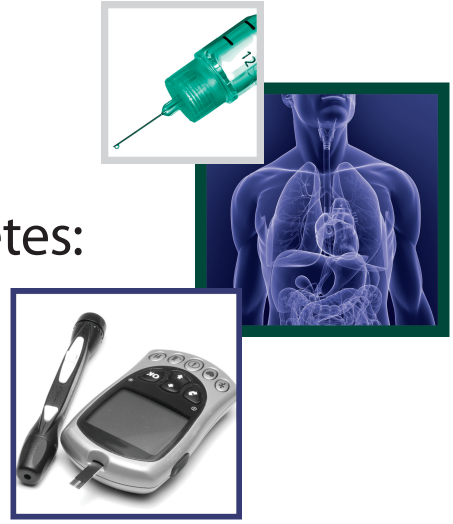
REVIEW

Effective interventions to improve medication adherence in Type 2 diabetes: a systematic review



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Practice Points

- Medication adherence is an important element in diabetes management, but may not be solely responsible for achieving glycemic control.
- Three critical components of any intervention are education, skills training and problem-solving. Most of the interventions in this review focused on education rather than the other components. Based on this finding, more research is needed to identify effective interventions for improving medication adherence in Type 2 diabetes. Interventions targeting diabetes self-management are needed and must be developed.
- One-on-one counseling was the method used in many of the randomized controlled trials reviewed, and was found to be effective.
- Interventions led by pharmacists demonstrated the most statistically significant results. Although small in number, interventions using other types of facilitators such as nurse educators, community health workers and certified diabetes educators were also effective.
- Uniform definitions for medication adherence must be constructed.
- Interventions should be simple and tailored to patients' individual needs to increase the likelihood of effectiveness and improved outcomes.
- Clinical outcomes may not adequately reflect medication adherence.
- Benefits of medication adherence must continue to be reinforced.

SUMMARY **Aim:** Medication adherence is associated with improved outcomes in diabetes. Interventions have been established to help improve medication adherence; however, the most effective interventions in patients with Type 2 diabetes remain unclear. The goal of this study was to distinguish whether interventions were effective and identify areas for future research. **Methods:** Medline was searched for articles published between January 2000 and May 2013, and a reproducible strategy was used. Study eligibility criteria

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included interventions measuring medication adherence in adults with Type 2 diabetes. **Results:** Twenty seven studies met the inclusion criteria and 13 showed a statistically significant change in medication adherence. **Conclusion:** Heterogeneity of the study designs and measures of adherence made it difficult to identify effective interventions that improved medication adherence. Additionally, medication adherence may not be solely responsible for achieving glycemic control. Researchers must emphasize tailored interventions that optimize management and improve outcomes, and examine the need for clear indicators of medication adherence.

Medication adherence is one of several behaviors vital to diabetes self-management and clinical outcomes. The variables believed to contribute to adherence behaviors include treatment and disease characteristics, intra- and inter-personal factors, and environmental characteristics [1]. Patients, providers and health systems, in addition to the treatment plan itself, may contribute to the success of adherence [2,3].

Adherence has been associated with better glycemic control, fewer diabetes-related complications, reduced hospitalizations, reduced healthcare costs, and lower all-cause mortality [4–8]. Despite the known benefits of medication adherence in patients with Type 2 diabetes mellitus (T2DM), adherence rates vary, with patients taking between 36 and 93% of prescribed recommended doses [4]. Additionally, national clinical practice guidelines emphasize the need for composite control of blood glucose, blood pressure and cholesterol to improve glycemic control and reduce adverse outcomes, but only 43, 29 and 52% of patients with T2DM have controlled blood sugar (HbA1c ≥7%), blood pressure (systolic blood pressure <130 mmHg and diastolic blood pressure <80 mmHg) and cholesterol levels (LDL-cholesterol <100 mg/dl), respectively [9,10].

Prior research suggests that patients with chronic diseases such as diabetes were themselves the cause of poor adherence, with the role of providers in adherence regarded as secondary [1]. It has since been acknowledged that a systems approach to medication adherence might achieve greater effectiveness and lead to improved adherence, better health outcomes and decreased healthcare costs [1]. Furthermore, the WHO stressed that increasing the effectiveness of interventions targeting adherence may have a greater impact on population health than improving specific medical treatments [1]. Addressing the factors that increase and improve adherence is necessary to reduce the burden of diabetes and other chronic illnesses.

Finally, there is no gold standard for measuring medication adherence, thus making it difficult to discern the impact of any given measure on T2DM outcomes. In research studies and clinical practice, multiple methods for measuring medication adherence have been used inconsistently [11,12]. Some interventions define adherence directly by measuring the actual pills taken by a patient and others measure it indirectly by assuming that medications have been taken. Each method has its own advantages and disadvantages. Therefore, the measure selected for use in research and/or clinical practice should be practical and applicable for achieving desired outcomes. This does not appear to always be the case, thereby making it difficult to assess actual medication adherence.

Box 1. Search strategy.

Type 2 diabetes
- Exploded MeSH 'diabetes mellitus', 'non-insulin-dependent'
- Exploded MeSH 'insulin resistance'
- Text word 'insulin resistance'
- Text word 'MODY' or 'NIDDM'
- Text word 'non-insulin dependent' or 'noninsulin dependent'
- Text word 'Type 2 diabetes' or 'Type II diabetes'
- Any in 'Type 2 diabetes' category

Compliance/adherence
- Exploded MeSH 'patient compliance'
- Exploded MeSH 'self-care'
- Text word 'self-care' or 'self-management'
- Text word 'compliance' or 'adherence'
- Text word 'treatment refusal'
- Text word 'empowerment'
- Any in 'compliance/adherence' category

Intervention
- Text word 'intervention'
- Any in 'Type 2 diabetes' category and any in 'compliance/adherence' category and text word 'intervention'

Given the complex assignment of role responsibility in medication adherence and the variety of methods used to determine adherence to medication regimens, we aimed to identify interventions targeted at improving medication adherence and T2DM-related clinical outcomes in adults. The goal of this systematic review was to distinguish whether interventions were effective and identify areas for future research.

Methods

Information sources, eligibility criteria & search

A reproducible strategy was used to identify interventions addressing medication adherence in patients with T2DM. Studies were identified by searching Medline on 23 May 2013 for articles published in the English language between 2000 and 2013. The search terms were based on the Cochrane Metabolic and Endocrine Disorder Group search strategy for T2DM [13] and the Cochrane search strategy for medication compliance/adherence [14]. Some search terms in the Cochrane strategies were not used based on the goals of this review. The search strategy is given in **Box 1**.

Study selection & data collection

Eligibility assessment was performed by four independent authors (JLS Williams, RJ Walker, BL Smalls and JA Campbell) in a standardized manner and disagreements were resolved by the fifth author (LE Egede). The process used to identify eligible citations is shown in **Figure 1**. Titles and abstracts were reviewed using a standardized checklist. Abstracts were eliminated if they did not investigate a T2DM patient population, measure medication adherence/compliance as an outcome or describe an intervention. Interventions included randomized controlled trials (RCTs) and quasiexperimental studies, with and without a control arm.

