Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study

Jaana Lindström, Pirjo Ilanne-Parikka, Markku Peltonen, Sirkka Aunola, Johan G Eriksson, Katri Hemiö, Helena Hämäläinen, Pirjo Härkönen, Sirkka Keinänen-Kiukaanniemi, Mauri Laakso, Anne Louheranta, Marjo Mannelin, Merja Paturi, Jouko Sundvall, Timo T Valle, Matti Uusitupa, Jaakko Tuomilehto, on behalf of the Finnish Diabetes Prevention Study Group

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Diabetes Unit, Department of Health Promotion and Chronic Disease Prevention, National Public Health Institute, Mannerheimintie 166, 00300 Helsinki, Finland (J Lindström MSc, M Peltonen PhD, Prof J G Eriksson MD, K Hemiö MSc, T T Valle MD, Prof J Tuomilehto MD); **The Diabetes Centre, Finnish Diabetes Association, Tampere, Finland** (P Ilanne-Parikka MD); **Research Unit of Tampere University Hospital, Tampere, Finland** (P Ilanne-Parikka); **Laboratory for Population Research, National Public Health Institute, Turku, Finland** (S Aunola PhD); **Research Department, Social Insurance Institution, Turku, Finland** (H Hämäläinen PhD); **Department of Sports Medicine, Oulu Deaconess Institute, Oulu, Finland** (P Härkönen MSc, M Mannelin MSc); **Department of Public Health Science and General Practice, University of Oulu, Oulu, Finland** (Prof S Keinänen-Kiukaanniemi MD, M Laakso MD); **Unit of General Practice, Oulu University Hospital, Oulu, Finland** (S Keinänen-Kiukaanniemi, M Laakso); **Department of Public Health and Clinical Nutrition, University of Kuopio, Kuopio, Finland** (A Louheranta PhD, Prof M Uusitupa MD); **Nutrition Unit, Department of Epidemiology and Health Promotion, National Public Health Institute, Helsinki, Finland** (M Paturi MSc); **Laboratory of Analytical Biochemistry, Department of Health and Functional Capacity, National Public Health Institute, Helsinki, Finland** (J Sundvall MSc); **Health Centre of Oulu, Oulu, Finland** (S Keinänen-Kiukaanniemi); **Department of Public Health, University of Helsinki, Helsinki, Finland** (J Lindström, J Tuomilehto, J G Eriksson); **South Ostrobothnia Central Hospital, Seinäjoki, Finland** (J Tuomilehto)

Correspondence to:
Jaana Lindström
jaana.lindstrom@ktl.fi

Summary

Background **Lifestyle interventions can prevent the deterioration of impaired glucose tolerance to manifest type 2 diabetes, at least as long as the intervention continues. In the extended follow-up of the Finnish Diabetes Prevention Study, we assessed the extent to which the originally-achieved lifestyle changes and risk reduction remain after discontinuation of active counselling.**

Methods **Overweight, middle-aged men (n=172) and women (n=350) with impaired glucose tolerance were randomly assigned to intensive lifestyle intervention or control group. After a median of 4 years of active intervention period, participants who were still free of diabetes were further followed up for a median of 3 years, with median total follow-up of 7 years. Diabetes incidence, bodyweight, physical activity, and dietary intakes of fat, saturated fat, and fibre were measured.**

Findings **During the total follow-up, the incidence of type 2 diabetes was 4·3 and 7·4 per 100 person-years in the intervention and control group, respectively (log-rank test p=0·0001), indicating 43% reduction in relative risk. The risk reduction was related to the success in achieving the intervention goals of weight loss, reduced intake of total and saturated fat and increased intake of dietary fibre, and increased physical activity. Beneficial lifestyle changes achieved by participants in the intervention group were maintained after the discontinuation of the intervention, and the corresponding incidence rates during the post-intervention follow-up were 4·6 and 7·2 (p=0·0401), indicating 36% reduction in relative risk.**

Interpretation **Lifestyle intervention in people at high risk for type 2 diabetes resulted in sustained lifestyle changes and a reduction in diabetes incidence, which remained after the individual lifestyle counselling was stopped.**

Introduction

The pandemic of type 2 diabetes is an enormous public health problem.[1,2] Studies using lifestyle intervention in people with impaired glucose tolerance have shown that the progress to manifest type 2 diabetes can be prevented or postponed.[3–8] Lifestyle intervention in these studies lasting for 3–6 years emphasised bodyweight control, physical activity, and dietary modification. Reduction in relative risk achieved in the intervention group compared with the control group ranged from 30% to 67%, as shown in a recent meta-analysis.[9] The Finnish Diabetes Prevention Study[5] and the US Diabetes Prevention Program[6] both revealed a 58% relative risk reduction in the progression from impaired glucose tolerance to type 2 diabetes, during a mean intervention period of about 3 years.

