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International Diabetes Federation: a consensus on Type 2 diabetes prevention

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Abstract

Aims Early intervention and avoidance or delay of progression to Type 2 diabetes is of enormous benefit to patients in terms of increasing life expectancy and quality of life, and potentially in economic terms for society and health-care payers. To address the growing impact of Type 2 diabetes the International Diabetes Federation (IDF) Taskforce on Prevention and Epidemiology convened a consensus workshop in 2006. The primary goal of the workshop and this document was the prevention of Type 2 diabetes in both the developed and developing world. A second aim was to reduce the risk of cardiovascular disease in people who are identified as being at a higher risk of Type 2 diabetes.

The IDF plan for prevention of Type 2 diabetes is based on controlling modifiable risk factors and can be divided into two target groups:

- People at high risk of developing Type 2 diabetes
- The entire population.

Conclusions In planning national measures for the prevention of Type 2 diabetes, both groups should be targeted simultaneously with lifestyle modification the primary goal through a stepwise approach. In addition, it is important that all activities are tailored to the specific local situation.

Further information on the prevention of diabetes can be found on the IDF website: http://www.idf.org/prevention.

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Keywords International Diabetes Federation, population, prevention, risk factors, Type 2 diabetes

Abbreviations NCEP-ATP III, National Cholesterol Education Program—Third Adult Treatment Panel; BMI, body mass index; DEHKO, Development Programme for the Prevention and Care of Diabetes in Finland; DPP, Diabetes Prevention Program; DPS, Diabetes Prevention Study; DREAM, Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication; GI, gastro-intestinal; HDL, high-density lipoprotein; IDF, International Diabetes Federation; IDPP, Indian Diabetes Prevention Programme; IGT, impaired glucose tolerance; ILC, intensive lifestyle changes; LDL, low-density lipoprotein; NGT, normal glucose tolerance; PPAR, peroxisome proliferators-activated receptors; RRR, relative risk reduction; STOP-NIDDM, Study to Prevent Non-Insulin-Dependent Diabetes Mellitus; TRIPOD, Troglitazone in Prevention of Diabetes; WHO, World Health Organization; XENDOS, XENical in the Prevention of Diabetes in Obese Subjects

Introduction

Type 2 diabetes mellitus is now found in almost every population and epidemiological evidence suggests that without effective prevention and control programmes, the prevalence will continue to increase globally [1]. The impact of this increase in diabetes prevalence on costs is well illustrated in the Australian setting, where a 3.7-fold increase in disease-attributable costs of diabetes has been projected by 2051 [2].

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Table 1 Modifiable and non-modifiable risk factors and associated disorders for Type 2 diabetes

Modifiable risk factors	Non-modifiable risk factors
Overweight* and obesity† (central and total)	Ethnicity
Sedentary lifestyle	Family history of Type 2 diabetes
Previously identified glucose intolerance (IGT and/or IFG)	Age
Metabolic syndrome:	Gender
Hypertension	History of gestational diabetes
Decreased HDL cholesterol	Polycystic ovary syndrome
Increased trigylcerides	
Dietary factors	
Intrauterine environment	
Inflammation	

*World Health Organization (WHO) criteria define overweight as a BMI ≥ 25 kg/m^2 [50].
†WHO criteria define obesity as a BMI ≥ 30 kg/m^2 [50]. For country/ethnic specific values for waist circumference as a measure of central obesity see table 4.
HDL, high-density lipoprotein; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

Approximately 75–80% of people with diabetes die of cardiovascular disease. People with Type 2 diabetes have a two to four times higher risk of coronary heart disease than the rest of the population, and their prognosis is poorer. The risk of cerebrovascular and peripheral vascular disease is also significantly higher [3]. Premature mortality caused by diabetes results in an estimated 12–14 years of life lost [4].

To address the growing impact of Type 2 diabetes and the need for its prevention, the International Diabetes Federation (IDF) convened a consensus workshop in Lisbon, Portugal in 2006. The 19 participants included experts in the fields of diabetes, public health, epidemiology, metabolism, exercise, nutrition and health economics. There were participants from each continent as well as from the World Health Organization (WHO), the American Diabetes Association (ADA) and the National Cholesterol Education Program—Third Adult Treatment Panel (NCEP-ATP III).

The primary goal of the workshop and this document is the prevention of Type 2 diabetes in both the developed and developing world. A second aim is to reduce the risk of cardiovascular disease in people who are identified as being at a higher risk of Type 2 diabetes. Further information on the prevention of diabetes can be found on the IDF website: www.idf.org/prevention.

Causes of diabetes

Type 2 diabetes is caused by a combination of genetic and lifestyle factors [5]. Although genes that predispose an individual to diabetes are considered to be an essential factor in the development of the disease, activation of a genetic predisposition requires the presence of environmental and behavioural factors, particularly those associated with lifestyle. The most significant factors are overweight, abdominal obesity and physical inactivity [6]. Intrauterine and early childhood influences may also play a role.

The rapidly increasing prevalence of Type 2 diabetes demonstrates the important role played by lifestyle factors and provides the potential for reversing the global epidemic of Type 2 diabetes. The most dramatic increases in Type 2 diabetes have occurred in populations where there have been rapid and major lifestyle changes. These include changes in diet, and reductions in physical activity, with consequent increases in the prevalence of overweight and obesity [7]. Risk factors for Type 2 diabetes can be classified as non-modifiable and modifiable (Table 1).

Non-modifiable risk factors

Genetic factors

Type 2 diabetes is associated with a strong genetic predisposition. It has not yet been possible to definitely identify the genes to which this susceptibility is linked. The magnitude of the differences between ethnic groups when exposed to similar environments implies a significant genetic contribution (Table 2).

