A Narrative Review of Diabetes Intervention Studies to Explore Diabetes Care Opportunities for Pharmacists

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1. Introduction

Diabetes contributed to 1.2 million worldwide deaths in 2012 [1]. In people with diabetes, approximately 50–80% of mortality is attributed to cardiovascular disease [2]. Diabetes is the leading cause of kidney failure [3] and also contributes to one percent of global blindness [4]. In terms of healthcare burden it was estimated that in 2010 diabetes contributed to 4–7 billion United States Dollar (USD) in health expenditure in Australia, USD 7–15 billion in the United Kingdom (UK), and USD 197–344 billion in the United States of America (USA) [5].

As the incidence of diabetes and health burden continues to rise [3] a new approach in diabetes management is imminent. The overall aim of diabetes care is to improve patients’ quality of life, prevent early death and reduce the burden of disease [6]. Nevertheless, diabetes is a complex disease as there is a need to address multiple factors in order to achieve quality diabetes care. Addressing multiple factors is referred to as multifactorial intervention or multifactorial treatment and has been described in previous studies [7–13].

This is a narrative review of multifactorial intervention studies from selective literature and explores potential opportunities for pharmacists to deliver quality diabetes care in patients with type 2 diabetes. Findings from this review are useful in addressing current practice challenges.

Aim of Narrative Review. The aim of this research is to review current diabetes management practices targeted towards improved diabetes control and prevention of diabetes related complications. The objectives are to

(1) critique diabetes studies in terms of diabetes guidelines,
(2) determine intervention methods used by healthcare professionals involved in diabetes care with a particular focus towards diabetes intervention services by pharmacists,
(3) identify key areas where multifactorial interventions are lacking and explore opportunities for pharmacists in diabetes care.

2. Method

Keywords used in database searches were “diabetes”, “pharmacist”, “intervention” or “tool”, and “randomised controlled trial” (RCT). Databases used included the Cochrane Library, PubMed, Medline (Web of Science), ProQuest, Scopus, and Medline Ovid. Searches were limited to articles in the English Language, published between January 2010 and August 2015 and included both type 1 and type 2 diabetes. The findings from the search are presented as a narrative review.

3. Results and Discussion

3.1. Multifactorial Diabetes Care. There were several landmark trials that provided significant evidence that led to improved diabetes management outcomes, namely:

(1) The United Kingdom Prospective Diabetes Study (UKPDS) carried out in the UK [14].

(2) The Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation (ADVANCE) study carried out in 20 countries throughout Asia, Australia, Europe, and North America [15].

(3) The Veterans Affairs Diabetes Trial (VADT) in the USA [16].

(4) The Diabetes Control and Complications Trial (DCCT) in the USA [17].

(5) The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study carried out in the USA and Canada [18].

Table 1 is a summary of these trials. Findings from the trials provided evidence that three main factors need to be addressed to achieve therapeutic targets and consequently prevent diabetes complications, namely, glycaemic, blood pressure (BP), and cholesterol control.

These factors have been incorporated into clinical practice guidelines (CPGs) on diabetes management from Australia, Europe, the UK, and the USA. In addition, CPGs from these countries recommend management of four other factors in diabetes management. These are medication management, lifestyle, education, and cardiovascular risk management. These seven diabetes factors are summarised in Figure 1 and discussed in the following paragraphs.

(1) Glycaemic Control. Diabetes guidelines recommend a target HbA1c (glycated haemoglobin) of 7% or less. Glycaemic control should aim to reduce HbA1c by 1% or more for patients whose HbA1c is more than 7%, as this can lead to significant reduction in microvascular complications, as was shown in the UKPDS trial [14]. The results from the landmark trials highlight several factors that need to be emphasised to prevent hypoglycaemia such as individualised glycaemic targets, educating patients on hypoglycemia awareness, self-monitoring of blood glucose levels, adjusting therapy, and changing to treatment that causes low risk of hypoglycemia [20–23].

(2) BP Control. Blood pressure less than 150/85 mmHg has demonstrated a reduction of microvascular and macrovascular complications [14]. The American Association of Clinical Endocrinologists and American College of Endocrinology CPGs on diabetes strongly suggests a target BP of less than 140/80–90 mmHg and recommended an update from the previous target of less than 130/80 mmHg [24]. However Australian guidelines recommend a target of 130/80 mmHg or lower and 125/75 mmHg for diabetes patients with proteinuria. Diabetes guidelines from Australia and the USA advise on the need to reduce sodium intake, increase potassium intake, and moderate alcohol consumption [25, 26]. These guidelines recommend prescribing, unless contraindicated, an Angiotensin Converting Enzyme Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARBs) as the preferred anti-hypertensive.

(3) Cholesterol Control. Guidelines from Australia, the UK, and USA stress the importance of use of a lipid-regulation medication such as a statin unless contraindicated, to reduce the risk of developing cardiovascular disease (CVD). Although there is increased risk of developing diabetes with statin use [27, 28], several meta-analysis on randomised trials show evidence of increased benefit of statins in terms of reduction in cardiovascular risk [29, 30]. The current safety advice from the USA Food and Drug Administration [31] and Australian Diabetes Guidelines [25] outlines the benefits of statins in preventing cardiovascular events over the increased glycaemia risks.

(4) Medication Management. Medication management requires that each patient’s medicine related needs be addressed to achieve target therapy outcomes. Pharmacists play a main role in medication management that involves identifying, resolving, and preventing medication-related problems [32]. Medication-related problems include inappropriate medication, incorrect or inappropriate dose, medicine interactions, adverse medicine reactions, and unnecessary medicine use [32].

