Abstract

Background
The global prevalence of diabetes is increasing. Medications are a recommended strategy to control hyperglycaemia. However, patient adherence can be variable, impacting health outcomes. A range of interventions for patients with type 2 diabetes have focused on improving treatment adherence. This review evaluates the impact of these interventions on adherence to anti-diabetic medications and focuses on the methods and tools used to measure adherence.

Method
Medline, Embase, CINAHL, IPA, PUBmed, and PsychINFO were searched for relevant articles published in 2000–2013, using appropriate search terms.

Results
Fifty two studies addressing adherence to anti-diabetic medications in patients with type 2 diabetes met the inclusion criteria and were reviewed. Each study was assessed for research design, method(s) used for measuring medication adherence, and impact of intervention on medication adherence and glycaemic control. Fourteen studies were published in 2000–2009 and 38 in 2010–2013. Twenty two interventions led to improvements in adherence to anti-diabetic medications, while only nine improved both medication adherence and glycaemic control. A single strategy could not be identified which would be guaranteed to improve anti-diabetic medication adherence consistently. Nonetheless, most interventions were successful in influencing one or more of the outcomes assessed, indicating the usefulness of these interventions under certain circumstances. Self-report, particularly the Summary of Diabetes Self-Care Activities questionnaire was the most commonly used tool to assess medication adherence, although other self-report tools were used in more recent
studies. Overall, there was a slight increase in the number of studies that employed multiple methods to assess medication adherence in studies conducted after 2008.

**Conclusion**

The diversity of interventions and adherence measurements prevented a meta-analysis of the impact of interventions on adherence to therapy, highlighting the need for more consistency in methods in the area of adherence research. Whilst effective interventions were identified, it is not possible to conclude on an effective intervention that can be generalised to all patients with type 2 diabetes.

**Introduction**

The global prevalence of diabetes is on the rise. Over 347 million people worldwide have been estimated to be suffering from diabetes [1]. The World Health Organization (WHO) projects that diabetes will be the 7th leading cause of death in 2030 [2], and that the majority of the cases of diabetes will be type 2 [2]. Type 2 diabetes (T2D) is a chronic metabolic disease resulting from defects in insulin secretion and insulin action and glucagon suppression, which cause hyperglycaemia [3]. Adequate management of dysglycaemia in diabetes is extremely important, in particular to prevent or delay complications, and ensuring that patients have a good quality of life. Along with lifestyle management (such as diet and adequate physical activity) [4, 5], treatment with oral anti-diabetic agents and/ or insulin is recommended to control hyperglycaemia. Different classes of oral anti-diabetic medications are available for treatment, with metformin (a biguanide) being the optimal first line medication. Dual and then triple combination therapy is recommended if mono-therapy is insufficient. Due to progressive beta cell dysfunction, patients with T2D may ultimately require insulin replacement therapy to adequately manage their diabetes [5]. Therapy also needs to be individually tailored depending upon their age, co-morbidities and risks of developing complications [4].

Diabetes is further complicated by a multitude of other factors, such as, the ’chronic’ nature of the disease, lifelong requirement for medications, requirement for changes in lifestyle, and the need to cope with social, cultural and psychological distress that may occur with the disease. In the midst of such complexities, remaining adherent to treatment recommendations may be a challenge [6]. Treatment adherence, in the context of diabetes, covers adherence to an array of self-care behaviours, constituting home glucose monitoring, adjustment of food intake, administration of medication(s), regular physical exercise, foot care and regular medical visits [7]. Although adherence to each self-care measure contributes to the effective management of diabetes, this review focuses only on adherence to anti-diabetic medications.

Adherence to oral hypoglycaemic medications in patients with T2D is 36 to 93% and to insulin is 63% [8]. The low level of medication adherence is likely to be one of the major factors contributing to sub-optimally controlled diabetes [9, 10]. Treatment non-adherence is well recognised, and interventions to promote adherence, improve glycaemic control, self-care behaviours and other key outcomes, have been designed and implemented. Several reviews and meta-analyses published over the last decade have addressed these interventions in patients with T2D [11–23]. Some reviews have focused on the wider aspect of treatment adherence in diabetes, incorporating adherence to anti-diabetic medications and treatment adherence as a whole [14, 19, 23]. Similarly, two reviews have discussed the interventions delivered by nurses [23] and pharmacists [14] to improve adherence to ’medical treatment’. Where adherence to
medications is specifically discussed [12, 16, 21, 22], one review included studies that analysed adherence to a range of medications taken by patients with T2D (anti-diabetic, anti-hypertensives and lipid lowering) rather than being specific to anti-diabetic medications [12]; two focused on analysing the methodological quality of the interventions [21, 22], and one focused on pharmacists' interventions to improve adherence to oral anti-diabetic medications and included only controlled trials [16]. Thus reviews have to-date not focused on the range of interventions addressing anti-diabetic medication adherence. This review aimed to:

i. investigate the impact of interventions on anti-diabetic medication adherence,

ii. identify measures of adherence used, and

iii. explore the changes in adherence measurement/assessment methods used over time.

Methods

Literature search

A review of the literature was conducted to identify research articles that have evaluated the impact of interventions on adherence to anti-diabetic medications in patients with T2D. Studies were searched in the following databases: Medline, Embase, CINAHL, International Pharmaceutical Abstracts (IPA), PUBmed, and PsychINFO. Each database was searched using the appropriate terms for medication adherence (concept 1), type 2 diabetes/anti-diabetic medications (concept 2) and intervention studies (concept 3). Key words/terms were used to denote these concepts (S1 Fig.) and combined using 'and' operator (concept 1 and concept 2 and concept 3). The search strategy (S1 Appendix) was limited to English language articles published from January 2000 to April 2013 (inclusive). The references of relevant publications (all studies included in this review and relevant systematic reviews) [12, 14, 16, 19, 20, 22] were hand searched to find additional studies that met the inclusion criteria (S1 Table).

Data extraction and analysis

For each study included in the review, the following 'study characteristics' were recorded: authors, year of publication, country where the study was conducted, study design, study population/sample, study site/setting, sample size, study duration, outcomes analysed and findings. Each study was analysed to determine whether medication adherence was the primary outcome measure, how medication adherence was measured, and adherence pre and post-intervention. The impact of the interventions on medication adherence and other outcomes were evaluated.

Operational definitions

For the purposes of this review, the term 'medication adherence/adherence' was used and defined as the extent to which individuals take their medication. However, the terms used in S3 Table, S4 Table and S2 Appendix reflect those used in the reviewed studies. S2 Table demonstrates other operational definitions used in this review.

Results

1. Study selection

The literature search identified 6,662 citations (S2 Fig.), of which 230 appeared to meet the inclusion criteria and were retrieved in full text. Of these, 49 met the study criteria and were reviewed.
Three additional studies were identified from hand searching. Thus, a total of 52 studies [24–75] were included in the review.

2. Study characteristics

The studies included in the review were conducted in 15 different countries, with the majority (57.7%) conducted in the USA, followed by countries in Europe (17.3%), Asia (15.4%) and the rest of the world. Majority of the studies (n = 38) were published in the past 5 years (since 2009) whilst only 8 were published during 2000 to 2005. S3 Table outlines the characteristics of the studies presented in this review.

