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H.M. Saris, Ellen E Blaak

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PREDICTORS OF LIFESTYLE INTERVENTION OUTCOME AND DROPOUT: THE SLIM STUDY

Running title: lifestyle intervention in IGT

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Cheryl Roumen, PhD^a
Edith J.M. Feskens, PhD^b
Eva Corpeleijn, PhD^a
Marco Mensink, MD, PhD^b
10 Wim H. M. Saris, MD, PhD^a
Ellen E. Blaak, PhD^a

15

^aDepartment of Human Biology, Nutrition and Toxicology Research Institute Maastricht, NUTRIM, Maastricht University, Maastricht, The Netherlands; ^bDivision of Human Nutrition, Wageningen University, Wageningen, The Netherlands

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Correspondence and reprint requests:
Ellen E. Blaak
Department of Human Biology
P.O. Box 616
6200 MD Maastricht
Telephone: +31433881503
25 Fax: +31 43 3670976
E-mail: e.blaak@maastrichtuniversity

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Abbreviations: BMI, Body Mass Index; DPP, Diabetes Prevention Program; DPS, Diabetes Prevention Study; HDL, High Density Lipoprotein; IDF, International Diabetes Federation; IDPP-1, Indian Diabetes Prevention Program-1; IFG, Impaired Fasting Glucose; IGT, Impaired Glucose Tolerance; INT, Intervention group; LDL, Low Density Lipoprotein; OGTT, Oral Glucose Tolerance Test; SLIM, Study on Lifestyle intervention and Impaired glucose tolerance Maastricht; CON, Control group.

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ABSTRACT

Objectives: To evaluate the effect of a 4.1 year (range 3-6 years) lifestyle intervention according to general public health recommendations on glucose tolerance and dropout in a Dutch population with impaired glucose tolerance (IGT).

5 *Methods:* In the Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM), 147 Caucasian IGT subjects were randomized to an intervention group (n=74, 38 male, 36 female (INT)) and control group (n=73, 37 male, 36 female (CON)). Annually, subjects underwent measurements of body weight, anthropometry, glucose tolerance (OGTT), insulin resistance (HOMA-IR), maximal aerobic capacity
10 (VO₂ max), blood lipids and blood pressure. INT received individual advice regarding a healthy diet and physical activity.

Results: INT decreased their saturated fat intake, increased their carbohydrate intake (p<0.05) and VO₂ max (p=0.04) compared to CON. Body weight did not change significantly (p=0.20) between groups. After an initial decrease, 2-Hr glucose levels
15 overall increased in INT (+0.11 mmol/l), but significantly less than CON (+1.18 mmol/l; p=0.04). Diabetes incidence was lower in INT versus CON (30% versus 56%, p=0.04). Change in body weight was associated with change in 2-hr glucose levels (β =0.399 mmol/l/kg, p=0.02). Dropouts had a lower aerobic fitness and social economic status and a higher BMI and 2-hr glucose compared to non-dropouts.

20 *Conclusions:* Prolonged feasible changes in diet and physical activity prevent deterioration of glucose tolerance and reduce diabetes risk. Low social economic status, low aerobic fitness and high BMI and 2-hr glucose are indicative of dropout to the program.

Key words: long-term lifestyle intervention, glucose metabolism, predictors of success

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INTRODUCTION

Type 2 diabetes needs effective prevention measures for curbing the growing burden worldwide. Diabetes incidence is 10–20 times greater in those with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) than those with normal glycemia (Magliano et al, 2008).

Lifestyle interventions in IGT are an efficacious (Gillies et al, 2007, Roumen et al, 2008) and cost-effective (Jacobs-van der Bruggen et al, 2007) way to prevent type 2 diabetes (Knowler et al, 2002, Tuomilehto et al, 2001), even after active counselling is stopped (Lindstrom et al, 2006).