Addressing patients’ medication-related problems facilitates achievement of treatment goals, as documented in a study of 2620 patients in the USA seen by pharmacists [33]. In a similar randomised prospective study of 107 Latino patients in the USA, followed up for two years, adherence to medication was the strongest predictor of reaching the target HbA1c [34]. Reducing hypoglycaemia episodes has also been associated with increased patient adherence and satisfaction with medication [35]. Several studies suggest that diabetes patients who are adherent in taking their medication reduce overall healthcare burden, even though this could mean an increase in medication costs [36–40].

(5) Lifestyle. Lifestyle factors such as diet intervention, exercise, smoking cessation, moderation of alcohol consumption,
Table 1: Summary of landmark diabetes trials.

| Trials     | Number of patients | Country (ethnicity) | Measure                                                                                                                                   | Outcome                                                                                                                                                                                                 |
|------------|--------------------|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| UKPDS      | 5102               | UK                  | (1) Intensive blood glucose control using metformin (to achieve HbA1c of 7%) versus conventional treatment. Patient followed up for median of 10.7 years (2) Intensive BP control (less than 150/85 mm Hg) (3) Efficacy of captopril or atenolol as antihypertensive and in controlling microvascular and macrovascular complications | (1) A reduction of 1% in HbA1c produced significant risk reduction (12%) for any diabetes related end point, 25% risk reduction for microvascular end points, 21% risk reduction for retinopathy and 33% risk reduction for albuminuria at 12 years, and 36% risk reduction for myocardial infarction (2) Significant effect on microvascular and macrovascular complications (3) Captopril and atenolol were equally effective antihypertensives in preventing microvascular and macrovascular complications |
| ADVANCE    | 10000              | 20 countries from Asia, Europe and North America, and Australia | Intensive lowering of blood glucose to HbA1c of 6.5% (gliclazide modified release) in addition to other therapies and BP (perindopril/indapamide combination) compared to UKPDS trial Median follow-up of 5 years | (1) Significant reduction in microvascular events (2) Severe and minor hypoglycemia more frequent in intensive arm (3) Hospitalisation more frequent in intensive arm                                                                                      |
| DCCT       | 1441               | USA and Canada      | Intensive therapy using three or more daily injections compared to conventional treatment (one or two insulin injections daily) among type 1 diabetes patients Mean follow-up of 6.5 years | (1) Intensive therapy reduced microalbuminuria: 39%, albuminuria: 54%, neuropathy: 60%, progression of retinopathy: 54%, and risk of retinopathy: 76% (2) Significant weight gain and diabetic ketoacidosis were reported more on intensive arm |
| ACCORD*    | (1) 10251          | USA and Canada      | (1) Intensive intervention to control hyperglycemia to less than HbA1c of 6.0% (2) Two targets for systolic levels in BP control (<120 versus <140) (3) Two regimens for plasma lipid levels. Fenofibrate and simvastatin versus simvastatin alone Mean follow-up of 3.4 years | (1) All cause mortality was significantly greater in the intensive arm (2) No reduction in macrovascular, mortality, or myocardial infarctions (3) No significant difference between the two arms |
| VADT       | 1791               | USA                 | Comparison between intensive and standard glucose control Mean follow-up of 5.6 years                                                      | (1) No significant difference in the rates of CVD events, death, or microvascular complications (2) More hypoglycemia in intensive group                                                                 |

Note: HbA1c (glycated hemoglobin) reflects average plasma glucose over the previous eight to 12 weeks. It is used as a marker for diabetes control [19].

*The ACCORD trial is divided into three different groups of patients, namely, the glycemic, lipid, and blood pressure groups.
and stress reduction contribute to achievement of glycaemic control [41, 42]. Intensive lifestyle interventions resulted in reduction of more than 5% weight loss and the loss was maintained at the fourth year in the Look AHEAD (Action for Health in Diabetes) study [43]. However, there is lack of intervention studies on other lifestyle issues such as foot care despite neuropathy being a major diabetes related complication. In 2005, there were about 10,000 hospital admissions for diabetes related foot ulcers in Australia resulting in lower limb amputations [44]. In the USA, the annual cost of diabetes foot ulcers is USD9-13 billion in addition to other diabetes costs [45].

(6) Education. A Malaysian study showed that one of the barriers to achieving good glycaemic control includes lack of understanding and knowledge of diabetes [46]. Educating diabetes patients on the management of their disease can significantly improve glycaemic [47–50], BP [49] and cholesterol control [48, 51], physical activity [49–51], dietary management [51], and medication understanding and adherence [49, 50].

(7) CVD Risk Prevention Strategies. Guidelines from Europe, the UK, and USA suggest aspirin therapy (75 mg–162 mg/day) as primary preventative strategy for increased CVD risk (10 year risk >10%) [24, 52, 53]. Cardiovascular disease risk can be estimated using risk prediction formulae such as the Framingham Risk Score and the UKPDS tool for diabetics. In Australia, the absolute CVD disease risk chart/calculator was developed using the Framingham risk equation [54]. USA guidelines recommend the use of the Framingham risk score. The Framingham risk score calculates percentage of CVD risk in 10 years using a patient’s information on age, family history of CVD, gender, total cholesterol level, HDL cholesterol level, whether he/she is a smoker, has diabetes, or has systolic BP level, and whether the patient is treated for high blood pressure [55].