2.1. Study design and setting

Nearly half of the studies (n = 25) [25, 26, 28, 31, 32, 34, 36, 40, 44–47, 53, 56, 57, 59–61, 63, 64, 66, 69, 72–74] were ‘randomized controlled’ trials (S3 Table). However, a few studies utilised pre- and post-intervention designs [26, 34, 44]. Two studies were cluster randomized trials [42, 62], where either the participating general practices [62] or the clinicians [42] were randomized; four were controlled trials without randomization [27, 35, 48, 55], and one followed time-series design where the subjects served as their own controls [52]. Other studies varied in their designs and were cross-sectional [24, 41], quasi-experimental [33, 37, 43, 54, 75], and case series analyses [51]. The method of patient recruitment and research design were not clear in two studies [29, 70]. One study discussed the impact of two retrospective observational studies [65] and 8 studies were reported as pilot studies [24, 35, 37, 42, 47, 49, 61, 71].

Patients received the intervention mostly in community settings (n = 36) [24–27, 30, 33, 35–37, 40, 42–45, 47–50, 52–54, 57–59, 61, 64–72, 74, 75]. Other studies were conducted in hospitals (n = 6) [29, 32, 46, 51, 60, 73] clinics (n = 8) [28, 31, 34, 39, 55, 56, 62, 63], and one study involved multiple settings, community locations, clinic or patient’s home [38]. One study was not clear about the setting used [41].

2.2. Study subjects and recruitment criteria

Inclusion criteria varied between studies and included age, HbA1c level, taking an oral anti-diabetic medication and/or the duration the patient was on medication, and the duration since diagnosis with diabetes.

The subjects’ age groups varied and some studies were more inclusive, recruiting patients who were ≥18 years [31, 40, 48, 49, 53, 56, 73], or >18 years [35, 62, 72]. A vast majority did not specify the exact age [24–29, 33, 37–39, 41–43, 45, 46, 50–52, 58, 60, 63, 65, 69, 71, 75]. Others included adults who were ≥21 years [59], ≥30 years [64, 66], >40 years [30], ≥40 years [67], and ≥50 years [47]. A few provided age ranges for inclusion, such as, 18–65 years [44, 74], 18–70 years [36, 55], 18–75 years [34], 21–60 years [32], 21–80 years [68], 30–65 years [61], and 45–75 years [57]. One study included only the older adults 65 years and above [54], in contrast to another that included patients below 75 years of age [70].

The HbA1c level was sometimes specified as an inclusion criterion. However, the specifications varied and were >6.5% [44], ≥6.5% [30], >7% [26, 47, 58], ≥7% [55], ≥7.5% [36, 64, 69], 7–9.5% [42], 7–10% [61], ≥9% [31] and <8% [35].

Some studies used duration since diagnosis or taking an oral anti-diabetic medication as inclusion criteria. For example, patients with a diagnosis of T2D for at least 3 months [69], 6 months [38], one year [35, 42, 53, 68], 5 years [61], less than 10 years [32] prior to the study, or newly diagnosed (within 3–33 months of diagnosis) [45], were only included in the studies. One study only recruited ‘newly diagnosed T2D patients’ without defining the duration since diagnosis [39]. Thirteen studies explicitly stated the requirement for the patients to be taking an oral anti-diabetic medication in order to be eligible for participation [29–32, 42, 47, 53, 57, 64, 66, 69, 72, 75].
A few studies focused on specific patient groups, for example: African American [24, 37, 47, 52, 71], Mexican American [34] and Hispanics/Latinos [38, 49]. Four studies [47, 51, 59, 66] included patients with diabetes and depression.

2.3. Sample size and study duration

Sample sizes were highly variable (S3 Table), ranging from 5 patients in a case-series pre/post analysis [51] to 5,123 patients in a prospective cohort pre/post analysis [67]. Likewise, the duration of the studies varied, from 10 weeks [49] to 4 years [43]. With the exception of one study [41], all other studies reported the duration of the intervention and/or the study. Most of the studies were conducted for 3 months (n = 14) [25, 26, 33–36, 46, 47, 50, 56, 60, 66, 68, 71], 6 months (n = 17) [24, 27, 29, 32, 37–40, 42, 44, 53, 57, 58, 67, 70, 74, 75], or 12 months (n = 10) [31, 45, 48, 52, 55, 59, 61, 63, 64, 72]. In one study [57], outcomes were also analysed eighteen months after the formal end of the study. In contrast, in a 6-month study, data were presented and analysed for a 3 month period only [75]. The maximum duration noted were for studies that involved the analysis of medical and pharmacy claims to determine the effect of ‘value based plan design’ [43]; the impact of U.S. Medicare part D [54], and the ‘value based insurance design’ programs [65] on adherence.

2.4. Outcomes analysed

A range of clinical and non-clinical outcomes were reported together with medication adherence, either as a primary or secondary outcome measure (S3 Table). With the exception of 14 studies [27, 29, 39, 41–43, 45, 54, 65, 67, 70, 72, 74], all other studies analysed one or more clinical and/or biological outcomes. In addition, many studies also assessed patient specific outcomes, for example health related Quality of Life (QoL) [27, 59], diabetes specific QoL [32, 52] or QoL in general [60, 73]; diabetes knowledge [24, 32, 34, 38, 41, 42, 44, 49, 56, 68], and self-efficacy [34, 35, 37, 39, 40, 44, 45, 49, 56, 62, 68].

3. Assessing medication adherence

3.1. Medication adherence as a primary or secondary focus

In most studies (n = 38) medication adherence was assessed as a primary outcome [24–30, 32–35, 37, 39–47, 50–54, 56, 58, 61, 65–69, 71–74] (S4 Table). Adherence was measured as a self-management/ self-care behavioural outcome at the same time as other measures, for example adherence to diet, exercise, foot care, and blood glucose testing. Only 15 studies [25, 28, 41–43, 46, 47, 54, 60, 65–67, 69, 72, 74] assessed the impact of the intervention on medication adherence alone. Other studies specified medication adherence as a secondary outcome. Clinical measures (primarily the HbA1c) were the primary outcome measure in most of these studies [31, 48, 49, 55, 57, 59, 62–64].

3.2. Measuring medication adherence

Overall, the studies included measured adherence to medications as the measure of medication taking compared to the prescribed regimen (S4 Table). Some studies used ‘compliance’ to describe this medication taking. Only one study measured persistence to therapy in addition to adherence [42]. Studies reported adherence as number or proportion of adherent/non-adherent patients, adherence scores, or number of days the patient reported adherent behaviour.

Patient self-report, pharmacy refills and claims data and electronic measures were used to assess adherence. Six studies [28, 47, 51, 66, 69, 74] used electronic measures to assess adherence. Medication Event Monitoring System (MEMS) was used in five and the Real Time Medication Monitoring (RTMM) system in another [74]. Three of the six also used self-report [28, 51, 69]. Ten studies used prescription refill claims (pharmacy and medical claims data) [29, 30, 42, 43, 54, 57, 64, 65, 67, 72], with four also measuring adherence through self-report [30, 42, 57, 64]. Self-report alone was used in all other remaining studies.
Self-report was used in 82.7% of the studies (n = 43). Most (n = 16) [25, 27, 32–37, 44, 45, 49, 51, 52, 56, 64, 68] used the medication subscale (1 or 2 items) questions in the Summary of Diabetes Self-Care Activities (SDSCA) questionnaire [76] to assess adherence. A study [42] used ‘the number of days patient missed taking the pill in the last 7 days’ and another analysed the response to the question ‘have you missed a medication dose in the past week?’ [53], as opposed to the approach by SDSCA, which takes into consideration the number of days the patient was adherent to their medication in the last 7 days.Morisky Medication Adherence Scale (MMAS) [38, 53, 56, 59, 60, 64, 73], Medication Adherence Report Scale (MARS) [39, 45, 62, 69, 70], Morisky-Green test [48, 55], Brief Medication Questionnaire (BMQ) [46, 58] and Hill Bone compliance questionnaire [40] were other self-report tools used. A few studies reported the use of validated questionnaires without giving the details of the questions asked [26, 41, 61, 63, 75]. One study simply tabulated medication adherence using a ‘yes’ and ‘no’ response [24].

