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Effect of Pharmacist's Interventions on Glycemic Control in Diabetic Patients: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Abstract

Several clinical trials have evaluated the effect of pharmacists' interventions. However, the results have been inconsistent. We performed a systematic review to evaluate the effect of pharmacists' interventions on glycemic control in diabetes. Clinical trials of pharmacists' interventions aimed at improving glycemic control in diabetes patients were identified through a systematic search of MEDLINE, CINAHL, Web of Science, the Cochrane Library, and THAILIS. The bibliographic databases were searched from their inceptions to the end of February 2012. The references lists of relevant articles were checked and experts were consulted. Studies were included if they were: i) randomized controlled trials of pharmacists' interventions aimed at improving glycemic control in diabetes patients, ii) reporting HbA_{1c} as an outcome measure, iii) published in English or Thai, and iv) clearly describing details of pharmacists' intervention. Treatment effect was estimated with the mean difference in the change of HbA_{1c} levels from baseline between the intervention and the control groups. Twenty-two trials involving 2,808 patients were included. Pharmacists' interventions included an assessment and adjustment of anti-diabetic medications, identification of drug-related problems, co-operation with physicians and other members of the health care team, offering diabetes booklets and special medication containers, providing education concerning self-management of diabetes, and reinforcement of diabetes management with pharmacotherapy and non-pharmacotherapy. This meta-analysis showed that pharmacists' interventions can improve glycemic control in diabetes patients (mean difference -0.68%, 95% CI -0.87% to -0.49%, $p < 0.00001$). Thus, pharmacists can play an important role in diabetes management.

Keyword: systematic review, pharmaceutical care, glycemic control, diabetes

INTRODUCTION

Uncontrolled diabetes leads to micro-vascular complications, namely, retinopathy, nephropathy, and neuropathy, and macrovascular complications, namely, congestive heart failure (CHF), cerebrovascular disease (CVD), and peripheral arterial disease (PAD).[1] Pharmacist has recently been involved in multidisciplinary team. The role of pharmacist in diabetes care, including discharged counseling and providing patient education regarding disease and medication, especially, drug related problem (DRP) monitoring,[2-4] is the most important responsibility of pharmacist to their patients for positive outcomes such as improving quality of life and keeping targeted goal of hemoglobin A_{1c} (HbA_{1c}). Evidence is clear that improving glycemic control and preventing complications result in significant cost saving and improved quality of life.[5]

There have been a large number of clinical trials evaluating pharmacists'

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interventions in diabetes mellitus (DM). However, the outcomes of these studies remain controversial. We conducted a systematic review and meta-analysis to assess the effect of pharmacists' interventions on HbA_{1c} level in diabetes patients.

METHODS

Data sources

Reports of randomized controlled trials of pharmacists' interventions aimed for good glycemic control in diabetes patients were identified through a systematic literature search of MEDLINE, CINAHL, the Cochrane Library, Web of Science, and the THAIland Library Integrated System (THAILIS). Literature searches were conducted from inception to the end of February 2012. The MeSH terms "pharmaceutical services", "pharmacists", and "diabetes mellitus" were used together with keywords "pharmaceutical care" and "pharmacy counseling". Hand search was also performed on relevant journals in Thailand such as Journal of the Medical Association of Thailand, Thai Journal of Hospital Pharmacy. References of retrieved studies and reviews of the topic were hand searched and experts in the field were contacted for additional papers not captured by the search strategy.

Study selection

The studies were included in the review if they: 1) were randomized controlled trials of any pharmacists' interventions compared with usual care in diabetes patients, including type 1, type 2, Gestational diabetes mellitus (GDM), or unspecified DM; 2) reported HbA_{1c} as an outcome measure; 3) were published in English or Thai language; and 4) clearly described pharmacists' intervention. Abstract presentation was excluded.

