Available online on 15.07.2020 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

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Research Article

Pharmacist-Led Interventions on Improving Outcomes in Patients with Diabetes Mellitus: Evidence from the Literature

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ABSTRACT

Diabetes mellitus is a rapidly growing major health problem world-wide. The management of type 2 diabetes mellitus is complex, requiring continuous medical care by health care professionals and considerable self-care efforts by patients. A collaborative and integrated team approach in which pharmacists can play a pivotal role should be sought when managing patients with diabetes. Pharmacist-led care programs have been shown to help patients with diabetes succeed in achieving treatment goals and improving outcomes. Hence, the aim of this narrative review is to address and summarize the effectiveness of pharmacist interventions in the management of diabetic patients. A comprehensive literature search was conducted in PubMed/Medline, Scopus, web of Science and the Cochrane Library were searched from the date of database inception to June 2019. All randomized controlled trials evaluating the effectiveness of pharmacist-based interventions on diabetic patients in comparison with usual care were included in study. Outcomes of interest included short-term and long-term measures such as glycated haemoglobin (HbA1c), and secondary outcomes were blood glucose level, blood pressure (BP), lipid profile, body mass index (BMI), 10-year coronary heart disease (CHD) risk, medication adherence, health related quality of life (HRQoL), and economic outcomes. Twenty-five studies were included in this systematic study. They were heterogeneous in terms of interventions, participants, settings and outcomes. Pharmacist-led self-management interventions included education on diabetes and its complications, medication adherence, lifestyle and education of self-management skills. Few studies even focussed on patients need through a tailored intervention. We found that those who received the pharmacist care had a statistically significant improvement in HbA1c, blood pressure, lipid profile, health-related quality of life, and CHD risk. These results underline the added value of pharmacists in patient-related care. Hence this review supports the involvement of pharmacists as a member of health-care teams in managing diabetic patients at diverse settings worldwide.

Keywords: diabetes, self-management, HbA1c, pharmaceutical care, randomized controlled trial**Article Info:** Received 26 April 2020; Review Completed 17 June 2020; Accepted 25 June 2020; Available online 15 July 2020

Cite this article as:

Inasu ST, Kumudavalli MV, Pharmacist-Led Interventions on Improving Outcomes in Patients with Diabetes Mellitus: Evidence from the Literature, Journal of Drug Delivery and Therapeutics. 2020; 10(4):49-58
<http://dx.doi.org/10.22270/jddt.v10i4.4195>

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INTRODUCTION

Diabetes mellitus is a major chronic health problem for decades to come. Indeed, it was estimated that 463 million people globally suffered from diabetes in 2019, and this number is predicted to increase to 700 million people by 2045.¹ Diabetes, if left uncontrolled, may cause microvascular and macrovascular complications in the long term, which are the main causes of increased morbidity and mortality and decreased health-related quality of life among patients.²

The management of diabetic mellitus is very difficult and it became a persisted task all over the world.³ Overtime, several studies have shown that prolonged high levels of glycaemia lead to micro- and macrovascular complications.⁴ The overall goal of diabetes treatment is, therefore, to

reduce the risk of diabetes-related complications by achieving and maintaining near normal glycaemic control with lifestyle changes and drug therapy⁵. Despite the benefits of effective therapies, literature demonstrates that achievement of desired therapeutic outcomes in patients with diabetes remains suboptimal that could increase the disease burden.^{6,7} Barriers to adherence may consist of complex treatment regimens, medication side effects, poor patient-provider communication, socio-economic issues, memory impairment psychological well-being and personal beliefs.⁸

Due to the complexities associated with managing diabetes population, new models of health care delivery should be developed and implemented for better glycaemic control.^{9,10} Thus, evidences has shown that a multidisciplinary team

with collaboration among different healthcare professionals can provide a more holistic treatment and to obtain better outcomes.¹¹ A larger role of the pharmacist, in diabetes treatment by helping patients improve their chances of reaching therapeutic and lifestyle goals. The responsibilities of pharmacist involve patient education, monitoring treatment goals, adherence, drug-related problem assessment.¹² They can positively influence patients individually or with other health professionals in improving diabetes management by providing pharmaceutical care programs and prudent pharmacological therapy to improve disease state outcomes.¹³ Several studies have recommended the involvement of a pharmacist in a diabetes multidisciplinary healthcare team including those by the American Diabetes Association and Canadian Diabetes Association.^{12,14} Previous literature reviews have proven that the contribution of pharmacists in achieving better control of diabetes is significant¹⁵⁻¹⁶. These reviews focused on many types of pharmacist interventions including self-care related interventions, adherence, and compliance or on counselling but always resulted in a significant effect on the outcomes of diabetes mellitus¹⁷⁻¹⁸.