Medication adherence was measured as a single entity for the entire therapeutic class (anti-diabetic medications), rather than for individual anti-diabetic medication in almost all of the studies, except for one study that specifically addressed adherence to metformin [28].

3.3. Longitudinal changes in methods of assessing adherence

The self-report tools used to measure adherence have changed over time. SDSCA was used in all studies published during 2006 to 2008, compared to only 25% of the studies in 2000–2005. Since 2009, a range of approaches have been used to measure adherence. Although SDSCA has remained an important tool, other methods, such as the Morisky scales, MARS, Hill Bone compliance questionnaire, and BMQ have also been employed. Of 38 studies published since 2009, eight used SDSCA [44, 45, 49, 51, 52, 56, 64, 68], four [45, 51, 56, 64] of which also utilised an additional method to assess adherence, either another self-report tool [45, 56, 64] or an electronic measure [51]. While only two studies [28, 30], both published in 2004 used multiple methods to analyse adherence, seven studies [42, 45, 51, 56, 57, 64, 69], conducted (after 2008) used either two different tools or different methods for assessing adherence. Electronic methods, pharmacy claims and pharmacy refills have been reported.

4. Interventions and their impact

4.1. Impact on anti-diabetic medication adherence

S2 Appendix provides a description of the interventions and their impact. Forty nine articles dealt with interventions directed at the patient [24–26, 28, 30–48, 50–75], two directed at the healthcare provider [27, 29], and one directed at both [49]. Twenty two studies [28, 29, 33, 41, 46–51, 53, 54, 58, 60, 64, 66, 67, 69, 71–74] reported improvements in medication adherence. In two of these studies [28, 69] there were contradictory results between the two methods of measuring adherence. Rosen et al [28] reported a significant improvement in medication adherence when MEMS was used, but the improvement was not significant when assessed using ‘self-report’. Furthermore an improvement was detected using MEMS at the 16th week i.e. immediately after the intervention, and a decline in medication adherence was observed in subsequent analysis after 16 weeks. Similarly, Farmer et al [69] demonstrated that medication adherence improved significantly when analysed objectively (using MEMS) and but did not when self-report (MARS) was used.

Two studies [46, 48] reported a significantly positive impact of their interventions on adherence, however, did not include their control groups in the analysis. Therefore, they did not report how the interventions impacted adherence when taking into account the control groups’ data. A study on the impact of SMS showed an improvement in the number of doses taken within an agreed time period for the intervention group in comparison to control [74]. However, the intervention did not have a significant effect on days without dosing and missed doses.
In addition, a few comparable intervention strategies delivered different results; for example, continuous education and reinforcement text messages delivered to patients based on their blood glucose level, significantly improved medication adherence [33]; however, a similar intervention consisting of tailored feedback and reminders based on patient-specific data via messages on cellular phone failed to show an impact on adherence [35]. In both studies nurses delivered the interventions. Likewise, while a regular multidisciplinary education program positively influenced medication adherence in Nigerian patients [41], two educational sessions on diabetes self-management failed to impact medication adherence in Korean immigrants in the USA [68]. Furthermore, pharmacist delivered ‘care plans’ have been effective [48] in one study and ineffective in another [30].

4.2. Impact on clinical outcomes

HbA1c was an outcome measure (S3 Table) in 34 studies [24–26, 28, 30–38, 40, 44, 47–53, 55–57, 59, 61–64, 66, 68, 71, 75]. Nine studies reported a positive impact of the intervention on both medication adherence and HbA1c [33, 47–51, 53, 64, 66]. Sixteen of the 34 studies [30, 33, 36, 47–52, 55, 57, 61, 63, 64, 66, 68] reported a significant impact of intervention on HbA1c levels. In two studies however, the significant impact was observed only for part of the duration of the intervention [55, 63]. Garcia-Huidobro et al [55] demonstrated a significant positive impact on HbA1c during the 2nd 6 months of the 12 month intervention period. Wakefield et al showed a significant impact in the first 6 months which was not sustained at 12 months [63].

A small number of studies reported significant improvements in HbA1C levels of participants in the intervention groups, however, the difference was not significant when control group data were taken into consideration (between group differences were not statistically significant) [26, 38, 53]. Furthermore, in one study [53] the improvements observed in HbA1c levels were only significant amongst the patients who had baseline HbA1c ≥7.0 and not for the entire sample.

Other clinical or biological parameters measured varied between the studies and included blood glucose levels, blood pressure, and lipid profiles (S3 Table). Twenty five studies measured one or more clinical/biological parameters other than HbA1c [25, 30, 34, 35, 38, 40, 44, 46–50, 55–63, 66, 68, 71, 73], of which eighteen reported improvements in one or more parameters [30, 34, 38, 44, 47–50, 55, 58–61, 63, 66, 68, 71, 73]. In three [51, 59, 66] of the four studies [47, 51, 59, 66] that included patients with depression and diabetes, the interventions were successful in reducing depression symptoms. Blood glucose was improved in six studies [34, 48, 50, 58, 60, 73].

4.3. Impact on non-clinical outcomes

A range of non-clinical outcomes were evaluated highlighting the diversity of interventions and the range of non-clinical outcomes important in diabetes (S3 Table). A majority (94.2%) of the studies reported an impact on one or more non-clinical outcomes. Improvements were observed in adherence to exercise [25, 33, 44, 49–51, 53, 57], diet [26, 39, 44, 50, 51, 57, 71] blood glucose testing [26, 49, 51], foot care [33, 44, 49, 51, 57, 71], QoL [27, 73], self-efficacy [34, 35, 44, 45], patient knowledge [30, 32, 34, 41, 42, 49, 57, 58, 60] and goal achievements [37, 44].

Other medication related issues were influenced by some interventions, such as, identification and resolution of medication discrepancies [25, 36], improvements in medication appropriateness index [31], identification of drug therapy problems [48], pharmacotherapeutic changes [57], and intensification of oral diabetic therapy [56].

Discussion

A number of studies were identified which had investigated the impact of interventions on adherence to anti-diabetic medications, as well as a range of clinical and non-clinical patient
outcomes. Only a few interventions demonstrated a significant positive impact on adherence to anti-diabetic medication, and even fewer had shown improvements in both medication adherence and HbA1c levels. A range of tools were used in the studies to evaluate adherence, and consequently adherence was reported in several ways (e.g. proportion of adherent patients, adherence scores), preventing meta-analyses or direct comparisons of the findings. Despite the variability in study designs observed, including subject inclusion criteria, a range of sample sizes and variability in the duration of time since diagnosis, the review has highlighted an overall improvement in medication adherence and other secondary outcomes as a result of some interventions delivered to patients. Interestingly, the review also revealed a change in the tools and methods used to evaluate adherence to therapy, in particular, over the past 5 years.

