SYSTEMATIC REVIEW

A SYSTEMATIC REVIEW ON SELF-REPORTED QUESTIONNAIRES TO ASSESS MEDICATION ADHERENCE IN DIABETIC PATIENTS

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ABSTRACT

Adherence to pharmacological therapies are keys to effective treatments in diabetic patients. Previous reviews found that most adherence measurement studies on chronic diseases used a self-reported scale. However, there is no consensus on the best scale to measure adherence in diabetic patients. The purpose of this systematic review was to identify the potential self-reported scale that could be considered for measuring medication adherence in diabetic patients and to provide recommendations for researchers or clinicians to determine appropriate adherence self-reported scales in diabetic patients. This review follows general guidelines in the implementation of systematic reviews. After further review, it was found that 33 studies met all inclusion criteria from 4 databases (Wiley, Science Direct, Scopus, and PubMed). The articles were done by the PRISMA, while the keywords were determined by the PICO method. Most research was conducted in Asia (69.7%) and America (18.2%) on patients with type 2 diabetes (81.3%), patients in hospitals (54.5%), suffering for 1-6 months (54.5%), and using a cross-sectional study design (78.8%). HbA1c clinic data (57.6%) were used in most studies as biological markers of adherence. The measurement scales of medication adherence in diabetic patients are MMAS-8 (57,.5%), MMAS-4 (12.1%), BMQ (9%), MCQ (6%), ARMS (3%), ARMS-D (3%), GMAS (3%), LMAS-14 (3%), and MARS-5 (3%). This review provides information on the different self-reported scales most widely used in diabetic medication adherence research. Various aspects need to be considered before choosing the scale of adherence.

Keywords: *Diabetes mellitus, medication adherence, self-report scale, MMAS-8, MMAS-4, BMQ, ARMS*

INTRODUCTION

The prevalence of diabetes increases in various countries, primarily type 2 diabetes in adults[1]. This increase causes an increase in disease burden because of micro and macro-vascular complications disease caused by diabetes[2]. The combination of prevalence and high cost of diabetes treatment leads to the need for effective treatment[1,3]. Lifestyle modification and adherence to pharmacological therapy are critical to effective therapies and treatments in the disease[4]. Increasing the efficacy of adherence interventions will have a much more impact on the population of diabetic patients than increasing specific clinical treatments[4].

Some review literature found variations in adherence to medication rates in diabetic patients[5,6]. In 2007, a review describing barriers to taking medication in diabetic patients found that this population's adherence rates ranged from 31% to 87%[6]. Subsequently, the latest review literature conducted in 2020 shows that adherence to the treatment of diabetes patients in developing countries ranged from 4% to 88%[5]. Diabetes mellitus medication adherence in developed countries is relatively better than in developing countries, but this still needs to focus on health services[5,6]. Non-adherence medication in diabetic patients is associated with an increased risk of complications, mortality, increased use of services, health care costs, decreased quality of life, and even an increase in a country's economic burden[2-5]. Measuring, understanding, and knowing medication adherence will reduce this problem's negative impacts[7]. The assessment of medication adherence plays a pivotal role in the effectiveness of diabetic therapy. Therefore, it is necessary to find and evaluate an accurate scale for medication adherence assessment. However, medication adherence to some chronic diseases, especially diabetes, has not been identified and measured optimally[7].

Several literature reviews have been conducted to summarize studies measuring medication adherence in chronic and diabetic disease[8-10]. The reviews found methodological problems and stated that the self-report method was more common in studies of medication adherence in the population of diabetic patients because of their ease of use in clinical settings. However, none of

them specifically address self-reported methods in diabetics populations. The purpose of this systematic review was to summarize a self-reported scale update that could be considered for measuring medication adherence in the diabetic population and to provide recommendations for researchers or clinicians to determine appropriate adherence self-reported scales in diabetic patients.

METHODS

Study identification

Keywords and electronic database combinations are performed to get more relevant research studies through an extensive search from Wiley Online, Science Direct, Scopus, and PubMed[11]. The last searching process was run in July 2020. A preliminary hand search of the literature was completed to identify appropriate keywords based on PICO (population, intervention, comparison, outcome) search strategies are shown in Figure 1[12]. The inclusion and exclusion criteria are shown in Table 1. Two research members screened all titles/abstracts and reviewed them to determine whether they meet the inclusion criteria or not. Papers that were not based on original research (i.e., the study was an Editorial, Case Report, Brief Report, Pilot Study, Commentary, Qualitative Study, Systematic Review, Literature Review, Guideline) were discarded.

