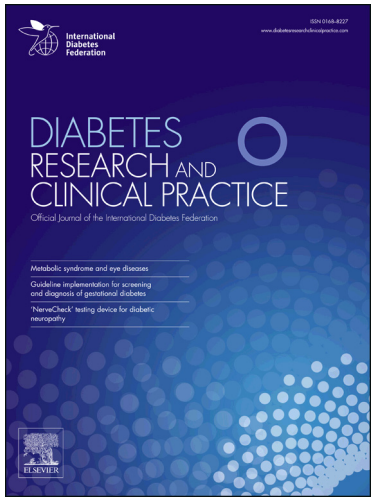


Review

Factors associated with medication adherence among patients with diabetes in the Middle East and North Africa region: A systematic mixed studies review

Myriam Jaam, Mohamed Izham Mohamed Ibrahim, Nadir Kheir, Ahmed Awaisu

PII: S0168-8227(16)31858-7
DOI: http://dx.doi.org/10.1016/j.diabres.2017.04.015
Reference: DIAB 6938

To appear in: *Diabetes Research and Clinical Practice*

Received Date: 29 December 2016
Revised Date: 7 April 2017
Accepted Date: 19 April 2017

Please cite this article as: M. Jaam, M. Izham Mohamed Ibrahim, N. Kheir, A. Awaisu, Factors associated with medication adherence among patients with diabetes in the Middle East and North Africa region: A systematic mixed studies review, *Diabetes Research and Clinical Practice* (2017), doi: http://dx.doi.org/10.1016/j.diabres.2017.04.015

Factors associated with medication adherence among patients with diabetes in the Middle East and North Africa region: A systematic mixed studies review

Myriam Jaam[1] MSc (Pharm), **Mohamed Izham Mohamed Ibrahim**[1] PhD, **Nadir Kheir**[1] PhD, **Ahmed Awaisu**[1]* PhD

[1]College of Pharmacy, Qatar University, Doha, Qatar

***Corresponding author:**

Dr. Ahmed Awaisu

Associate Professor of Clinical Pharmacy and Practice

College of Pharmacy, Qatar University, Doha, Qatar.

E-mail address: aawaisu@qu.edu.qa

Tel: (+974) 44035596 (GMT +3hrs)

Word count (Excluding abstract and references): 5,463

Number of Tables: 3

Number of Figures: 2

Summary

Multiple systematic reviews were conducted investigating factors associated with medication adherence worldwide. However, investigations from the Middle East and North Africa (MENA) region were largely underrepresented in those reviews. Therefore, the objective of this systematic review is to identify the factors influencing medication adherence among patients with diabetes in the MENA region. A systematic literature search was conducted through Cochrane Library, EBSCO, EMBASE, Google Scholar, ISI Web of Science, PubMed, ScienceDirect, SCOPUS, and ProQuest. Studies were included if they determined factors associated with medication adherence among patients with diabetes within the MENA region. Quality was assessed using Crow Critical Appraisal Tool. Thirty primary studies from 10 MENA countries were included. The factors associated with medication adherence were categorized into demographics-related; disease- and medication-related; perception, attitude and psychological feelings-related; and societal-related factors. Positively associated factors included knowledge about the disease and medications, regular follow-up visits, and patients' positive beliefs about effectiveness and motivations about medications, while negatively associated factors included forgetfulness, side effects, and polypharmacy. Factors associated with medication adherence among patients with diabetes in the MENA region are highly diverse. The identified factors can serve as potential targets for culturally-relevant interventions to improve medication adherence and overall health outcomes.

Keywords: barriers; diabetes; facilitators; medication adherence; MENA; systematic review

1. Background

Diabetes mellitus is a chronic disease that affects a large proportion of people worldwide. The International Diabetes Federation (IDF) reported that about 382 million people had diabetes in 2013 [1, 2]. The number of people diagnosed with diabetes is projected to increase by more than 50% globally within the next 20 years [3]. This consequently adds to the total health expenditure particularly in the Middle East and North Africa (MENA) region where people of working age group (40 to 60 years old) are expected to have the highest incidence of diabetes compared to the rest of the world [3]. This unfortunate projection can be attributed to the continuous increase in the prevalence of obesity, sedentary lifestyle, and the poor dietary habits with minimal efforts to contain it within this region [4].

The management of diabetes comprises a complex network of activities and components including education, nutritional therapy, physical activity, and drug therapy [5]. Due to the multidimensionality and complexity of the management and the burden associated with the disease, self-care and adherence to the different aspects of the treatment regimen is challenging. Medication non-adherence rate in diabetes has been reported to range from 36% to 93% [6, 7]. Moreover, it is well documented that non-adherence to medications leads to poor metabolic control which ultimately results in complications including, but not limited to, hospitalizations; morbidities such as nephropathy, retinopathy, neuropathy, myocardial infarction, and stroke; and mortality [1, 2, 8-11]. This necessitates more thorough investigations of the factors influencing medication adherence (barriers and facilitators) in this population in an effort to determine potential targets for promoting adherence to medications.

Several systematic reviews on medication adherence in diabetes have been conducted worldwide [12-15]. An unpublished systematic review of systematic reviews aimed at identifying barriers to medication adherence reported globally and evaluating the quality of the existing evidence on the topic was recently conducted. Despite the inclusion of a large number of primary investigations from across the different regions of the world, these systematic reviews did not adequately feature studies from the MENA region, and thus, the region was largely underrepresented in these reviews [12-28]. This revelation prompted us to undertake a scoping literature review to navigate the available evidence on factors influencing medication adherence within the MENA region. Barriers to medication adherence identified in one population or region may not necessarily be the same as those in other populations or regions due to environmental, socio-economic, and cultural differences across countries. Therefore, the primary aim of this systematic review is to determine the rates of and factors (barriers and facilitators) associated with medication adherence in patients with diabetes in the MENA region. These factors could serve as targets for promoting adherence to medications when designing intervention strategies that are tailored to specific regions or populations.

2. Methods

This systematic review has been registered in PROSPERO International Prospective Register of Systematic Reviews (registration number: CRD42016042474)[29].

2.1. Data sources and search strategy

In order to answer the research question, a comprehensive systematic literature search was initially conducted using the following databases and search engines: The Cochrane Library, EBSCO, EMBASE, Google Scholar, ISI Web of Science, PubMed, ScienceDirect, SCOPUS, and ProQuest. Bibliographies of the articles retrieved were also manually searched for relevant studies. The search included original studies from the conception of the respective databases to 31 May 2016. No limits or restrictions in terms of language or date were applied in the respective databases in order to obtain all relevant articles.

Varying search terms were used to retrieve relevant articles including terms relating to adherence such as “adherence, compliance”; the disease such as “diabetes, diabetic”; influencing factors such as “factors, barriers”; and the relevant countries within the MENA region. Boolean connectors (AND/OR) were applied in such a way that articles related to factors associated with adherence or non-adherence among patients with diabetes were retrieved. The terms were also modified based on individual databases (e.g. the use of MeSH and Emtree terms in MEDLINE and EMBASE, respectively). Table 1 highlights the search strategy applied in one of the databases (i.e. PubMed).

Table 1: Search strategy in PubMed

Search Strategy	Number of hits
((Diabetes [Title/Abstract]) OR Diabetes mellitus[Title/Abstract]) OR Diabetic [Title/Abstract] AND ((((((((Compliance[Title/Abstract]) OR Adherence [Title/Abstract]) OR Comply*[Title/Abstract]) OR Adher*[Title/Abstract]) OR Noncompliance[Title/Abstract]) OR Noncomplying[Title/Abstract]) OR Nonadher* [Title/Abstract]) OR non-compliance) OR non-adher*[Title/Abstract] AND ((((((((((((((((((((Algeria) OR Bahrain) OR Egypt) OR Iran) OR Iraq) OR Jordan) OR	138

Kuwait) OR Lebanon) OR Yemen) OR United Arab Emirates) OR UAE) OR Libya) OR Morocco) OR Oman) OR Palestine) OR Qatar) OR Saudi Arabia) OR KSA) OR Syria) OR MENA region) OR Arab) AND (((((Barrier*[Title/Abstract]) OR Facilitator* [Title/Abstract]) OR determinant[Title/Abstract]) OR factor*[Title/Abstract]) OR Predictor*[Title/Abstract]) OR Challenge[Title/Abstract])	

2.2. Study selection

Original qualitative, quantitative and mixed-method studies targeting the factors influencing adherence to medications in patients with diabetes in the MENA region were included in the review. A Study was eligible for inclusion in the review if it: (1) included adults (18 years and above) with either type 1 or type 2 diabetes who received antidiabetic medications; (2) investigated factors associated with medication adherence and; (3) was conducted in one or more countries within the MENA region (Algeria, Bahrain, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Yemen, United Arab Emirates, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Syria, and Tunisia).

