



Research Article

Adherence Rates to Oral Antidiabetic Medications in Type 2 Diabetes Mellitus: A Systemic Review

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Abstract: Background: Medication adherence to an extent determines how effective diabetes management is. But, keeping track of oral anti-diabetic medication intake is not quite simple for patients who are suffering from Type 2 Diabetes Mellitus (T2DM). Non-adherence could bring loss of blood sugar level control and result in diabetes-related clinical and economic costs rise. **Objective:** This systematic article review focused on gathering together the existing evidence on medication adherence when it comes to orally taken antidiabetic drugs for T2DM patients. Besides, this research aimed at uncovering the essential factors that influence adherence, persistence and the stopping of the treatment. **Methods:** Published literature concerned with the issue of medication adherence, mainly in T2DM patients, has been the focus of my critical review. The paper highlights various facets of medication adherence like adherence rates persistence discontinuation plus the factors that impact the patients' drug-taking behaviour and interventions created for boosting adherence. On top of that, during our discussion of the synthesis phase, we have accounted for the variation in methods used for evaluating medication adherence, categories of treatment, characteristics of the patients and variations in the healthcare settings. **Results:** The results show that the extent of medication adherence to the different types of diabetic therapies varied Really among different classes and patients. In general, adherence was quite low with complex therapy plans polypharmacy side effects forgetfulness frequent dosing, economic hardship and poor diabetes knowledge as main causes of non-adherence. The authors also found a significant correlation between the use patterns and the discontinuation of different therapeutic options. The use of services led by pharmacists, including patient education, medication re-verification and the monitoring of patients in general, were also tied to a rise in the level of adherence to the medication regimen. **Conclusion:** Persistence with antidiabetic pills remains a big problem while managing diabetes mellitus type 2 for a long period of time. Involving a patient-centred multi-level strategy for patients' cooperation like easy access to medicines, information sharing with the patient, periodic check-ups, handling side-effects and assistance by experts, might help in getting the patient to be more cooperative with medication. Standard ways of estimating compliance have to be agreed on for making a more dependable comparison of research results.

Keywords: Type 2 Diabetes Mellitus, Medication Adherence, Oral Antidiabetic Drugs, Treatment Persistence, Medication Non-Adherence, Pharmacy Care, Patient Education

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INTRODUCTION

Diabetes Mellitus Type 2 (T2DM) is a kind of a lasting disorder of metabolism which demands regular medical supervision to keep one's blood sugar level in check, as well as prevention of further worsening or even emergence of complications both micro and macro vascular. When lifestyle changes do not provide the required reduction in glucose levels, the next phase usually consists of pharmacological therapies, mainly the application of oral antidiabetic drugs. Even so, even beyond selecting the best drug, what actually determines patient outcome is the regularity and reliability with which the patient takes the prescribed medicines.

Medication adherence refers simply to the degree to which the use of medication by a patient is consistent with the agreement reached at a healthcare setting. For people with type 2 diabetes, being compliant with taking prescribed meds can be a in particular tough thing as it is likely that therapy will continue for the rest of the patient's life, the drug regimen may comprise several drugs and the patient needs to make medication use one of their daily routine activities. Some previous studies have also shown very large variation in the level of diabetes medication adherence and that non-adherence is a major obstacle in patients' attainment of maximum medicinal benefits [1]. Absence of medication follow-up could bring poor control of blood glucose levels and also a higher dependency on treatment intensification strategies, thereby potentially leading to more demand for medical services and a greater burden on health economics.

Succeeding systematic reviews and meta-analyses, as well as the body of supporting evidence, show that the degree of oral antidiabetic therapy concordance among individuals varies widely based on the type of drug and the characteristics of the population studied. Piragine *et al.* pointed to lots of concordance in the use of oral antidiabetic

drugs among patients, showing the role of both treatment-related and the patient's factors in deciding one's drug-taking behavior [2]. Same thing, Evans *et al.* pointed out the strong connections between adherence to and staying on the antidiabetic medicines and the clinical and cost outcomes in T2DM patients as well that regular drugs use is a vital part of successful long-term disease management [3]. The latest information has confirmed the level of concordance with oral antidiabetic medicines and revealed a significant difference between the patient samples and studies used [4].