Data extraction and quality assessment

Data extraction and study quality assessment were performed independently by two investigators using a standardized form. Disagreements were resolved by a third investigator. Data from individual studies were abstracted. Data recorded were the year of publication, setting, country, duration of study, intervention frequency, number of visit, inclusion criteria and exclusion criteria of each trial, type of DM, concomitant drug and disease, sample size, age, duration of DM, details of pharmacists' interventions and control intervention, and primary outcomes. Quality of randomized controlled trials included in this review was assessed using Maastricht-Amsterdam scale.[6] The scale comprises 11 items to evaluate internal validity of the study results. Studies that met at least 6 of 11 quality criteria were of high quality. Those scoring less than 6 of the criteria were of low quality.

Statistical analysis

Treatment effect was estimated with a mean difference in the change of HbA_{1c} level from baseline to final assessment between the intervention group and the control group. If the variances of change values were not provided, but the exact p-value of the mean difference between the intervention and the control groups was available, the p-value was used to impute the variance.[7] If the variances of change values and the exact p-values of the mean difference were not provided, the pooled interstudy variances were imputed from studies reporting variances.

The inverse variance-weighted method was used for the pooling of mean difference and the estimation of 95% confidence interval (CI).[8] A random effects model was used when the Q-statistic for heterogeneity was significant at the level of 0.1,[9] otherwise the fixed effects model was used.[8] The degree of heterogeneity was quantified using the I^2 statistic which is the percentage of total variation across studies due to heterogeneity.[10] A funnel plot and Egger's method[11] were performed to assess publication bias. Statistical analysis was undertaken with RevMan version 5.1 (Cochrane Collaboration, Oxford, UK). The significant level was set at $p < 0.05$.

RESULTS

Study characteristics

The initial search of the computerized

database and hand search identified a total of 1,160 articles (Figure 1). After the initial screening, 44 trials were attained in the selection process. Among the 44 trials, 16 trials were excluded because they did not report glycemic control/HbA_{1c}. Five trials were further excluded because they did not state clearly the role of pharmacist in the intervention group. One trial reported results in terms of median and interquartile range and was then excluded. Only 22 randomized controlled trials met inclusion criteria and were included in the systematic review and meta-analysis. Characteristics of these trials are presented in Table 1. In general, there were no significant differences between patients in the intervention group and those in the control group with respect to age and duration of diabetes.