Data collected from the eligible articles are shown in **Tables 1–4**. For each study, data were extracted on the number of participants, sample population, duration of intervention, setting of intervention, study design and type of control **(Table 1)**. An outcome table for medication adherence was created to include the mean baseline medication adherence score, mean change (or baseline and postintervention if not reported) and statistical significance **(Table 2)**. **Table 2** also reports the method used to measure medication adherence, categorized as pharmacy claims, electronic monitoring, pill count, self-report or serum/blood levels. If the article measured HbA1c, it was included in **Table 3**, which provides mean baseline HbA1c, mean change (or baseline and postintervention if not reported) and statistical significance. Each article was analyzed for relevant intervention characteristics, including whether it was culturally tailored, educational or skills focused, device driven (i.e., mobile phone, computers with internet access or landline telephone) and/or personnel administered (i.e., community health worker [CHW] or pharmacist) **(Table 4)**. A narrative review was performed as the heterogeneous measures used to determine medication adherence precluded conducting a meta-analysis. Although risks of bias exist, articles were not excluded due to the limited

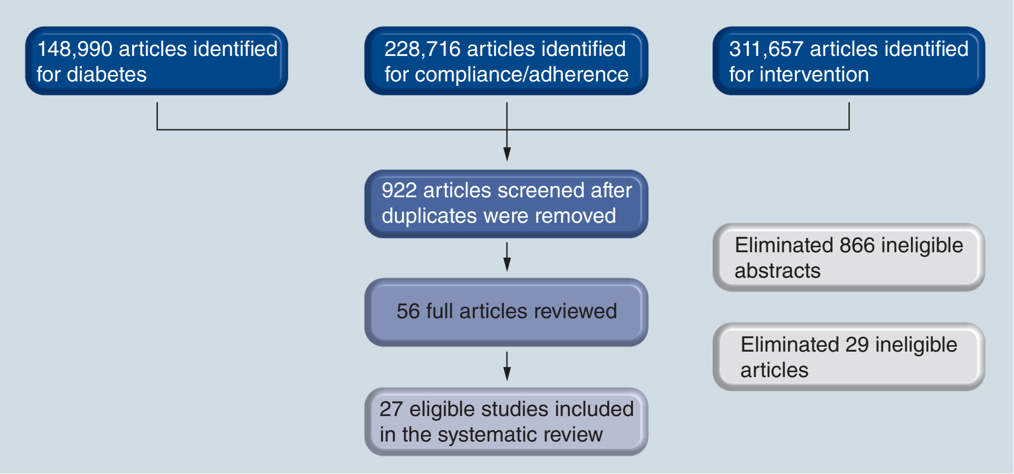

Figure 1. Process for eligible article selection.

Table 1. Studies meeting inclusion criteria.

Study (year)	Patients (n)	Sample population	Duration	Setting	Intervention description	Study design	Type of control	Ref.
Al Mazroui *et al.* (2009)	240	Adults with T2DM	12 months	Military hospital outpatient clinic in the United Arab Emirates	Patients received education about their illness from a research pharmacist that included complications, proper medication dosage and storage, as well as a healthy lifestyle	RCT	Standard provider care and noncontact control group	[15]
Arora *et al.* (2012)	23	Adults with T2DM	3 weeks	Emergency department at Los Angeles County Hospital (CA, USA)	Participants received daily text messages with health information including knowledge, healthy eating, exercise, self-efficacy and medication adherence	Pre–post-test	None	[16]
Babamoto *et al.* (2009)	318	Hispanic/Latinos newly diagnosed with T2DM	6 months	Inner-city family health center in Los Angeles (CA, USA)	Diabetes education and monitoring services incorporating participant preferences using CHWs or CMs	Pre–post-test	Standard provider care and noncontact control group	[17]
Bogner *et al.* (2010)	58	African–American adults aged 50+ years with HbA1c >7 and diagnosis of depression	4 weeks	Community-based primary care practice in Philadelphia (PA, USA)	An integrated CM worked with patient and provider to provide education about depression and diabetes	RCT	Usual care	[18]
Bogner *et al.* (2012)	180	Individuals with T2DM ≥30 years with diagnosis of depression	2-week run-in, 3 months	Primary care practices in Philadelphia (PA, USA)	Run-in phase and intervention phase. Integrated CM worked with patient and provider to provide education about depression and T2DM	RCT	Usual care	[19]
Brennan *et al.* (2012)	Intervention: 5123 Control: 24,124	Employees with T2DM working in a heavy industry company in the midwest where CVS Caremark was the pharmacy benefit manager	18 months	12 CVS retail pharmacies in northwest Indiana (USA)	There were two intervention groups (retail and pharmacy benefit management) and four intervention programs: general information; initiation of ACE inhibitors and/or statins; adherence enforcement; and first-fill counseling	Prospective cohort	Usual care	[20]
Castillo *et al.* (2010)	70 enrolled and 47 completed pre–post-test data	Hispanic/Latino residents with T2DM	10 weeks	Community self-care (nonclinical) centers	CHWs conducted 2-h T2DM education sessions addressing self-management	Pre–post-test design	N/A	[21]
Chan *et al.* (2011)	105	Adults with at least 5 drugs and HbA1c ≥8	9 months	Public hospital in Hong Kong	Structured pharmacist care program providing 15–30 min with pharmacist before each physician visit	RCT	Usual care	[22]
Farmer *et al.* (2012)	211	Individuals with T2DM and HbA1c value ≥7.5%, and prescribed at least one glucose-lowering oral medication	12 weeks	13 primary care practices in Oxfordshire, Buckinghamshire, Suffolk, Essex and Huntingdonshire (UK)	Patients were asked questions about their beliefs regarding taking medication regularly, positive behaviors were reinforced and problem-solving was used for negative beliefs. Patients were asked to write the exact circumstances in which they would take their medication	RCT	Usual care	[23]

BGSM: Blood glucose monitoring; CHW: Community health worker; CM: Case manager; DMSM: Diabetes mellitus self-management; N/A: Not applicable; RCT: Randomized controlled trial; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus; TOFHLA: Test of Functional Health Literacy in Adults.

Table 1. Studies meeting inclusion criteria (cont.).