However, whether the risk reduction achieved during active counselling for lifestyle changes will last after discontinuation of the intervention is not known. The extended follow-up of the Diabetes Prevention Study was designed to assess the long-term results of the lifestyle intervention originally aimed at reducing the risk for developing type 2 diabetes in high-risk individuals.

Methods

The Diabetes Prevention Study was a randomised controlled trial aimed at prevention of type 2 diabetes by lifestyle intervention. The study design has been described in detail previously.[10] The study protocol was approved by the ethics committee of the National Public Health Institute in Helsinki, Finland, and all study participants gave written informed consent. Randomisation started in 1993 and was completed in 1998 (figure 1). The first interim analysis was done in March, 2000.[5] According to the recommendation of the endpoint committee, the intervention period was discontinued at each participant's next yearly clinic visit, after a median follow-up of 4 years. Subsequently, we decided to continue to monitor the participants who had remained free of diabetes. This report consists of the data obtained until Dec 31, 2004, ie, post-intervention follow-up for a median of 3 years, with median total follow-up of 7 years.

Participants

Originally, 522 men and women in five study centres were randomised at the baseline visit to one of the two treatment modalities, the intervention group with intensive diet-exercise counselling (n=265, the proportion

of women 66%) or the control group (n=257, the proportion of women 69%). Overweight (mean body-mass index 31·1 kg/m^2), middle-aged (mean age 55 years) participants with impaired glucose tolerance based on two 75 g oral glucose tolerance tests by the WHO 1985 criteria[11] were eligible for the study. Mean fasting plasma glucose at baseline was 6·1 (SD 0·8) mmol/L and mean plasma glucose value 2 h after the 75 g oral glucose load was 8·9 (1·5) mmol/L without significant differences between the two groups. The overall proportion of participants who were lost to follow-up was 10% in the intervention group and 8% in the control group (p=0·3619 Fisher's exact test; figure 1).

Intervention

The main goals of the intervention were: weight reduction of 5% or more; less than 30% of the daily energy intake from fat; less than 10% of the daily energy intake from saturated fat; fibre intake 15 g per 1000 kcal or more; and moderately intense physical activity 30 min per day or more. The duration of intervention ranged from less than 1 year (indicating withdrawal before the first yearly visit) up to 6 years, with median length of 4 years. The implementation of the intervention programme has been previously reported.[12] Briefly, the participants in the intervention group were given detailed and individualised counselling to achieve the lifestyle goals. They had seven personal counselling sessions with the study nutritionist during the first year and every 3 months thereafter. The median number of dietary counselling sessions per participant was 20 thus indicating excellent compliance with the study protocol. The participants were also advised to increase their level of physical activity, and were offered free of charge, supervised, individually tailored circuit-type moderate-intensity resistance training sessions to improve the functional capacity and strength of the large muscle groups of the upper and lower body.

The participants in the control group were given general verbal and written health behaviour information at baseline without specific individualised advice. At the last intervention period visit all the participants were given a summary of their laboratory test results during the intervention period, including the glucose values, and they were also told about the findings of the randomised trial.

