Long-Term Benefits From Lifestyle Interventions for Type 2 Diabetes Prevention

Time to expand the efforts

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The potential to prevent type 2 diabetes in high-risk individuals by lifestyle intervention was established in several clinical trials. These studies had a strong focus on increased physical activity and dietary modification as well as weight reduction among overweight participants. The key issue seems to be a comprehensive approach to correct several risk factors simultaneously. Furthermore, long-term follow-up studies of lifestyle interventions lasting for a limited time period seem to have a long-lasting carry-over effect on risk factors and diabetes incidence (Table 1).

The research evidence has inspired national and local authorities and health care providers all over the world to start programs and activities to prevent type 2 diabetes and its complications. Based on the experiences from the clinical trials, as well as from the "real world" implementation programs, the IMAGE (Development and Implementation of a European Guideline and Training Standards for Diabetes Prevention) Study Group collated information in a systematic manner. The IMAGE deliverables include a European evidence-based guideline for the prevention of type 2 diabetes, a toolkit for the prevention of type 2 diabetes in Europe, and the quality indicators for the prevention of type 2 diabetes in Europe.

What is needed now is political support to develop national action plans for diabetes prevention. The prerequisites for successful prevention activities include involvement of a number of stakeholders on the governmental and nongovernmental level as well as on different levels of health care. Furthermore, structures to identify high-risk individuals and manage intervention, follow-up, and evaluation have to be established.

Observational studies have provided firm evidence that multiple lifestyle-related factors either increase or decrease the risk of type 2 diabetes. Thus, in type 2 diabetes prevention, it is important to pay attention not only to one single factor such as obesity but also to several factors simultaneously. This method was unequivocally demonstrated by the Finnish Diabetes Prevention Study (DPS), where none of the high-risk individuals with impaired glucose tolerance (IGT) developed diabetes during the initial trial period if they reached four or five out of five predefined lifestyle targets (1). These targets were as follows: weight loss >5%, intake of fat <30% energy, intake of saturated fats <10% energy, increase of dietary fiber to ≥15 g/1,000 kcal, and increase of physical activity to at least 4 h/week. Such targets are relatively modest and therefore possible to reach by many people. Moreover, to practice such a lifestyle is feasible for the long term, even for an entire lifetime. However, the trial data have been criticized for presenting an over-optimistic outlook, since the trial population comprised individuals who volunteered to participate in such a lifestyle intervention trial. It has been questioned whether or to what extent such trial results can be translated to the general population. Although this critique may be valid, the individuals participating in the trial were typical Finnish people with IGT who were overweight, were relatively sedentary, and whose diet was discordant with recommendations in many ways (2).

To provide evidence about the effects of a healthy lifestyle in the general population, a prospective cohort study was recently carried out among older U.S. adults (3). The particular aim of the study was to evaluate the association of multiple lifestyle factors, including physical activity level, dietary habits, smoking habits, alcohol use, and adiposity measures, with risk of new-onset type 2 diabetes. Each factor was independently associated with diabetes, but in combination, these lifestyle risk factors strongly predicted type 2 diabetes incidence. To investigate how modest differences in lifestyle factors were related to diabetes risk, each lifestyle risk factor was dichotomized. The incidence of type 2 diabetes was ~50% lower in people whose physical activity level and dietary habits indicated low risk and ~80% lower in individuals with physical activity level, dietary habits, smoking habits, and alcohol use all indicating the low-risk group. Because 8 in 10 cases of type 2 diabetes in this population of older adults appeared to be attributable to these four lifestyle factors, results suggest that 8 in 10 new cases of diabetes might have been prevented if all older adults were considered to be low risk based on these lifestyle factors. Adding either not being

Table 1—*Long-term effectiveness of diabetes prevention trials*

Study	Intervention	n	Intervention duration (years)	Risk reduction (%)*	Total follow-up time (years)	Follow-up risk reduction (%)	CVD events/total mortality reduction (%)
Da-Qing Study China (6,10)	Diet	130	6	31	20	43	2/4
	Exercise	141		46			
	Diet + exercise	126		42			
	Control	133					
DPS Finland (1,14,15)	Diet + physical activity	265	3.2	58	7	43	4†/43
	Control	257					
DPP U.S. (16,17)	Diet + physical activity	1,079	2.8	58	10	34	No data
	Metformin	1,073		31			
	Placebo	1,082					

