diabetesresearchandclinicalpractice185(2022)109238

Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.journals.elsevier.com/diabetes-research-and-clinical-practice

Enhancing diabetes care with community pharmacist-involved collaborative care model: A multi-centre randomised controlled trial

Zheng Kang Lum [a], Kai Li Chang [a], Keith Yu-Kei Tsou [b], Jia Yeong Tan [c], Cynthia Sze Mun Wong [b], Zi Yin Kok [c], Sing Cheer Kwek [b], Paul John Gallagher [a,*], Joyce Yu-Chia Lee [d,*]

[a] Department of Pharmacy, National University of Singapore, Singapore
[b] National University Polyclinics, Singapore
[c] Keat Hong Family Medicine Clinic, Singapore
[d] School of Pharmacy and Pharmaceutical Sciences, University of California, Irvine, USA

ARTICLE INFO

Keywords:
Collaborative care
Community pharmacist
Diabetes
HbA1c
Hypoglycaemia
Polypharmacy. quality of life
Self-care

ABSTRACT

Aim: To evaluate the clinical and humanistic outcomes of a community pharmacist-involved collaborative care model in diabetes management.
Methods: This was a parallel arm, open-label, multi-centre randomized controlled trial conducted over 6 months. Subjects with type 2 diabetes, HbA1c $\geq$ 7.0% (53 mmol/mol) and taking $\geq$ 5 medications were included. Participants were randomized into intervention (collaborative care) and control groups (physician-centric care). The intervention included medication therapy management and telephonic follow-up with visits to family physicians, nurses, and dietitians. Clinical outcomes included changes in HbA1c, systolic blood pressure (SBP), lipids, and hypoglycaemic incidences. Humanistic outcomes included self-care capabilities and quality of life. Linear mixed models were constructed. Intention-to-treat analyses, with sensitivity analyses, were conducted.
Results: A total of 264 participants were randomized (intervention: 131, control: 133). Significantly greater reduction in HbA1c was observed in the intervention group (intervention: −0.32% (-3.52 mmol/mol) vs. control: −0.06% (-0.66 mmol/mol), p = 0.038). Changes in SBP, lipids, and incidences of hypoglycaemia were not significant over 6 months between both groups. Significantly greater improvements in self-management (p < 0.001) and quality of life (p = 0.003) were observed within the intervention group.
Conclusion: Partnering community pharmacists in a collaborative care team improved glycaemic control, quality of life and self-care capabilities of patients with diabetes and polypharmacy.

1. Introduction

The rising global burden of chronic diseases in the community, coupled with complexity of patient's individual needs, poses significant challenges to the healthcare system. Individuals with multiple chronic diseases require multi-faceted care approaches, from optimal pharmacotherapy to active health behavioural and lifestyle modifications. [1] Diabetes, a major public health concern, is one of such chronic non-communicable disease that requires frequent monitoring and active lifestyle engagements.

People with diabetes often suffered from multiple chronic diseases such as hypertension, ischemic heart disease, and dyslipidaemia, leading to increased use of medications, known as polypharmacy. [2] Polypharmacy, defined as usage of five or more medications, can be a cause of adverse events, increased risk of hypoglycaemia, frailty, worsened quality of life, increased hospital readmission rates, and mortality among patients with diabetes. [3,4] In order to overcome challenges among people with diabetes on multiple medications, studies have suggested to incorporate pharmacists as part of patient's multidisciplinary care team. [5,6] A *meta*-analysis of 11 randomized controlled trials found that pharmacist-led interventions resulted in significantly greater reduction in HbA1c as compared to the control group

* Corresponding authors at: Department of Clinical Pharmacy Practice, School of Pharmacy and Pharmaceutical Sciences, University of California, Irvine. 101 Theory, Suite 100, Irvine, CA 92697, USA and Department of Pharmacy, Faculty of Science, National University of Singapore. Block MD1, Tahir Foundation Building, 12 Science Drive 2, #06-03C, Singapore 117549, Singapore.
E-mail addresses: phapjg@nus.edu.sg (P.J. Gallagher), j.lee@uci.edu (J.Y.-C. Lee).

https://doi.org/10.1016/j.diabres.2022.109238
Received 1 September 2021; Received in revised form 28 January 2022; Accepted 1 February 2022
Available online 5 February 2022

(difference: −0.66% (-7.26 mmol/mol), p = 0.008). [7]

Community pharmacists, who are based in retail pharmacies, can serve as an accessible collaborative partner of patient's care team in providing medical advice in the community. Community pharmacists have been identified as the "first port of call" for medical advice for community-dwelling individuals. [8] This easy access for people with diabetes also allows the community pharmacists to address the self management aspect, including monitoring of blood glucose and hypoglycaemia promptly. [9] Community pharmacists also facilitate communications between the patient and their primary healthcare provider, and ensuring continuity of care. [8] Most published studies focused on clinical pharmacists in the hospitals and ambulatory care clinics, the benefits of engaging retail community pharmacists in collaboration with patient's multidisciplinary care team in the primary care setting has yet to be elucidated. In this trial, we have proposed a novel collaborative care model by partnering retail community pharmacists with family physicians, nurses, and dietitians to care for patients with type 2 diabetes and polypharmacy. The objective of this trial was to examine the impact of this novel collaborative care approach on patients' clinical outcomes, hypoglycaemic events, quality of life, and self-care capabilities.

2. Methods

2.1. Trial design and setting

This was a six-month, prospective, parallel arm, open label, multicentre randomized controlled trial conducted at two primary healthcare institutions in Singapore. Singapore is a multi-ethnic society, with residents of Chinese, Malay and Indian origins, and has a prevalence of diabetes at 14.2% in 2019. [10] Singapore adopts a mixed financing healthcare system with mandatory health insurance. [11] The public health system in Singapore comprises of primary care clinics, tertiary hospitals, and intermediate and long term care facilities, but chronic diseases are largely managed in the primary care clinics. [11] Pharmacists are generally accessible through dispensary pharmacies in retail settings and large public and private healthcare institutions. Engaging community pharmacists to assist patients and work jointly with patient's care team in the community clinics as presented in this study is yet to be established. This trial is approved by the National University of Singapore Institutional Review Board and the National Healthcare Group Domain Specific Review Board. This trial is registered with clinicaltrials.gov (NCT03531944).

2.2. Trial participants

The inclusion criteria were individuals ≥ 21 years with documented type 2 diabetes and baseline glycated haemoglobin (HbA1c) of above 7.0% (53 mmol/mol), taking five or more chronic medications. [3] Patients who were not able to converse in the English, Chinese or Malay language were excluded from the trial.