Studies investigating factors associated with or barriers to disease control without focusing on medication adherence as well as studies that reported adherence/non-adherence levels alone without investigating associated factors were excluded from the review. Moreover, studies targeting substance abusers, patients with mental illnesses, tuberculosis, HIV/AIDS, cancer, and gestational diabetes were also excluded because each of these population groups has its own circumstances that affect medication adherence. Titles and abstracts of the searched results were first screened for relevance to the study objective (MJ and AA). Furthermore, eligibility for

inclusion/exclusion was assessed using the full-text articles of studies considered for inclusion. Discrepancies in judgment were resolved through consensus.

2.3. Outcome measures

The primary outcome of this systematic review was factors influencing medication adherence identified through quantitative or qualitative methods or both. Factors reported by the studies were extracted regardless of their significance, in order to gain an insight into the issue within the MENA region. The secondary outcome measure was the prevalence of medication adherence/non-adherence presented as a percentage of the overall participants.

2.4. Quality assessment

Methodological quality of the included studies was assessed using the Crowe Critical Appraisal Tool (CCAT) [30]. This tool was designed to rigorously assess the quality of a wide range of research designs including cross-sectional quantitative, qualitative and mixed method studies. The tool was previously proven to be reliable and valid. The quality of a study was classified as follows: ✶ for a score of 0 – 39%, ✶✶ for a score of 40 – 59%, ✶✶✶ for a score of 60 – 79%, and ✶✶✶✶ for a score of 80 – 100%. To ensure consistency and reliability of scoring, the tool was used along with the tool guide and the assessment was independently conducted for each study by two authors. Discrepancies were resolved through discussions and consensus.

2.5. Data synthesis and analysis

The review is reported using the PRISMA guidelines. A data extraction tool was created and piloted on three randomly selected articles. The tool included the following information: title, authors, year of publication, country, setting, definition of adherence, study objective(s), study design, sample recruitment method, inclusion and exclusion criteria, number of participants and their characteristics, rate of adherence/non-adherence and method of measurement, factors influencing medication adherence, conclusion, limitations and CCAT score. The process was conducted by two independent reviewers and consensus was sought through discussion were disagreements exist. Qualitative and quantitative data were combined in an effort to identify all possible factors affecting medication adherence in patients with diabetes. The identified factors were also further classified into modifiable (if they were judged to be susceptible to interventions) and non-modifiable (if they were foreseen to be unamenable to interventions) by one of the authors [MJ] and agreed upon by all other authors who have extensive experiences in diabetes- and adherence-related research (AA, MI, NK).

3. Results

Of the 2788 articles initially identified from the databases, search engines, and grey literature, a total of 78 primary studies were identified for full-text screening (**Fig 1**). Studies were excluded due to the following reasons: focusing on disease control rather than medications (n=12), not conducted within the MENA region (n=9), irrelevant (n=9), and not investigating barriers to medication adherence (n=5), and other reasons (n=13). References of excluded articles can be

found in Supplementary 1. Overall, 30 studies from 10 different countries met the inclusion criteria and were included in this review [31-60].

Insert Fig 1 Flow diagram for articles selection

The 30 studies included in the present review were published between 1993 and 2015. Six studies were conducted in each of the following countries: Saudi Arabia, Iran, and Egypt, while three studies were conducted in Palestine and United Arab Emirates each. Other countries represented include Kuwait, Jordan, Oman, Libya, and Qatar. Only one study was qualitative, while the rest were quantitative in nature. The studies included a total of 11,859 participants and mostly investigated type 2 diabetes (n=20). None of the studies was exclusively conducted among patients with type 1 diabetes, six studies included both patients with type 1 and type 2 diabetes, while four studies did not specify the type of diabetes investigated. The primary method used to identify factors associated with medication adherence was self-reported approach using different types of questionnaires. The overall quality of the studies using the CCAT averaged to 51% with only one-third of the articles (n=10) scoring 80% or above (Table 2).

The overall average medication non-adherence among patients with diabetes within the MENA region was 38.3%, while for the gulf region alone (Saudi Arabia, Oman, United Arab Emirates, Kuwait, and Qatar) was 40.9%. The definition of medication adherence was not clear, and there were disparities in measurement tools across the studies. Adherence level was mainly determined by using questionnaire's cut-off points. The questionnaires used in the studies were mostly developed by the authors to fulfill the objectives of their studies, with minimal evidence

of validity and reliability (n=14) and only one study used pill count in addition to self-reporting. Other commonly used self-reported measures included Morisky Medication Adherence Scale (MMAS) (n=7), Beliefs about Medicines Questionnaire (n=2) and others (n=20) (Table2).

The factors identified from the included studies were classified into different categories: demographics-related; disease- and medication-related; disease management-related; perceptions, attitude and psychological feeling-related; and societal-related. These categories were determined based on consensus among the authors to represent the factors influencing medication adherence within the MENA region. Overall, the factors could be viewed as those that were positively associated with adherence, those that were negatively associated with adherence, and those that were insignificant (Table 3). The classification of factors into modifiable (e.g. knowledge about diabetes and its medications) vs. non-modifiable (e.g. age and gender) is represented in **Fig 2.**

Table 2: Characteristics of included studies

Author/ Year	Country/ setting	Study design	No. of pts	Type of DM	Avg. duration of diabetes	Diabetes medications	Avg. HbA1c	Avg. age (years)	Level of education	Adherence measure	Non-Adh. %	Quality CCAT % Score
Jeragh-Alhaddad et al., 2015	Kuwait / Outpatient clinics, hospitals and home visits	Cross-sectional – semi structured interview	20	Type 2	Majority (80%) more than 4 yrs	OAD (70%), Insulin (5%), Combination (25%)	NI	53.7	15% illiterate	• Semi structured interview	NI	98 ★★★★
Heissam et al., 2015	Egypt /Medical center	Cross-sectional – survey	372	Type 2	NI	OAD	NI	51.64 ± 10.76	42.3% illiterate	• Treatment Adherence survey	26	43 ★★
El-Khawaga et al., 2015	Egypt/ Outpatient clinic	Cross-sectional – survey	750	Type 1 and type 2	Majority (67.4%) more than 4 yrs	OAD (71.3%), Insulin (34.3%)	NI	Majority (94.8%) above 29	31.3% illiterate	• Author designed survey	39.9	60 ★★★
Ashur et al., 2015	Libya/ National Center for Diabetes	Cross-sectional – survey	523	Type 2	9.4 ± 7.3	Oral (38%), Insulin with or without oral (62%)	NI	54.43 ± 10.03	58.1% Primary school	• Revised Illness Perception Questionnaire • Morisky	36.1	90 ★★★★
Alatawi et al., 2015	Saudi Arabia/ Outpatient hospitals	Cross-sectional – survey	217	Type 2	8.9 ± 7.1	OAD (58%), Insulin (6.4%), combination (35.6%)	8.3 ± 1.5	52.1 ± 11.3	59.1% less than high school education	• Expanded Health Belief Model Questionnaire	43.0	93 ★★★★
Sweileh et al., 2014	Palestine/ Primary healthcare center	Cross-sectional – survey	405	Type 2	8.5 ± 6.0	monotherapy (35.6%), Combination (64.4%) Insulin (32.6%)	NI	58.3 ± 10.4	12.1% illiterate	• Morisky • Belief About Medicines • Michigan Knowledge Scale	42.7	95 ★★★★
Salam et al., 2014	Saudi Arabia/ Primary healthcare center	Cross-sectional – survey	406	Type 2	NI	OAD	NI	Majority (70.4%) between 40-60 yrs old	42.1% illiterate	• Author designed survey	22.9	25 ★
Koprulu et al., 2014	United Arab Emirates/ Diabetes clinic and outpatient hospital	Cross-sectional – interviewer-administered survey	200	Type 2	Majority (63.5%) less than 5 yrs	NI	45% more than 6.5% 55% of 6.5 or less	52.5% less than 50 yrs, 47.% above 49 yrs old	10% illiterate	• Author designed survey	40.0	70 ★★★