*During the randomized trial period. †Higher in the intervention than control group.

overweight or not having a large waist circumference, nearly 9 in 10 new cases of type 2 diabetes appeared attributable to not being in the low-risk group for one or more of these lifestyle factors. Although these results provide an estimate of the public health burden of combined nonoptimal lifestyle risk factors for incidence of type 2 diabetes, they also confirm in a nonselected population that the majority of the cases of diabetes can be avoided with a modestly healthy lifestyle. This U.S. study among older people also confirms that a healthy lifestyle pattern provides long-term, lifelong benefits in terms of type 2 diabetes prevention. The key issue seems to be that several lifestyle issues related to the gluco-metabolic status, if they are not in balance, should be corrected simultaneously.

The potential to prevent type 2 diabetes in high-risk individuals by lifestyle intervention has been firmly established by several randomized controlled trials; based on a meta-analysis by Gillies et al. (4), the number needed to treat to prevent one case of type 2 diabetes is 6.4 when the duration of intervention ranges from 1.8 to 4.6 years. Lifestyle intervention in these clinical trials had a strong focus on increased physical activity (2.5–4 h/week) and dietary modification (increased whole grains, fiber, vegetables, and fruit; reduced total and saturated fat, sugar, and refined grains). Weight reduction among overweight participants was also an important goal and predictor of decreased diabetes risk (5); however, beneficial changes in type 2 diabetes incidence were also achieved independently of weight reduction (6,7). The interventions used behavior modification techniques such as motivational interviewing, self-monitoring, and individualized short- and long-term

goals. Several of the major type 2 diabetes prevention trials have revealed interesting long-term evidence regarding the sustaining effects of lifestyle changes on the risk of type 2 diabetes among the people who received intensified lifestyle advice.

LONG-TERM EFFECTS OBSERVED DURING THE EXTENDED FOLLOW-UP OF LIFESTYLE INTERVENTION TRIALS—A promising finding is that lifestyle interventions lasting for a limited time period seem to have a long-lasting carry-over effect on type 2 diabetes incidence. The first study to suggest that a sustained risk reduction may exist was the Malmö Feasibility Study (8). Originally, the effect of exercise and diet ($n = 161$) on incidence of type 2 diabetes among men with IGT was compared with a reference group ($n = 56$) of similar men who did not want to join the lifestyle intervention. Thus, the groups were not assigned at random. By the end of the 5-year study period, 11% of the intervention group and 29% of the reference group had developed diabetes. The 12-year follow-up results (9) revealed that all-cause mortality among men in the former IGT intervention group was lower than that among the men in the nonrandomized IGT group who received "routine care" only (6.5 vs. 14.0 per 1,000 person-years, $P = 0.009$). Mortality in the former IGT intervention group was actually similar to that in men with normal glucose tolerance.

A large population-based screening program (110,660 individuals screened with an oral glucose tolerance test) to identify people with IGT was carried out in Da Qing, China, in 1986 (6). The randomization of study subjects was not

done at random, but the 33 participating clinics (cluster randomization) were randomized to carry out the intervention according to one of the four specified intervention protocols (diet alone, exercise alone, diet-exercise combined, or none). Altogether, 577 men and women with IGT participated in the trial, and of them, 533 participated in the measurements at the end of the 6-year lifestyle intervention in 1992.

The Da Qing study participants were relatively lean; the mean BMI was 25.8 kg/m^2 at baseline. In clinics assigned to dietary intervention, the participants were encouraged to reduce weight if BMI was >25 kg/m^2, aiming for <24 kg/m^2; otherwise, a high-carbohydrate (55–65%) and moderate-fat (25–30%) diet was recommended. The overall changes in risk factor patterns were relatively small. Body weight did not change in lean subjects, and there was a modest <1 kg reduction in subjects with baseline BMI >25 kg/m^2. Again, this indicates that body weight alone may not be the most critical issue in the prevention of type 2 diabetes; also, other lifestyle issues are important, whereas body weight may work as a summary indicator of several dietary and activity factors.