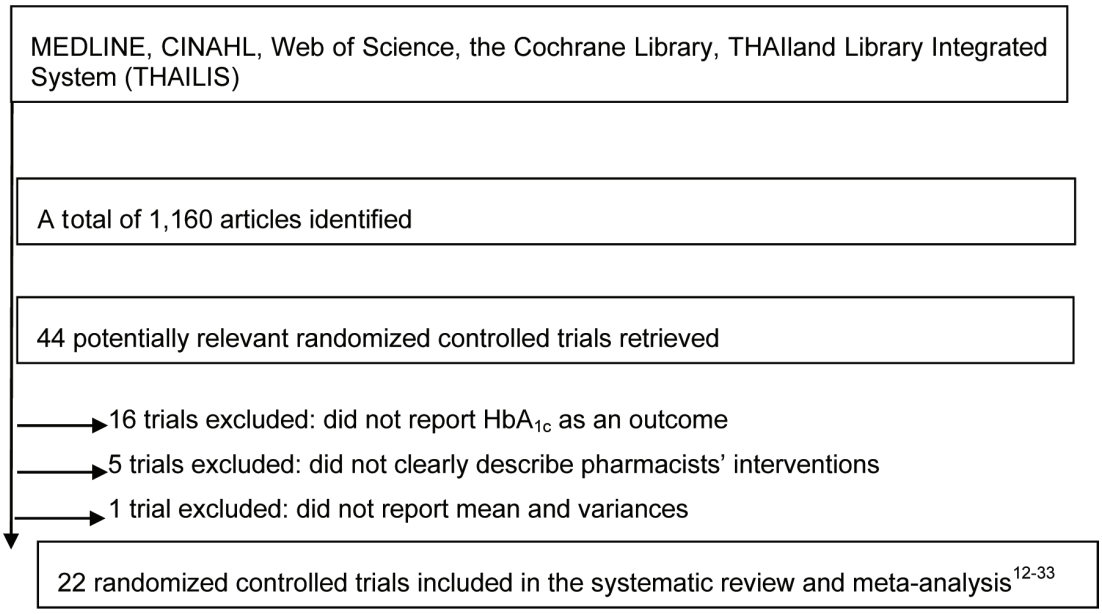

Figure 1. Flow diagram of study selection for meta-analysis

Those trials, involved patients with type 1, type 2, GDM, or unspecified DM and were reported between 1996 and 2012. The setting of trials included primary care unit, home care, community pharmacy, primary care hospital, tertiary care hospital, a university-affiliated internal medicine outpatient clinic, endocrine clinic, military hospital, and veteran medical center in the USA, Canada, Australia, Sweden, Spain, UAE, and Thailand. The duration of trials varied from 3 months to 2 years. Pharmacists' intervention was given at different frequency, for example, once a week and once every 6 months. Number of visit ranged between 1 and 24 times. Pharmacists involved included registered pharmacist,[12,20,26,32] clinical pharmacist,[14,16-18,21,23,25,27,29,30] community pharmacist,[22,24,28,32] clinical pharmacist with multidisciplinary team,[19,31] certified diabetes educator pharmacists,[13] specially trained pharmacists.[15] The methods of follow-up were face-to-face encounter and/or by telephone. Details of pharmacist' interventions differed from trial to trial (Table 2 and 3) and encompassed the followings: diabetes education and counseling about drug, disease, diet, exercise, life style modification, and self-management, assessment and adjustment of antidiabetic medications, identifying and solving drug-related problems, co-operating with physician and other diabetes health care team, providing materials, leaflet, diabetes booklet and special medication containers, and monthly newsletter that enforced patients to achieve a target goal, reminding about annual eye and foot examinations, and providing additional information about smoking cessation, stop drinking alcohol.

For the usual care group, patients continued to receive standard medical care provided by their physicians, other health care team, and with/without pharmacists depending on each study design (Table 2).

Table 1. Characteristics of the studies included in the meta-analysis

No.	Study	Setting	Country	Duration of study	Intervention frequency	Inclusion criteria
1	Jaber LA 1996[12]	A University-affiliated internal medicine outpatient clinic	US	4 mo	2-4 weeks/time	T2DM
2	Guirguis LM 2001[13]	Chain pharmacy, shoppers drug mart	Canada; Edmonton,	6 mo	< 1 month/time	T2DM for Alberta a minimum of 1 year, non-institutionalized
3	Clifford RM 2002[14]	Frementle Hospital, diabetes outpatient clinic	Australia	6 mo	6 weeks/time	Aged > 18 years with either T1DM or T2DM and was high-risk for the development of diabetes complications.
4	Sarkadi A 2004[15]	Stockholm Diabetes Association	Sweden	24 mo	6 months/time	T2DM and, if treated with insulin, only for 2 years or less
5	Clifford RM 2005[16]	Frementle Hospital, Frementle Diabetes Study (FDS)	Australia	12 mo	6 weeks/time	T2DM
6	Choe HM 2005[17]	University-affiliated primary care internal medicine clinic	US	24 mo	1 month/time	T2DM, HbA_{1c} levels > 8.0%
7	Odegard PS 2005[18]	The University of Washington medicine clinics	US	6 mo	1 week/time	Aged ≥ 18 years, T2DM, taking at least one oral diabetes medication, with an HbA_{1c} ≥9%
8	Suksomboon N 2005[19]	Primary care unit, Samutsakorn Hospital	Thailand	3 mo	3 months/time	T2DM, 18-60 years old, take OAD as metformin, glipizide and/or glibenclamide, HbA_{1c} > 7%
9	Suppapitiporn S 2005[20]	Endocrine clinic in King Chulalongkorn Memorial Hospital (out patients)	Thailand	6 mo	3 months/time	T2DM, aged > 40 years
10	Rothman RL 2005[21]	University of North Carolina General Internal Medicine Practice	US	12 mo	2-4 weeks/time	Aged >18 years old, T2DM, HbA_{1c} level >8.0%, life expectancy >6 months
11	Fornos JA 2006[22]	Community pharmacies	Spain; Pontevedra	13 mo	1 month/time	treatment with oral antidiabetics for more than 2 months
12	Scott DM 2006[23]	Siouxland Community Health Center (SCHC)	US	9 mo	2 weeks/time	T2DM, aged > 18 years

Table 1. Characteristics of the studies included in the meta-analysis (cont.)