Study quality assessment

There were 856 abstracts obtained from four databases, 45 articles fulfilling the full-text screening requirements. After further review, it was found that 33 studies met all inclusion criteria. The screening was accomplished according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method shown in Figure 2. Two reviewers independently assessed the possibility of bias using 14 items from the National Institute of Health (NIH) quality assessment tool for observational cohort and cross-sectional studies[13].

Data extraction

Data were extracted from selected papers by one reviewer and were then double-checked by another. There were no conflicts between the reviewers and authors of the articles in final selection decisions. Studies that met the following predetermined inclusion criteria were considered for data extraction and analysis. The extracted papers summarize the general characteristics of included studies compiled in Table 2a and 2b. Another extracted data summarizes the correlation between scale validation and biological markers of diabetes compiled in Table 3. Finally, the summarizes of the self-reported scale for medication adherence in diabetic patients is compiled in Table 4.

Table 1: Criteria for inclusion and exclusion for the article reviewed

No	Inclusion Criteria	Exclusion Criteria
1.	Measuring adherence to at least one type of diabetes medication as a primary or secondary outcome.	The article was not based on original research (i.e., the study was a Editorial, Case Report, Brief Report,Pilot Study, Commentary, Qualitative study, Systematic, review, literature Review, Guideline)
2.	Mention the details of the methods used to measure the level of adherence	Adherence to self-monitoring, diet, exercise, guideline, clinical care, self-care, lifestyle
3.	Published in the English language	
4.	Published in the period 2009-2019	
5.	Accessible in full-text	

RESULTS

Details of selected studies

The summary of systematic searching is originated from various scientific journal databases. Most of the studies were conducted in Asian and American countries to type 2 diabetes patients in hospitals. Most research used HbA1c (Glycated hemoglobin) clinic data (57.6%) (n = 19) as a biological marker of adherence compared to blood sugar data and used a cross-sectional research design (78.8%) (n = 26). The majority of studies did not carry out a scale adaptation process through validation tests or adequate psychometric tests. However, ten of them conducted a scale adaptation process based on the World health organization (WHO), The Professional Society for Health Economics and Outcomes Research (ISPOR), or Agency for Healthcare Research and Quality (AHRQ) for Translation and Cultural Adaptation guidelines[14-16]. The summary of selected studies was listed in Table 2a and 2b.

Methodological characteristics

The most of selected studies were cross-sectional research design (78.8%) (n = 26), Prospective study: 1 (3.0%), RCT: 1 (3.0%), Survey: 1 (3.0%), Cohort study: 1 (3.0%), NA: 3 (9.1%) and 20 (60.6%) of these were primary studies measuring medication adherence in diabetes patients. Most of the research recruitment locations were carried out in hospitals or public health clinics with an average sample population of 50-200 samples.

diabetes OR “diabetes mellitus” OR “type 2 diabetes mellitus” OR “type II diabetes mellitus” OR “type 1 diabetes mellitus” OR “type I diabetes mellitus” OR “non-insulin anti diabetic treatment” OR hyperglycemic OR "glycemic control" OR insulin OR "diabetic control" OR antidiabetic OR “Uncontrolled diabetes” OR “oral antidiabetics”

AND

adherence OR persistence OR persistency OR compliance OR concordance OR cooperation OR noncompliance OR "non compliance” OR non-compliance OR “patient compliance” OR nonadherence OR non-adherence OR "non adherence" OR “medication adherence" OR "guideline adherence" OR "patient compliance" OR "treatment refusal" OR "refusal of treatment" OR “diabetes medication adherence scale” OR “evaluation of adherence” OR “medication adherence scale” OR “oral medication adherence” OR “treatment adherence” OR “diabetes medication adherence scale” OR assessment OR evaluation OR assessing OR “Adherence to treatment”