Study characteristics and methodological limitations

There has been a significant increase in the number of studies evaluating the impact of interventions on anti-diabetic medication adherence in recent years. This signifies broader awareness of non-adherence as an important issue in diabetes therapy, and an ongoing effort to find interventions that could improve adherence to anti-diabetic medications in patients with T2D.

Whilst most of the studies identified were conducted in the USA, there were a number of studies conducted in a broad range of countries. Diabetes is a global problem [2], with an increasing prevalence. The management of diabetes is influenced by social, cultural and environmental practices [77, 78]. It is therefore important that intervention studies are conducted in diverse populations globally to gain a better understanding of how to influence the range of factors that impact adherence to anti-diabetic therapy.

Characteristics of the subjects for enrolment into the study differed across the intervention studies. The reasons for apparent inconsistency in the subjects’ age groups is difficult to comprehend, especially as ‘age’ has been recognized, although inconsistently, as a factor that could affect adherence [7]. It is possible that the variations in age range, and the number of subjects recruited across different age brackets, have an impact on the effectiveness of the interventions in improving adherence to anti-diabetic medications, which may not have been detected or taken into account during the analyses.

In the same way, criteria set for HbA1c level varied across studies and the basis of demarcation was inconsistent and unclear. Ideally, the target HbA1c levels for most people with diabetes is recommended to be <7% to reduce the incidence of complications, particularly microvascular disease [4]. A better judgment of the impact of any intervention on glycaemic outcome is likely to be derived from patients who have high HbA1c levels, rather than ones who are already within the recommended range.

The duration since diagnosis and therefore the period of time that the patient has had diabetes, is likely to impact on patients’ self-management behaviours [79, 80], including medication adherence. For example, for all chronic diseases, it has been found that the first year after starting chronic medication is the period of highest risk for non-adherence [81]. While some studies have clearly defined the ‘duration of disease’, many have not. Therefore, consistency in sample selection, and inclusion of a clearly defined sample population with comparable traits could yield a better interpretation of the findings. Alternatively, a larger sample size can be recruited and the impact of characteristics such as duration of diagnosis, age and other variables as confounders can be determined.

Most of the studies in the review either used a control or comparison group or a pre/post research design. A randomized controlled trial is regarded as the most powerful research design [82], and most of the studies reviewed were randomized controlled trials. However, despite having the control group, some studies reported the impact of the intervention on the study...
group using pre and post-intervention data rather than comparing with the data from the control group, or they compared the effect size between the study and control groups without conducting appropriate statistical analyses to consider the change in outcome measures in the control groups. Therefore, it is not possible to determine the true impact of the intervention on adherence to anti-diabetic medication in these studies.

The setting in which the intervention is delivered is likely to have an influence on the delivery and impact of the intervention. For example, a noisy, crowded place may be considered unsuitable for effective delivery of educational sessions or counselling a patient. Most interventions in the review were conducted in community settings, and information about the settings and the environment of intervention delivery was not provided in any of the studies. It is therefore not clear how the setting and environment impacted intervention delivery.

Medication adherence

Adherence to anti-diabetic medications was assessed as a primary outcome in most studies, using mainly self-report as the method of assessment. Although there was consistency in the use of the term adherence or compliance, the definition and interpretation of medication adherence was variable. For most studies, ‘taking or not taking the medication’ was the basis of the adherence measure, while others used number of patients reporting/not reporting a missed dose. To add complexity to the adherence definition, studies tended to use a cut-off point at which they considered patients as adherent or non-adherent, usually ‘≥80%’, for example MPR ≥80%, and number of patients who were adherent to ≥80% of their OHA doses. In another study, where adherence percentage was tabulated, the range ‘0–25% adherent’ was interpreted as non-adherent, while ‘50–100%’ as adherent. In most of the studies the method/tool used for measuring medication adherence was the only clue to the definition/interpretation of adherence. For example, for those studies that used the SDSCA question, ‘medication adherence’ was defined as ‘the number of days in the past week the patient took their medication’. Therefore, with each different measurement approach used, the interpretation of ‘medication adherence’ varied. Thus, lack of a consistent approach in defining and interpreting medication adherence is apparent, preventing comparison between studies.

Furthermore, adherence to anti-diabetic medications was measured collectively, i.e. adherence to the whole therapeutic class, rather than to an individual anti-diabetic medication. Patients with T2D often take more than one medication for their diabetes, and whether or not adherence to each medication differs, needs to be assessed, particularly when comparing oral agents with injection therapy. Addressing medication adherence for each medication a patient is taking, could also be a way of determining patients’ perceptions of their individual medications and investigating whether the medication itself has an impact on adherence, and whether this impact varies depending on the total number of medications taken.

A range of tools are available to measure medication adherence, each having its own pros and cons [83]. The choice generally depends on the ease of use, validity and reliability [84]. Overall, self-report tools were the more common tools used in the studies reviewed, as seen in most adherence studies [85]. Self-report tools are popular because of their flexibility, ease of use, cost effectiveness and ability to gather social, situational and behavioural data [85]. SDSCA was the most commonly used self-report tool to estimate adherence in T2D patients. In addition to the inherent advantages that SDSCA has as a self-report tool, including being brief, reliable and valid for use in both research and clinical practice [76], its popularity can be explained by the fact that medication adherence in patients with T2D can be assessed as an outcome together with other important outcomes, for example adherence to diet, medication, blood glucose testing, lifestyle, foot care, and attending clinics. SDSCA allows assessment of the
overall treatment adherence behaviours in patients with T2D, while also making it possible to assess adherence to a single component, using a single tool. Despite SDSCA remaining a popular method for measuring medication adherence, other self-report tools were also used to assess medication adherence, particularly after 2008, either alone, or in combination with another self-report tool or a different method. Specifically, MARS, MMAS, BMQ, and Hill Bone compliance scale, which is a scale generally used to measure adherence in hypertensive patients, were used, signifying the availability of a range of adherence measures and the lack of a universal measure.

Studies that used more than one method to assess medication adherence, either employed a second self-report tool, or a different method, for example electronic measure. Use of an additional method of measuring adherence was more common in studies published after 2008. Using two or more different methods could be an important means of validating, and/or triangulating the data, leading to improvements in medication adherence data collection. Nonetheless, a careful evaluation of the results obtained from both measures is required. For example, in two studies, where MEMS and self-report were used to assess medication adherence, although the trend appeared consistent for the intervention groups (from both measures), results for the control groups varied. The control groups, in each case, reported a better medication adherence based on the data from the self-report tool. Therefore, whilst it’s important to use more than one adherence measure to triangulate the data collected, these findings highlight the need to determine the aspect of adherence (initiation, compliance, persistence) being measured by each tool, as well as the tools’ characteristics, when choosing the tool and interpreting the data.

Diversity in the interpretation of the term ‘medication adherence’, methods of assessment, and reporting of the assessment results, thus, makes it very difficult to bring together the findings of all of the retrieved studies to make an effective comparison and conclude on the impact of interventions to promote adherence to anti-diabetic medication therapy. Moreover, a key aspect of intervention studies aimed at improving adherence is the appropriateness and validity of the methods and tools employed to determine the impact of the interventions.

