Journal of Diabetes and Metabolism
ISSN: 2155-6156
Matte and Velonakis, J Diabetes Metab 2014, 5:11
DOI: 10.4172/2155-6156.1000460
Review Article
Open Access

Type 2 Diabetes Prevention Programs; How Far are we?

Margarita E Matte[1,2]* and Emmanuel G Velonakis[2]

[1]Department of Nutrition, Eastern Achaia General Hospital, Greece
[2]Department of Nursing, National and Kapodistrian University of Athens, Athens, Greece

Abstract

Type 2 diabetes is the most costly chronic disease for both, the individual and the society. Many randomized controlled trials of structured lifestyle modification have consistently demonstrated that achieving and maintaining a healthy body weight through a combination of a change in dietary behaviors and an increase of physical activity reduces the risk of incidence of type 2 diabetes in adults at high risk. Although, their results have demonstrated the efficacy of lifestyle modification for diabetes prevention, long-term compliance with these lifestyle changes has proven difficult, however, and the benefits wane with weight regain. Small community-based programs have reported some success in modifying surrogate markers for diabetes through lifestyle intervention. The cost-effectiveness of lifestyle interventions has been examined in a number of clinical trials and computer modelling simulations. Short time-horizon studies have shown prediabetes lifestyle interventions to be cost-effective and even cost saving. Long time-horizon studies based on 10- to 30-year predictive mathematical models have used different models with different data, and have come to different conclusions about the cost-effectiveness of prediabetes lifestyle interventions. It is difficult to base a long time-horizon policy decision on predictive models when long-term randomized controlled trial data are not available to support the conclusions of those models. In conclusion, for large-scale implementation of preventive strategies, the future plan should focus on health education of the public, improving the national capacity to detect and manage non-communicable diseases and development of innovative, cost effective, and scalable methodologies.

Keywords: Community-based programs; Cost-effectiveness; Lifestyle interventions; Primary health care; Prevention; Type 2 diabetes

Abbreviations: CDQDPS: Chinese Da Qing Diabetes Prevention Study; CVD: Cardiovascular Disease; DEHKO: Development Programme for the Prevention and Care of Diabetes in Finland; DE-PLAN: Diabetes in Europe – Preventing using Lifestyle, Physical Activity and Nutritional Intervention; DEPLOY: Diabetes Education and Prevention with Lifestyle intervention Offered at the Young Men's Christian Association; DPPOS: Diabetes Prevention Program Outcomes Study; DPP: Diabetes Prevention Program; DPS: Finnish Diabetes Prevention Study; FIN-D2D: National Type 2 Diabetes Prevention Programme in Finland; FINDRISC: Finnish Diabetes Risk Score; GGT: Greater Green Triangle Diabetes Prevention Project in Australia; GOAL: Good Ageing in Lahti Region Lifestyle Implementation Trial in Finland; IDF: International Diabetes Federation; IGT: Impaired Glucose Tolerance; NGR: Normal Glucose Regulation; T2D: Type2 Diabetes

Introduction

Diabetes is the one of the most common non-communicable diseases. It is the fourth or fifth leading cause of death in most high-income countries and there is substantial evidence that it is epidemic in many economically developing and newly industrialized countries. Diabetes imposes a large economic burden on individuals and families, national health systems and countries. Health expending on diabetes accounted for 11% of total health expenditure worldwide in 2013 [1-3].

The most recent estimates indicate that 8.3% of adults - 382 million people have diabetes and the number of people with the disease will increase by 55% - 592 million in less than 25 years. Type2 diabetes (T2D), which is the most common condition and a serious global health problem, accounts for 85% to 95% of all diabetes in high-income countries and may account for an even higher percentage in low- and middle-income countries. A further 316 million people or 6.9% of adults with Impaired Glucose Tolerance (IGT) are at risk from the disease as well as at increased risk from Cardiovascular Disease (CVD) – an alarming number that is set to reach 471 million by 2035. The majority of adults with IGT are under the age of 50 (153 million) and are therefore likely to spend many years at high risk [4].

In most countries diabetes has increased alongside rapid culture and social changes: ageing populations, increasing urbanization, dietary changes, reduced physical activity and unhealthy behaviors [5-7]. Population growth and prolonged life expectancy have contributed to a steady increase in the number of older people aged 60 years or over who constitute more than 11.1% of the world's population. The International Diabetes Federation (IDF) estimates the global prevalence of diabetes in people aged between 60 and 79 to be 18.6%, more than 134.6 million people, accounting for over 35% of all cases of diabetes in adults. It is important to know that one-third of all people with IGT are in this age group [4].

At present, type 1 diabetes cannot be prevented, although there is a lot of evidence that lifestyle changes can help prevent the development of T2D. Landmark clinical trials have shown than primary prevention can delay and possibly prevent the onset of diabetes in individuals at high risk [8-13]. Intensive lifestyle and pharmacological interventions reduce the rate of progression to T2D in people with IGT. The results of the prevention trials seemed that the interventions to change dietary

***Corresponding author:** ME Matte, Department of Nutrition, Eastern Achaia General Hospital, Ano Voulomeno, 25100 Aegio, Achaia, Greece, Tel: +30 2691059403; Fax: +30 2691059678; E-mail: mattemargarita@yahoo.gr

Received September 10, 2014; **Accepted** October 17, 2014; **Published** October 19, 2014

Citation: Matte ME, Velonakis EG (2014) Type 2 Diabetes Prevention Programs; How Far are we? J Diabetes Metab 5: 460 doi:10.4172/2155-6156.1000460

habits and increase physical activity are the most effective strategies, representing the first steps of T2D prevention programs, while the effect of pharmacological interventions decreased after intervention was terminated [13-18]. Encouraged by these results, there have been many attempts to translate the prevention trials into community-based programs [8,19-21]. In this review, results from long-term follow-up of diabetes prevention and the outcomes of community-based interventions in "real world" settings will be presented. Furthermore, it will provide evidence-based data on the cost-effectiveness of primary prevention of diabetes at the long-term clinical and community-based level. Finally, this review will also focus on older adults as there is a profound lack of clinical trials, although little evidence is showed that lifestyle interventions had greater impact in older participants.

Long-term Follow Up of Diabetes Prevention

Many randomized controlled trials of structured lifestyle modification have consistently demonstrated that achieving and maintaining a healthy body weight through a combination of a change in dietary behaviors and an increase of physical activity reduces the risk of incidence of T2D in adults at high risk by 42-67% [8,21]. Long-term post-intervention follow up evidence of lifestyle modification are only provided by three major clinical trials providing encouraging results (Table 1). However, no long-term follow-up of drug intervention to prevent diabetes has been published except for the Diabetes Prevention Program Outcomes Study (DPPOS).