No.	Study	Setting	Country	Duration of study	Intervention frequency	Inclusion criteria
13	Krass I 2007[24]	Communities pharmacies	Australia	6 mo	1 month/time	T2DM, $HbA_{1c} \geq 7.5\%$, taking at least one oral glucose lowering medication or insulin, or $HbA_{1c} \geq 7.0\%$, taking at least one oral glucose lowering medication or insulin, on at least one anti-hypertensive, angina or lipid-lowering drug.
14	Elnour AA 2008[25]	Al Ain Hospital, gynaecology outpatient clinics	UAE	6 mo	1 month/time	Patient provided within the first 20 weeks of gestation, diagnosis of GDM, and aged 20- 39 years
15	Phumipamorn S 2008[26]	Community hospital in Krabi province	Thailand	10 mo	2 months/time	Muslim diabetic patients, aged > 18 years, and $HbA_{1c} > 7\%$
16	Pavasudthipaisit A 2009[27]	Diabetes Clinic, Out-patient department, Nongbualamphu hospital	Thailand	12 mo	6 months/time	T2DM, HbA_{1c} levels > 8.0% without macrovascular complications
17	Doucette WR 2009[28]	Community pharmacy practice site	US; IOWA	12 mo	3 months/time	T2DM, $HbA_{1c} > 7.0\%$
18	Mazroui NRA 2009[29]	Zayed Military Hospital, general medical wards and endocrinology & medical outpatient clinics	UAE	12 mo	4 months/time	T2DM, receiving oral hypoglycaemic therapy
19	Taveira TH 2010[30]	Veterans Health Affairs	US	22 mo	4 weeks/time	T2DM, aged > 18 years, or HbA_{1c} 7%-9% within the previous 6 months
20	Edelman D 2010[31]	Veterans Affairs Medical Centers	US; Carolina & Virginia	12.8 mo	2 months/time	Patients had both diabetes and hypertension, receiving medication for diabetes, and HbA_{1c} level >7.5% and hypertension (SBP >140 mm Hg or DBP >90 mm Hg)
21	Mehuys E 2011[32]	Community pharmacies	Belgium	6 mo	6 weeks/time	T2DM, receiving oral hypoglycaemic medication for at least 12 months, aged 45 – 75 years, BMI> 25 kg/m2, and regular visitor of pharmacy
22	Sriram S 2011[33]	A private tertiary care hospital	South India	8 mo	3 months/time	Indian, T2DM, aged > 18 years, with or without other diseases