In this study, a narrative and systematic review was performed to determine the relative efficacy of various pharmacist based interventions involving diabetes education alone and in combination with pharmaceutical care, and those interventions in which diabetes education was provided by health care team including pharmacist as team member, on clinical outcomes of the type 2 diabetes patients. We choose to use glycosylated hemoglobin (HbA1c) as primary outcome, as it has been shown to be a good surrogate marker for diabetes related complications¹⁹. Other secondary outcomes include fasting blood sugar (FBS), body mass index (BMI), blood pressure control (BP), cardiovascular incidences (CV) and lipid profile.

MATERIALS AND METHODS

Study design

A comprehensive literature search was done in PubMed/Medline, Scopus, web of Science and the Cochrane Library from the date of database inception to November 2019. The PubMed search strategy served as a reference for the development of search strategies for the remaining database. The standardized search strategy included the use of medical subject headings terms or text words related to pharmacist interventions (pharmacists, pharmaceutical care, medication therapy management, pharmaceutical services); to the disease (diabetes, diabetes mellitus type2, glycosylated haemoglobin, glycaemia, blood glucose, glycaemic); and to clinical trials (randomized controlled trial, controlled clinical trial, random allocation). The electronic database searches were complemented by manually reviewing the reference of relevant reviews and included studies.

Inclusion criteria

Studies were included in this review if they were randomized controlled trials or cluster-randomized controlled trials evaluating the effectiveness of interventions delivered only or mainly by pharmacists and directed at patients with type 2 diabetes in comparison with usual care. Studies that took place in a community pharmacy and in outpatient primary care and hospital settings were also included. Studies were included if they reported one or more outcome measures were reported, for example: glycosylated haemoglobin (A1c); blood glucose (fasting, postprandial, or random); blood pressure; lipid profile [total cholesterol, low-density lipoprotein cholesterol [LDL], high-density

lipoprotein cholesterol [HDL], and triglycerides; body mass index (BMI), medication adherence or health-related quality of life (HRQoL). It must be an original study published in a peer-reviewed journal and the full text article was published in English language.

Study selection

Two independent reviewers screened all titles and abstracts retrieved from the electronic databases using the pre-defined inclusion criteria. Then, the full text of each potentially eligible article was obtained and screened independently by two reviewers to determine their eligibility for further analysis. Any discrepancies regarding study inclusion was resolved through discussion.

Data extraction and Synthesis

One of the researchers extracted the data from the studies included in this review. No blinding for author or journal was applied in the extraction process. The data extracted from the studies includes publication details (title, authors, publication year and journal name); study design characteristics (country where the study took place, type of the study, sample size, period of study); study characteristics (patients age, gender, follow-up duration, details of pharmacist interventions and usual care, inclusion and exclusion criteria) and study outcomes. The description of the intervention includes counselling on diabetes education, quality of life, medication details, lifestyle modifications, patient compliance toward the treatment, and clinical outcomes (HbA1c, fasting and random blood glucose levels, BP, BMI, and lipid profile). Pharmacist interventions were evaluated in all the included studies. Outcomes in the form of HbA1c, random and fasting glucose levels, BP, BMI, and lipid profiles were evaluated in all included studies. The risk of bias in the included studies was measured by two independent reviewers according to pre-defined criteria based on the Cochrane risk-of-bias tool (Rob 2.0). Any divergences were deliberated till consensus was reached. Results for all the outcomes (HbA1c, FBS, BMI, CV incidence, BP, lipid profile etc) and intervention across the included studies were analysed and described narratively.

RESULTS

In total 5919 articles were identified from the electronic database searches. On the basis of title and abstract evaluation 3930 studies were excluded as they did not meet the inclusion criteria of the study. The full text of 66 papers was assessed, with 25 papers finally being included in the review. (Figure 1). The main characteristics and study population of the included studies are presented in Table 1.