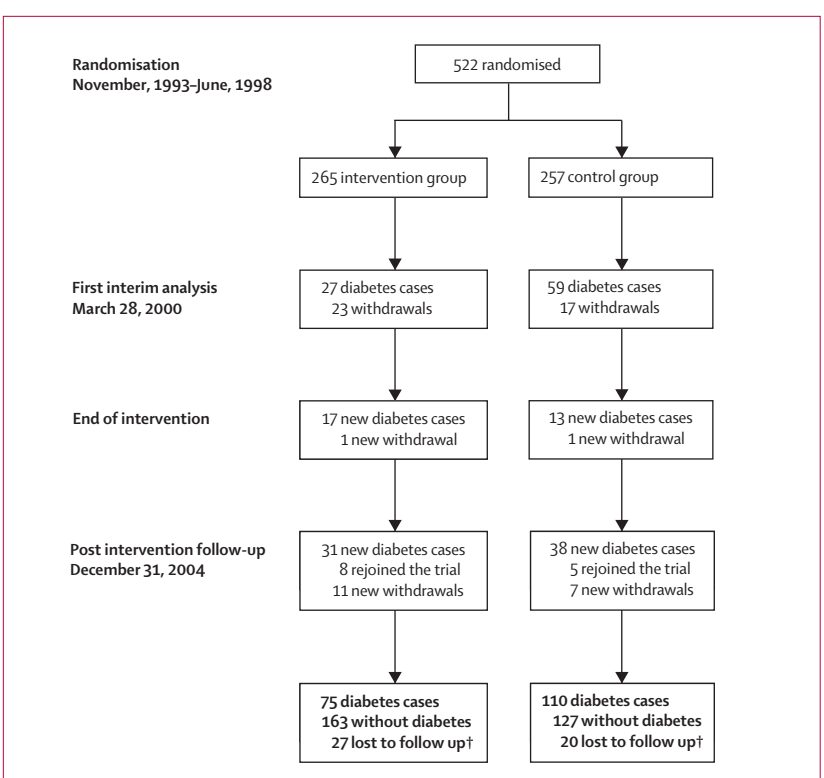

Figure 1: **Trial profile**
*After the decision to end the intervention period, the intervention was continued until each participant's next scheduled yearly clinic visit. End date thus varied from March, 2000, to Dec, 2001. †Participants who were lost to follow-up were treated as censored observations in the analyses.

Post-intervention follow-up

All individuals who participated in the Diabetes Prevention Study were invited to take part in the post-intervention follow-up. During this follow-up, all study participants had a yearly visit with the study nurse. The visits included the same procedures as during the intervention period, and were similar for all participants irrespective of their former randomisation group. No specific diet or exercise counselling was provided.

Procedures and measurements

The parameters measured every year included fasting and post load (75 g oral glucose tolerance test) plasma glucose after a 12-h fast. During the intervention, plasma glucose was measured locally according to standard guidelines. During the post-intervention follow-up, centralised glucose assays were established enzymatically with the hexokinase method (Thermo Electron Oy, Vantaa, Finland).

A clinical examination was done and questionnaires including questions about physical activity were obtained at baseline and at every yearly visit. Individuals who reported that they "mostly read, watch TV, and spend time in other ways that are not physically demanding" during their spare time were categorised as physically inactive, and those who reported "walking, bicycling, or other exercise for at least 4 hours per week" were categorised as achieving the physical activity goal. All study participants completed a 3-day food record with a picture booklet of portion sizes of typical foods.[13] The average intakes of total fat (proportion of the total daily energy intake), saturated fat (proportion of the total daily energy intake), and dietary fibre (g per 1000 kcal) from the baseline and 1-year, 2-year, and 3-year visits of the intervention period were calculated using a dietary analysis programme and the Finnish Food Composition

Database (Fineli) developed at the National Public Health Institute, Helsinki, Finland.[14] The dietary analyses were repeated at the first post-intervention follow-up visit to clarify the maintenance of the dietary changes after the intervention had been discontinued.

The study participants were categorised according to their success in achieving the five predefined lifestyle goals (0=not achieved, 1=achieved) by the 3-year visit, with mean physical activity and nutrient intakes during the years 1, 2, and 3. For those who either dropped out or were diagnosed with diabetes before the 3-year visit, the last observation for bodyweight was used for calculating weight reduction. A success score from 0 to 5 was calculated as the sum of the achieved goals. The analysis was repeated at the first post-intervention follow-up-visit.

The development of type 2 diabetes was the primary endpoint. Since the study was started before the current criteria for diabetes were introduced,[15] diabetes was defined according to WHO 1985 criteria,[11] ie, either fasting plasma glucose of 7·8 mmol/L or more, or 2-hour post-challenge plasma glucose of 11·1 mmol/L or more. The diagnosis of diabetes was confirmed by a second oral glucose tolerance test.

Statistical analysis

Kaplan-Meier survival curves were calculated to estimate the probability of remaining free of diabetes in the two groups. Participants who were lost during follow-up were treated as censored observations. The difference between the survival curves was tested with the log-rank test. The Cox proportional hazards model was used to estimate the hazard ratio for development of diabetes. The proportionality assumption of the model was assessed with graphical methods (ie, the log-log plot). All comparisons of the endpoints were based on the intention-to-treat principle.

Mean levels of bodyweight, nutrient intakes, and physical activity during the study were compared between the groups with analysis of covariance, adjusting for the level of respective variable at baseline. Further, analysis of covariance was used to examine changes in these variables from the last intervention period visit until the first post-intervention examination. In this analysis, adjustment was made for the level of respective variable at the last visit during intervention. In further analyses, the Cox model was used to analyse the relation between the success score and the incidence of diabetes. First, the success score variable was included in the model as categorical variable, with those who did not achieve any of the lifestyle goals as reference category. Additionally, test of linear trend was done including the success score as continuous variable in the model. In these analyses the groups were pooled. The analyses were adjusted for treatment group, study centre, sex, age, and the baseline 2-h post-challenge plasma glucose concentration. Analyses were done with the statistics package Stata version 8.0.