Despite the promising results of lifestyle interventions, it is unclear which factors determine changes in glucose tolerance and insulin sensitivity. Changing lifestyle towards general guidelines for diet and physical activity seems to be inversely associated with diabetes risk (Simmons et al, 2006), suggesting that the more strict compliance to the regime, the better the outcome. The Diabetes Prevention Program (DPP) has shown that a lifestyle-induced reduction in body weight was strongly associated with a reduced diabetes risk (Hamman et al, 2006). The current study, the Study on Lifestyle intervention and Impaired glucose tolerance Maastricht (SLIM), showed that subjects who adhered to both the dietary as well as the physical activity recommendations had the greatest one-year improvement in bodyweight, waist circumference and fasting insulin (Mensink et al, 2003) and prevented deterioration of 2-hr glucose levels after 3 years (Roumen et al., 2008). Another factor of importance is non-adherence to a lifestyle program. Overall, dropout rate varies highly between lifestyle interventions. Knowledge on determinants of adherence and intervention outcome (2-hr glucose tolerance) may contribute to a more efficient and targeted intervention to prevent and/or treat type 2 diabetes in the future.

The aim of the present SLIM report is to assess the long-term results of a lifestyle intervention aimed at improving glucose tolerance in a Dutch population at high risk for type 2 diabetes. The present paper extends previously published 3-year results by providing novel information on determinants of intervention outcome and dropout, which
5 can help optimize identification, lifestyle effect and adherence in high-risk subjects.

EXPERIMENTAL METHODS

10 The SLIM study (Study on Lifestyle intervention and Impaired glucose tolerance Maastricht) is a randomized controlled trial, evaluating the effect of a combined dietary and physical activity intervention program on glucose tolerance in IGT subjects (Mensink et al., 2003). Changes in body composition, fasting and 2-hr insulin and plasma glucose concentrations, serum lipids, blood pressure and maximal aerobic capacity are determined
15 annually. The Medical Ethical Review Committee of Maastricht University approved the study protocol and all subjects gave their written informed consent before the start of the study.

Study design and subjects

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The study design has been described previously (Mensink et al., 2003). Briefly, subjects with impaired glucose tolerance were selected from a cohort in the area of Maastricht. For inclusion, mean 2-hr glucose concentration of both OGTTs had to be between 7.8 and 12.5 mmol/l and fasting glucose concentration < 7.8 mmol/l. Data obtained during the

second (venous) OGTT were used as baseline values. The incidence of type 2 diabetes was determined according to WHO criteria of 1999 (WHO, 1999).

Screening and inclusion started in 1999. Originally, the study follow-up was 3 years, but this was extended to 6 years in 2002. In 2002, a second screening period was performed, and an additional 33 subjects were included in the study. In total, the study population consists of 147 subjects. The study was completed in June 2006 (see figure 1). Subjects were randomized, with stratification for sex and mean 2-hr plasma glucose concentration, to either the intervention group (INT: 74 subjects; 38 male, 36 female) or the control group (CON: 73 subjects; 37 male, 36 female). At the end of the intervention, 57 INT (77%) and 58 CON (79%) completed at least 3 years of lifestyle intervention, of whom 6 INT and 3 CON did not attend all measurements. In total 32 subjects (16 INT, 16 CON) discontinued study participation and were classified as dropout. Reason for discontinuation did not differ between study groups ($p=0.85$). It was calculated that based on the results of the Finnish DPS that 50-60 subjects per group would be sufficient to detect a 1.0 mmol/l difference in 2-hour glucose concentration between groups (Eriksson et al, 1999).

Lifestyle Intervention

The intervention program consisted of a dietary and physical activity part. The study design has been described in detail previously (Roumen et al, 2008). Dietary recommendations were based on the Dutch guidelines for a healthy diet (Dutch Nutrition Council). After consideration of a 3-day physical activity record, subjects received personalized advice by the researcher and/or dietician on how to increase their level of physical activity to at least 30 minutes a day for at least 5 days a week.

Measurements

In both groups, all measurements were performed annually. Measurements have been
5 described previously (Roumen et al, 2008). Additionally, in a questionnaire, subjects were
asked to fill in their highest educational background. At baseline and annually until year 3,
physical activity was measured with the Short QUestionnaire to ASsess Health-enhancing
physical activity (SQUASH) in all participants, which proved to be fairly reliable and
reasonably valid (Wendel-Vos et al, 2003). This Dutch questionnaire contains 10 questions
10 about the number of days spent per week, the average time spent per day and intensity
regarding four activity categories: commuting activities, leisure time activities, household
activities and activities at work and school. The questionnaire categorizes all activities into
light, moderate and vigorous intensity activities, based on MET (metabolic equivalent)
values defined by Ainsworth's compendium of physical activities (Ainsworth et al, 1993)
15 and the respondents' age.