Finnish Diabetes Prevention Study (DPS)

A total of 522 middle-aged individuals with IGT were randomized to an intensive lifestyle intervention group or to a control group. After 3.2 years of intervention, the relative risk reduction of T2D between lifestyle intervention and control group was 58% (p<0.001) [9]. After a median post-intervention follow up of 4 and 9 years (7 and 13

Study	Subjects	Intervention	Relative Risk Reduction of T2D/ mean duration of intervention	Relative Risk Reduction of T2D/ mean duration of follow-up
DPS	522 individuals mean age 55 ± 7 years, and mean BMI 31.2 ± 4,5 kg/m^2 with IGT	1. Control group: general advice about healthy lifestyle at baseline. 2. Intervention group: Individualized lifestyle intervention included 7 face-to-face counseling sessions with nutritionist during the first year and every 3 months thereafter. Intervention goals: body weight reduction of ≥ 5%, total fat intake <30% of energy, saturated fat intake <10% of energy, fibre intake of ≥15gr/1000kcal and moderate exercise for ≥ 30/day	58% (p<0.001) Compared with control group / 3.2 years	42% (p=0.0001) Compared with control group / a median post-intervention follow up of 4 years (7 from baseline) 38% (p<0.001) Compared with control group / a median post-intervention follow up of 9 years (13 years from baseline)
CDQDPS	577 people mean age of 45 ± 9.1 years and BMI 25.8 ± 3.8kg/m^2 with IGT	1. Control group: general advice about healthy lifestyle at baseline 2. Dietary intervention: individual counseling+ compliance evaluation by physician/nurse every 3 months + small groups weekly for 1 month, monthly for 3 months and every 3 months thereafter. Intervention goals: weight reduction aiming at <24 kg/m^2, 55-65% of energy carbohydrate, 25-30% of energy fat and 10-15% of energy protein. Increase vegetables, decrease alcohol and sugar. 3. Exercise intervention: physical activity by at least 30 minutes of moderate activities and 20 minutes of vigorous activities daily 4. Diet+Exercise intervention: diet-plus- exercise combined intervention	33% of dietary group (p<0.03) 47% of exercise group (p<0.0005) 38% diet + exercise group (p<0.005) Compared with control group / 6 years	43% all intervention group (p<0.01) Compared with control group / 20 years from baseline
DPP	3234 US adults mean age of 50.6 ± 10.7 years and mean BMI 34 ± 6.7 kg/m^2 with IGT	1. Placebo group: general advice about healthy lifestyle at baseline. 2. Intervention group: 16 face-to-face counseling sessions with registered dietitian during the first 24 week and every 2 months thereafter. Intervention goals: ≥ 7% weight loss, total fat intake <25% of energy, energy reduction of 500-1000 kcal/day and 150 min or more per week of moderate-intenp physical activity 3. Metformin intervention: 850 mg twice per day	58% of lifestyle group (p<0.01) 31% of metformin (p<0.01) Compared with placebo group / 2.8 years	
DPPOS post-intervention ongoing observational follow-up to the DPP	2766 DPP participants mean age of 55.2 ± 10.3 years and mean BMI 32.7 ± 6.6 kg/m^2	all three groups of DPP were offered group-implemented lifestyle intervention with registered dietitian metformin treatment was continued in the original metformin groupt the original lifestyle intervention group was offered additional lifestyle support		34% of lifestyle group 18% of metformin group (p<0.001) Compared with placebo group / 10 years (DPP + DPPOS)

Table 1: Long-term follow-up of diabetes prevention programs.

years from baseline), the relative risk were 42% (p=0.0001) and 38% (p<0.001) respectively [22]. Body weight reductions from baseline to years 1 and 3 were 4.5 ± 5 kg and 3.5 ± 5.1 kg (p<0.0001) respectively in the intervention group and 1.0 ± 3.7 kg and 0.9 ± 5.4 kg (p<0.0001) in the control group [9]. Body weight increased gradually in the course of follow-up in the both groups. However, a statistically significant difference between the study groups prevailed (p=0.006 at year 10) [22]. Finally, it is important to be mentioned that lifestyle intervention among person with IGT did not decrease CVD morbidity during the first 10 years of follow up [23].

Chinese Da Qing Diabetes Prevention Study, (CDQDPS)

Cluster randomization was used to allocate 577 people with IGT attending 33 participating clinics to diet alone, exercise alone, diet-plus-exercise combined or no intervention [24]. After 6 years intervention, the relative risk reduction of T2D in the diet alone, exercise alone, diet-plus-exercise combined intervention groups were 33% (p<0.03), 47% (p<0.0005) and 38% (p<0.005) respectively. Compared with control participants, those in the combined lifestyle intervention groups had a 43% (p<0.01) lower incidence of T2D over the 20 year follow-up [11]. Finally, a 23-year follow-up study indicates that the 6-year lifestyle intervention programme for Chinese people with IGT can reduce incidence of CVD and all-cause mortality. Specifically, cumulative incidence of CVD mortality was 11.9% in the intervention group versus 19.6% in the control group (p=0.033) and all-cause mortality was 28.1% versus 38.4% (p=0.049) [25].

Diabetes Prevention Program Outcomes Study, (DPPOS)

The DPPOS is a post-intervention ongoing observational follow-up to the US Diabetes Prevention Program (DPP), one of the largest randomized controlled clinical trials to date.

The DPP was conducted in 3234 US adults with IGT. Unlike most previous studies, the cohort was diverse and included a large proportion of women (68%), ethnic and racial minorities (45%) and 20% aged 60 years or older. Participants were randomly assigned centrally to one of three interventions: intensive lifestyle; metformin 850 mg twice per day; or placebo [26].The mean duration of intervention was 2.8 years. Compared with placebo, both lifestyle intervention and metformin group reduced T2D risk by 58% (p<0.01) and 31% (p<0.01) respectively [10].

For a median additional follow-up of 5.7 years, 2766 (mean age of 55.2 ± 10.3 years and mean BMI 32.7 ± 6.6 kg/m^2) of 3150 (88%) enrolled in DPPOS. On the basis of the benefits from the intensive lifestyle intervention in DPP, all three groups of DPP were offered group-implemented lifestyle intervention, while metformin treatment was continued in the original metformin group and the original lifestyle intervention group was offered additional lifestyle support [27].

During the 10 year follow-up since randomization to DPP, the T2D incidence rate of lifestyle group was reduced by 34% (p<0.001) and metformin by 18% (p<0.001) compared with placebo. It is important to mention that lifestyle effect was greatest in participants aged 60-85 years at randomization (49% rate reduction), in whom metformin had no significant effect [28]. Furthermore, it should be noted that participants who were able to achieve Normal Glucose Regulation (NGR) status at least once during DPP had a 56% lower risk of diabetes during DPPOS (0<0001). Generalized mixed did demonstrate a positive effect of female sex on regression to NGR [29].