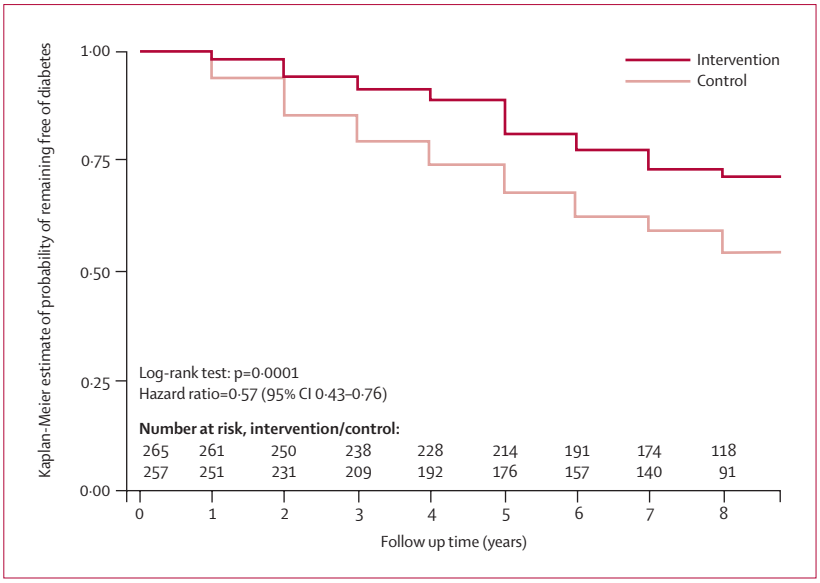

Figure 2: **Diabetes by treatment group**
Follow-up time is truncated at 8 years, since number of participants at risk beyond this point was low, but they are included in the calculation of hazard ratios.

Role of the funding source

The sponsors of the study had no role in study design, the collection, analysis, or interpretation of the data, or in the writing of the report. The corresponding author had full access to all data in the study and had the final responsibility to submit for publication.

Results

The total number of cases of diabetes diagnosed during the overall follow-up of 7 years was 75 in the intervention group and 110 in the control group (figure 1). The incidence rates were 4·3 (95% CI 3·4–5·4) and 7·4 (6·1–8·9) per 100 person-years in the intervention and control group, respectively (p=0·0001 log-rank test). The corresponding hazard ratio was 0·57 (0·43–0·76; figure 2). The cumulative incidence of diabetes at year 6 was 23% in the intervention group and 38% in the control group, with an absolute risk reduction of 15% (7·2–23·2). The number of people needed to be treated to prevent one case of type 2 diabetes by lifestyle intervention was 22 for 1 year. The mean bodyweight and the intake of total and saturated fat were lower in the intervention group compared with that in the control group during the intervention (table 1). Further, intake of dietary fibre and physical activity were higher in the intervention group.

In the intervention and the control group, respectively, 10% and 27% of the participants did not achieve any of the predefined goals by the 3-year examination, whereas 14% and 6% achieved four or five goals (p<0·0001 for Fisher's exact test). There was a strong inverse correlation between the success score and the incidence of diabetes during the total follow-up. Incidence rate per

100 person-years ranged from 8·4 (95% CI 6·2–11·3) in the participants who did not achieve any of the goals at the 3-year visit, to 2·0 (1·0–4·3) in those who achieved four or five of the goals. The hazard ratios were 1·00, 0·85 (0·57–1·28), 0.66 (0·40–1·09), 0·69 (0·38–1·26), and 0·23 (0·10–0·52) for success score from 0, 1, 2, 3, to 4–5, respectively (test for trend p=0·0004).

To assess the independent effects of achieving the success score components at the 3-year examination on diabetes incidence during the total follow-up, all five variables for lifestyle goal were first individually included in a Cox model. Univariate hazard ratios (95% CI) were 0·45 (0·31–0·64) for weight reduction from baseline, 0·65 (0·45–0·95) for intake of fat, 0·59 (0·31–1·13) for intake of saturated fat, 0·69 (0·49–0·96) for intake of fibre, and 0·62 (0·46–0·84) for physical activity, comparing those who did or did not achieve the respective goal. When all five success score components were simultaneously included in the Cox model, the multivariate-adjusted hazard ratios for diabetes (95% CI) were 0·43 (0·30–0·61) for weight reduction, 0·80 (0·48–1·34) for intake of fat, 0·55 (0·26–1·16) for intake of saturated fat, 0·97 (0·63–1·51) for intake of fibre, and 0·80 (0·57–1·12) for physical activity. Furthermore, weight change from baseline was significantly associated with the achievement of each of the other four lifestyle goals, and consequently, success score was strongly and inversely correlated with weight reduction. The 3-year weight reduction was 0·5%, 2·1%, 4·3%, 4·7%, and 8·7% for success score from 0, 1, 2, 3, to 4–5, respectively (test for trend p<0·0001). Additionally, all the dietary goals (total fat, saturated fat, and fibre) were significantly associated with each other (p for all <0·0001). Achievement of the fat intake goal or the fibre intake goal was associated also with the physical activity goal (p=0·0019 and p<0·0001, respectively).