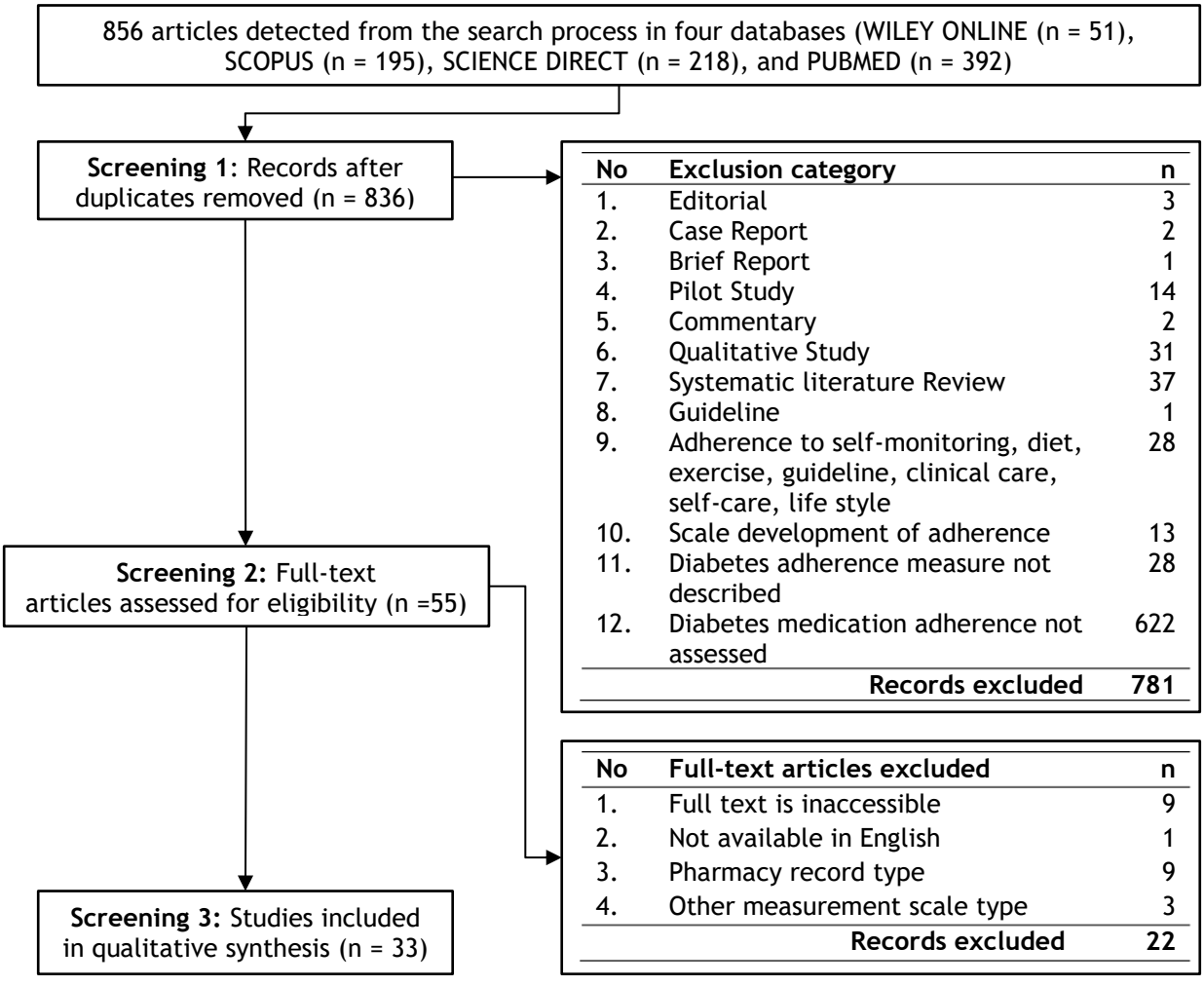
AND

“oral medication adherence” OR “treatment adherence” OR “diabetes medication adherence scale” OR assessment OR evaluation OR assessing OR “Adherence to treatment” AND "Infusion Pumps" OR regimen OR "multiple daily injections" OR "insulin therapy" OR oral OR therapy OR "medication use" OR treatment OR "drug therapy" OR insulin

AND

"monitoring device" OR "electronic device" OR "self monitor" OR "self monitoring" OR "Drug Monitoring" OR "Blood Glucose Self-Monitoring" OR "Self Administration" OR "Reminders" OR "Drug Administration Schedule" OR "medication possession ratios" OR self-report

Figure 1 : Search strategies on the database Wiley Online, ScienceDirect, Scopus, and PubMed[12].



No	Exclusion category	n
1.	Editorial	3
2.	Case Report	2
3.	Brief Report	1
4.	Pilot Study	14
5.	Commentary	2
6.	Qualitative Study	31
7.	Systematic literature Review	37
8.	Guideline	1
9.	Adherence to self-monitoring, diet, exercise, guideline, clinical care, self-care, life style	28
10.	Scale development of adherence	13
11.	Diabetes adherence measure not described	28
12.	Diabetes medication adherence not assessed	622
	Records excluded	**781**

No	Full-text articles excluded	n
1.	Full text is inaccessible	9
2.	Not available in English	1
3.	Pharmacy record type	9
4.	Other measurement scale type	3
	Records excluded	**22**

Figure 2 : PRISMA screening diagram of retrieved studies[17].