Age and gender

The prevalence of Type 2 diabetes increases markedly with age. The age of onset has moved down into younger adults and even adolescents in recent decades, especially in countries where a major imbalance between energy intake and expenditure has emerged.

Previous gestational diabetes

With gestational diabetes, glucose tolerance usually returns to normal following delivery; however, these women have a substantially higher risk of developing Type 2 diabetes in later life.

Modifiable risk factors

Obesity

Obesity is the most important single risk factor for Type 2 diabetes. The WHO estimates that there are currently 1.1 billion people who are overweight and expect this total to rise to over 1.5 billion by 2015 [8]. Longitudinal studies have shown obesity

Table 2 Prevalence of diabetes in communities exposed to westernized lifestyle

Indigenous people in North America and Australia [7,51]	20–30%
Pacific Islanders and Australian Aboriginies [19,52]	20–30%
India and Middle East [53]	10–20%
Europe and North America [1]	5–10%
Africa [1]*	3.1%

*There are marked discrepancies between the rates of diabetes prevalence among different communities in sub-Saharan Africa. Studies suggest that there will be an increase in the number of people with diabetes as more people move to urban areas [1].

to be a powerful predictor of Type 2 diabetes development [9,10]. Furthermore, interventions directed at reducing obesity also reduce the incidence of Type 2 diabetes. Several studies indicate that waist circumference or waist-to-hip ratio, which reflect visceral (abdominal) fat, may be better indicators of the risk of developing Type 2 diabetes than body mass index [11,12]. These data confirm that the distribution of fat has importance over and above the total amount.

Physical inactivity

Physical activity levels have decreased over recent decades in many populations, and this has been a major contributor to the current global rise of obesity. Physical inactivity has been found, in both cross-sectional and longitudinal studies, to be an independent predictor of Type 2 diabetes in men and women [13–15]. For equivalent degrees of obesity, more physically active subjects have a lower incidence of diabetes.

Nutritional factors

Much uncertainty still surrounds the dietary factors involved in developing diabetes, partly because of the difficulty in collecting accurate dietary data. Nevertheless, some of the more consistent messages indicate that a high total calorie and low dietary fibre intake, a high glycaemic load and a low polyunsaturated to saturated fat ratio may predispose to the disease [16].

Other risk factors

While genetic and lifestyle factors appear to impart the greatest risk for Type 2 diabetes, there are other potential risk determinants that may have a modifiable element. Their importance on a population level is less likely to play a role, but these include low birthweight, exposure to a diabetic environment *in utero* and a potential inflammatory component [17,18].

Clustering of glucose intolerance and cardiovascular risk factors

Many high-risk ('pre-diabetic') individuals have a clustering of other cardiovascular disease risk factors, e.g. abdominal obesity, elevated levels of total triglycerides, low levels of high-density lipoprotein (HDL) cholesterol and elevated blood pressure, known as the metabolic syndrome, as well as raised low-density lipoprotein (LDL) cholesterol levels [19,20]. Because individuals with pre-diabetes are at a particularly high risk of developing cardiovascular disease, other cardiovascular risk factors such as smoking also need to be addressed. However, results of targeted trials specifically designed to prevent the metabolic syndrome are not currently available.

Review of prevention studies

The rapid escalation in the number of people with Type 2 diabetes and diabetes-related cardiovascular disease demands urgent preventative action.

Lifestyle intervention

Most interventions targeted at preventing Type 2 diabetes have aimed at achieving and maintaining a healthy body weight through a combination of dietary measures and physical activity in individuals who already have impaired glucose tolerance, a particularly high-risk group. Dietary recommendations across studies are quite similar, and stress the reduction of fat intake and an increase in vegetable consumption with moderate calorie restriction in overweight/obese populations. Most interventions also recommend 30–40 min of moderate physical activity on all or most days of the week with variable emphasis on high-intensity and resistance training exercise. However, the approach used to promote physical activity in the interventions range from simply providing exercise goals and tips on how to increase daily physical activity, to providing weekly supervised exercise training sessions [7,21,22]. (see Table 3)

Malmö Study

One of the earliest lifestyle intervention studies for the prevention of Type 2 diabetes was conducted in men aged 47–49 years in Malmö, Sweden [23]. Some impaired glucose tolerant (IGT) and all normal glucose tolerant (NGT) men received usual care, while all Type 2 diabetic men and the other IGT men underwent a lifestyle intervention. Of these, approximately 40% of individuals participating in the lifestyle intervention underwent 6 months of supervised physical training and 6 months of dietary treatment in a randomized crossover design. Men who participated in the lifestyle intervention had a lower incidence of Type 2 diabetes, and had a greater reversal of glucose intolerance compared with men who received usual care. At the 12-year follow-up, the IGT men who underwent the lifestyle intervention showed no difference

Table 3 Summary of major diabetes intervention studies

Study	Intervention	*n*	Relative risk reduction of T2DM vs. placebo (%)	Duration (years)
Malmö [23]	Lifestyle	181	63	6
Da Qing [24]	Lifestyle	577	42	6
DPS [17,25]	Lifestyle	522	58	3
DPP [18]	Lifestyle	3234	58	3
Japanese study [54]	Lifestyle	458	67	4
Indian study [28]	Lifestyle	531	28	3
DPP [18]	Metformin	3234	31	3
Indian study [28]	Metformin	531	26	3
Indian study [28]	Metformin + lifestyle	531	28	3
TRIPOD [31]	Troglitazone	266	55	2.5
DPP [18]	Troglitazone	3234	75	1
STOP-NIDDM [29]	Acarbose	1429	25	3
XENDOS [34]	Orlistat	3305	37	4
DREAM [32]	Rosiglitazone	5269	60	3

DPP, Diabetes Prevention Program; DPS, Diabetes Prevention Study; STOP-NIDDM, Study to Prevent Non-Insulin-Dependent Diabetes Mellitus; T2DM, Type 2 diabetes mellitus; TRIPOD, Troglitazone in Prevention of Diabetes; XENDOS, XENical in the Prevention of Diabetes in Obese Subjects.

in mortality rates when compared with NGT men, and had less than half the mortality rate when compared with IGT men who received usual care.