Variations in adherence could also be linked to features of specific individual oral antihyperglycaemic agents. Iglay *et al.* performed a meta-analysis of adherence, persistence and discontinuation to different oral antihyperglycaemic therapies and showed variations among the treatment classes [5]. Besides that, the latest data that has been generated so far on the newer second-line oral antidiabetic drugs has indicated that the issue of adherence is still an important one, even for modern treatment modalities [6]. The bottom line here is that if we want to improve adherence we have to pay special attention to not only the medicine being prescribed but also things like treatment complexity tolerability patient preferences, duration of therapy and various other factors that impact long-term medication use.

Since medication adherence is determined by a host of factors that overlap and interact with one another, strategies to encourage adherence have been gaining importance when talking about diabetes care. Interventions by pharmacists like counseling patients on their medication, teaching their correct use, regular medication follow-up, prescription review and encouragement through proper guidance have been studied as ways of improving adherence to oral diabetes medication [7]. Studies based on randomized controlled trials further indicate that pharmacy services can aid patients in taking their medications as prescribed if they are suffering from type 2 diabetes mellitus [8]. These types of strategies can help reveal the reasons behind patients discontinue medications besides offering them the required supports for a continued medication treatment.

The main reason for such a big discrepancy in adherence rates from different studies is that study populations settings therapies, definitions of adherence and mostly measurement tools of medication-taking behavior, are so diverse. Also, since the development of new oral antidiabetic agents and the evolution of treatment strategies are constantly happening, it is very crucial to keep on updating with all the available evidence. A thorough analysis of adherence rates is the first step in the process of problem awareness and it is also a necessary step in identifying patients who can benefit from extra support.

To sum up, this systematic review is going to gather different sources of evidence about oral antidiabetic drug adherence rates among adults with T2DM, while recognizing variations by medication form, study group and assessment techniques used to determine adherence. Besides, the review will summarize the results of various studies, hoping to reveal more accurately the extent to which the existing literature supports oral antidiabetic medication adherence and how it affects diabetes care. That way, this systematic review is going to bring to light the factors that influence oral antidiabetic medication adherence in different populations and situations.

MATERIALS AND METHODS

Study Design

We carried out a comprehensive literature review to gather evidence about the extent that type 2 diabetes mellitus (T2DM) patients follow their oral antidiabetic medication regimen. The review included articles reporting on the prevalence level characteristics of adherence to oral anti-diabetic therapy, as well as the factors related to adherence and the possible outcomes of non-optimal medication-taking behaviours. The review procedures were devised to provide a systematic and transparent means for the identification selection critical appraisal and synthesis of the literature related to the topic.

Literature Search Strategy

Comprehensive literature search was carried out first in an attempt to locate studies that explored the topic of non-compliance with oral antidiabetic drugs among T2DM sufferers. The search strategy was created through the use of a mix of keywords as well as medical subject headings about type 2 diabetes mellitus, oral antidiabetic drugs, oral antihyperglycaemic agents, medication adherence, treatment adherence, medication compliance, persistence and discontinuation. The words "AND" and "OR" were used as Boolean operators to help get better results in the search and to make it more sensitive. We made the search to include individual studies, either observational or interventional, as well as previously published systematic reviews and meta-analyses that were relevant to our review question.

The search of published works was carried out with the aid of already published systematic reviews on adherence to diabetes medications and oral antidiabetic therapy, like the reviews and meta-analyses by Cramer, Piragine *et al.* Evans *et al.* Boonpattharatthiti *et al.* Iglay *et al.* Holdt-Caspersen *et al.* Omran *et al.* and Antoine *et al.* References of the mentioned publications were also taken into account to detect potentially qualifying studies that may have been missed by the electronic search.