2.3. Trial procedures and randomization

Research team screened for potential subjects prior to their upcoming medical appointments. Research team then approached eligible subjects on the day of their clinic appointments and invited them to participate in the study. Upon providing written informed consent, the participants completed the humanistic questionnaires before being randomized into the intervention or control group. Stratified randomization was conducted to randomly allocate subjects into the intervention and control groups. Participants were stratified first in accordance with their baseline HbA1c levels [7.1% to 8.0% (54 to 64 mmol/mol), 8.1% to 10.0% (65 to 86 mmol/mol), and ≥ 10.1% (≥87 mmol/mol)]. Participants were then allocated randomly with a ratio of 1:1 into the intervention or control group using outcomes of flipping a coin. A trained research assistant who was not involved in the administration of questionnaires and other trial procedures conducted the randomization and allocation.

The intervention group received collaborative care which consisted of community pharmacists from a retail chain pharmacy and family physicians with as needed referral to nurses and dietitians. The control group received usual care from family physicians with as needed referral to nurses and dietitians. Both groups of patients received their medications from the clinic dispensary, managed by Pharmacy technicians. Both groups were provided with a complementary glucose meter and supplied with six months of lancets and test strips free of charge.

2.4. Community pharmacist intervention

Over the six-month period, community pharmacists were engaged for two face-to-face visits in the family physicians' clinics followed by telephonic follow-up sessions conducted every 4 to 6 weeks in their own pharmacy chain store. These community pharmacists were selected from a pool of pharmacists who have completed a 3-day diabetes certificate workshop and had at least 2 years of clinical experience in a retail pharmacy. These pharmacists were engaged on a part-time basis and renumerated according to the number of hours contributed for the collaborative care service. The physical presence of the community pharmacists in the clinic during the face-to-face consultations facilitated timely communication with patient's care team as well as improved understanding of their patients through authorized access to medical data which included patient history and updated laboratory investigations.

During the first face-to-face session with a community pharmacist, the pharmacist would prepare an individualized medication action plan (MAP) which detailed actual prescription and non-prescription medications taken by the patients. [12] This MAP was structured in the subjective, objective, assessment and plan (SOAP) format, which allowed community pharmacists to make recommendations that were specific to patient's disease control, medication-related problems, and non-pharmacological plan with a focus on self-care. [13] The MAP encouraged holistic documentation of patient care which allowed care team to communicate and endorse care plans jointly. During the patient care process, physician, pharmacist, and patient came together and discussed assessments and plans using the MAP prepared by the pharmacist. The final plans endorsed by physicians and agreed by patients may also include referrals to dietitians, nurses, or other investigational measures.

The second face-to-face consultation with a community pharmacist took place four weeks after the first visit and focused on diabetes self-management. This included glucose meter teaching and techniques, individualized goal setting, and interpretation of blood glucose results. The second visit also consisted of counselling on lifestyle modifications and update of MAP with relevant recommendations. Each face-to-face session lasted approximately 30 to 45 minutes.

Upon completion of the two face-to-face consultations, the participants were followed up regularly every 4 to 6 weeks over phone calls conducted by the community pharmacists. During each telephonic call, community pharmacists assessed SMBG techniques, interpretation of SMBG results, and provided lifestyle counselling and disease-related education. The participants provided their regular SMBG readings for the pharmacists to review and telephonic calls were conducted to follow up with the participants. The conversation was documented and made available to the patient's care team. Each telephonic session lasted approximately 15 to 30 min. The intervention workflow is illustrated in Fig. 1.

2.5. Training received by the community pharmacists

All community pharmacists had undergone a 3-day diabetes certificate workshop conducted by the National University of Singapore, and a

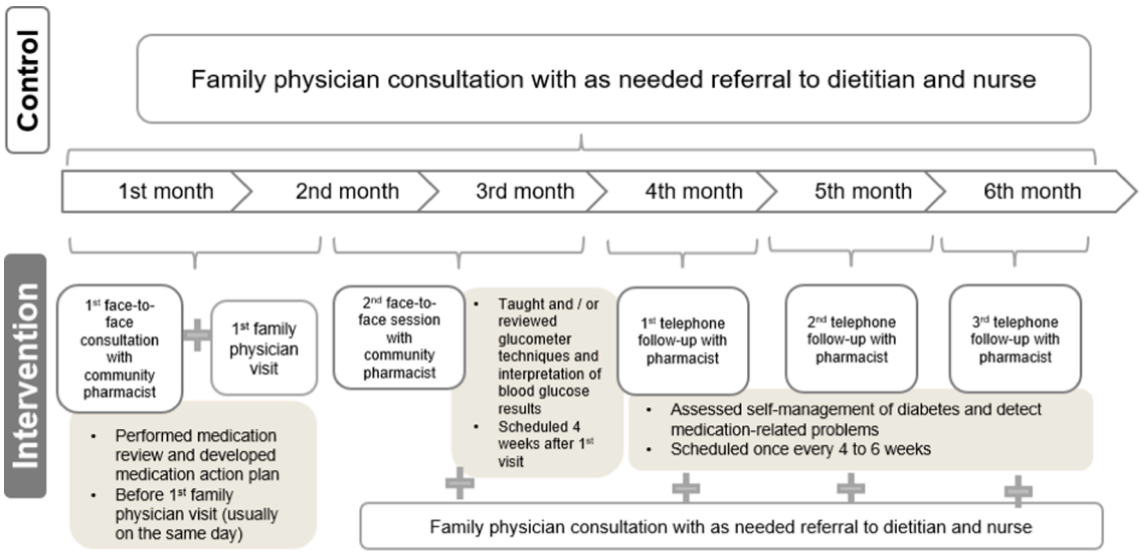

Fig. 1. Workflow of Intervention and Control Groups.

2-week Diabetes, Multidisciplinary, Experiential (DIAMANTE) program prior to participation in this trial. [14,15] The 3-day diabetes workshop delivered by a multi-disciplinary healthcare professionals covered different aspects of diabetes management and clinical case discussion, and served as a pre-requisite to attend the DIAMANTE program. The DIAMANTE program was specifically tailored for community pharmacists to engage in team-based care in the management of individuals with diabetes through active experiential workplace-based learning. [14] The DIAMANTE program included 80 hours of experiential learning with endocrinologists, clinical pharmacists, diabetes nurse educators, dietitians, and podiatrists in their clinics. [14] Participants of the DIAMANTE program were certified after successfully passing the exit assessment. [14]

2.6. Data collection and outcome measures

2.6.1. Clinical outcomes

Participant demographics, medication records and past medical histories were collected at enrolment. Data were collected at baseline, 3-month, and 6-month intervals during the trial period. Clinical outcomes included changes in HbA1c, systolic blood pressure (SBP), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-c) over 6 months. All measurements were conducted at a validated laboratory using a single instrument, except for blood pressure which was measured in the clinic using the same blood pressure monitor [OMRON HEM-7121] for all participants. Clinical and laboratory data were obtained from the electronic medical records available at the trial sites.