Da Qing Study

The Da Qing Study examined the effect of a 6-year diet and exercise intervention in Chinese subjects with IGT and a mean age of 45 years [24]. The diet intervention alone was associated with a 31% reduction, while the exercise intervention alone showed a 46% reduction in the risk of developing Type 2 diabetes. However, the combined diet and exercise group had a similar 42% reduction in the risk of developing Type 2 diabetes during follow-up.

The Finnish Diabetes Prevention Study

The Finnish Diabetes Prevention Study (DPS) was the first randomized controlled trial to specifically examine the effect of a lifestyle intervention in preventing Type 2 diabetes [17,25]. This study randomized 522 overweight/obese subjects with IGT to either a lifestyle intervention or a control group and followed them for approximately 3.2 years. The lifestyle intervention provided individualized counselling focused on achieving and maintaining healthy body weight, reducing fat intake, increasing fibre intake and increasing physical activity. At 2-year follow-up, the incidence of Type 2 diabetes in the intervention group was less than half that observed within the control group. Further, the reduction in diabetes was related to the number and magnitude of the lifestyle changes made. Each component of the intervention: weight loss, increase in physical activity, reduction of total and saturated fat intake, and increase in dietary fibre contributed to the risk reduction. More recently, the DPS group has reported that the impact of lifestyle changes in reducing incidence of diabetes persisted for at least 4 years after the intensive intervention finished [26].

Diabetes Prevention Program

One of the largest randomized controlled clinical trials to date is the Diabetes Prevention Program (DPP), which was conducted in 3234 US adults with glucose intolerance. Unlike most previous studies, the cohort was diverse and included a large proportion of women (68%) and ethnic minorities (45%), and compared lifestyle intervention with drug intervention (metformin) and with a placebo control group over 2.8 years. The DPP reported that both lifestyle intervention and metformin had positive effects on the prevention of Type 2 diabetes and restoring normal glucose tolerance. However, the lifestyle intervention was more effective in preventing Type 2 diabetes, particularly in older adults. The lifestyle intervention group also tended to have a lower mortality rate than the metfomin intervention group. The cost-effectiveness of metformin vs. lifestyle is highly dependent on the costs of metformin. For example, considering the current generic metformin pricing in the USA, the price of both interventions is comparable.

A recent paper relating to the DPP concluded that an increase in physical activity helps sustain weight loss and independently reduces diabetes risk in those who do not lose weight [27]. Although the DPP was not originally intended to examine the metabolic syndrome per se, the DPP reports that lifestyle intervention also improves lipid parameters of the metabolic syndrome (fasting triglycerides and high-density lipoprotein cholesterol), and reduced the incidence of hypertension in addition to its positive effect on fasting glucose and glucose tolerance.

The Indian Diabetes Prevention Programme (IDPP)

The IDPP was a prospective community-based study, that examined whether the progression to diabetes could be influenced by interventions in Asian Indians with IGT who were leaner and more insulin resistant than populations studied

previously (multi-ethnic American, Finnish and Chinese populations) [28]. Results showed that progression of IGT to diabetes was high in Asian Indians. Both lifestyle modification and metformin significantly reduced the incidence of diabetes in Asian Indians with IGT, but there was no added benefit from combining them. The relative risk reduction was 28.5% with lifestyle modification, 26.4% with metformin and 28.2% with lifestyle modification combined with metformin.

Drug treatment

DPS and DPP have demonstrated the efficacy of intensive lifestyle intervention, but both of these trials had considerable health professional support to maintain dietary and exercise interventions [17,18,25]. Therefore, it is likely that the effect of lifestyle changes will be less in a real-life setting than in the published trials. Potential criteria to determine a reasonable lifestyle response include a 2-kg weight loss in 1 month or 5% loss at 6 months. Equally, a substantial fall in plasma glucose would indicate a reasonable response. As not all high-risk individuals are able to accept lifestyle changes and achieve these results, other interventions including drug treatment are needed.

Pharmacological intervention for the prevention of diabetes is therefore generally recommended as a secondary intervention to follow (or to be used in conjunction with) lifestyle intervention. If sufficient weight loss has not occurred, consideration should be given to the use of drug therapy. However, there is no trial-based evidence of the magnitude of preventative effect of pharmacotherapy in individuals who have failed to respond to lifestyle intervention.

Metformin

The rationale for the use of metformin is largely based on its 40-year long-term safety record and the results of the DPP and the more recent IDPP [18,28]. The DPP showed that metformin in the dose of 850 mg twice daily with meals reduced the 2.8-year incidence of diabetes by 31% compared with placebo and the incidence of metabolic syndrome by 17%. Metformin, however, is not recommended for everyone with IGT. Apart from the standard contraindications, metformin may predispose to lactic acidosis (renal, hepatic and ischaemic disorders), the DPP results suggest that metformin may be less effective in terms of diabetes prevention or delay in those aged 60 years or older.

Other potential limitations of metformin's use in the prevention of diabetes include GI side-effects in a minority of patients, which can often be reduced by building up the dose gradually. Moreover, those with a lower body mass index (BMI; 22–30 kg/m^2 range) responded less well, with a 3% relative risk reduction, compared with 16 or 35% for those with a BMI of 30–34 or ≥ 35 kg/m^2, respectively.