Table 2. Details of pharmacists' intervention and usual care of each trial

No.	Study	Pharmacist intervention	Usual care
1	Jaber LA 1996[12]	Diabetes education, medication counseling, instructions on dietary regulation, exercise, and home blood glucose monitoring, and evaluation and adjustment of their hypoglycemic regimen.	Continued to receive standard medical care provided by their physicians.
2	Guirguis LM 2001[13]	Usual care plus service provide; diabetes and its complication, hypoglycemia, monitoring blood glucose level, use of blood glucose monitor, nutrition, exercise, insulin use, insulin device, medication use, and foot care; and teaching provide; evaluated teaching needs, addressed participant concerns, reviewed blood glucose levels, reviewed HbA1c, measured BP, reviewed cholesterol levels, screened for microalbuminuria, reviewed medication profile, advised on non-prescription medications, contacted physician, contacted other members of diabetes team, and meter maintenance.	Control pharmacies provided usual care, pharmacist offered patients some form of blood glucose meter training , other training on diabetes management (in-store courses or continuing education course).
3	Clifford RM 2002[14]	Completed a comprehensive, self-directed revision of diabetes management prior to the study, saw each patient at every visit, and co-operation with the diabetes physician and other health team.	Received standard outpatient care, not completed the patient satisfaction survey.
4	Sarkadi A 2004[15]	The educational program; a video on how to "live well" with diabetes, exemplifying lifestyle changes made by those interviewed, a dice game where questions had to be answered, and a booklet or guide on "how to manage your diabetes".	Usual care and assigned to a waiting list of 2 years, then they were invited to participate in the educational program.
5	Clifford RM 2005[16]	Face-to-face meeting goal-directed medication and lifestyle counseling, telephone assessments and provision of other educational material	Had a standard assessment by primary care physician.
6	Choe HM 2005[17]	Pharmacists provided evaluation and modification of pharmacotherapy, self-management diabetes education, and reinforcement of diabetes complications screening processes through clinic visits and telephone follow-up.	Kept as a natural control, they received only regular care including regular follow up visits with their primary care physicians, received no special contact during the intervention, did not have exit interviews or process measurements at the end of the study.

Table 2. Details of pharmacists' intervention and usual care of each trial (cont.)

No.	Study	Pharmacist intervention	Usual care
7	Odegard PS 2005[18]	The pharmacist intervention was composed of development of a diabetes care plan (DCP), regular pharmacist-patient communication on diabetes care progress, pharmacist-provider communication on the subject's diabetes care progress, and DRP.	Patients were constructed to continue normal care with their primary care provider. Diabetes education was not provided during the baseline interview to avoid introducing an intervention for patients in the control group.
8	Suksomboon N 2005[19]	Self-efficacy training program by multidisciplinary team including pharmacist, pharmacist also provided education on self-care behaviors, self-monitoring of blood glucose, and knowledge in diabetes.	The control group did not enter perceived self-efficacy training program.
9	Suppapitiporn S 2005[20]	Usual care plus diabetic drug counseling, added diabetes booklet, special medication containers.	Patients were interviewed demographic information, blood test, and medical records.
10	Rothman RL 2005[21]	Intensive education sessions, evidence-based algorithm, proactive management.	Patients received usual care from their primary care provider and had no further management from the disease management team.
11	Fornos JA 2006 [22]	Usual care plus pharmacotherapy follow up program (individualized program) which consists of the detection and resolution of DRPs and diabetes education, involves patients in their own care in order to obtain maximum benefit from the medication.	Usual dispensing by pharmacist.
12	Scott DM 2006[23]	Patient education about disease, testing blood glucose levels, drug therapy, psychological adjustment in diabetes, signs and symptoms of hyper-glycemia, hyperglycemia, and diabetic ketoacidosis and course of action.	Patients received standard diabetes care and were managed by a nurse.
13	Krass I 2007[24]	Services from pharmacists included of review of self monitoring of blood glucose; disease, medication, and lifestyle education; adherence support and detection of drug-related problems; and referrals to the patients' GPs when appropriate.	The control patients had two visits with the pharmacist, one at the beginning and one at the end of the study. During the intervening 6 months, they received 'usual care' (i.e. no specialized diabetes service in the pharmacy).
14	Elnour AA 2008[25]	Ensured that intervention patients received based treatment and treatment for any other concomitant illness, educated on GDM and its management, educational booklet, Clinical assessments.	Patients received traditional care: monthly clinic visits and self-monitoring of plasma glucose using diary cards.

Table 2. Details of pharmacists' intervention and usual care of each trial (cont.)