Self-reported Adherence Scale Commonly Reported

There are nine self-reported scales on 33 research on diabetic medication adherence (2009–2019). The self-reported scale identified in the research papers and used to measure medication adherence in diabetic patients:

Morisky Medication Adherence Scale (MMAS-4 and MMAS-8)

During 2009 - 2019 the self-reported scale of medication adherence in diabetic patients was dominated by the Morisky Medication Adherence Scale-8 (MMAS-8) (57.6%) (n = 19)[18-35] and Morisky Medication Adherence Scale-4 (MMAS-4) (12.1%) (n = 4) (Table 2a)[36-39]. The majority of these studies were conducted in hospitalized type 2 diabetes patients with a study period of 2 - 12 months. This review found that eight studies have used the MMAS (4-item or 8-item) scale that has been independently validated by researchers or using a scale validated by other researchers. The eight studies of MMAS (4-item or 8-item) scale found a correlation between adherence levels and HbA1c or blood glucose levels[35,37,40-45] (Table 3). There are at least eight versions of MMAS-8 in various countries and languages for diabetes patients. Internal consistency values or Cronbach alpha of MMAS-8 for diabetics ranged from 0.47 to 0.70 (Table 4)[15,46-53]. The Cronbach alpha value is categorized as low - moderate, whereas if MMAS-8 performed in hypertensive patients, the Cronbach alpha value is 0.83.

Brief Medication Questionnaire (BMQ)

The BMQ scale was used by three studies in different countries (USA, Brazil, and Indonesia) with a study time of 6-19 months (9.1%) (n = 3) (Table 2b)[54-56]. All three studies were conducted in hospitals on type 2 diabetes patients. One study in Indonesia[57] carried out a local language translation and adaptation process based on WHO guidelines[14]. In contrast, two other studies in the USA[54] and Brazil[56] did not carry out this process (Table 3). The study of medication adherence used the BMQ scale in Indonesia, carried out the adaptation process and scale validation but did not analyze the predictive validity (Table 3). Scale adaptation and scale validation of BMQ in diabetic patients were carried out by research in Sri Lanka and Indonesia following WHO-recommended translation and cultural adaptation procedures (Table 4)[14,55,58]. The Cronbach alpha values of these studies were relatively the same as the BMQ study in hypertensive patients (Table 4)[57-59].

Medication Compliance Questionnaire (MCQ)

Two studies in Malaysia and Cameroon from this review used the MCQ scale (6.1%) (n= 2) (Table 2b)[60,61]. The study was conducted on type 2 diabetes patients in hospitals and primary health care for 2 – 6 months. The validity and reliability of the MCQ were determined by using 20 diabetes patients before use in Malaysia[60], whereas the Cameroon study did not[61] (Table 3). Although the research in Malaysia performed scale validation, the study did not measure clinical indicators of diabetes patients, so it was unable to determine its predictive validity. The MCQ scale was developed to measure medication adherence in diabetic patients with a Cronbach alpha value in the good category (0.782 > 0.7).

Adherence to Refill Medication Scale (ARMS) and Adherence to Refills and Medication Scale for Diabetes (ARMS-D)

Two studies were using the ARMS (3.2%) (n= 1)[62] and ARMS-D (3.2%) (n= 1)[63] scales conducted in two different countries (Table 2b). One study using the ARMS scale was performed in Indonesia[62], and another study using the ARMS-D scale was performed in Qatar[63]. Both studies were performed on diabetic patients in primary health care for 2 - 4 months. Research in Qatar finds a clear correlation between HbA1c and adherence levels, whereas the Indonesian study did not measure the biological markers of diabetes patients. The ARMS scale is validated in diabetic patients and translated to the Indonesian language with the forwarding and backward translation method from the WHO research tool. The Cronbach alpha value in the validation is categorized as good and acceptable (0.865> 0.7). The ARMS-D scale used in Qatar also performs validation in diabetic patients using a pre-validated researcher-administered questionnaire (Table 4).

General Medication Adherence Scale (GMAS)

The GMAS scale was published in 2018 in Pakistan to measure adherence to some chronic diseases[64]. One study found using the GMAS scale to measure diabetes patients taking the drug (3.0%) (n= 1)[39]. The study was conducted in a state hospital in Saudi Arabia for two months using the GMAS scale, adapted using the new report from the ISPOR Task Force for Translation and Cultural Adaptation. The study found a clear correlation between the biological marker tests for diabetic patients with adherence levels (Table 4). Several studies have been conducted to test the psychometric of GMAS scale in Saudi Arabia and Pakistan (Table 4)[65,66]. Both translation and validation studies stated that the Arabic and English versions of GMAS were valid and reliable research instruments to measure medication adherence in patients with chronic illnesses [65,66].

Lebanese Medication Adherence Scale (LMAS-14)

The LMAS-14 instrument was developed in 2015 in Lebanon to measure adherence in chronic disease populations. It was validated in several chronic disease populations such as hypertension, diabetes, and hypothyroidism (Table 4)[67-70]. One study found using the LMAS-14 scale for measuring medication adherence of patients with diabetes (3.0%) (n = 1) (Table 2b)[71]. The study was conducted in a Lebanese state hospital for four months using a scale made by previous rese-

archers in the same country[68]. The LMAS-14 study found a correlation between adherence and HbA1c levels even though the scale was not validated in diabetic patients (Table 3).