Study characteristics

The studies included were heterogenous in terms of interventions, participants, settings and outcomes. They varied in their quality and reporting of their findings conducted in several setting including: standard care, pharmaceutical care or family practice in the UK, Spain or elsewhere in the world²⁰⁻²⁸. Among the included studies 24 were randomised controlled studies^{20-35,37-44} and one was cluster randomised³⁶. All studies were published from 2009 onwards. Most of the included studies (n = 12) were conducted in Asia,^{22 24 27 28 30 34 35 39 40 41 43 44} followed by Europe (n = 5),^{21 31 33 36 38} North America (n = 5),^{25 26 29 32 42} South America (n = 2),^{23 37} and Africa (n = 1).³⁰

The median follow-up time was 6 months,^{22,23,25,28,30,33,36,37,38,40,41,42,44} two studies had a follow-up time of less than 6 months^{27,39} and ten of more than 6 months.^{20,21,24,26,29,31,32,34,35,43}

The majority of the studies focused primarily on diabetes mellitus type 2 patients,^{20,22-28,30,31,33-44} (n=22), one study included both type 1 and type 2 patients,³² and one study did not specify the type of diabetes.²⁹

Description of Intervention

The settings in which the studies took place included community pharmacies, primary care clinics or health centres, and hospitals. The nature of interventions provided by pharmacist varied among the included studies and covered one or more of the following topics: counselling and education on diabetes, medication, lifestyle modification, and self-monitoring; reinforcement of medication adherence or complications screening; provision of materials such as educational leaflets and pill boxes; medication review; identification and resolution of drug-related problems; discussions with the primary care provider regarding pharmacotherapy; adjustment of pharmacotherapy; and referrals to other health care professionals. Two studies mentioned motivational interviews as a technique used to deliver advice to patients.^{20,28} In most studies, the control group received usual care from medical and nursing staff and/or community pharmacists, depending on the study setting.

The intervention in the included studies were all provided by a trained pharmacist, either by pharmacist alone^{20-24,26-}

^{33,35-37,39,40,43,44} or within a multi-disciplinary team.^{25,34,41,42} one study did not specify the intervention team, besides including a pharmacist.³⁸ Most interventions targeted the individual patient^{20-24,26,28-33,35-40,43,44} whereas some interventions used group sessions^{25,34,41,42}. One study did not specify whether the intervention was offered in an individual or group setting²⁷.

Thirteen studies included diabetes education as interventions^{21-23,25,28,30,31,36,39-42,44} either about diabetes in general or about acute and chronic complications. Patient education on medication was provided by the pharmacists in 16 included studies and this included education about adherence, dosage, drug-related problems, indication, storage, and use^{20-29,31,37-40,42,44}.

In eighteen studies the intervention included self-management skills support^{20-22,25-27,29-32,34,38-44} and in around 10 studies participants were trained in self-monitoring glucose.^{22,23,25,28,30-32,39,40,42}

In most of the studies, education was given on lifestyle modifications, exercise requirements, foot cares, management of proper diet and smoking cessation were included as the part of the intervention by the pharmacists. Other interventions such as the use of a diabetes diary and provision of written educational material were reported in the included studies.