The IDPP-1 metformin data are generally consistent with DPP and show a similar relative risk reduction (RRR) of 26%, over 2.5 years, in a younger and thinner population of 531 subjects with IGT (mean age of 46 years and BMI of 26 kg/m^2) treated with a lower dose of metformin (250 mg b.i.d.) [28]. There was a similar benefit in those assigned to both metformin and lifestyle modification (28%) with no added benefit with both together. In contrast to DPP, IDPP shows a benefit with metformin in those with BMI well below 30 kg/m^2 (although it should be noted that obesity is often considered to be present in Asians at a lower BMI, e.g. > 25 kg/m^2).

Acarbose

Acarbose inhibits enzymes needed to digest carbohydrates. In the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM), acarbose achieved a 25% RRR in 714 subjects over 3.3 years without any major subgroup (e.g. age, gender or BMI) variations [29]. However, the pronounced GI side-effects and a 31% dropout rate (vs. 19% in the placebo group) in this study have somewhat limited its use for diabetes prevention. In addition to the reduced diabetes incidence, a remarkable 49% reduction in major cardiovascular events over 3 years was also noted (2.2 vs. 4.7%) with acarbose treatment. This could not be fully explained by weight loss and favourable cardiovascular risk factor reduction (notably a 34% reduction in incident hypertension). While caution should be advised against over interpretation of these findings, given the small number of total events (15 vs. 32), the STOP-NIDDM results clearly support the use of acarbose in those who can tolerate the GI side-effects to reduce diabetes and, potentially, cardiovascular risk [29]. Acarbose may reduce body weight in some patients, although in the clinical trials its weight reducing effect was negligible.

Glitazones

In the DPP, one group was treated initially with troglitazone. This was withdrawn after about a year because of hepatotoxicity [30]. In the Troglitazone in Prevention of Diabetes (TRIPOD) study, the cumulative incidence of diabetes dropped to zero in subjects treated with troglitazone for more than 3 years, suggesting true diabetes prevention [31]. Very recently the DREAM (Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication) study using rosiglitazone and an ACE inhibitor, ramipril, in a 2 × 2 factorial design reported their results in a large international multiethnic cohort of subjects with impaired fasting glucose (IFG) and/or IGT [32]. The rosiglitazone arm showed a greater than 60% decrease in progression to diabetes (from 25% with placebo to 10.6% with rosiglitazone) over a 3-year period, with 70% returning to normal glucose tolerance. Importantly, better results were seen in those with a higher BMI at the start of the trial. The results in DREAM were at the expense of weight gain (which was more around the hip leading to a decrease in waist–hip ratio, while waist circumference did not change) and a small but highly significant number of subjects developing congestive heart failure [32]. The results of repeat testing after a 2–3-month washout of rosiglitazone suggested that the effect was a delay rather than actual prevention, although it could be argued that this may well delay the development of microvascular complications.

Orlistat

Orlistat inhibits an enzyme that breaks down triglycerides in the intestine. In one study, orlistat caused a placebo-corrected weight loss of 3–5 kg over 6 months, which was maintained over 4 years. Treatment of obese subjects with IGT by orlistat as an adjuvant to diet and lifestyle modification has been associated with a lower incidence of Type 2 diabetes. Thus, in a retrospective analysis, orlistat reduced the 1-year incidence of Type 2 diabetes from 7.6% in the placebo group to 3.0% [33]. In the XENical in the Prevention of Diabetes in Obese Subjects (XENDOS) trial, 3304 non-diabetic obese subjects received intensive lifestyle modification and were randomized to either orlistat or placebo for 4 years [34]. There was a weight loss of 6.9 kg in the orlistat group (compared with 4.1 kg in the placebo group) after 4 years that was associated with a RRR in diabetes incidence of 37% (6.2 v 9.0%). The low rate of completion (52% in the orlistat group) limits the conclusions that can be drawn. GI side-effects are the main factors limiting its use.

Other agents

Sibutramine The role of the weight loss agent sibutramine in diabetes prevention remains to be established. No studies have been reported.

Rimonabant Rimonabant is the first selective endocannabinoid receptor antagonist to be developed. The RIO-Diabetes trial assessed the efficacy and safety of rimonabant in overweight or obese patients with Type 2 diabetes who were inadequately controlled by metformin or sulphonylureas. It found that rimonabant in combination with diet and exercise can produce a clinically meaningful reduction in body weight and improve HbA_{1c} and a number of cardiovascular and metabolic risk factors [35]. The results of a number of trials with rimonabant, particularly the RAPSODI (Rimonabant in Prediabetic Subjects to Delay Onset of Type 2 Diabetes) study which is examining the prevention of Type 2 diabetes in patients with pre-diabetes, are awaited with interest.

ACE inhibitors A number, but not all, trials using ACE inhibitors or ARB agents for hypertension, renal or cardiovascular risk reduction, have suggested a potential diabetes preventative effect, perhaps linked to improved insulin sensitivity. A recent meta-analysis of 12 clinical trials of ACE inhibitors or ARBs, showed that these agents were associated with reductions in the incidence of newly diagnosed diabetes of 27 and 23% respectively [36]. In the recently reported DREAM study, ramipril did not reduce the risk of diabetes, which affected 18% of participants on ramipril and 20% of those taking placebo [32].

The polypill Finally, given the multiplicity of medications (which may also include statins, aspirin and anti-hypertensive agents) that have proven benefit in subjects at higher risk of Type 2 diabetes and/or cardiovascular disease, the concept of the 'polypill' combining all appropriate drugs is attractive. Although this will need development and evaluation, its potential for improving adherence would seem considerable, and a very convenient way to provide a basic preventive intervention on to which further medications or higher doses can be added, as clinically indicated.

