

# Effectiveness of pharmacist-led educational interventions on self-care activities and glycemic control of type 2 diabetes patients: a systematic review and meta-analysis

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**Background:** Effectiveness of pharmacist-led educational interventions on self-care activities and glycemic control of type 2 diabetes mellitus (T2DM) patients is vague. The purpose of this review is to appraise the effect of pharmacist-led educational interventions on self-care activities and levels of glycated hemoglobin of T2DM patients.

**Methods:** Five electronic databases were searched from date of database inception to September 2017. Randomized clinical trials examining the effectiveness of pharmacist-led educational interventions, directed at T2DM patients only, were included for systematic review and meta-analysis. The protocol is available with PROSPERO (CRD42017078854).

**Results:** Eleven studies, involving n=1,544 T2DM patients, were included in this systematic review. Meta-analysis demonstrated that pharmacist-led interventions had a significant effect on lowering of the levels of glycated hemoglobin (-0.66; 95% CI [-0.83, -0.50];  $I^2=58.3\%$ ;  $P=0.008$ ), in comparison to usual care. Self-care activities were assessed by using Summary of Diabetes Self-care Activities tool in eight studies. Overall meta-analysis of self-care activities for included studies demonstrated a significant effect of pharmacist-led interventions on improvement of self-monitoring of blood glucose (1.62; 95% CI [0.92, 2.32];  $I^2=70.5\%$ ;  $P=0.005$ ), foot care (1.20; 95% CI [0.49, 1.90];  $I^2=95.0\%$ ;  $P<0.001$ ), and overall diet (1.16; 95% CI [0.38, 1.93];  $I^2=64.2\%$ ;  $P=0.094$ ).

**Conclusion:** The findings of this review demonstrate a significantly positive effect of pharmacist-led educational interventions on HbA1c levels and self-care practices among T2DM patients.

**Keywords:** self-care, pharmacist, glycemic control, type 2 diabetes, meta-analysis, HbA1c

## Introduction

A steady and continuous growth in the number of reported cases of diabetes mellitus has been observed over the past decades.<sup>1</sup> According to the Global Diabetes Report by World Health Organization (WHO), there were approximately 422 million patients suffering from diabetes mellitus in 2014. The global prevalence of diabetes mellitus in the adult population has nearly doubled since 1980, rising from 4.7% to 8.5% in 2014. Diabetes prevalence is increasing more rapidly in low- and middle-income countries than in high-income countries. As such, the South-East Asian Region of WHO has seen a substantial increase in diabetes with roughly 96 million of diabetes patients in the region.<sup>2,3</sup> In Ethiopia, 0.8 million diabetes cases were reported in 2000 and the figure is expected to skyrocket to 1.8 million by year 2030.<sup>4</sup>

Keeping in view this massive increase in the number of diabetes cases, most of the diabetes foundations are emphasizing on the need to educate the patients about diabetes self-care which will further help in improving the clinical outcomes of the diabetes patients. Diabetes self-care is undertaken by individuals with or at risk of diabetes. It is a process in which necessary information and skills are acquired by the patients to successfully self-manage the disease and its complications for better health outcomes.<sup>5</sup> According to American Association of Diabetes Educators, there are seven key self-care activities in order to produce positive and efficacious outcomes. These activities include, proper diet, being physically active (regular exercising), monitoring of blood glucose level, adherence and compliance of medications, problem-solving skills, healthy coping skills, and finally, risk reducing behaviors.<sup>6</sup> Positive correlation has been proven between all seven activities with favorable glycemic control, significant reduction in late complications, and improved quality of life.<sup>7</sup> In other words, nonadherence to self-care activities can lead to lower health-related quality of life.<sup>8,9</sup>

Additionally, it is noticed that diabetes self-care also assists in improving adherence to the medications, which assists in controlling the medication cost and morbidity and mortality rates. In acknowledgement to this problem, the involvement of different health care professionals in interdisciplinary health care approach is seen to be a useful strategy to educate the public about the importance of adherence and subsequently improving overall health outcomes especially in patients with diabetes.<sup>10</sup> Health care providers can collaborate with public health agencies and come out with programs to assist diabetic patients and their families.<sup>11</sup> In the United States, programs such as state Diabetes Control Program and Living with Type 2 Diabetes Program assist health care professionals to implement diabetes interventions, increase access to quality diabetes care, and promote public awareness about diabetes.<sup>12</sup>

In the last few years with the emergence of pharmacist's role in direct patient care, clinical pharmacists with pharmacotherapeutic knowledge are playing a vital role in educating patients during dispensation process. Accurate directions for use of medicines and self-care advises incorporated into the counseling process are essential in educating people with diabetes. According to American College of Clinical Pharmacy, one of the key roles of clinical pharmacists is to educate the patients by giving them advises on important strategies for best possible treatment outcomes so as to improve or maintain their health.<sup>13</sup>

Pharmacist-led interventions include variety of services, ranging from education on diabetes, complications associated with diabetes, self-management, medication adherence, telemedicine, and pharmaceutical care planning. Clinically significant effect of pharmacy-based interventions have been reported by few systematic reviews.<sup>14-19</sup> The positive impact of pharmacist-led interventions is directly associated with reductions in micro- and macrovascular complications associated chronic diabetes.<sup>16</sup> Systematic reviews have previously been conducted to appraise the effect of pharmacy-based interventions on clinical and nonclinical parameters of people with diabetes.<sup>14,16</sup> However, to date, there is hardly any summative evidence in the form of meta-analysis that scrutinize the impact of pharmacist-led educational interventions on self-care activities and glycemic control of type 2 diabetes patients. This systematic review will assess the impact of pharmacist-led educational interventions on patients' self-care practices and glycated hemoglobin (HbA1c) levels.

## Methods

This systematic review and meta-analysis was performed according to PRISMA guidelines.

## Database and search strategies

An online search was made from date of database inception till September 2017, from five databases, namely, PubMed, ProQuest, Scopus, EBSCOhost, and Ovid, by using the following search strategy: Diabetes Mellitus, Type 2 OR T2DM OR Non-insulin dependent diabetes mellitus OR NIDDM OR Type 2 diabetes AND Pharmaceutical care OR Clinical pharmacy OR Community pharmacy OR Pharmacist\* OR Pharmaceutical services OR Education OR Intervention OR "Self-care" OR Self-management OR Medication Management AND Knowledge OR Haemoglobin A, Glycosylated OR HbA1c OR glycemic control OR Behavior change.

## Outcomes

The outcomes of interest were glycemic control, which was measured by HbA1c, and self-care activities, such as, diet control, physical activity, and self-monitoring of blood glucose (SMBG).

## Selection criteria

The studies were included in this systematic review if they were 1) randomized controlled trials (RCTs); 2) evaluating the effectiveness of educational interventions delivered by pharmacists (alone or in collaboration with other health care

professionals); 3) conducted on patients with type 2 diabetes only; 4) reporting both self-care activities and HbA1c; and 5) available in English language. Conference abstracts, review articles, and non-RCT interventional studies were excluded.

## Data extraction

After completion of the literature search, two researchers (AB and TMK) reviewed the titles and abstracts of all identified studies and selected the articles that fulfilled the study selection criteria. One researcher (AB) independently extracted the data from each identified study and recorded on a standardized data extraction form. The data extraction form was piloted on a selection of included studies in order to check whether it is adequate to capture all relevant information.

The data extracted from the selected studies in this review included the following: author names, year of publication, study design, health care setting and country where this study was conducted, duration of study, patient characteristics (number of participants, gender, and age), contents of the intervention, and outcome measures. AB extracted the data, which was checked and verified by another researcher (TMK); inconsistencies in the extracted data were resolved by discussion and consensus.

## Risk of bias (quality) assessment

Quality assessment of the included studies was done by two reviewers (AB and XT) by using Cochrane risk of bias (ROB) tool. This quality assessment was checked by a third researcher (TMK). The criteria that were used for quality assessment included the following: biasness associated with random sequence generation, allocation concealment, blinding for outcome evaluation, the extent of outcome data completeness, selective reporting, and other sources of bias. Each item of tool was rated, either as “low risk” (if it was unlikely that a bias would seriously alter the results), or “unclear” (if it was likely that a bias would raise some doubt about the results), or “high risk” (if it was likely that a bias would seriously alter the results). Disagreements were resolved through discussion.

## Data analysis

Meta-analysis was performed by using STATA version 14®. Weighted mean difference (WMD) was estimated to calculate the overall comparative effect of all interventions using random-effects model. For the meta-analysis, WMD > 0 will indicate an improvement in the self-care activities (specific diet, general diet, overall diet, physical activity, SMBG and

foot care), however WMD < 0 will represent reduction of HbA1c levels. All the *P*-values were set to be <0.05 with 95% CIs (according to whether the confidence interval included the null value) to assess significance. Subgroup analyses were performed on the basis of quality of the studies, in order to explain the heterogeneity among the studies. Inconsistency among the included studies was quantified by using *I*<sup>2</sup> statistic, which was appraised by the following criteria: 0%–40%, might not be important; 30%–60%, may represent moderate heterogeneity; 50%–90%, may represent substantial heterogeneity, and 75%–100%, considerable heterogeneity.<sup>20</sup>

Sensitivity analysis was done to check the robustness of the results by performing subgroup analysis regarding baseline HbA1c levels (<8% and ≥8%), duration of interventions, and geographical areas of the studies and their influence on HbA1c.

## Study protocol registration

The study protocol is registered with PROSPERO (Registration No CRD42017078854).