**Intervention**

A large number of interventions identified in the review failed to show a positive impact on medication adherence. Of the small number of ‘successful’ interventions, a few employed similar strategies that were also reported to be unsuccessful in improving medication adherence in other studies. It is therefore extremely difficult to conclude and predict what type of interventions will be the most effective in promoting adherence to anti-diabetic medications. While 65.4% of the total studies assessed the impact of their intervention on HbA1c, about half of these reported improvements in HbA1c, and only about a quarter reported improvements in both HbA1c and medication adherence. Improving HbA1c is the key in diabetes control, and all management efforts are aimed at bringing HbA1c levels to an acceptable range. Studies have indicated that adherence to therapy results in better controlled HbA1c [9, 10, 86]. However, this could not be confirmed from the studies included in the review, as the results obtained from studies which assessed an impact on both medication adherence and HbA1c, were inconsistent. Some improved medication adherence only, some HbA1c only and some improved both. Such inconsistencies lead us to question the level of adherence to anti-diabetic medications required in order to improve HbA1c levels; it also necessitates a clearer understanding of the role of other self-care measures (e.g. adherence to diet and exercise) in impacting on the HbA1c value, independently of, and together with, medication adherence. Anti-diabetic medication adherence could therefore be only one factor amongst a range of factors that contributes...
to the glycaemic control in T2D patients. A clearer understanding of how much being adherent to medication counts in terms of effective glycaemic control will help to guide effective patient education.

To understand the relative “weightings” of adherence to medications and self-care behaviours in impacting and improving HbA1c levels, it is important to have a better understanding of how each intervention (and its components) influences medication adherence and self-care behaviours. Most interventions in the studies have been designed with an intention to influence patients’ adherence to more than one self-care behaviour rather than just ‘medication adherence’. Some studies were able to impact one or more self-care behaviours, even if they did not have a positive impact on anti-diabetic medication adherence. A specific behaviour might be particularly susceptible to certain influences, for example, dietary behaviour is particularly susceptible to social influences [87], and might require a different approach to create a change. Quantifying the level of impact of an intervention on adherence to medication and other self-care behaviours will provide valuable information on the type of intervention that would be beneficial in not only improving medication adherence and adherence to a range of self-care behaviours, but also in improving and reaching HbA1c goal levels.

The majority of interventions reported an impact on one or more outcomes assessed, either clinical or non-clinical. For example, adherence to foot care, adherence to blood glucose testing, patient knowledge, quality of life, blood glucose levels and lipid profiles. Thus, although most of the interventions did not improve anti-diabetic medication adherence or HbA1c, the intervention(s) improved other important patient-related outcomes, highlighting that each of the interventions could have one or more characteristics crucial to improving outcomes important in overall diabetes care.

The evidence presented in this review, therefore, suggests that a single strategy may not be suitable to effectively address all self-care behaviours and HbA1c levels in patients with diabetes. However, it may also not be practical to have several interventions each aimed at influencing different patient-related outcomes, including medication adherence. Additionally, it is equally important to be able to quantify the relative importance and weighting of the different self-care measures in impacting HbA1c in diabetics. This could help both the carers and the patients to better understand the role of medication related and non-medication related self-management strategies in patients with T2D. Thus, an ideal intervention would be one that has specific and targeted strategies addressing all key factors and which can be tailored to each patient, to specifically address the individual issues that impact medication adherence and glycaemic control.

**Conclusion**

Most of the interventions identified in the reviewed studies aimed to influence a range of self-care behaviours, including medication adherence as well as clinical/non-clinical outcome(s). Interestingly, almost all interventions were successful in impacting one or more of the outcomes analysed, thus signifying that while the search for an effective strategy to influence adherence to anti-diabetic medication is yet not over, the interventions, and/or their components could be utilized singly or in combination to impact different clinical or non-clinical patient outcomes. While an ideal perspective would demand a single strategy, there is no evidence to support an effective single intervention to promote adherence to anti-diabetic medication(s) for all patients.

The intervention studies have used different methods to assess anti-diabetic medication adherence, with self-report tools being the most common. The tools have evolved over the years, and although SDSCA remained the most commonly used self-report tool, more recent studies
have employed other novel approaches. Accurate assessment of medication adherence is critical for the correct interpretation of the effect of interventions on medication adherence. Clarity in the definition of medication adherence, and how it is measured are the issues that researchers have to consider when designing and implementing interventions.

It is evident from the review that although numerous strategies have been utilised to improve anti-diabetic medication adherence in patients with T2D, only few have succeeded, and even fewer have had an impact on HbA1c, the major indicator of glycaemic control. The successful interventions, akin to the overall studies in the review, employed variable strategies and methods of assessing medication adherence; it is therefore not possible to deduce the best possible strategy to address anti-diabetic medication adherence in patients with T2D.

**Limitations of the review**

One of the limitations of this review was the heterogeneous nature of the studies included, which is inherent in adherence intervention studies and a fundamental issue that needs to be addressed in this area. The diversity in methods and measures used prevented a meta-analysis from being conducted. A further limitation is that as part of the review we did not consider the quality of the research design as an inclusion/exclusion criterion as we were interested in including all studies which had implemented and evaluated interventions to promote adherence to anti-diabetic therapy in T2D.

**Supporting Information**

S1 PRISMA Checklist. PRISMA Checklist. S1_Checklist.doc
(DOC)

S1 Table. Review inclusion and exclusion criteria. S1_Table.docx
(DOCX)

S2 Table. Operational definitions. S2_Table.docx
(DOCX)

S3 Table. Study Characteristics. S3_Table.docx
(DOCX)

S4 Table. Medication Adherence Assessment. S4_Table.docx
(DOCX)

S1 Fig. Literature review search strategy. S1_Figure.docx
(DOCX)

S2 Fig. Citation selection flowchart for the review. S2_Figure.docx
(DOCX)

S3 Fig. PRISMA 2009 Flow diagram. S3_Figure.doc
(DOC)

S1 Appendix. Full electronic search strategy for Medline database. S1_Appendix.docx
(DOCX)

S2 Appendix. Intervention Summary and Impact. S2_Appendix.docx
(DOCX)
Author Contributions
Conceived and designed the experiments: SS JAB PA. Performed the experiments: SS PA. Analyzed the data: SS PA. Wrote the paper: SS PA JAB JG.