No.	Study	Pharmacist intervention	Usual care
15	Phumipamorn S 2008[26]	Usual care plus reminded the patients, refilled prescriptions, discussed the uses of medication, check the pill count, education on diabetes about appropriate lifestyle, correct diet, and provided diabetic pamphlet; diabetic complications, target of treating diabetes, life style change, and diabetic medications.	Patients received usual schedule care by primary care physician every 4-8 weeks., dispensing by pharmacist filled and gave general advice on medication uses over the dispensary counter on a routine basis.
16	Pavasudthipaisit A 2009[27]	Intervention group received intensive management from pharmacist practitioners; received an assessment of medication-taking adherence and their understanding of diabetes then applied algorithms for managing glucose control and other cardiovascular risk factors.	Patients were provided care by their physicians of interns.
17	Doucette WR 2009[28]	Discussing medications, clinical goals, self-care activities with patients and recommending medication changes to physicians when appropriate.	Patients received usual diabetes care from their primary care provider.
18	Mazroui NRA 2009[29]	The research pharmacist had discussions with their physicians regarding drug therapy, treatment modification, educated for illness and medication, printed leaflet, and behavioral modification.	Patients received normal care from medical and nursing staff, did not receive the clinical pharmacy service.
19	Taveira TH 2010[30]	Usual care plus treatment of hyperglycemia, hypertension, hyperlipidemia, and cigarette smoking.	Patients received the standard care provided by primary care providers, frequency average 4 months.
20	Edelman D 2010[31]	Pharmacist reviewed patient medical records, BP, and home blood glucose readings during each session and developed individualized plans for medication or lifestyle management. Pharmacist and physician adjusted medication to manage each patient HbA1c level and BP.	Patients continued to receive their usual primary care, no active intervention.
21	Mehuys E 2011[32]	Education about T2DM and complications, correct use of oral hypoglycaemic agents, facilitation of medication adherence, healthy lifestyle education, and reminders about annual eye and foot examinations.	Patients received usual pharmacist care.
22	Sriram S 2011[33]	Patients received pharmaceutical care; medication counseling instructions on dietary regulation, exercise and other lifestyle modification.	Patients received usual diabetes care.

Table 3. Component of pharmacists' intervention in individual trials

Study	Materials provided	Education and counseling	Identifying and resolving drug-related problems
Jaber LA 1996[12]	-	✓	✓
Guirguis LM 2001[13]	glucose meter maintenance	✓	-
Clifford RM 2002[14]	-	✓	✓
Sarkadi A 2004[15]	video, booklet	✓	✓
Clifford RM 2005[16]	educational material	✓	✓
Choe HM 2005[17]	-	✓	✓
Odegard PS 2005[18]	-	-	✓
Suksomboon N 2005[19]	-	✓	-
Suppapitiporn S 2005[20]	booklet, containers	✓	-
Rothman RL 2005[21]	-	✓	-
Fornos JA 2006[22]	-	✓	✓
Scott DM 2006[23]	-	✓	✓
Krass I 2007[24]	monthly newsletter	✓	✓
Elnour AA 2008[25]	booklet	✓	✓
Phumipamorn S 2008[26]	pamphlet	✓	✓
Pavasudthipaisit A 2009[27]	-	✓	✓
Doucette WR 2009[28]	-	✓	✓
Mazroui NRA 2009[29]	leaflet	✓	-
Taveira TH 2010[30]	smoking cessation handout	✓	-
Edelman D 2010[31]	-	✓	✓
Mehuys E 2011[32]	educational material	✓	-
Sriram S 2011[33]	leaflet, diabetic diet chart, diabetic diary	✓	✓

Effect on HbA_{1c}

Twenty two trials involving a total of 2,808 diabetes patients were pooled. HbA_{1c} levels at baseline, final assessment are presented in Table 4. HbA_{1c} levels were significantly reduced with pharmacists' interventions compared with usual care. The pooled mean difference in the change of HbA_{1c} was -0.68% (95%CI, -0.87% to -0.49%; $p< 0.00001$) (Figure 2). No publication bias was detected (Egger bias -0.35; 95% CI -2.89 to 2.19, P= 0.7785).