Table 2a: General characteristics of included studies.

No	Author and Research design	Self-reported scale	DM Type	Clinical indicator	Country	Setting	Duration of study (Month)	Limitations related to the adherence scale
1.	(Al-Qazaz et al., 2011), Cross-sectional[18]	MMAS-8	T2DM	HbA1c	Malaysia	Hospital	7 Month	Overestimated and socially desirable answer
2.	(Hernandez-Tejada et al., 2012), Cross-sectional[24]	MMAS-8	T2DM	Blood sugar	USA	Primary-Care	3 Month	Not mention in the study
3.	(Bailey et al., 2012), Cross-sectional[25]	MMAS-8	T1DM & T2DM	N/A	USA and Mexico	Community Clinic	3 Month	Not mention in the study
4.	(Sweileh et al., 2014), Cross-sectional[19]	MMAS-8	T2DM	N/A	Palestina	Primary Health	4 Month	The scale was not translated and not validated to the Arabic version
5.	(Farsaei et al., 2014), Cross-sectional[20]	MMAS-8	T1DM & T2DM	N/A	Iran	Diabetes Clinic	NA	Not mention in the study
6.	(Sankar et al., 2015), Cross-sectional[26]	MMAS-8	T1DM & T2DM	Blood sugar	India	Community	3 Month	Overestimated answer
7.	(Wong et al., 2015), Cross-sectional[21]	MMAS-8	T2DM	HbA1c	Hong Kong	Hospital	NA	Not mention in the study
8.	(Jackson et al., 2015), Cross-sectional[27]	MMAS-8	T2DM	N/A	Nigeria	Hospital	8 Month	Recall bias
9.	(Shams et al., 2016), Cross-sectional[22]	MMAS-8	T2DM	HbA1c	Pakistan	Hospital	10 Month	Not mention in the study
10.	(Alfian et al., 2016), Cross-sectional[28]	MMAS-8	T2DM	N/A	Indonesia	Secondary Health Care	3 Month	Recall bias
11.	(Butt et al., 2016), RCT[34]	MMAS-8	T2DM	HbA1c	Malaysia	Hospital	6 Month	Not mention in the study
12.	(Samu et al., 2017), A prospective study[29]	MMAS-8	T2DM	HbA1c	India	Hospital	12 Month	Not mention in the study
13.	(Waari et al., 2018), Cross-sectional[35]	MMAS-8	T2DM	HbA1c	Kenya	Hospitals	3 Month	Not mention in the study
14.	(Khotkar et al., 2017), Cross-sectional[33]	MMAS-8	T2DM	Blood glucose	India	Hospital	12 Month	Recall bias
15.	(Balasubramaniam et al., 2019), Cross-sectional[31]	MMAS-8	T2DM	HbA1c	Malaysia	Hospital	5 Month	Recall bias
16.	(Olorunfemi and Ojewole, 2019), Cross-sectional[30]	MMAS-8	T1DM & T2DM	N/A	Nigeria	Hospitals	NA	Not mention in the study

Table 2b: General characteristics of included studies.