Study (year)	Patients (n)	Sample population	Duration	Setting	Intervention description	Study design	Type of control	Ref.
Gialamas *et al.* (2009)	Recruited: 4968 Data analyzed: 4381	Individuals with T1DM or T2DM with hyperlipidemia or requiring anticoagulant therapy	2 years	53 Australian general practices in urban, rural and remote areas	Blood and urine samples tested using point-of-care devices within their general practices	RCT	Usual care: blood tested by usual pathology laboratory	[24]
Glasgow *et al.* (2010)	463	Heterogeneous sample of adults with T2DM	4 months	5 primary care clinics within Kaiser Permanente Colorado (CO, USA)	Internet-based DMSM program	RCT	Enhanced usual care	[25]
Glasgow *et al.* (2012)	463	Adults aged 25–75 years with a BMI of ≥25 and biweekly access to the internet	12 months	Primary clinics within Kaiser Permanente Colorado (CO, USA)	Internet-based, computer-assisted DMSM compared with computer-based program with social support	Pragmatic RCT	Enhanced usual care: computer-based risk appraisal	[26]
Grant *et al.* (2003)	232	Individuals with T2DM who had undergone laboratory testing in the preceding year and had visited the clinic 6 months preceding the study	3 months	Academic-affiliated community health center	Pharmacist administered detailed questionnaires, provided tailored education regarding medication use and help with appointment referral	Prospective RCT	Usual care	[27]
Jarab *et al.* (2012)	171	Adults with T2DM attending an outpatient diabetes clinic	6 months	Royal Medical Services Hospital (Jordan)	A clinical pharmacist-led pharmaceutical care program delivered antidiabetic therapy and adjunct therapy to patients	RCT	Usual care	[28]
Kim *et al.* (2006)	45	Individuals aged ≥30 years with internet at home	12 weeks	Urban area in South Korea	Used online site to enter and monitor blood glucose levels and drug information, with support from a nurse through weekly SMS messages	Quasi-experimental, 1 group, pre–post-test	N/A	[29]
Krass *et al.* (2005)	188	Diagnosed with T2DM, taking >3 medications, aged 18–85 years, able to complete questionnaires	9 months	Regions of New South Wales (Australia)	Patients were given instructions on BGSM using MediSense; diabetes history, information on quality of life, medication adherence, clinical data and medication history were used to develop patient protocols; intervention strategies included BGSM levels, education about the disease and medications, adherence devices, reminders, and regular follow-up	Parallel group, repeated measure design	Usual care	[30]
Negarandeh *et al.* (2013)	135	Adults diagnosed for >6 months with low literacy (TOFHLA ≤59)	6 weeks	Diabetes clinic in Kurdistan	Two educational strategies (teach back and pictorial image) using the same educational content	RCT	Usual diabetes education	[31]

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Table 1. Studies meeting inclusion criteria (cont.).

Study (year)	Patients (n)	Sample population	Duration	Setting	Intervention description	Study design	Type of control	Ref.
Odegard *et al.* (2005)	77	Adults with T2DM taking at least one oral T2DM medication and HbA1c ≥9%	12 months	Nonprofit medical clinics in greater Seattle area (WA, USA)	Pharmacist intervention with a developed T2DM care plan and pharmacist–patient/ pharmacist–provider communication on patient progress	RCT	Usual care	[32]
Odegard *et al.* (2012)	265	Patients with T2DM taking oral T2DM medications and late for refills by ≥6 days	18 months	Four community chain pharmacies in Seattle (WA, USA)	Telephone-initiated adherence support by pharmacists following missed refill alerts from computer	RCT	Usual care	[33]
Rubak *et al.* (2011)	80	Individuals aged 40–69 years with T2DM	12 months	Denmark	Effect of motivational interview training on general practitioners and quality of care measures in patients with T2DM	RCT	Standard care	[34]
Tan *et al.* (2011)	164	Adults with poorly controlled T2DM	12 weeks	Malaysia	Brief structured diabetes education program based on self-efficacy	Single-blinded RCT	Standard care	[35]
Thiebaud *et al.* (2008)	2598	Adults that did not opt out of care management	2 years	Florida Medicaid beneficiaries (FL, USA)	Telephone education of Medicaid beneficiaries on chronic diseases and increasing self-management abilities	Cohort	Matched moderate-to-high risk beneficiaries with diabetes	[36]
Thoolen *et al.* (2008)	227	Individuals aged 50–70 years and receiving treatment	12 weeks	The Netherlands	Group meetings to teach necessary skills to anticipate and deal with potential barriers to goal maintenance through proactive coping	RCT	Brochure on diabetes self-management	[37]
Vervloet *et al.* (2011)	104	Adults using medication for at least 1 year with low adherence	6 months	Dutch pharmacies (The Netherlands)	Two intervention groups with electronic dispensers; one group received a SMS reminder if they had not opened their dispenser	RCT	No use of SMS with electronic monitoring	[38]
Wakefield *et al.* (2012)	302	Adults with T2DM and hypertension treated by a Veterans Affairs primary care provider	12 months	Iowa City Veterans Affairs Medical Center (IA, USA)	Patients in the intervention group entered blood pressure and blood glucose measures into a home telehealth device and received educational feedback	RCT	Usual care	[39]
Wolever *et al.* (2010)	56	Diverse sample of adults with T2DM	6 months	Community serviced by Duke University School of Medicine (NC, USA)	14 30-min integrative coaching sessions by telephone	Pre–post-test	Usual care	[40]
Zolfaghari *et al.* (2012)	77	Recruited from the Iranian Diabetes Association, aged 18–65 years, must have telephone access in their homes and have a mobile phone, must be only using oral medication	6 months	Tehran University of Medical Science (Iran)	The SMS group received 6 messages/week regarding exercise, taking T2DM medication, diet, BGSM and stress management. The telephone group involved scheduling appointments, counseling about the nature of the disease, risk factors, importance of maintaining normal blood glucose levels, diet, exercise, medication taking, illness management and how to record blood glucose levels	Quasi-experimental, 2 groups, pre–post-test	Parallel intervention, no control group	[41]

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evidence available in the literature. The risk of bias across studies is discussed in this article and the discussion gives more weight to studies using a RCT design.

Results

■ Study selection

Figure 1 shows the results of the search. After duplicates were removed, the search resulted in 922 citations for review. Title review produced 171 abstracts to examine, after which 56 articles were determined eligible for full article review. Twenty-seven eligible studies were identified based on the predetermined eligibility criteria [15–41]. Seventeen studies showed a statistically significant change in medication adherence for interventions with or without comparison groups, and ten studies reported significant statistical changes in glycemic control. Seven of the studies described interventions that significantly improved both medication adherence and HbA1c.

■ Study characteristics & results of individual studies

Table 1 provides a summary of the 27 studies that were eligible for inclusion; these studies are heterogeneous in terms of sample size, sample population, length of duration, setting, intervention description, study design and use of a control group. Sample sizes ranged from 23 to 29,247, and intervention duration stretched from 2 weeks to 2 years. Eighteen of the studies were RCTs [15,18–19,22–28,31–35,37–39], four were pre–post-test [16–17,21,40], two combined quasiexperimental with pre- and post-tests [29,41], two were cohorts [20,36], and one used a parallel group with repeated measure design [30]. Twenty-three of the studies used a control group for comparisons [15,17–20,22–28,30–40]. All of the studies focused on adults with T2DM [15–41], but one study also included individuals diagnosed with Type 1 diabetes [24]. Thirteen of the 27 articles were conducted in international locations [15,22–24,28–31,34–35,37–38,41].

Table 2 presents the medication adherence outcomes of studies meeting the inclusion criteria [15–41]. The mean baseline medication adherence was wide ranging and fluctuated throughout the studies, particularly given the variety of adherence methods – direct and indirect – used. Direct measures of adherence indicate that medications have actually been taken by the patients and indirect measures, those most commonly used, infer an assumption that medications have been taken by patients [11]. No direct methods for measuring medication adherence were used. All forms of indirect methods were used, with 18 studies measuring medication adherence by self-report [15–17,21,23–32,35,37,39–41], two by pill count [22,33], three by electronic devices [18–19,38], and three by pharmacy claims data [20,34,36]. Of the 27 studies, 13 reported statistically significant differences in medication adherence in the intervention group compared with the control group [15,17–20,22,24,28,30–31,33,36,40]. All four studies without a control group reported statistically significant changes in medication adherence [16,21,29,41].