3.2. Practice Guidelines and Multifactorial Intervention Studies. Diabetes practice guidelines aim to achieve a range of outcomes such as the reduction of microvascular and macrovascular complications, improvement in quality of life (QOL), and prevention of premature mortality. Reductions in several diabetes complications such as kidney failure and amputation were observed as more patients received guideline-adherent therapy [56]. However, there is evidence that guidelines are not always being followed in clinical practice. In a recent cross-sectional study, it was found that among 650 Malaysian outpatients, 32.1% of diabetes patients with hypertension were not on an antihypertensive such as an ACEI or ARB as per guideline recommendations, although these patients had no contraindications to these antihypertensives [57]. A similar study conducted among 430 Australian diabetes patients found evidence-based practice gaps especially in the prescribing of antihypertensive and lipid lowering medications [38].

The multifactorial interventions described in diabetes studies often do not encompass all seven factors addressed in the diabetes guidelines. Diabetes intervention studies led by healthcare professionals other than pharmacists indicated improvements in patients’ outcomes. However, there are inconsistencies in terms of the number of diabetes factors being addressed. While some studies emphasised self-management [59–62], others focused only on diet [41] or adherence [63]. Some studies evaluated motivational interviewing to promote behavioural changes and belief among diabetes patients which resulted in improved glycaemic control, adherence, and lifestyle changes [64–69]. Interventions which focused on four factors, namely, nutrition, blood glucose monitoring, medication taking, and lifestyle improved HbA1c and health related QOL [12, 70, 71]. These studies are summarised in Table 2. However, data on the number of patients seeking emergency treatment or who had adverse events in comparison to the usual care group were not always mentioned. Adverse events such as hypoglycemia are not
Pharmacist RCTs on medication management services do not provide evidence of the seven diabetes management factors that should be addressed in diabetes care as these factors were not consistently incorporated in patient interactions. Despite some studies showing more than 1% reduction of HbA1c, other studies which used the same intervention method showed less reduction or in some cases no difference. The range of HbA1c reduction in RCTs which focused on three or less of the seven factors were 0.8% to 1.0% [78, 83, 85, 90] while RCTs which incorporated four to five factors produced a reduction of 0.6% to 1.7% [47, 75, 80, 84, 86]. In studies which incorporated six to seven evidence-based factors, the HbA1c range improved by 0.5% to 1.8% [77, 79, 91].

It is uncertain if other variables are responsible for these outcomes, for instance, frequent face-to-face contact with patients. RCTs mentioned in Table 3 included frequent visits to the pharmacy every two to four weeks. These studies reported a HbA1c reduction which ranged between 0.5% and 1.7%. However these intervention groups may have had positive outcomes due to the regular contact with the pharmacist and not due to the nature of the intervention itself, as suggested by several studies [96, 97]. Therefore, patients who show less commitment to intervention programs may obtain less benefit. In addition, it is uncertain whether positive clinical outcomes continue after patients' face-to-face management ends.

The methods used to assess the patients' adherence towards medications were not clearly defined in some studies [78, 80, 82, 91] while other studies used varied assessment methods [79, 85–87]. These unstandardised methods could have contributed to the difference in patient outcomes. The assessment methods mentioned in these RCTs were the ASK-20 (Adherence starts with knowledge), prescription refill rates and self report, eight-item modified Morisky adherence assessment score, and the four-item Morisky adherence assessment score.

Lack of access to patients' medical notes and laboratory data may be a barrier for community pharmacists to provide quality medication management compared to pharmacists in hospital settings. In a study conducted in a GP clinic in Australia where pharmacists had access to patient's medical data the results showed increased medication adherence and improved patient satisfaction [98]. The importance of electronic health records in improving healthcare delivery has prompted the USA government to pass legislation to better integrate information technology into healthcare delivery in 2009 [99]. This enabled community pharmacists providing medication management services in the USA to access patients' medical records including information about medications, laboratory, and radiology results. Nevertheless, access to patients' medical notes remains limited to most community pharmacists in the USA [100]. In the UK, pharmacists were only given access to patients' summary care records in 2015 [101].

The majority of the interventions in the clinical trials were conducted by pharmacists with a minimum of three years of experience [75–82, 87]. Thus, there are uncertainties as to whether pharmacists with limited experience can produce similar clinical outcomes in practice settings. Another issue
Table 2: RCT studies led by healthcare professionals other than pharmacists grouped together according to type of interventions.