No	Author and Research design	Self-reported scale	DM Type	Clinical indicator	Country	Setting	Duration of study (Month)	Limitations related to the adherence scale
17.	(Acharya et al., 2019), Cross-sectional[23]	MMAS-8	T2DM	HbA1c	India	Hospital	2 Month	Recall bias
18.	(Jannoo and Mamode Khan, 2019), Cross-sectional[32]	MMAS-8	T2DM	HbA1c	Malaysia	Hospitals	NA	Not mention in the study
19.	(Nazir et al., 2016), Cross-sectional[72]	MMAS-8	T2DM	HbA1c	Pakistan	Public clinic	4 Month	Not mention in the study
20.	(Aikens and Piette, 2013), Cross-sectional[37]	MMAS-4	T2DM	HbA1c	USA	Primary Care	NA	Overestimated answer
21.	(Grandy et al., 2013), Survey study[38]	MMAS-4	T2DM	N/A	USA	General Population	24 Month	Not mention in the study
22.	(Mann et al., 2009), Cohort study[73]	MMAS-4	T2DM	N/A	USA	Primary-Care	7 Month	Overestimated answer
23.	(Alqarni et al., 2019), Cross-sectional[74]	MMAS-4	T1DM & T2DM	HbA1c	Saudi Arabia	Primary Health	4 Month	Overestimated answer
24.	(Kreyenbuhl et al., 2011), N/A[54]	BMQ	T2DM	HbA1c	USA	Hospital	19 Month	Overestimated answer
25.	(Istilli et al., 2015), N/A[56]	BMQ	T2DM	HbA1c	Brazil	Hospital	6 Month	Overestimated answer
26.	(Perwitasari and Urbayatun, 2016), Cross-sectional[55]	BMQ	T2DM	N/A	Indonesia	Hospital	6 Month	Not mention in the study
27.	(Sufiza Ahmad et al., 2013), Cross-sectional[60]	MCQ	T2DM	N/A	Malaysia	Primary health care	6 Month	Not mention in the study
28.	(Aminde et al., 2019), Cross-sectional[61]	MCQ	T2DM	N/A	Kamerun	Hospital	2 Month	Recall bias and overestimate answer
29.	(Andanalusia et al., 2019), Cross-sectional[62]	ARMS	T2DM	N/A	Indonesia	Primary health care	2 Month	Not mention in the study
30.	(Jaam et al., 2018), Cross-sectional[63]	ARMS-D	T1DM & T2DM	HbA1c	Qatar	Primary Healthcare	4 Month	Social desirability bias and recall bias
31.	(AlQarni et al., 2019), Cross-sectional[39]	GMAS	T2DM	HbA1c	Saudi Arabia	Hospital	2 Month	Not mention in the study
32.	(Mroueh et al., 2018), Cross-sectional[71]	LMAS-14	T2DM	HbA1c	Lebanon	Hospitals	4 Month	Social desirability bias and recall bias
33.	(Lee et al., 2017), Cross-sectional[75]	MARS-5	T2DM	HbA1c	Singapura	Primary Care	10 Month	Not mention in the study

N/A: not available; T2DM: Type 2 diabetes; T1DM: Type 1 diabetes; HbA1c: Glycated hemoglobin; MMAS-4: Morisky Medication Adherence Scale 4; MMAS-8: Morisky Medication Adherence Scale 8; BMQ: Brief Medication Questionnaire; MCQ: Medication Compliance Questionnaire; ARMS: Adherence to Refill Medication Scale; ARMS-D: Adherence to Refills and Medication Scale for Diabetes; GMAS: General Medication Adherence Scale; LMAS-14: Lebanese Medication Adherence Scale 14; MARS-5: Medication Adherence Report Scale.

Table 3. Information of validation of adherence scale and predictive validation

		Predictive validation (scale measurement and biological markers)		
		Correlated	**Not correlated**	**N/A**
Adherence scale validation	**Validated**	1. (Al-Qazaz et al., 2011) MMAS-8[41] 2. (Sankar et al., 2015) MMAS-8[45] 3. (Butt et al., 2016) MMAS-8[43] 4. (Balasubramaniam et al., 2019) MMAS-8[42] 5. (Jannoo and Mamode Khan, 2019) MMAS-8[44] 6. (Waari et al., 2018) MMAS-8[35] 7. (Alqarni et al., 2018) MMAS-4[40] 8. (Aikens and Piette, 2013) MMAS-4[37] 9. (AlQarni et al., 2019) GMAS[39] 10. (Jaam et al., 2018) ARMS-D[63]	-	1. (Andanalusia et al., 2019) ARMS[62] 2. (Ahmad et al., 2013) MCQ[60] 3. (Perwitasari and Urbayatun, 2016) BMQ[57]
	Not validated	1. (Samu et al., 2017) MMAS-8[29] 2. (Lee et al., 2017) MARS-5[75] 3. (Mroueh et al., 2018) LMAS-14[71]	1. (Wong et al., 2015) MMAS-8[21] 2. (Khotkar et al., 2017) MMAS-8[33] 3. (Acharya et al., 2017) MMAS-8[23] 4. (Nazir et al., 2016) MMAS-8[72] 5. (Istilli et al., 2015) BMQ[56] 6. (Kreyenbuhl et al., 2011) BMQ[54]	1. (Hernandez-Tejada et al., 2012) MMAS-8[24] 2. (Bailey et al., 2012) MMAS-8[25] 3. (Sweileh et al., 2014) MMAS-8[19] 4. (Farsaei et al., 2014) MMAS-8[20] 5. (Jackson et al., 2015) MMAS-8[27] 6. (Shams et al., 2016) MMAS-8[22] 7. (Alfian et al., 2016) MMAS-8[28] 8. (Olorunfemi and Ojewole, 2019) MMAS-8[30] 9. (Grandy et al., 2013) MMAS-8[38] 10. (Mann et al., 2009) MMAS-8[73] 11. (Aminde et al., 2019) MCQ[61]
	N/A	-	-	-

N/A: not available; MMAS-4: Morisky Medication Adherence Scale 4; MMAS-8: Morisky Medication Adherence Scale 8; BMQ: Brief Medication Questionnaire; MCQ: Medication Compliance Questionnaire; ARMS: Adherence to Refill Medication Scale; ARMS-D: Adherence to Refills and Medication Scale for Diabetes; GMAS: General Medication Adherence Scale; LMAS-14: Lebanese Medication Adherence Scale 14; MARS-5: Medication Adherence Report Scale.