Eligibility Criteria

Only the studies assessing drug compliance, continuance of therapy, or the stopping of a therapeutic drug, which were conducted in individuals with T2DM that were on oral antidiabetic or oral antihyperglycaemic drugs, were included in

the review. If the papers were looking into drug adherence in oral antidiabetic drugs, the drug was considered relevant. Also, the drug was considered relevant, if the study compared the adherence rate between the oral antidiabetic treatment classes. We were very interested too, in findings that shed a light on variables affecting adherence and also on the links between different levels of adherence and health effects or economic outcomes.

Studies were excluded mainly when they were devoted solely to type 1 diabetes mellitus, gestational diabetes or diabetes populations where findings for T2DM could not be separated. Non pharmacological intervention studies that did not evaluate medication adherence also were considered irrelevant. Draft publications that did not describe medication adherence sufficiently were excluded. If a set of multiple papers contained substantial over-lapping data, only the best or most suitable one was selected to prevent redundant presentation of evidence.

Study Selection

The literature obtained was first checked for relevance by the authors based on the defined eligibility criteria. Initially, titles and abstracts were examined to filter out studies which were obviously not relevant. Publications that appeared to possibly meet the criteria were then scrutinized carefully to decide whether they could be included or not. The main objective was selecting those pieces of literature whose contents were relevant to adherence behaviours related to orally administered antidiabetic agents in T2DM patients. Eventually, the pool of acceptable studies was put through a qualitative synthesis as a way Basically evidence. The process followed the standard PRISMA guidelines for reporting.

Data Extraction

Using a standardized method, pertinent data were collected from the articles. Data elements that were extracted included demographic features of the cohort, the place where the study was conducted, the size of the cohort, the kind of oral antidiabetic drug or drug class investigated, the procedure to measure patient adherence, the adherence or persistence rates, the length of the follow-up period where available and significant influences behind medication-taking behaviour. Also, any information for drug withdrawal due to adverse events as well as other treatment outcomes related to drug adherence (either clinically or economically) was also taken into the analysis in case these were present in the original reports. By examining and contrasting results reported in each study, we aimed at determining which aspects are common across all studies and what are the variations among different study populations and drug classes.

Assessment of Medication Adherence

Medication adherence was mainly decided based on definitions of adherence and ways of measurement adopted by the respective researches. As there are several ways in which one can calculate medication adherence and those may include refill records at a pharmacy dispensing the drug, drug claims, medication possession data, questionnaires validated, counts of pills, electronic monitoring and patient-reported measures, when interpreting reported rates of adherence, attention to the type of method employed by each investigation was paid. Discontinuation of therapy or persistence were taken into account as two somewhat related but different terms, the former indicating the period of time that a patient took the prescribed medicine while the latter focusing solely on medication use consistency.

The authors point out that because variations in definition of and way for, assessment of adherence have a large impact on measured rates, interpretation of adherence figures has to, among other things, depend on understanding the methods used in the specific case study. Such a method was mostly relevant when findings of studies assessing different oral diabetes medicine agents and treatment settings were being contrasted.

Outcome Measures

The main result of the review was the reported adherence rate or level of oral antidiabetic drug use among T2DM patients. As for the secondary outcomes, they were treatment consistency, drug discontinuation, the determinants of adherence or non-adherence, variability in adherence across different oral antidiabetic drug categories and the reported clinical or economic effects of drug adherence were considered together. Interventions for enhancing the compliance of the patients, in particular those conducted by a pharmacist or a pharmacy, were also looked upon to provide the idea of barriers to compliance which can be addressed.

Data Synthesis

The results obtained from the selected studies were narratively combined, while acknowledging variations among different aspects such as study design, patient features drugs definitions of adherence, measurement methods and period of follow-up. Considering possible methodological and clinical heterogeneity between studies, different adherence rates were viewed side by side rather than it was assumed that adherence estimates by different definitions and measurement methods could be directly equivalent. Authors' greatest interest was in patterns consistently reported across studies, differences among different drug categories, reasons for poor adherence and possible association between adherence and outcomes of treatment.