The cumulative 6-year incidence of type 2 diabetes was lower in the three (diet alone, exercise alone, diet-exercise combined) intervention groups (41–46%) compared with the control group (68%). The 20-year follow-up analyses of the original Da Qing study cohort were published in 2008 (10). The results showed that the reduction in type 2 diabetes incidence persisted in the combined intervention group compared with control participants with no intervention; furthermore, the risk reduction remained

essentially the same during the postintervention period. However, type 2 diabetes incidence during the follow-up was generally high: in the final analyses, 80% of the intervention participants and 93% of the control participants had developed type 2 diabetes.

Furthermore, the 20-year follow-up study aimed to assess whether the lifestyle intervention had a long-term effect on the risk of cardiovascular disease (CVD) or mortality. The results showed no statistically significant differences in CVD events, CVD mortality, or total mortality either in the control group or the three intervention groups combined. A nonsignificant 17% reduction in CVD death was observed, which can be seen at least suggestive for benefits of lifestyle intervention.

The Finnish DPS was a multicenter trial carried out in five clinics in Finland from 1993 to 2001. The main aim of the study was to find out whether type 2 diabetes is preventable with lifestyle modification alone among high-risk individuals with IGT. A total of 522 men and women were recruited into the study. The participants were randomly allocated either into the control group or the intensive intervention group (2).

Body weight reduction from baseline was on average 4.5 kg in the intervention group and 1.0 kg in the control group subjects ($P < 0.001$) after the first year and at 3 years, weight reductions were 3.5 and 0.9 kg ($P < 0.001$), respectively. Also, indicators of central adiposity and glucose tolerance improved significantly more in the intervention group than in the control group at both the 1-year and 3-year follow-up examinations. At the 1-year and 3-year examinations, intervention group subjects reported significantly more beneficial changes in their dietary and exercise habits, based on dietary and exercise diaries (2). The components of the metabolic syndrome also improved significantly in the intervention group compared with the control group (11).

By March 2000, a total of 86 incident cases of diabetes had been diagnosed among the 522 subjects with IGT randomized into the DPS when the median follow-up duration of the study was 3 years. The cumulative incidence of diabetes was 11% (95% CI 6–15) in the intervention group and 23% (95% CI 17–29) in the control group after 4 years; thus, the risk of diabetes was reduced by 58% ($P < 0.001$) during the trial in the intervention group compared with the

control group (1). Post hoc analyses have shown that in addition to weight reduction, adopting a diet with moderate fat and high fiber content (12), as well as increasing physical activity (13), was independently associated with diabetes risk reduction.

An analysis using the data collected during the extended follow-up of the DPS revealed that after a median of 7 years total follow-up, a marked reduction in the cumulative incidence of type 2 diabetes was sustained (14). The relative risk reduction during the total follow-up was 43%. The effect of intervention on diabetes risk was maintained among patients who after the intervention period were without diabetes: after the median postintervention follow-up time of 3 years, the number of incident new cases of type 2 diabetes was 31 in the intervention group among 221 people at risk and 38 in the control group among 185 people at risk. The corresponding incidences were 4.6 and 7.2 per 100 person-years, respectively (log-rank test, $P = 0.0401$) (i.e., 36% relative risk reduction).

The 10-year follow-up results of the DPS showed that total mortality (2.2 vs. 3.8 per 1,000 person-years) and cardiovascular morbidity (22.9 vs. 22.0 per 1,000 person-years) were not different between the intervention and control groups (15). Interestingly, when the DPS groups (all IGT at baseline) were compared with a Finnish population–based cohort of people with IGT, the adjusted hazard ratios were lower in the DPS cohort: 0.21 (95% CI 0.09–0.52) and 0.39 (0.20–0.79) for total mortality in the intervention and control groups, respectively, and 0.89 (0.62–1.27) and 0.87 (0.60–1.27) for cardiovascular events.

The Diabetes Prevention Program (DPP) was a multicenter randomized clinical trial carried out in the U.S. (16). It compared the efficacy and safety of three interventions: an intensive lifestyle intervention or standard lifestyle recommendations combined with metformin or placebo. The goals of the dietary intervention were to achieve and maintain 7% weight reduction by consuming a healthy low-calorie low-fat diet and to engage in physical activities of moderate intensity (such as brisk walking) ≥150 min per week.