Health economics of diabetes prevention

Early intervention and avoidance or delay of progression to Type 2 diabetes is of enormous benefit, both to patients in terms of increasing life expectancy and quality of life, and potentially in economic terms for society and health-care payers. The cost-effectiveness of interventions aimed at halting or slowing the progress of impaired glucose tolerance to Type 2 diabetes has been examined in a number of clinical trials and computer modelling simulations. Because the costs of patient management programmes, medications and treatment of complications of Type 2 diabetes vary widely from country to country, country-specific analyses of the cost-effectiveness of diabetes prevention is essential. Intensive lifestyle changes (ILC), rosiglitazone, metformin and acarbose all provide significant health benefits, with ILC and rosiglitazone appearing to provide larger improvements than metformin and acarbose [18,37,38]. The majority of health economic studies performed to date demonstrate that diabetes prevention is highly cost-effective.

A number of other pharmacological interventions are currently under investigation in the prevention of diabetes. As the clinical results are published, health economics analyses of each new intervention will be required. Head-to head clinical trials will allow more robust direct cost-effectiveness comparisons between different pharmacological approaches to diabetes prevention.

In the absence of long-term follow-up data (> 10 years) from diabetes prevention studies, computer simulation modelling represents the best available approach to assess the long-term clinical and economic impact of diabetes prevention programs.

Reimbursement decisions made by health-care payers have to be based on appropriate time horizons. The relatively short-term studies such as the DPP Research Group (within Trial Analysis) are at risk of substantially underestimating the cost-effectiveness of treatments designed to delay or prevent the onset of diseases with long-term complications such as diabetes [39]. Such short-term comparisons fail to capture long-term complications, which may lead to an underestimate of cost savings as a result of complications avoided.

To provide relevant information for the health-care payer, analyses must be tailored to their specific setting. The economic variations observed when implementing the DPP interventions in a European or an Australian setting graphically demonstrate the need for this [40]. The same treatment can be dominant, cost-effective or not attractive at all depending upon variations in settings. No assumptions should be made on the suitability

of any course of action based on the results seen in a different setting. Any analysis must consider the costs of treating diabetes complications and costs of medications in the relevant country.

The IDF strategy for diabetes prevention

There is clearly growing evidence that earlier detection of people with IGT and others at high risk, followed by interventions to delay or prevent Type 2 diabetes and improve glucose control, can result in clinically important reductions in the incidence of diabetes and its complications and co-morbidities.

The IDF plan for the prevention of Type 2 diabetes is based on controlling modifiable risk factors and can be divided into two target groups:

- people at a high risk of developing Type 2 diabetes;
- the entire population.

In planning national measures for the prevention of Type 2 diabetes, both groups should be targeted simultaneously. In addition, it is important that all activities are tailored to the specific local situation.

The high-risk approach

The IDF proposes a simple three-step plan for the prevention of Type 2 diabetes in those at increased risk:

The high-risk approach

Step 1: *Identification* of those who may be at higher risk
Step 2: *Measurement* of risk
Step 3: *Intervention* to prevent the development of Type 2 diabetes

Step 1—identification of those at high risk

The first step is the identification of individuals from the overall population who may be at higher than average risk of developing Type 2 diabetes. The IDF recommend the use of opportunistic screening by health-care personnel including those working in general practice, nurses and pharmacists.

Strategies to predict future risk of diabetes have generally used demographic and clinical data from prospective cohort studies and statistical models and risk scores. In general, they have not relied on measurements of blood glucose, but have included some measure of personal or family history of glucose intolerance. In this longitudinal approach, age and family history of high blood glucose appear to be most important. Such strategies appear to perform moderately well, with area under the ROC curve between 71 and 84% [41].

However, it should be noted that most of the strategies have been developed and tested in Europid populations. When applied to other Europid populations with similar distributions of risk factors, these strategies perform reasonably well. However, application of the same strategy to different populations often gives substantially different sensitivities, specificities, positive predictive values, and percentages of the population requiring further testing. A number of screening strategies also have been applied to populations with different ethnic origins. In general, these strategies do not perform well in different patient populations, most likely because of differences in population characteristics. This suggests a need for ethnic-specific screening strategies.

Questionnaire

Simple, practical, non-invasive and inexpensive methods are needed to identify individuals at high risk for IGT and diabetes and to limit the proportion of the population requiring diagnostic glucose tolerance tests. The IDF recommend the use of brief questionnaires to help health-care professionals to quickly identify people who may be at a higher risk and who need to have their level of risk further investigated. This type of questionnaire could also be used by individuals for self-assessment.

Questionnaire—suggested assessments

The following criteria should be included in the questionnaire. The presence of any of them puts an individual at a higher risk and further investigations should be undertaken to assess the level of risk.

Obesity
Central obesity is most easily measured by waist circumference with cut-points that are gender and ethnic group specific. For example, the waist-circumference cut point for Europid males is ≥ 94 cm and for Europid females is ≥ 80 cm (see Table 4 for ethnic specific cut points).

Family history
Immediate family member or other relatives diagnosed with diabetes.

Age
People over the following ages are at an increased risk:
≥ 45 years in Europids
≥ 35 years in rest of the world.

Cardiovascular history
History of raised blood pressure and/or heart disease.

Gestational history
Previous occurrence of gestational diabetes.

Drug history
Use of drugs that predispose a patient to Type 2 diabetes, including: nicotinic acid; glucocorticoids; thyroid hormone; beta-adrenergic antagonists; thiazides; dilantin; pentamidine; anti-psychotic agents; interferon-alpha therapy.