Hypoglycaemia and its management were assessed using a self-reported 5-item questionnaire, in which the first item assessed the symptoms of hypoglycaemia as either "yes", "no", or "not sure". [16] Items 2 to 4 assessed if the participant resolved hypoglycaemia through ingesting fast-acting glucose, requires assistance from another person to resolve hypoglycaemic symptoms, and whether the symptoms were resolved, respectively. Item 5 assessed the number of times that the participant performed SMBG in the past 7 days. Participants' self-reported hypoglycaemia was classified into severe hypoglycaemia and minor hypoglycaemia. Severe hypoglycaemia was defined as any signs and symptoms that require assistance from another person, while minor hypoglycaemia was defined as any signs and symptoms precipitated by known or modifiable causes that were resolved with or without ingesting fast-acting glucose. [17]

2.6.2. Humanistic outcomes

Humanistic outcomes included changes in quality of life and degree of self-care management among participants. These outcomes were measured using self-reported questionnaires administered at baseline and after 6 months. Permission for use of all questionnaires have been obtained from the respective copyright owners.

Quality of life was assessed using the valid and reliable Audit of Diabetes-Dependent Quality of Life (ADDQoL). [18] The ADDQoL is a 19-item questionnaire measuring participants' perception of the weighted impact of diabetes on their quality of life. [18] For each item, respondents provided both impact and importance ratings with ranges from −3 to + 1 and 0 to 3 respectively. [18] The average weighted impact (AWI) score was calculated from averaging the product of impact and importance ratings. [18] The more negative the AWI score is, the greater the negative impact diabetes has on participant's quality of life. [18]

Degree of self-care was assessed using the revised Summary of Diabetes Self-Care Activities (SDSCA) questionnaire. [19] SDSCA focusses on 5 domains, namely general diet (items 1 and 2), specific diet (items 3 and 4), exercise (items 5 and 6), blood-glucose testing (items 7 and 8), and foot-care (items 9 and 10), scored on a scale from 0 to 7 (i.e. number of days in a week in which the participant engaged with the asked activity). [19] The scores for items 1 to 10, with item 4 reversed coded, were summed up to a total score out of 70, with higher scores indicating greater degree of self-care management. [19]

2.7. Statistical analysis

Sample size was calculated using an estimate of 0.44% (4.8 mmol/mol) difference in mean HbA1c change between intervention and control arms over 6 months. [5] With a standard deviation of 1%, type I error rate of 5%, and power of 80%, the calculated total sample size was 164 participants.

Descriptive summary of the baseline characteristics between the intervention and control groups were reported. Analysis of baseline characteristics between the two groups was conducted using independent-sample *t*-test, Mann-Whitney *U* test or chi-square test as appropriate.

Separate linear mixed models were constructed to assess the changes in HbA1c, SBP, TG, LDL-c, quality of life, and self-care management over 6 months. Covariates such as duration of diabetes since documented diagnosis, smoking status, and total number of comorbidities were adjusted. In order to include appropriate covariates in this study, the

selection of covariates in each model was based on statistical evaluation on best fit, as well as clinical reasoning behind influences of covariates on specific outcomes. Fixed effects of time, trial arm and arm-time interactions, and random effects of trial sites, random intercepts, and random slopes were added where applicable for best model fit. Pairwise comparison with Bonferroni correction was also conducted for comparison between time points within each group. Analyses were based on intention-to-treat (ITT). Among those participants who have completed the trial, proportions of them who experienced severe and minor hypoglycaemia were compared between baseline and 6-month using McNemar's test. We conducted sensitivity analyses using linear mixed models to examine the possible influence of participant attrition.

All analyses were performed using the SPSS statistical software (V26.0; SPSS Inc, Chicago, Illinois). All statistical tests were two-tailed with a significance level (α) of 0.05.

3. Results

Among 3,339 potential patients screened for eligibility, 2,463 did not meet the inclusion criteria, while 612 declined participations. A total of 264 eligible patients were recruited and randomized into the intervention (n = 131) and control (n = 133) groups. Over the course of 6 months, a total of 89 (33.7%) participants (Intervention (INT): 61 [68.5%] vs. Control (CTL): 28 [31.5%]) dropped out of the study. Reasons for dropout included general disinterest or uncontactable (n = 17 [19.1%]; INT: 7 and CTL: 10), unwillingness to perform SMBG (n = 7 [7.9%]; INT: 7 and CTL: 0), no longer receiving care at trial sites (n = 22 [24.7%]; INT: 11 and CTL: 11), not keen on pharmacist intervention (n = 43 [40.4%]; INT: 36 and CTL: 0), not keen on survey participation (n = 5 [5.6%]; INT: 0 and CTL: 5) and deaths (n = 2 [2.2%]; INT: 0 and CTL: 2). This resulted in 175 participants (INT: 70 vs CTL: 105) completing the trial (Fig. 2).

The mean age of the trial participants was 67.2 ± 8.9 years (INT: 67.4 years vs. CTL: 66.9 years). Majority were female (52.3%) and Chinese in ethnicity (73.5%). The mean duration of diabetes diagnosed was 14.6 ± 9.5 years. The trial participants were taking on average 7.1 ± 1.9 chronic medications. Overall, the baseline demographic, medical and medication data were comparable between both groups, except for smoking status (INT: 3.8% smokers vs. CTL: 12.8% smokers, p = 0.013) (Table 1).

3.1. Clinical outcomes

3.1.1. Changes in HbA1c

The mean improvement in HbA1c level was significantly greater between the intervention and control groups over 6 months (INT: −0.32% (-3.52 mmol/mol) vs. CTL: −0.06% (-0.66 mmol/mol), 95% confidence interval (CI): 0.31 to 4.01, p = 0.038) (Table 2). The mean HbA1c level among participants in the intervention group improved significantly from 8.2 ± 1.0% (66 ± 11 mmol/mol) at baseline to 8.0 ± 1.2% (64 ± 13 mmol/mol) at 3-month to 7.8 ± 1.2% (62 ± 13 mmol/mol) at 6-month (p = 0.017). Glucose fluctuation was observed in the control group where the mean HbA1c level changed from 8.2 ± 1.2% (66 ± 13 mmol/mol) at baseline to 8.1 ± 1.2% (65 ± 13 mmol/mol) at 6-month (p = 0.922).