No. of pts: Number of patients, Avg.: Average, Non-Adh.: Non-adherence, NI: Not indicated, yrs: years

Table 2: Characteristics of included studies

Author/ Year	Country/ setting	Study design	No. of pts	Type of DM	Avg. duration of diabetes	Diabetes medications	Avg. HbA1c	Avg. age (years)	Level of education	Adherence measure	Non-Adh. %	Quality CCAT % Score
Khan et al., 2014	Saudi Arabia/ Diabetes center	Cross-sectional – survey	112	Type 2	15.8 ± 7.27	NI	9.2 ± 2.2	59.8 ± 9.03	44.4% illiterate	• Author designed survey	47.1	13 ⋆
Jimmy et al., 2014	Oman/ Home visits	Cross-sectional – survey	158	Type 2	Majority (89.2%) more than 1 yr	NI	NI	Majority (66.5%) were above 45 yrs old	55.7% illiterate	• Author designed survey	NI	73 ⋆⋆⋆
Jarab et al., 2014	Jordan/ Outpatient diabetes clinic	Cross-sectional – survey	171	Type 2	9.9 ± 7.5	Insulin (63.8%), Metformin (70.2%),Sulfonylurea (63.8%)	NI	64 ± 9.8	74.3% Secondary or high school	• Morisky • The ADKnowl survey • EQ-5D • EQ-VAS for quality of life scale	72.5	88 ⋆⋆⋆⋆
Farsaei et al., 2014	Iran/ Outpatient diabetes center	Cross-sectional – telephone-administered survey	507	Type 1 and type 2	11.2 ± 8.2	Insulin	NI	38.2 ± 2	10.9% illiterate	• Morisky	21.6	83 ⋆⋆⋆⋆
Bener et al., 2014	Qatar/ Primary healthcare center	Cross-sectional – survey	2582	NI	7.69 ± 5.1	None (20.26%), diet only (19.4%), OHA (22.46%), insulin (22.78%), Combination (15.1%)	9.15 ± 1.41	Majority (80.1%) were above 40 yrs old	16.3% illiterate	• Morisky	NI	75 ⋆⋆⋆
Arifulla et al., 2014	United Arab Emirates/ Outpatient hospitals	Cross-sectional – interviewer-administered survey	132	Type 2	Majority (81.82%) were less than 6 yrs	NI	NI	54 ± 10.2	88.6% university graduates	• Author designed survey	16.0	80 ⋆⋆⋆⋆
Al-Majed et al., 2014	Kuwait/ Primary healthcare center	Cross-sectional – interviewer-administered survey	693	Type 2	Majority (61.1%) more than 4 yrs	OAD (65.95%), insulin (6.49%), combination (27.56%)	NI	43.9% less than 50 yrs,	63.1% primary school or less	• Author designed survey	26.1	70 ⋆⋆⋆
Ahrari et al., 2014	Iran/ Diabetes center	Cross-sectional – survey	208	Type 2	9.32 ± 1.83	NI	9.32 ± 1.83	55 ± 11.1	28.4% illiterate	• Cognitive Appraisal of Health Scale	NI	70 ⋆⋆⋆

No. of pts: Number of patients, Avg.: Average, Non-Adh.: Non-adherence, NI: Not indicated, yrs: years

Table 2: Characteristics of included studies

Author/ Year	Country/ setting	Study design	No. of pts	Type of DM	Avg. duration of diabetes	Diabetes medications	Avg. HbA1c	Avg. age (years)	Level of education	Adherence measure	Non-Adh. %	Quality CCAT % Score
Khalil et al., 2013	Egypt/ Outpatient clinic	Cross-sectional – survey	1100	Type 2	Majority (73.5%) more than 4 yrs	NI	NI	Majority (96.5%) were above 39 yrs old	41.1% illiterate	• Author designed survey	52.0	83 ★★★★
Aflakseir et al., 2013	Iran/ Outpatient clinic	Cross-sectional – survey	93	Type 2	7.3	NI	NI	44.2 ± 12.1	15% primary school	• Subscale of Cause of Illness Perception Questionnaire •Medication Adherence Rating Scale	NI	58 ★★
Abdul Salam et al., 2013	Saudi Arabia/ Primary healthcare center	Cross-sectional – interviewer-administered survey	406	Type 2	NI	NI	NI	Majority (70.4%) were between 40-60 yrs old	42.1% illiterate	• Author designed survey	52.5	55 ★★
Khan et al., 2012	Saudi Arabia/ Primary healthcare center	Cross-sectional – interviewer-administered survey	468	NI	Majority (79.7%) more than 5 yrs	NI	67.9% had HbA1c above 7%	58 ± 11.64	64.7% illiterate	• Author designed survey	57.5	68 ★★★
Aflakseir et al., 2012	Iran/ Outpatient diabetes clinic	Cross-sectional – Survey	102	Type 2	9.5	NI	NI	40.7 ± 11.4	85% high school or above	• Illness Perception Survey Revised • Beliefs about Medication Survey •Medication Adherence Report Scale	13.0	68 ★★★
Ibrahim et al., 2011	United Arab Emirates/ Outpatient clinic	Cross-sectional – interviewer-administered	240	Type 1 and type 2	NI	NI	78.4% had HbA1c above 7%	56.6 ± 12.4	62.5% illiterate	• Author designed survey	83.3	38 ★

No. of pts: Number of patients, Avg.: Average, Non-Adh.: Non-adherence, NI: Not indicated, yrs: years

Table 2: Characteristics of included studies

Author/ Year	Country/ setting	Study design	No. of pts	Type of DM	Avg. duration of diabetes	Diabetes medications	Avg. HbA1c	Avg. age (years)	Level of education	Adherence measure	Non-Adh. %	Quality CCAT % Score
Mahfouz et al., 2011	Egypt/ Home visits	Cross-sectional – interviewer-administered survey	206	Type 2	12 ± 8	Diet (8.7%), OAD (56.8%), Insulin (34.5%)	NI	54 ± 6.3	62.1% illiterate	• Author designed survey	8.7	63 ⋆⋆⋆
Jamous et al., 2011	Palestine/ Military service clinic	Cross-sectional – Survey	130	Type 1 and type 2	8.2 ± 5.8	OAD	NI	56.3 ± 9.8	20% illiterate	• Morisky • Treatment Satisfaction Survey for Medication	61.5	88 ⋆⋆⋆⋆
Farsaei et al., 2011	Iran/ Outpatient clinic	Cross-sectional – interview	248	Type 2	10.8 ± 6.1	Metformin and glyburide	7.4 ±1.3 HbA1c	56.6 ± 8.9	18.8% illiterate	• Pill count • Morisky • Treatment Satisfaction Survey for Medication	50.8	60 ⋆⋆⋆
Shams et al., 2010	Egypt/ Outpatient clinic	Cross-sectional – interviewer-administered survey	226	Type 2	NI	OAD	NI	Majority (75.2%) were above 40 yrs old	12.8% illiterate	• Measure Treatment Adherence Scale	15.9	65 ⋆⋆⋆
Morowatisheta ll., 2010	Iran/ Diabetes center	Cross-sectional interviewer-administered survey	120	Type 1 and type 2	9.8 ± 6.8	NI	NI	53.28 ± 10	33.3% illiterate	• Diabetes Locus of Control Scale • Diabetes Self-care Activities Scale	NI	88 ⋆⋆⋆⋆
Ibrahim et al., 2010	Egypt/ Primary healthcare center	Cross-sectional – interviewer-administered survey	600	NI	NI	NI	NI	47.68 ± 1.94	34.5% illiterate	• Author designed survey	43.4	70 ⋆⋆⋆
Khattab et al., 1999	Saudi Arabia/ Primary healthcare center	Cross-sectional – Physician assessment	294	Type 1 and type 2	6.4 ± 5	Diet (8.9%), Diet and drugs (91.1%),	NI	54.0 ± 12.8	55.6% illiterate	• Physician reported	1.4	47 ⋆⋆
Alrowais et al., 1993	Saudi Arabia/ Inpatient and outpatient hospitals	Cross-sectional – Survey	170	NI	NI	NI	NI	71.7+/-11.8	65% illiterate	• Author designed survey	60.6	25 ⋆

No. of pts: Number of patients, Avg.: Average, Non-Adh.: Non-adherence, NI: Not indicated, yrs: years

Several factors were reported by the studies to have a positive association with medication adherence. These included knowledge about the disease and medications (n=10), regular follow-up visits (n=2), patient's belief **about medication effectiveness** and motivation about the medications (n=3), and perceived need for medications (n=2). Although six studies have demonstrated the positive association of patient's educational status on medication adherence, eight other studies failed to show any significant influence of this factor on adherence. Similarly, five studies have shown positive association of patient's income on medication adherence, while one study showed no significant influence of income (Table 3).