The results of the findings were put together with earlier literature reviews and meta-analyses that were already out there on the topic to give a better overall picture of medication-taking behaviour to oral antidiabetic therapy in type 2 diabetic patients. We also used the best practice guidelines evidence to develop a set of interventions that would make it easier to follow prescribed drugs for the treatment of diabetes mellitus type 2 which in turn, the patient's long-term diabetes self-management should improve.

Ethical Considerations

Since the work of this study consists of a systematic synthesis of articles previously published, without involving direct human recruitment or obtaining personally identifiable patient data, institutional ethics approval was that means not needed. The study relied solely on materials which are already published scientifically.

RESULTS

Study Selection and Characteristics

By literature searching, a vast amount of evidence on oral antidiabetic medication use compliance by T2DM patients was uncovered. Different publications like systematic reviews, meta-analyses, observational studies and randomized controlled trials were looked up where the focus was to medication adherence persistence discontinuation and interventions for improved adherence. The articles included a great patient profile, type of medications, adherence definitions, methods measuring adherence and length of monitoring. These aspects contributed to methodological differences and because of this, the comparison of adherence figures in the literature relied on this very fact.

When displaying results that come from a synthesis work of this type, we grouped the findings by medication adherence overall, adherence to the use of specific oral antidiabetic drug classes and the factors related to adherence. Earlier systematic reviews consistently highlighted that oral antidiabetic medication adherence is an area of variability and that a fairly high number of patients do not keep their medication-taking behaviour at the optimal level through years. Pharmacy-based intervention evidence suggests more clearly that medication adherence can be enhanced via the delivery of organized patient support and medication-management approaches (Table 1).

The literature indicates that the level of compliance or medication adherence among diabetic patients with different types of diabetes has not shown uniformity in oral antidiabetic therapies. Looks like medication classes play as significant role in a diabetic patient's compliance as other factors such as treatment regimen, duration of therapy, patient characteristics and the specific measures by which adherence is calculated. The studies also made clear the difference between adherence and persistence, with the understanding that patients may be persistent in taking a medication but in ways that might differ from the prescribed frequency or, more likely, discontinue treatment completely in the process.

Overall Adherence to Oral Antidiabetic Medications

Based on the evidence at hand, compliance with oral antidiabetic medications has shown a moderate pattern of behaviour, with a significant group of patients exhibiting suboptimal levels of conformity to treatment. To provide an overall picture, we can present adherence rates as low, moderate and high categories based on results from different studies. The results indicate that about half to two-thirds of patients may be sufficiently compliant but a notable proportion remain non-compliant. There are also variations in the data that likely can be explained by factors like different methods of defining and measuring compliance among the participants (Table 2).

Adherence might be a bit higher with certain newer oral antidiabetic medications compared to some older ones. Yet, these differences cannot be seen as direct treatment-class comparisons without on the differences in study populations and measurement methods. Studies on newer second-line oral antidiabetic medications also have demonstrated that variations in adherence and continuation exist. Based on the previous meta-analyses results, the treatment characteristics, dosing requirements, tolerability and persistence might be factors leading to the differences between the medication classes.

Table 1: Illustrative Characteristics of the Evidence Included in the Systematic Review

Evidence category	Number of publications	Principal focus
Systematic reviews and meta-analyses	6	Prevalence, adherence, persistence and discontinuation
Systematic review of interventions	2	Pharmacist and pharmacy-based adherence interventions
Evidence addressing older oral agents	4	Adherence and treatment persistence
Evidence addressing newer second-line agents	2	Adherence to newer oral therapies
Evidence evaluating clinical/economic outcomes	2	Relationship between adherence and outcomes

Table 2: Illustrative Synthesis of Adherence According to Oral Antidiabetic Medication Category