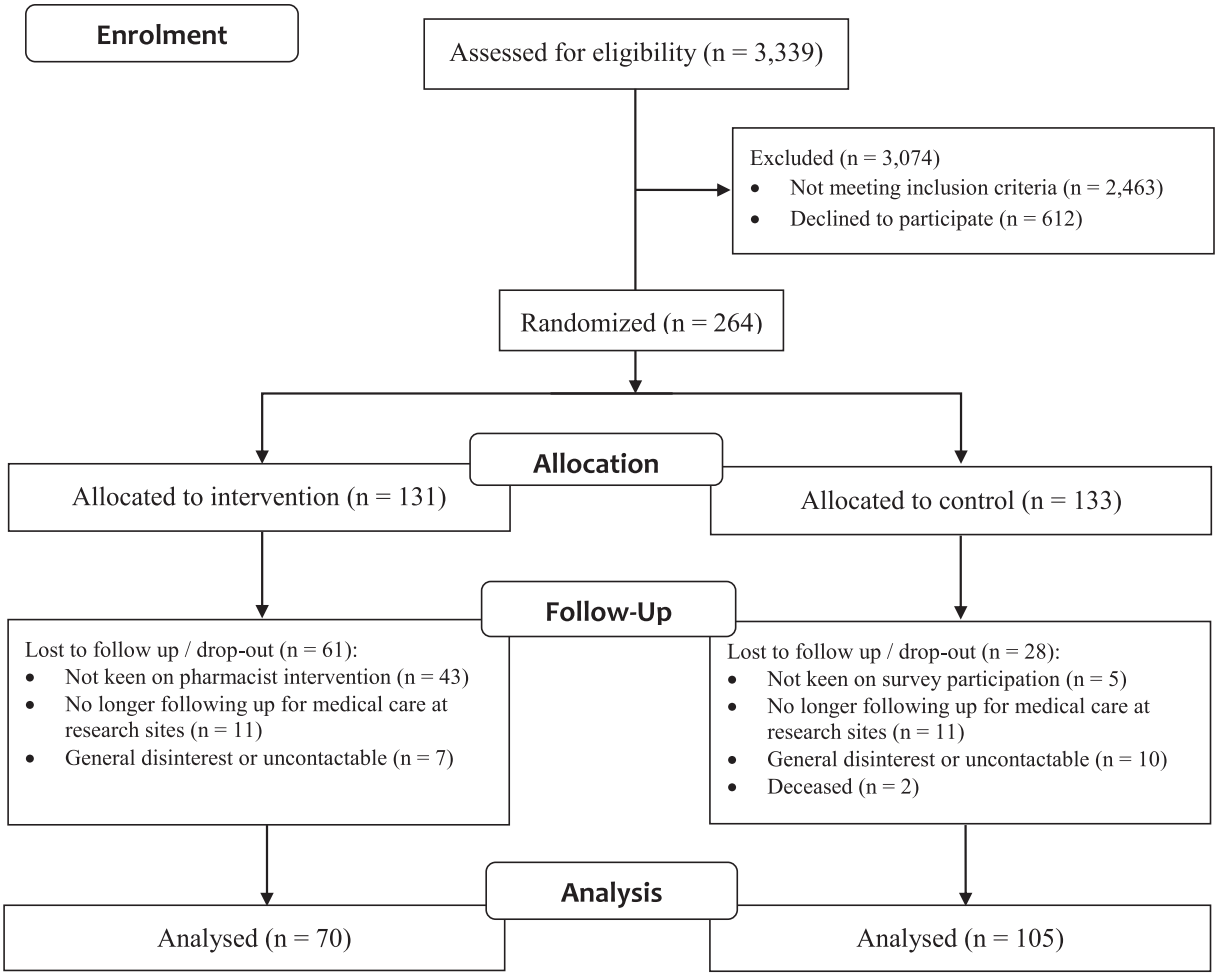

Fig. 2. CONSORT Flow Diagram of Study Participants.

Table 1
Baseline characteristics of trial participants (ITT Analysis).

Characteristics	Overall (N = 264) †	Intervention (n = 131) †	Control (n = 133) †	p-value
Age, years	67.2 ± 8.9	67.4 ± 8.0	66.9 ± 9.6	0.606
Gender				0.265
Male	126 (47.7)	58 (44.3)	68 (51.1)	
Female	138 (52.3)	73 (55.7)	65 (48.9)	
Ethnicity				0.737
Chinese	194 (73.5)	93 (71.0)	101 (75.9)	
Malay	41 (15.5)	21 (16.0)	20 (15.0)	
Indian	27 (10.2)	16 (12.2)	11 (8.3)	
Others	2 (0.8)	1 (0.8)	1 (0.8)	
Educational status				0.863
No formal education	40 (15.2)	18 (13.7)	22 (16.5)	
Elementary	85 (32.2)	45 (34.4)	40 (30.1)	
High school	98 (37.1)	48 (36.6)	50 (37.6)	
College / University	41 (15.5)	20 (15.3)	21 (15.8)	
Employment status				0.438
Unemployed	157 (59.5)	81 (61.8)	76 (57.1)	
Employed	107 (40.5)	50 (38.2)	57 (42.9)	
Marital status				0.284
Single	10 (3.8)	5 (3.8)	5 (3.8)	
Married	211 (79.9)	100 (76.3)	111 (83.5)	
Divorced / widowed	43 (16.3)	26 (19.8)	17 (12.8)	
Body mass index, kg m^{-2}	26.6 ± 4.9	26.7 ± 4.8	26.5 ± 4.9	0.658
Smoking status				0.013
Non-smoker	242 (91.7)	126 (96.2)	116 (87.2)	
Smoker	22 (8.3)	5 (3.8)	17 (12.8)	
Comorbidities	5.2 ± 1.5	5.3 ± 1.5	5.2 ± 1.5	0.386
IHD	62 (23.5)	32 (24.2)	30 (22.6)	0.772
Hypertension	242 (91.7)	119 (90.8)	123 (92.5)	0.629
Hyperlipidaemia	258 (97.7)	129 (98.5)	129 (97.0)	0.684
Stroke	31 (11.7)	15 (11.5)	16 (12.0)	0.884
Duration of diagnosed diabetes, years	14.6 ± 9.5	14.7 ± 9.1	14.4 ± 10.0	0.812
Diabetes regimen				0.674
Insulin only	5 (1.9)	2 (1.5)	3 (2.3)	
OHA only	167 (63.3)	80 (61.1)	87 (65.4)	
Insulin and OHA	53 (20.1)	22 (16.8)	31 (23.3)	
Chronic medications	7.1 ± 1.9	7.2 ± 1.9	7.0 ± 1.9	0.437
Diabetes medications	2.1 ± 0.9	2.1 ± 0.9	2.1 ± 0.8	0.860
Non-diabetes medications	4.9 ± 1.9	5.0 ± 2.0	4.8 ± 1.9	0.497

Abbreviations: ITT, intention-to-treat; IHD, ischemic heart disease; OHA, oral hypoglycaemic agents.
† Reported in mean ± standard deviation or number (percentage) as appropriate.