Statistical analysis

Data analysis was conducted using SPSS for Windows (version 14.1). Insulin and serum
20 lipid concentrations were not normally distributed and were ln-transformed. Data are
presented as mean \pm SD in the tables and text, and as mean \pm SEM in the figures to
improve graphical presentation. Differences between groups at baseline were tested with a
Student's t test for independent samples or a chi-square test. Changes over time between
groups were assessed using mixed model analysis on intention to treat, which included all
25 available observations, including those from later dropouts. P-values of interaction

between group and time were used to indicate differences between the groups as a result of the lifestyle intervention. Survival analysis was used to determine the hazard ratio for diabetes development and to produce a Kaplan-Meier graph. Stepwise backward linear regression analysis was used to determine which parameters were associated with changes in glucose tolerance. A p-value of less than 0.05 was considered statistically significant. All tests were two-sided.

RESULTS

At baseline, no differences between the randomized groups were seen apart from age, which was higher in the control subjects (58.8 ± 8.4 years) compared to the intervention subjects (55.0 ± 6.5 years, $p=0.001$ for differences between groups; table 1).

Lifestyle-induced changes

In INT, total fat intake decreased ($p=0.01$ time x group interaction, figure 2A) and carbohydrate intake increased from 40.9 ± 7.5 E% at baseline to 46.7 ± 5.9 E% at the end of the study ($p=0.002$), whereas the increase was smaller in CON ($+1.2$ E%). INT decreased their saturated fat intake with 2.4%, while a minor decrease of 0.9% was observed for CON ($p<0.001$). Fiber intake increased in INT from 2.7 ± 0.7 mg/MJ to 3.4 ± 1.1 mg/MJ and increased less in CON from 2.7 ± 0.9 mg/MJ to 3.3 ± 1.2 mg/MJ ($p=0.05$). Changes in energy, cholesterol, protein and alcohol intake were similar between study groups ($p>0.05$, data not shown). Data on energy intake from baseline to year 3 have been published previously (Roumen et al., 2008).

During the lifestyle intervention, body weight decreased in INT after 1 year (-2.47 kg) and during the first 4 years (-0.32 kg) (table 1), but increased to baseline value at the end of the study, whereas body weight did not change in CON ($p=0.20$, figure 2B). Maximal aerobic capacity (VO_2 max) improved more in INT, compared to CON ($p=0.042$, figure 2C). To verify the association between physical activity and aerobic capacity we looked at the number of days that subjects were at least 30 minutes physically active doing walking, bicycling, gardening or doing sports after 3 years. Statistical analyses revealed that the number of active days per week increased significantly in the intervention group from 2.9 ± 2.4 days at baseline to 3.8 ± 2.5 days after 3 years (change: 0.9 ± 2.8 days), while those of the control group decreased from 3.0 ± 2.6 days at baseline to 2.5 ± 2.7 days (change: -0.55 ± 3.31 days). In the total population, the increase in number of days was significantly correlated with an increase in aerobic capacity ($r=0.343$, $p=0.01$). 2-Hr glucose levels decreased in INT in the first 4 years and thereafter increased slightly. In CON, 2-hr glucose increased from 8.80 ± 2.09 mmol/l to 9.38 ± 2.45 mmol/l ($p=0.041$) for average difference between groups (figure 2D). No differences between groups or over time were observed in fasting glucose, fasting insulin and 2-hr insulin, HOMA-IR, triglycerides, total cholesterol, HDL and LDL cholesterol, diastolic and systolic blood pressure or medication use ($p>0.05$, table 1). Diabetes incidence was higher in the control group compared to the intervention group with a p-value of the log-rank test that amounted to 0.04 and a relative risk of 0.53 (95% CI 0.29-0.97) (Figure 3).