## Results

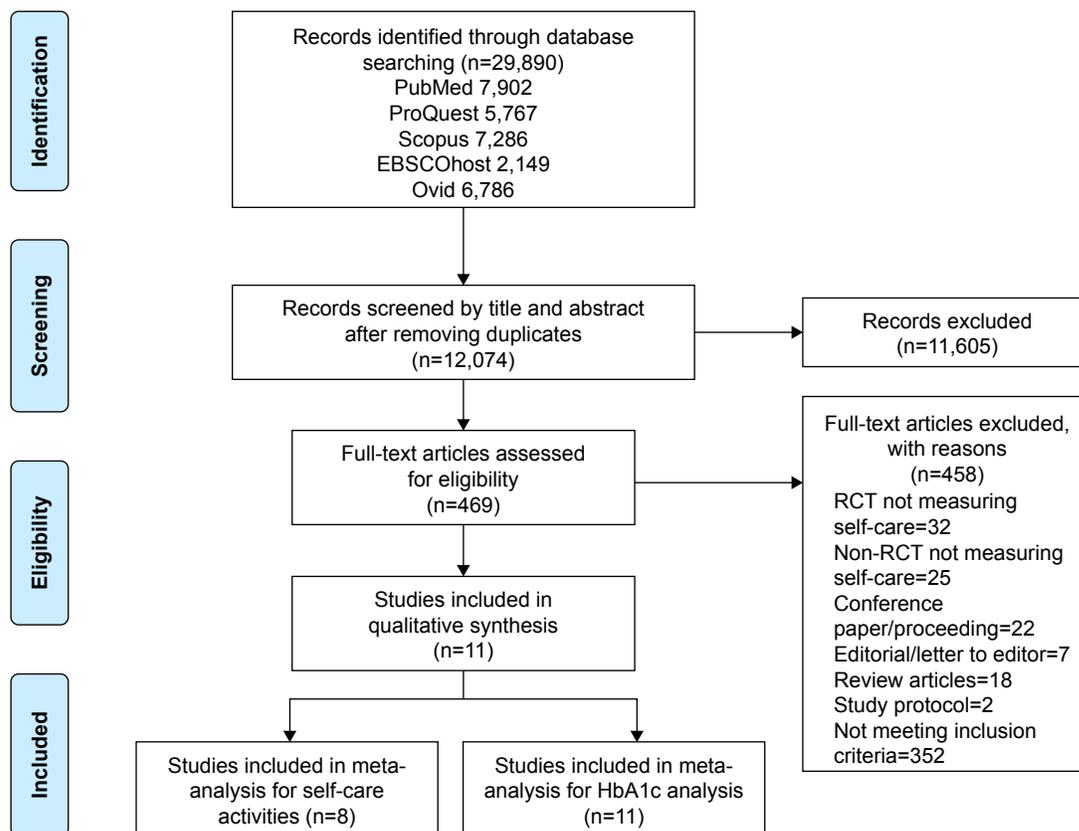
In total, 29,890 articles were identified initially from five electronic databases. After removing duplication and performing title and abstract screening, 469 articles were identified. Full-text assessment of these 469 articles resulted in identification of 11 articles meeting our inclusion criteria; the details are presented in PRISMA flow diagram of Figure 1.

## Description of the included studies

Among the n=11 included studies, parallel-group design of RCTs was adopted.<sup>21–31</sup> The study duration of all studies ranged from 4 months to 12 months. Three studies had a study duration <6 months,<sup>28,30,31</sup> n=6 studies' duration was 6 months,<sup>21,23,24,26,27,31</sup> and n=2 studies' duration was 12 months.<sup>22,25</sup> All of the included studies (n=11) were conducted on type 2 patients (n=1,544). Some studies imposed certain criteria on the type 2 patients' recruitment, such as patients who were using oral hypoglycemic medications,<sup>28</sup> and poorly controlled type 2 diabetes.<sup>24</sup> Majority of the studies included in this review (n=5) were conducted in Asia subcontinent,<sup>23,24,28,29,31</sup> followed by North America (n=4),<sup>21,22,25,30</sup> and Europe (n=2).<sup>26,27</sup>

## Description of pharmacist-led educational interventions

In most of the studies (n=8), educational intervention was performed by the pharmacist alone,<sup>22,23,25–29,31</sup> whereas, in rest



**Figure 1** PRISMA flow diagram of the study selection.

**Abbreviation:** RCT, randomized controlled trial.

of the studies ( $n=3$ ) it was performed by a multidisciplinary health care team, such as nurses, physicians, dieticians, involving pharmacist as a member of team.<sup>21,24,30</sup> Summary of Diabetes Self-care Activities (SDSCA) was the most frequently used tool ( $n=8$ ) in the included studies for assessment of the impact of educational interventions on self-care behaviors of the diabetes patients.<sup>21–23,25–28,31</sup> This eleven items tool is comprised of five domains of self-care, which include, diet (first four items), exercise (two items), blood glucose testing (two items), foot care (two items), and smoking (one item). This tool requires the respondents to rate their diabetes-related self-care activities of past 7 days on eight-point Likert scale. The diet domain (overall diet) of the tool is further composed of two subdomains, namely, General diet (first two items of the scale) and Specific diet (items three and four of the tool).<sup>32</sup>

One study used Diabetes self-care (DSC) scale,<sup>24</sup> and the other two studies used nonvalidated diabetes self-care assessment tool.<sup>29,30</sup> Details of contents of pharmacist-led educational interventions are presented in Table 1.

## Risk of bias assessment

The ROB of the included RCTs ( $n=11$  studies) by using Cochrane ROB tool is presented in Figure S1 (ROB

summary) and Figure S2 (ROB graph). Most of the studies ( $>80\%$ ) were free from attrition bias, selection bias, performance bias, detection bias, and reporting bias. Publication bias was checked by using funnel plot, and the Egger test was performed to check the funnel-plot asymmetry in meta-analysis.

## Outcomes

### Self-care activities

Effect of pharmacist-led educational intervention on self-care activities was measured by using a validated SDSCA tool in majority of the studies (8 out of 11). The results of eight studies that used SDSCA tool were pooled together for meta-analysis. Overall, a significant effect of pharmacist-led interventions was observed on different domains of patients' self-care practices, such as overall diet (1.16; 95% CI [0.38, 1.93];  $I^2=64.2\%$ ;  $P=0.094$ ), foot care (1.20; 95% CI [0.49, 1.90];  $I^2=95.0\%$ ;  $P<0.001$ ), and SMBG (1.62; 95% CI [0.92, 2.32];  $I^2=70.5\%$ ;  $P=0.005$ ).

Whereas, among rest of the three studies, which did not use SDSCA tool, statistically insignificant change ( $P=0.61$ ) in the self-care behaviors was reported by Kang et al, in type 2 diabetes patients, after 6 months of the intervention.<sup>24</sup> On the other hand, significantly improved compliance was observed

**Table 1** Characteristics of the included studies (n=11)

Author, Year, Country	Study design, duration of study (months)	No of type 2 diabetes patients (n), lost to follow-up (n), Mean age in years (SD), Gender (%) Female, Duration of type 2 diabetes in years (SD)	Pharmacist intervention and its characteristics	Control	Study tool for measurement of diabetes self-care
Cohen et al, 2011, <sup>21</sup> USA	Parallel RCT, 6	No of patients (IG/CG): 53/50 Lost to follow-up (IG/CG): 5/2 Age (IG/CG): 69.8 (10.7)/67.2 (9.4) Gender (IG/CG) female (%): 0/4 Duration of T2DM (IG/CG): Not mentioned	<b>Pharmacist-led group medical visit program:</b> Education about diabetes and its complications, self-management education, medication adherence counseling, identification and resolution of medication-related problems requiring intervention, education on lifestyle modification.	Standard primary care	SDSCA
Doucette et al, 2009, <sup>22</sup> USA	Parallel RCT, 12	No of patients (IG/CG): 36/42 Lost to follow-up (IG/CG): 5/7 Age (IG/CG): 58.7 (13.3)/61.2 (10.9) Gender (IG/CG): 61.8/53.7 Duration of T2DM (IG/CG): not mentioned	<b>Pharmaceutical care:</b> Self-management education, counseling for medication use, medication adherence counseling, SMBG education, medication review, identification of therapy-related issues and recommendations for therapy modification.	Usual care	SDSCA
Jahangard-Rafsanjani et al, 2015, <sup>26</sup> Iran	Parallel RCT, 5	No of patients (IG/CG): 51/50 Lost to follow-up (IG/CG): 6/10 Age (IG/CG): 57.3 (8.6)/55.9 (8.7) Female gender (IG/CG): 49/52 Duration of T2DM (IG/CG): 4.6 (4.3)/5.7 (5.9)	<b>Diabetes Education Program:</b> Education about diabetes and its complications, self-management education, medication adherence counseling, provision of written educational material, provision of free glucometer and/ pill counter, provision of SMBG data entry log book, SMBG education.	Usual care	SDSCA
Jarab et al, 2012, <sup>23</sup> Jordan	Parallel RCT, 6	No of patients (IG/CG): 85/86 Lost to follow-up (IG/CG): 8/7 Age (IG/CG): 63.4 (10.1)/65.3 (9.2) Gender (IG/CG) female (%): 36/38 Duration of T2DM (IG/CG): 9.7 (7.4)/10.1 (7.7)	<b>Comprehensive clinical pharmacy service:</b> Education about diabetes and its complications, self-management education, counseling for medication use, medication adherence counseling, provision of written educational material, education on lifestyle modification.	Usual care	SDSCA
Kang et al, 2010, <sup>24</sup> Taiwan	Parallel RCT, 6	No of patients (IG/CG): 33/34 Lost to follow-up (IG/CG): 5/6 (IG/CG): 55.3 (7.7)/51.7 (8.5) Gender (IG/CG): 42.8/50 Duration of T2DM (IG/CG): 3.8 (3.2)/4.4 (3.0)	<b>Family partnership intervention care:</b> Self-management education, counseling for medication use, Provision of SMBG data entry log book, education on lifestyle modification.	Conventional care	DSC
Korcegez et al, 2017, <sup>25</sup> USA	Parallel RCT, 12	No of patients (IG/CG): 79/80 Lost to follow-up (IG/CG): 4/3 Age (IG/CG): 61.80±10.38/62.22±9.54 Gender (IG/CG) female (%): 77.3/74 Duration of T2DM (IG/CG): not mentioned	<b>Pharmacist-led program:</b> Education about diabetes and its complications, self-management education, counseling for medication use, provision of written educational material, education on lifestyle modification, SMBG education, medication and treatment review, discussion sessions on revision of medications.	Usual care	SDSCA