3.1.2. Changes in SBP

The SBP at baseline for both groups were controlled (INT: 134.4 ± 16.4 mm Hg vs. CTL: 131.9 ± 18.5 mm Hg) and maintained throughout the study (between-group difference: 13.5 mm Hg, p = 0.136). There was an insignificant but clinically reasonable improvement and maintenance of SBP among participants in the intervention group between baseline and 6 months (from 134.4 mm Hg at baseline to 130.6 mm Hg at 3-month to 130.4 mm Hg at 6-month, p = 0.058). For the control group, trends of significant worsening in SBP were observed over 6 months from baseline (from 131.9 mm Hg at baseline to 139.9 mm Hg at 3-month to 141.4 mm Hg at 6-month, p < 0.001).

3.1.3. Changes in TG and LDL-c

The changes in triglyceride level were not significantly different between both intervention and control groups (between-group difference: 0.254 mmol/L, p = 0.339). Similarly, changes in low-density lipoprotein cholesterol level were also not significantly different between both groups (between-group difference: 0.509 mmol/L, p = 0.589).

3.2. Hypoglycaemic events

The overall proportion of participants who experienced any hypoglycaemic events decreased from 47.4% at baseline (INT: 36 [51.4%] vs. CTL: 47 [44.8%]) to 34.3% at 6-month (INT: 25 [35.7%] vs. CTL: 35 [33.3%]) (Table 3).

The proportion of participants in the intervention group who experienced severe hypoglycaemia significantly decreased from 7 (10.0%) at baseline to 0 (0.0%) at 6-month (p = 0.016). The decrease in proportion of participants in the control group who experienced severe hypoglycaemia from 8 (7.6%) at baseline to 6 (5.7%) at 6-month was not statistically significant (p = 0.687) (Table 3).

The proportion of participants in the intervention group who experienced minor hypoglycaemia decreased from 29 (41.4%) at baseline to 25 (35.7%) at 6-month (p = 0.608); compared to that of the control group from 40 (38.1%) at baseline to 29 (27.6%) at 6-month (p = 0.052) (Table 3).

3.3. Humanistic outcomes

3.3.1. Changes in quality of life

Participants in the intervention group showed greater improvement in their quality of life as compared to the control group over 6 months (between-group difference: 0.219, p = 0.003). Within the intervention group, significant improvements in quality of life over the trial period was observed (change: 0.550, p = 0.001). Changes in quality of life within the control group over 6 months was not significant (p = 0.977).

3.4. Changes in self-care management

Similarly, participants in the intervention group showed greater improvement in the degree of self-care management as compared to the control group (between-group difference: 5.621, p < 0.001). Within the intervention group, improvements in degree of self-care management were also observed among the participants (change: 12.16, p < 0.001). No significant changes were observed in the degree of self-care management among participants in the control group (p = 0.698).

In terms of general diet, the score for participants in the intervention group increased from 3.5 ± 2.7 days at baseline to 4.6 ± 1.8 days at 6-month (p < 0.001) (compared to the control group from 3.9 ± 2.7 days to 3.7 ± 2.1 days after 6 months, p = 0.595). Specific diet remained similar over 6 months for participants in the intervention group (baseline: 4.3 ± 1.8 days vs. 6-month: 4.2 ± 1.4 days, p = 0.878). However, participants in the control group showed significant decrease in score for specific diet (baseline: 4.2 ± 1.8 days vs. 6-month: 3.7 ± 1.5 days, p = 0.042). Participants in the intervention group showed improvements in exercise scores (baseline: 2.7 ± 2.5 days vs. 3.3 ± 2.2 days, p = 0.098) (compared to the control group from 2.8 ± 2.4 days to 2.6 ± 2.1 days over 6 months). SMBG frequency showed significantly greater improvements in the intervention group (baseline: 1.1 ± 2.0 days to 6-month: 4.4 ± 2.4 days, p < 0.001) as compared to the control group (baseline: 0.8 ± 1.8 days to 6-month: 1.2 ± 1.9 days, p = 0.081). Foot care also improved significantly for participants in the intervention group (baseline: 3.0 ± 2.8 days to 6-month: 4.2 ± 1.7 days, p < 0.001), compared to control group (baseline: 3.1 ± 2.7 days to 6-month: 3.3 ± 2.0 days, p = 0.633).

3.5. Sensitivity analyses

Sensitivity analyses on the outcomes for participants who have completed the trial (N = 175; intervention: 70 vs. control: 105) found that the results did not differ from the ITT analyses (Table 2). The mean improvement in HbA1c level was significantly greater between the intervention and control groups over 6 months (INT: −0.23% (-2.53 mmol/mol) vs. CTL: −0.03% (-0.33 mmol/mol), p = 0.022). The changes in SBP between both groups from baseline to 6 months were comparable (p = 0.077). Similarly, the changes in TG (p = 0.828) and LDL-c (p = 0.487) between both groups over 6 months were not significantly different.

Table 2
(a). Outcomes of clinical and humanistic measures.