During DPP, weight loss was associated with diabetes prevention. Body weight at baseline and weight reduction during intervention was most important predictors of T2D risk. At one-year of DPP the mean weight loss of the lifestyle group participants was 7.4 kg (about 7%) of body weight, diminishing to 4.2 kg (about 4%) after 3 years [10]. During the DPPOS, the lifestyle group participants gradually regained, although still weighing 2.1 kg less than they did at randomization [27]. The metformin group lost a mean of 2.5kg during DPP and maintained most of the weight loss. Although, during the DPPOS every age-group in the lifestyle intervention gained weight, on average, participants in both metformin and placebo group who were aged 60-85 years at DPP randomization lost weight [27,28].

Finally, although no differences in CVD events were noted after 3 years of DPP, lifestyle intervention reduced known CVD risk factors including hypertension, high triglyceride levels, low HDL levels, and small dense LDL compared with placebo and metformin therapy. During 10 years of DPPOS, assessing the association between the regression to NGR and a long-term decrease in CVD risk using the Framingham 10-year

CVD risk score, the mean scores were highest in the group with IGT (16.2%), intermediate in the NGR group (15.5%), and 14.4% in people with diabetes (p<0.05). The lower score in the diabetes group versus other groups and a declining score in the group with IGT were probably explained by higher or increasing antihypertensive medication and pharmacologic therapy for dyslipidemia [30,31].

Translating Diabetes Prevention Trials to the Public Health

Preventing diabetes is of enormous value for any nation particularly in the developing world because of the high cost of treating diabetes and its complications. However, there is less agreement with respect to the intensive and costly lifestyle intervention of the DPP and DPS [32-34]. Although, their results have demonstrated the efficacy of lifestyle modification for diabetes prevention, long-term compliance with these lifestyle changes has proven difficult, however, and the benefits wane with weight regain (Table 2).

Small community-based programs have reported some success in modifying surrogate markers for diabetes through lifestyle intervention. The Greater Green Triangle (GGT) Diabetes Prevention Project in Australia, the Diabetes Education and Prevention with Lifestyle intervention Offered at the Young Men's Christian Association (DEPLOY) and the Good Ageing in Lahti Region (GOAL) Lifestyle Implementation Trial in Finland confirmed that short-term lifestyle modification programs can reduce risk factors for diabetes in primary care settings.

The DEPLOY study aimed to deliver a formal, group-based adaptation of the DPP lifestyle intervention. Among 92 overweight adults with abnormal glucose metabolism, the 46 participants (mean age of 60.1 ± 10.5 years and mean BMI 30.8 ± 5.1 kg/m^2) in the intervention arm participated in the new DPP assembled into 16 classroom-style meetings of 8-12 people over 16-20 weeks. At the control group 46 participants (mean age of 56.5 ± 9.7 years and mean BMI 32 ± 4.8 kg/m^2) were offered information about existing wellness programs to help participants achieve modest weight loss through gradual lifestyle changes. After 6 months, compared to baseline levels,

Study	1st year	2nd year	3rd year	4th year	5th year	10th year
DPS	4.5	4	3.5	2.9	2.5	0.9
DPP-DPPOS	7.4	5.6	4.2	3.2	2.6	1.9

Table 2: Weight loss of intervention group over the diabetes prevention programs.

body weight decreased by 6% in intervention participants and 2% in control participants (p<0.001). This equated to a mean weight loss of 5.7 kg for intervention participants and 1.8 kg for controls. Intervention participants also had greater changes in total cholesterol (p<0.001). These differences were sustained after 12 months [35,36].

In the Finland, 352 middle-aged participants (mean age of 58.5 ± 4 years and mean BMI 32.3 ± 4.9 kg/m^2) with elevated T2D risk were recruited from the health care centres in Finland. The GOAL intervention included six group counselling sessions implemented lifestyle objectives derived from DPS. At 12 months, only 20% of participants achieved at least four of five keys lifestyle outcomes and physical activity and weight loss goals were achieved significantly less frequently [37].

The Australian GGT intervention study included 237 individuals (mean age of 56.7 ± 8.7 years and mean BMI 33.5 ± 5.9 kg/m^2) 40-75 years of age with moderate or high risk of developing T2D. A structured group programme with six 90 minute group-sessions delivered during an eight month period by trained nurses in Australian primary health care. The intervention model used in the study was based on the diabetes prevention project in the Finnish GOAL study. At 12 months participants' mean weight reduced by 2.52 kg. Between baseline and 12 months, statistically significant improvements were observed in participants' mean clinical indicators except systolic blood pressure. 75% of participants experienced some waist reduction and 68% experienced weight reduction [38,39].

While early results from these are encouraging, the samples were small and largely self-selected, follow-up was short, the interventions remained relatively intensive and many studies lacked formal comparison. Furthermore, the low level of participation in the community-based diabetes risk-screening events suggests that a range of different approaches may be needed to engage people who are at risk for diabetes.

The design of effective 'real world' models for implementing the DPP and DPS lifestyle intervention requires a collaborative effort that balances fidelity to the design with additional incentives, communications and organizational elements that predispose, enable and reinforce behavioural changes in both practitioners and patients and that optimize reach, adoption and implementation and effectiveness, minimize cost and improve sustainability for capable community partners.

The current challenge is to translate evidence of the trials and the small community-based programs into cost-effective large scale community-wide programs. There is increasing acknowledgement that the best way to do this is through studies which have an explicit focus on generalisation and feasibility and which report information on contextual variables such as representativeness, reach, implementation and adaption, costs and other outcomes important to policy makers [21,40,41].

Finland is one of the first countries to implement a large-scale diabetes prevention strategy. The Development Programme for the Prevention and Care of Diabetes in Finland 2000-2010 (DEHKO) includes a population strategy aimed at nutritional interventions and increased physical activity in the entire nation, an individualised strategy for those at high risk, and a programme of early detection and management for people with T2D [42].

The primary strategy of the Finnish National T2D Prevention Programme (FIN-D2D) was a 'high-risk strategy' aiming at preventing diabetes and reducing cardiovascular risk factor levels among high-risk individuals in daily routines in healthcare centres and occupational healthcare outpatient clinics. The aim of the 'high-risk strategy' was first to identify individuals aged 18-87 years at elevated risk of developing type 2 diabetes and to support their lifestyle changes required to reduce their future risk. Altogether, 400 primary healthcare centres or occupational healthcare clinics were involved in the programme. To identify high-risk individuals for type 2 diabetes, the modified Finnish Diabetes Risk Score (FINDRISC; scoring ≥ 15) was used. Intervention visits were either individual counselling visits or group sessions, at which the intervention visit form was filled. The frequency of intervention visits varied between health centres depending on local circumstances and resources, and the total number of intervention visits was recorded [43].