(Continued)

Table 1 (Continued)

Author, Year, Country	Study design, duration of study (months)	No of type 2 diabetes patients (n), lost to follow-up (n), Mean age in years (SD), Gender (%) Female, Duration of type 2 diabetes in years (SD)	Pharmacist intervention and its characteristics	Control	Study tool for measurement of diabetes self-care
Mehuys et al, 2011, <sup>26</sup> Belgium	Parallel, RCT, 6	No of patients (IG/CG): 153/135 Lost to follow-up (IG/CG): 5/3 Age (IG/CG): 63.0 (40–84)/62.3 (45–79) Gender (IG/CG) female (%): 49/46.3 Duration of T2DM (IG/CG): not mentioned	<b>Standard diabetes education program:</b> Education about diabetes and its complications, counseling for medication use, medication adherence counseling, education on lifestyle modification.	Usual pharmacist care	SDSCA
Nascimento et al, 2015, <sup>27</sup> Spain	Parallel RCT, 6	No of patients (IG/CG): 44/43 Lost to follow-up (IG/CG): 0/0 Age (IG/CG): 74.2 (5.4)/72.3 (4.5) Gender (IG/CG): 43.2/41.9 Duration of T2DM (IG/CG): 10.4 (6.9)/14.7 (8.5)	<b>Individualized pharmacotherapy management service:</b> Education about diabetes and its complications, provision of written educational material.	Standard medical care consultation	SDSCA
Samtia et al, 2013, <sup>29</sup> Pakistan	Parallel RCT, 5	Age (IG/CG): 46.1 (23–74)/42.3 (21–77) Lost to follow-up (IG/CG): 4/2 Age (IG/CG): 54 (13)/57 (11) Gender (IG/CG): 47.2/51.2 Duration of T2DM (IG/CG): not mentioned	<b>Multifactorial intervention:</b> Education about diabetes and its complications, self-management education, medication adherence counseling, education on lifestyle modification, SMBG education	Usual medical care	Generic self-care assessment tool
Taveira et al, 2010, <sup>30</sup> USA	Parallel RCT, 4	No of patients (IG/CG): 64/54 Lost to follow-up (IG/CG): 6/3 Age (IG/CG): 62.2 (10.3)/66.8 (10.2) Gender (IG/CG) female (%): 8.6/0 Duration of T2DM (IG/CG): not mentioned	<b>Pharmacist-led group medical visit programs:</b> Patient education and counseling for medication use.	Usual care	Nonvalidated diabetes self-care behavior survey
Wishah et al, 2015, <sup>31</sup> Jordan	Parallel RCT, 6	No of patients (IG/CG): 52/54 Lost to follow-up (IG/CG): 2/3 Age (IG/CG): 52.9 (9.6)/53.2 (11.2) Gender (IG/CG) female (%): 61.5/51.9 Duration of T2DM (IG/CG): 5.5 (4.5)/5.1 (4.9)	<b>Pharmaceutical care interventions developed by the clinical pharmacist:</b> Education about diabetes and its complications, self-management education, counseling for medication use, medication adherence counseling, provision of written educational material, therapeutic efficacy monitoring by laboratory results, recommendations for initiation of oral hypoglycemic agents, titration of drug therapeutic dosage, and current therapy modifications due to ineffectiveness.	Usual care provided by the medical and nursing staff	SDSCA

**Abbreviations:** CG, control group; DSC, Diabetes Self-Care Scale; IG, investigational group; RCT, randomized controlled trial; SDSCA, Summary of Diabetes Self-Care Activities; SMBG, self-monitoring of blood glucose; T2DM, type 2 diabetes mellitus.

by Samtia et al, among intervention group patients, toward foot care ( $P<0.001$ ) and SMBG ( $P=0.001$ ).<sup>29</sup> Similar findings were also observed by Taveira et al, where a significant improvement ( $P=0.01$ ) in adherence toward self-care behaviors was observed, especially for SMBG ( $P=0.01$ ).<sup>30</sup>

## Exercise

By using SDSCA tool,  $n=8$  studies measured the effect of pharmacist-led educational intervention on exercise for type 2 diabetes patients, which is one of the key factors for diabetes self-care. The results of an overall meta-analysis favored the pharmacist-led education on exercise (WMD =0.94; 95% CI [0.72, 1.16];  $I^2=17.9\%$ ;  $P=0.288$ ), as shown in Figure 2.

## Foot care

Foot care was examined by  $n=7$  studies, and the results of an overall meta-analysis favored pharmacist-led education (WMD =1.20; 95% CI [0.49, 1.90];  $I^2=95.0\%$ ;  $P<0.001$ ; Figure 2). Due to significant heterogeneity among these ( $n=7$ ) studies ( $I^2=95.0\%$ ), subgroup analyses were performed based on the ROB (unclear, low, and high) of the seven studies. It was found that the heterogeneity of the unclear ROB group<sup>21,27</sup> notably decreased from 95.0% to 70.2%. However, the studies in low ROB group<sup>23,26,28,31</sup> showed only a slight decrease in heterogeneity ( $I^2=94.1\%$ ; Figure 3). There was no  $I^2$  value for the high ROB group, as there was only one study with high ROB,<sup>25</sup> thus there was no comparison of data to obtain  $I^2$  value. Significantly high effect of interventions

was observed by the studies with low ROB (WMD =1.46; 95% CI [0.58, 2.35];  $I^2=94.1\%$ ;  $P<0.001$ ), when compared with the studies with unclear ROB (WMD =0.36; 95% CI [-0.57, 1.30];  $I^2=70.2\%$ ;  $P=0.067$ ).

## General diet

Effect of pharmacist-led educational interventions on general diet was examined by  $n=4$  studies. Results of overall meta-analysis were in favor of the pharmacist-led education (WMD =0.68; 95% CI [0.15, 1.22];  $I^2=74.6\%$ ;  $P=0.008$ ), however the overall heterogeneity was high, as shown in Figure 2. Therefore, a subgroup analysis based on the ROB of each study was performed. The studies with low ROB<sup>26,31</sup> showed greater effect on general diet (WMD =0.94; 95% CI [-0.13, 2.02];  $I^2=88.4\%$ ;  $P=0.003$ ) when compared with the studies with unclear ROB<sup>21,27</sup> (WMD =0.43; 95% CI [0.04, 0.82];  $I^2=0\%$ ;  $P=0.688$ ); details are presented in Figure 3.

## Overall diet

Another analysis was performed with two studies for overall diet. The results favored the pharmacist-led intervention, toward overall diet in type 2 diabetes patients (WMD =1.16; 95% CI [0.38, 1.93];  $I^2=64.2\%$ ;  $P=0.094$ ; Figure 2).

## Self-monitoring of blood glucose

By using SDSCA scale,  $n=6$  studies examined the effect of pharmacist-led interventions on SMBG. The results of overall meta-analysis were in favor of pharmacist-led education on

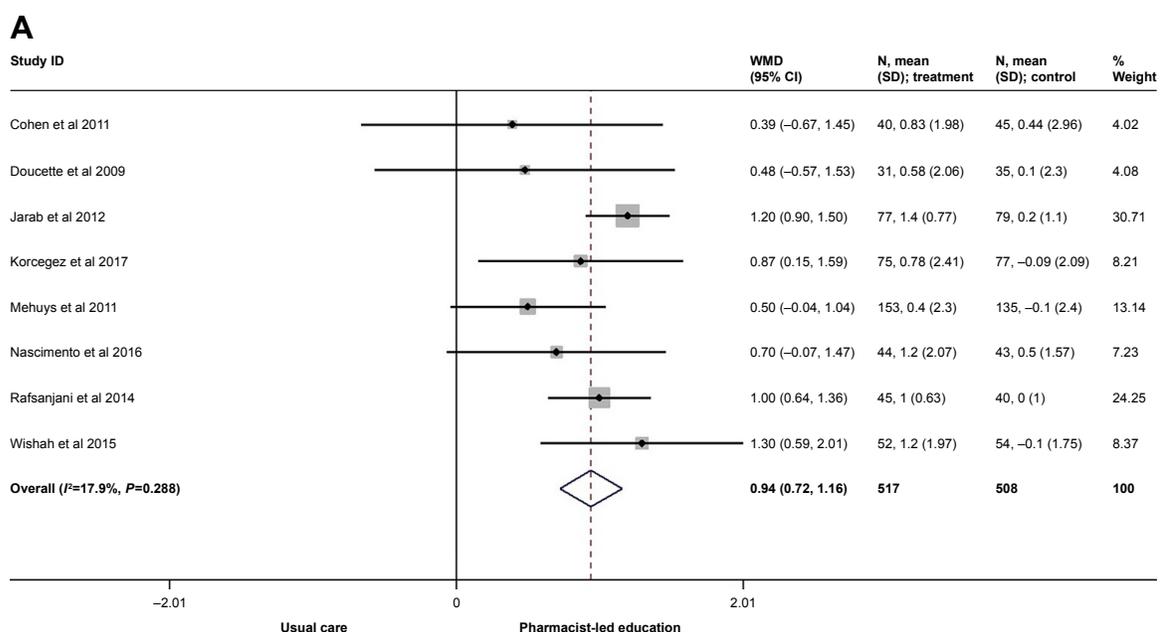


Figure 2 (Continued)