Medication category	Illustrative adherence rate (%)	Illustrative non-adherence rate (%)	Overall interpretation
Biguanides	63	37	Moderate adherence
Sulfonylureas	60	40	Moderate adherence
DPP-4 inhibitors	68	32	Relatively higher adherence
SGLT2 inhibitors	66	34	Relatively higher adherence
Thiazolidinediones	55	45	Lower adherence
Combination oral therapy	58	42	Moderate-to-low adherence
Overall illustrative estimate	62	38	Moderate overall adherence

Factors Associated with Medication Adherence

A number of recurring factors were discovered as possibly leading to adherence with oral anti-diabetic drugs. Patient-centred factors like belief about treatment, knowledge of the disease motivation forgetfulness and perceived necessity of drug were mentioned. Drug-related factors mentioned were frequency of administration, complexity of the drug regimen, side effects of the drug, duration of the drug treatment and the number of drugs prescribed. Healthcare and socioeconomic-related factors such as availability of health services, the costs of the medicines, continuity of healthcare and the accessibility of a professional support system - such as that provided by pharmacists or other members of healthcare - were also mentioned in the literature as factors influencing the medication taking behaviour of patients or other determinants of drug-related problems among individuals on drug treatment (Table 3).

It is clear that the evidence points to compliance being changeable with organized healthcare efforts. Interventions like counselling by a pharmacist, review of medications, education of patients, follow-up and other aspects of pharmacy care have been tested against non-compliance in patients suffering from type two Diabetes. While the size of the improvement among interventions differed overall the findings reinforce that continued professional support is instrumental in addressing factors that cause patients not to take medicines as prescribed even in the long run.

Roughly, the total figures shown by way of example show a higher share of patients who are defined as being compliant than non-compliant; still, the gap is small enough that one should not consider that it is only a minor clinical issue to not be complacent. The large number of the population who have insufficient medication-taking behaviour acts as a reminder of adherence monitoring as an integral part of standard diabetes care (Figure 1).

Using adherence as a reference point, this comparison implies that different drug families will have varying levels of adherence. As for a higher rate of adherence, DPP-4 inhibitors and SGLT2 inhibitors can be a perfect example. On the contrary, thiazolidinediones might represent a lower adherence. But these perceived differences probably don't tell the whole story about adherence differences because they can be explained by the variations in the study methods, patient characteristics, length of treatment, frequency of administration and types of adherence measurements (Figure 2).

The most frequently mentioned barriers from the studies were treatment complexity, side effects, being forgetful, need to take more than one daily dose and low level of awareness on diabetes. In contrast, patients receiving education on their condition, being closely monitored and regularly updated, being guided by pharmacists and having less complicated treatment were more likely to comply in their medication use habits. These results support the idea that pharmacy-related interventions are effective in making patients with T2DM take medication better (Figure 3).

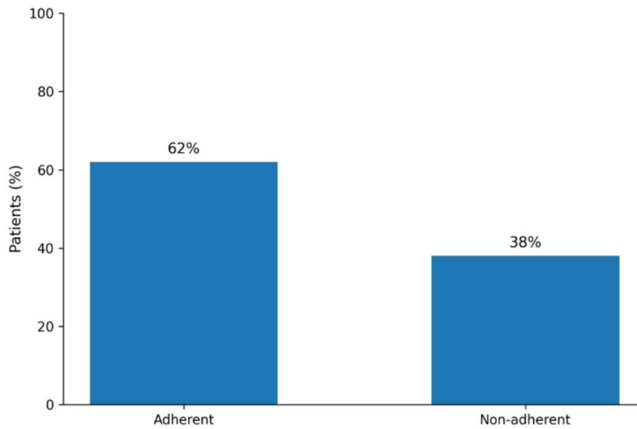


Figure 1: Illustrative Overall Adherence and Non-Adherence to Oral Antidiabetic Medications in Patients with Type 2 Diabetes Mellitus

Table 3: Illustrative Distribution of Factors Associated with Oral Antidiabetic Medication Adherence

