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Prevention of Type 2 Diabetes and Its Complications in Developing Countries: A Review

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Abstract
Background Type 2 diabetes mellitus (T2DM) is a significant global public health problem affecting more than 285 million people worldwide. Over 70% of those with T2DM live in developing countries, and this proportion is increasing annually. Evidence suggests that lifestyle and other nonpharmacological interventions can delay and even prevent the development of T2DM and its complications; however, to date, programs that have been specifically adapted to the needs and circumstances of developing countries have not been well developed or evaluated.
Purpose The purpose of this article is to review published studies that evaluate lifestyle and other non-pharmacological interventions aimed at preventing T2DM and its complications in developing countries.
Methods We undertook an electronic search of MEDLINE, PubMed, and EMBASE with the English language restriction and published until 30 September 2009.
Results Nine relevant publications from seven studies were identified. The reported interventions predominantly used counseling and educational methods to improve diet and physical activity levels. Each intervention was found to be effective in reducing the risk of developing T2DM in people with impaired glucose tolerance, and improving glycemic control in people with T2DM.
Conclusions The current evidence concerning the prevention of T2DM and its complications in developing countries has shown reasonably consistent and positive results; however, the small number of studies creates some significant limitations. More research is needed to evaluate the benefits of low-cost screening tools, as well as the efficacy, cost-effectiveness, and sustainability of culturally appropriate interventions in such countries.

Keywords Type 2 diabetes · Complications · Prevention · Developing countries

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Introduction

Type 2 diabetes mellitus (T2DM) is a significant global public health problem [1, 2]. The International Diabetes Federation recently reported that the number of people with diabetes will escalate from 285 million in 2010 to 438 million by 2,030, with more than 70% of cases already from developing countries [2]. Despite a number of significant global and regional initiatives being undertaken to prevent diabetes and diabetes-related complications [3–7], seven out of the top ten countries with the greatest number of people living with diabetes are low- or middle-income countries. These include China, India, Russia,

Brazil, Pakistan, Indonesia, and Bangladesh [8–11], with China now having the largest number of individuals with diabetes (92.4 million) in the world [8].

Each year, almost four million deaths are directly attributable to diabetes, constituting 6.8% of the total global (all-age and all-cause) mortality [12, 13]. Diabetes is the fourth leading cause of disease-related death and almost 80% of diabetes-related deaths occur in developing countries. It has been projected that diabetes-related deaths will increase by 50% in the next 10 years if no urgent action is taken [14]. T2DM poses a significant economic burden to individuals, families, health systems, and nations, particularly in resource-poor countries [14, 15]. Despite this, over 80% of the world's diabetes care-related expenditure occurs in developed countries [16]. Given the rapidly escalating financial and societal costs associated with diabetes care in developing countries, where resources to address the disease are severely limited, there is an urgent need for the development, implementation, and evaluation of programs to prevent T2DM and its complications [4].

Since the concept of T2DM prevention on a mass scale was first proposed early in the twentieth century [17], and was more recently emphasized by the World Health Organization (WHO) [18] and other international organizations, a number of very well-conducted intervention trials have now evaluated the prevention of diabetes and its complications in developed countries. These trials include the Malmo Feasibility Study in Sweden [19], the Finnish Diabetes Prevention Study (DPS) [20–22] and the US Diabetes Prevention Program (DPP) [23]; all of which have demonstrated comparable efficacy, by reducing the risk of developing T2DM by up to 63% in lifestyle intervention groups compared with controls. A recent systematic review and meta-analysis by Gillies et al. confirmed these findings, reporting that non-pharmacological interventions were effective in reducing the risk of T2DM in people with impaired glucose tolerance (IGT) by up to 60% compared with control groups [24].

Trials focused on the prevention of T2DM complications conducted in developed countries have not directly examined the effects of non-pharmacological interventions on complication incidence. However, studies have demonstrated that non-pharmacological interventions are effective in reducing glycemic levels in people with T2DM [19, 20] and work from the UK and Japan indicates that optimal control of glycemic levels in people with newly diagnosed T2DM can reduce the development of complications [25, 26].

Despite the evidence concerning prevention of T2DM and its complications in developed countries, the translation of these programs to developing countries, where resources are limited to address the problem, still presents a very significant challenge. Therefore, it is important to develop and evaluate culturally appropriate interventions in developing countries [3, 27]. This paper reviews the study characteristics, efficacy, and cost-effectiveness of those non-pharmacological interventions aimed at preventing T2DM and its related complications in developing countries.