To explore whether the reduced long-term risk of type 2 diabetes in the intervention group could be attributed solely to a reduced risk during the actual intervention of the study, we excluded all participants who were diagnosed with diabetes during the intervention (n=116) and calculated the incidence rates exclusively for the post-intervention follow-up. The median post-intervention follow-up time was 3 years, and the number of incident new cases of type 2 diabetes was 31 in the intervention group of 221 people at risk, and 38 in the control group of 185 people at risk. The corresponding incidence rates were 4·6 and 7·2 per 100 person-years, respectively (log-rank test p=0·0401), ie, 36% relative risk reduction (figure 3).

Bodyweight, physical activity, and nutrient intakes in those without diabetes at the end of the intervention are shown in table 2. The differences in these variables between the groups remained favourable for the intervention group during the post-intervention follow-up. The proportion of physically active individuals decreased in the control group. Conversely, the participants in the control group reduced their intake of saturated fat more but, since they had a higher intake to start, still maintained a higher intake of saturated fats than the intervention group.

	Intervention		Control		p*
	n	Mean	n	Mean	
Bodyweight (kg)					
Baseline	265	86·7	257	85·5	0·3267
Year 1	256	82·2	250	84·8	<0·0001
Year 3†	256	83·4	251	85·2	<0·0001
Last intervention period visit†	257	84·3	251	85·6	<0·0001
Proportion of physically active (%)‡					
Baseline	261	64	257	67	0·5192
Year 1	252	86	245	69	<0·0001
Year 3†	256	82	251	71	0·0003
Last intervention period visit†	256	81	251	71	0·0013
Energy proportion of fat (%)					
Baseline	264	36	255	37	0·0670
Year 1	254	33	245	35	0·0001
Year 3†	254	32	246	34	<0·0001
Energy proportion of saturated fat (%)					
Baseline	264	16	255	17	0·0188
Year 1	254	14	245	16	<0·0001
Year 3†	254	13	246	15	<0·0001
Dietary fibre (g per 1000 kcal)					
Baseline	264	11·7	255	11·7	0·9431
Year 1	254	14·2	245	12·5	<0·0001
Year 3†	254	14·1	246	12·7	<0·0001

*p for test of equality between groups, adjusting for baseline level. †Last observation brought forward for individuals who dropped out or became diabetic during the study. ‡Individuals who reported walking, cycling, or other moderate intensity activity for at least 4 h per week categorised as physically active.

Table 1: **Bodyweight, physical activity, and dietary intake during the intervention period of the study**

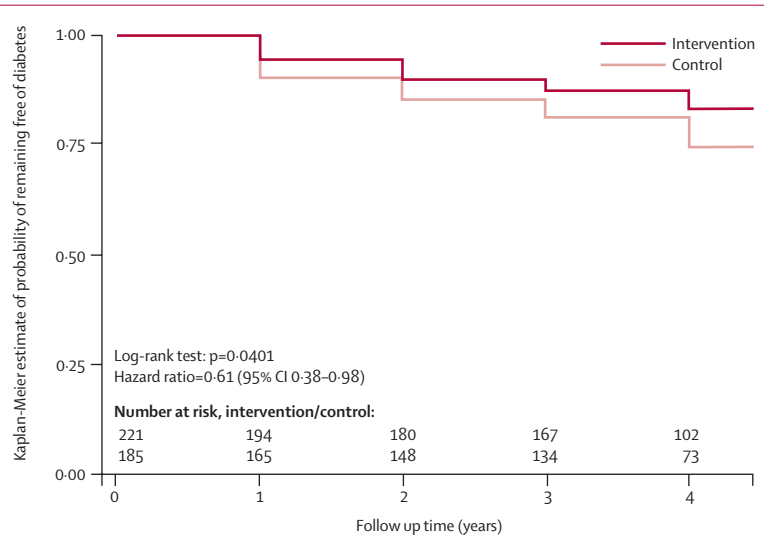

Figure 3: **Diabetes by treatment group during the post-intervention follow-up period**
Follow-up time is truncated at 4 years, since number of participants at risk beyond this point was low, but they are included in calculation of hazard ratios.