| Author, year                  | Study duration (months) | Country | Group size (usual care versus intervention) | Intervention strategy                                                                 | Results                                                                                                                                 |
|------------------------------|-------------------------|---------|--------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------|
| 1 Barrera et al., 2012 [69]  | 12                      | USA     | 138 142                                    | Culturally adapted diabetes intervention                                             Improvement in sources for dietary practice, problem solving, and physical activity                                    |
| 2 Farmer et al., 2012 [63]   | 5                       | UK      | 81 114                                     | Intervention on adherence, reinforcement of positive belief by nurse                  Percentage of adherence days in intervention group was 77.4 and usual care group was 69% |
| 3 Keogh et al., 2011 [65]    | 6                       | Ireland | 61 60                                      | Motivational interviewing                                                            Significant lower AIC levels (0.66%), significant improvements in beliefs about diabetes, psychological well-being, diet, exercise, and family support |
| 4 DePue et al., 2013 [59],   | 3–12                    | USA     | 34–134                                     | Community nurse intervention on self-management among diabetes patients               Significant reduction in HbA1c (0.5%–1.1%), understanding of diabetes self-management and performing diabetes self-management |
| Sinclair et al., 2013 [62],  |                         |         | 48–134                                     |                                                                                      |                                                                                                                                                 |
| Spencer et al., 2011 [60]    |                         |         |                                             |                                                                                      |                                                                                                                                                 |
| 5 Fischer et al., 2012 [67]  | 20                      | USA     | 381 381                                    | Nutrition, blood glucose monitoring, medication taking, and lifestyle through telephone | Significant improvement in HbA1c (0.8%–1.9%) and health related quality of life。                                                                 |
| 6 Williams et al. 2012 [71],| 6–12                    | USA     | 60–82 60–81                                | Psychological family intervention by healthcare professionals (nurse, pharmacist, physician, physiotherapist, dietitians, foot therapist, and social workers)  | Statistically significant improvements in HbA1c (1.35%), beliefs about diabetes, psychological well-being, diet, exercise, and family support |
| Quinn et al., 2011 [70]      |                         |         |                                             |                                                                                      |                                                                                                                                                 |
| 7 Kang et al., 2010 [66]     | 6                       | USA and Taiwan | 28 28                                     | Motivational interview using Miller and Rollnick’s (2002) approach. Intervention based on readiness to change | Improvement in self-management, self-efficacy, quality of life, and HbA1c (0.8%)                                                                 |
| 8 Chen et al., 2012 [64]     | 3                       | Taiwan  | 111 104                                    | Dietician in primary care                                                            Increased intake of vegetable and reduced intake of mean energy intake and HbA1c reduction of 0.7% |                                                                                                                                                 |
| 9 Wu et al., 2011 [61]       | 6                       | Taiwan  | 73 72                                      | Diet, exercise, BP, cholesterol, and glycaemic by endocrinologist in hospital         Reduction in macrovascular outcomes                                                                                                       |
| 10 Adachi et al., 2013 [41]  | 6                       | Japan   | 93 100                                     | Dietician in primary care                                                            Increased intake of vegetable and reduced intake of mean energy intake and HbA1c reduction of 0.7% |                                                                                                                                                 |
| 11 Weinger et al., 2011 [68] | 12                      | USA     | 96 & 92                                    | Diet, exercise, BP, cholesterol, and glycaemic by endocrinologist in hospital         Reduction in macrovascular outcomes                                                                                                       |
| 12 Yang et al., 2013 [12]    | 84 (7 years)            | China   | 68 70                                      | Diet, exercise, BP, cholesterol, and glycaemic by endocrinologist in hospital         Reduction in macrovascular outcomes                                                                                                       |
| Country                          | Duration (month) | Group size control versus intervention | Types of intervention                                                                 | Pharmacist participants                                                                                                      | Results                                                                                                                                 |
|--------------------------------|------------------|----------------------------------------|----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Pakistan [75]                  | 5                | 170                                    | Education and glycaemic control                                                        | Clinical pharmacists with minimum experience of 3 years in hospital setting                                                | Reduced body mass index and waist circumference, fasting blood glucose, and HbA1c (−1.01%). Increase in compliance, foot care, and SMBG |
| Nigeria and Hong Kong [76, 77] | 9–12             | 54–110                                | Education, lifestyle, and medication                                                    | Experienced hospital pharmacists                                                                                               | Improved quality of life significant reduction in CVD risk, HbA1c levels (1.57%), LDL and increased level of medication understanding |
| Brazil, Jordan, Belgium, and USA [78, 80, 82, 85–88] | 6–14             | 23–2303                               | Education and medication                                                               | Community pharmacists with minimum of 4 years of experience in diabetes management, board-certified pharmacotherapy specialists trained in diabetes | Significant reduction of HbA1c (0.5%–1.6%), FBG, total cholesterol, LDL cholesterol, TGL, BP and increase in HDL, improvement in self-management, and medication adherence |
| Iran [47]                      | 3                | 87                                    | Education                                                                              | Clinical pharmacists                                                                                                         | Improvements in FBG and HbA1c (1.7%)                                                                                     |
| USA [89]                       | 1                | 39                                    | Medication                                                                             | Clinical pharmacists with 2 years' experience                                                                                     | No significant difference in HbA1c, LDL, and BP                                                                             |
| USA [90]                       | 4                | 28                                    | Medication                                                                             | Clinical pharmacists                                                                                                         | Significant improvement in HbA1c (0.9%)                                                                                     |
| Malaysia and USA [79, 91]      | 9–12             | 42–201                                | Glycaemic control, BP, cholesterol, CVS risk, education, lifestyle, and medication       | Experienced clinical pharmacists trained as diabetes pharmacists                                                              | Significant improvement in HbA1c (1.7–1.8% reduction) and medication adherence levels                                        |
| Canada [81]                    | 12               | 93                                    | Medication, BP, cholesterol, and glycaemic                                             | Community pharmacists certified as diabetes educators with >5 years of practice experience                                     | Reduction in Framingham risk score, 1.2%                                                                                   |
| USA [84]                       | 3                | 24                                    | Education, lifestyle, and medication                                                    | Community pharmacists trained as diabetes pharmacists                                                                        | Reduction in HbA1c of 0.93% and mean body mass index                                                                       |
| USA [83]                       | 6                | 49                                    | Medication and behavioural interventions                                                | Community pharmacist certified as diabetes educators                                                                        | Significant improvements in exercise, foot care, HbA1c (0.41%), LDL, and BP                                              |
| Hawaii [92]                    | 7                | 62                                    | Medication and life coach counselling                                                   | Community pharmacists trained as diabetes pharmacists                                                                        | Significant effect on QOL and body mass index                                                                             |
| USA [93]                       | 6                | 24124                                 | Statin, ACE/ARB initiation, and total days of medication supply per month (adherence)  | Community pharmacists trained to deliver intervention                                                                      | Increased adherence and GP initiation of ACE/ARB and statin                                                               |
to consider is that although medication management services are accepted and being practised in many countries, pharmacists are still burdened with dispensing workloads, inadequate staff, and lack of time in carrying out services [102–104].