At the end of the study, 115 (57 INT/58 CON) subjects were still participating and 32 (16 INT/16 CON) had dropped out. At baseline, adherent subjects had a higher VO_2 max ($p<0.05$), were higher educated and had a lower BMI and 2-hr glucose levels compared to dropouts ($p<0.01$, table 2). Results were similar when tested for the intervention group and control group separately.

Factors that determine intervention outcome

5 Regression analysis in INT (n=49) revealed that in a model including Δ body weight, Δ maximal aerobic capacity, Δ total fat intake and Δ fiber intake as covariates, only Δ body weight was significantly associated with changes in 2-hr glucose levels (standardized $\beta=0.303$ mmol/l per kg $p=0.04$). When replacing Δ bodyweight with Δ waist circumference, this parameter was slightly more strongly associated with Δ 2-hr glucose ($\beta=0.316$ mmol/l per cm, $p=0.03$). In the control group, suprailiacal skinfold thickness and 10 age at baseline predicted worsening in 2-hr glucose levels ($\beta=0.19$ mmol/l per cm, $p=0.05$; $\beta=0.23$ mmol/l per year, $p=0.01$).

DISCUSSION

15 The present study demonstrates novel information on factors associated with dropout and intervention outcomes, as well as confirms the long-term effectiveness of lifestyle intervention in the Dutch setting. Our findings add to the knowledge about identification, lifestyle effect and adherence in certain high-risk subgroups, and optimize implementation.

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Diabetes risk

In our lifestyle intervention the difference in 2-hr plasma glucose levels between groups 25 remained as high as 0.72 mmol/l, which was associated with a diabetes risk reduction of

47%, despite no significant differences in body weight between groups. Nevertheless, in agreement with previous results from the DPP (Hamman et al., 2006), stepwise regression analyses revealed that variation in body weight loss and waist circumference was the most important determinant of the change glucose tolerance. Adherence to a more rigid regime regarding weight loss, compared to what we have achieved in our study, may result in even greater improvements. The control group showed a relatively small increase in 2-hr glucose levels and one may argue that the control group would not reflect the actual general population. However, at present, self-monitoring, self-tests, multimedia attention and increasing information availability and presentation of diabetes and diabetes-related complications may well increase awareness of the general population and induce small changes in their dietary and physical activity habits. The control group in our study may therefore be reflective of the informed general population at present.

Subjects in the intervention group had a sustained higher aerobic compared to the control group and they increased their total number of physically active days per week.

Unfortunately, we were not able to analyze whether attendance to the exercise program predicted the outcome of the intervention due to limited power. However, since approximately 70% of the intervention subjects also used other exercise facilities or physical activities, the total number of physically active days per week may be more indicative for the whole intervention group. Physical activity may independently reduce diabetes risk (Hamman et al., 2006), also by sustaining weight loss (Hamman et al., 2006). Even small sustained increases in physical activity, as was also observed in this study, seem beneficial in the long term. Surprisingly, changes in aerobic capacity were not correlated with changes in glucose tolerance, possibly due to lack of statistical power for aerobic capacity (n=48 for the intervention group).

Similar to the DPS, our lifestyle intervention did not have an effect on total or HDL-cholesterol, triglyceride levels and blood pressure, or on medication use, which could have masked the lifestyle effects (Ilanne-Parikka et al, 2008).

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Dropouts to the intervention program

A limitation in the present study is the seemingly high dropout rate, 21% in total (31 out of the 147 subjects). This percentage is higher compared to previous reports of the DPS (Tuomilehto et al., 2001) and the DPP (Knowler et al., 2002). On the other hand, our dropout percentage is similar to that of other lifestyle interventions after 1-2 year follow-up (Oldroyd et al, 2006, Swinburn et al, 2001) and to that observed in the DREAM trial after a follow-up for a median of 3 years (Gerstein et al, 2006), with 29.3% (772/2635) dropout in the rosiglitazone group and 25.0% (658/2634) in the control group. Two explanations for the difference between the DPS, DPP and SLIM can be given. First, our participants were originally extracted from the general population and they may have had less internal motivation to participate in the study, as compared to subjects recruited via advertisements, as was done in the DPS (Eriksson et al, 1999). Second, no specific weight loss program was provided which may have led to dissatisfaction for participants. In our study, subjects unable to participate until the end of the study had a lower social economic status, a lower VO₂ max and a higher BMI and 2-hr glucose levels at baseline, than those who completed the study. This clustering of factors is known from previous studies, which have found that a low educational background is associated with increased risk for obesity (BallCrawford, 2005) and that a low occupational position in adulthood is

associated with a higher prevalence of type 2 diabetes in men and women (Agardh et al, 2007).