Methods

Search Strategy

We undertook an electronic search of MEDLINE, PubMed, and EMBASE with the search terms "Diabetes Mellitus Type 2," "Glucose Intolerance," "Primary Prevention," "Secondary Prevention," "Diabetes Complications," and "Lifestyle Intervention." These search terms were combined with the search term "Developing Countries" to identify relevant articles. In addition, we performed a search of policy and program documents developed by different national and international organizations. Furthermore, all relevant reference lists from the main papers were hand searched for additional papers of interest. The article search, inclusion and selection process is shown in Fig. 1.

Inclusion Criteria

The search was restricted to English language with papers published until 30 September 2009. We applied the World Bank 2008 classification criteria [28] to identify developing countries. Those studies/trials that employed lifestyle or non-pharmacological interventions conducted in developing countries with a glucose measure as a primary outcome were included. There was no restriction on sample size or duration of the intervention.

Information Assessment

Two independent reviewers examined each full-text paper for eligibility and extracted and tabulated all relevant information. Any differences were resolved by discussion and consensus with other authors. Inclusion or exclusion of the studies was determined by consensus between authors. The information assessment and synthesis were primarily based on the main findings of the publications.

Results

We initially identified 247 research articles by Medline, PubMed, and EMBASE searches. After a review of the titles and abstracts, 84 papers closely matched our inclusion criteria. The full papers were examined, however, 75 papers did not meet our inclusion criteria (i.e., evaluation of non-pharmacological interventions aimed at prevention of the development of T2DM or its associated complications, the

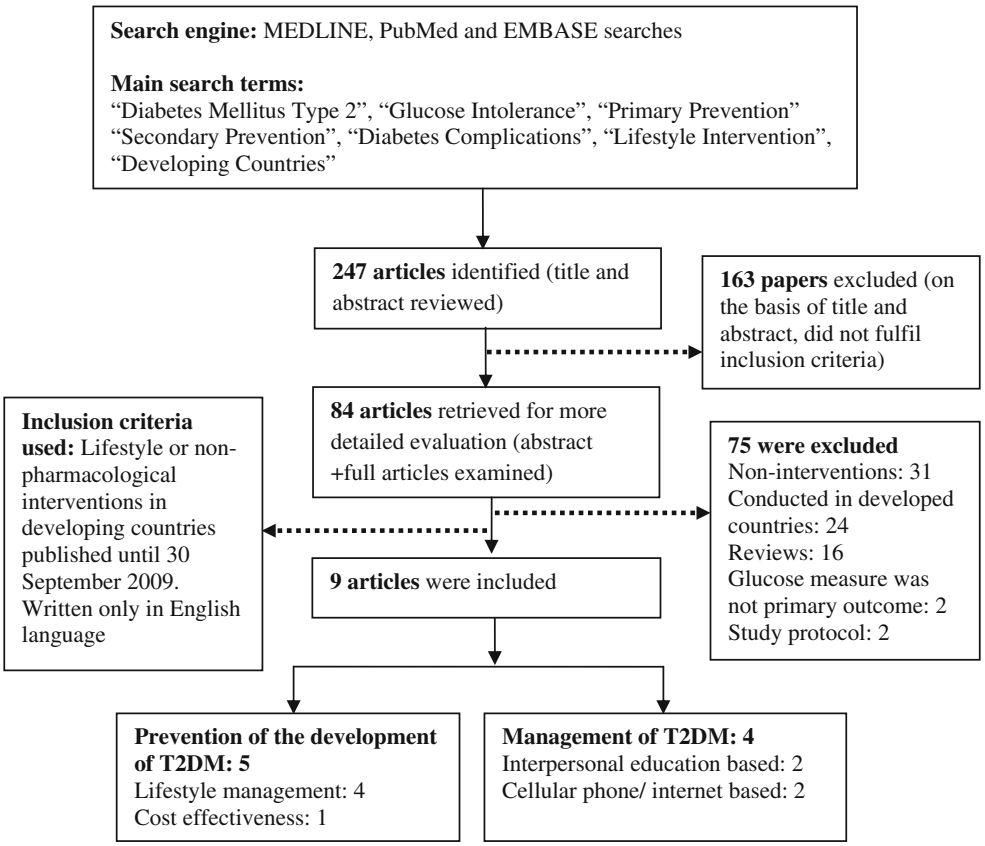

Fig. 1 Flow chart showing articles search, inclusion criteria, and selection process

inclusion of blood glucose or glycosylated hemoglobin (HbA1c) as a primary outcome and the study being undertaken in a developing country), so they were subsequently excluded. Consequently, nine publications from seven studies were included in this review. A summary of each intervention and the findings are presented in this section. The main findings of the studies are divided into four subsections: (1) sample characteristics, (2) intervention or program characteristics, (3) effectiveness of the programs and (4) cost-effectiveness. The key sample characteristics and the findings of the study are summarized in Tables 1 and 2 and intervention characteristics in Tables 3 and 4.