The success score analysis was repeated to analyse the effect of maintained lifestyle changes on the diabetes incidence during the post-intervention follow-up. In the intervention and control groups, respectively, 7% and 14% of the participants did not achieve any of the lifestyle goals at the first follow-up visit, 32% and 40% achieved one, while 18% and 7% achieved at least four out of the five goals (p=0·0042 for Fisher's exact test). The incidence rate of diabetes per 100 person-years was 8·0 (95% CI 4·2–15·4) in the group that did not achieve any of the goals, compared with 3·8 (1·7–8·5) in the group with 4 or 5 goals achieved. The hazard ratios were 1·00, 0·96 (0·45–2·04), 0·37 (0·15–0·93), 0·78 (0·32–1·91) and 0·54 (0·20–1·49) for the success score from 0, 1, 2, 3, to 4 or 5, respectively (p=0·1089).

Univariate hazard ratios (95% CI) for diabetes incidence during the post-intervention follow-up were 0·55 (0·30–1·02) for achieving the weight reduction goal, 0·74 (0·44–1·27) for achieving the fat intake goal, 1·01 (0·54–1·89) for achieving the saturated fat intake goal, 0·72 (0·40–1·30) for achieving the fibre intake goal, and 0·62 (0·36–1·06) for achieving the physical activity goal, compared with those who did not achieve the respective goal at the first post-intervention follow-up examination. When all five variables for lifestyle goals were simultaneously analysed, the adjusted hazard ratios were 0·52 (0·28–0·96) for weight reduction from baseline, 0·67 (0·35–1·31) for the intake of fat, 1·62 (0·68–3·85) for the intake of saturated fat, 0·77 (0·38–1·57) for the intake of fibre, and 0·82 (0·46–1·48) for physical activity.

	Intervention		Control		p*	p†
	n	Mean	n	Mean		
Bodyweight (kg)						
Baseline	190	84·9	165	84·0	0·5174	
Last intervention visit	190	81·8	165	83·3	<0·0001	
First post-intervention follow-up visit	190	83·1	165	84·0	0·0032	0·1482
Proportion of physically active (%)‡						
Baseline	184	70	164	70	0·9102	
Last intervention visit	187	88	164	76	0·0035	
First post-intervention follow-up visit	187	86	164	71	0·0005	0·0273
Energy proportion of fat (%)						
Baseline	187	36	159	37	0·1879	
Year 3‡	187	31	159	34	0·0002	
First post-intervention follow-up visit	187	31	159	33	0·0174	0·1189
Energy proportion of saturated fat (%)						
Baseline	187	16	159	17	0·0676	
Year 3‡	187	13	159	15	<0·0001	
First post-intervention follow-up visit	187	12	159	14	0·0001	0·0128
Dietary fibre (g per 1000 kcal)						
Baseline	187	11·9	159	11·9	0·9750	
Year 3‡	187	14·5	159	12·9	0·0003	
First post-intervention follow-up visit	187	13·6	159	12·6	0·0071	0·4577

*p for test of equality between the groups, adjusting for the baseline level. †p for test of equal change between the groups from the last intervention period visit to the first post-intervention follow-up visit, adjusting for the level at the last intervention visit. ‡Individuals who reported walking, cycling, or other moderate intensity activity for at least 4 h a week were categorised as physically active.

Table 2: **Bodyweight, physical activity, and dietary intakes of participants of the post-intervention follow-up period who were without diabetes at the end of the intervention**

Discussion

Individually randomised controlled lifestyle intervention studies have shown the benefit of healthy lifestyle on delaying the deterioration of glucose tolerance to manifest type 2 diabetes, at least as long as the intervention continues.[5–8] Our study with a median of 7 years total follow-up shows that a marked difference in the cumulative incidence of diabetes can be sustained after the discontinuation of active counselling. The absolute difference in diabetes risk between the intervention and control groups was about 15% during the initial trial period and also remained the same during the post-intervention follow-up. The relative risk reduction of 43% was, however, less than the 58% seen during the original study,[5] as expected from the increasing cumulative diabetes incidence in both groups.

The earlier Da Qing IGT and Diabetes Study[4] with clinics randomly assigned either to diet, exercise, or diet plus exercise intervention showed a 31%, 46%, and 42% risk reduction, respectively, after a 6-year intervention. The relative risk reduction achieved in our study was about the same after a similar period even though the duration of active intervention was shorter. Thus, from a public health point of view there is an important message: an intensive lifestyle intervention lasting for a limited time can yield long-term benefits in reducing the risk of type 2 diabetes in high-risk individuals.

The achieved changes in physical activity and dietary habits seemed to be maintained at least 1 year after the discontinuation of the intervention. The differences between the groups persisted despite a possible dilution effect, since the control group participants can be considered to have received a reinforced mini-intervention when they were provided with their own glucose results and told about the main findings of the Diabetes Prevention Study at the end of the intervention period. Still, a modest difference in bodyweight change from baseline between the intervention and control groups was preserved. Our results confirm the findings from earlier studies showing that interventions can have long-term effect on lifestyle,[16,17] and offer encouraging evidence for the efficacy of comprehensive lifestyle intervention even without large reduction in weight.