Outcomes †	Intention-to-Treat Analysis (N = 264)							Per-Protocol Analysis (N = 175)						
	Intervention Group (n = 131)			Control Group (n = 133)			p-value (between-group)	Intervention Group (n = 70)			Control Group (n = 105)			p-value (between-group)
	Baseline	3-Month	6-Month	Baseline	3-Month	6-Month		Baseline	3-Month	6-Month	Baseline	3-Month	6-Month	
HbA1c, % (mmol/mol)	8.2 ± 1.0 (66 ± 11)	8.0 ± 1.2 (64 ± 13)	7.8 ± 1.2 (62 ± 13)	8.2 ± 1.2 (66 ± 13)	8.2 ± 1.2 (66 ± 13)	8.1 ± 1.2 (65 ± 13)	0.038 *	8.1 ± 1.1 (65 ± 12)	7.8 ± 0.8 (62 ± 9)	7.8 ± 1.2 (62 ± 13)	8.2 ± 0.9 (66 ± 10)	8.0 ± 1.1 (64 ± 12)	8.2 ± 1.2 (66 ± 13)	0.022 *
SBP, mm Hg	134.4 ± 16.4	130.6 ± 13.4	130.4 ± 14.2	131.9 ± 18.5	139.9 ± 18.2	141.4 ± 19.1	0.136	132.4 ± 16.8	133.5 ± 17.3	130.4 ± 14.2	132.4 ± 19.0	137.0 ± 16.9	141.4 ± 19.1	0.077
TG, mmol/dL	2.0 ± 1.5	1.8 ± 0.9	1.8 ± 1.6	1.9 ± 1.5	2.0 ± 1.0	1.9 ± 1.0	0.339	2.0 ± 1.9	1.9 ± 1.1	1.8 ± 1.6	2.0 ± 1.6	1.9 ± 1.0	1.9 ± 1.0	0.828
LDL-c, mmol/dL	2.4 ± 1.0	2.3 ± 0.6	2.1 ± 0.8	2.1 ± 0.7	2.3 ± 0.7	2.3 ± 0.8	0.589	2.3 ± 1.0	2.3 ± 0.6	2.1 ± 0.7	2.0 ± 0.6	2.2 ± 0.6	2.3 ± 0.8	0.487
Quality of Life	−2.66 ± 1.92	–	−2.11 ± 1.37	−2.57 ± 1.89	–	−2.51 ± 1.57	0.003 *	−2.71 ± 1.99	–	−2.11 ± 1.37	−2.46 ± 1.91	–	−2.51 ± 1.57	0.003 *
Self-care	29.2 ± 13.9	–	41.3 ± 11.4	29.6 ± 12.8	–	29.2 ± 11.6	< 0.001 *	29.7 ± 13.8	–	41.3 ± 11.4	29.3 ± 12.3	–	29.2 ± 11.6	0.012 *

Abbreviations: HbA1c, glycated haemoglobin; SBP, systolic blood pressure; SMBG, self-monitoring of blood glucose; TG, triglyceride; LDL-c, low-density lipoprotein cholesterol.
† Reported in mean ± standard deviation.
* Statistically significant between intervention and control groups (i.e. $p < 0.05$).

Table 2
(b). Outcomes of self-care components.

Outcomes †	Intention-to-Treat Analysis (N = 264)						Per-Protocol Analysis (N = 175)					
	Intervention Group (n = 131)			Control Group (n = 133)			Intervention Group (n = 70)			Control Group (n = 105)		
	Baseline	6-Month	p-value (within-group)	Baseline	6-Month	p-value (within-group)	Baseline	6-Month	p-value (within-group)	Baseline	6-Month	p-value (within-group)
General	3.5 ±	4.6 ±	< 0.001*	3.9 ±	3.7 ±	0.595	3.6 ±	4.6 ±	0.009*	3.7 ±	3.7 ±	0.769
Diet	2.7	1.8	0.878	2.7	2.1	0.042 *	2.6	1.8	0.709	2.8	2.1	0.173
Specific	4.3 ±	4.2 ±	0.098	4.2 ±	3.7 ±	0.691	4.2 ±	4.2 ±	0.252	4.1 ±	3.7 ±	0.921
Diet	1.8	1.4	< 0.001*	1.8	1.5	0.081	1.7	1.4	< 0.001*	1.8	1.5	0.002*
Exercise	2.7 ±	3.3 ±	< 0.001*	2.8 ±	2.6 ±	0.633	2.8 ±	3.3 ±	0.003	2.7 ±	2.6 ±	0.862
SMBG	2.5	2.2		2.4	2.1		2.5	2.2		2.3	2.1	
Foot Care	1.1 ±	4.4 ±		0.8 ±	1.2 ±		1.3 ±	4.4 ±		0.8 ±	1.2 ±	
	2.0	2.4		1.8	1.9		2.1	2.4		1.8	1.9	
	3.0 ±	4.2 ±		3.1 ±	3.3 ±		3.0 ±	4.2 ±		3.3 ±	3.3 ±	
	2.8	1.7		2.7	2.0		2.7	1.7		2.6	2.0	

† Reported in mean ± standard deviation.
* Statistically significant within intervention or control group (i.e. $p < 0.05$).

Table 3
Hypoglycaemic incidences among trial participants (N = 175).

	Overall hypoglycaemia			Severe hypoglycaemia			Minor hypoglycaemia		
	Baseline	6-Month	P Value	Baseline	6-Month	P Value	Baseline	6-Month	P Value
Intervention (n = 70)	36 (51.4%)	25 (35.7%)	0.062	7 (10.0%)	0 (0.0%)	0.016*	29 (41.4%)	25 (35.7%)	0.608
Control (n = 105)	48 (45.7%)	35 (33.3%)	0.067	8 (7.6%)	6 (5.7%)	0.687	40 (38.1%)	29 (27.6%)	0.052

* Statistically significant between baseline and 6-month (i.e. $p < 0.05$).

Participants in the intervention group showed greater improvement in their quality of life as compared to the control group over 6 months (between-group difference: 0.621, $p = 0.003$). Similarly, participants in the intervention group showed greater improvement in the degree of self-care management as compared to the control group (between-group difference: 11.62, $p = 0.012$).

4. Discussion

This trial was one of the first to evaluate the impact of a novel care model on the clinical and humanistic outcomes of community-dwelling patients with diabetes and polypharmacy. The care model strategically brought together the key providers in the community and formed a health safety net to better address the gaps of today's diabetes care. Through this trial, it was found that community pharmacist-involved collaborative care model resulted in improved glycaemic control, less hypoglycaemic events and better quality of life and self-care capabilities.

The novel aspect of our trial intervention was the shared decision-making between the patient and the community pharmacist in drawing up the MAP and subsequently utilized by the family physician to guide patient care. [12] This component addresses the previously

established challenge of lack of communication between healthcare providers and enhanced the connections between patients and their healthcare providers to minimize polypharmacy and medication-related problems. The community pharmacist played an intermediary role in facilitating communication between the family physician and the patient. Communication is key to enhancing effectiveness of the entire consultancy process, especially with regards to diabetes that relies on optimal self-management. [8] Furthermore, the integration of telephonic follow up of self-management provided by the community pharmacists added convenience and flexibility for the participants to seek medical care timely.

This care model involved remote monitoring of the participants' blood glucose and follow up with telephonic calls and allowed the collaborative care team to continue monitoring and providing medical care for people with diabetes. This mode of delivery ensures continuity of care for people with diabetes, especially during times of pandemic such as the COVID-19, in which this group of people is exceptionally vulnerable to COVID-19 and its complications. [20] Telephonic follow-up allowed these people to be cared for without them having to visit the healthcare institutions, and hence minimising their risk to infections. [21] Taken together, this novel care model not only enhances communication between patients and their healthcare providers, but also facilitates care adaptability when face-to-face consultations are restricted.