3.5. Long Term Outcomes. The duration of most diabetes intervention studies ranges between three to 14 months. The improvement in clinical outcomes could therefore be evaluated over a short-term period. As the main goal in diabetes management is prevention of diabetes related complications such as nephropathy and CVD, there is a need for a long term study incorporating multifactorial interventions. One RCT study of 150 patients followed up for seven years in China [12] found that diabetes nephropathy can be delayed and macrovascular disease can be prevented using tightly controlled BP, cholesterol, and glycaemic targets as defined in USA guidelines. However this study was carried out in a hospital rather than a community setting. As such it remains uncertain if these methods can be translated into primary healthcare settings.

3.6. Opportunities for Pharmacists in Preventing Diabetes Complications. In comparison to other healthcare professionals involved in diabetes care, pharmacists are better qualified in pharmacology of medicines and assessment of medication-related problems. In contrast to GPs, community pharmacists are easily accessible to the public with extended opening hours and without the need for prior appointments. They are therefore able to provide medication review services to most people with diabetes. Undoubtedly, pharmacists play an important role and therefore should take on a bigger role in providing diabetes care and further ease the burden off general practitioners.

In order to support pharmacists in delivering consistent quality diabetes care that addresses all the seven evidence-based factors, a structured intervention method may be beneficial. This could take the form of a tool with support materials, checklists, or structured interview questions. Currently there are no published studies on the effectiveness of a standardised and structured method for pharmacists delivering diabetes management.

4. Conclusion

This narrative review has highlighted the seven evidence-based factors involved to prevent or delay diabetes related complications and achieve target therapy outcomes. While our findings identified a lack of consistent and systematic multifactorial evidence-based approaches in delivering diabetes care, it did demonstrate pharmacists’ contributions towards improving clinical and QOL outcomes. This review has revealed some questions in need of further investigations, in particular, the impact of pharmacists’ interventions on all seven evidence-based factors and the effect of long term clinical and health related QOL outcomes.

Competing Interests

The authors declare that they have no competing interests.

References

[1] World Health Organization (WHO), Global Health Estimates: Deaths by Cause, Age, Sex and Country, 2000–2012, World Health Organization (WHO), Geneva, Switzerland, 2014.

[2] N. J. Morrisey, S.-L. Wang, L. K. Stevens et al., “Mortality and causes of death in the WHO multinational study of vascular disease in diabetes,” Diabetologia, vol. 44, supplement 2, pp. S14–S21, 2001.

[3] World Health Organization (WHO), Global Status Report on Noncommunicable Diseases 2010, World Health Organization (WHO), Geneva, Switzerland, 2011.

[4] WHO, Global Data on Visual Impairments 2010, World Health Organization, Geneva, Switzerland, 2012.

[5] P. Zhang, X. Zhang, J. Brown et al., “Global healthcare expenditure on diabetes for 2010 and 2030,” Diabetes Research and Clinical Practice, vol. 87, no. 3, pp. 293–301, 2010.

[6] Ministry of Health, Management of Type 2 Diabetes Mellitus, Ministry of Health, Putrajaya, Malaysia, 2009.

[7] S. J. Griffin, K. Borch-Johnsen, M. J. Davies et al., “Effect of early intensive multifactorial therapy on 5-year cardiovascular outcomes in individuals with type 2 diabetes detected by screening (ADDITION–Europe): a cluster-randomised trial,” The Lancet, vol. 378, no. 9786, pp. 156–167, 2011.

[8] O. Vaccaro, L. Franzini, R. Miccoli et al., “Feasibility and effectiveness in clinical practice of a multifactorial intervention for the reduction of cardiovascular risk in patients with type 2 diabetes: the 2-year interim analysis of the MIND.IT study: a cluster randomized trial,” Diabetes Care, vol. 36, no. 9, pp. 2566–2572, 2013.

[9] P. S. Koekkoek, C. Ruis, M. Van Den Donk et al., “Intensive multifactorial treatment and cognitive functioning in screen-detected type 2 diabetes—the ADDITION-Netherlands study: a cluster-randomized trial,” Journal of the Neurological Sciences, vol. 314, no. 1-2, pp. 71–77, 2012.

[10] J. M. Gamble, H. Holly, D. T. Eurch, K. K. Jindal, and P. A. Senior, “Patient-level evaluation of community-based, multifactorial intervention to prevent diabetic nephropathy in Northern Alberta, Canada,” Journal of Primary Care & Community Health, vol. 3, no. 2, pp. 111–119, 2012.

[11] S.-T. Tu, S.-J. Chang, J.-F. Chen et al., “Prevention of diabetic nephropathy by tight target control in an Asian population with type 2 diabetes mellitus: a 4-year prospective analysis,” Archives of Internal Medicine, vol. 170, no. 2, pp. 155–161, 2010.

[12] Y. Yang, J.-J. Yao, J.-L. Du et al., “Primary prevention of macroangiopathy in patients with short-duration type 2 diabetes by intensified multifactorial intervention: seven-year follow-up of diabetes complications in Chinese,” Diabetes Care, vol. 36, no. 4, pp. 978–984, 2013.