Table 4. HbA_{1c} levels at baseline and final assessment reported in individual trials

Study	HbA1c (%)			
	Control		Intervention	
	Baseline	Final	Baseline	Final
Jaber LA 1996[12]	11.5±2.9	12.1±3.3	12.2±3.5	9.2±2.1
Guirguis LM 2001[13]	7.9*	7.1*	7.9*	6.9*
Clifford RM 2002[14]	8.5±1.6	8.1±1.6	8.4±1.4	8.2±1.5
Sarkadi A 2004[15]	6.44*	6.60*	6.44*	6.09*
Clifford RM 2005[16]	7.1*	6.7*	7.5*	7.3*
Choe HM 2005[17]	10.2±1.7	9.3±2.1	10.1±1.8	8.0±1.4
Odegard PS 2005[18]	10.6±1.4	9.2*	10.2±0.8	8.7*
Suksomboon N 2005[19]	9.73±1.88	10.23±2.59	9.03±1.67	8.69±1.82
Suppapitiporn S 2005[20]	8.01±1.51	8.80±1.36	8.16±1.44	7.91±1.27
Rothman RL 2005[21]	11±2	9.4*	11±3	8.5*
Fornos JA 2006[22]	7.8±1.7	8.5±1.9	8.4±1.8	7.9±1.7
Scott DM 2006[23]	8.7*	8.0*	8.8*	7.08*
Krass I 2007[24]	8.3±1.3	8.0±1.2	8.9±1.4	7.9±1.2
Elnour AA 2008[25]	6.87 (95%CI 6.81, 6.93)	6.55 (95%CI 6.43, 6.67)	6.85 (95%CI 6.78, 6.90)	6.38 (95%CI 6.33, 6.42)
Phumipamorn S 2008[26]	8.7±1.6	8.1±1.9	8.7±1.5	7.9±1.4
Pavasudthipaisit A 2011[27]	9.9±1.6	9.1*	9.8±1.4	7.8*
Doucette WR 2009[28]	7.91±1.91	8.03*	7.99±1.45	7.72*
Mazroui NRA 2009[29]	8.4 (95%CI 8.6, 8.6)	8.3 (95%CI 8.1, 8.5)	8.5 (95%CI 8.3, 8.7)	6.9 (95%CI 6.7, 7.1)
Taveira TH 2010[30]	7.9±1.1	7.9*	8.1±1.5	7.2*
Edelman D 2010[31]	9.2±1.3	8.6*	9.2±1.5	8.3*
Mehuys E 2011[32]	7.3 ± 1.2	7.2 ± 1.0	7.7 ± 1.7	7.1 ± 1.1
Sriram S 2011[33]	9.03 ± 0.46	8.31 ± 0.16	8.44 ± 0.29	6.73 ± 0.21