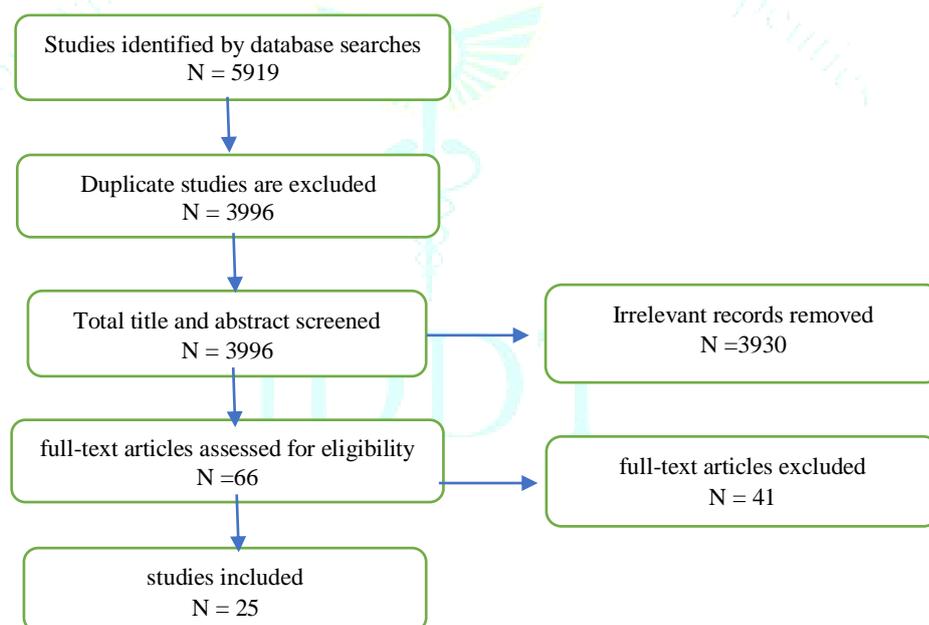


Figure 1: Flow chart of study selection

DISCUSSION

This review found evidence of the importance of the clinical pharmacist/ pharmacist care program that targeted immediate and long-term risk factors associated with diabetes mellitus. This extended across multiple health care settings and cultures worldwide. In most of the included studies, pharmacist's role was mainly to specify all drug related problem including poor drug compliance and side effects and communicating these to the physician. such rapport is crucial in building professional working relations necessary to ensure optimal patient care. However, pharmacist involvement is not meant to replace the formal diabetes education or physician direct care, nevertheless, the

program provides a usual supplement or enhancement to the care of diabetic patients.

The type, intensity, and frequency of the interventions were different in all the included studies. The number of visits for face-to-face interactions varied once in a week to once in a year. Some of the included studies do have face-to-face contact with the pharmacists or pharmacy departments^{20,22,35} and some have combination of face-to-face contacts along with telephone contact with the pharmacists or department of pharmacy.^{25,28} The evidence indicate that telephone interventions are effective and significant improvement in glycaemic level.⁴⁵

Table No.1: Characteristics of the included studies.

Author, Year, Country	Study design	No. of Patients Lost to Follow-up Age in Years (Mean [SD]) Gender (%)	Follow-up Duration	Pharmacist Intervention	Control	Outcome measure
Adibe et al. 2013 ²⁰ Nigeria	Randomized, controlled study	No. of patients (IG/CG):110/110 Lost to follow-up (IG/CG):11/17 Age (IG/CG): 52.4[7.6]/52.8 [8.2] Gender (IG/CG): 44.6%/40.0% male	12 months	Pharmaceutical care including education on diabetes, self-monitoring, medication, lifestyle modification, counselling, and effective interaction with health providers	Usual care offered by hospitals	HbA1c, LDL, CVD risks, HRQoL, medication understanding, cost-utility analysis
Ali et al. 2012 UK ²¹	Randomized, controlled study	No. of patients (IG/CG):25/23 Lost to follow-up (IG/CG): 2/0 Age (IG/CG): 66.4[12.7]/66.8 [10.2] Gender (IG/CG): 43.5%/56.5% male	12 months	Pharmaceutical care including medicine use review; education regarding diabetes and its complications; and counselling on lifestyle modification with referral to other health care professional when appropriate	Usual service from general practitioner, practice nurse, and community pharmacy	A1c, BG, SBP, DBP, TC, LDL, HDL, TG, BMI, DQoL, HRQoL, diabetes knowledge, SIMS, beliefs about medicines, other
Butt et al. 2016 ²² Malaysia	Randomized, controlled study	No. of Patients (IG/CG):33/33 Lost to follow-up (IG/CG):4/3 Age (IG/CG) 57.42 [7.17]/57.12[10.78] Gender (IG/CG): 60.6/57.6	6 months	Pharmaceutical care including education on diabetes and its complication, self-management education, counselling on medication use and medication adherence	Usual care	HbA1c, FBS, BMI, TC, HDL-C, LDL-C, triglycerides, QoL, diabetes education and MMAS scores
Cani et al. 2015 ²³ Brazil	Parallel randomized controlled trial	No. of Patients (IG/CG):37/41 Lost to follow-up (IG/CG):3/5 Age(IG/CG): 61.91(9.58)/61.58(8.14) Gender (IG/CG):61.7/61.1	6 months	Individualized pharmacotherapeutic care plan consisting of education about diabetes, education on lifestyle modification and provision of free glucometer and pill counter	Standard care	HbA1c, FBS, BMI, QoL, medication adherence, insulin injection and home blood glucose monitoring techniques, diabetes education
Chan et al. 2012 ²⁴ Hong Kong	Parallel randomized controlled trial	No. of Patients (IG/CG):51/54 Lost to follow-up (IG/CG):0/0 Age (IG/CG): 63.2(9.5)/61.7(11.2) Gender (IG/CG) female(%): 41.2/48.1	9 months	Pharmaceutical care program addressing medication adherence, knowledge and beliefs, skills, perceived health and cognitive functions, and identification of DRPs	Routine medical care	HbA1c, SBP, DBP, TC, LDL, HDL, TG, BMI, Albumin-creatinine ratio, CHD risk, stroke risk medication knowledge, medication adherence, cost-effectiveness analysis
Cohen et al. 2011 ²⁵ USA	Randomized controlled trial	No. of patients (IG/CG):53/50 Lost to follow-up (IG/CG): 5/2 Age (IG/CG):	6 months	Part of a multidisciplinary diabetes specific healthy lifestyle education intervention and behavioural and pharmacologic interventions, including	Standard primary care	HbA1c, SBP, LDL, HRQoL, perceived competence, adherence to self-care activities,