On the other hand, forgetfulness was reported as a negative factor by half of the included studies (n=15). Eleven studies found the experience with side effects as a negative factor on medication adherence. Other negatively associated factors included polypharmacy (n=7), traveling abroad (n=4), and fear of side effects (n=4). Having comorbidities was also negatively associated with adherence (n=5), yet one study conducted in Palestine indicated that having comorbidities act as a positive factor instead (Table 3).

Table 3: Factors associated with medication adherence

Factor	Statistically significant positive association Country, Reference	Statistically significant negative association Country, Reference	No statistically significant association Country, Reference
Demographics-related			
Age	n=2 Palestine[31] Jordan[32]	n=2 Iran[33, 34]	n=9 Saudi Arabia[35, 36] Iran[37] Egypt[38] Iran[39] Iran[40] Oman[41] Palestine[42] Libya[43]
Age 35-49	n=1 Egypt[44]		
Age 40-60	n=1 Saudi Arabia[45]		
Age above 60	n=1 Egypt[46]		
Gender			n=12 Saudi Arabia[35, 36, 45] Iran[37, 39, 40] Palestine[31, 42] Egypt[38] Jordan[32] Oman[41] UAE[47]
Gender (female)	n=1 Iran[48]		
Gender (male)	n=2 Egypt[46]	n=2 Saudi Arabia[49] Libya[43]	
Marital status			n=6 Egypt[44] Iran[39] Jordan[32] UAE[47] Libya[43] Saudi Arabia[36]
Married	n=1 Saudi Arabia[45]		
Single		n=2 Saudi Arabia[49] Palestine[42]	

Table 3: *Cont.* Factors influencing medication adherence

Factor	Statistically significant positive association Country, Reference	Statistically significant negative association Country, Reference	No statistically significant association Country, Reference
Demographics-related *Cont.*			
Education status	n=6 Saudi Arabia[35, 45] Iran[37] Libya[43] Egypt[46] Kuwait[50]		n=8 Egypt[44] UAE[51] Iran[33, 34] Jordan[32] Oman[41] Palestine[42] Saudi Arabia[36]
Education level	n=2 Saudi Arabia[49] UAE[47]	n=1 Kuwait[52]	n=3 Saudi Arabia[35] Egypt[38] Iran[39]
Nationality			n=1 Saudi Arabia[35]
Income	n=5 Kuwait[52] UAE[47] Libya[43] Egypt[46, 53]		n=1 Egypt[44]
Insurance	n=1 UAE[47]		n=1 Iran[39]
Occupation	n=2 Libya[43] Egypt[46]	n=1 Saudi Arabia[54]	n=7 Egypt[38, 44] Jordan[32] UAE[47] Iran [39] Oman[41] Saudi Arabia[36]
Living in an urban area	n=1 Egypt[46]	n=1 Saudi Arabia[49]	
Family history			n=1 Egypt[46]
Comorbidities	n=1 Palestine [31]	n=5 Kuwait[52] Jordan[32] UAE[47] Palestine[42] Libya[43]	
Smoking			n=1 Jordan[32]

Table 3: *Cont.* Factors influencing medication adherence

Factor	Statistically significant positive association Country, Reference	Statistically significant negative association Country, Reference	No statistically significant association Country, Reference
Disease management-related			
Regular follow- up visits	n=2 Kuwait[52] UAE[47]		
Physical activity /Exercise	n=1 Kuwait[52]		n=1 Iran[40]
Interference with food/ Diet	n=1 Kuwait[52]	n=1 UAE[55]	n=1 Iran[40]
Level of HbA1c		n=2 Kuwait[52] UAE[47]	n=1 Iran[39]
Monitoring blood glucose levels	n=4 Egypt[53, 56] Kuwait[52] Jordan[32]		n=1 UAE[47]
Patient-physician relationship	n=1 Egypt[53]		n=3 Egypt[44, 56] Saudi Arabia[49]
Disease- and medication-related			
Duration of diabetes	n=1 Palestine[31]	n=2 UAE[55] Egypt [46]	n=10 Iran[34, 37, 40] Egypt[38] Jordan[32] Oman[41] UAE[47] Palestine[42] Libya[43] Saudi Arabia[36]
Type of diabetes			n=1 Saudi Arabia[36]
Knowledge about diabetes and the medications	n= 10 Egypt[44, 46, 53, 56] Palestine[42] Iran[34] Saudi Arabia[35, 49] UAE[47] Kuwait[50]		n=1 Jordan[32]
Self-care management skills	n=1 Egypt[44]		
Medications adequate onset of action	n=1 Saudi Arabia[49]		

Table 3: *Cont.* Factors influencing medication adherence

Factor	Statistically significant positive association Country, Reference	Statistically significant negative association Country, Reference	No statistically significant association Country, Reference
Disease- and medication- related *Cont.*			
The use of complementary medicines		n=2 Egypt[57] UAE[47]	
Frequency of medications		n=2 Iran[40] Jordan[32]	
Combination of medication		n=1 Palestine[31]	
Side effects		n= 11 Egypt[56] Iran[37, 40] Saudi Arabia[49] UAE[47, 55] Qatar[58] Palestine[59] Jordan[32] Oman[41] Egypt[53]	
Drug regimen (simple)	n=1 Egypt[56]		
Drug regimen (complex)		n=3 Iran[37] UAE[55] Egypt[53]	
Shortage of medications		n=2 Iran[40] Kuwait[50]	
Cost of medications		n=2 Egypt[56] UAE[47]	
Complications	n=1 Kuwait[52]		n=1 Jordan[32]
Number of medications (monotherapy)	n=2 Egypt[56] Saudi Arabia[49]		n=1 Saudi Arabia[36]
Type of medication			n=4 Jordan[32] Palestine [42] Libya[43] Saudi Arabia[36]

Table 3: *Cont.* Factors influencing medication adherence

Factor	Statistically significant positive association Country, Reference	Statistically significant negative association Country, Reference	No statistically significant association Country, Reference
Disease- and medication-related *Cont.*			
Polypharmacy		n=7 UAE[47, 51, 55] Jordan[32] Oman[41] Libya[43] Egypt[53]	n=2 Iran[40] Oman[41]
Changes in therapy			n=1 UAE[47]
Societal-related			
Lack of social support		n=1 Kuwait[50]	
Too busy		n=1 UAE[55]	
Social stigma		n=1 Kuwait[50]	
Traveling abroad		n=4 Qatar[58] Palestine[42, 59] Saudi Arabia[54]	
Disruption of routine		n=1 Iran[37]	
Perception, attitude, and emotions			
Forgetfulness		n=15 Palestine[31, 42, 59] UAE[47, 51, 55] Iran[34, 37, 40] Qatar[58] Jordan[32] Oman[41] Saudi Arabia[53, 54, 60]	
Carelessness		n=1 Iran[34]	
Confusion		n=1 Iran[37]	
Treatment satisfaction	n=1 Palestine[31]		
Fasting in Ramadan		n=1 Iran[37]	