Sample Characteristics

Prevention of the Development of T2DM Five relevant publications from three studies assessing effectiveness of the lifestyle interventions for prevention of the development of T2DM were identified. There was significant heterogeneity in the sample characteristics, such as sample size, age, inclusion criteria, type of sample, and length of follow-up, across the studies (Table 1). The Da-Qing study, a randomized controlled trial (RCT) designed to prevent diabetes progression in people with IGT in an urban area in China, recruited 283 men and 247 women over 25 years of age (mean age, 45±9.1 years) [29, 30]. The active intervention of this program lasted 6 years. The Indian Diabetes Prevention Program (IDPP-1) was a 3-year prospective RCT that recruited an urban population aged 35–55 years old with persistent IGT [31]. The sample of 421 men and 110 women were leaner and yet more insulin resistant than the subjects included in the Finnish DPS [20–22] and US DPP [23] studies. A community-based diabetes prevention study by Balagopal et al., undertaken in rural India, recruited 703 villagers aged 10–92 years old [32]. The mean age of participants was 35.8±17.0 years and follow-up lasted 7 months.

Blood Glucose Measurements and Criteria for Participant Selection in Studies to Prevent the Development of T2DM The Da-Qing and IDPP-1 studies used oral glucose tolerance tests to assess blood glucose levels. The Da-Qing study [29] implemented the WHO 1985 criteria [33] to survey and identify people with normoglycemia, impaired fasting glucose (IFG), IGT, and T2DM. The IDPP-1 [31] used the WHO 1999 criteria [34] and the community-based program in India [32] used a glucometer to measure blood glucose and the American Diabetes Association (ADA) criteria 2005 to classify IGT [35]. The WHO 1999 and the ADA 2005 use the same criteria for classifying people with diabetes, IGT and IFG, however, the WHO 1985 classification included higher cut-off values for fasting and 2-h blood glucose levels compared with the later WHO 1999 and ADA 2005 criteria.

Table 1 Summary of studies for prevention of development of T2DM in developing countries

Reference	Objective	Study design	Sample characteristics		Duration	Main findings	
			n	Mean age (years)			
Da-Qing, 1997 [29, 30]	Determine whether diet and exercise intervention in those with IGT would reduce incidence of T2DM and related complications (e.g., cardiovascular/ renal/retinal disease and excess mortality)	RCT	577 adults aged >25 years with IGT	45±9.1	6 years	Diabetes incidence after 6 years of intervention	67.7% in control, 43.8% in diet, 41.1% in exercise, and 46.0% in diet+exercise groups
						Relative risk reduction for T2DM:	31% with diet, 46% with exercise, and 42% with diet+ exercise groups compared with control group
						Diabetes incidence at 20-year follow-up	Cumulative incidence: 80% in intervention groups compared with 93% in control group
							Intervention group participants spent an average of 3.6 fewer years with DM compared with control group
							No significant difference in rate of first CVD events/CVD mortality/all-cause mortality
IDPP-1, 2006 [31, 40]	Determine whether incidence of T2DM could be modified by lifestyle interventions	RCT	531 adults aged 35–55 years with IGT	45.9±5.7	3 years	Diabetes incidence after 3 years of intervention	55% in control, 39.3% in lifestyle management (LSM), 40.5% in metformin (MET), and 39.5% in LSM+MET groups
						Relative risk reduction for T2DM	28.5% with LSM, 26.4% with MET, and 28.2% with LSM+MET groups compared with control group
						Cost-effectiveness	Direct medical cost to identify 1 subject with IGT: $117
							Direct medical cost of interventions over a 3-year period: $61 per subject in control group, $225 in LSM group, $220 in metformin group, and $270 in LSM+metformin group
							Cost to prevent 1 case of diabetes: $1,052 with LSM, $1,095 with metformin, and $1,359 with LSM+metformin
Community based, India 2008 [32]	Evaluate community-based non-pharmacological lifestyle intervention to prevent/reduce risk of developing diabetes/ complications	Community based	703 residents aged 10–92 years	35.8±17	7 months	Crude prevalence of diabetes and pre-diabetes	In adults: 5.1% diabetes and 13.5% pre-diabetes
							In youths aged 10–17 years: 5.1% pre-diabetes
						Fasting blood glucose level reductions	11% in pre-diabetic adult, 17% in pre-diabetic youth, and 25% in T2DM adults
							Improved obesity parameters and dietary intake