		69.8[10.7]/67.2 [9.4] Gender (IG/CG): 100.0/96.0 % male		medication changes		disease knowledge
Doucette et al. 2009 ²⁶ USA	Parallel randomised controlled trial	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 % male	12 months	Pharmaceutical care including education on diabetes, self-monitoring and pharmacologic interventions including medication changes	Standard primary care	HbA1c, BP, LDL-C, adherence to self-care activities
Farsaei et al 2011 ²⁷ Iran	Parallel randomized controlled study	No. of patients (IG/CG):87/87 Lost to follow-up: NR Age (IG/CG): 53.4[9.8]/52.9 [8.5] Gender(IG/CG): 63.2%/68.2% female	3 months	Pharmacist-led program including education on medications adherence and self-management and provision of SMBG data entry log book	General education offered by the nursing staff	HbA1c, FBG
Jarab et al 2012 ²⁸ Jordan	Parallel randomized controlled study	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): 42.4/44.2 % female	6 months	Comprehensive clinical pharmacy care including education on diabetes, medication and lifestyle changes; review of prescribed treatment; referral to a smoking cessation program; and provision of booklet about diabetes medications and lifestyle changes	Usual care	HbA1c, FBS, BP, lipid levels BMI, diabetes self-care activities, medication adherence
Jameson et al 2010 ²⁹ USA	Parallel randomized controlled study	No. of Patients (IG/CG):52/51 Lost to follow-up (IG/CG): not mentioned Age (IG/CG): 49.3(10.8)/49.7(10.9) Gender (IG/CG):]51.1/5% female	12 months	Evaluation and adjustment of therapeutic regimen, and patient education on self-care activities, medication and insulin, and medication adherence	Usual care	HbA1c
Jahangard-Rafsanjani et al. 2015 ³⁰ Iran	Parallel randomized controlled study	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) Gender (IG/CG): 49/52%Female	6 months	Pharmaceutical care involving education about diabetes and its complication and on self-management, counselling on medication adherence, provision of written educational material and SMBG data entry log book	Usual care	HbA1c, BP, Medication adherence, Diabetes self-care activity, BMI, satisfaction, diabetes knowledge
Korcegez et al. 2017 ³¹ Cyprus	Parallel randomized controlled study	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	12 months	Pharmaceutical care including education about diabetes and its complication, self-management and on lifestyle modification, counselling for medication use, provision of written educational material	Usual care	HbA1c, FBS, SBP, DBP, TC, LDL-C, HDL-C, TGs, BMI, Medication adherences, diabetes knowledge, self-care activities
Kraemer et al. 2012 ³² USA	Parallel randomized controlled study	No. of Patients (IG/CG):36/31 Lost to follow-up	12 months	pharmacist counselling and empowering with diabetes education and its complication, self-management and on	Usual care with written educational	HbA1c, FBS, SBP, DBP, TC, LDL-C, HDL-C, TGs, BMI