Table 3: *Cont.* Factors influencing medication adherence

Factor	Statistically significant positive association Country, Reference	Statistically significant negative association Country, Reference	No statistically significant association Country, Reference
Perception, attitude, and emotions *Cont.*			
Embarrassment		n=1 Iran[40]	
Fear of side effects		n=4 Palestine[42, 59] UAE[51] Iran[34]	
Fear of hypoglycemia		n=1 Kuwait[50]	n=1 Iran [40]
Feeling unwell		n=1 Iran[34]	
Feeling better		n=3 Qatar[58] Oman[41] Palestine[42]	
Limited faith in medications and their effectiveness		n=2 UAE[[51, 55]	
Patients' positive beliefs and motivation about medications	n=3 Egypt[53, 56] Kuwait[50]		
Locus of control	n=2 Iran[48] Libya[43]		
Low self-efficacy		n=3 Saudi Arabia [54] Kuwait [50]	
God-centered locus of control		n=1 Kuwait [50]	
Perceived need for medications	n=2 Palestine [42, 59]		
Quality of life			n=1 Jordan [32]

Insert Fig 2 Factors influencing medication adherence

4. Discussion

Despite the availability of several primary studies conducted in the MENA region on the topic of medication adherence in diabetes, current systematic reviews did not capture these studies [12-28]. Barriers to medication adherence identified in one country or region may not necessarily be the same as those in another country or region due to environmental, socio-economic, and cultural differences across countries. Therefore, to identify whether the same influencing factors to medication adherence exist in this region compared to the rest of the world, we conducted this systematic review using rigorous systematic review methodology. It was noted that the majority of the studies focused on type 2 diabetes. This could be due to the much lower prevalence of type 1 diabetes, which ranges between 7% and 12%, compared to type 2 diabetes [2]. Moreover, type 1 diabetes is still considered to be limited to children rather than adults with an expected increase of 3% annually [2]. Nonetheless, investigating factors associated with medication adherence within type 1 population in the MENA region is highly needed particularly that its prevalence is increasing [2].

Overall, it was found that non-adherence to medications among patients with diabetes ranged from 1.4 to 83.3%. This large variability can be attributed to the diversity of methods used in assessing medication adherence whereby investigator-designed questionnaires with no sufficient evidence of validity and reliability were mostly used in the studies. The average rate of medication non-adherence reported by the studies that used the MMAS questionnaire alone was 47.4% which is relatively high, while good quality studies (CCAT score of 80 and above) indicated an average nonadherence of 43%. The average HbA1c level across the studies was

8.7%. Noting that there is a positive direct correlation between adherence and disease control [61], these findings necessitate urgent interventions to reduce the risk of disease complications and their possible associated costs.

The negatively influencing factors reported in this review are similar to those reported elsewhere [12, 13, 62]. In more than half of the studies, patients reported forgetfulness as a major barrier to medication adherence. This barrier can be addressed through many interventions such as mobile phone reminders, modifying regimen schedule, keeping the medication close by, or creating a routine [63, 64].

Similar to another review conducted by *Sarayani* [20], this systematic review showed that knowledge about the disease and medications is positively associated with medication adherence. Therefore, any form of education provided by the healthcare provider in relation to the disease and its management will potentially contribute positively to the patients' adherence to drug therapy, which in fact has been proven in intervention studies targeting this factor [65, 66].

Overall, the factors identified in this systematic review appear to be largely similar to those reported from other parts of the world, a finding that was initially unpredicted. Other factors influencing medication adherence that may be unique to the region need to be further investigated using rigorous methodological approaches. For instance, religious convictions and God-centered beliefs, and fasting during the month of Ramadan, although reported in one study, need to be more thoroughly investigated especially that the MENA region is rich in

religious and cultural beliefs. An aspect that is considered to be unique to this region, but not reported within the included primary studies, includes the involvement of family members in the care of patients with diabetes. Within the MENA region, the majority of the elderly individuals are being cared for by their family members; therefore, family involvement in the care planning and their understanding of the medication regimen need to be further explored. Other important factors such as social stigma and social support were surprisingly investigated in only one study. It is well known that these factors play a major role in diabetes management, particularly among those who are on insulin therapy [14, 15, 67-69]. Therefore, further studies are needed to confirm whether these factors are common across the MENA region or limited to a few countries. Finally, MENA-specific factors such as climatic conditions which may influence insulin storage condition, beliefs in traditional and complementary healing practices, and the rapid economic growth observed in the GCC states merit further investigations. This could potentially result in culturally-relevant and region-specific interventions to improve medication adherence in the MENA region.

Our classification of factors into modifiable and non-modifiable categories based on perceived amenability for modification creates meaningful opportunities for intervention strategies. Generally, interventions should be carefully designed to be holistic targeting multiple factors at the same time in order to maximize the benefits to be achieved. For instance, in addition to counseling about the disease and medications, it is important to emphasize on educating the patient about the expected side effects and their management. Moreover, more than one-quarter (27.4%) of the patients with diabetes are of limited literacy skills, indicating that

counseling should be carefully tailored to the level of understanding of the patient. The provision of pictograms, for example, as tools to indicate the dosing regimen can be of significant help to those who cannot read medication labels [70].

The healthcare provider should also look into providing diabetic patients with the simplest drug regimen possible. Currently, multiple antidiabetic medications exist in combination forms, so healthcare provider can prescribe a combination product instead of two separate medications which would reduce pill burden and improve adherence [71]. Moreover, insulin can be prescribed with pens which are easier to administer than vials, and this has been reported to be associated with better adherence [72]. However, such changes should take into consideration availability, accessibility, affordability and patient's ability to pay for the medications especially that studies indicated medication cost as a negative influencing factor to medication adherence [47, 56].

As for the societal-related factors, healthcare institutions can implement the use of social service personnel who can educate families about the patients' health condition and how to provide the best possible support. In relation to social stigma, stakeholders including policymakers, healthcare providers, non-profit health and consumer organizations can work on creating public campaigns educating the public on how to help patients with diabetes [73]. Patients with diabetes believe that community-based interventions are highly needed to overcome the disease-associated stigma [73].

This review has some limitations some of which are inherent to all systematic reviews. The results obtained from the studies included in this review should be interpreted with caution as most of the studies were not of high quality. Despite assessing the quality of the studies using the CCAT, some studies had serious methodological flaws and weaknesses, mostly lacking power analysis, using non-validated instruments that have not been rigorously designed, all of which increase the risk of bias and reduce the generalizability of the results. This factor clearly reflects the diversity of the results obtained from different countries within the MENA region. In addition, clear definitions of medication adherence were lacking within these studies. Having clear definitions would improve the quality of the conducted research since a valid and reliable measure would be used to produce standardized results which can then be compared across different studies. Future original studies should investigate the barriers to medication adherence among patients with type 1 diabetes as well as use qualitative or mixed methodology which would allow for in-depth identification of barriers and facilitators to medication adherence.

5. Conclusion

Factors influencing medication adherence are highly diverse in the MENA region. Nonetheless, the factors identified in this systematic review reaffirm what has been reported in the literature. The main influencing factors identified in the present review were forgetfulness, knowledge about diabetes and its medications as well as side effects. It is hard to draw a conclusion on the rates of non-adherence to antidiabetic medications and factors influencing these in the MENA region due to the diverse methodology used to assess adherence, disparities

in the measurement tools and their validities as well as the lack of clear definition of adherence. However, the rate of medication nonadherence identified in good quality studies (CCAT score of 80 and above) indicated an average nonadherence of 43%. Some factors such as cultural and religious aspects were understudied and merit further investigations. The current findings suggest that the identified factors influencing medication adherence in patients with diabetes, although inconclusive, can serve as potential targets for intervention strategies to improve adherence and overall patients' health outcomes.

Acknowledgment: None

Funding: This research did not receive any specific grants from funding agencies in the public, commercial or non-profit sectors.