Table 2 Summary of studies for prevention of diabetes complications in developing countries

Reference	Objective	Study design	Sample characteristics		Duration (months)	Main findings	
			n	Mean age (years)			
Sun et al. 2008 [36]	Evaluate structured and integrated intervention program on diabetes management	RCT	150 with T2DM	51±1.0	6	Mean change in HbA1c	Intervention group: −0.6% and −0.8% in 12 and 24 weeks, respectively Control group: +0.1% and +0.1% in 12 and 24 weeks, respectively
						Blood glucose	Intervention group: −1.3 and −0.9 mmol/l in 12 and 24 weeks, respectively Control group: −1.0 and +0.2 mmol/l in 12 and 24 weeks, respectively
Wattana et al. 2007 [37]	Determine effects of diabetes self-management program on glycemic control, CHD risk and Quality of Life	RCT	147 adults with T2DM	Int, 58.40±10.05; control, 55.14±10.22	6	Mean change in HbA1c	Intervention group: −0.68% Control group: −0.07%
						CHD risk factors	Intervention group: −4.83% Control group: −1.54%
						Quality of life (out of 100)	Intervention group: +9.82 Control group: −0.67
Kim, 2007 [38]	Investigate effectiveness of educational intervention using cellular phone and Internet on plasma glucose levels	RCT	51 patients with T2DM	Int, 46.8±8.8; control, 47.5±9.1	3	Mean change in HbA1c	Intervention group: −1.15% Control group: +0.07%
						Mean change in FPG	Intervention group: −0.4 mmol/l Control group: +0.3 mmol/l
						Mean change in 2-h glucose level	Intervention group: −4.7 mmol/l Control group: +0.8 mmol/l
Kim and Song, 2008 [39]	Evaluate nurse-led intervention using short message service (via cellular phones) and Internet to improve levels of plasma glucose and serum lipids	RCT	34 obese patients with T2DM	Int, 45.5±9.1; control, 48.5±8.0	6	Mean change in HbA1c	Intervention group: −1.22% (3 months) and −1.09% (6 months). Significant Control group: −0.05% (3 months) and no change (6 months). Not significant
						Mean change in fasting plasma glucose	Intervention group: −10.8 (3 months) and −4.6 mg/dl (6 months). Significant Control group: +4.2 mg/dl (3 months) and +6.0 mg/dl (6 months). Not significant

Int intervention

Table 3 Summary of study intervention characteristics for prevention of development of T2DM

Study/Ref	Intervention characteristics	Intensity, duration, and regularity
Da-Qing, China [29, 30]	Intervention groups—received individual/small-group counseling, delivered by trained physicians, nurses, and technicians	1 individual counseling session
	Diet group—those with body mass index (BMI) of ≥25 kg/m^2 advised to lose weight, through goal setting on healthy diets. Those with BMI of <25 kg/m^2 encouraged to eat healthy diets with prescribed proportions of carbohydrates, fat, and protein	Weekly small-group counseling sessions for 1 month, monthly for 3 months and then once every 3 months
	Exercise group—advised to increase amount of leisure time physical exercise	
	Diet+exercise group—received both interventions as above	
	Control group—received usual care (general information on diabetes/IGT, brochures containing information on improving diet/physical activity)	
IDPP-1, India [31, 40]	Intervention groups—received individual counseling, followed up by telephone	1 individual counseling at the beginning of the study
	Lifestyle group—those performing "moderate" activity (physical labor/walk or cycle for >30 min/day/perform exercise regularly) advised to continue routine activities. Those performing sedentary/light physical activity advised to walk briskly for ≥30 min/day	Telephonic contact after 2 weeks or by letter
	Advice on diet modification given, including reduction in total calories and refined carbohydrates/fats, avoidance of sugar, and inclusion of fiber-rich foods	Monthly telephonic contacts personal sessions at 6 monthly intervals
	Metformin group—received metformin tablets for 3 months and provided diaries to record daily intake of tablets	
	Lifestyle+metformin group—received both interventions as above	
	Control group—received advice on standard healthcare	
Community based, India [32]	Individual face-to-face culturally sensitive (Tamil language) educational sessions on dietary modification (increasing fiber, reducing fat, portion control), increasing physical activity, and relaxation breathing techniques conducted	10 face-to-face individual education sessions
		Group events for reinforcement
	Group events, such as cooking/physical activity demonstrations, organized as reinforcement	Additional counseling sessions for individuals with impaired FBG