Table 3 shows glycemic control outcomes of the studies that met the eligibility criteria [15–23,25–30,32,34–35,39–42] for which the impact on glycemic control was noted. The mean baseline HbA1c ranged from 6.8 to 10.6. One of the studies included in this review [39] reported outcomes for medication adherence and glycemic control in two separate papers; thus, a second article using the same population and intervention, reporting the differences in HbA1c between groups, is reported in **Table 3** [42]. Eight out of 18 studies demonstrated statistically significant improvements in HbA1c between the intervention groups and the control groups [15,17–19,22,28,34–35]. In these studies, the percentage change in HbA1c in the intervention group ranged from -1.57 to -0.15 compared with -2.1 to +0.2 in the control group; this also varied at different time points within the studies. Of the four studies without a control group, two described statistically significant changes in HbA1c [21,29]. For one study, there was a -0.6% drop in the HbA1c, while the percentage change was -1.1% in the other.

Table 4 illustrates intervention characteristics of the 27 studies included in this review. Most studies did not employ a theoretical foundation [15–16,20–22,24–25,27–34,36,38–41], but for those that did, one study used the Theory of Planned Behavior [23], one used the Transtheoretical Model [17], two used a self-efficacy theory [35,37], two used integrated care [18–19], and one used the Social–Cognitive Theory [26]. As for the intervention characteristics, five out of the 27 studies were culturally tailored [16,18,31,38–39], of which four were significant for changes in medication adherence and HbA1c. Self-management was the focus of several interventions, with 18 concentrating on

Table 2. Medication adherence outcomes of studies meeting inclusion criteria.

Study (year)	Measure of medication adherence	Mean ± SD baseline medication adherence	Intervention mean ± SD change in medication adherence	Control mean ± SD change in medication adherence	Statistical significance	Ref.
Al Mazroui *et al.* (2009)	Self-report: forgetting, missing or increasing doses	Intervention: 48.3% nonadherent Control: 49.1% nonadherent	21.4% of intervention group were nonadherent at 12-month follow-up	32.5% of control group were nonadherent at 12-month follow-up	Glycemic control and health-related quality of life were significantly improved after receiving patient education and medication adherence advice ($p = 0.003$)	[15]
Arora *et al.* (2012)	Self-report: MMAS	Score of 3.5 on MMAS	Score of 4.75 on MMAS at 3-week follow-up	No control group	The pilot intervention demonstrated increased healthy behaviors with improved diabetes self-efficacy and medication adherence	[16]
Babamoto *et al.* (2009)	Self-report (percentage who never forget to take medication)	Intervention: CHW: 69% never forgot to take medication CM: 77% never forgot to take medication Control: 67% never forgot to take medication	79% never forgot to take medication in the CHW intervention, 55% never forgot to take medication in the CM intervention	50% never forgot to take medication in the control group	Medication-taking behavior remained unchanged ($p > 0.05$) in the CHW group, but worsened in the CM and control groups ($p < 0.05$)	[17]
Bogner *et al.* (2010)	Electronic monitoring (MEMS >80% adherent)	34.5% intervention 20.7% control	62.1%	24.1%	Proportion of participants who had 80% adherence to hypoglycemic agent was greater in the intervention than the control group ($p = 0.004$)	[18]
Bogner *et al.* (2012)	Electronic monitoring (MEMS >80% adherent)	42.0% intervention 35.9% control	At 6 weeks, the intervention group was 61% adherent, and 65% adherent at 12 weeks	At 6 weeks, the control group was 35% adherent, and 30% adherent at 12 weeks	At 6 and 12 weeks, those in the intervention group had significant improvement in adherence compared with usual care ($p \leq 0.001$)	[19]
Brennan *et al.* (2012)	Total number of days of medication supplied per month	CVS Retail: Intervention: No recent use of ACE inhibitors: 31.2% No recent use of statins: 32.6% Control: No recent use of ACE inhibitors: 31.6% No recent use of statins: 32.4% Mail order: Intervention: No recent use of ACE inhibitors: 32.1% No recent use of statins: 32.8% Control: No recent use of ACE inhibitors: 31.3% No recent use of statins: 31.9%	3.9% increase in supply per month in retail intervention group compared with control group; 1.7% increase in supply per month in mail order intervention group compared with control group	N/A	There was a statistically significant difference between the two interventions ($p < 0.01$)	[20]

BMQ: Brief medication questionnaire; CHW: Community health worker; CM: Case manager; MARS: Medication adherence report scale; MEMS: Medication Event Monitoring System; MMAS: Morisky Medication Adherence Scale; MPR: Medication possession rate; N/A: Not applicable; RTMM: Real-time medication monitoring; SD: Standard deviation; SDSCA: Summary of diabetes self-care activities; T2DM: Type 2 diabetes mellitus.

Table 2. Medication adherence outcomes of studies meeting inclusion criteria (cont.).

Study (year)	Measure of medication adherence	Mean ± SD baseline medication adherence	Intervention mean ± SD change in medication adherence	Control mean ± SD change in medication adherence	Statistical significance	Ref.
Castillo *et al.* (2010)	Self-report: SDSCA	5.5 ± 2.5 (pretest)	6.6 ± 1.3 (post-test)	N/A	Significant pre–post improvement in adherence (p = 0.009)	[21]
Chan *et al.* (2012)	Pill count (percentage that are at least 80% compliant based on number taken as a percentage of correct amount)	73.6% intervention 82.1% control	The proportion of individuals who were at least 80% adherent increased by 22.5 ± 13.4%	The proportion of individuals who were at least 80% adherent increased 2 ± 5.0%	Intervention group had greater improvement in compliance compared with control (p < 0.001)	[22]
Farmer *et al.* (2012)	Self-report: MARS (scale: 5–25)	Intervention: 23.6 ± 2.3 score on MARS Control: 23.6 ± 2.8 score on MARS	23.6 ± 2.6 score on MARS; -0.4 (95% CI: -1.0 to 0.2)	24.1 ± 1.6 score on MARS	There was no statistically significant difference between the control and intervention groups (p = 0.2)	[23]
Gialamas *et al.* (2009)	Self-report via the MARS-5	Median score of 24 (maximum score: 25)	N/A	N/A	Intervention group had higher adherence than controls with a noninferiority margin of -4.1% (39.3 vs 37.0%; p < 0.001)	[24]
Glasgow *et al.* (2010)	Self-report: Hill–Bone Compliance Scale (scale: 0–1)	Intervention score: 3.80 ± 0.29 Control score: 3.77 ± 0.30	3.84 ± 0.29	3.79 ± 0.39	No significant improvements in adherence (p = 0.262)	[25]
Glasgow *et al.* (2012)	Self-report: Hill–Bone Compliance Scale (scale: 0–1)	Intervention score: 0.35 ± 0.03 Control score: 0.34 ± 0.04	Postintervention scores: 4 months: 0.42 ± 0.03 12 months: 0.43 ± 0.03	Poststudy scores: 4 months: 0.38 ± 0.04 12 months: 0.41 ± 0.04	No statistical significance between interventions and control groups	[26]
Grant *et al.* (2003)	Self-report: number of days without missing medication	Intervention: 6.7 ± 0.9 days without missing medication in the past 7 days Control: 6.9 ± 0.4 days without missing medication in the past 7 days	0.1 ± 1 days without missing medication in the past 7 days at 3-month follow-up	0.1 ± 0.4 days without missing medication in the past 7 days at 3-month follow-up	There was not a statistically significant difference when comparing the intervention and control groups (p = 0.8)	[27]
Jarab *et al.* (2012)	Self-report: MMAS	Intervention: 74.1% nonadherent Control: 70.9% nonadherent	28.6% of the intervention group were nonadherent postintervention at 6-month follow-up	64.6% of the control group were nonadherent postintervention at 6-month follow-up	At the 6-month follow-up intervention patients were more adherent to medications than the control group (p = 0.003)	[28]
Kim *et al.* (2006)	Self-report: number of days in week when medication was taken	4.8 ± 2.6 days	+1.1 days	N/A	There was a statistically significant change in the number of days of medication adherence in a week in the intervention group (p = 0.032)	[29]