References
1. Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, et al. (2011) National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. The Lancet. 2011; 378(9785):31–40. doi:10.1016/S0140-6736(11)60679-X PMID: 21705069
2. Alwan A (2011) Global status report on noncommunicable diseases 2010: World Health Organization; 2011.
3. World Health Organization (2003) Screening for type 2 diabetes: report of a World Health Organization and International Diabetes Federation meeting: World Health Organization; 2003.
4. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, et al. (2012) Management of hyperglycemia in type 2 diabetes: a patient-centered approach position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes care. 2012; 35(6):1364–79. doi:10.2337/dc12-0413 PMID: 22517736
5. Kamar ME Management of Type 2 Diabetes:: From guidelines to personalized medicine.
6. Lerman I (2005) Adherence to treatment: the key for avoiding long-term complications of diabetes. Archives of medical research. 2005; 36(3):300–6. PMID:15925020
7. Sabatâe E (2003) Adherence to long-term therapies: evidence for action: World Health Organization; 2003.
8. Cramer JA (2004) A systematic review of adherence with medications for diabetes. Diabetes care. 2004; 27(5):1218–24. PMID: 15111553
9. Bailey CJ, Kodack M (2011) Patient adherence to medication requirements for therapy of type 2 diabetes. International Journal of Clinical Practice. 2011; 65(3):314–22. doi: 10.1111/j.1742-1241.2010.02544.x PMID: 21314869
10. Rhee MK, Slocum W, Ziener DC, Culler SD, Cook CB, et al. (2005) Patient adherence improves glycemic control. Diabetes Educator. 31(2):240–50. PubMed PMID: PMID: 15797853.
11. Blenkinsopp A, Hassey A (2005) Effectiveness and acceptability of community pharmacy-based interventions in type 2 diabetes: A critical review of intervention design, pharmacist and patient perspectives. International Journal of Pharmacy Practice. 2005; 13(4):231–40.
12. Doggrell SA (2010) Does intervention by an allied health professional discussing adherence to medicines improve this adherence in Type 2 diabetes? Diabetic Medicine. 2010 Dec; 27(12):1341–9. PubMed PMID: PMID: 21059085. English. doi:10.1111/j.1464-5491.2010.03137.x
13. Graziano JA, Gross CR (2009) The effects of isolated telephone interventions on glycemic control in type 2 diabetes: A literature review. Advances in Nursing Science. 2009; 32(3):E28–E41. doi: 10.1097/ANS.0b013e3181b0d6d6 PMID: 19707085
14. Lindenmeyer A, Hearmshaw H, Vermeire E, Van Royen P, Wens J, et al. (2006) Interventions to improve adherence to medication in people with type 2 diabetes mellitus: A review of the literature on the role of pharmacists. Journal of Clinical Pharmacy and Therapeutics. 2006; 31(5):409–19. PMID: 16958818
15. Montori VM (2004) Review: interventions focusing on patient behaviors in provider-patient interactions improve diabetes outcomes. ACP Journal Club. 140(2):51. PubMed PMID: PMID: 200498223.
16. Omran D, Guirguis LM, Simpson SH (2012) Systematic review of pharmacist interventions to improve adherence to oral antidiabetic medications in people with type 2 diabetes. Canadian Journal of Diabeties. 36(5):292–9.
17. Sigurdardottir AK, Jonsdottir H, Benediktsson R (2007) Outcomes of educational interventions in type 2 diabetes: WEKA data-mining analysis. Patient Education and Counseling. 67(1–2):21–31. PMID: 17574367
18. van Dam HA, van der Horst FG, Knoops L, Ryckman RM, Crebolder HF, et al. (2005) Social support in diabetes: a systematic review of controlled intervention studies. Patient education and counseling. 59(1):1–12. PMID: 16198213
19. Vermeire EL, Wens J, Van Royen P, Biot Y, Hearmshaw H, et al. (2005) Interventions for improving adherence to treatment recommendations in people with type 2 diabetes mellitus. Cochrane Database of Systematic Reviews. 2005 (2:2). PubMed PMID: PMID: 2009824422.
20. Wens J, Vermeire E, Hearnshaw H, Lindenmeyer A, Biot Y, et al. (2008) Educational interventions aiming at improving adherence to treatment recommendations in type 2 diabetes. A sub-analysis of a systematic review of randomised controlled trials. Diabetes Research and Clinical Practice. 2008; 79(3):377–88. PMID: 17643546

21. Wilke T, Mueller S, Groth A (2010) The methodological quality and effectiveness of adherence interventions: A review of diabetes type II interventions. Value in Health. 2010; 13(7):A295–A6.

22. Zomahoun HTV, Guenette L, Moisan J (2012) Interventions that improve adherence to oral antidiabetic in adults with type 2 diabetes: A systematic review. Journal of Population Therapeutics and Clinical Pharmacology. 2012; 19(2):e135.

23. Hearnshaw H, Lindenmeyer A, Vermeire E, Van Royen P, Wens J, et al. (2008) Educational interventions aiming at improving adherence to treatment recommendations in type 2 diabetes mellitus: the role of nurses. European Diabetes Nursing. 3(2):73–7. PubMed PMID: 2009547320.

24. Hendricks LE, Hendricks RT (2000) The effect of diabetes self-management education with frequent follow-up on the health outcomes of African American men. The Diabetes educator. 26(6):995–1002. PubMed PMID: 11912812

25. Grant RW, Devita NG, Singer DE, Meigs JB (2003) Improving adherence and reducing medication discrepancies in patients with diabetes. Annals of Pharmacotherapy. 37(7–8):962–9.

26. Kim HS, Oh JA (2003) Adherence to diabetes control recommendations: impact of nurse telephone calls. Journal of Advanced Nursing. Nov; 44(3):256–61. PubMed PMID: 14641395. English.

27. Maddigan SL, Majumdar SR, Guirguis LM, Lewanczuk RZ, Lee TK, et al. (2004) Improvements in patient-reported outcomes associated with an intervention to enhance quality of care for rural patients with type 2 diabetes: results of a controlled trial. Diabetes Care. Jun; 27(6):1306–12. PubMed PMID: 15161780.

28. Rosen MI, Rigsby MO, Salahi JT, Ryan CE, Cramer JA (2004) Electronic monitoring and counseling to improve medication adherence. Behav Res Ther. Apr; 42(4):409–22. PubMed PMID: 14998735.

29. Schectman JM, Schorling JB, Nadkarni MM, Voss JD (2004) Can Prescription Refill Feedback to Physicians Improve Patient Adherence? American Journal of the Medical Sciences. 2004; 327(1):19–24. PMID: 14722392

30. Wermelle J, Bennie M, Brown I, McKnight J (2004) Pharmaceutical care model for patients with type 2 diabetes: integration of the community pharmacist into the diabetes team–a pilot study. Pharmacy World and Science. 2004; 26(1):18–25. PMID: 15018255

31. Odegard PS, Goo A, Hummel J, Williams KL, Gray SL (2005) Caring for poorly controlled diabetes mellitus: A randomized pharmacist intervention. Annals of Pharmacotherapy. 2005; 39(3):433–40. PMID: 15701763

32. Keeratiyutawong P, Hanucharumkul S, Melkus GDE, Panpakdee O, Vorapongsathorn T (2006) Effectiveness of a self-management program for Thais with type 2 diabetes. Thai Journal of Nursing Research. 2006; 10(2):85–97. PubMed PMID: 20091937.

33. Kim HS, Kim NC, Ahn SH (2006) Impact of a nurse short message service intervention for patients with diabetes. Journal of nursing care quality. 2006; 21(3):266–71. PMID: 16816608

34. Vincent D, Pasvogel A, Barrera L (2007) A feasibility study of a culturally tailored diabetes intervention for Mexican Americans. Biol Res Nurs. 2007; 9(2):130–41. PMID: 17909165

35. Faridi Z, Liberti L, Shuval V, Northrup V, Ali A, et al. (2008) Evaluating the impact of mobile telephone technology on type 2 diabetic patients’ self-management: the NICHE pilot study. Journal of evaluation in clinical practice. 2008; 14(3):465–9. doi: 10.1111/j.1365-2753.2007.00881.x PMID: 18373577

36. Quinn CC, Clough SS, Minor JM, Lender D, Okafor MC, et al. (2008) WellDoc mobile diabetes management randomized controlled trial: change in clinical and behavioral outcomes and patient and physician satisfaction. Diabetes technology & therapeutics. 2008; 10(3):160–8.