During the one-year follow-up, 17.5% of the subjects lost ≥ 5% weight. On average this meant an 8.5 kg (p<0.001) reduction in weight, a 3.0 kg/m^2 (p<0.001) reduction in BMI and a 6.6 cm (p<0.001) reduction in waist circumference. During the follow-up, 16.8% of the subjects lost 2.5–4.9% weight and 46.1% maintained weight. Only 19.6% of the subjects gained 2.5% weight. Men were as successful as women in losing weight. Weight loss was on average 1.3 kg (p<0.0001) in 919 men (mean age of 56.0 ± 9.9 years and mean BMI 30.9 ± 3.6 kg/m^2) and 1.1 kg (p<0.0001) in 1879 women (mean age of 54.0 ± 10.7 years and mean BMI 31.6 ± 5.4 kg/m^2). 9.6% of the men reported both an increase in physical activity and improved dietary pattern, 4.1% an increase in physical activity, 39.3% an increase in improved dietary pattern, while 47.0% reported no lifestyle changes. Corresponding numbers for women were 14.2%, 3.8%, 39.2% and 42.7%.Those who increased their activity decreased their weight by 3.6 kg (p<0.001), BMI by 1.27 kg/m^2 (p<0.001) and waist circumference by 3.6 cm (p<0.001) more than those who did not increase their activity. Those who increased their physical activity also reported more changes in their diet, but the main results remained either statistically significant or borderline significant after adjustment for the number of intervention visits and after the adjustment for dietary change [44,45].

Estimated 10-year risk for CVD events decreased 3.5% in men and 1.5% in women reporting an increase in physical activity and improvement in diet, compared to an increase of 0.15% in men (p<0.001) and decrease of 0.43% (p=0.027, between groups) in women with no lifestyle changes [46].

The relationship between weight loss and incidence of diabetes was almost stepwise. The relative risk of diabetes was only 0.31 (95% CI 0.16 – 0.59; p<0.001), which translates to 69% risk reduction in the group who lost 5% weight compared with the group who maintained weight. The relative risk was 0.72 (0.46–1.13, risk reduction of 29%; p<0.001) in the group who lost 2.5– 4.9% weight and 1.10 (95% CI 0.77–1.58, risk increase 10%; p<0.001) in the group who gained 2.5% compared with the group who maintained weight. This unexpected reduction in the risk of diabetes emphasizes that moderate weight loss in this very high-risk group representing early converters is especially effective in reducing risk of diabetes or at least postponing diabetes. Longer follow-up is needed to see whether this effect will last over time [44].

Although encouraging first results of the first large-scale diabetes prevention strategy, it must be noted that only 50% of the total cohort had any follow-up data. The first loss to follow-up occurred after screening; only 78% of the screened high-risk subjects had an OGTT. The second loss to follow-up occurred after the OGTT. Only 69% of subjects who had an OGTT at baseline had any follow-up data. These data reflect a real-life setting and the difficulty in following up on patients in primary healthcare settings [44-47].

The Diabetes in Europe – Preventing using Lifestyle, Physical Activity and Nutritional Intervention (DE-PLAN) project is another large-scale diabetes prevention initiative, which aims to develop community-based T2D prevention programmes for individuals at high risk in each local project centre across Europe [48-50].

The national programs such as the FIN-D2D, the Singapore Diabetes Prevention Programme and the Cameron Diabetes Prevention Plan initiated by the government should be taken as model endeavours to formulate strategies to promote and implement community health programs [43,51,52].

Cost-effectiveness of Diabetes Prevention

The increasing health and economic burden of T2D has made preventing the disease a public health priority. Implementation of diabetes prevention interventions in real-life settings requires a comprehensive evaluation approach. In most countries health care costs are rapidly rising, and the obesity epidemic plays an important role in this process. Several studies have shown that the risk of developing T2D and associated CVD reduces with weight loss and improved lifestyle behaviours [8-13]. The cost-effectiveness of lifestyle interventions has been examined in a number of clinical trials and computer modelling simulations. Although pharmacological interventions have also been shown to prevent diabetes, the cost effectiveness and risk-benefit ratio are less clear [32-34,53-63].

The 10-year, within trial, intention-to-treat economic analysis of the DPP/DPPOS demonstrates that lifestyle, when compared with placebo, is cost-effective, and metformin is marginally cost-saving. Even when compared with metformin, lifestyle was cost-effective from both a health system and societal perspective [64]. Follow-up of the DPP cohort for 10 years after randomization showed that lifestyle intervention for people older than 65 years with prediabetes can prevent many cases of diabetes. Prediabetes lifestyle interventions for relatively healthy people aged 65 years or older seem to be highly cost-effective and possibly cost saving to a health care insurance payer, although evidence is little [65-67].

Another analysis indicates that, compared with no prevention program, the DPP lifestyle program would reduce a high-risk person's 30-year chances of getting diabetes from about 72% to 61%, the chances of a serious complication from about 38% to 30%, and the chances of dying of a complication of diabetes from about 13.5% to 11.2%. Metformin would deliver about one third the long-term health benefits achievable by immediate lifestyle modification [68].

Furthermore, modelling studies for diabetes prevention which encompass a screening stage indicate that screening for T2D and IGT, with appropriate intervention for those with IGT, in an above average risk, overweight and obese, population aged 55 and older with systolic blood pressure ≥130 mmHg, seems to be cost effective. The cost effectiveness of a policy of universal screening for undiagnosed T2D alone, which offered no intervention to those with IGT, is still uncertain, since its high cost effectiveness ratio was primarily attributable to the small gain in health benefit [60-63,69,70-77].

Cost-effectiveness analyses of lifestyle interventions are more complicated than evaluations of treatment where all important health effects can be expected to manifest in the short term. Their results are dependent, in part, on trial data as well as mathematical models. Short time-horizon studies have shown prediabetes lifestyle interventions to be cost-effective and even cost saving. Long time-horizon studies based on 10 to 30 year predictive mathematical models have used different models with different data, and have come to different conclusions about the cost-effectiveness of prediabetes lifestyle interventions [54-56,68-77]. Predictive models are useful, but they also have limitations. It is difficult to base a long time-horizon policy decision on predictive models when long-term randomized controlled trial data are not available to support the conclusions of those models.

The adoption of diabetes prevention programs by health plans and society will result in important health benefits over 10 years and represents a good value for the money spent. If the lifestyle intervention could be delivered at one-third lower cost than the intensive lifestyle interventions of the existing studies and achieve the same outcomes, it would be more cost-saving or cost-effective compared with placebo [32,55,56,61,70]. This might be achieved by changing the setting in which the intervention is provided. Although most large intensive lifestyle interventions seem to be cost-effective, medical nutrition therapy would be even more cost saving and/or cost-effective. Medical nutrition therapy is one form of lifestyle intervention that includes individual diet and exercise counselling and is administered by registered dieticians or other nutrition professionals. It has been shown to reduce diabetes risk factors, including body weight and blood glucose levels, and has shown success in diabetes management. The provision of medical nutrition therapy by registered dieticians or other nutrition professionals, who are experts in offering individualized nutrition counseling, will improve the quality of counseling offered to patients and alleviate the burden on physicians to provide nutrition education [65,78-84]. Although the cost of medical nutrition therapy is less than an intensive lifestyle intervention, more research is needed in the area of this form of intervention and community diabetes prevention programs to assess the effectiveness at decreasing diabetes incidence in the long term.