BMQ: Brief medication questionnaire; CHW: Community health worker; CM: Case manager; MARS: Medication adherence report scale; MEMS: Medication Event Monitoring System; MMAS: Morisky Medication Adherence Scale; MPR: Medication possession rate; N/A: Not applicable; RTMM: Real-time medication monitoring; SD: Standard deviation; SDSCA: Summary of diabetes self-care activities; T2DM: Type 2 diabetes mellitus.

Table 2. Medication adherence outcomes of studies meeting inclusion criteria (cont.).

Study (year)	Measure of medication adherence	Mean ± SD baseline medication adherence	Intervention mean ± SD change in medication adherence	Control mean ± SD change in medication adherence	Statistical significance	Ref.
Krass *et al.* (2005)	Self-report: BMQ (scale: 0–7)	Intervention: 1.38 ± 1.20 BMQ score Control: 1.01 ± 0.88 BMQ score	BMQ score of 0.94 ± 0.89	BMQ score of 1.16 ± 0.88	The BMQ scores were statistically significant when comparing the intervention and control groups ($p = 0.009$)	[30]
Negarandeh *et al.* (2013)	Self-report: MMAS (scale: 1–7)	Intervention: Picture intervention: 4.33 ± 1.62 Teach back intervention: 4.37 ± 1.46 Control: 4.52 ± 1.74	Picture intervention: 6.73 ± 1.52 Teach back intervention: 7.03 ± 0.99	Control: 4.32 ± 1.58	Significant difference between two intervention groups and the control group ($p < 0.001$), but no difference between intervention groups ($p = 0.56$)	[31]
Odegard *et al.* (2005)	Self-report: two-question recall validated in a chronic disease model	Intervention: 56% had difficulty remembering to take medications as prescribed Control: 35% had difficulty remembering to take medications as prescribed ($p = 0.07$)	Not reported	N/A	The intervention had no effect on adherence ($p = 0.49$) and the control group had better adherence throughout the study ($p = 0.03$)	[32]
Odegard *et al.* (2012)	Refill rate based on MPR at 6 and 12 months	Intervention: 74% had MPR above 80% for previous 12 months Control: 65% had MPR above 80% for previous 12 months	MPR scores at 6 and 12 months improved significantly within the group ($p = 0.16$ and $p<0.01$, respectively)	MPR remained unchanged at 6 and 12 months	Intervention group significantly more likely to have an MPR >80% at 12 months (odds ratio: 4.77; 95% CI: 2.00–11.4)	[33]
Rubak *et al.* (2011)	Number of prescriptions 'cashed in' by patients at pharmacy compared with number of prescriptions prescribed	N/A	Oral antidiabetic medication: 37% cashed in compared with 39% prescribed	Oral antidiabetic medication: 36% cashed in compared with 36% prescribed	There were no statistically significant differences in the number of prescriptions cashed in compared with the number of prescriptions prescribed. No effect of motivational interviewing on medication adherence was found	[34]
Tan *et al.* (2011)	Self-report (percentage that are 90% adherent based on number of times in a week medications are missed)	Intervention: 84.48% Control: 85%	89.21% reported 90% adherence based on number of times in a week medications are missed (91.42% were adherent when adjusted for changed adherence due to hyperglycemia)	84.48% were 90% adherent based on number of times in a week medications are missed	No difference in adherence between groups unless adjustments in insulin were considered adherent, in which case there was a significant difference ($p = 0.008$)	[35]

BMQ: Brief medication questionnaire; CHW: Community health worker; CM: Case manager; MARS: Medication adherence report scale; MEMS: Medication Event Monitoring System; MMAS: Morisky Medication Adherence Scale; MPR: Medication possession rate; N/A: Not applicable; RTMM: Real-time medication monitoring; SD: Standard deviation; SDSCA: Summary of diabetes self-care activities; T2DM: Type 2 diabetes mellitus.

Table 2. Medication adherence outcomes of studies meeting inclusion criteria (cont.).

Study (year)	Measure of medication adherence	Mean ± SD baseline medication adherence	Intervention mean ± SD change in medication adherence	Control mean ± SD change in medication adherence	Statistical significance	Ref.
Thiebaud *et al.* (2008)	Pharmacy claims data (proportion users with MPR ≥80%)	Intervention: 30.3% had an MPR ≥80% Control: 33% had an MPR ≥80%	Care managed vs not care managed +8.7% nonusers at baseline +6.9% users at baseline	N/A	Care-managed patients were more likely to have a higher MPR ($p < 0.001$)	[36]
Thoolen *et al.* (2008)	Self-report: MARS (scale: 1–5)	Intervention: 4.8 MARS score Control: 4.9 MARS score	MARS score of 4.9 at 3 and 12 months	MARS score of 5.0 at 3 and 12 months	There was no statistically significant difference between the intervention and control groups	[37]
Vervloet *et al.* (2011)	Electronic monitoring (RTMM measuring the number of days without dosing, proportion of missed doses and proportion of doses in standardized time)	Not reported	Days without dosing: 11.9 ± 18.8 Missed doses: 14.5 ± 15.7 Doses taken in agreed time: 56.7 ± 23.8	Days without dosing: 13.8 ± 14.5 Missed doses: 19.2 ± 16.0 Doses taken in agreed time: 38.7 ± 23.0	Patients who received reminders took doses within agreed upon window ($p = 0.003$), but showed no difference in days without dosing ($p = 0.283$) or missed doses ($p = 0.065$)	[38]
Wakefield *et al.* (2012)	Self-report: T2DM Regimen Adherence Scale	Low- and high-intensity intervention: 99.7% adherence Control: 99.5% adherence	Low-intensity intervention: 99.8% adherence at 6-month follow-up and 99.7% at 12 months High-intensity intervention: 99.6% at 6-month follow-up and 100% at 12-month postintervention	99.6% at 6-month follow-up; 98.9% at 12-month postintervention	Reported medication adherence was high across groups at all three time points. No significant changes were found. At 12 months postintervention $p = 0.20$	[39]
Wolever *et al.* (2010)	Self-report: MMAS	Intervention: 6.7 ± 0.96 MMAS score Control: 6.7 ± 1.25 MMAS score	Postintervention: 7.2 ± 0.97 MMAS score	Poststudy: 6.9 ± 1.25 MMAS score	There was a statistically significant improvement in the intervention group compared with control goup ($p = 0.004$)	[40]
Zolfaghari *et al.* (2012)	Self-care: T2DM questionnaire	SMS: 75.48 ± 14.33 Telephone: 73.27 ± 14.75	SMS: 15.65 ± 2.72 change in adherence score Telephone: 21.46 ± 7.12 change in adherence score	N/A	There was a statistically significant difference between the intervention and control groups ($p = 0.000$)	[41]

BMQ: Brief medication questionnaire; CHW: Community health worker; CM: Case manager; MARS: Medication adherence report scale; MEMS: Medication Event Monitoring System; MMAS: Morisky Medication Adherence Scale; MPR: Medication possession rate; N/A: Not applicable; RTMM: Real-time medication monitoring; SD: Standard deviation; SDSCA: Summary of diabetes self-care activities; T2DM: Type 2 diabetes mellitus.