Finnish Type 2 Diabetes Risk Assessment Form

The Finnish Type 2 Diabetes Risk Assessment Form developed in 2001 is an example of an effective patient questionnaire and should be used as the basis for developing national questionnaires which take into account local factors [42,43]. It has eight scored questions, with the total test score providing a measure of the probability of developing Type 2 diabetes over the following 10 years. The reverse of the form contains brief advice on what the respondent can do to lower their risk of developing the disease, and whether they should seek advice or have clinical examinations. The test takes only a few minutes to complete and can be carried out on the Internet, in pharmacies or at various public campaign events.

The risk test is based on a highly representative random sample of the Finnish population. Seven variables clearly correlated with the risk of developing diabetes were chosen for the test: age; body mass index; waist circumference, use of anti-hypertensive medication; history of elevated blood glucose; meeting the criterion for daily physical activity and daily consumption of fruit and vegetables. The variables were assigned scores according to the relative risk they conferred, resulting in a range of 0–21 for the total score. History of diabetes in the family was incorporated in the final Risk Test, which made the maximum score 26. The respondent's likelihood of developing diabetes is higher, the more points they receive in the test. (*The Finnish Type 2 Risk Assessment form is available for download at www.idf.org/prevention.)*

Other currently available questionnaires

The American Diabetes Association has an interactive Diabetes Risk Test available on its website [44]. This test uses seven simple questions to calculate the risk category for an individual: very low risk; low to medium risk; or high risk of developing Type 2 diabetes.

In addition, a risk score has recently been developed to predict people at high risk of diabetes in Thailand [45]. This simple diabetes risk score, based on a set of variables not requiring laboratory tests, can be used to identify individuals who are likely to develop diabetes in the near future. The variables included are age, BMI, waist circumference, history of hypertension, and history of diabetes in parents or siblings. Moreover, the Cambridge Scoring System uses a simple risk score, based on characteristics that are routinely recorded in primary care, and can identify individuals at increased risk of having previously undiagnosed Type 2 diabetes for subsequent diagnostic testing [46].

In resource-poor settings where questionnaires are not available or impractical, measurement of waist girth gives a simple prescreening tool allowing those at highest risk to be identified.

Step 2—measuring level of risk

If, following step 1, a person is considered to be at increased risk for the development of Type 2 diabetes, they will proceed to step 2 and the measurement of risk by a health-care professional. The key investigation in step 2 is the measurement of plasma glucose. Other diabetic risk factors are also assessed at this stage.

Plasma glucose

Measurement of plasma glucose will not only detect cases of IFG or IGT, but also cases of undiagnosed diabetes. If fasting plasma glucose is ≥ 6.1–6.9 mmol/l or 110–125 mg/dl then an oral glucose tolerance test (OGTT) is recommended. The presence of IGT and IFG gives a considerably increased risk of developing Type 2 diabetes. Interventions targeted at such individuals therefore provide an opportunity to delay or prevent the onset of Type 2 diabetes.

Other risk factors

Other risk factors for diabetes that should also be assessed at this stage include the presence of increased waist circumference; high blood pressure; family history of diabetes; raised triglycerides; or a pre-existing cardiovascular disease (Table 5). The presence of any of these factors will increase a person's risk of developing diabetes. In addition, there should be assessment of additional cardiovascular risk factors such as HDL cholesterol, LDL cholesterol and smoking, the presence of which should receive appropriate treatment.

Step 3—intervention to lower risk

There is substantial evidence that lifestyle changes can help prevent the development of Type 2 diabetes and should be the initial intervention for all patients [17,18]. However, some patients, including those with a high level of risk of developing diabetes who cannot change their lifestyle sufficiently, will also require pharmacotherapy and should be encouraged to still maintain lifestyle changes, as they will continue to deliver long-term health benefits.

Lifestyle changes

Lifestyle modification should be the first choice to prevent or delay diabetes. Moreover, as lifestyle intervention has a number of other benefits, health-care providers should urge all overweight and/or sedentary individuals to adopt these changes, and such recommendations should be made at every opportunity. However, in order for lifestyle changes to be successfully implemented, serious societal changes are required (discussed later).

Weight Obesity, particularly abdominal obesity, is central to the development of Type 2 diabetes and related disorders and is therefore a focus for attention in the reduction of risk of diabetes. Weight loss improves insulin resistance, hyperglycaemia and dyslipidaemia in the short term, and reduces hypertension.

Subjects should therefore be encouraged to achieve and maintain a healthy body composition. A structured approach such as that taken during the Diabetes Prevention Program, can produce long-term weight loss of 5–7% of baseline body weight [18]. The aim is gradual weight loss (0.5–1.0 kg per week) through moderate calorie restriction and increased physical activity. This should be supported by regular daily/weekly self-monitoring of weight or waist circumference. Standard weight-loss diets recommend reducing the daily calorie intake below that necessary for weight maintenance (depending on the individual's age and gender) by 500–1000 calories. Although very-low calorie diets and meal-replacement plans can produce impressive short-term results, they are of limited value in long-term weight-loss regimens. A complete change of dietary habits, particularly restricting fat consumption, is the most important approach to achieving sustained weight loss. Control of carbohydrate intake is also

Table 4 Country/ethnic specific values for waist circumference (as a measure of central obesity)

Country/ethnic group		Waist circumference (as measure of central obesity; measured at the midpoint between the bottom of the ribs and the top of the pelvis)
Europids*	Male	≥ 94 cm
	Female	≥ 80 cm
South Asians	Male	≥ 90 cm
	Female	≥ 80 cm
Chinese	Male	≥ 90 cm
	Female	≥ 80 cm
Japanese†	Male	≥ 90 cm
	Female	≥ 80 cm
Ethnic South and Central Americans		Use South Asian recommendations until more specific data are available
Sub-Saharan Africans		Use European data until more specific data are available
Eastern Mediterranean and Middle East (Arab) populations		Use European data until more specific data are available

These are pragmatic cut points and better data are required to link them to risk. Ethnicity should be the basis for classification, not the country of residence.
*In the USA the ATP III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes [55].
†There is lack of agreement about the ideal waist cut-off points for Japanese. The best correlates with visceral fat are a waist of 85 cm in males and 90 cm in females. However, the best agreement with cardiovascular disease and diabetes risk factors are 90 cm and 80 cm, respectively. Further work is required to resolve this problem.

important, as simple carbohydrates (with a high glycaemic index) exert an additional metabolic challenge to patients.