Many studies have methodological deficiencies since a minority of cost-effectiveness models for diabetes prevention accounted for the multivariate impacts of interventions on risk factors for T2D. While many studies mentioned above show that a health gain can be achieved by people at risk for diabetes, other analysis on reducing risk by lifestyle change did not show the expected effects and proved to be not cost-effective for health plans or a national program to implement [55,69].

Discussion

The increasing prevalence of T2D, the increase in modifiable risk factors for the disease (obesity, sedentary behaviour and poor nutritional choices), as well as the severe and costly complications which can be difficult to prevent and treat, mean that prevention is an important strategy for reducing the burden of diabetes. Improved nutritional habits like Mediterranean diet and increased physical activity are of particular importance to reduce the risk of T2D incident and to decelerate the manifestations of the disease [8,21,40,78,85-91].

Lifestyle modification has been shown to effectively reduce the risk of incident diabetes in randomised controlled trials. In addition, lifestyle modification is likely to produce beneficial other effects like reduction in risk of hypertension, hyperlipidemia, CVD and certain cancers. The main challenge is to translate this evidence into a routine community-wide setting and provide a feasible, effective and cost-effective intervention [6,8,19,21,40,41,92,93].

The key factor that reduces diabetes risk is weight loss and thus all efforts to translate the prevention trials to a community setting have focused on weight reduction. Weight regain is very common in weight loss studies that use a behaviour intervention [93-96]. Thus, it is extremely difficult to maintain weight loss, even in studies where

the intervention is still in full force and the enrolees are extremely well motivated. In addition, more evidence is needs to establish whether such intensive face-to-face individual implementation strategies are feasible in the long-term, whether group-based or remote contacts provides comparable efficacy in a more cost effective manner, and whether less-skilled personnel can deliver these same interventions [83,84,92-99]. Actually, the most successful interventions were obtained using many personnel and intensive supervision while the current practice requests less expensive, simple interventions which can be easily carried out in daily practice.

The key questions which can be addressed by all randomized controlled trials relate to the delivery, effects, costs and structure of community-based lifestyle modification programs, including key barriers and facilitators and key determinants of process and impact outcomes. Barriers in translating intensive interventions to a 'real life' setting include lengthy and unpleasant diagnostic testing procedures to identify pre-diabetes such as 2-hour oral glucose tolerance tests, the cost of highly educated personnel to provide the intervention and offering the intervention in locations such as single medical centres which are near to the homes of the participants [21,92-103].

Continued data from randomized controlled trials are needed to more fully understanding the long-term effects of these interventions and compare interventions with predictive models. Realistic cost-effectiveness studies of lifestyle interventions in people at risk for lifestyle-related diseases, addressing 'real-world' implementation, are also needed [21,104,105].

Still it is concluded that combined lifestyle interventions are likely to have great potential as a strategy to prevent diabetes. Finally, it may be more beneficial to achieve diabetes prevention by attacking the problem through national policies that reduce the overall consumption of food. In the long run, a combination of a societal and medical solution to the obesity/diabetes epidemic may end up being the best option.

In conclusion, for large-scale implementation of preventive strategies, the future plan should focus on health education of the public, improving the national capacity to detect and manage non-communicable diseases and development of innovative, cost effective, and scalable methodologies. Undoubtedly diabetes is one of the most challenging health problems of the 21st century.

References

1. Seaquist ER (2014) Addressing the burden of diabetes. JAMA 311: 2267-2268.
2. World Health Organization (2010) World Health Statistics 2010. WHO Press, Geneva, Switzerland.
3. World Health Organization (2013) Global action Plan for the Prevention and Control of non-communicable Disease 2013-2020. WHO Press, Geneva, Switzerland.
4. International Diabetes Federation Diabetes (2013) International Diabetes Federation Diabetes Atlas 6th Edition. Brussels.
5. Kolb H, Mandrup-Poulsen T (2010) The global diabetes epidemic as a consequence of lifestyle-induced low-grade inflammation. Diabetologia 53: 10-20.
6. Hossain P, Kawar B, El Nahas M (2007) Obesity and diabetes in the developing world--a growing challenge. N Engl J Med 356: 213-215.
7. Lyssenko V, Jonsson A, Almgren P, Pulizzi N, Isomaa B, et al. (2008) Clinical risk factors, DNA variants, and the development of type 2 diabetes. N Engl J Med 359: 2220-2232.
8. Simmons RK, Unwin N, Griffin SJ (2010) International Diabetes Federation: An update of the evidence concerning the prevention of type 2 diabetes. Diabetes Res Clin Pract 87: 143-149.
9. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, et al. (2003) The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity. Diabetes Care 26: 3230-3236.
10. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, et al. (2002) Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 346: 393-403.
11. Li G1, Zhang P, Wang J, Gregg EW, Yang W, et al. (2008) The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 371: 1783-1789.
12. Venditti EM, Bray GA, Carrion-Petersen ML, Delahanty LM, Edelstein SL, et al. (2008) First versus repeat treatment with a lifestyle intervention program: attendance and weight loss outcomes. Int J Obes (Lond) 32: 1537-1544.
13. Ramachanran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, et al (2006) The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). Diabetologia 49:289-297
14. Coutinho W (2009) The first decade of sibutramine and orlistat: a reappraisal of their expanding roles in the treatment of obesity and associated conditions. Arq Bras Endocrinol Metabol 53: 262-270.
15. Chiasson JL (2006) Acarbose for the prevention of diabetes, hypertension and cardiovascular disease in subjects with impaired glucose tolerance: The Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) Trial. Endocr Pract 12:S25-S30.
16. DREAM Trial Investigators, Dagenais GR, Gerstein HC, Holman R, Budaj A, et al. (2008) Effects of ramipril and rosiglitazone on cardiovascular and renal outcomes in people with impaired glucose tolerance or impaired fasting glucose: results of the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) trial. Diabetes Care 31: 1007-1014.
17. Defronzo RA, Banerji M, Bray GA, Buchanan TA, Clement S, et al. (2009) Actos Now for the prevention of diabetes (ACT NOW) study. BMC Endocr Disord 9: 17.
18. Ramachandran A, Snehalatha C, Mary S, Selvam S, Kumar CK, et al (2009) Pioglitazone does not enhance the effectiveness of lifestyle modification in prevention conversion of impaired glucose tolerance to diabetes in Asian Indians: results of the Indian Diabetes Prevention Programme-2 (IDPP-2). Diabetologia 52:1019-1026.
19. Fradkin JE, Roberts BT, Rodgers GP (2012) What's preventing us from preventing type 2 diabetes? N Engl J Med 367: 1177-1179.
20. Thorpe KE (2012) Analysis & commentary: The Affordable Care Act lays the groundwork for a national diabetes prevention and treatment strategy. Health Aff (Millwood) 31: 61-66.
21. Green LW, Brancati FL, Albright A; Primary Prevention of Diabetes Working Group (2012) Primary prevention of type 2 diabetes: integrative public health and primary care opportunities, challenges and strategies. Fam Pract 29 Suppl 1: i13-23.
22. Lindström J, Peltonen M, Eriksson JG, Ilanne-Parikka P, Aunola S, et al. (2013) Improved lifestyle and decreased diabetes risk over 13 years: long-term follow-up of the randomised Finnish Diabetes Prevention Study (DPS). Diabetologia 56: 284-293.
23. Uusitupa M, Peltonen M, Lindström J, Aunola S, Ilanne-Parikka P, et al. (2009) Ten-year mortality and cardiovascular morbidity in the Finnish Diabetes Prevention Study--secondary analysis of the randomized trial. PLoS One 4: e5656.
24. Pan XR, Li GW, Hu YH, Wang JX, Yang WY, et al. (1997) Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 20: 537-544.
25. Li G, Zhang P, Wang J, An Y, Gong Q, et al. (2014) Cardiovascular mortality, all-cause mortality, and diabetes incidence after lifestyle intervention for people with impaired glucose tolerance in the Da Qing Diabetes Prevention Study: a 23-year follow-up study. Lancet Diabetes Endocrinol 2: 474-480.
26. Diabetes Prevention Program (DPP) Research Group (2002) The Diabetes Prevention Program (DPP): description of lifestyle intervention. Diabetes Care 25: 2165-2171.
27. Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, Hamman RF, Christophi CA, et al. (2009) 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study. Lancet 374: 1677-1686.