Analysis of the success score showed that most people who maintained the lifestyle goals at 3-year visit remained free of diabetes during the extended follow-up. This finding indicates that the true effect of healthy lifestyle results in a dramatically better outcome than that seen by the intention-to-treat analysis of the treatment effect. Each of the success score components at the 3-year visit

(except that for saturated fat intake) was significantly associated with the reduction in diabetes risk in univariate analyses, but when all the components were included into the model simultaneously, only the effect of weight reduction remained significant. Analyses from the first post-intervention follow-up visit revealed similar tendency; however, the only significant association was between weight reduction and diabetes risk in the multivariate model. The findings suggest that dietary composition and physical activity are important in diabetes prevention but their effect on diabetes risk is in large part, although not entirely, mediated through resulting weight reduction. Nevertheless, because of the multicollinearity shown by the fact that weight change correlated with all the other intervention goals, the interpretation of the results should be made cautiously.

Our findings do not allow us to distinguish between the carry-over effect from the intervention, and the ongoing effect of lifestyle during the post-intervention follow-up, on diabetes incidence. In a subgroup analysis of the Diabetes Prevention Study population, we showed a marked improvement in insulin sensitivity concomitantly with weight loss, whereas insulin secretion did not change significantly.[18] This finding suggests that the prolonged benefit of the lifestyle intervention on the diabetes risk could partly be attributed to a correction of insulin resistance, which, on the other hand, might result in a preservation of the beta cell function. Even so, we cannot rule out the effect of maintaining lifestyle changes after the original intervention period. The question concerning the risk reduction in those in whom the success score or its components changed during the post-intervention follow-up period would be of interest, but unfortunately at the present our data have restricted statistical power for this kind of subgroup analyses.

About a third of participants in the intervention group met none or only one of the predefined goals 1 year after the intervention. Adherence to the intervention is a specific challenge for future diabetes prevention programmes. Oral antidiabetic medications have been shown to prevent diabetes, and could be an option for those who have not responded satisfactorily to lifestyle intervention. However, medications seem to lower blood glucose as long as they are taken, but much of their effect dissipates as soon as the drug is discontinued.[6,19–21] Unfortunately, there has thus far been no pharmacological trial specifically targeted to people at high risk of diabetes and who were unable to change their lifestyle.

Some limitations of the present study have to be addressed. The analyses related to the post-intervention follow-up period of the Diabetes Prevention Study were not planned in the original study protocol, and post hoc analyses have to be interpreted with caution. The post-intervention follow-up was not foreseen while calculating the original sample size,[10] and because of low numbers of people at risk and cases of diabetes the statistical power remains restricted. Furthermore, the study participants were volunteers and willing to take part in a long-lasting trial and thus were probably more health-conscious than the general population. A low number of withdrawals is a marker of high commitment, but since there was no difference between the groups it is also an advantage in the analyses. Future studies will reveal if the results from this clinical trial can be transposed into usual health-care settings. Also the generalisability of our findings in other populations must be studied.

Based on the Kaplan-Meier analysis, around 50% of people with impaired glucose tolerance will develop diabetes during 10 years when no active intervention is applied. Although a lifestyle intervention alone, even if successful, does not necessarily prevent type 2 diabetes in all individuals, it will still postpone the onset of the disease. Even delaying the onset of diabetes can have a substantial effect on subsequent morbidity, and therefore on the cost-effectiveness of diabetes prevention.[22] Whether the lifestyle intervention used in the Diabetes Prevention Study reduces diabetes-related microvascular and macrovascular complications in the long run is still to be proven, and such an assessment is planned in the future after an adequate number of cases and person-years have been accumulated.

The high diabetes incidence even in the intervention group of our study suggests that preventive actions should probably be targeted to all high-risk individuals, even before impaired glucose tolerance is present. The lifestyle intervention used in the Diabetes Prevention Study has formed the basis for the implementation programme for the prevention of type 2 diabetes in Finland.[23] This programme identifies high risk individuals with a simple, validated risk score questionnaire[24,25] and thus is likely to reach people at an earlier stage in the process leading to diabetes. Although a population-based strategy to fight the pandemic of type 2 diabetes is urgently needed, an individualised approach to guide people at high risk is also warranted. A simple lifestyle intervention seems to work well. However, further research is needed to reveal the optimum and most cost-efficient strategy, intensity, and duration of such an intervention. The results from the extended follow-up of the Finnish Diabetes Prevention Study nevertheless show that the effect of lifestyle intervention on diabetes risk does not disappear after active lifestyle counselling is stopped.