37. Utz SW, Williams IC, Jones R, Hinton I, Alexander G, et al. (2008) Culturally tailored intervention for rural African Americans with type 2 diabetes. The Diabetes Educator. Sep-Oct; 34(5):854–65. PubMed PMID: 2008–14587–009. doi: 10.1177/0145721708323642

38. Babamoto KS, Sey KA, Camilleri AJ, Karlan VJ, Catalanaj J, et al. (2009) Improving diabetes care and health measures among hispanics using community health workers: Results from a randomized controlled trial. Health Education and Behavior. 2009; 36(1):113–26. doi: 10.1177/1090198108325911 PMID: 19188371

39. Clarke A (2009) Effects of routine education on people newly diagnosed with type 2 diabetes. European Diabetes Nursing. 2009; 6(3):88–94. PubMed PMID: 2010528855.

40. Glasgow RE, Edwards LL, Whitesides H, Carroll N, Sanders TJ, et al. (2009) Reach and effectiveness of DVD and in-person diabetes self-management education. Chronic Illness. 2009 Dec; 5(4):243–9. PubMed PMID: 19933245. doi: 10.1177/1742395309343978

---

**Review of Interventions Addressing Adherence to Anti-Diabetics**
41. Kolawole B, Adeola O, Adegbenro C, Akintan T, Adegoke S, et al. (2009) Effectiveness of a structured diabetes education program on some non-glycemic endpoints in Nigerians with type 2 diabetes mellitus. International Quarterly of Community Health Education. 2009; 29(4):381–8. doi: 10.1177/0145721709356115

42. Mullan RJ, Montori VM, Shah ND, Christianson TJ, Bryant SC, et al. (2009) The diabetes mellitus medication choice decision aid: a randomized trial. Archives of Internal Medicine. 2009 Sep 28; 169 (17):1560–8. PubMed PMID: 19786674; doi: 10.1001/archinternmed.2009.293

43. Rodin HA, Heaton AH, Wilson AR, Garrett NA, Piocher DW (2009) Plan designs that encourage the use of generic drugs over brand-name drugs: An analysis of a free generic benefit. American Journal of Managed Care. 2009; 15(12):881–8. PMID: 20001169

44. Sacco WP, Malone JI, Morrison AD, Friedman A, Wells K (2009) Effect of a brief, regular telephone intervention by paraprofessionals for type 2 diabetes. Journal of Behavioral Medicine. 2009 Aug; 32 (4):349–59. PubMed PMID: 19365719. doi: 10.1007/s10865-009-9209-4

45. Thoolen BJ, de Ridder D, Bensing J, Gorter K, Rutten G (2009) Beyond good intentions: The role of proactive coping in achieving sustained behavioural change in the context of diabetes management. Psychology & Health. 2009 Mar; 24(3):237–54. PubMed PMID: 2009-03307-001.

46. Adepu R, Ari SM (2010) Influence of structured patient education on therapeutic outcomes in diabetes patients with type 2 diabetes mellitus. Journal of Pharmaceutical and Clinical Research. 2010; 3(3):174–8.

47. Bolger HR, de Vries HF (2010) Integrating type 2 diabetes mellitus and depression treatment among African Americans: a randomized controlled pilot trial. Diabetes Educator. 2010 Mar-Apr; 36(2):284–92. PubMed PMID: 20040705. Pubmed Central PMCID: NIHMS168821 PMC2858776. doi: 10.1177/0145721709356115

48. Borges APDS, Guidoni CM, Ferreira LD, Freitas OD, Pereira LRL (2010) The pharmaceutical care of patients with type 2 diabetes mellitus. Pharmacy World and Science. 2010; 32(8):730–6. doi: 10.1007/s11096-010-9428-3 PMID: 20734138

49. Castillo A, Giachello A, Bates R, Concha J, Ramirez V, et al. (2010) Community-based diabetes education for latinos: The diabetes empowerment education program. Diabetes Educator. 2010; 36(4):586–94. doi: 10.1177/0145721710371523 PMID: 20538970

50. Cinar Fl, Akbayrak N, Cinar M, Karadurmufl N, Fiahin M, et al. (2010) The effectiveness of nurse-led telephone follow-up in patients with type 2 diabetes mellitus. Turkish Journal of Endocrinology and Metabolism. 2010; 14(1):1–5.

51. Gonzalez JS, McCarl LA, Wexler DJ, Caglierio E, Delahanty L, et al. (2010) Cognitive-behavioral therapy for adherence and depression (CBT-AD) in type 2 diabetes. Journal of Cognitive Psychotherapy. 2010; 24(4):329–43. PubMed PMID: 2011–09229-007.

52. Tang TS, Funnell MM, Brown MB, Kurlander JE (2010) Self-management support in ‘real-world’ settings: An empowerment-based intervention. Patient Education and Counseling. 2010 May; 79(2):178–84. PubMed PMID: 2010–07961–009. doi: 10.1016/j.pec.2009.09.029

53. Wolever RQ, Dreusicke M, Fikkan J, Hawkins TV, Yeung S, et al. (2010) Integrative health coaching for patients with type 2 diabetes: A randomized clinical trial. Diabetes Educator. 2010; 36(4):629–39. doi: 10.1177/0145721710371523 PMID: 20534872

54. Zhang Y, Lave JR, Donohue JM, Fischer MA, Chernew ME, et al. (2010) The impact of medicare part D on medication adherence among older adults enrolled in medicare-advantage products. Medical Care. 2010; 48(5):409–17. doi: 10.1097/MLR.0b013e3181d68978 PMID: 20393580

55. Garcia-Huidobro D, Bittner M, Brahm P, Puschel K (2011) Family intervention to control type 2 diabetes: A controlled clinical trial. Diabetes Educator. 2011 Mar; 37(2):284–91. doi: 10.1177/0145721711011096 PMID: 21143256

56. Khan MA, Shah S, Grudzien A, Onyeyekwe N, Banskota P, et al. (2011) A diabetes education multimedia program in the waiting room setting. Diabetes Therapy. 2011; 2(3):178–88. doi: 10.1007/s13300-011-0007-y PMID: 22127826

57. Mehuys E, Van Bortel L, De Bolle L, Van Tongelen I, Annemans L, et al. (2011) Effectiveness of a community pharmacist intervention in diabetes care: A randomized controlled trial. Journal of Clinical Pharmacy and Therapeutics. 2011; 36(5):602–13. doi: 10.1111/j.1365-2710.2010.01218.x PMID: 21143256

58. Mitchell B, Armour C, Lee M, Song YJ, Stewart K, et al. (2011) Diabetes Medication Assistance Service: the pharmacist’s role in supporting patient self-management of type 2 diabetes (T2DM) in Australia. Patient Educ Couns. 2011 Jun; 83(3):289–94. PubMed PMID: 21616627; doi: 10.1016/j.pec.2011.04.027

59. Piette JD, Richardson C, Himle J, Duffy S, Torres T, et al. (2011) A randomized trial of telephonic counseling plus walking for depressed diabetes patients. Medical Care. 2011 Jul; 49(7):641–8. PubMed PMID: 2011–01319–005. doi: 10.1097/MLR.0b013e318215d0c9
60. Ramanath KV, Santosh YL (2011) Impact of clinical pharmacist provided patient education on QOL outcome in type II diabetes mellitus in rural population. Asian Journal of Pharmaceutical and Clinical Research. 2011; 4(4):15–20.