28. Diabetes Prevention Program Research Group1, Crandall J, Schade D, Ma Y, Fujimoto WY, et al. (2006) The influence of age on the effects of lifestyle modification and metformin in prevention of diabetes. J Gerontol A Biol Sci Med Sci 61: 1075-1081.

29. Perreault L, Pan Q, Mather KJ, Watson KE, Hamman RF, et al. (2012) Effect of regression from prediabetes to normal glucose regulation on long-term reduction in diabetes risk: results from the Diabetes Prevention Program Outcomes Study. Lancet 379: 2243-2251.

30. Perreault L, Temprosa M, Mather KJ, Horton E, Kitabchi A, et al. (2014) Regression from prediabetes to normal glucose regulation is associated with reduction in cardiovascular risk: results from the Diabetes Prevention Program outcomes study. Diabetes Care 37: 2622-2631.

31. Goldberg RB, Mather K (2012) Targeting the consequences of the metabolic syndrome in the Diabetes Prevention Program. Arterioscler Thromb Vasc Biol 32: 2077-2090.

32. Ackermann RT, Marrero DG, Hicks KA, Hoerger TJ, Sorensen S, et al. (2006) An evaluation of cost sharing to finance a diet and physical activity intervention to prevent diabetes. Diabetes Care 29: 1237-1241.

33. Lindgren P, Lindström J, Tuomilehto J, Uusitupa M, Peltonen M, et al. (2007) Lifestyle intervention to prevent diabetes in men and women with impaired glucose tolerance is cost-effective. Int J Technol Assess Health Care 23: 177-183.

34. Wylie-Rosett J, Herman WH, Goldberg RB (2006) Lifestyle intervention to prevent diabetes: intensive and cost effective. Curr Opin Lipidol 17: 37-44.

35. Ackermann RT, Finch EA, Brizendine E, Zhou H, Marrero DG (2008) Translating the Diabetes Prevention Program into the community. The DEPLOY Pilot Study. Am J Prev Med 35: 357-363.

36. Ackermann RT, Finch EA, Caffrey HM, Lipscomb ER, Hays LM, et al. (2011) Long-term effects of a community-based lifestyle intervention to prevent type 2 diabetes: the DEPLOY extension pilot study. Chronic Illn 7: 279-290.

37. Absetz P, Valve R, Oldenburg B, Heinonen H, Nissinen A, et al. (2007) Type 2 diabetes prevention in the “real world”: one-year results of the GOAL Implementation Trial. Diabetes Care 30: 2465-2470.

38. Laatikainen T, Dunbar JA, Chapman A, Kilkkinen A, Vartiainen E, et al. (2007) Prevention of type 2 diabetes by lifestyle intervention in an Australian primary health care setting: Greater Green Triangle (GGT) Diabetes Prevention Project. BMC Public Health 19: 249.

39. Kilkkinen A, Heistaro S, Laatikainen T, Janus E, Chapman A, et al. (2007) Prevention of type 2 diabetes in a primary health care setting. Interim results from the Greater Green Triangle (GGT) Diabetes Prevention Project. Diabetes Res Clin Pract 76: 460-462.

40. Mastellos N, Gunn LH, Felix LM, Car J, Majeed A (2014) Transtheoretical model stages of change for dietary and physical exercise modification in weight loss management for overweight and obese adults. Cochrane Database Syst Rev 2: CD008066.

41. Yoon U, Kwok LL, Magkidis A (2013) Efficacy of lifestyle interventions in reducing diabetes incidence in patients with impaired glucose tolerance: a systematic review of randomized controlled trials. Metabolism 62: 303-314.

42. Finnish Diabetes Association (2003) Program for the Prevention of Type 2 Diabetes in Finland 2003-2010.

43. Saaristo T, Peltonen M, Keinänen-Kiukaanniemi S, Vanhala M, Saltevo J, et al. (2007) National type 2 diabetes prevention programme in Finland: FIN-D2D. Int J Circumpolar Health 66: 101-112.

44. Saaristo T, Moilanen L, Korpi-Hyövälti E, Vanhala M, Saltevo J, et al. (2010) Lifestyle intervention for prevention of type 2 diabetes in primary health care: one-year follow-up of the Finnish National Diabetes Prevention Program (FIN-D2D). Diabetes Care 33: 2146-2151.

45. Salopuro TM, Saaristo T, Oksa H, Puolijoki H, Vanhala M, et al. (2011) Population-level effects of the national diabetes prevention programme (FIN-D2D) on the body weight, the waist circumference, and the prevalence of obesity. BMC Public Health 11: 350.

46. Kujala UM, Jokelainen J, Oksa H, Saaristo T, Rautio N, et al. (2011) Increase in physical activity and cardiometabolic risk profile change during lifestyle intervention in primary healthcare: 1-year follow-up study among individuals at high risk for type 2 diabetes. BMJ Open 1: e000292.