Conflicts of interest: None

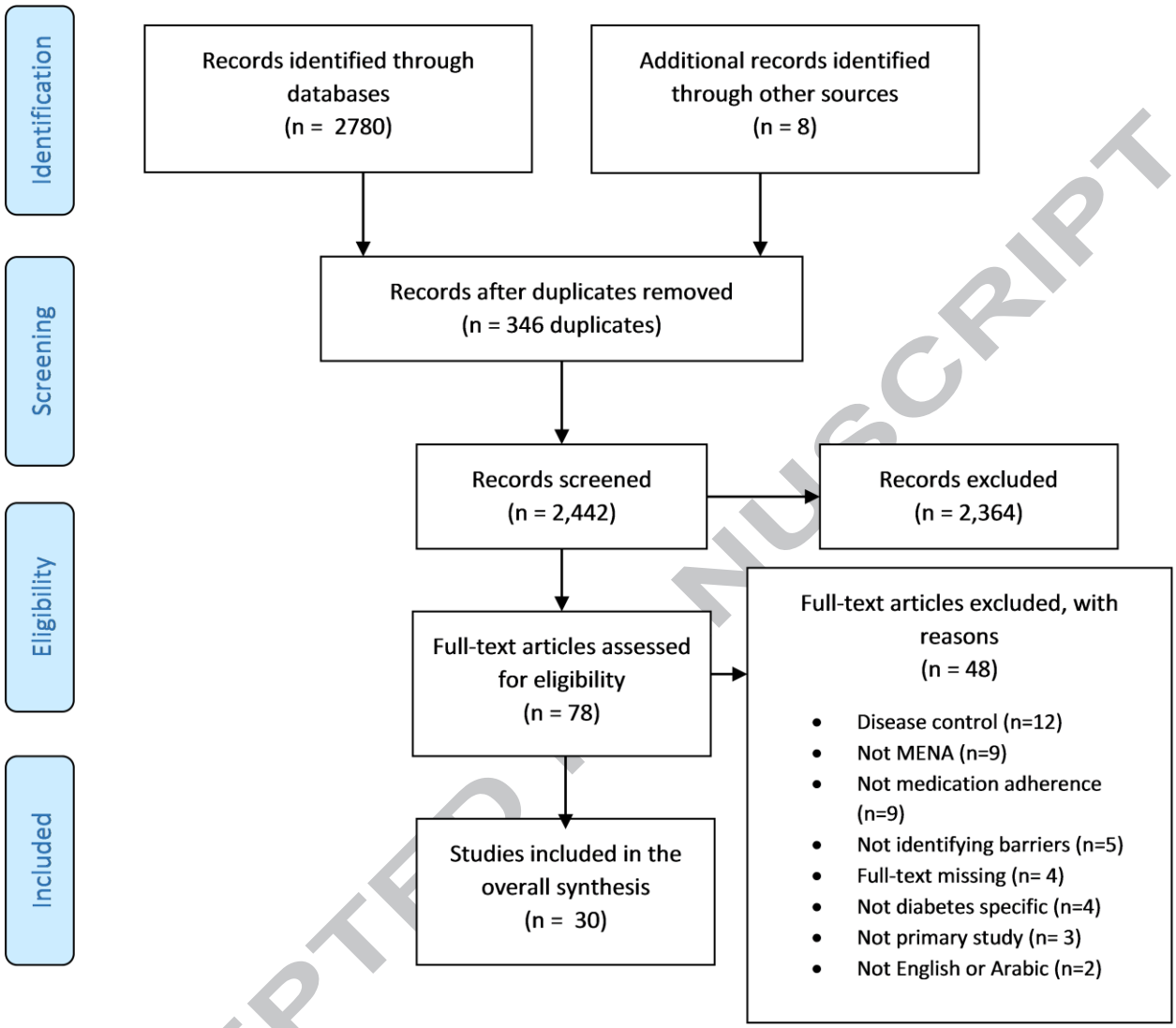
6. References

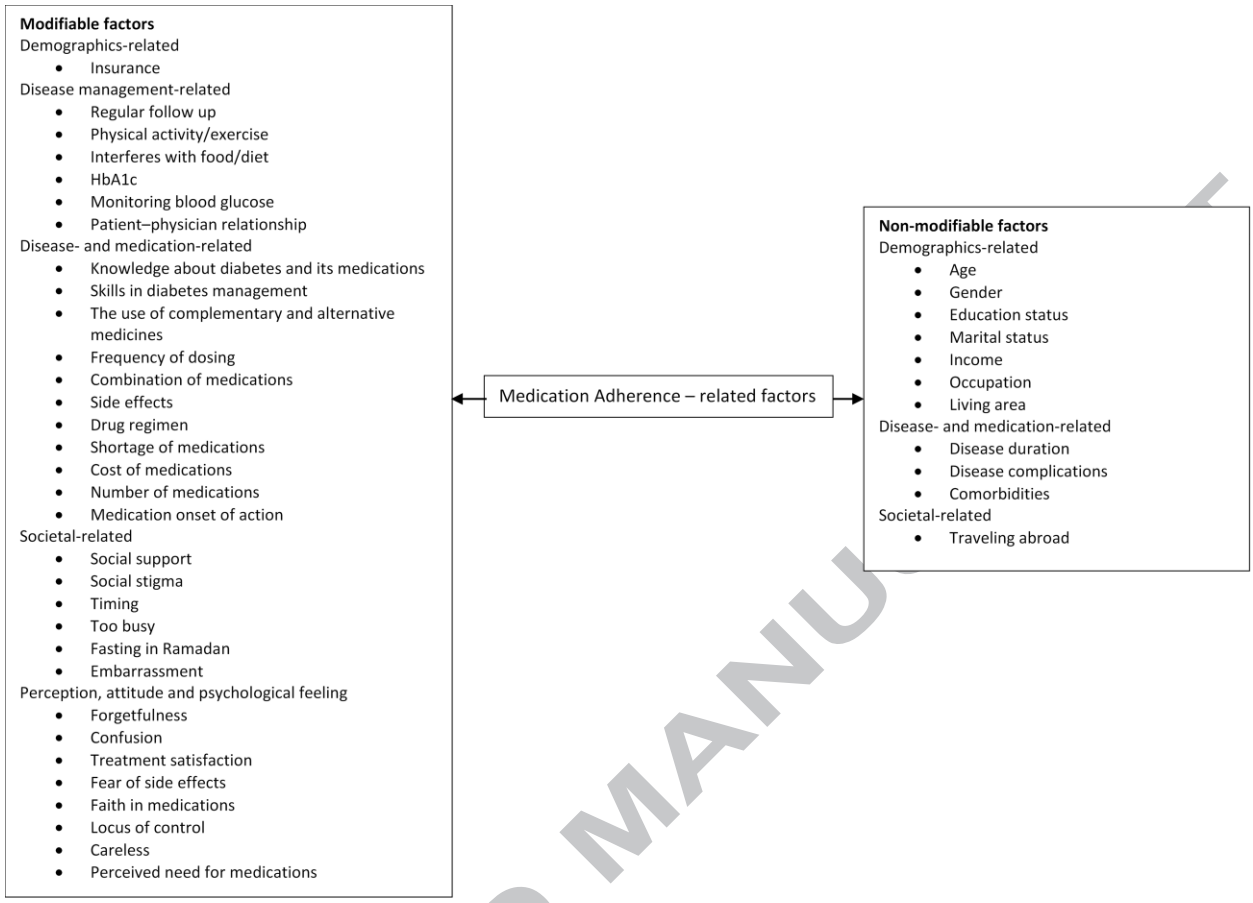
[1] van Dieren S, Beulens JW, van der Schouw YT, Grobbee DE, Neal B. The global burden of diabetes and its complications: an emerging pandemic. European journal of cardiovascular prevention and rehabilitation : official journal of the European Society of Cardiology, Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology. 2010;17 Suppl 1:S3-8.
[2] Intrnational Diabetes Federation. IDF Diabetes Atlas. 7th Ed. Brussels, Belgium. 2015.
[3] Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes research and clinical practice. 2010;87:4-14.
[4] Musaiger AO. Overweight and obesity in Eastern Mediterranean Region: prevalence and possible causes. J Obes. 2011;2011:407237.
[5] Nyenwe EA, Jerkins TW, Umpierrez GE, Kitabchi AE. Management of type 2 diabetes: evolving strategies for the treatment of patients with type 2 diabetes. Metab Clin Experimental. 2011;60:1-23.
[6] Cani CG, Lopes Lda S, Queiroz M, Nery M. Improvement in medication adherence and self-management of diabetes with a clinical pharmacy program: a randomized controlled trial in patients with type 2 diabetes undergoing insulin therapy at a teaching hospital. Clinics 2015;70:102-6.
[7] Kirkman MS, Rowan-Martin MT, Levin R, Fonseca VA, Schmittdiel JA, Herman WH, et al. Determinants of adherence to diabetes medications: findings from a large pharmacy claims database. Diabetes care. 2015;38:604-9.
[8] Young BA, Lin E, Von Korff M, Simon G, Ciechanowski P, Ludman EJ, et al. Diabetes complications severity index and risk of mortality, hospitalization, and healthcare utilization. Am J Manag Care. 2008;14:15-23.
[9] Bener A, Al-Laftah F, Al-Hamaq AO, Daghash M, Abdullatef WK. A study of diabetes complications in an endogamous population: an emerging public health burden. Diabetes & metabolic syndrome. 2014;8:108-14.
[10] Bener A, Kim EJ, Mutlu F, Eliyan A, Delghan H, Nofal E, et al. Burden of diabetes mellitus attributable to demographic levels in Qatar: an emerging public health problem. Diabetes & metabolic syndrome. 2014;8:216-20.
[11] Mason BJ, Matsuyama JR, Jue SG. Assessment of sulfonylurea adherence and metabolic control. The Diabetes educator. 1995;21:52-7.
[12] Capoccia K, Odegard PS, Letassy N. Medication adherence with diabetes medication: a systematic review of the literature. Diabetes Educ. 2016;42:34-71.
[13] Brundisini F, Vanstone M, Hulan D, DeJean D, Giacomini M. Type 2 diabetes patients' and providers' differing perspectives on medication nonadherence: a qualitative meta-synthesis. BMC health services research. 2015;15:516.
[14] Sohal T, Sohal P, King-Shier KM, Khan NA. Barriers and facilitators for type-2 diabetes management in South Asians: a systematic review. PloS one. 2015;10:e0136202.
[15] Al Hamid A, Ghaleb M, Aljadhey H, Aslanpour Z. A systematic review of qualitative research on the contributory factors leading to medicine-related problems from the perspectives of adult patients with cardiovascular diseases and diabetes mellitus. BMJ Open. 2014;4:e005992.
[16] Tiktin M, Celik S, Berard L. Understanding adherence to medications in type 2 diabetes care and clinical trials to overcome barriers: a narrative review. Current medical research and opinion. 2016;32:277-87.
[17] Krass I, Schieback P, Dhippayom T. Adherence to diabetes medication: a systematic review. Diabetic medicine : a journal of the British Diabetic Association. 2015;32:725-37.
[18] Davies MJ, Gagliardino JJ, Gray LJ, Khunti K, Mohan V, Hughes R. Real-world factors affecting adherence to insulin therapy in patients with Type 1 or Type 2 diabetes mellitus: a systematic review. Diabetic medicine : a journal of the British Diabetic Association. 2013;30:512-24.