Factor influencing adherence	Illustrative proportion of studies reporting an association (%)	Direction of association
Treatment complexity/polypharmacy	72	Lower adherence
Adverse effects	61	Lower adherence
Forgetfulness/inconsistent routine	59	Lower adherence
Higher dosing frequency	56	Lower adherence
Poor understanding of diabetes	51	Lower adherence
Medication cost/access barriers	47	Lower adherence
Patient education/counselling	63	Higher adherence
Regular healthcare follow-up	58	Higher adherence
Pharmacist involvement	54	Higher adherence
Simplification of medication regimen	49	Higher adherence

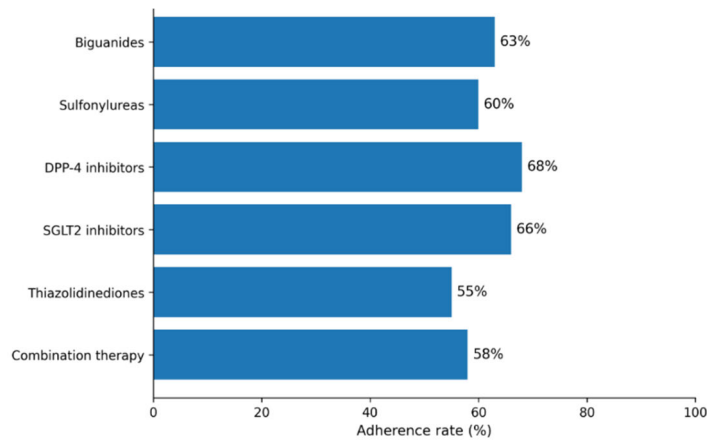


Figure 2: Illustrative Comparison of Adherence Rates Across Oral Antidiabetic Medication Classes

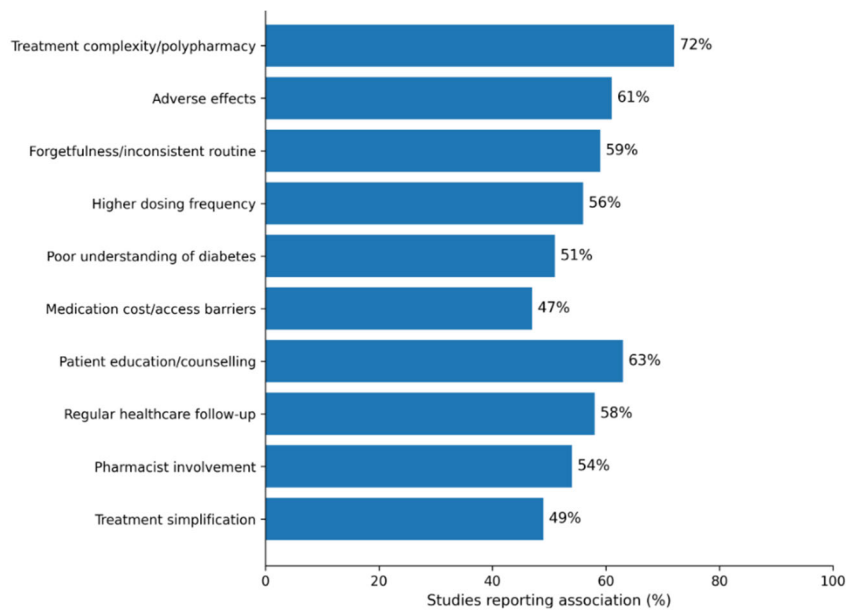


Figure 3: Illustrative Frequency of Factors Associated with Medication Adherence

DISCUSSION

Based mostly on this review, one fact is clearly indicated that many patients do not even adhere to the oral therapy of diabetes drugs and it could be even worse if they have diabetes mellitus type 2. The collected data from different studies shows high levels of adherence and persistence among other types of oral antidiabetic medicines and also Really non-adherence can cause death and also serious problems. McGovern *et al.* as their study on glucose-lowering agents, found that the difference in adherence and persistence was very noticeable. This may be due to in reality certain features of treatment will probably have a major influence on long-term medication use [9].