		(IG/CG):1/1 Age(IG/CG): 55.6(6.8)/52.6 (9.2) Gender (IG/CG) female(%): 38.8/61.29		lifestyle modification, medication use, provision of written educational material	informatio n about managing diabetes	
Kjeldsen et al. 2015 ³³ Denmark	Randomized controlled study	No. of patients (IG/CG):41/125 Lost to follow-up (IG/CG):4/23 Age (IG/CG): 63.4 [7.8]/62.1 [10.2] Gender (IG/CG): 59.5/62.4% male	6 months	Pharmaceutical care by nonadherence screening, medication review, patient education and coaching regarding metabolic syndrome, support to structure and remember medication intake, feedback to PCP, and referral to other health services	NR	BG, SBP, HRQoL, disease knowledge, medication adherence, patient satisfaction with service, others
Lau et al. 2018 ³⁴ Malaysia	Pilot retrospective cohort study	No. of Patients (IG/CG):29/29 Lost to follow-up (IG/CG):0/0 Age (IG/CG): 54.24 (9.97)/ 59.07 (10.25) Gender (IG/CG): 48.1/51.9 % female	12 months	Multidisciplinary collaborative care by educating patients regarding diabetes control, nutrition restriction and requirement, management of co-morbid conditions, and lifestyle modification. medication adjustment,	Standard primary care	HbA1c, diabetic related hospitalization
Lim et al. 2016 ³⁵ Malaysia	Prospective randomized open-labelled study	No. of Patients (IG/CG):50/50 Lost to follow-up (IG/CG):11/13 Age (IG/CG): 55.62(1.49)/57.00(1.56) Gender(IG/CG): 53.8/54.1 % female	12 months	Education regarding life style modification, diabetes and its complication, counselling for medication use and medication adherence and provision of written educational material	Usual care	HbA1c, FBG, BMI, SBP, DBP
Mehuys et al 2011 ³⁶ Belgium	Cluster randomized controlled study	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	6 months	Education on diabetes and its complications, medication and healthy lifestyles, facilitation of medication adherence, and reminders about annual eye and foot examinations	Usual pharmacist care	HbA1c, FBG, medication adherence, diabetes knowledge, adherence to self-care activities
Mourao et al 2013 ³⁷ Brazil	Parallel randomized controlled study	No. of patients (IG/CG):65/64 Lost to follow-up (IG/CG):12/9 Age (IG/CG): 60.0[10.2]/61.3 [9.9] Gender (IG/CG): 68.0%/66.0% female	6 months	Pharmaceutical care, providing patient education about diabetes; non pharmacological issues, and pharmacological treatments proposals for pharmacotherapy changes forwarded to PCP;	Usual health care	HbA1c, FBG, SBP, DBP, TC, LDL, HDL, TG, BMI, medication use,
Nascimento et al 2016 ³⁸ Portugal	Parallel randomized controlled study	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 %female	6 months	Individualized pharmacotherapy management service including education about diabetes and its complication and medication use, self-management skills	NR	HbA1c, FBG, medication adherence, adherence to self-care activities

Samtia et al 2013 ³⁹ Pakistan	Parallel randomized controlled study	No. of Patients (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 %female	5 months	Multifactorial Intervention consisting of education on diabetes, medication use and lifestyle modification, counselling for medication adherence and SMBG education	NR	HbA1c, FBG, BMI, medication adherence, Diabetes knowledge
Shao et al 2017 ⁴⁰ China	Parallel randomized controlled study	No. of Patients (IG/CG):120/120 Lost to follow-up (IG/CG):20/21 Age (IG/CG): 58.86 ±10.59/59.20±10.34 Gender (IG/CG): 49/42.5%female	6 months	Pharmaceutical care including education on diabetes and its complications, medication and healthy lifestyles, and also on self-management skills	Usual care	HbA1c, FBS, SBP, DBP, TC, LDL-C, HDL-C, TGs, BMI, Medication adherences, self-care activities
Siaw et al 2017 ⁴¹ Singapore	Parallel randomized controlled study	No. of Patients (IG/CG):214/197 Lost to follow-up (IG/CG):0/0 Age (IG/CG): 59.2±8.2/60.1±8.1 Gender (IG/CG): 47.7/39.1% female	6 months	Multidisciplinary collaborative care including education on diabetes and its complications, and on self-management skills	Usual care	HbA1c, cost-effective analysis
Taveira et al 2010 ⁴² USA	Parallel randomized controlled study	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	6 months	Part of multidisciplinary education intervention regarding self-care behaviours and behavioural and pharmacological interventions, including medication change	Usual care	HbA1c, SBP, DBP, LDL, non-HDL, BMI, tobacco use, CHD risk factor, adherence to self-care behaviours
Tourkmani et al 2016 ⁴³ Saudi Arabia	Parallel randomized controlled study	No. of Patients (IG/CG):140/122 Lost to follow-up (IG/CG):73/8 Age (IG/CG): 55.12 (12.76)/56.06 (11.08) Gender (IG/CG):60/66.4	9 months	Education program on diabetes and its complications, medication and healthy lifestyles, and also on self-management skills, provision of written educational material	Standard diabetic care	HbA1c, SBP, DBP, LDL, HDL, TC, TG BMI,
Wishah et al 2015 ⁴⁴ Jordan	Parallel randomized controlled study	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): 61.5%/51.9% female	6 months	Pharmaceutical care, including optimization of drug therapy; education and counselling on diabetes and medication; enhancement of adherence to medication and self-care activities; and provision of educational leaflet and brochures	Usual care provided by the medical and nursing staff	HbA1c, FBG, TC, LDL, HDL, TG, BMI, diabetes knowledge, medication adherence, diabetes self-care activities