47. Rautio N, Jokelainen J, Oksa H, Saaristo T, Peltonen M, et al. (2012) Participation, socioeconomic status and group or individual counselling intervention in individuals at high risk for type 2 diabetes: one-year follow-up study of the FIN-D2D-project. Prim Care Diabetes 6: 277-283.

48. Schwarz PE, Linstrom J, Kissimova-Scarbeck K, Szybinski Z, Barengo NC et al. (2008) The European Perspective of Diabetes Prevention: Diabetes in Europe – Preventiong Using Lifestyle, Physical Activity and Nutritional Intervention (DE-PLAN) Project. Exp Clin Endocrinol Diabetes 116: 167-172.

49. Makrilakis K, Liatis S, Grammatikou S, Perrea D, Katsilambros N (2010) Implementation and effectiveness of the first community lifestyle intervention programme to prevent Type 2 diabetes in Greece. The DE-PLAN study. Diabet Med 27: 459-465.

50. Kontogianni MD, Liatis S, Grammatikou S, Perrea D, Katsilambros N, et al. (2012) Changes in dietary habits and their association with metabolic markers after a non-intensive, community-based lifestyle intervention to prevent type 2 diabetes, in Greece. The DEPLAN study. Diabetes Res Clin Pract 95: 207-214.

51. Singapore Diabetes Prevention Program (2008).

52. Cameron Diabetes Prevention Plan (2014).

53. Herman WH, Hoerger TJ, Brandle M, Hicks K, Sorensen S, et al. (2005) The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. Ann Intern Med 142: 323-332.

54. Colagiuri S, Walker AE (2008) Using an economic model of diabetes to evaluate prevention and care strategies in Australia. Health Aff (Millwood) 27: 256-268.

55. Neumann A, Schwarz P, Lindholm L (2011) Estimating the cost-effectiveness of lifestyle intervention programmes to prevent diabetes based on an example from Germany: Markov modelling. Cost Eff Resour Alloc 9: 17.

56. Saha S, Carlsson KS, Gerdtham UG, Eriksson MK, Hagberg L, et al. (2013) Are lifestyle interventions in primary care cost-effective?--An analysis based on a Markov model, differences-in-differences approach and the Swedish Björknäs study. PLoS One 8: e80672.

57. Gillett M, Royle P, Snaith A, Scotland G, Poobalan A, et al. (2012) Non-pharmacological interventions to reduce the risk of diabetes in people with impaired glucose regulation: a systematic review and economic evaluation. Health Technol Assess 16: 231-236.

58. Lawlor MS, Blackwell CS, Isom SP, Katula JA, Vitolins MZ, et al. (2013) Cost of a group translation of the Diabetes Prevention Program: Healthy Living Partnerships to Prevent Diabetes. Am J Prev Med 44: S381-389.

59. Vojta D, Koehler TB, Longjohn M, Lever JA, Caputo NF (2013) A coordinated national model for diabetes prevention: linking health systems to an evidence-based community program. Am J Prev Med 44: S301-S306.

60. Gillies CL, Lambert PC, Abrams KR, Sutton AJ, Cooper NJ, et al. (2008) Different strategies for screening and prevention of type 2 diabetes in adults: cost effectiveness analysis. BMJ 336: 1180-1185.

61. Herman WH, Edelstein SL, Ratner RE, Montez MG, Ackermann RT, et al. (2013) Effectiveness and cost-effectiveness of diabetes prevention among adherent participants. Am J Manag Care 19: 194-202.

62. Chatterjee R, Narayan KM, Lipscomb J, Phillips LS (2010) Screening adults for pre-diabetes and diabetes may be cost-saving. Diabetes Care 33: 1484-1490.

63. Echouffo-Tcheugui JB, Ali MK, Griffin SJ, Narayan KM (2011) Screening for type 2 diabetes and dysglycemia. Epidemiol Rev 33: 63-87.

64. Diabetes Prevention Program Research Group (2012) The 10-year cost-effectiveness of lifestyle intervention or metformin for diabetes prevention: an intent-to-treat analysis of the DPP/DPPOS. Diabetes Care 35: 723-730.

65. Anderson JM (2012) Achievable cost saving and cost-effective thresholds for diabetes prevention lifestyle interventions in people aged 65 years and older: a single-payer perspective. J Acad Nutr Diet 112: 1747-1754.

66. Zhuo X, Zhang P, Gregg EW, Barker L, Hoerger TJ, et al. (2012) A nationwide community-based lifestyle program could delay or prevent type 2 diabetes cases and save $5.7 billion in 25 years. Health Aff (Millwood) 31: 50-60.

67. Thorpe KE, Yang Z (2011) Enrolling people with prediabetes ages 60-64 in a proven weight loss program could save Medicare $7 billion or more. Health Aff (Millwood) 30: 1673-1679.

68. Eddy DM, Schlessinger L, Kahn R (2005) Clinical outcomes and cost-effectiveness of strategies for managing people at high risk for diabetes. Ann Intern Med 143: 251-264.

69. van Wier MF, Lakerveld J, Bot SD, Chinapaw MJ, Nijpels G, et al. (2013) Economic evaluation of a lifestyle intervention in primary care to prevent type 2 diabetes mellitus and cardiovascular diseases: a randomized controlled trial. BMC Fam Pract 14: 45.

70. Li R1, Zhang P, Barker LE, Chowdhury FM, Zhang X (2010) Cost-effectiveness of interventions to prevent and control diabetes mellitus: a systematic review. Diabetes Care 33: 1872-1894.

71. Johnson SL, Tabaei BP, Herman WH (2005) The efficacy and cost of alternative strategies for systematic screening for type 2 diabetes in the U.S. population 45-74 years of age. Diabetes Care 28: 307-311.

72. Waugh N, Scotland G, McNamee P, Gillett M, Brennan A, et al. (2007) Screening for type 2 diabetes: literature review and economic modelling. Health Technol Assess 11: iii-iv, ix-xi, 1-125.

73. Waugh NR, Shyangdan D, Taylor-Phillips S, Suri G, Hall B (2013) Screening for type 2 diabetes: a short report for the National Screening Committee. Health Technol Assess 17: 1-90.

74. Simmons RK, Echouffo-Tcheugui JB, Sharp SJ, Sargeant LA, Williams KM, et al. (2012) Screening for type 2 diabetes and population mortality over 10 years (ADDITION-Cambridge): a cluster-randomised controlled trial. Lancet 380: 1741-1748.

75. Chatterjee R, Narayan KM, Lipscomb J, Jackson SL, Long Q, et al. (2013) Screening for diabetes and prediabetes should be cost-saving in patients at high risk. Diabetes Care 36: 1981-1987.

76. Gulliford MC, Bhattarai N1, Charlton J, Rudisill C (2014) Cost-effectiveness of a universal strategy of brief dietary intervention for primary prevention in primary care: population-based cohort study and Markov model. Cost Eff Resour Alloc 12: 4.