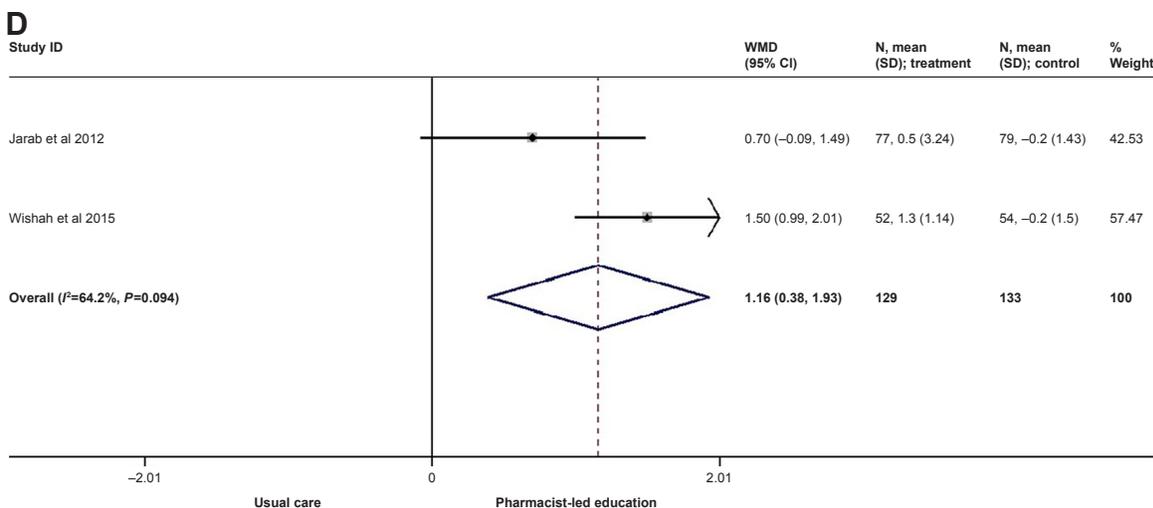
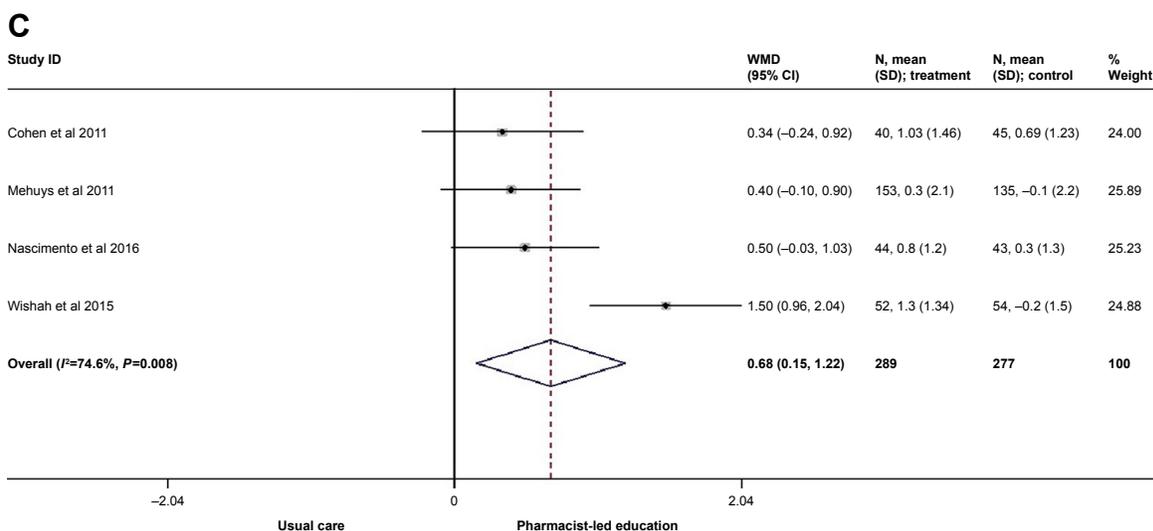
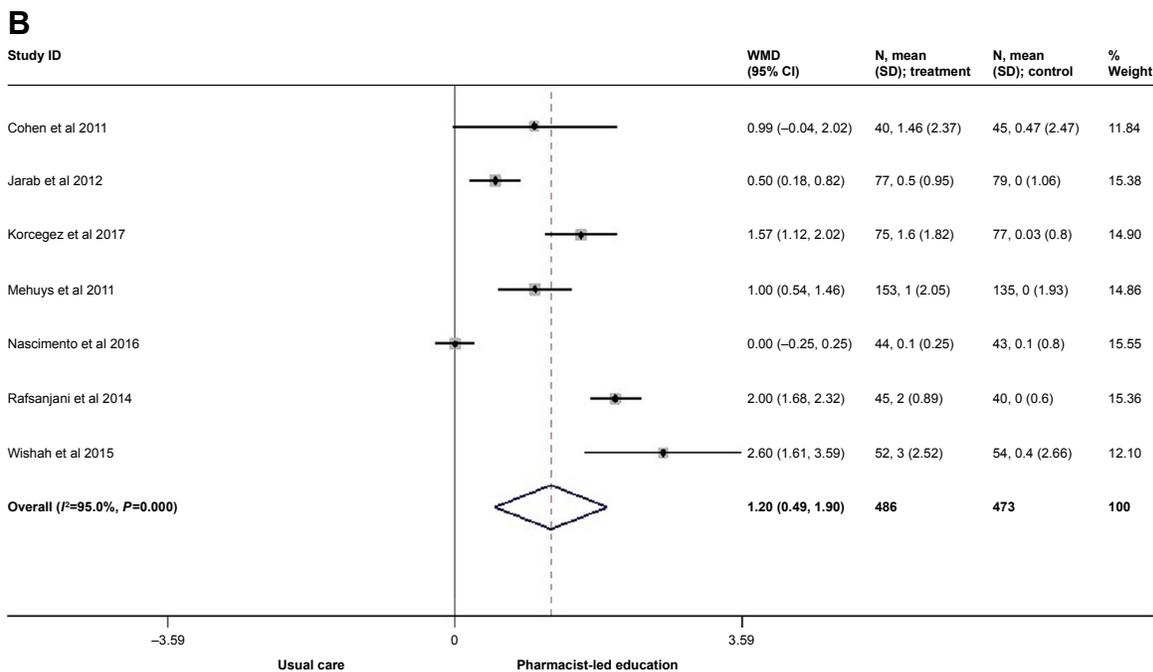
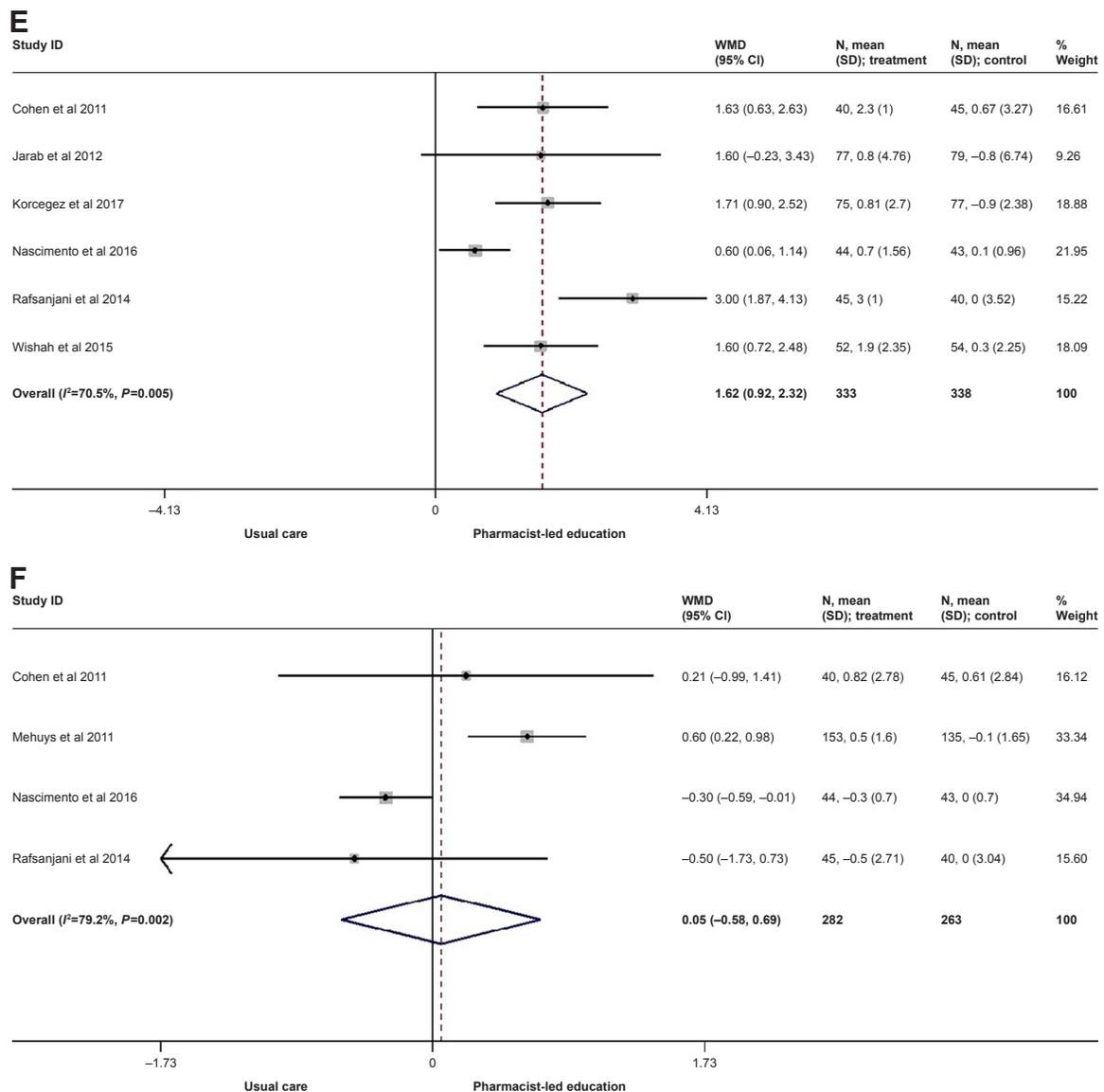


Figure 2 (Continued)



**Figure 2** Overall meta-analysis of all categories of Summary of Diabetes Self-care Activities.

**Notes:** (A) Exercise. (B) Foot care. (C) General diet. (D) Overall diet. (E) Self-monitoring of blood glucose. (F) Specific diet. Weights are from random-effects analysis.