The intensive lifestyle intervention reduced type 2 diabetes risk after 2.8 years mean follow-up by 58% compared with the placebo control group. Lifestyle intervention was also superior to metformin

treatment, which resulted in a 31% type 2 diabetes risk reduction compared with placebo. At the 1-year visit, the mean weight loss was 7 kg (~7%).

After finding that also in the DPP a 58% risk reduction in type 2 diabetes incidence was associated with lifestyle intervention, similar to that in the DPS, the randomized trial was stopped and the participants were invited to join the Diabetes Prevention Program Outcomes Study (17). During the follow-up, all participants, regardless of their original treatment group, were offered lifestyle counseling. During the overall follow-up of 10 years (from the initial randomization), type 2 diabetes incidence in the original lifestyle intervention group was reduced by 34% compared with the control group. However, during the postintervention follow-up, type 2 diabetes incidence was similar in all treatment groups (5.9 per 100 person-years in the former intervention group and 5.6% in the placebo control group), confirming that lifestyle intervention that was initiated in the former placebo control group was successful, even after several years of follow-up without any active intervention.

WHAT IS NEEDED TO SUCCESSFULLY IMPLEMENT DIABETES PREVENTION PROGRAMS?

—Type 2 diabetes can be delayed or prevented among people who have IGT with lifestyle interventions or medication, as shown by major clinical trials of diabetes prevention, but it is a completely different issue to translate this message derived from the lifestyle trials to clinical practice. We are still learning how this challenge may be achieved at a population level.

The research evidence has inspired national and local authorities and health care providers all over the world to start programs and activities to prevent type 2 diabetes and its complications (18). The first large-scale national program for the prevention of type 2 diabetes was launched in Finland (19,20). It was based on evidence derived from the DPS and was implemented through the Finnish National Diabetes Prevention Program implementation project (called FIN-D2D) between 2003 and 2007 in the Finnish primary health care. The FIN-D2D included population, high-risk, and early treatment strategies. The high-risk strategy was directed at implementing screening and lifestyle interventions in people at high risk of type 2 diabetes as part of

routine primary health care, aiming at both type 2 diabetes prevention and cardiovascular risk factor reduction.

The DE-PLAN initiative (Diabetes in Europe–Prevention Using Lifestyle, Physical Activity, and Nutritional Intervention) was designed to develop the evidence for diabetes prevention practice in 17 European countries (21). The European Union–supported IMAGE project went one step further, and it was established to collate the evidence in a systematic manner. A group of ~100 European experts in this field has worked for 2.5 years to prepare the main deliverables of the projects, which are the evidence-based guidelines on type 2 diabetes prevention (22), a toolkit for diabetes prevention (23), and a guideline for evaluation and quality indicators and management in type 2 diabetes prevention (24). Furthermore, a European training curriculum for prevention managers to perform type 2 diabetes prevention intervention programs was developed.

TOOLKIT FOR THE PREVENTION OF TYPE 2 DIABETES—The major output of the IMAGE project (relevant for prevention practice) is the practical guideline called "toolkit for the prevention of type 2 diabetes." This toolkit is meant for all people involved in type 2 diabetes prevention: individuals working in primary and specialized health care services, physicians, physical activity experts, dietitians, nurses, and teachers, but also stakeholders and politicians.

The toolkit (23) includes in a condensed form in essence what is necessary to build a type 2 diabetes prevention program and covers management, financial, intervention, and quality assurance aspects and refers to the latest scientific evidence on type 2 diabetes prevention and how to translate this knowledge into practice. The toolkit addresses issues such as how to budget and finance a prevention program and how to identify people at risk. The core of the toolkit describes elements of an effective lifestyle intervention program. A process model for supporting lifestyle behavior change is presented and described in its phases (motivation, action, and maintenance). The toolkit gives the core goals of lifestyles (physical activity and diet) and gives practical instructions about how to address these with the client. Other behavioral aspects to consider in type 2 diabetes prevention include smoking, stress/depression, and sleeping patterns.