Prevention of Diabetes Complications Four relevant studies assessing effectiveness of lifestyle interventions for the prevention of diabetes complications were identified. The sample characteristics of the intervention studies preventing the development of complications in people with T2DM were heterogeneous (Table 2). One RCT conducted in China aimed at improving glycemic control among overweight people with diabetes recruited 150 individuals, with 100 in the intervention arm and 50 in the control group [36]. With a mean age of 51±1.0 years, this sample was followed up for 6 months. A hospital-based RCT in Thailand recruited 147 adults over 35 years of age [37]. This follow-up lasted 6 months. Of the two RCTs conducted in Korea, one recruited 51 patients [38] and the other 34 patients with T2DM [39], each with a mean age of 47 years. The first sample was followed up over 3 months and the second over 6 months.

Intervention Characteristics

Prevention of the Development of T2DM The three studies undertaken to prevent the development of T2DM in developing countries included a range of interventions (Table 3). The Da-Qing study comprised three lifestyle intervention groups (diet, exercise, and diet+exercise), with one control group [29]. Overweight participants were advised to improve healthy food habits and increase physical activity through individual and small-group sessions, until they had reached a target body mass index of 23 kg/m^2. The IDPP-1 included a lifestyle intervention, medication (metformin tablets) group, combined lifestyle and metformin group and control group [31]. Participants in the lifestyle intervention group received individual advice regarding diet modification and exercise promotion. The intervention by Balagopal et al. comprised an educational intervention for the rural community; however, no control condition was included [32]. Culturally sensitive and linguistically appropriate sessions on dietary modification, physical activity, and simple relaxation breathing techniques constituted the main components of this intervention.

Prevention of Diabetes Complications There was a significant variation in the interventions employed across the four studies aimed at preventing T2DM complications in developing countries (Table 4). Two studies included an educational intervention [36, 37] and two involved telemedicine-based nurse-led educational intervention [38, 39]; all with

Table 4 Summary of study intervention characteristics for prevention of complications

Study/Ref	Intervention characteristics	Intensity, duration, and regularity
Sun et al., China [36]	Intervention group—received monthly group sessions on diabetes management/ lifestyle modification delivered by an experienced nutritionist	Weekly individual consultation sessions (30 min each) for 6 months
	Participants received weekly consultation sessions on diet and medical evaluations including assessment of adverse events, review of blood glucose measurements and adjustment of medications Participants were provided with blood glucose monitors	Additional monthly group sessions
	Control group—received monthly group sessions providing diabetes education	
Wattana et al., Thailand [37]	Intervention group—participated in small-group diabetes education classes (120 min) and discussions (90 min) Received individual home visits from researcher (45 min) and patient education manual	1 small-group diabetes education class, followed by 4 small-group discussions
	Participants were taught how to make lifestyle changes, monitor symptoms, record, and interpret their blood glucose levels, blood pressure, and blood lipid levels	2 individual home visit sessions in 6 months
	Control group—received usual nursing care, health education during waiting time at hospital and diabetes education class at the end of the study	
Kim, Korea [38]	Intervention group—received education and reinforcement on diet, exercise, medication adjustment, and frequent self-monitoring of blood glucose levels led by nurse via mobile phones and internet Participants were provided with blood glucose monitors	Weekly individual sessions via cellular phone and Internet for 6 months
	Control group—met an endocrinologist once or twice during a 3-month study	
	Those in control group who visited program intervention center received advice on medication, medication dosage, and lifestyle modification from endocrinologist	
Kim and Song, Korea [39]	Intervention group—received education and reinforcement on diet, exercise, medication adjustment, and frequent self-monitoring of blood glucose levels led by nurse via mobile phones and internet Participants were provided with blood glucose monitors	Weekly individual sessions via cellular phone or wired Internet for 3 months
	Control group—met an endocrinologist 2–4 times during a 6-month study	
	Those in control group who visited program intervention center received advice on medication, medication dosage, and lifestyle modification from endocrinologist	

comparison control groups. The educational interventions provided information on behavioral and lifestyle change. In one study, individuals in the intervention group received monthly group sessions on the management of diabetes and lifestyle modification delivered by an experienced nutritionist [36]. This group also received weekly consultation sessions on diet and medical evaluation. In comparison, the control group received monthly group sessions comprising diabetes education. In another study, individuals in the intervention group participated in small-group diabetes education classes and received a patient education manual [37]. A researcher also conducted home visit sessions for each of these participants. The control group, in contrast, received usual nursing care before they began diabetes education classes at the end of the study. The two telemedicine-based nurse-led educational interventions comprised education and reinforcement of healthy diet, physical exercise, and medication adjustment to those participants in the intervention groups [38, 39]. The reminders for frequent self-monitoring of blood glucose levels were sent to each participant in the intervention groups, using short message services via cellular mobile phone.