**Abbreviation:** WMD, weighed mean difference.

better practices toward SMBG, when compared with usual care (WMD=1.62; 95% CI [0.92, 2.32];  $I^2=70.5%$ ;  $P=0.005$ ; Figure 2). A subgroup analysis was performed according to the ROB of each study. The heterogeneity of the unclear ROB subgroup<sup>21,23,27</sup> decreased significantly compared with the previous overall  $I^2$  value ( $I^2=46.8%$ ). There was only  $n=1$  study in the high ROB subgroup;<sup>25</sup> therefore, the  $I^2$  value cannot be obtained, but the result was still in favor of the pharmacist-led education. For the low ROB subgroup, the  $I^2$  value increased slightly to 72.9%. Also, the studies with low ROB showed significantly better effect (WMD =2.25; 95% CI [0.88, 3.62];  $P=0.055$ ) when compared with the studies with Unclear ROB (WMD =1.08, 95% CI [0.30, 1.87];  $P=0.153$ ; Figure 3).

## Specific diet

Effect of pharmacist-led educational interventions on specific diet was examined by  $n=4$  studies. The results of overall meta-analysis showed no effect on specific diet (WMD=0.05; 95% CI [-0.58, 0.69];  $P=0.002$ ; Figure 2). However, the heterogeneity was high ( $I^2=79.2%$ ). A subgroup analysis was performed according to the ROB of each study. The studies with low ROB<sup>26,28</sup> (WMD =0.21; 95% CI [-0.82, 1.24];  $I^2=64.4%$ ;  $P=0.094$ ) as well as with unclear ROB<sup>21,27</sup> (WMD =-0.27; 95% CI [-0.56, 0.01];  $I^2=0%$ ;  $P=0.417$ ) showed insignificant effect on specific diet (Figure 3).

## Glycated hemoglobin

Glycemic control of the all the included studies ( $n=11$ ) was measured by HbA1c. WMD was estimated for overall

meta-analysis of the included studies. The meta-analysis showed an overall effect in favor of the pharmacist-led educational interventions on HbA1c, where the levels of HbA1c reduced with a mean difference of  $-0.66\%$  (95% CI  $[-0.83, -0.50]$ ;  $I^2=58.3\%$ ;  $P=0.008$ ), as shown in Figure 4.

### Moderation of effectiveness of intervention and study features on HbA1c

The findings of subgroup meta-analysis revealed that the studies that were conducted in Asian countries ( $n=5$ ) showed a comparatively larger effect on HbA1c level reduction

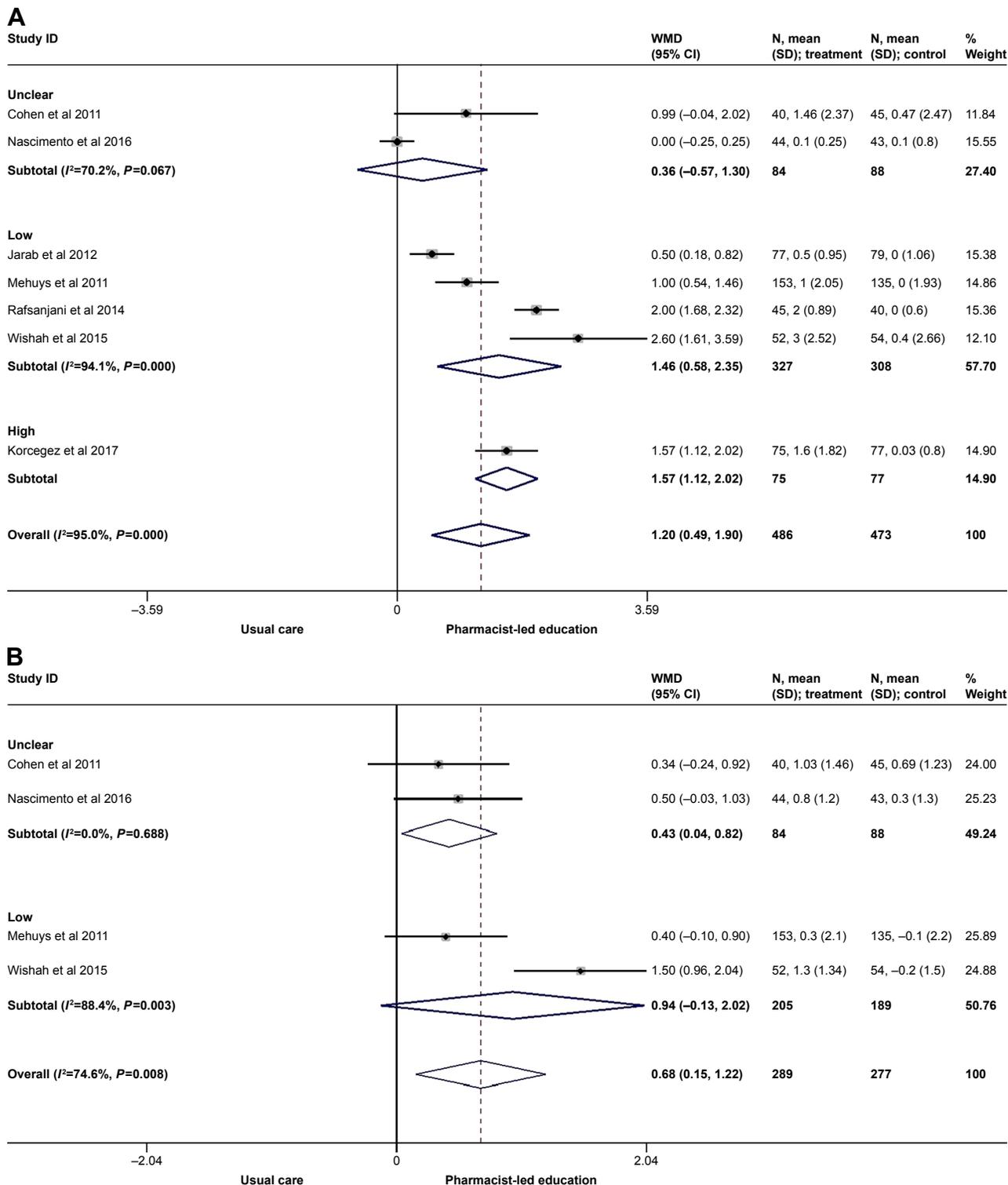
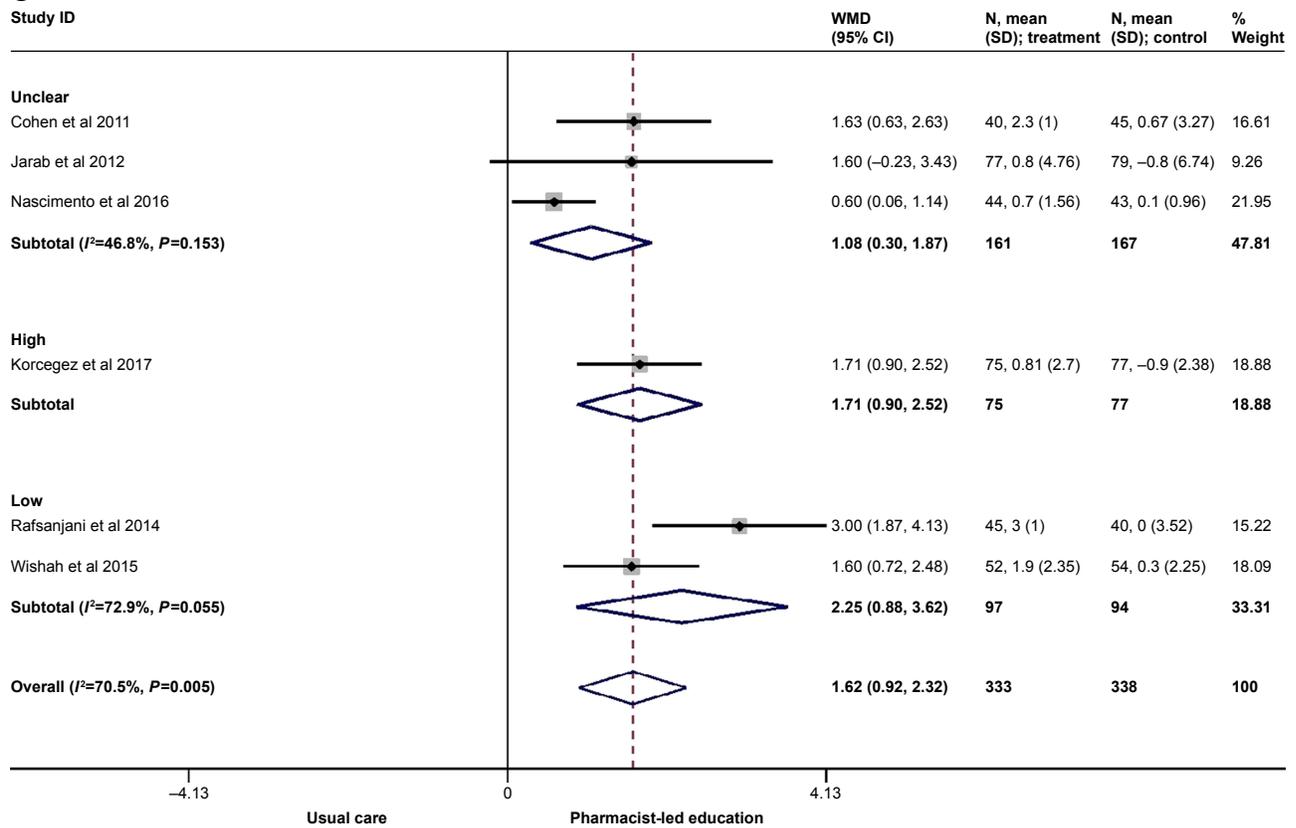