Physical activity Increased physical activity is particularly important in maintaining weight loss. Regular physical activity also improves insulin sensitivity; reduces plasma levels of insulin in patients with hyperinsulinaemia; improves dyslipidaemia and lowers blood pressure. Moreover, physical activity increases metabolically active muscle tissue and improves general cardiovascular health. Increased physical activity also reduces the risk of Type 2 diabetes.

The IDF recommends a goal of at least 30 min of moderate physical activity (e.g. brisk walking, swimming, cycling, dancing) on most days of the week. Regular walking for at least 30 min per day reduces diabetes risk by 35–40%. This can comprise several bouts of activity adding up to 30 min.

It is important to assess patients carefully before they commence any exercise regimen to identify any contraindications. For patients who have had a sedentary lifestyle, exercise programmes should start slowly and gradually build up.

Pharmacological intervention

The IDF recommends that when lifestyle intervention alone has not achieved the desired weight loss, and/or improved glucose tolerance goals, as set by the health-care provider, metformin in the dose of 250–850 mg b.i.d. (depending on tolerance) should be considered as a diabetes prevention strategy (particularly in those aged less than 60 years with a BMI > 30 kg/m^2 (greater than 27 kg/m^2 in certain ethnic populations) and a FPG > 6.1 mmol/l or 110 mg/dl who do not have any contraindications).

Acarbose is also worthy of consideration for those who can tolerate it. PPAR gamma agonists such as rosiglitazone have shown promising results, but concerns must remain about side-effects including weight gain and congestive heart failure as well as durability, and so we do not recommend them for routine use at present. A further option for the obese might be orlistat.

Similarly, newer agents such as rimonabant show some promise, but long-term safety and specific diabetes preventive efficacy data are lacking and are not currently recommended for diabetes prevention in those at increased risk. The IDF working group awaits with interest the results of ongoing studies into newer therapies.

The population approach

The IDF population approach to the prevention of Type 2 diabetes aims to bring about important changes in the health of a large percentage of the population. It is based on promoting healthy lifestyles that are effective in the prevention of Type 2 diabetes, as well as other chronic diseases including cardiovascular disease, hypertension and many other non-communicable diseases. The dominant effect of obesity in precipitating glucose intolerance and its consequences suggests that reversal of the diabetes epidemic can only come about with urgent and substantial changes to lifestyles. The prevention of obesity is founded on an increase in daily activity and healthier eating habits, thus rendering the balance between energy intake and energy utilization more favourable. Type 2 diabetes is a disease of slow onset, the prevalence of which increases with age. Its prevention therefore cannot be accomplished rapidly or with a single measure, and the approach must instead be methodical and sustained over a long period of time.

Table 5 Other risk factors for diabetes

Other diabetic risk factors	
Raised triglycerides	TG ≥ 1.7 mmol/l (150 mg/dl), or specific treatment for this lipid abnormality
Reduced HDL cholesterol	< 1.03 mmol/l (40 mg/dl) in males < 1.29 mmol/l (50 mg/dl) in females or specific treatment for this lipid abnormality
Waist circumference	See Table 4
Blood pressure	Raised blood pressure is defined as systolic pressure ≥ 130 mmHg and/or ≥ 85 mmHg Or treatment of previously diagnosed hypertension
Family history of diabetes	First-degree relative with diabetes
Pre-existing cardiovascular disease	Ischaemic heart disease, cerebrovascular disease, peripheral arterial disease

HDL, high-density lipoprotein; TG, triglyceride.

Simply distributing information on health hazards and how to avoid them is not sufficient for the prevention of chronic diseases such as Type 2 diabetes in the general population. In the past, efforts have been directed at improving the knowledge and skills of individuals, but this approach has not proved to be very successful in reducing obesity and increasing physical activity levels. In societies that encourage unhealthy lifestyles, information and education alone will not succeed. Attention must be paid to the creation of an environment and conditions that are conducive to achieving and maintaining an active lifestyle and healthy eating habits. An environment that promotes physical activity and optimum nutrition will help prevent those at high risk from developing diabetes, while also preventing those at low risk from becoming high risk.

The IDF population approach recognizes that the health sector on its own cannot accomplish population-wide changes. New strategic relationships with groups not normally associated with health but whose activities have an impact on health are needed. For example, the food industry (producers, processors, distributors, retailers and restauranteurs) is a key partner for reducing the energy density and fat content of food.