Intervention Effectiveness

Prevention of the Development of T2DM Each study showed significant reductions in the development of T2DM in the intervention group compared with controls. The Da-Qing study successfully reduced the risk of developing T2DM up to 46% in the lifestyle intervention group compared with the control group [29]. The 20-year follow-up showed that the group-based lifestyle intervention implemented over 6 years prevented or delayed diabetes for up to 14 years, although the long-term effects on reduced cardiovascular disease morbidity and mortality were less clear [30]. The IDPP-1 reported high rates of progression of IGT to T2DM in control participants (18.3%

incidence per year), while both lifestyle modification and medication reduced T2DM incidence, with a relative risk reduction of 28.5% and 26.4%, respectively, over the 3-year study [31]. Interestingly, the IDPP-1 program did not show an additional benefit of combined lifestyle intervention and medication. The community-based, non-pharmacological diabetes prevention program in rural India was successful in reducing fasting blood glucose levels in adults with IFG by 11%, in youths by 17%, and in adults with T2DM by 25% over the 7-month study, although the numbers in each group were small [32]. In addition, the authors reported improvements in obesity parameters and dietary intake.

Prevention of Diabetes Complications Significant improvements were observed in glycemic control across the range of diabetes complications prevention studies. One RCT in China improved glycemic control and markers of cardiovascular health in people with T2DM [36]. This program reduced HbA1c levels by 0.8% in the intervention group, compared with an elevation of 0.1% in the reference group over the 6-month study timeframe. Participants in both the intervention and reference groups achieved modest weight loss of 3.7% and 2.5%, respectively. The hospital-based RCT in Thailand demonstrated the efficacy of educational interventions by reducing HbA1c levels by 0.68% in the intervention group, compared with 0.07% in the control group over 6 months [37]. The program also demonstrated reductions in risk factors for coronary heart disease of 4.83% in the intervention group, as opposed to 1.54% in the control group. Similarly, the two RCTs conducted in Korea showed reductions in HbA1c levels in adults with T2DM [38, 39]. One demonstrated reduced HbA1c levels of 1.15% in the intervention group compared with an elevation of 0.07% in the control group over 3 months [38, 39], and the other reduced HbA1c levels by 1.09% in the intervention group, compared with no changes in the control group over the 6-month study [38, 39].

Cost-effectiveness

Prevention of Development of T2DM The economic evaluation of the IDPP-1 was the only cost-effectiveness study of a diabetes prevention intervention program identified in a developing country [40]. This work concluded that the lifestyle intervention was cost-effective for preventing diabetes among high-risk individuals. The total cost spent to identify one subject with IGT was the equivalent of US $117. The total direct medical cost of the intervention in different groups over the 3-year intervention period was US $61 per subject in the control group, US $225 with lifestyle modification and US $270 with the lifestyle modification+medication group. The cost of the intervention to prevent one case of diabetes was US $1,052 with lifestyle modification and US $1,359 with lifestyle modification+medication. In addition, the number of individuals needed to treat to prevent a case of diabetes was 6.4 with lifestyle modification and 6.5 with lifestyle modification+medication.

Prevention of Development of Complications No cost-effectiveness studies for preventing T2DM complications in developing countries were identified.

Discussion

Diabetes in developing countries contributes to an increasing proportion of the total global burden of diabetes [2, 14, 41]. Prevention studies have now been conducted in China [29, 30, 36], India [31, 32, 40], Thailand [37], and Korea [38, 39]. Despite the limited number of studies, these studies do provide some important information concerning the efficacy and cost-effectiveness of non-pharmacological interventions for the prevention of T2DM and its related complications in developing countries.