[13] S. D. Prato, J. LaSalle, S. Mattheai, and C. J. Bailey, “Tailoring treatment to the individual in type 2 diabetes practical guidance from the Global Partnership for Effective Diabetes Management,” International Journal of Clinical Practice, vol. 64, no. 3, pp. 295–304, 2010.

[14] P. King, I. Peacock, and R. Donnelly, “The UK Prospective Diabetes Study (UKPDS): clinical and therapeutic implications for type 2 diabetes,” British Journal of Clinical Pharmacology, vol. 48, no. 5, pp. 643–648, 1999.

[15] S. R. Heller, “A summary of the ADVANCE trial,” Diabetes Care, vol. 32, supplement 2, pp. S357–S361, 2009.
[16] W. Duckworth, C. Abraira, T. Moritz et al., “Glucose control and vascular complications in veterans with type 2 diabetes,” New England Journal of Medicine, vol. 360, no. 2, pp. 129–139, 2009.

[17] G. Worrall, “Results of the DCCT trial. Implications for managing our patient with diabetes,” Canadian Family Physician, vol. 40, pp. 1955–1963, 1994.

[18] J. B. Buse, “Action to control cardiovascular risk in diabetes (ACCORD) trial: design and methods,” The American Journal of Cardiology, vol. 99, no. 12, supplement, pp. S21–S33, 2007.

[19] D. M. Nathan, H. Tugeon, and S. Regan, “Relationship between glycated haemoglobin levels and mean glucose levels over time,” Diabetologia, vol. 50, no. 11, pp. 2239–2244, 2007.

[20] H. Rodbard, P. Jellinger, J. Davidson et al., “Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: an algorithm for glycemic control,” Endocrine Practice, vol. 15, no. 6, pp. 540–559, 2009.

[21] L. C. Hay, E. G. Wilmshurst, and G. Fulcher, “Unrecognized hypo- and hyperglycemia in well-controlled patients with type 2 diabetes mellitus: the results of continuous glucose monitoring,” Diabetes Technology and Therapeutics, vol. 5, no. 1, pp. 19–26, 2003.

[22] J. P. Jansen, “Self-monitoring of glucose in type 2 diabetes mellitus: a Bayesian meta-analysis of direct and indirect comparisons,” Current Medical Research and Opinion, vol. 22, no. 4, pp. 671–681, 2006.

[23] D. C. Klonoff, R. M. Bergensdal, L. Blonde et al., “Consensus report of the coalition for clinical research—self-monitoring of blood glucose,” Journal of Diabetes Science and Technology, vol. 2, no. 6, pp. 1030–1035, 2008.

[24] American Association of Clinical Endocrinologists and American College of Endocrinology, “Clinical practice guidelines for developing a diabetes mellitus comprehensive care plan,” Endocrine Practice, vol. 21, no. 1, pp. 1–87, 2015.

[25] Diabetes Management in General Practice, Australian Guidelines for Type 2 Diabetes, 2014-2015.

[26] American Diabetes Association, “Standards of medical care in diabetes,” Diabetes Care, vol. 37, pp. 1–67, 2015.

[27] N. Sattar, D. Preiss, H. M. Murray et al., “Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials,” The Lancet, vol. 375, no. 9716, pp. 735–742, 2010.

[28] S. M. Liew, P. Y. Lee, N. S. Hanafi et al., “Statins use is associated with poorer glycaemic control in a cohort of hypertensive patients with diabetes and without diabetes,” Diabetology & Metabolic Syndrome, vol. 6, article 53, 5 pages, 2014.

[29] P. M. Ridker, A. Pradhan, J. G. MacFadyen, P. Libby, and R. J. Glynn, “Cardiovascular benefits and diabetes risks of statin therapy in primary prevention: an analysis from the JUPITER trial,” The Lancet, vol. 380, no. 9841, pp. 565–571, 2012.

[30] S. N. Rajpathak, D. J. Kumbhani, J. Crandall, N. Barzilai, M. Alderman, and P. M. Ridker, “Statin therapy and risk of developing type 2 diabetes: a meta-analysis,” Diabetes Care, vol. 32, no. 10, pp. 1924–1929, 2009.

[31] U.S. Food and Drug Administration, FDA Drug Safety Communication: Important Safety Label Changes to Cholesterol-Lowering Statin Drugs, 2012, http://www.fda.gov/Drugs/DrugSafety/ucm293101.htm.

[32] C. D. Hepler and L. M. Strand, “Opportunities and responsibilities in pharmaceutical care,” American Journal of Hospital Pharmacy, vol. 47, no. 3, pp. 533–543, 1990.

[33] L. M. Strand, R. J. Cipolle, and M. J. Frakes, Medication Adherence: Improved Results with Comprehensive Medication Therapy Management Services, Medication Management Systems, 2007.

[34] V. Ruelas, G. M. Roybal, Y. Lu, D. Goldman, and A. Peters, “Clinical and behavioral correlates of achieving and maintaining glycemic targets in an underserved population with type 2 diabetes,” Diabetes Care, vol. 32, no. 1, pp. 54–56, 2009.

[35] F. Á. Guisasola, S. T. Povedano, G. Krishnarajah, R. Lyu, P. Mavros, and D. Yin, “Hypoglycaemic symptoms, treatment satisfaction, adherence and their associations with glycaemic goal in patients with type 2 diabetes mellitus: findings from the Real-Life Effectiveness and Care Patterns of Diabetes Management (RECAP-DM) Study,” Diabetes, Obesity and Metabolism, vol. 10, no. 1, pp. 25–32, 2008.