Figure 3 (Continued)

**C**



**D**

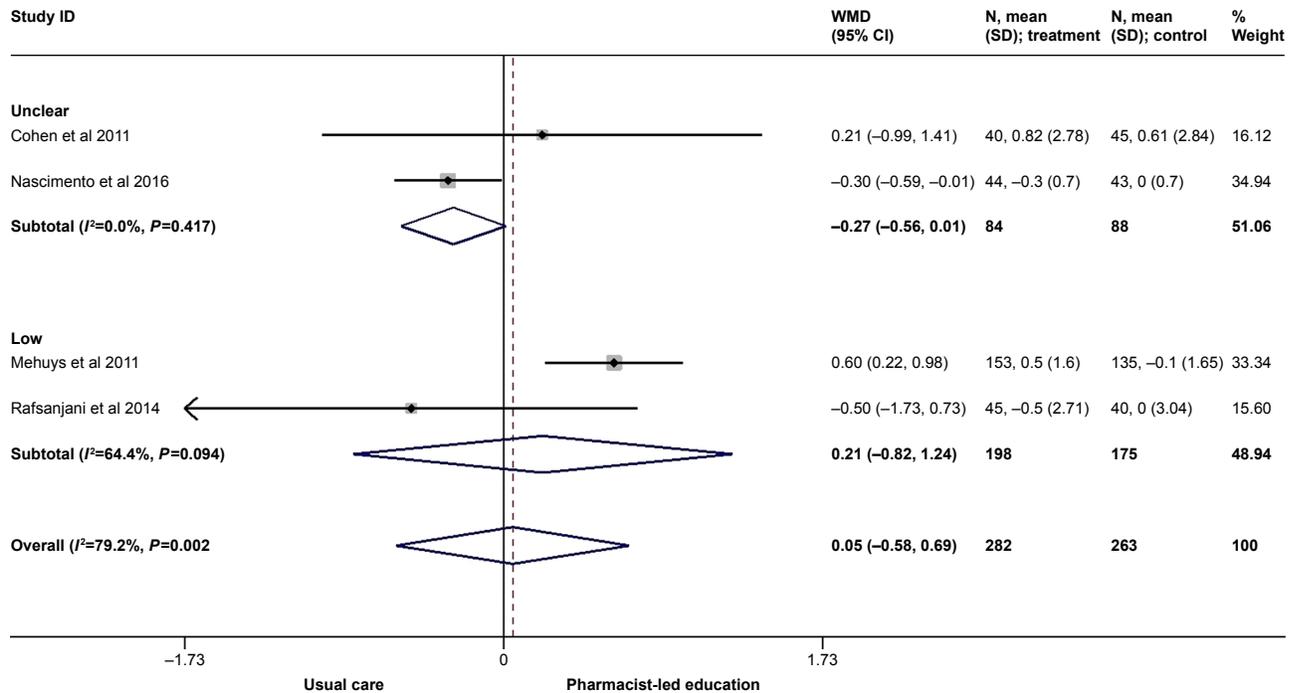
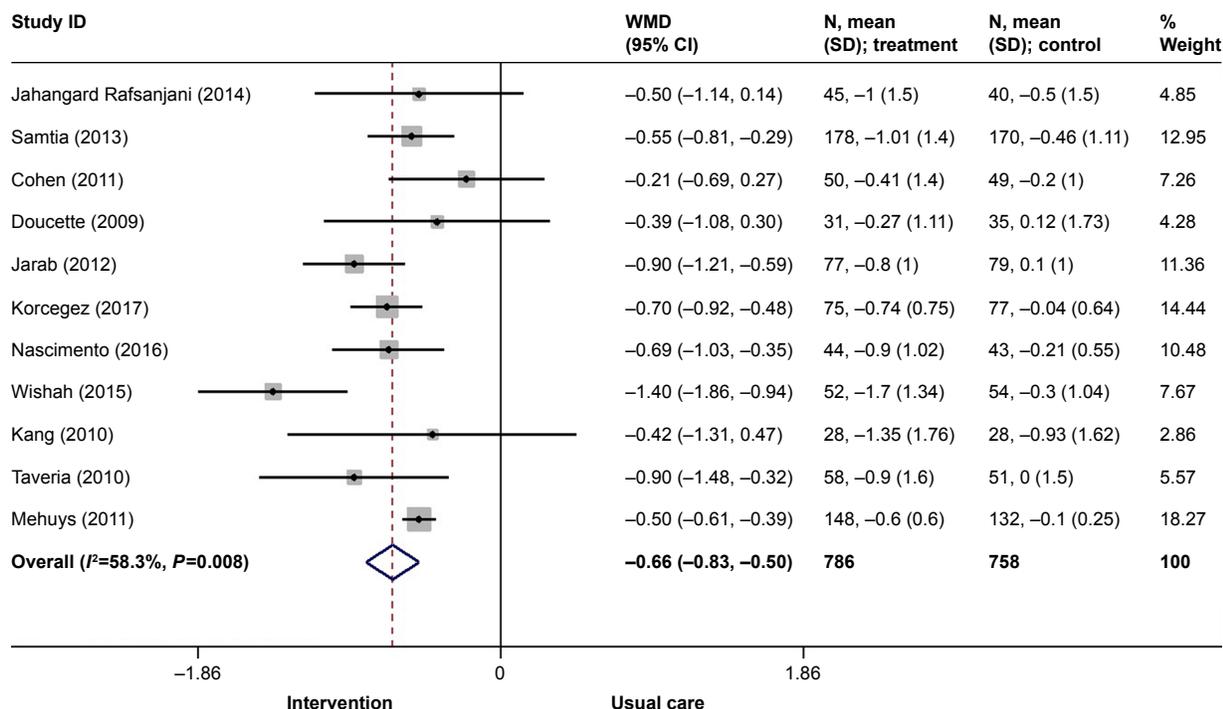


Figure 3 Subgroup meta-analysis for different categories of Summary of Diabetes Self-care Activities scale.

Notes: (A) Foot care. (B) General diet. (C) Self-monitoring of blood glucose. (D) Specific diet. Weights are from random-effects analysis.

Abbreviation: WMD, weighed mean difference.



**Figure 4** Overall meta-analysis for glycosylated hemoglobin of the included studies (n=11).

**Note:** Weights are from random-effects analysis.

**Abbreviation:** WMD, weighted mean difference.

(WMD = -0.80; 95% CI [-1.14, -0.46];  $I^2=66.3%$ ;  $P=0.018$ ) when compared with the studies (n=4) that were conducted in North America (WMD = -0.58; 95% CI [-0.86, -0.31];  $I^2=35.1%$ ;  $P=0.201$ ) and Europe n=2 (WMD = -0.52; 95% CI [-0.64, -0.40];  $I^2=7%$ ;  $P=0.300$ ; Figure S3). When self-care education was provided by pharmacist alone, comparatively more reduction in HbA1c level was examined (WMD = -0.70; 95% CI [-0.88, -0.52];  $I^2=65.5%$ ;  $P=0.005$ ) in comparison to the intervention where education was given by pharmacist in a team (WMD = -0.50; 95% CI [-0.95, -0.04];  $I^2=38.3%$ ;  $P=0.198$ ; Figure S4). No significant difference on WMD of HbA1c was observed when other features of the studies, such as, duration of intervention and baseline HbA1c levels were examined (Figures S5 and S6, respectively).

## Publication bias

The symmetrical presentation of the funnel plot for HbA1c for all studies (n=11) indicated slight publication bias, as the majority of the studies were with 95% CI (Figure S7) along with Egger test, where the bias was -0.86 (95% CI = -2.63, 0.90;  $P=0.298$ ).

## Discussion

Based on the evidence synthesized from the overall meta-analysis of RCTs (n=11), included in this review, it is

evident that pharmacist-led educational interventions have clinically significant effect on glycosylated hemoglobin (-0.66; 95% CI [-0.83, -0.50];  $I^2=58.3%$ ) and on various domains of self-care activities, such as, on SMBG (1.62; 95% CI [0.92, 2.32];  $I^2=70.5%$ ), foot care (1.20; 95% CI [0.49, 1.90];  $I^2=95.0%$ ), and overall diet (1.16; 95% CI [0.38, 1.93];  $I^2=64.2%$ ).

The ROB of most of the included studies was low in different domains; however, there is still a significant percentage of unclear and low ROB in few studies. Among the included studies, Korcegez et al,<sup>25</sup> has the highest percentage of high ROB, whereas Samtia et al,<sup>29</sup> has the highest percentage of unclear ROB. These studies might lead to an overestimate or underestimate for the effect of pharmacist-led education toward the observed outcomes of people with diabetes. Slight evidence of publication bias was confirmed by funnel plot and Eggers test. To address the issue of high heterogeneity, subgroup meta-analysis was performed on the basis of quality of the studies. The findings of subgroup meta-analysis revealed that the studies with low ROB had a comparatively larger effect of pharmacist-led interventions on foot care (1.46; 95% CI [0.58, 2.35];  $I^2=94.1%$ ), general diet (0.94; 95% CI [-0.13, 2.02];  $I^2=88.4%$ ), SMBG (2.25; 95% CI [0.88, 3.62];  $I^2=72.9%$ ), and specific diet (WMD = 0.21; 95% CI [-0.82, 1.24];  $I^2=64.4%$ ), when compared with studies with unclear or high ROB.

Similarly, clinically important reductions were observed in HbA1c levels when self-care education was provided by pharmacist ( $-0.70$ ; 95% CI  $[-0.88, -0.52]$ ;  $I^2=66\%$ ), as evident from subgroup meta-analysis. A similar effect of pharmacist-led interventions on HbA1c levels was reported by van Eikenhorst et al,<sup>15</sup> ( $-0.70$ ; 95% CI  $[-0.91, -0.51]$ ) and Cranor et al.<sup>33</sup> Likewise, Pousinho et al<sup>16</sup>  $[-0.18\%$  to  $-2.1\%$ ] and Machado et al<sup>17</sup>  $[1.00\% \pm 0.28\%$ ;  $P<0.001$ ] in their systematic reviews also reported statistically significant reductions in HbA1c. Inclusion of pharmaceutical care component to the pharmacist-led educational intervention resulted in comparatively more reductions in HbA1c levels as shown by Wishah et al<sup>31</sup>  $[-1.40$ ; 95% CI  $-1.86, -0.94]$ . Further research is required to examine the effect of components, cost and delivery of interventions on clinical and patient-reported outcomes of patients with type 2 diabetes, in order to design a cost-effective intervention.

