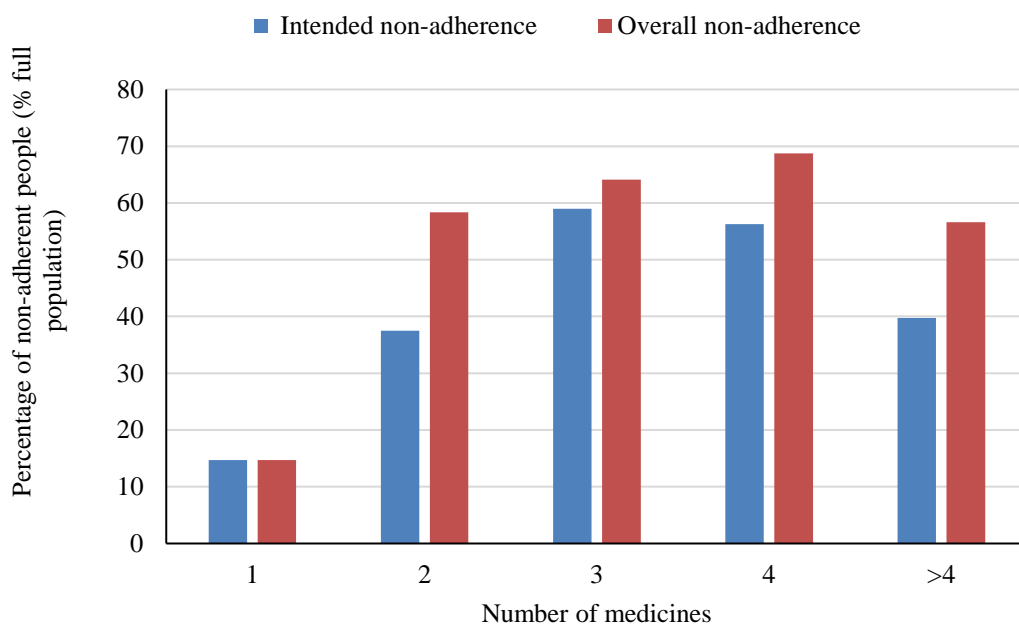
Figure 4: The relationship between the number of medicines that patient take and the patient adherence (**Al Assaf S**, 2023).

Patients' perspectives on the accessibility of pharmacist services were a crucial aspect explored in my study, as illustrated in Figure 4. 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.
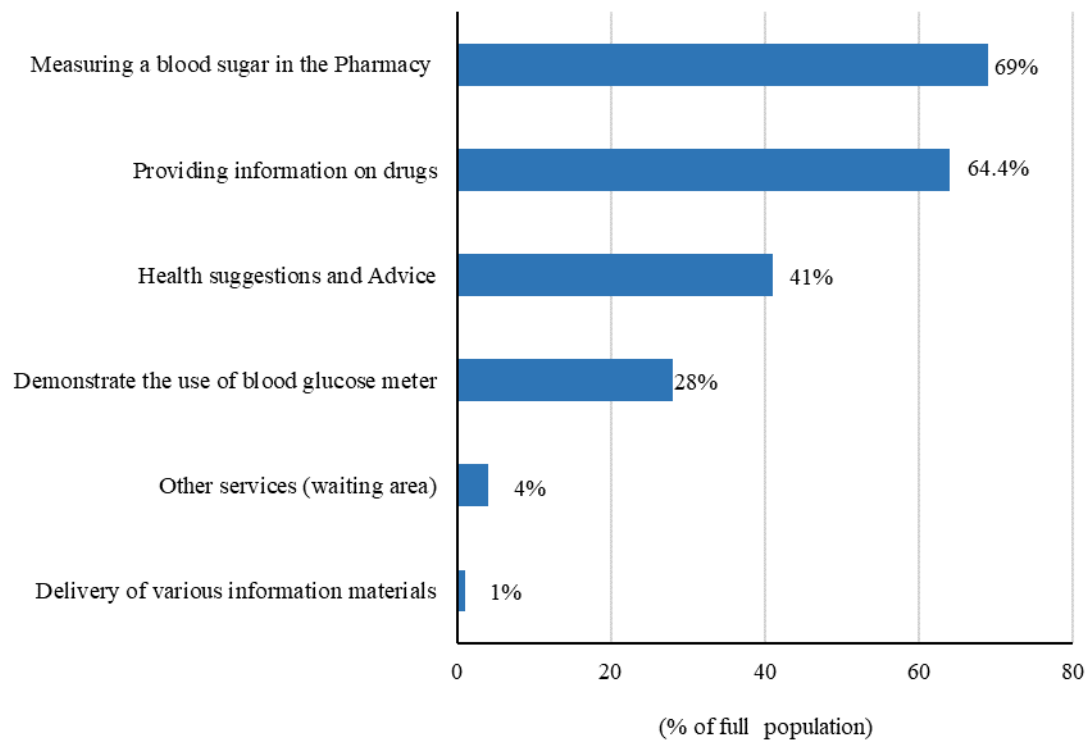
Figure 5: Percentage of patients' satisfaction towards the availability of pharmacy services (**Al Assaf S**, 2023).

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.
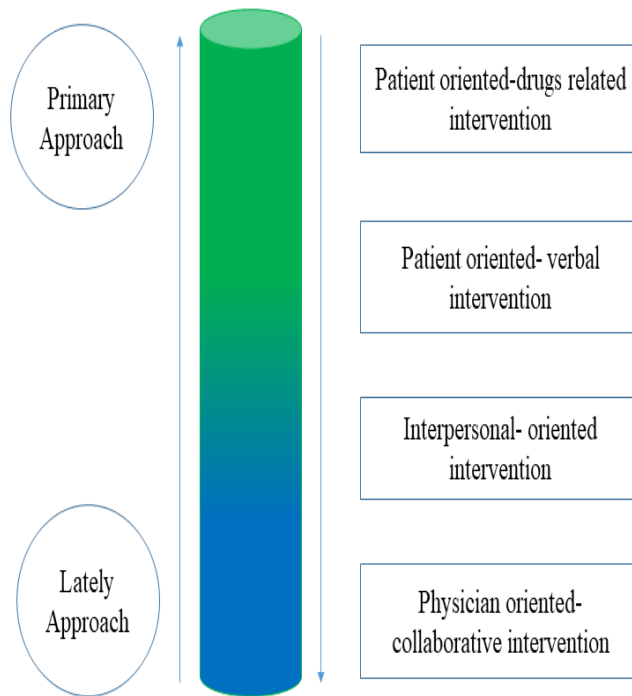
Figure 6: Primary and lately goals of the enhancement therapeutic adherence process (**Al Assaf S**, 2023).

5.   Conclusion

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.

Based on the thesis findings the design of pharmacist services in Syria should prioritize a patient oriented related to drugs interventions.

Simplifying the complex regimes and Medication Use Review (MUR)

By employing MUR, pharmacists can actively contribute to resolving medication availability challenges and ensuring patients receive appropriate and effective treatments. 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.

The forthcoming step in improving this method:

- Research implication (community pharmacy viewpoint)
- Practice implication (Availability of medicines)

6. Bibliography

All publications 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. https://doi.org/10.3390/ijerph19106188

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. https://doi.org/10.3390/healthcare11121720