Table 3. Glycemic control outcomes of studies meeting inclusion criteria.

Study (year)	Mean ± SD baseline HbA1c (%)	Intervention mean ± SD change in or mean ± SD postintervention HbA1c (%)	Control mean ± SD change in medication adherence	Statistical significance	Ref.
Al Mazroui *et al.* (2009)	Intervention: 8.5 Control: 8.4	7.6 at 4-month follow-up 7.1 at 8-month follow-up 6.9 at 12-month follow-up	8.0 at 4-month follow-up 8.4 at 8-month follow-up 8.3 at 12-month follow-up	The care program resulted in better glycemic control for intervention patients compared with control ($p < 0.001$)	[15]
Babamoto *et al.* (2009)	CHW: 8.6 CM: 8.5 Standard care control: 9.5 Noncontact control: 7.5	CHW: 7.2 CM: 7.4	Standard care control: 7.4 Noncontact control: 7.7	Mean HbA1c decreased in CHW, CM and standard care control ($p < 0.05$). No decrease seen in noncontact control group ($p > 0.05$)	[17]
Bogner *et al.* (2010)	Intervention: 7.3 Control: 7.3	6.7 ± 2.3	7.9 ± 2.6	Participants who received intervention had lower HbA1c ($p = 0.019$)	[18]
Bogner *et al.* (2012)	Intervention: 7.2 Control: 7.0	-0.70 ± 1.32	0.50 ± 1.11	Significantly improved mean change in HbA1c compared with usual care ($p < 0.001$)	[19]
Castillo *et al.* (2010)	8.39 ± 1.96	7.79 ± 1.67	N/A	Significant pre–post-test reduction in HbA1c ($p < 0.001$)	[21]
Chan *et al.* (2012)	Intervention: 9.7 Control: 9.5	-1.57	-0.4	HbA1c reduced in intervention group compared with control group ($p < 0.001$)	[22]
Farmer *et al.* (2012)	Intervention: 8.37 ± 1.25 Control: 8.28 ± 1.22	8.34 ± 1.24	Control: 8.21 ± 1.32	There was no statistically significant difference between the intervention and control group ($p = 0.64$)	[23]
Glasgow *et al.* (2010)	Intervention: 8.13 ± 1.80 Control: 8.06 ± 1.76	7.95 ± 1.58	8.00 ± 1.58	No significant improvements in HbA1c ($p = 0.145$)	[25]
Glasgow *et al.* (2012)	Intervention: 8.14 ± 0.10 Control: 8.16 ± 0.16	8.00 ± 0.09 at 4 months 8.16 ± 0.09 at 12 months	8.02 ± 0.14 at 4 months 8.04 ± 0.14 at 12 months	No significant difference between combined interventions and control	[26]
Grant *et al.* (2003)	Intervention: 7.7 ± 1.7 Control: 7.5 ± 1.1	Not reported	Not reported	Not reported	[27]
Jarab *et al.* (2012)	8.5	-0.8 at 6 months postintervention	+0.1 at 6 months postintervention	Patients in the intervention showed significant improvement in HbA1c levels compared with the control group ($p = 0.019$)	[28]
Kim *et al.* (2006)	8.1 ± 2.1	-1.1 ± 2.1	No control	Significant change in mean HbA1c in intervention ($p = 0.006$)	[29]
Odegard *et al.* (2005)	Intervention: 10.2 ± 0.8 Control: 10.6 ± 1.4 ($p = 0.11$)	-1.5 at 6 months -2 at 12 months		Mean HbA1c did not differ between groups after 12 months ($p = 0.61$); however, there was a significant decrease in HbA1c over time for both groups ($p = 0.001$)	[32]
Rubak *et al.* (2011)	Intervention: 6.9 Control: 6.8	-0.7 at 12 months postintervention	-0.7 at 12 months postintervention	Significant improvements were seen in both groups postintervention ($p < 0.01$). No statistically significant difference reported between groups	[34]
Tan *et al.* (2011)	Intervention: 9.9 Control: 9.6	8.75	9.67	Significant decrease in HbA1c relative to control ($p < 0.001$)	[35]

CHW: Community health worker; CM: Case manager; SD: Standard deviation.

Table 3. Glycemic control outcomes of studies meeting inclusion criteria (cont.).

Study (year)	Mean ± SD baseline HbA1c (%)	Intervention mean ± SD change in or mean ± SD postintervention HbA1c (%)	Control mean ± SD change in medication adherence	Statistical significance	Ref.
Wakefield *et al.* (2012)	Low-intensity intervention: 7.2 High-intensity intervention: 7.1 Control: 7.2	Low intensity: -0.4 at 6 months, -0.44 at 12 months High intensity: -0.17 at 6 months, -0.19 at 12 months	-0.07 at 6 months 0.33 at 12 months	Intervention subjects had decreased HbA1c compared with control group at 6 months ($p = 0.003$), but did not significantly differ from control group at 12 months ($p = 0.65$)	[39]
Wolever *et al.* (2010)	Intervention: 7.9 ± 1.98 Control: 8.1 ± 1.92	7.5 ± 1.76	8.2 ± 1.92	No significant effects on HbA1c, but intervention group with HbA1c ≥7% showed 0.64% reduction by 6 months ($p = 0.03$)	[40]
Zolfaghari *et al.* (2012)	Interventions: SMS: 8.97 ± 1.65 Telephone: 9.44 ± 1.72	SMS: -1.01% ± 0.01 Telephone: -0.93% ± 0.13	Not reported	There was no statistically significant difference between the interventions ($p = 0.489$)	[41]

CHW: Community health worker; CM: Case manager; SD: Standard deviation.