Micro- and macrovascular complications in chronic patients with type 2 diabetes are directly associated with glycemic control. Effective diabetes self-care education provided by health care providers can minimize the chances of such complications, which occur as a consequence of poor glycemic control. Being an expert in pharmacotherapy and easily approachable, when compared with other overburdened health care providers, pharmacists can play an effective role by providing self-care education in addition to pharmaceutical care in a variety of health care settings. Especially, people with diabetes from low- and middle-income countries can rely more on pharmacists within the community and it will decrease dependence on the limited public hospitals and will facilitate in achieving favorable health outcome.

## Limitations

One of the limitation of this systematic review is the relatively small sample size of the included studies, thus the results are subject to greater sampling variation and hence might be interpreted with care. In addition, heterogeneity among the included studies was another limitation to this study, which could be due to variability of patient populations and interventions. Despite the heterogeneity, most of the outcomes were in favor of the pharmacist-led education. To address the issue of high heterogeneity, subgroup analysis and funnel plot for publication bias were performed for the pooled results of HbA1c. The symmetrical shape of funnel plot indicated low risk of publication bias, but the heterogeneity remained same after subgroup analysis, which could possibly be due to varied population characteristics. Thus, the high heterogeneity values should not greatly affect the conclusion of this systematic review.

## Conclusion

This systematic review demonstrates a positive impact of pharmacist-led educational interventions on glycemic control and diabetes-related self-care activities of type 2 diabetes patients, which are surrogate markers for disease progression and its related complications. Therefore, pharmacists should take an active role in providing diabetes self-care education in conjunction with euglycemic medicines, in order to improve patient outcomes.

## Disclosure

AB received a PhD Merit Scholarship from Monash University. KGC received a grant from the University of Malaya (PG089-2015B). The authors report no other conflicts of interest in this work.

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## Supplementary materials

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cohen et al, 2011	?	?	+	+	+	+	+
Doucette et al, 2009	?	?	?	+	-	+	+
Jarab et al, 2012	+	?	?	?	+	+	+
Kang et al, 2010	+	+	+	+	+	+	+
Korcegez et al, 2017	-	-	-	?	+	+	+
Mehuys et al, 2011	+	+	?	+	+	+	+
Nascimento et al, 2016	?	?	+	?	+	-	+
Rafsanjani et al, 2014	+	+	+	+	+	+	+
Samtia et al, 2013	?	?	?	+	?	+	-
Taveira et al, 2010	+	+	+	+	+	+	+
Wishah et al, 2015	?	+	+	-	+	+	-

Figure S1 Risk of bias summary of included studies (n=11).

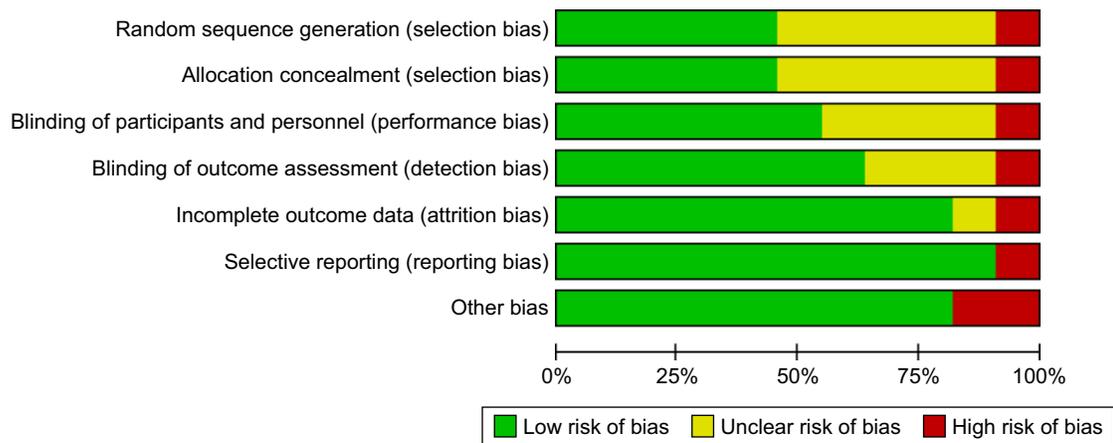


Figure S2 Risk bias graph of included studies (n=11).

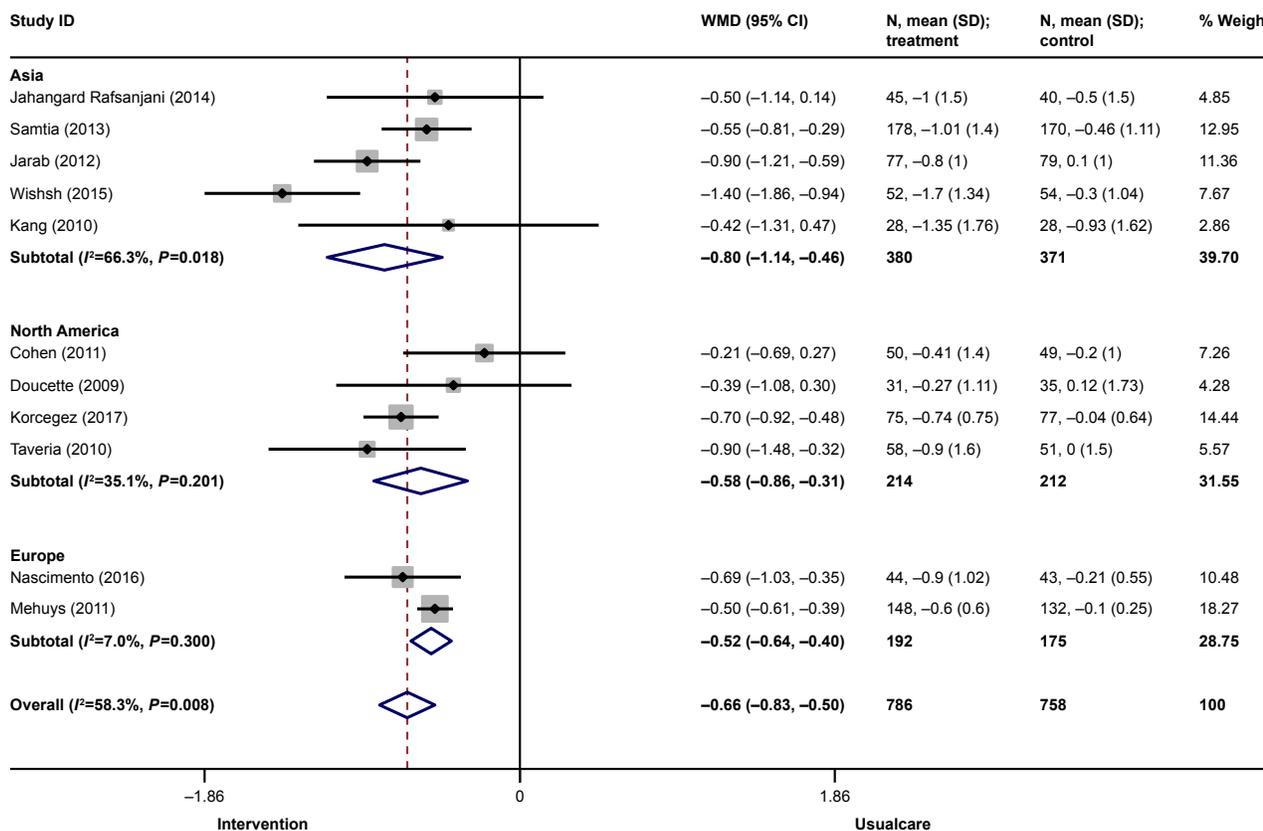


Figure S3 Sub-group meta-analysis for HbA1c on the basis of region (n=11). Weights are from random effects analysis.