Medication Adherence Report Scale (MARS-5)

The MARS-5 scale is a modification of the MARS-10 scale, which measures patients' medication intake with psychotic disorders[76]. The results of the modification eliminated five questions that were irrelevant in diabetic patients. MARS-5 was used by one study (3.0%) (n = 1) in Singapore as a scale to measure adherence to diabetic patients receiving large amounts of medication (Table 2b)[77]. MARS-5 has been validated in various clinical settings and used in several clinical trials to determine adherence. However, the study using MARS-5 in a Singapore diabetic population without any prior scale validation (Table 4)[77-79].

Table 4: Self-reported scale for medication adherence in diabetic patients.

No	Self-reported Adherence Scale	Original language	Population in initial validation study	The Cronbach's α value in initial validation study	Validation processes in the diabetic population	The Cronbach's α value in diabetic patients (Country)
1	MMAS-8[80]	English	Hypertension	0.83	Validated in diabetic population and translated to the Malaysian, Thai, Spanish, English (American and Singaporean), Arabic, Korean, French language with forward and backward translation method from the Report of the ISPOR Task Force for Translation and Cultural Adaptation[15,46-53].	0.675 (Malaysia) 0.61 (Thailand) 0.4 (Spain) 0.68 (America) 0.65 (Singapore) 0.70 (Arab) 0.66 (Korea) 0.47 (French)
2	MMAS-4[81]	English	Hypertension	0.61	Validated in diabetic population and translated to the Arabic language with AHRQ translation method[16,82].	0.76 (Arab)
3	BMQ[59]	English	Hypertension	0.66	Validated in diabetic patients and translated to the Indonesian language and Sinhalese language (Sri Lanka) with forwarding and backward translation method from the WHO research tool[14,57,58].	0.775 (Indonesia) 0.65 (Sri Lanka)
4	MCQ[83]	Malay	Diabetes	0.782	An internal consistency test was done by using 20 diabetic patients[83].	0.782 (Malaysia)
5	ARMS[84]	English	Hypertension	0.814	Validated in diabetic patients and translated to the Indonesian language with forwarding and backward translation method from the WHO research tool[14,85].	0.865 (Indonesia)
6	ARMS-D[86]	English	Diabetes	0.86	Validated in diabetic patients using a pre-validated researcher-administered questionnaire[86].	0.86 (English)
7	GMAS[64]	Urdu	Chronic illness	0.84	Validated in diabetic population and translated to the Arabic and English language with forwarding and backward translation method from the Report of the ISPOR Task Force for Translation and Cultural Adaptation[15,65,66].	0.865 (Arabic) 0.82 (English)
8	LMAS-14[68]	Arabic	Hypertension	0.695	Not validated in diabetic patients	N/A
9	MARS-5[76]	English	Schizophrenia	0.75	Not validated in diabetic patients	N/A

N/A: not available; MMAS-4: Morisky Medication Adherence Scale 4; MMAS-8: Morisky Medication Adherence Scale 8; BMQ: Brief Medication Questionnaire; MCQ: Medication Compliance Questionnaire; ARMS: Adherence to Refill Medication Scale; ARMS-D: Adherence to Refills and Medication Scale for Diabetes; GMAS: General Medication Adherence Scale; LMAS-14: Lebanese Medication Adherence Scale 14; MARS-5: Medication Adherence Report Scale; ISPOR: The Professional Society for Health Economics and Outcomes Research; AHRQ: Agency for Healthcare Research and Quality; WHO: World Health Organization

This systematic review summarizes self-reported medication adherence scales in diabetic patients in the original study published from 2009 to 2019. The review has identified 33 studies from different countries and found new scales developed to measure medication adherence rates in the diabetic patient population (Table 4)[64]. The scale used in 33 research is the original type of medication adherence scales (MMAS-8, MMAS-4, BMQ, MCQ, ARMS, GMAS, and LMAS-14) or modified medication adherence scales (ARMS-D and MARS-5). Most research on medication adherence used the MMAS-8 self-reported scale as translation and adaptation to the local or used in its original form. It is the most studied and validated scale for several chronic diseases, including diabetes. MMAS-8 has been performed on psychometric tests in eight different diabetic populations and has acceptable internal consistency, excellent test-retest reliability. However, it showed moderate sensitivity and specificity when used in diabetic patients[15,46-53] (Table 4).