[19] Polinski JM, Smith BF, Curtis BH, Seeger JD, Choudhry NK, Connolly JG, et al. Barriers to insulin progression among patients with type 2 diabetes: a systematic review. Diabetes Educ. 2013;39:53-65.
[20] Sarayani A, Jahangard-Rafsanjani Z, Hadjibabaie M, Ahmadvand A, Javadi M, Gholami K. A comprehensive review of adherence to diabetes and cardiovascular medications in Iran; implications for practice and research. Journal of diabetes and metabolic disorders. 2013;12:57.
[21] Peeters B, Van Tongelen I, Boussery K, Mehuys E, Remon JP, Willems S. Factors associated with medication adherence to oral hypoglycaemic agents in different ethnic groups suffering from type 2 diabetes: a systematic literature review and suggestions for further research. Diabetic medicine : a journal of the British Diabetic Association. 2011;28:262-75.
[22] Gherman A, Schnur J, Montgomery G, Sassu R, Veresiu I, David D. How are adherent people more likely to think? A meta-analysis of health beliefs and diabetes self-care. Diabetes Educ. 2011;37:392-408.
[23] Nam S, Chesla C, Stotts NA, Kroon L, Janson SL. Barriers to diabetes management: patient and provider factors. Diabetes research and clinical practice. 2011;93:1-9.
[24] Fu AZ, Qiu Y, Radican L. Impact of fear of insulin or fear of injection on treatment outcomes of patients with diabetes. Current medical research and opinion. 2009;25:1413-20.
[25] Pun SPY, Coates V, Benzie IFF. Barriers to the self-care of type 2 diabetes from both patients' and providers' perspectives: literature review. Journal of Nursing and Healthcare of Chronic Illness. 2009;1:4-19.
[26] Gonzalez JS, Peyrot M, McCarl LA, Collins EM, Serpa L, Mimiaga MJ, et al. Depression and diabetes treatment nonadherence: a meta-analysis. Diabetes care. 2008;31:2398-403.
[27] Lee WC, Balu S, Cobden D, Joshi AV, Pashos CL. Prevalence and economic consequences of medication adherence in diabetes: a systematic literature review. Managed care interface. 2006;19:31-41.
[28] Nagasawa M, Smith MC, Barnes JH, Jr., Fincham JE. Meta-analysis of correlates of diabetes patients' compliance with prescribed medications. Diabetes Educ. 1990;16:192-200.
[29] Jaam M, Awaisu A, Mohamed Ibrahim MI, Kheir N. Factors associated with medication non-adherence in patients with diabetes in the Middle East and North Africa region: a systematic mixed studies review. . PROSPERO. 2016;CRD42016042474.
[30] Crowe M, Sheppard L. A review of critical appraisal tools show they lack rigor: Alternative tool structure is proposed. Journal of clinical epidemiology. 2011;64:79-89.
[31] Jamous RM, Sweileh WM, Abu-Taha AS, Sawalha AF, Zyoud SH, Morisky DE. Adherence and satisfaction with oral hypoglycemic medications: a pilot study in Palestine. International journal of clinical pharmacy. 2011;33:942-8.
[32] Jarab AS, Almrayat R, Alqudah S, Thehairat E, Mukattash TL, Khdour M, et al. Predictors of non-adherence to pharmacotherapy in patients with type 2 diabetes. Int J Clin Pharm. 2014;36:725-33.
[33] Aflakseir A, Farmani A. Exploring illness causal beliefs and its relationship with medication adherence and demographic characteristics among a sample of patients with type 2 diabetes in Isfahan-Iran. Iranian J Diabetes Obesity. 2013;5:121-5.
[34] Aflakseir A. Role of illness and medication perceptions on adherence to medication in a group of Iranian patients with type 2 diabetes. Journal of diabetes. 2012;4:243-7.
[35] Alrowais NA, Alhaider AA, Alhassan MI, Abou-Auda HS, Jarallah JS. A look at the diabetic patient compliance in Riyadh district. Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society. 1993;1:50-5.
[36] Khattab MS, Aboifotouh MA, Khan MY, Humaidi MA, al-Kaldi YM. Compliance and control of diabetes in a family practice setting, Saudi Arabia. Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit. 1999;5:755-65.
[37] Farsaei S, Sabzghabaee AM, Zargarzadeh AH, Amini M. Effect of pharmacist-led patient education on glycemic control of type 2 diabetics: A randomized controlled trial. J Res Med Sci. 2010;15:317-23.