77. Gulliford MC, Charlton J, Bhattarai N, Charlton C, Rudisill C (2014) Impact and cost-effectiveness of a universal strategy to promote physical activity in primary care: population-based cohort study and Markov model. Eur J Health Econ 15: 341-351.

78. Franz MJ, Boucher JL, Evert AB3 (2014) Evidence-based diabetes nutrition therapy recommendations are effective: the key is individualization. Diabetes Metab Syndr Obes 7: 65-72.

79. Dalziel K, Segal L (2007) Time to give nutrition interventions a higher profile: cost-effectiveness of 10 nutrition interventions. Health Promot Int 22: 271-283.

80. Delahanty LM1, Nathan DM (2008) Implications of the diabetes prevention program and Look AHEAD clinical trials for lifestyle interventions. J Am Diet Assoc 108: S66-72.

81. Delahanty LM (2010) Research charting a course for evidence-based clinical dietetic practice in diabetes. J Hum Nutr Diet 23: 360-370.

82. Delahanty LM (2010) An expanded role for dietitians in maximising retention in nutrition and lifestyle intervention trials: implications for clinical practice. J Hum Nutr Diet 23: 336-343.

83. Fitzgerald N, Morgan KT, Slawson DL (2013) Practice paper of the Academy of Nutrition and Dietetics abstract: the role of nutrition in health promotion and chronic disease prevention. J Acad Nutr Diet 113: 983.

84. Loveman E, Frampton GK, Shepherd J, Picot J, Cooper K, et al. (2011) The clinical effectiveness and cost-effectiveness of long-term weight management schemes for adults: a systematic review. Health Technol Assess 15: 1-182.

85. Ajala O, English P, Pinkney J (2013) Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes. Am J Clin Nutr 97: 505-516.

86. Looney SM, Raynor HA (2013) Behavioral lifestyle intervention in the treatment of obesity. Health Serv Insights 6: 15-31.

87. Wong ND, Patao C, Malik S, Iloeje U (2014) Preventable coronary heart disease events from control of cardiovascular risk factors in US adults with diabetes (projections from utilizing the UKPDS risk engine). Am J Cardiol 113: 1356-1361.

88. Karstoft K, Winding K, Knudsen SH, James NG, Scheel MM, et al. (2014) Mechanisms behind the superior effects of interval vs continuous training on glycaemic control in individuals with type 2 diabetes: a randomised controlled trial. Diabetologia 57: 2081-2093.

89. Schwingshackl L, Missbach B, Dias S, König J, Hoffmann G (2014) Impact of different training modalities on glycaemic control and blood lipids in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetologia 57: 1789-1797.

90. Mitjavila MT, Fandos M, Salas-Salvadó J, Covas MI, Borrego S, et al. (2013) The Mediterranean diet improves the systemic lipid and DNA oxidative damage in metabolic syndrome individuals. A randomized, controlled, trial. Clin Nutr 32: 172-178.

91. Salas-Salvadó J, Bulló M, Estruch R, Ros E, Covas MI, et al. (2014) Prevention of diabetes with Mediterranean diets: a subgroup analysis of a randomized trial. Ann Intern Med 160: 1-10.

92. Uusitupa M, Tuomilehto J, Puska P (2011) Are we really active in the prevention of obesity and type 2 diabetes at the community level? Nutr Metab Cardiovasc Dis 21: 380-389.

93. Rautio N, Jokelainen J, Saaristo T, Oksa H, Keinänen-Kiukaanniemi S; FIN-D2D Writing Group, et al. (2013) Predictors of success of a lifestyle intervention in relation to weight loss and improvement in glucose tolerance among individuals at high risk for type 2 diabetes: the FIN-D2D project. J Prim Care Community Health 4: 59-66.

94. Lindström J, Absetz P, Hemiö K, Peltomäki P, Peltonen M (2010) Reducing the risk of type 2 diabetes with nutrition and physical activity - efficacy and implementation of lifestyle interventions in Finland. Public Health Nutr 13: 993-999.

95. Lakerveld J, Bot SD, Chinapaw MJ, van Tulder MW, Kostense PJ, et al. (2013) Motivational interviewing and problem solving treatment to reduce type 2 diabetes and cardiovascular disease risk in real life: a randomized controlled trial. Int J Behav Nutr Phys Act 10: 47.

96. Hardcastle SJ, Taylor AH, Bailey MP, Harley RA, Hagger MS (2013) Effectiveness of a motivational interviewing intervention on weight loss, physical activity and cardiovascular disease risk factors: a randomised controlled trial with a 12-month post-intervention follow-up. Int J Behav Nutr Phys Act 10: 40.

97. Steyn NP, Lambert EV, Tabana H (2009) Conference on "Multidisciplinary approaches to nutritional problems". Symposium on "Diabetes and health". Nutrition interventions for the prevention of type 2 diabetes. Proc Nutr Soc 68: 55-70.

98. Eichler K, Wieser S, Brügger U (2009) The costs of limited health literacy: a systematic review. Int J Public Health 54: 313-324.

99. Schwarz PE, Li J, Lindström J, Bergmann A, Gruhl U, et al. (2007) How should the clinician most effectively prevent type 2 diabetes in the obese person at high risk? Curr Diab Rep 7: 353-362.

100. Kutob RM, Siwik VP, Aickin M, Ritenbaugh C (2014) Families United/Familias Unidas: family group office visits to reduce risk factors for type 2 diabetes. Diabetes Educ 40: 191-201.

101. Ramachandran A, Snehalatha C, Ram J, Selvam S, Simon M, et al. (2013) Effectiveness of mobile phone messaging in prevention of type 2 diabetes by lifestyle modification in men in India: a prospective, parallel-group, randomised controlled trial. Lancet Diabetes Endocrinol 1: 191-198.

102. Chen P, Chai J, Cheng J, Li K, Xie S, et al. (2014) A smart web aid for preventing diabetes in rural China: preliminary findings and lessons. J Med Internet Res 16: e98.

103. Recio-Rodríguez JI, Martín-Cantera C, González-Viejo N, Gómez-Arranz A, Arietaleanizbeascoa MS, et al. (2014) Effectiveness of a smartphone application for improving healthy lifestyles, a randomized clinical trial (EVIDENT II): study protocol. BMC Public Health 14: 254.

104. Duijzer G, Jansen SC, Haveman-Nies A, van Bruggen R, Ter Beek J, et al. (2012) Translating the SLIM diabetes prevention intervention into SLIMMER: implications for the Dutch primary health care. Fam Pract 29 Suppl 1: i145-145i152.

105. Duijzer G, Haveman-Nies A, Jansen SC, ter Beek J, Hiddink GJ, et al. (2014) SLIMMER: a randomised controlled trial of diabetes prevention in Dutch primary health care: design and methods for process, effect, and economic evaluation. BMC Public Health 14: 602.