Data are mean±SD, * mean value

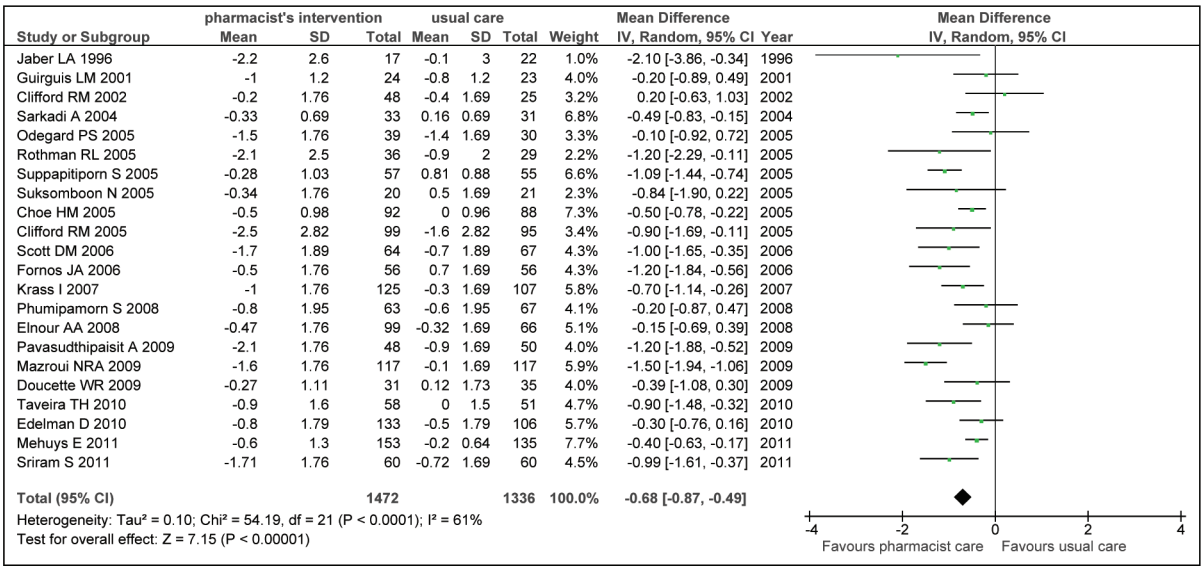

Figure 2. Mean difference (95% confidence interval) of HbA_{1c} between pharmacist intervention group and usual care group

DISCUSSION

Pharmacist is part of a multidisciplinary team. This team normally consists of pharmacist, physician, nurse, technician, nutritionist, and other health care professions. All of the members in multidisciplinary team have important roles in diabetes management in achieving the goal of treatment, improving quality of life, controlling disease and its complications, delaying complication, and decreasing mortality and morbidity. Pharmacists' interventions are an important factor to improve glycemic control in diabetic patients. Pharmacists' interventions include diabetes education and counseling on drug, disease, diet, exercise, life style modification, and self-management, assessment and adjustment of anti-diabetic medications, identifying and solving drug-related problems, co-operation with physician and other diabetes health care team, providing materials that reinforce patients to achieve a target goal, providing additional information on smoking cessation. All of these interventions aimed at improving glycemic control.

In our study, HbA_{1c} levels significantly reduced with pharmacists' interventions compared with usual care. The pooled mean difference in the change of HbA_{1c} was -0.68% (95%CI, -0.87% to -0.49%; p< 0.00001). This reduction is the same as the ability in reducing HbA_{1c} by taking some oral anti-hyperglycemic drugs for example, DPP-4 inhibitors and alpha-glucosidase inhibitors. This would help patients meeting the target of their treatment.

To ensure that the meta-analysis included quality study, the Maastricht Amsterdam scale was used to assess the quality of individual study. The majority of the studies[12-13, 15-20, 22-31,33] were rated as low quality, only three studies[14, 21, 32] were of high quality. Most of these studies were open (not blinded) in study design. Performance bias in both intervention and control groups was likely in these trials as patients may seek other interventions to help control their blood glucose. This was evident when only high quality studies[14, 21, 32] were pooled, showing a slight reduction in the effect of pharmacists' interventions on HbA_{1c} (mean difference -0.39%, 95% CI -0.61% to -0.17%, p = 0.0005).

There were limitations in individual studies included in this meta-analysis. In most of the trials, both pharmacists and patients were not blinded and therefore,

contamination between groups was possible. This may affect the final outcomes. Secondly, Hawthorne effect may occur when study participants improved because of the only fact that they were participating in a research study.

The findings of our study suggest several practice implications. First, pharmacists' interventions effectively improve glycemic control when compared with usual care; and thus, pharmacist should be part of a diabetes care team. Second, the approprite components of intervention should include both pharmacotherapy and non-pharmacotherapy. Interventions on pharmacotherapy are screening and solving drug-related problems; if necessary, pharmacists provide feedback to physician, deliver patient education and counseling on medication. Non-pharmacotherapy interventions include education and counseling on diet, exercise, disease, adherence, and life-style modification.

CONCLUSION

The available evidence suggests that pharmacists' interventions are more effective than usual care in decreasing HbA_{1c} levels in diabetes patients. Pharmacists' interventions included diabetes education and counseling on drug, disease, diet, exercise, life style modification, and self-management, an assessment and adjustment of anti-diabetic medications, identifying and solving drug-related problems, co-operation with physician and other diabetes health care team.

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