education [16–18,20–23,25–26,28,31–32,34–36,39,41], nine focusing on skills training [15–18,20–21,35–37], and 13 helping with problem-solving [16–18,20–21,26–28,31,35–37,41]. Twelve of the studies emphasizing education – five focusing on skills and seven assisting with problem-solving – were significant for variations in medication adherence and/or HbA1c between groups and/or at different time points. Eight used monitoring data, such as providing results of self-monitored blood glucose readings to the provider [15,25,27,29,31,40–41] and, of these, four were significant for differences in medication adherence and/or HbA1c. Fifteen studies provided one-on-one counseling to patients [17–20,22,24,28–29,31–33,35–36,40–41] and 13 studies were significant for changes in medication adherence and/or HbA1c. The study designs for most of the interventions using one-on-one interactions were RCTs. A total of 14 studies utilized telehealth/telemedicine technology: mobile phones [22,28,33,40], telephones [15,17,23,26,30,36,38–40] and the internet [18]. Of those using health technologies, three of the mobile usage studies and seven of the studies using telephones were significant for differences in medication adherence and/or HbA1c. The study using internet delivery did not show significant differences. Facilitators were used for intervention delivery in some studies: eight used nurse educators [17,25,27,31,34,36–37,40], one used certified diabetes educators (CDEs) [35] and three used CHWs [16,31,34]. Six involved collaboration with the patients' physicians [23,26,29–30,38–39]. Of the studies using facilitators that demonstrated statistical significance in medication adherence, five used nurses, three used CHWs and six used pharmacists. Five of the six studies collaborating with physicians were significant for medication adherence and/or HbA1c. Using CDEs showed statistical significance only for HbA1c, as did two of the studies using nurses and CHWs, and three using pharmacists and physician collaborations.

In this review, effective medication adherence was defined as a significance improvement at $p < 0.05$. It is worth mentioning that out of the 17 articles showing statistical significance in medication adherence, eight were RCTs, four used a pre–post design, two were cohort studies, two were quasiexperimental with pre–post designs, and one used a parallel-group, repeated-measure design. The remaining studies were all RCTs, one of the strongest research designs, and did not show a statistically significant difference

Table 4. Characteristics of interventions in studies meeting inclusion criteria.

Study (year)	Theoretical basis	Culturally tailored	Education	Skills training	Uses monitoring results	Mobile phone use	One-on-one interaction	Internet based
Al Mazroui *et al.* (2009)	None reported		x	x				
Arora *et al.* (2012)	Not reported		x			x		
Babamoto *et al.* (2009)	Transtheoretical Model	x	x		x		x	
Bogner *et al.* (2010)	Integrated care	x	x				x	
Bogner *et al.* (2012)	Integrated care	x	x				x	
Brennan *et al.* (2012)	Not reported						x	
Castillo *et al.* (2010)	Not reported	x	x	x				
Chan *et al.* (2012)	Not reported		x				x	
Farmer *et al.* (2012)	Theory of Planned Behavior				x			
Gialamas *et al.* (2009)	Not reported						x	
Glasgow *et al.* (2010)	Not reported	x	x	x				x
Glasgow *et al.* (2012)	Social–Cognitive Theory		x		x			
Grant *et al.* (2003)	Not reported		x					
Jarab *et al.* (2012)	Not reported		x				x	
Kim *et al.* (2006)	Not reported				x	x	x	
Krass *et al.* (2005)	Not reported				x			
Negarandeh *et al.* (2013)	None reported		x				x	
Odegard *et al.* (2005)	None reported		x	x			x	
Odegard *et al.* (2012)	None reported			x	x		x	
Rubak *et al.* (2011)	None reported							
Tan *et al.* (2011)	Self-efficacy		x	x	x		x	
Thiebaud *et al.* (2008)	None reported		x	x			x	
Thoolen *et al.* (2008)	Self-efficacy; proactive coping			x				
Vervloet *et al.* (2011)	None reported					x		
Wakefield *et al.* (2012)	None reported		x		x			
Wolever *et al.* (2010)	None reported		x	x			x	
Zolfaghari *et al.* (2012)	Not reported		x			x	x	

in medication adherence. The study design of those showing and not showing statistically significant differences in glycemic control varied. Likewise, the studies showing a statistically significant impact on both medication adherence and glycemic control simultaneously, had RCT, pre–post and quasiexperimental designs.

Discussion

■ Summary of evidence

This systematic review was conducted to determine whether interventions for improving medication adherence in adult patients with T2DM were effective. The findings demonstrate that interventions can be designed to improve medication adherence; however, heterogeneity of the studies meeting inclusion criteria made it difficult to determine the most effective interventions. The findings may also suggest that medication adherence alone is not sufficient for achieving glycemic control and managing diabetes. This is noted by several interventions that improved medication adherence, but did not significantly improve glycemic control.

The characteristics of these interventions varied, but there are some consistencies between the studies selected for review. Education, skills training and problem-solving are vital components of diabetes management [43–46], and psychological and behavioral factors also contribute [1]. According to the US 2012 Standards for Diabetes Self-Management Education and Support, diabetes care should not simply consist of one-off education classes [47]. Instead, education should be an ongoing exchange of information between the patient and care team, and be in congruence with the progression of the chronic disease [48]. Furthermore, according

Telephone use	Assist in problem-solving	Nurse educators/case managers	Diabetes educator	Collaboration with physicians	Community health worker	Pharmacist	Statistical significance in medication adherence	Statistically significant difference in HbA1c	Ref.
	x					x	x	x	[15]
							x		[16]
	x	x			x		x	x	[17]
x				x			x	x	[18]
x				x			x	x	[19]
x				x		x	x		[20]
	x				x		x	x	[21]
						x	x	x	[22]
	x	x							[23]
							x		[24]
	x								[25]
x	x								[26]
x	x			x		x			[27]
x				x		x	x	x	[28]
		x					x	x	[29]
				x		x	x		[30]
		x			x		x		[31]
	x					x			[32]
x						x	x		[33]
								x	[34]
	x		x					x	[35]
x	x	x					x		[36]
	x	x							[37]
						x			[38]
		X							[39]
x	x	x					x		[40]
	x						x		[41]

to the American Diabetes Association (ADA), guidelines for treatment and interventions targeting T2DM should focus on patient-centered care such as increasing physical activity, modifying diet plans and improving weight loss efforts [49–50]. Of the studies reviewed, more focused on education than skills training and problem-solving. It is gratifying to observe the use of education in the interventions, but an ideal intervention would also include skills training and problem-solving, both of which are crucial to achieve glycemic control. Among the studies addressing education, skills training or problem-solving, the topics included diabetes knowledge and beliefs, self-management and use of medications. Some interventions addressed problem-solving through action plans and goal setting, while others used open-ended questions and time for discussion of patient concerns. The importance of education, skills training and problem-solving are evident and must be utilized when discussing medication adherence and glycemic control with patients.