[36] A. K. Jha, R. E. Aubert, J. Yao, J. R. Teagarden, and R. S. Epstein, “Greater adherence to diabetes drugs is linked to less hospital use and could save nearly $5 billion annually,” Health Affairs, vol. 31, no. 8, pp. 1836–1846, 2012.

[37] W. C. Lee, S. Balu, D. Cobden, A. V. Joshi, and C. L. Pashos, “Prevalence and economic consequences of medication adherence in diabetes: a systematic literature review,” Managed Care Interface, vol. 19, no. 7, pp. 31–41, 2006.

[38] L. Breitscheidel, S. Stamenitis, F.-W. Dippel, and O. Schöffski, “Economic impact of compliance to treatment with antidiabetes medication in type 2 diabetes mellitus: a review paper,” Journal of Medical Economics, vol. 13, no. 1, pp. 8–15, 2010.

[39] K. L. Hepke, M. T. Martus, and D. A. Share, “Costs and utilization associated with pharmaceutical adherence in a diabetic population,” The American Journal of Managed Care, vol. 10, no. 2, pp. 144–151, 2004.

[40] M. C. Sokol, K. A. McGuigan, R. R. Verbrugge, and R. S. Epstein, “Impact of medication adherence on hospitalization risk and healthcare cost,” Medical Care, vol. 43, no. 6, pp. 521–530, 2005.

[41] M. Adachi, K. Yamaoka, M. Watanabe et al., “Effects of lifestyle education program for type 2 diabetes patients in clinics: a cluster randomized controlled trial,” BMC Public Health, vol. 13, article 467, 2013.

[42] R. H. Bishay, A. Omari, J. Zang et al., “Divide and conquer: the multidisciplinary approach to achieving significant long-term weight loss and improved glycemic control in obese patients with type 2 diabetes,” Clinical Diabetes, vol. 31, no. 1, pp. 14–20, 2013.

[43] T. A. Wadden, R. H. Neiberg, R. R. Wing et al., “Four-year weight losses in the look AHEAD study: factors associated with long-term success,” Obesity, vol. 19, no. 10, pp. 1987–1998, 2011.

[44] Australian Institute of Health and Welfare, Diabetest: Australian Facts, Australian Institute of Health and Welfare, Canberra, Australia, 2008.

[45] J. B. Rice, U. Desai, A. K. G. Cummings, H. G. Birnbaum, M. Skornicki, and N. B. Parsons, “Burden of diabetic foot ulcers for medicare and private insurers,” Diabetes Care, vol. 37, no. 3, pp. 651–658, 2014.

[46] S. M. Ali, “Barriers to optimal control of type 2 diabetes in Malaysian Malay patients,” Global Journal of Health Science, vol. 1, no. 2, pp. 106–118, 2009.

[47] S. Farsaei, A. M. Sabzghabaee, A. H. Zargarzadeh, and M. Amini, "Effect of pharmacist-led patient education on glycemic control of type 2 diabetics: a randomized controlled trial," Journal of Research in Medical Sciences, vol. 16, no. 1, pp. 43–49, 2011.
[48] A. Philis-Tsimikas, A. Fortmann, L. Lleva-Ocana et al., “Peer-led diabetes education programs in high-risk Mexican Americans improve glycemic control compared with standard approaches: a Project Dulce promotora randomized trial,” Diabetes Care, vol. 34, no. 9, pp. 1926–1931, 2011.

[49] E. Beyazit and M. Mollaoglu, “Investigation of effect on glycosylated hemoglobin, blood pressure, and body mass index of diabetes intensive education program in patients with Type 2 diabetes mellitus,” American Journal of Men’s Health, vol. 5, no. 4, pp. 351–357, 2011.

[50] M. Y. Tan, J. M. Magarey, S. S. Chee, L. F. Lee, and M. H. Tan, “A brief structured education programme enhances self-care practices and improves glycaemic control in Malaysians with poorly controlled diabetes,” Health Education Research, vol. 26, no. 5, pp. 896–907, 2011.

[51] M. Moriyama, M. Nakano, Y. Kuroe, K. Nin, M. Niitani, and T. Nakaya, “Efficacy of a self-management education program for people with type 2 diabetes: results of a 12 month trial,” Japan Journal of Nursing Science, vol. 6, no. 1, pp. 51–63, 2009.

[52] International Diabetes Federation, Global Guideline for Type 2 Diabetes, vol. 2, International Diabetes Federation, Brussels, Belgium, 2012.

[53] National Institute for Health and Care Excellence (NICE), The Management of Type 2 Diabetes, National Institute for Health and Care Excellence (NICE), London, UK, 2014.

[54] National Vascular Disease Prevention Alliance, Guidelines for the Management of Absolute Cardiovascular Disease Risk, NVDPA, 2012.

[55] R. B. D’Agostino Sr., R. S. Vasan, M. J. Pencina et al., “General cardiovascular risk profile for use in primary care: the Framingham Heart study,” 2008, http://www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php.

[56] P. J. O’Connor, N. L. Bodkin, J. Fradkin et al., “Diabetes performance measures: current status and future directions,” Diabetes Care, vol. 34, no. 7, pp. 1651–1659, 2011.

[57] N. Ahmad, Y. Hassan, B. Tangiisuran et al., “Guidelines adherence and hypertension control at a tertiary hospital in Malaysia,” Journal of Evaluation in Clinical Practice, vol. 19, no. 5, pp. 798–804, 2013.