DISCUSSION

This review provides information on the various self-reported scales that are the most broadly used in diabetic medication adherence research. Most studies used a validated scale through previous psychometric tests, modified the previous scale, or used the scale validated in other countries with another disease. They used the scale in a limited context because there were no psychometric studies in the appropriate population and conditions. Psychometric tests on an established adherence scale are still needed, even for a predetermined compliance scale, because validity is not on the adherence scale itself. However, it characterizes conclusions derived from data generated using the adherence scale in a particular context[87]. Studies using validated scales generally find clear correlations between the results of the adherence measures and HbA1c level (Table 3)[18,31,32,34,35,37,39,45,63,74]. However, several studies stated a correlation even though they did not use a validated scale (Table 3)[29,71,77]. Psychometric testing is necessary because the question's characteristics, the response to the scale, and the measurement time could impact the results[15,88]. Most research in this review uses the validity tests that have been carried out by other researchers in settings and populations that differ from the population to be studied (Table 4). These differences may reduce adherence measures in diabetic patients, as each scale was constructed and validated in a specific patient population[15]. It should be understood that different scales are needed for diverse populations, contexts, and conditions. These findings should be of particular concern to researchers and clinicians who will perform studies on medication adherence.

Measuring medication adherence in diabetic patients using a self-reported scale is a substantial challenge. First, the absence of gold standard measurement; secondly, the primary therapeutic outcome measures, namely blood glucose status or HbA1c, did not always correlate with the treatment adherence level as found in this review[21,23,33,54,56,72]. This review found several studies in Asia and America concluded that MMAS-8 scale scores[21,23,33,72] and BMQ[54,56] did not correlate with the clinical outcome. Most studies did not measure HbA1c levels in their research populations as a comparison for the objective scale. The comparison helps assess scale accuracy based on correlation analysis between scale measurement and HbA1c data. That correlation is a predictive validity that an adherence scale has adequate specificity and sensitivity to measure medication adherence in patients with diabetes[89]. A clear correlation between self-reported adherence levels and glycemic regulation implied that the scale could separate patients with (or without) regulated blood glucose using HbA1c or blood glucose levels.

A limitation of the self-reported scale mentioned in the study was the possibility of patients overestimating their adherence ratings because of the perceived benefits of high adherence levels, questions that the respondent did not understand, and patients' failure to remember or not they took medication[18,19,21,27,28,33,38,39,54,56,60,61,71,75] (Table 2a and Table 2b). For these reasons, the results of self-report scales may experience a limitation with an unrealistic perfect adherence recorded by most respondents. One way to overcome this is by implementing an adherence scale selection criteria based on the population's characteristics and research purposes. These criteria may include a method, study design, patient population, and research resource[88,90]. Medication adherence is a complex problem; therefore, some studies suggest combining two or more measurement categories according to measurement objectives[88,90,91]. For clinical purposes, it is advisable to use a combination of several types of indirect measurements because they are less expensive. For research purposes, it is advisable to use a combination of direct and indirect measurements. Using these criteria and combinations is possible to overcome the limitations of the self-reported scale. It may be necessary to develop self-reported scales for specific populations for specific diseases for more accurate measurements.

The following recommendations could be applied to medication adherence studies: (1) Using a self-report medication adherence scale that was validated in a population of disease, sociodemographic conditions, and language that was relatively the same as the population to be studied or performed scale validation on the population studied which is the best practice recommended by psychometrics[87]; (2) Measuring

the biological marker of disease using an appropriate instrument for assessing scale accuracy as predictive validity[9]; (3) Combining two or more types of medication adherence measurement strategies[88,90,91]. Our review emphasizes the importance of understanding the strengths and weaknesses inherent in using self-report treatment adherence measures. This review also emphasizes using a self-report adherence scale validated based on standard validation test guidelines. Finally, we would like to point out that our study may have limitations of the systematic review process. We did not include unpublished studies, and our findings may be distorted by publication bias. Several adherence studies did not analyze the correlation between adherence measures and HbA1c because medication adherence was not the study's primary outcome. Therefore, it is desirable to undertake a further specific review of medication adherence as the primary outcome.

CONCLUSION

In conclusion, while this is not a comprehensive review of all the methods used in adherence studies, it does provide information on the various types of self-reported scales that can be applied to diabetic patients. The MMAS-8 self-report scale is the most widely used in diabetes patients; however, evidence of adequate psychometric testing is needed to use it in diabetes patients. Choosing the appropriate scale requires several considerations, such as using specific self-reported scales and performing a scale validation, using the biological marker of diabetes (blood glucose or HbA1c), and perform a combination of other direct or indirect methods. Creating and developing a new scale according to the predictor factors in a particular disease population could be another alternative.

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COMPETING INTEREST

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