The significant improvement in glycaemic control in this trial also corroborated with a cluster randomized controlled trial in France, which found that tailored intervention on medication management and lifestyle education performed by community pharmacists resulted in reduction in HbA1c level (INT: −0.5% (-5.5 mmol/mol) vs. CTL: −0.2% (-2.2 mmol/mol), $p = 0.005$). [22] Given that the blood pressure and lipid markers of the participants were well-controlled at baseline, there were no significant improvements after 6 months. This could be due to the short duration of the trial as effects on these cardiovascular markers require a longer duration of intervention. This was supported by a systematic review in which significant changes in blood pressure and lipids due to pharmacist-involved collaborative care model were only observed for studies of duration beyond 6 months. [23] These findings supported the fact that involvement of community pharmacist for as short as 6 months can already result in improvements in glycaemic control. [24]

In addition, compared to the usual care, the collaborative care approach also resulted in significant improvements in patients' self-management and quality of life. Specifically, these improvements may be partially attributed to the effective self-management counselling and address of polypharmacy issues provided by the community pharmacists. [25] In addition, the convenient and easy access to community pharmacists also allow patients to have their self management and self care issues addressed promptly. [9] Studies have shown that active engagement of patient by healthcare professionals empower patient self-capabilities and self-efficacy, leading to enhanced quality of life. [26,27]

Furthermore, our novel approach to partner retail community pharmacists with primary care team also formed a diabetes safety net in the community. Numerous studies have reported family physicians' frustration on not being able to fulfil their patients' needs due to a lack of time and resources. [28,29] These challenges faced by the family physicians often led to delayed disease control, which resulted in development of complications requiring specialist care. [30] By working with retail community pharmacists, patients can be monitored effectively in the community with added flexibility in availability and location. In addition to building the communication bridge between patients and their providers, the community pharmacists also serve as a safety net for emotional support. [31] A prospective multi-centre study that examined the impact of pharmaceutical care provided by community pharmacists for people with diabetes found an improvement in mental well-being over 6 months ($p = 0.022$). [31] The community pharmacists in this trial were also able to identify patients who may require closer monitoring or early follow up to minimize complications.

This trial had several limitations. Physicians participating in the collaborative care process were also attending to other patients who may be in the control group. The possibility of cross-contamination between the two arms cannot be eliminated, and true benefits of the collaborative care may be under-estimated. The intervention group had higher dropout rate ($n = 43$, 32.8%) than the control group. This attrition rate was within the reported rate of approximately 30% to 60% in a systematic review. [32] Furthermore, sensitivity analyses conducted found that the results did not differ after excluding participants who dropped out of the trial. However, implementation research anchored on patient perception and perspectives towards this novel collaborative care model should be conducted to eventually translate this effective care model to real-world practice. In this study, patient-reported outcomes were elucidated through questionnaires and inherently subjected to recall bias. [33] To address this limitation, the 6-month questionnaires were administered within 4 weeks of completing the intervention [32,33].

5. Conclusion

Partnering retail community pharmacists with patient's primary care team improved glycaemic control, self-care capabilities and quality of life. The multidisciplinary collaborative care model can form a safety net for community-dwelling individuals with chronic diseases.

Funding

This randomized controlled trial was funded by the National Medical Research Council Health Services Research Competitive Research Grant awarded to Dr. Joyce Yu-Chia Lee. The funder was not involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; and decision to submit the manuscript for publication.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The authors would like to acknowledge the medical and administrative staff from Keat Hong Family Medicine Clinic and Bukit Batok Polyclinic in supporting the conduct of this randomized controlled trial. The authors would also like to acknowledge the community pharmacists, Kng Li Lin Grace, Koh Jia Lei, and Siti Rahil Bte Mohd Yussof for their invaluable support in conducting the interventional activities.

ClinicalTrials.gov number: NCT03531944

References

[1] Reynolds R, Dennis S, Hasan I, Slewa J, Chen W, Tian D, et al. A systematic review of chronic disease management interventions in primary care. BMC Fam Pract. 2018;19(1). https://doi.org/10.1186/s12875-017-0692-3.

[2] Bauer S, Nauck MA. Polypharmacy in people with Type 1 and Type 2 diabetes is justified by current guidelines–a comprehensive assessment of drug prescriptions in patients needing inpatient treatment for diabetes-associated problems. Diabet Med J Br Diabet Assoc. 2014;31(9):1078–85. https://doi.org/10.1111/dme.12497.

[3] Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. J Clin Epidemiol. 2012;65(9):989–95. https://doi.org/10.1016/j.jclinepi.2012.02.018.

[4] Noale M, Veronese N, Cavallo Perin P, Pilotto A, Tiengo A, Crepaldi G, et al. Polypharmacy in elderly patients with type 2 diabetes receiving oral antidiabetic treatment. Acta Diabetol. 2016;53(2):323–30. https://doi.org/10.1007/s00592-015-0790-4.

[5] Siaw MYL, Ko Y, Malone DC, Tsou KYK, Lew Y-J, Foo D, et al. Impact of pharmacist-involved collaborative care on the clinical, humanistic and cost outcomes of high-risk patients with type 2 diabetes (IMPACT): a randomized controlled trial. J Clin Pharm Ther. 2017;42(4):475–82. https://doi.org/10.1111/jcpt.12536.