The toolkit finishes with an overview on how to evaluate intervention programs and how to establish quality assurance.

The IMAGE toolkit aims at providing a good balance between clear, accurate information and practical guidance. It is not intended to be a comprehensive source of information. Specifically, detailed instructions about how to achieve and maintain weight reduction, which evidently is one of the main issues in diabetes prevention, are not given because local and national guidelines as well as other information are abundantly available elsewhere. Furthermore, the staff members delivering intervention are assumed to have basic knowledge about diet and physical activity and their health effects and about the support needed for behavioral changes. Furthermore, the toolkit is not designed to be used as the intervention material to be delivered directly to individuals participating in preventive interventions, although it does contain some examples of information sheets and materials that could be shared with participants.

Content of the IMAGE toolkit
The toolkit starts with an executive summary including the rationale for diabetes prevention. It is followed by chapters that represent the background (type 2 diabetes prevalence, risk factors, consequences, evidence of successful prevention) and gives instructions about the development of diabetes prevention programs and identification and recruitment of participants at high risk for type 2 diabetes.

One of the core items of the toolkit is the description of what to do and how to do it. Behavior change is a process that requires individual attention and effective communication to achieve motivation, self-monitoring, sustained support, and other interventions to prevent and manage relapses. This section includes an intervention model including empowerment and patient-centered messages. It is followed by key messages on behavior (physical activity and diet) that are important in prevention of diabetes and practical advice for patient-centered counseling. The focus is on long-term sustainable lifestyle changes.

Finally, a brief guide for evaluation and quality assurance in reference to the "quality and outcome indicators" is included. This section is followed by consideration of possible risks and adverse effects. The IMAGE toolkit main text ends with a positive mission statement, emphasizing what can be achieved if we work together.

The appendices give the reader a set of easy-to-use tools including a checklist for prevention program development, templates for goal-setting and for food and physical activity diaries, an example of a risk screening questionnaire (the FINDRISC [Finnish Diabetes Risk Score] questionnaire), and a template for evaluation and quality assurance data collection.

NETWORK "WHO IS ACTIVE IN DIABETES PREVENTION?"—An important current new initiative is the launch of an international network, "Who is active in diabetes prevention?" This network is primarily for people who are interested in the prevention of type 2 diabetes and who want to use such a professional network to meet others with this cause (free registration at www.activeindiabetesprevention.com). The network itself encourages exchanging knowledge and discusses recent intervention material as well as educational standards, but the most important focus of the network is the exchange of experiences in type 2 diabetes prevention practices. It is also thought of as a platform to exchange scientific information or up-to-date study information between research groups and people active in diabetes prevention. People from 140 countries have thus far joined the network, and it is worth noting that many participants come from low- and middle-income "developing" countries.

FUTURE CHALLENGES AND OPPORTUNITIES—As estimated by the International Diabetes Federation, the number of type 2 diabetic patients is likely to increase during the upcoming years and may increase for decades in many parts of the world. This pattern needs to be stopped and can only be done through the implementation of the evidence-based recommendations on the prevention of type 2 diabetes. The first prerequisite is political support and the development of a national action plan for type 2 diabetes prevention in all countries. This step requires involving a number of stakeholders—not only the health sector, but also other governmental and nongovernmental as well as scientific organizations. Second, we need dramatic changes within the health sector, where the most urgent issue is to use people who have training in lifestyle management, diet, physical activity, psychological issues, etc. Third, the

research targeted to the prevention of type 2 diabetes must be expanded. The trials documented thus far have provided a good basis, but there is a lot to do to find the most effective methods of type 2 diabetes prevention in various societies and cultural settings. Also, it is important to find out how a "personalized medicine" approach could be applied in type 2 diabetes prevention. The most important issue, however, is to implement and evaluate community-based efforts aimed at preventing type 2 diabetes; this cannot be done without actual programs implemented in real-life settings. The International Diabetes Federation, with other organizations representing chronic diseases, is planning a Noncommunicable Disease Alliance and will hold a United Nations Summit in September 2011. One part of the summit will be to develop a Global United Nations Diabetes Plan on noncommunicable disease prevention and control that will call for political action and support.

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