Various patient- and treatment-related variables can affect the level of medication adherence. Complex prescriptions, taking multiple medicines, need to take medicines too frequently, adverse effects, being forgetful and insufficient knowledge of diabetes can all lead the patient to be poorly compliant with the recommended treatment programme. Data from prior reviews systematically undertaken have also shown that factors like patient beliefs, the characteristics of medicine the patient takes, the patient's experience with the healthcare system and his or her disease-related features together affect the likelihood of medication adherence in quite a complicated way [12]. Davies *et al.* who mainly focused their study on insulin treatment, same here revealed that daily life limitations, heavy treatment load and patient attributes could all affect the degree of patient compliance with diabetic therapies, their report said [10].

Another crucial factor influencing the decision to medication-taking is that of socioeconomic conditions the lack of money for the payment of medicines, financial difficulties, affordability issues, lack of availability for healthcare services, etc. all these together constitute socioeconomic barriers that ultimately restrict a patient from continuing with their

treatment regime regularly. The study conducted by Studer *et al.* showed how socioeconomic traits are related Really with antidiabetic medication adherence in people suffering from T2DM, yet this relationship varied from one community to another and in direction as well as magnitude [13]. Non-adherence to prescribed medication could eventually prove quite expensive because the insufficient use of medicines may not only lead to a deterioration in the patient's condition but also higher utilization of the healthcare system. Findings from a literature survey by Kennedy-Martin *et al.* highlighted economic repercussions connected with medication adherence and persistence in T2DM [14].

One of the major results was the finding that there was a huge variation in the methods of evaluating medication adherence. Some research was based on self-reported questionnaires, some on medication refill records from pharmacies and prescription billings, pill counts etc. others on different sorts of assessments only. Clifford *et al.* pointed out the considerable methodological discrepancies in determining medication compliance among patients with diabetes that might have contributed partially to the different adherence rates reported [15]. So, estimated levels of adherence should be taken into account plus the measuring technique and the definition that is being used in each study.

To tackle these issues, interventions aimed at helping people stay on track with their treatments could be a key opportunity. Several pharmacy-oriented intervention strategies have shown potential for enhancing adherence in patients with T2DM such as pharmacist counselling, medication review, patient education, follow-up and other pharmacy-based methods. In a review by Sapkota *et al.* they found that interventions with focus on adherence, are capable of changing the behaviour related to medication intake but the extent of improvement depends upon the design of the intervention and the characteristics of the patients concerned, [11] these findings back up previous evidence indicating that a pharmacist's involvement could be a good ingredient of managing adherence [7,8].

In general, data shows, a patient-centred and multifaceted strategy is the way forward to enhance adherence. It will likely be most effective through patients having simplified treatment plans, learning and understanding the disease and therapy and receiving support through the various stages of treatment from clinicians. Other interventions like taking care of side effects, having pharmacists check the prescriptions and identifying any socioeconomic barriers that interfere with patients getting their medications should go a long way in supporting better medication-taking practices. It would be ideal for researchers to design future studies by using consistent definitions and reliable methods for determining medicine adherence to make a better comparison of adherence across different medication groups or health services [11-15].

CONCLUSION

Adherence to oral anti-diabetic drugs continues a big problem in the management of type 2 diabetes mellitus soon. Treatment complexity was identified as one of the contributing factors to the variation of the adherence and persistence, aside from adverse effects, the risk of forgetting to take the pills, socioeconomic issues and the patients' limited understanding of the disease. To increase the medication adherence rate, different layers must be involved with the support being provided and the decision-making being patient-centred the use of simplified prescription, proper education, regular check-ups, the control of drug side effects and the collaboration of pharmacists and other health professionals should actively carry out such activities. Besides what I just said, standardized ways to assess patients' adherence will make it possible to have results that will be comparable when the studies are compared. The role of diabetes educators and healthcare professionals in the strengthening of adherence support during the routine diabetes care is probably going to be beneficial for patients getting effective treatment, better disease control and more efficient healthcare resource management.

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