61. Shetty AS, Chumukattan S, Nanditha A, Raj RKC, Ramachandran A (2011) Reinforcement of adherence to prescription recommendations in Asian Indian diabetes patients using short message service (SMS)-a pilot study. Journal of Association of Physicians of India. 2011; 59(11):711–4.

62. Smith S, Paul G, Kelly A, Whitford D, O'Shea E, et al. (2011) Peer support for patients with type 2 diabetes: Cluster randomised controlled trial. BMJ: British Medical Journal. 2011 Feb; 342(7795):No Pagina-tion Specified. PubMed PMID: PMID: 2011–06060–002.

63. Wakefield BJ, Holman JE, Ray A, Scherubel M, Adams MR, et al. (2011) Effectiveness of home tele-health in comorbid diabetes and hypertension: a randomized, controlled trial. Tehemedicine journal and e-health: the official journal of the American Telemedicine Association. 2011; 17(4):254–61. doi: 10.1089/tmj.2010.0176 PMID: 21476945

64. Walker EA, Shmukler C, Ullman R, Blanco E, Scollan-Koliopoulos M, et al. (2011) Results of a successful telephonic intervention to improve diabetes control in urban adults: a randomized trial. Diabetes Care. 2011 Jan; 34(1):2–7. PubMed PMID: PMID: 21193619. Pubmed Central PMCID: PMC3005454. doi: 10.2337/dc10-1005

65. Barron JJ, Cai Q, Turner RM, White JT, Amirpoor LW (2012) Analyzing the impact of different value-based insurance design programs. American Journal of Pharmacy Benefits. 2012; 4(1):29–36.

66. Bogner HR, Morales KH, de Vries HF, Cappola AR (2012) Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. Annals of family medicine. 2012; 10(1):15–22. doi: 10.1370/afm.1344 PMID: 22230826

67. Brennan TA, Dollear TJ, Hu M, Matlin OS, Shrank WH, et al. (2012) An integrated pharmacy-based program improved medication prescription and adherence rates in diabetes patients. Health Aff (Millwood). 2012 Jan; 31(1):120–9. PubMed PMID: PMID: 22232102.

68. Choi SE, Rush EB (2012) Effect of a short-duration, culturally tailored, community-based diabetes self-management intervention for Korean immigrants: A pilot study. The Diabetes Educator. 2012 May; 38 (3):377–85. PubMed PMID: PMID: 2012–13333–008. doi: 10.1177/0145721712443292

Farmer A, Hardeman W, Hughes D, Prevost AT, Kim Y, et al. (2012) An explanatory randomised controlled trial of a nurse-led, consultation-based intervention to support patients with adherence to taking glucose lowering medication for type 2 diabetes. BMC family practice. 2012; 13:30. doi: 10.1186/1471-2296-13-30 PMID: 22480341

70. Kroese FM, Adriaanse MA, De Ridder DTD (2012) Boosters, anyone? Exploring the added value of booster sessions in a self-management intervention. Health Education Research. 2012; 27(5):825–33. PubMed PMID: PMID: 2011688559. doi: 10.1093/her/cys062

71. Collins-McNeil J, Edwards CL, Batch BC, Benbow D, McDougal CS, et al. (2012) A Culturally Targeted Self Management Program for African Americans With Type 2 Diabetes Mellitus. Canadian Journal of Nursing Research. 2012; 44(4):126–41. PubMed PMID: PMID: 201189755.

72. Odegard PS, Christensen DB (2012) MAP study: RCT of a medication adherence program for patients with type 2 diabetes. J Am Pharm Assoc (Wash). 2012; 52(6):753–56. doi: 10.1331/japha.2012.11001 PMID: PMID: 22962017. doi: 10.1111/j.1520-669X.2012.01975.x

73. Ramanath KV, Bhanuprakash M, Nagakishore CH, Mahesh Kumar S, Balaji DBSS (2012) Study the clinical pharmacist influence on medication adherence & quality of life of rural type-2 diabetes mellitus patients in a tertiary care hospital. Archives of Pharmacy Practice. 2012; 9(2):170–80.

74. Vervloet M, van Dijk L, Santen-Reestman J, van Vlijmen B, van Wingerden P, et al. (2012) Peer support for patients with type 2 diabetes: Cluster randomised controlled trial. BMJ: British Medical Journal. 2011 Feb; 342(7795):No Pagina-tion Specified. PubMed PMID: PMID: 2011–06060–002.

75. Zolfaghari M, Mousavifar SA, Pedram S, Haghani H (2012) 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(13–14):1922–31.

76. Toobert DJ, Hampson SE, Glasgow RE (2000) The summary of diabetes self-care activities measure: results from 7 studies and a revised scale. Diabetes care. 2000; 23(7):943–50. PMID: 10895844

77. Cha E, Yang K, Lee J, Min J, Kim KH, et al. (2012) Understanding cultural issues in the diabetes self-management behaviors of Korean immigrants. The Diabetes Educator. 2012; 38(6):635–44. doi: 10.1177/0145721712460283 PMID: 23001928

78. Kim G, Ford KL, Chiriboga DA, Sorkin DH (2012) Racial and ethnic disparities in healthcare use, delayed care, and management of diabetes mellitus in older adults in California. Journal of the American Geriatrics Society. 2012; 60(12):2319–25. doi: 10.1111/j.1532-5415.2012.03896.x
79. Blackburn DF, Swidrovich J, Lemstra M (2012) Non-adherence in type 2 diabetes: practical considerations for interpreting the literature. Patient preference and adherence. 2012; 7:183–9.

80. Grégoire J-P, Sirois C, Blanc G, Poirier P, Moisan J (2010) Persistence patterns with oral antidiabetes drug treatment in newly treated patients—a population-based study. Value in Health. 2010; 13(6):820–8. doi: 10.1111/j.1524-4733.2010.00761.x PMID: 21054658

81. Brown MT, Bussell JK, editors (2011) Medication adherence: WHO cares? Mayo Clinic Proceedings; 2011: Elsevier.

82. Campbell M, Fitzpatrick R, Haines A, Kinmonth AL, Sandercock P, et al. (2000) Framework for design and evaluation of complex interventions to improve health. BMJ: British Medical Journal. 2000; 321 (7262):694. PMID: 10987780

83. Osterberg L, Blaschke T (2005) Adherence to medication. New England Journal of Medicine. 2005; 353(5):487–97. PMID: 16079372

84. Horne R, Weinman J, Barber N, Elliott R, Morgan M, et al. (2005) Concordance, adherence and compliance in medicine taking. London: NCCSDO. 2005:40–6.

85. Lehmann A, Aslani P, Ahmed R, Celio J, Gauchet A, et al. (2014) Assessing medication adherence: options to consider. International journal of clinical pharmacy. 2014; 36(1):55–69. doi: 10.1007/s11096-013-9865-x PMID: 24166659

86. Pladevall M, Williams BK, Potts LA, Divine G, Xi H, et al. (2004) Clinical outcomes and adherence to medications measured by claims data in patients with diabetes. Diabetes Care. 2004 Dec; 27 (12):2800–5. PubMed PMID: PMID: 15562188. Pubmed Central PMCID: PMC1262687. Epub 2004/11/25.

87. Gallant MP (2003) The influence of social support on chronic illness self-management: a review and directions for research. Health Education & Behavior. 2003; 30(2):170–95.