Contributors

J Lindström and P Ilanne-Parikka had joint responsibility for writing this manuscript and share the primary authorship of this paper. M Peltonen did the statistical analyses and participated in writing the manuscript. S Aunola, J G Eriksson, K Hemiö, H Hämäläinen, P Härkönen, S Keinänen-Kiukaanniemi, M Laakso, A Louheranta, M Paturi, J Sundvall, and T T Valle contributed to data extraction and revised the manuscript. J Tuomilehto and M Uusitupa are the principal investigators of the study and participated in writing the manuscript.

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Conflict of interest statement

We declare that we have no conflict of interest.

References

1 King H, Aubert RE, Herman WH. Global burden of diabetes, 1995–2025: prevalence, numerical estimates, and projections. *Diabetes Care* 1998; **21:** 1414–31.

2 Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004; **27:** 1047–53.

3 Eriksson KF, Lindgärde F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmo feasibility study. *Diabetologia* 1991; **34:** 891–98.

4 Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* 1997; **20:** 537–44.

5 Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; **344:** 1343–50.

6 The Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002; **346:** 393–403.

7 Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. 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* 2006; **49:** 289–97.

8 Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. *Diabetes Res Clin Pract* 2005; **67:** 152–62.

9 Yamaoka K, Tango T. Efficacy of lifestyle education to prevent type 2 diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care* 2005; **28:** 2780–86.

10 Eriksson J, Lindström J, Valle T, et al. Prevention of Type II diabetes in subjects with impaired glucose tolerance: the Diabetes Prevention Study (DPS) in Finland. Study design and 1-year interim report on the feasibility of the lifestyle intervention programme. *Diabetologia* 1999; **42:** 793–801.

11 WHO. Diabetes Mellitus: report of a WHO Study Group. Technical Report Series No 727. Geneva: World Health Organization, 1985.

12 Lindström J, Louheranta A, Mannelin M, et al. The Finnish Diabetes Prevention Study (DPS): lifestyle intervention and 3-year results on diet and physical activity. *Diabetes Care* 2003; **26:** 3230–36.

13 Haapa E, Toponen T, Pietinen P, Räsänen L. Annoskuvakirja. Helsinki: Painokaari Oy, 1985.

14 Ovaskainen M-L, Valsta L, Lauronen J. The compilation of food analysis values as a database for dietary studies–the Finnish experience. *Food Chemistry* 1996; **57:** 133–36.

15 WHO. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO Consultation: Part 1: Diagnosis and classification of diabetes mellitus. Geneva: World Health Organization, Department of Noncommunicable Disease Surveillance, 1999.

16 Pereira MA, Kriska AM, Day RD, Cauley JA, LaPorte RE, Kuller LH. A randomized walking trial in postmenopausal women: effects on physical activity and health 10 years later. *Arch Intern Med* 1998; **158:** 1695–701.

17 Simkin-Silverman LR, Wing RR, Boraz MA, Kuller LH. Lifestyle intervention can prevent weight gain during menopause: results from a 5-year randomized clinical trial. *Ann Behav Med* 2003; **26:** 212–20.

18 Uusitupa M, Lindi V, Louheranta A, Salopuro T, Lindström J, Tuomilehto J. Long-term improvement in insulin sensitivity by changing lifestyles of people with impaired glucose tolerance: 4-year results from the Finnish Diabetes Prevention Study. *Diabetes* 2003; **52:** 2532–38.

19 The Diabetes Prevention Program Research Group. Effects of withdrawal from metformin on the development of diabetes in the Diabetes Prevention Program. *Diabetes Care* 2003; **26:** 977–80.

20 The Diabetes Prevention Program Research Group. Prevention of type 2 diabetes with troglitazone in the Diabetes Prevention Program. *Diabetes* 2005; **54:** 1150–56.

21 Chiasson J-L, Josse RG, Gomis R, et al. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet* 2002; **359:** 2072–77.

22 Herman WH, Hoerger TJ, Brandle M, et al. The cost-effectiveness of lifestyle modification or metformin in preventing type 2 diabetes in adults with impaired glucose tolerance. *Ann Intern Med* 2005; **142:** 323–32.

23 The Finnish Diabetes Association. Programme for the prevention of type 2 diabetes in Finland 2003–2010. www.diabetes.fi/english. Tampere, 2003.

24 Lindström J, Tuomilehto J. The Diabetes Risk Score: A practical tool to predict type 2 diabetes risk. *Diabetes Care* 2003; **26:** 725–31.

25 Saaristo T, Peltonen M, Lindström J, et al. Cross-sectional evaluation of the Finnish Diabetes Risk Score: a tool to identify undetected type 2 diabetes, abnormal glucose tolerance and metabolic syndrome. *Diab Vasc Dis Res* 2005; **2:** 67–72.