[6] Abdulrhim SH, Saleh RA, Mohamed Hussain MA, Al Raey H, Babiker AH, Kheir N, et al. Impact of a Collaborative Pharmaceutical Care Service Among Patients With Diabetes in an Ambulatory Care Setting in Qatar: A Multiple Time Series Study. Value Health Reg Issues. 2019;19:45–50. https://doi.org/10.1016/j.vhri.2018.12.002.
[7] Bukhsh A, Tan XY, Chan KG, Lee LH, Goh BH, Khan TM. Effectiveness of pharmacist-led educational interventions on self-care activities and glycemic control of type 2 diabetes patients: a systematic review and meta-analysis. Patient Prefer Adherence. 2018;12:2457–74. https://doi.org/10.2147/PPA.S180256.
[8] Ilardo ML, Speciale A. The Community Pharmacist: Perceived Barriers and Patient-Centered Care Communication. Int J Environ Res Public Health. 2020;17(2):E536. https://doi.org/10.3390/ijerph17020536.
[9] Dhippayom T, Krass I. Supporting self-management of type 2 diabetes: is there a role for the community pharmacist? Patient Prefer Adherence. 2015;9:1085–92. https://doi.org/10.2147/PPA.S88071.
[10] Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep. 2020;10(1). https://doi.org/10.1038/s41598-020-71908-9.
[11] Thomas JS, Ong SE, Chia KS, Lee HP. A Brief History of Public Health in Singapore. In: *Singapore's Health Care System*. World Scientific Series on Singapore's 50 Years of Nation-Building. WORLD SCIENTIFIC; 2015:33-56. doi:10.1142/9789814696067_0002.
[12] Burns A. Medication therapy management in pharmacy practice: Core elements of an MTM service model (version 2.0). J Am Pharm Assoc JAPhA. 2008;48(3):341–53. https://doi.org/10.1331/JAPhA.2008.08514.
[13] Weed LL. Medical records that guide and teach. N Engl J Med. 1968;278(11):593–600. https://doi.org/10.1056/NEJM196803142781105.
[14] Siaw MYL, Ang SW, Lee JYC. Evaluation of the Diabetes, Multidisciplinary, Experiential (DIAMANTE) Program for Retail Pharmacists: A Mixed-Method Study. J Contin Educ Health Prof. 2017;37(2):116–22. https://doi.org/10.1097/CEH.0000000000000157.
[15] Lee J. A Multidisciplinary Approach to Diabetes Continuing Education for Healthcare Professionals. *CDTL Brief, First Look*. http://www.cdtl.nus.edu.sg/brief/firstlook/pdf/Joyce_Lee_dec2012.pdf. Published December 2012.
[16] Pratipanawatr T, Satirapoj B, Ongphiphadhanakul B, Suwanwalaikorn S, Nitiyanant W. Impact of Hypoglycemia on Health-Related Quality of Life among Type 2 Diabetes: A Cross-Sectional Study in Thailand. J Diabetes Res. 2019;2019:1–8. https://doi.org/10.1155/2019/5903820.
[17] Seaquist ER, Anderson J, Childs B, Cryer P, Dagogo-Jack S, Fish L, et al. Hypoglycemia and Diabetes: A Report of a Workgroup of the American Diabetes Association and The Endocrine Society. Diabetes Care 2013;36(5):1384–95. https://doi.org/10.2337/dc12-2480.
[18] Wee H-L, Tan C-E, Goh S-Y, Li S-C. Usefulness of the Audit of Diabetes-Dependent Quality-of-Life (ADDQoL) questionnaire in patients with diabetes in a multi-ethnic Asian country. PharmacoEconomics. 2006;24(7):673–82.
[19] Toobert DJ, Hampson SE, Glasgow RE. The summary of diabetes self-care activities measure: results from 7 studies and a revised scale. Diabetes Care 2000;23(7):943–50.
[20] Mantovani A, Byrne CD, Zheng MH, Targher G. Diabetes as a risk factor for greater COVID-19 severity and in-hospital death: A meta-analysis of observational studies. Nutr Metab Cardiovasc Dis NMCD. 2020;30(8):1236–48. https://doi.org/10.1016/j.numecd.2020.05.014.
[21] Danne T, Limbert C, Puig Domingo M, Del Prato S, Renard E, Choudhary P, et al. Telemonitoring, Telemedicine and Time in Range During the Pandemic: Paradigm Change for Diabetes Risk Management in the Post-COVID Future. Diabetes Ther Res Treat Educ Diabetes Relat Disord. 2021;12(9):2289–310. https://doi.org/10.1007/s13300-021-01114-x.
[22] Michiels Y, Bugnon O, Chicoye A, Dejager S, Moisan C, Allaert F-A, et al. Impact of a Community Pharmacist-Delivered Information Program on the Follow-up of Type-2 Diabetic Patients: A Cluster Randomized Controlled Study. Adv Ther. 2019;36(6):1291–303. https://doi.org/10.1007/s12325-019-00957-y.
[23] Pousinho S, Morgado M, Falcão A, Alves G. Pharmacist Interventions in the Management of Type 2 Diabetes Mellitus: A Systematic Review of Randomized Controlled Trials. J Manag Care Spec Pharm. 2016;22(5):493–515. https://doi.org/10.18553/jmcp.2016.22.5.493.
[24] Majumdar SR, Guirguis LM, Toth EL, Lewanczuk RZ, Lee TK, Johnson JA. Controlled trial of a multifaceted intervention for improving quality of care for rural patients with type 2 diabetes. Diabetes Care 2003;26(11):3061–6. https://doi.org/10.2337/diacare.26.11.3061.
[25] Shrivastava SR, Shrivastava PS, Ramasamy J. Role of self-care in management of diabetes mellitus. J Diabetes Metab Disord. 2013;12(1):14. https://doi.org/10.1186/2251-6581-12-14.
[26] Deters MA, Laven A, Castejon A, Doucette WR, Ev LS, Krass I, et al. Effective Interventions for Diabetes Patients by Community Pharmacists: A Meta-analysis of Pharmaceutical Care Components. Ann Pharmacother. 2018;52(2):198–211. https://doi.org/10.1177/1060028017733272.
[27] Carter EL, Nunlee-Bland G, Callender C. A Patient-Centric, Provider-Assisted Diabetes Telehealth Self-management Intervention for Urban Minorities. *Perspect Health Inf Manag AHIMA Am Health Inf Manag Assoc*. 2011;8(Winter). Accessed October 1, 2019. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3035826/.
[28] McInnes S, Peters K, Bonney A, Halcomb E. An integrative review of facilitators and barriers influencing collaboration and teamwork between general practitioners and nurses working in general practice. J Adv Nurs. 2015;71(9):1973–85. https://doi.org/10.1111/jan.12647.
[29] Zallman L, Ibekwe L, Thompson J, Ross-Degnan D, Oken E. Development of a Mapped Diabetes Community Program Guide for a Safety Net Population. Diabetes Educ. 2014;40(4):453–61. https://doi.org/10.1177/0145721714531076.
[30] Kauffman Y, Jonkman L, Lupu A, Connor S. Exploring the value of clinical pharmacy services for patients with diabetes in safety net settings. Res Soc Adm Pharm RSAP. 2013;9(6):770–6. https://doi.org/10.1016/j.sapharm.2012.11.001.
[31] Lum ZK, Siaw MYL, Lee MJX, Koh Z, Zhang PQ, Eng SK, et al. Impact of pharmaceutical care on mental well-being and perceived health among community-dwelling individuals with type 2 diabetes. Qual Life Res 2019;28(12):3273–9.
[32] Tan ECK, Stewart K, Elliott RA, George J. Pharmacist services provided in general practice clinics: a systematic review and meta-analysis. Res Soc Adm Pharm RSAP. 2014;10(4):608–22. https://doi.org/10.1016/j.sapharm.2013.08.006.
[33] Refolo P, Minacori R, Mele V, Sacchini D, Spagnolo AG. Patient-reported outcomes (PROs): the significance of using humanistic measures in clinical trial and clinical practice. Eur Rev Med Pharmacol Sci. 2012;16(10):1319–23.