[38] Mahfouz EM, Awadalla HI. Compliance to diabetes self-management in rural El-Mina Egypt. Cent Eur J Public Health. 2011;19:35-41.
[39] Ahrari S, Mohammadpour A, Amouzeshi Z, Agha-Yousefi A. The relationship between cognitive appraisal and adherence to medical regimens in type 2 diabetic patients. Journal of caring sciences. 2014;3:277-85.
[40] Farsaei S, Radfar M, Heydari Z, Abbasi F, Qorbani M. Insulin adherence in patients with diabetes: risk factors for injection omission. Primary care diabetes. 2014;8:338-45.
[41] Jimmy B, Jose J, Al-Hinai ZA, Wadair IK, Al-Amri GH. Adherence to medications among type 2 diabetes mellitus patients in three districts of Al Dakhliyah Governorate, Oman: A cross-sectional pilot study. Sultan Qaboos Univ Med J. 2014;14:e231-5.
[42] Sweileh WM, Zyoud SH, Abu Nab'a RJ, Deleq MI, Enaia MI, Nassar SM, et al. Influence of patients' disease knowledge and beliefs about medicines on medication adherence: findings from a cross-sectional survey among patients with type 2 diabetes mellitus in Palestine. BMC public health. 2014;14:94.
[43] Ashur ST, Shah SA, Bosseri S, Morisky DE, Shamsuddin K. Illness perceptions of Libyans with T2DM and their influence on medication adherence: a study in a diabetes center in Tripoli. The Libyan journal of medicine. 2015;10:29797.
[44] Ibrahim NKR, Attia SG, Sallam SA, Fetohy EM, El-Sewi F. Physicians' therapeutic practice and compliance of diabetic patients attending rural primary health care units in Alexandria. J Fam Community Med. 2010;17:121-8.
[45] Abdul Salam M, Farheen Siddiqui A. Socio-demographic determinants of compliance among type 2 diabetic patients in Abha, Saudi Arabia. J Clin Diagn Res. 2013;7:2810-3.
[46] El-Khawaga G, Abdel-Wahab F. Knowledge, attitudes, practice and compliance of diabetic patients in Dakhlia, Egypt. Int J Res Med Sci. 2015;3.
[47] Koprulu F, Bader RJK, Hassan NAGM, Abduelkarem AR, Mahmood DA. Evaluation of adherence to diabetic treatment in Northern Region of United Arab Emirates. Trop J Pharm Res. 2014;13:989-95.
[48] Morowatisharifabad MA, Mahmoodabad SS, Baghianimoghadam MH, Tonekaboni NR. Relationships between locus of control and adherence to diabetes regimen in a sample of Iranians. International journal of diabetes in developing countries. 2010;30:27-32.
[49] Khan AR, Al-Abdul Lateef ZN, Al Aithan MA, Bu-Khamseen MA, Al Ibrahim I, Khan SA. Factors contributing to non-compliance among diabetics attending primary health centers in the Al Hasa district of Saudi Arabia. Journal of Family & Community Medicine. 2012;19:26-32.
[50] Jeragh-Alhaddad FB, Waheedi M, Barber ND, Brock TP. Barriers to medication taking among Kuwaiti patients with type 2 diabetes: a qualitative study. Patient preference and adherence. 2015;9:1491-503.
[51] Mohamed Ibrahim OH, Jirjees FJ, Mahdi HJ. Barriers affecting compliance of patients with chronic diseases: A preliminary study in United Arab Emirates (UAE) population. Asian J Pharm Clin Res. 2011;4:42-5.
[52] Al-Majed HT, Ismael AE, Al-Khatlan HM, El-Shazly MK. Adherence of type-2 diabetic patients to treatment. Kuwait Med J. 2014;46:225-32.
[53] Heissam K, Abuamer Z, El-Dahshan N. Patterns and obstacles to oral antidiabetic medications adherence among type 2 diabetics in Ismailia, Egypt: A cross section study. Pan Afr Med J. 2015;20:1-7.
[54] Alatawi YM, Kavookjian J, Ekong G, Alrayees MM. The association between health beliefs and medication adherence among patients with type 2 diabetes. Research in social & administrative pharmacy : RSAP. 2015.
[55] Arifulla M, John LJ, Sreedharan J, Muttappallymyalil J, Basha SA. Patients' adherence to anti-diabetic medications in a hospital at Ajman, UAE. Malaysian J Med Sci. 2014;21:44-9.

[56] Shams ME, Barakat EA. Measuring the rate of therapeutic adherence among outpatients with T2DM in Egypt. Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society. 2010;18:225-32.
[57] Khalil SHA, Zaki A, Ibrahim AM, El-Moughazi AM, Khater AM, Youssef AM, et al. Pattern of use of complementary and alternative medicine among type 2 diabetes mellitus patients in Alexandria, Egypt. J Egypt Public Health Assoc. 2013;88:137-42.
[58] Bener A, Al-Hamaq AO, Yousafzai MT, Abdul-Ghani M. Relationship between patient satisfactions with diabetes care and treatment. Nigerian journal of clinical practice. 2014;17:218-25.
[59] Jamous RMF. Analysis of beliefs about medicines and medication adherence in patients with chronic diseases at the Military Medical Services, Nablus, Palestine. J Family Med Prim Care. 2014;3:224-9.
[60] Khan NA, Venkatachalam VV, Alavudeen SS, Alakhali KM, Dhanapal CK. Study on therapeutic outcome, attitude and awareness about type 2 diabetes among type 2 diabetes female patients in Aseer diabetes center. Pharmacie Globale. 2014;5:1-4.
[61] Schectman JM, Nadkarni MM, Voss JD. The association between diabetes metabolic control and drug adherence in an indigent population. Diabetes care. 2002;25:1015-21.
[62] Polinski JM, Shrank WH, Glynn RJ, Huskamp HA, Roebuck MC, Schneeweiss S. Beneficiaries with cardiovascular disease and the Part D coverage gap. Circulation Cardiovascular quality and outcomes. 2012;5:387-95.
[63] Jarab AS, Alqudah SG, Mukattash TL, Shattat G, Al-Qirim T. Randomized controlled trial of clinical pharmacy management of patients with type 2 diabetes in an outpatient diabetes clinic in Jordan. Journal of managed care pharmacy : JMCP. 2012;18:516-26.
[64] Zolfaghari M, Mousavifar SA, Pedram S, Haghani H. The impact of nurse short message services and telephone follow-ups on diabetic adherence: which one is more effective? Journal of clinical nursing. 2012;21:1922-31.
[65] Negarandeh R, Mahmoodi H, Noktehdan H, Heshmat R, Shakibazadeh E. Teach back and pictorial image educational strategies on knowledge about diabetes and medication/dietary adherence among low health literate patients with type 2 diabetes. Primary care diabetes. 2013;7:111-8.
[66] Al Mazroui NR, Kamal MM, Ghabash NM, Yacout TA, Kole PL, McElnay JC. Influence of pharmaceutical care on health outcomes in patients with Type 2 diabetes mellitus. Br J Clin Pharmacol. 2009;67:547-57.
[67] Woudenberg YJ, Lucas C, Latour C, Scholte op Reimer WJ. Acceptance of insulin therapy: a long shot? Psychological insulin resistance in primary care. Diabetic medicine : a journal of the British Diabetic Association. 2012;29:796-802.
[68] Brod M, Kongso JH, Lessard S, Christensen TL. Psychological insulin resistance: patient beliefs and implications for diabetes management. Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation. 2009;18:23-32.
[69] Snoek FJ, Skinner TC. Psychological aspects of diabetes management. Medicine. 2006;34:61-2.
[70] Negarandeh R, Mahmoodi H, Noktehdan H, Heshmat R, Shakibazadeh E. Teach back and pictorial image educational strategies on knowledge about diabetes and medication/dietary adherence among low health literate patients with type 2 diabetes. Primary care diabetes. 2013;7:111-8.
[71] van Galen KA, Nellen JF, Nieuwkerk PT. The effect on treatment adherence of administering drugs as fixed-dose combinations versus as separate pills: systematic review and meta-analysis. AIDS Res Treat. 2014;2014:967073.
[72] Baser O, Bouchard J, DeLuzio T, Henk H, Aagren M. Assessment of adherence and healthcare costs of insulin device (FlexPen) versus conventional vial/syringe. Advances in therapy. 2010;27:94-104.
[73] Irani MD, Abdoli S, Bijan I, Parvizy S, Fatemi NS, Amini M. Strategies to overcome type 1 diabetes–related social stigma in the Iranian society. Iranian J Nurs Midwifery Res. 2014;19:456-63.





Highlights

- Factors influencing medication adherence in patients with diabetes within Middle East and North Africa region are highly complex.
- Influencing factors within this region can be classified into demographics-related; disease- and medication-related; perception, attitude and psychological feelings-related; and societal-related factors.
- These factors can also be viewed as modifiable and non-modifiable based on their perceived amenability for interventions, creating meaningful opportunities for interventions.
- Primary studies identifying factors influencing medication adherence need to use standardized definitions as well as valid and reliable methods of measurement to truly reflect on the problem of medication non-adherence.