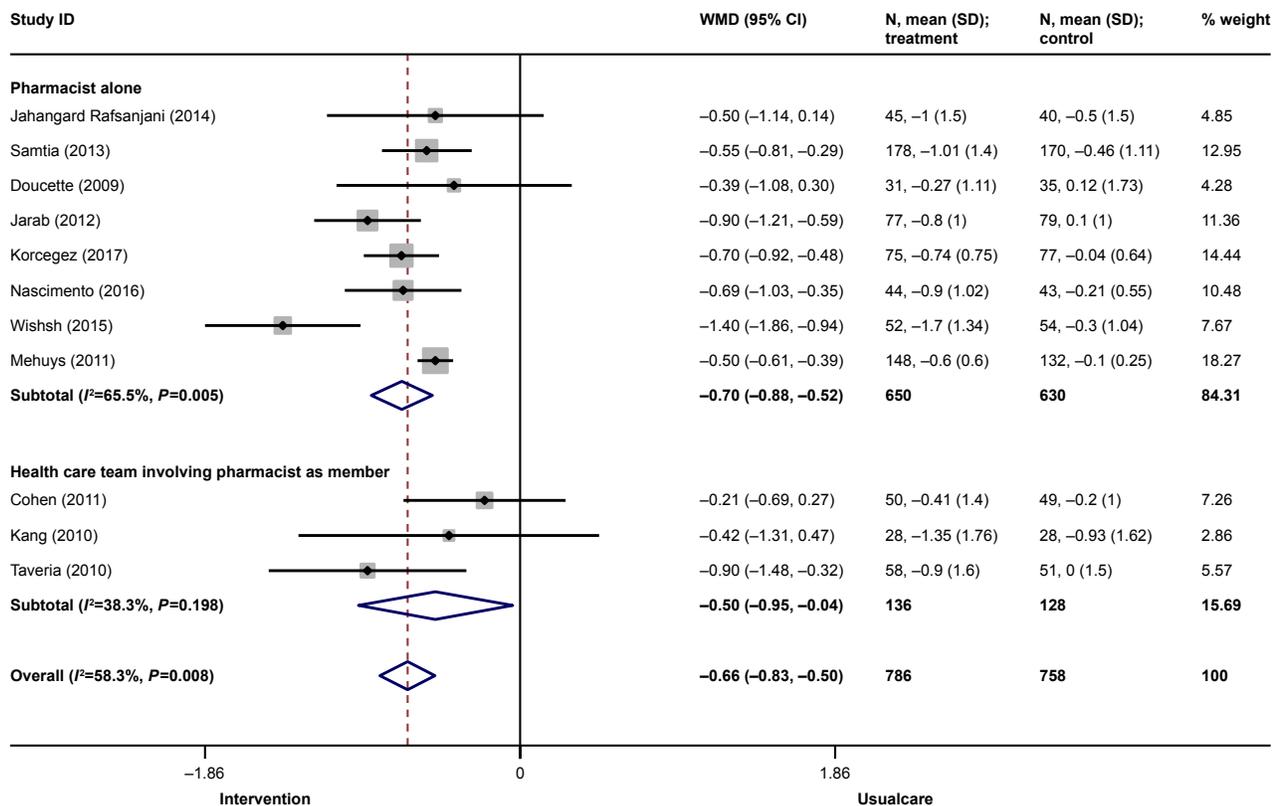


Figure S4 Sub-group meta-analysis for HbA1c of included RCTs on the basis of intervention provider (n=11).

Note: Weight are from random effects analysis.

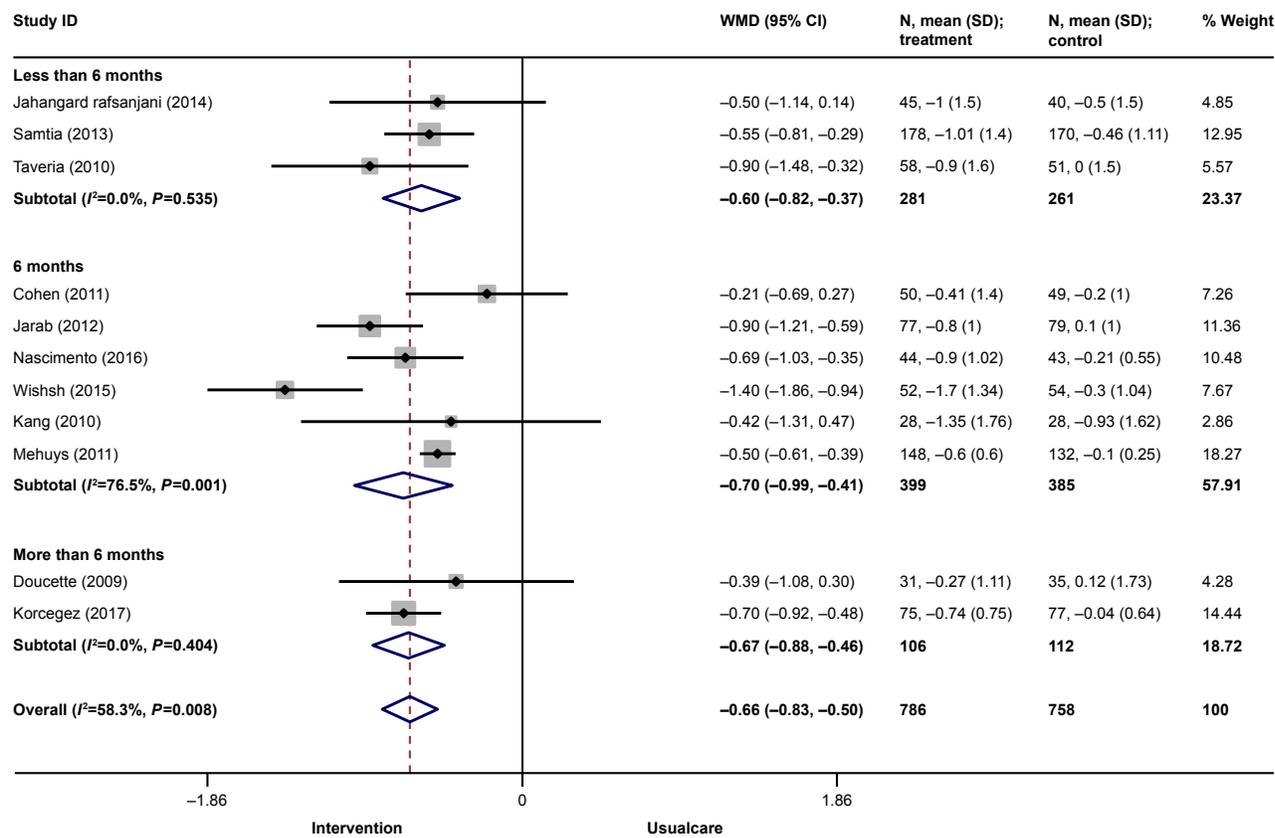


Figure S5 Sub-group meta-analysis for HbA1c of included RCTs on the basis of duration of study (n=11).

Note: Weights are from random effects analysis.

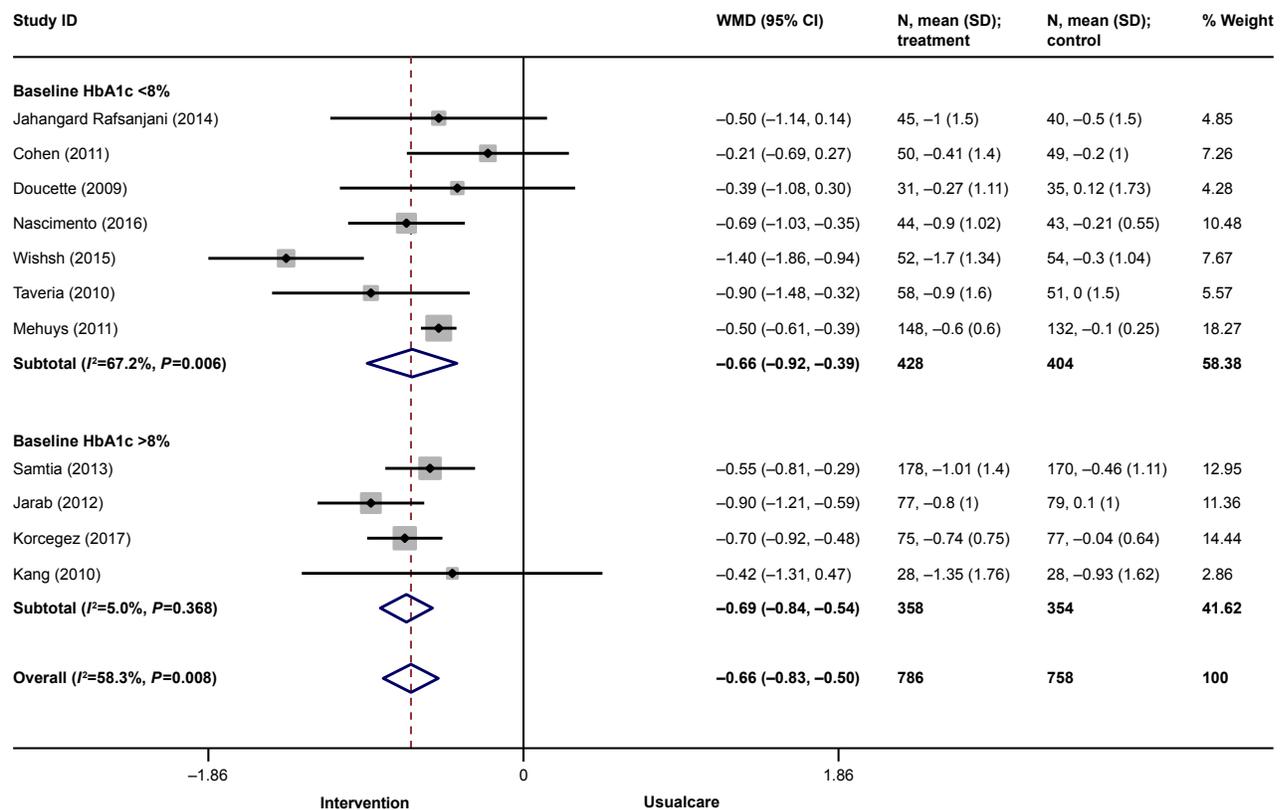
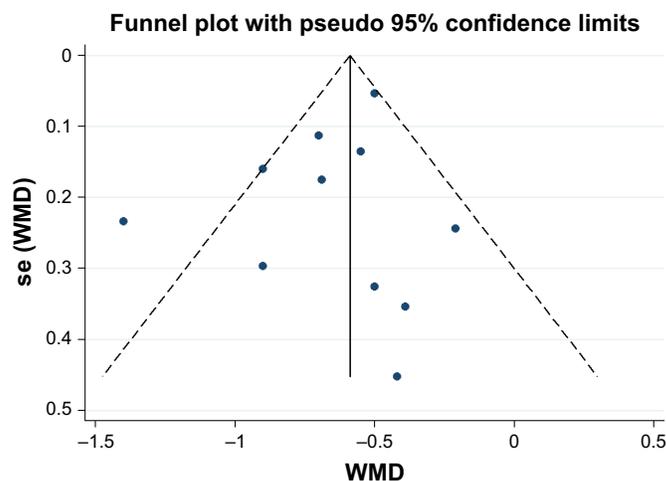


Figure S6 Sub-group meta-analysis for HbA1c of included RCTs on the basis of baseline HbA1c (n=11).

Note: Weights are from random-effects analysis.



**Figure S7** Funnel Plot of Publication Bias.

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