One-on-one counseling was an effective approach used in over half (55%) of the studies that included this method as an intervention component. Among studies using individual counseling, the topics discussed included self-efficacy, self-management, adherence and overcoming potential barriers to care. The US 2012 Standards for Diabetes Self-Management Education and Support reports the use of a continuous interdisciplinary team, including diabetes and community clinicians, and lay persons, for the ongoing treatment and support of diabetes care [47]. The facilitator used to conduct the interventions during these sessions varied, but used either nurse educators/case managers, CDEs, CHWs or pharmacists, and several documented collaborations with physicians, who are essential to any diabetes self-management plan [43]. Pharmacists seemed to be the most effective facilitators, but nurse educators and CHWs were also employed effectively. Research suggests that approximately 75% of patients receiving medications from community pharmacists are adherent [1]. Interventions using certified diabetes educators were not frequently designed and, compared with other facilitators, were not as effective in significantly improving medication adherence. Including physicians in the interventions and interactions with patients was beneficial in the studies reviewed in this article; however, there are inconsistent results in adherence when using clinicians such as nurses and dieticians [1]. These findings suggest that the use of facilitators, especially pharmacists, is effective in improving medication adherence. In addition, although smaller in numbers compared with pharmacists and nurse educators, using CHWs and CDEs was also effective. Rothschild and colleagues report that CHWs, for example, are ideal facilitators because they have similarities – culture, language and resources – with the patients enrolled in the studies, and may be more effective at engaging the patients compared with clinicians [51]. The efficacy of facilitators such as CHWs, however, has not been well established in the literature. Therefore, more research is needed to examine the role of facilitators in medication adherence. Furthermore, it is worth mentioning that future research should examine the role facilitators serve as sources of social support for patients with T2DM [52] and the impact this may have on glycemic control.

Health technologies were used in some studies included in this review. The use of telemedicine has grown as providers recognize its ability to increase access to expert care [53]. At present, the internet and mobile phones are often used to increase adherence and address unintentional causes of nonadherence such as forgetfulness and not knowing how to use or take medications, especially when complex medication regimens are prescribed [2]. The use of telemedicine in populations with T2DM may provide a way to increase contact with patients and expand the one-on-one contact beyond office visits. For example, Vervloet and colleagues found positive short-term effects on adherence in a systematic review of studies using SMS reminders on mobile phones [54]. Based on the success seen in the articles reviewed, the effectiveness of telemedicine in improving medication adherence should be further investigated.

In a previous review describing methods used for assessing medication adherence in research and clinical trials, Farmer explains that no single measure of medication adherence is superior and that the method used must be specific for the situation [11]. A Cochrane review of interventions for improving adherence to treatment recommendations in people with T2DM also stressed the difficulties of drawing solid conclusions from adherence research and the need for more research in this area [14]. Additionally, according to WHO, it may be necessary to assess the level of adherence by each individual component involved in treatment, such as self-monitoring of blood sugars, administering and taking prescribed medications, eating an appropriate diet, increasing physical activity and seeking preventive services, including eye and foot examinations, rather than using a single measure to assess medication adherence [1].

The variety of methods used for assessing medication adherence was evident in this review and may have influenced the significant differences observed. For example, several studies demonstrated statistical changes in medication adherence, but did not show the same in glycemic control. This may infer that taking medications alone is not sufficient for improving HbA1c. Furthermore, it was not always clear whether other aspects of diabetes management were used in the intervention and analyses, thus making it difficult to determine whether the intervention significantly impacted upon medication adherence or was a product of combined management efforts. More research should be conducted to assess the need for a clear and uniform definition and measure of adherence. In addition, future studies should examine whether medication adherence is an appropriate variable for reliably predicting glycemic control.

Finally, it is important to understand that the design of the intervention may also contribute to the significance or lack thereof in outcomes such as medication adherence and glycemic control. Significance may vary based on the short- and long-term goals of an intervention. In a study to identify causes of nonadherence with medications, Hugtenburg and colleagues recognized the reasons why patients might not adhere to medication regimens or might be unsuccessful in intervention trials [2]. These reasons included complex interventions and nontailored interventions not meeting the specific needs of the patients. These findings suggest the need for more research into simplifying medication regimens and interventions. Reasons for nonadherence must also be detected and discussed. Patients, in collaboration with their care teams, should examine methods for improving compliance and generating solutions to address problems with adherence.

Limitations

This study has four limitations that should be mentioned. First, the search was limited to articles published in the English language between January 2000 and May 2013. Second, the review was limited to studies using interventions addressing medication adherence as an outcome. By including the studies that assessed medication adherence by intervention only, evidence from other study designs, such observational and/or nonexperimental designs, was not presented here, and may have demonstrated different results. As a result of that exclusion, future reviews investigating medication adherence in multiple study designs are warranted. Third, since studies with positive results are more likely to be published, the studies in this review may reflect publication bias. Fourth, the diversity of the studies and the heterogeneous methodology prevented a meta-analysis from being performed. Conclusions from this review are, therefore, qualitative and meant to guide future research rather than serve as conclusive answers.

Conclusion & future perspective

Based on this review, more research is needed to identify effective interventions for improving medication adherence in T2DM. Our findings show that it is difficult to identify the interventions with the most profound effect on improving diabetes-related outcomes. However, this review did find a number of characteristics that may influence medication adherence based on statistical significance of results. These include targeted educational components that are used while engaging patients in skills building and problem-solving; one-on-one counseling using facilitators such as pharmacists, nurse educators or CHWs; and use of health technologies including cell phones and the internet.

Additionally, our findings suggest that medication adherence is not solely responsible for achieving glycemic control. Not all studies that found significant changes in medication adherence found similar changes in glycemic control. Previous evidence suggests that patient-level factors account for 90–95% of the variance seen in glycemic control [55,56]. This variance is not solely due to taking medications, but also to eating a healthy and appropriate diet, maintaining a healthy weight, increasing physical activity, identifying applicable risk factors, being motivated, and practicing preventive care [7]. This is supported by the definition of adherence reported by WHO, where adherence encompasses health-related behaviors in addition to taking prescribed medications [1]. Having access to the medications and taking the medications as prescribed are imperative; however, medications alone are not sufficient for successful disease management and treatment.

Providers and health systems must take the onus of the improving medication adherence and not consider adherence the sole responsibility of the patient. WHO suggests that patients must be supported and not blamed for problems with adherence [1]. Wolpert and Anderson recognized goal setting and encouragement as critical components to engaging patients in behavior changes that ultimately lead to improved glycemic control [57]. They stress the importance of distinguishing between standardized, clinical goals that may often be unattainable by the patient, and patient goals that are more realistic and likely to lead to tighter glycemic control. Additionally, the ADA suggests the development of personalized plans by the patient and care team that are specific to individual patients (i.e., patient-specific symptoms, comorbid conditions, age, weight, race/ethnicity, gender and lifestyle) [50]. This is an important factor in improving disease management, glycemic control and quality of life.

Finally, investigation into the clear, acceptable and applicable definitions and measures of medication adherence, and whether outcomes adequately predict or reflect appropriate adherence are important. The factors that influence medication adherence must be recognized and relayed to patients with T2DM in simple terms to improve empowerment, adherence and, ultimately, outcomes. This is particularly true since diabetes management is multidimensional and not solely based on adhering to a medication regimen. A Cochrane review on interventions for enhancing medication adherence reported current methods for improving medication adherence as being complex and ineffective [58].

In conclusion, research must continue to emphasize the benefits of medication adherence and tailor interventions that optimize diabetes management. Medication adherence may vary based on demographic characteristics (i.e., race/ethnicity, gender and age), culture and social determinants of health. Factors that influence medication adherence must be identified and addressed as they emerge and change to allow for better overall control of chronic disease burden. Patients, providers and health systems should take ownership of their respective roles in order to improve medical adherence and diabetes-related outcomes.

Financial & competing interests disclosure

This work was supported by the National Institute of Diabetes and Digestive Kidney Disease (NIDDK; award number 5K24DK093699-02). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

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