[58] I. Krass, R. Hebing, B. Mitchell et al., “Diabetes management in an Australian primary care population,” Journal of Clinical Pharmacy and Therapeutics, vol. 36, no. 6, pp. 664–672, 2011.

[59] J. D. DePue, S. Dunsiger, A. D. Seiden et al., “Nurse-community health worker team improves diabetes care in American Samoa: results of a randomized controlled trial,” Diabetes Care, vol. 36, no. 7, pp. 1947–1953, 2013.

[60] M. S. Spencer, A.-M. Rosland, E. C. Kieffer et al., “Effectiveness of a community health worker intervention among African American and Latino adults with type 2 diabetes: a randomized controlled trial,” American Journal of Public Health, vol. 101, no. 12, pp. 2253–2260, 2011.

[61] S.-F. V. Wu, M.-C. Lee, S.-Y. Liang, Y.-Y. Lu, T.-J. Wang, and H.-H. Tung, “Effectiveness of a self-efficacy program for persons with diabetes: a randomized controlled trial,” Nursing and Health Sciences, vol. 13, no. 3, pp. 335–343, 2011.

[62] K. A. Sinclair, E. K. Makahi, C. Shea-Solatorio, S. R. Yoshimura, C. K. M. Townsend, and J. K. Kaholokula, “Outcomes from a diabetes self-management intervention for native hawaiians and pacific people: partners in care,” Annals of Behavioral Medicine, vol. 45, no. 1, pp. 24–32, 2013.

[63] A. Farmer, W. Hardeman, D. Hughes et al., “An explanatory randomised controlled trial of a nurse-led, consultation-based intervention to support patients with adherence to taking glucose lowering medication for type 2 diabetes,” BMC Family Practice, vol. 13, article 30, 2012.

[64] S. M. Chen, D. Creedy, H.-S. Lin, and J. Wollin, “Effects of motivational interviewing intervention on self-management, psychological and glycemic outcomes in type 2 diabetes: a randomized controlled trial,” International Journal of Nursing Studies, vol. 49, no. 6, pp. 637–644, 2012.

[65] K. M. P. Keogh, S. M. M. D. Smith, P. White et al., “Psychological family intervention for poorly controlled type 2 diabetes,” The American Journal of Managed Care, vol. 17, no. 2, pp. 105–113, 2011.

[66] C.-M. Kang, S.-C. Chang, P.-L. Chen et al., “Comparison of family partnership intervention care vs. conventional care in adult patients with poorly controlled type 2 diabetes in a community hospital: a randomized controlled trial,” International Journal of Nursing Studies, vol. 47, no. 11, pp. 1363–1373, 2010.

[67] H. H. Fischer, S. L. Eisert, R. M. Everhart et al., “Nurse-run, telephone-based outreach to improve lipids in people with diabetes,” The American Journal of Managed Care, vol. 18, no. 2, pp. 77–84, 2012.

[68] K. Weinger, E. A. Beverly, Y. Lee, L. Sittinok, O. P. Ganda, and A. E. Caballero, “The effect of a structured behavioral intervention on poorly controlled diabetes: a randomized controlled trial,” Archives of Internal Medicine, vol. 171, no. 22, pp. 1990–1999, 2011.

[69] M. Barrera Jr., D. Toobert, L. Stryczek, and D. Osuna, “Effects of acculturation on a culturally adapted diabetes intervention for latinas,” Health Psychology, vol. 31, no. 1, pp. 51–54, 2012.

[70] C. C. Quinn, M. D. Shadrall, M. L. Terrin, E. A. Barr, S. H. Ballew, and A. L. Gruber-Baldini, “Cluster-randomized trial of a mobile phone personalized behavioral intervention for blood glucose control,” Diabetes Care, vol. 34, no. 9, pp. 1934–1942, 2011.

[71] E. D. Williams, D. Bird, A. W. Forbes et al., “Randomised controlled trial of an automated, interactive telephone intervention (TLC Diabetes) to improve type 2 diabetes management: baseline findings and six-month outcomes,” BMC Public Health, vol. 12, no. 1, article 602, 2012.

[72] J. Belsey and G. Krishnarajah, “Glycaemic control and adverse events in patients with type 2 diabetes treated with metformin + sulphonylurea: a meta-analysis,” Diabetes, Obesity and Metabolism, vol. 10, supplement 1, pp. 1–7, 2008.

[73] S. E. Inzucchi, R. M. Bergenstal, J. B. Buse et al., “Management of hyperglycemia in type 2 diabetes: a patient-centred approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD),” Diabetologia, vol. 35, no. 6, 2012.

[74] S. Pande, J. E. Hiller, N. Nkansah, and L. Bero, “The effect of pharmacist-provided non-dispensing services on patient outcomes, health service utilisation and costs in low- and middle-income countries,” Cochrane Database of Systematic Reviews, no. 2, Article ID CD010398, pp. 1–71, 2013.

[75] A. M. Samtia, M. F. Rasool, N. M. Ranjha, F. Usman, and I. Javed, “A multifactorial intervention to enhance adherence to medications and disease-related knowledge in type 2 diabetic patients in Southern Punjab, Pakistan,” Tropical Journal of Pharmaceutical Research, vol. 12, no. 5, pp. 851–856, 2013.

[76] M. O. Adibe, C. V. Ukwe, and C. N. Aguwa, “The impact of pharmaceutical care intervention on the quality of life of nigerian patients receiving treatment for type 2 diabetes,” Value in Health Regional Issues, vol. 2, no. 2, pp. 240–247, 2013.