IG – intervention group; CG -control group; HRQoL- health related quality of life; BG-blood glucose; SBP - systolic blood pressure; DBP- diastolic blood pressure; TC – total cholesterol; LDL – low-density lipoprotein cholesterol; HDL – high- density lipoprotein cholesterol; TG – triglycerides; BMI – body mass index; DQoL – diabetic quality of life; SIMS – satisfaction of information received about medicines; FBG – fasting blood glucose

Various guidelines for diabetes recommend that a target HbA1c of a diabetic patient should be 7% or less. In order to decrease the chances of diabetic complication in those patients who have HbA1c more than 7%, it is recommended to reduce the HbA1c up to 1% or more. Thus, a tight control of FBS and random blood sugar (RBS) is needed to decrease diabetes complications.¹⁷ Thus, pharmacist intervention is needed to reduce the FBS and RBS of patients as shown in the included studies of analysis. HbA1c was considered as an outcome measure in 24 studies. A1c mean value decreased in the intervention group during the follow-up period in all studies. Further analysis revealed that larger effect was made by studies which involved pharmacist-based diabetes education, followed by studies which involved pharmacist-based diabetes education plus pharmaceutical care and studies in which diabetes education was provided by health care team involving pharmacist.⁴⁶

Regarding the blood pressure, in this review it reveals that in comparison with the control, 11 out of 13 studies demonstrated a significant reduction in the blood pressure in the intervention group^{21,25,28,30-33,35,37,40,42,43,44}. The American Association of Clinical Endocrinologists and American College of Endocrinology CPGs on diabetes recommends that the target BP of diabetics should be less than 140/80–90 mm Hg to decrease the risk of microvascular and macrovascular complications.²³ According to Indian guidelines, currently recommend the standard BP target of <140 mm systolic and < 90 mm in patients with diabetes to decrease the chances of complications.

Ten studies described total cholesterol as an outcome measure^{21,22,24,28,31,32,37,40,43,44}. In all of these studies, there was a reduction in the intervention group from baseline to final follow up, and seven studies reported a greater improvement in this outcome in comparison with the control group. Regarding LDL cholesterol, 14 studies reported data on this outcome, and all of them demonstrated a decrease in the intervention group from baseline to final follow-up^{20-22,24-26,28,31,32,37,40,42-44}. Ten studies reported a greater reduction in this outcome in the intervention group compared with the control group. Among the 11 studies that reported HDL cholesterol as an outcome measure, 10 studies described an increase in the intervention group from baseline to final follow-up^{21,22,24,31,32,37,40,42,43,44} and one study observed a decrease in the parameter²⁸. Guidelines of various countries such as Australia, UK, USA, and Malaysia strongly recommend the use of a lipid-profile control medication such as a statin if it is not contraindicated to decrease the risk of cardiovascular disease (CVD) development¹⁷. Although the chances of development of diabetes with statin use are reported,^{47,48} many meta-analyses on randomized trials reported the advantages of statins to decrease the CV risks.^{17,49}

Fifteen studies described BMI as an outcome measure, in all studies mean BMI decreased in the intervention group from baseline to final follow-up.^{21-24,28,30-32,35, 37, 39,40, 42-44}