Prevention of the Development of T2DM

The non-pharmacological interventions in China [29, 30] and India [31, 32] have demonstrated that the lifestyle interventions can result in significant reductions of risk for the development of T2DM in people with IGT or IFG. The Da-Qing study and the IDPP-1 each reported a significant relative risk reduction in the development of T2DM in the intervention groups, however these were substantially lower than shown in similar trials conducted in developed countries, including the Finnish DPS [20–22] and US DPP [23]. These latter trials have reported a relative risk reduction of 58% in diabetes incidence in the lifestyle intervention groups over approximately 3-year intervention periods. The lifestyle interventions in these trials focused on weight loss, intake of healthy diet, and promoting modest physical activity, and were delivered by a nutritionist [20] and special educators (“case managers”) [23]. Although the risk reduction was lower in the developing countries, the progression of T2DM incidence in the control group was observed to be greater in the IDPP-1 [31] than in developed countries (IDPP-1 at 18.3% compared with DPS at 6% [42] and DPP at 11% per year [23]). Therefore, any reduction in the progression of T2DM in developing countries is particularly important. There are likely to be numerous explanations for the higher effectiveness in developed countries compared with low-income countries. For example, the existing structure of healthcare systems in developed countries provides a framework for effective

intervention studies [43]. Access to healthcare services is likely to be another important factor, as is the reduced level of health literacy in some developing countries. Poor adherence to standard diabetes care may be lower in developing countries as a result of competing priorities that are not present in developed countries.

It is interesting to note that, even in samples with comparable age ranges and obesity levels, Indian cohorts demonstrated an elevated progression rate of T2DM compared with Chinese groups [29]. High prevalence of diabetes and elevated levels of insulin resistance in South Asian populations [44] could have resulted in the observed high rates of T2DM incidence in the control group in the Indian sample. The China Da-Qing intervention [29, 30] was reported to be more effective than the IDPP-1 [31]. The increased intensity and the mode of intervention delivery through trained physicians and nurses in the China Da-Qing study are likely to have influenced these differences. In terms of features of the interventions with higher efficacy, the inclusion of exercise, either alone or in conjunction with diet [29–32], demonstrated the greatest improvements in risk reduction of diabetes.

Prevention of Diabetes Complications

Maintaining glycemic control, in particular HbA1c levels lower than 7% [45–47], is important for preventing diabetes-related complications. Early effective intervention for the management of hyperglycemia, hypertension, and dyslipidemia can reduce the risk of developing diabetes-related complications [48]. The non-pharmacological educational interventions in China [36], Thailand [37], and Korea [38, 39] demonstrated reductions of HbA1c levels and other cardiovascular disease risk factors, which might facilitate improvements in diabetes control and prevent disease-related complications. These findings are supported by other studies conducted in developed countries, which have resulted in reduced HbA1c levels, adiposity, and blood pressure in the intervention compared with control groups [25, 26, 49]. For example, a diabetes education and self-management program reduced HbA1c levels by 1.49% in people with newly diagnosed diabetes [25], and a weight reduction and exercise program for older African-American adults reduced HbA1c levels by 1.1% in the intervention compared with control groups [26]. Telehealth-delivered educational interventions in developing countries were also shown to be effective in reducing HbA1c levels in adults with T2DM [38, 39]. Previous work from developed countries has found similar results, demonstrating decreased HbA1c levels in patients receiving telephone-based nurse support programs [50–52].

The interventions conducted in developed countries that focused on prevention of diabetes-related complications [25, 26, 49–52] have shown greater improvements in glycemic control compared with those in developing countries [36–39] (reduction of HbA1c level 0.9–1.7% compared with 0.7–1.1%). As discussed in the earlier paragraph in relation to primary prevention, there are multiple explanations for lower efficacy of such trials in developing countries compared with developed countries. In addition, within the studies in developing countries, the telehealth-delivered educational interventions [38, 39] reported greater reductions in HbA1c compared with those with interpersonal education-based programs [36, 37]. It is possible that the delivery of the interventions via trained nurses in the telehealth studies had an impact on the differentials in efficacy across these studies.

Previous studies have shown that, in addition to lifestyle interventions, pharmacological interventions are effective in the prevention of diabetes-related complications [53–58]. The UKPDS, one of the most widely known studies, showed that anti-hypertensive medications reduced macrovascular endpoints by 37% and diabetes-related mortality by 32% [53]. Similarly, a Danish study conducting a multifactorial intervention, implementing behavioral modification alongside pharmacological therapy, found CVD risk reductions of up to 50% in the intervention compared with the conventional treatment group [57]. Although the studies included in this review did not implement pharmacological interventions, other studies from low- and middle-income countries have shown similar results to those from the developed world with medication therapy within their programs [59–62]. Therefore, the existing evidence indicates that the use of medication is also important in the management of diabetes and preventing the related complications.