Unlike the interventions that focus on high-risk individuals, the population-based approach to the prevention of Type 2 diabetes is not supported by a large database of clinical studies. One recent study used baseline and follow-up data from EPIC-Norfolk, a UK cohort of 24 155 [47]. It assessed the association between the achievement of five 'diabetes healthy behaviour prevention goals' (BMI < 25 kg/m^2, fat intake < 30% of energy intake, saturated fat intake < 10% of energy intake, fibre intake ≥ 15 g/1000 kcal, physical activity > 4 h/week) and the risk of developing diabetes at follow-up (mean 4.6 years). Diabetes incidence was inversely related to the number of goals achieved ($P < 0.001$). None of the participants who met all five of the goals developed diabetes, whereas diabetes incidence was highest in those who did not meet any goals. If the entire population were able to meet one more goal, the total incidence of diabetes would be predicted to fall by 20%. This finding suggests that interventions that result in an increase in healthy behaviour in the general population could significantly reduce the growing burden of diabetes-related morbidity and mortality.

With this in mind, the IDF population strategy requires the governments of all countries to develop and implement a National Diabetes Prevention Plan. This national plan would encompass many groups including schools; communities (for example, religious and ethnic groups); industry (marketing, investment policy, product development) and the workplace (health promotion within the working environment).

Finland is one of the first countries to implement such a large-scale diabetes prevention strategy. Following on from the DPS study, the Finnish Diabetes Association has devised a national strategy for preventing Type 2 diabetes: The Development Programme for the Prevention and Care of Diabetes in Finland 2000–2010 (DEHKO) [48]. This programme comprises three concurrent approaches: a population strategy aimed at promoting the health of the entire nation; an individualized strategy for those at high risk; and a strategy of early diagnosis and management for those with new-onset Type 2 diabetes. The population strategy focuses on nutritional interventions and increased physical activity so that the risk factors for Type 2 diabetes are reduced in all age groups. A pilot study (FIN-D2D) assessing practical feasibility and cost-effectiveness is currently under way in four hospital districts (2003–2007), and results from this pilot will direct the focus of the national scheme. In 2010, the population-level effects of the programme will be studied in terms of coverage, effectiveness, rate of adoption, feasibility and permanence.

Until the results from the Finnish DEHKO study are available, research from population-based interventions focusing on reducing cardiovascular risk can provide clues for a population approach to diabetes prevention. For example, in 1987 the government of Mauritius issued a national non-communicable disease intervention programme, aimed at modifying levels of risk factors related to lifestyle, including glucose intolerance, hypertension, hyperlipidaemia, obesity, cigarette smoking,

alcohol misuse and physical inactivity [49]. Primary prevention components of the programme included extensive use of the mass media, fiscal and legislative measures, and widespread community, school and workplace health education activities. After 5 years, the results suggested significant decreases in the prevalence of hypertension, cigarette smoking and heavy alcohol consumption. Moderate physical activity increased and the mean population cholesterol fell considerably from 5.5 to 4.7 mmol/l. This dramatic fall was linked to a regulated change to the saturated fat content of a widely used cooking oil [56]. While the prevalence of overweight and obesity increased, and rates of glucose intolerance changed little, the population frequency distributions of blood pressure, serum lipid concentrations and the composite risk factor score shifted advantageously. These results suggest that lifestyle intervention projects can be implemented and have positive effects in developing countries.

Clearly, the prevention of obesity and Type 2 diabetes in both the developed and developing world will require coordinated policy and legislative changes with greater attention given to the urban environment, transportation infrastructure and workplace opportunities for education and exercise. Governments, national and local, should commit to optimizing opportunities for exercise in a safe environment. A multidisciplinary, politically driven and co-ordinated approach in health, finance, education, sports and agriculture can contribute to a reversal of the underlying causes of the Type 2 diabetes epidemic.

Major legislative and other regulatory measures may be required similar to those needed to address illness arising from tobacco usage. For example, there must be political will to transform the school environment and curriculum to improve physical and nutritional education to reduce the impact of childhood obesity. There is a need for statutory food labelling as currently labels cannot be understood by most consumers and health claims are often misleading. Importantly, each National Diabetes Prevention Plan will need to take into account local and ethnic issues such as local perceptions of obesity and attitudes towards physical activity.

The IDF population approach to diabetes prevention

Based on the findings of lifestyle prevention studies, the IDF recommends that:

- Everyone is encouraged to engage in at least 30 min of moderately intense (e.g. brisk walking) most days of the week.
- Everyone should be encouraged to maintain a healthy weight.
- Adults with BMI > 25 kg/m^2 in Europids and > 23 kg/m^2 in Asians should be encouraged to attain and maintain a healthy weight and/or 5–10% weight reduction.
- Children should be encouraged to attain and maintain weight for height in the normal range.

Priorities in developed and developing worlds

- Approach needs to be culturally sensitive.
- Cultural beliefs (e.g. about obesity) need to be understood and addressed.

National Diabetes Prevention Plans
Government initiatives should include:

- Advocacy
  - —supporting national associations and non-government organizations
  - —promoting the economic case for prevention
- Community support
  - —Providing education in schools re: nutrition and physical activity
  - —Promoting opportunities for physical activity through urban design (e.g. to encourage cycling and walking)
  - —Supporting sports facilities for the general population
- Fiscal and legislative
  - —Examining food pricing, labelling and advertising
  - —Enforcing environmental and infrastructure regulation, e.g. urban planning and transportation policy to enhance physical activity
- Engagement of private sector
  - —Promoting health in the workplace
  - —Ensuring healthy food policies in food industry
- Media communication
  - —Improving level of knowledge and motivation of the population (press, TV and radio)

Competing interests

KGMMA receives periodic consultancy fees from AstraZeneca, GlaxoSmithKline, Novartis and Servier. PZ has received consultant fees from Novartis, GlaxoSmithKline, Bristol Myer Squibb, Bayer AG, Abbott and Merck and has received payment for speaking from E. Merck, Sanofi-Aventis, AstraZeneca, Kissei and Fournier. JS has received consultant fees from Merck, Eli Lilly and Novo Nordisk.

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