CHD risk was predicted among five of the included studies in diabetic patients^{20, 24,31,39,42}. The method used to estimate this risk varied between studies. All 5 studies recorded a decrease in CHD risk in the intervention group from baseline to final follow-up and reported a greater improvement in this group compared with the control group. Two studies used the United Kingdom Prospective Diabetes Study (UKPDS) risk engine,^{31, 42} Two studies used the Framingham prediction method^{20,39}, and one study used an equation specifically validated for the Hong Kong population²⁴. All the models incorporated the variables age, sex, and smoking status⁶.the equation validated for the Hong Kong population

also includes the duration of diabetes²⁴. while the Framingham prediction model considers the presence or absence of diabetes as a variable.⁵⁰ In addition to the duration of diabetes, the UKPDS risk engine also incorporates the A1c mean values. Regarding blood pressure, the UKPDS risk engine and the British National Formulary prediction charts include systolic blood pressure, while the Framingham prediction model integrates systolic and diastolic blood pressure. As for the lipid profile, the UKPDS risk engine and the British National Formulary prediction charts consider the total cholesterol/HDL cholesterol ratio as a variable, while the Framingham prediction model only includes HDL cholesterol, and the equation validated for the Hong Kong population incorporates non-HDL cholesterol. In addition to the previously mentioned variables, the UKPDS risk engine also considers ethnicity as a variable, and the equation validated for the Hong Kong population integrates glomerular filtration rate and urinary albumin to creatinine ratio.⁶

Adherence to medications was measured in 12 studies^{22-24,28,30,31,33,36,38,39,40,44}. The methods used to measure this outcome varied between the studies. Self-reported adherence was used to measure this outcome almost in all studies, while one study used pill count or prescription refill rate in combination with self-reported adherence³⁶. Eleven studies revealed an improvement in medication adherence in the intervention group from baseline to final follow-up.

Health-Related Quality of life was measured in six studies.^{20-23,25,33} Five studies used the validated EuroQol-5 Dimension questionnaire which can be applied in different health conditions and diseases and one study used generic and diabetes-specific tools²¹ to measure this outcome. All studies reported an improvement in HRQoL in the intervention group from baseline to final follow-up, which was greater than that observed in the control group.

The evidence regarding the cost-effectiveness of pharmacist interventions was limited. In fact, only 3 studies conducted an economic analysis. Chan et al. (2012) estimated the cost-effectiveness of the pharmacist care program being studied based on CHD risk reduction and the direct cost of time spent by the pharmacist in counselling and associated administrative work.²⁴The estimated potential saving in costs was \$5,086.30 USD per patient.²⁴ Adibe et al. (2013) conducted a cost-utility analysis of the pharmaceutical care intervention implemented.²⁰ The total cost per patient per year was \$326.00 USD for the control group and \$394.00 USD for the intervention group.²⁰ Siaw et al. (2017) also conducted a cost-effectiveness analysis for the pharmacist intervention being studied.⁴¹The 6-month mean cost for direct outpatient diabetes-related care was US\$516.77 for the intervention arm and US\$607.78 for the control arm ($p < .001$). Compared to the control arm, an average cost savings of US\$91.01 per patient over 6 months was achieved by the intervention arm.⁴¹ This is in accordance with the findings from the other 2 systematic reviews that evaluated the effects of pharmacist interventions on patients with diabetes, in which a small proportion of studies assessed the cost-effectiveness of the interventions under study.⁶ However, given the current resource restraints in the health care systems, and in order to inform policymakers and influence their decisions towards widespread implementation of pharmacist interventions on the management of type 2 diabetes, cost-utility studies proving the cost-effectiveness of such interventions are of the utmost importance. Indeed, a comprehensive evaluation of pharmaceutical services has to consider clinical and humanistic outcomes, as well as economic outcomes.⁵¹

CONCLUSION

This review demonstrates a comprehensive evidence on the pharmacist-led interventions is associated with better glycaemic control and medication adherence. This narrative review supports a potential role of the pharmacists in diabetic care to help and support other healthcare professionals to achieve the target therapy outcomes. Therefore, they are very valuable to the care of such patients and should be considered and involved in diabetes care to help patients more effectively control their disease.

Overall, our review revealed that the pharmacist-led group intervention program was an efficacious and sustainable collaborative care approach to manage diabetes, self-management interventions and reduce associated cardiovascular risk.

ACKNOWLEDGEMENT: The authors wishes to acknowledge Vinayaka Missions College of Pharmacy, Salem, Tamil Nadu-636008 and Ahalia School of Pharmacy, Palakkad, Kerala-678557, for providing their library support and other logistic facilities in framing the review article.

CONFLICTS OF INTEREST: The author declares no conflict of interest.

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