Cost-effectiveness of Programs

The 3-year IDPP-1 confirmed that a non-pharmacological intervention was cost-effective for preventing diabetes among high-risk Indian adults [40]. All the costs incurred in the different intervention groups of IDPP-1 were substantially lower and more cost-effective than the costs incurred in the US DPP [63], where the placebo group cost US $218, the lifestyle intervention group cost US $2,919 and medication group cost US $2,681 over the 3-year intervention period. Sparse data are available examining the costs and cost-effectiveness of the interventions related to prevention of T2DM and its complications, and the studies that do exist come predominantly from developed countries [19, 63–65]. However, the cost and the cost-effectiveness estimations from the IDPP-1 study suggest that non-pharmacological interventions for the prevention of T2DM in developing countries are, in absolute terms, cheaper and more cost-effective compared with studies

from the developed world, such as the DPP [63]. This evidence should encourage other developing countries to develop and implement cost-effective, non-pharmacological interventions to stem the escalating problem of T2DM and diabetes-related complications.

Limitations of the Studies/Programs

Prevention of the Development of T2DM The two Indian studies [31, 32] and the Da-Qing [29] study have some important limitations. Most importantly, these studies identified high-risk individuals using IGT or IFG classifications, which employ relatively expensive screening methods that require individuals to fast and undergo blood tests. In countries such as China and India, where rates of diabetes are extremely high, it is not feasible or cost-effective to screen everyone using such expensive screening methods for diabetes. Low-cost screening methods such as short questionnaires to identify high-risk individuals need to be developed and tested in diabetes prevention programs. Furthermore, in the IDPP-1, only one fifth of the subjects were female [31]; yet, the number of males and females in India with IGT are comparable [2, 9]. In addition, this program selected a sample from a middle class working people with persistent IGT in an urban setting; however it did not include people from rural areas, where two thirds of the population of India live, so generalizability to the whole population is problematic. Although the IDPP-1 estimated the direct medical costs and cost-effectiveness of the program [40], it did not estimate the longer-term cost-effectiveness of the program and the indirect costs which are often many times higher than the direct medical costs. The study by Balagopal et al. did not include a control group, comprised very small numbers of high-risk participants, and lacked sufficient follow-up (7 months) to determine the sustained effect of the intervention [32]. The Da-Qing study achieved a longer-term follow-up; however, it did not report the estimated cost and cost-effectiveness of the program [29, 30].

Prevention of Diabetes Complications A major limitation of these studies was the short follow-up periods, which varied between 3 [38] and 6 months [36, 37, 39]. This meant the sustainability of the intervention effects could not be evaluated [36–39]. The time frame did not allow an evaluation of the efficacy of the trials on incidence of complications, only the observation of reduced risk factors associated with the development of complications. In addition, the hospital-based study in China had a large discrepancy in the number of participants in the control and intervention groups [36]. The two Korean RCTs included sample sizes (n=51 and 34) that were too small to reliably establish intervention effects, particularly over the short follow-ups of 3 and 6 months, respectively [38, 39].

Future Directions

Given the escalating burden of noncommunicable diseases in low- and middle-income countries [66], research must begin to focus more heavily on effective chronic disease interventions [43]. Future programs to prevent diabetes and its associated complications in developing countries should focus on the appropriate development, adaptation, and implementation of efficacious, cost-effective intervention methods from developed and developing countries. However, it is also important to evaluate programs that combine more traditional educational and behavioral methods with peer support, telehealth, and other more contemporary approaches that are now being widely utilized around the world [67–72]. To date, diabetes prevention trials in developed as well as developing countries have primarily targeted those people with diagnosed pre-diabetes [20, 23, 29, 31]; however, in resource-constrained settings, it is not feasible to rely on the identification of such high-risk individuals using blood tests so the development of valid and reliable self-report risk assessment tools is also required [73]. In addition, it is very important to develop linguistically appropriate and context-specific lifestyle interventions that are tailored to meet the cultural, religious, and socioeconomic needs of the target communities, with long-term implementation to enable the sustainability of the targeted intervention outcomes.

It is also necessary to consider the development and evaluation of programs that link with local community resources, relevant non-government organizations, and in particular, local health services. Interventions focused on chronic disease prevention and management in developing countries must engage healthcare systems to initiate the improvements and reform that are urgently required to support the long-term primary and secondary prevention and care of those at risk and with these diseases [43].

Conclusions

We conclude that, despite the escalating burden of T2DM in developing countries, the current evidence concerning the prevention of T2DM and its complications in these countries still remains quite limited. Nevertheless, there is an urgent need to stem the growing epidemic of T2DM in rapidly developing countries that face significant resource constraints. This must be achieved by linking a significant primary prevention

effort in all countries with the use of low-cost behavioral medicine and related approaches to screen and identify high-risk individuals, followed by the development, implementation, and evaluation of community-based programs that are culturally relevant and cost-effective.

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Conflicts of Interest We declare that there was no conflict of interest.

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