Subjects with a low maximal aerobic capacity were more likely to become a dropout. This is an alarming finding, since it was previously reported in the U.S. that especially high-risk subjects do not engage in regular physical activity (Morrato et al, 2007). Therefore, these subjects may be especially prone to dropout en stay in their non-active physical behavior. This may lead to a vicious circle in which the non-active behavior accelerates overweight and an unfavorable body fat distribution. To verify this finding, results from larger randomized studies regarding dropout are warranted.

Overall, the high dropout rate in the SLIM study in subjects with the worst metabolic profile and a lower social economic status exemplifies the difficulty to reach and sustain lifestyle changes in this vulnerable group and, requires special programs to tailor the intervention in these groups.

Recommendations

Although, this study is already promising, better results may be achieved with special tailored programs for subjects with a low-socio-economic status to enable these subjects to change their lifestyle. Besides reducing costs of healthy food and facilities for physical activity, improving perceived susceptibility for getting diabetes and misconception about ones adherence, can improve this lifestyle program. Future research has to address the barriers and promoting factors for implementing this lifestyle intervention in the general public health setting with most likely a key role for the general practitioner.

Summary

Our results underscore that prolonged feasible changes in diet and physical activity prevent deterioration of glucose tolerance and reduce diabetes risk by 47% over a mean of 4.1 years. Variation in body weight loss and waist circumference was most strongly associated with the improved glucose tolerance, exemplifying the importance of body weight and central body fat reduction. Low social economic status and low aerobic fitness are indicative of dropout to the program, suggesting that these subjects may need special attention to achieve beneficial changes in their lifestyle and metabolic profile.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Table 1. Changes in body composition, glucose metabolism and blood lipid profile during the intervention period.

Parameter		Baseline	Year 1	Year 2	End	P Group	P Time	P* for Group x Time interaction
N	INT	74	64	56	57	-	-	-
	CON	73	65	58	58	-	-	-
Age (years)	INT	55.0 ± 6.5	-	-	-	<0.01	-	-
	CON	58.8 ± 8.4	-	-	-	-	-	-
Low Social economic status	N (% of total)					0.50	-	-
	INT	37 (50%)	-	-	-	-	-	-
Smoking status	CON	40 (55%)	-	-	-	-	-	-
	N (% of total)					0.60	-	-
Weight (kg)	INT	86.83 ± 13.24	84.36 ± 13.18	85.98 ± 13.52	85.74 ± 13.56	0.30	<0.01	0.20
	CON	84.08 ± 12.06	83.47 ± 11.38	83.32 ± 11.15	84.04 ± 11.99	-	-	-
BMI (kg/m ²)	INT	29.89 ± 4.16	28.78 ± 3.86	29.16 ± 3.84	29.19 ± 3.90	0.90	0.06	0.46
	CON	29.65 ± 3.42	29.35 ± 3.22	29.19 ± 3.14	29.37 ± 3.32	-	-	-
Waist (cm)	INT	103.6 ± 11.3	100.1 ± 11.2	102.1 ± 10.7	102.9 ± 11.1	0.70	<0.01	0.71
	CON	103.6 ± 9.7	101.6 ± 9.8	102.3 ± 9.5	104.2 ± 8.5	-	-	-
VO _{2max} (l/min)	INT	2.18 ± 0.59	2.38 ± 0.63	2.39 ± 0.62	2.35 ± 0.63	0.03	<0.01	0.04
	CON	2.06 ± 0.57	2.14 ± 0.60	2.04 ± 0.59	2.08 ± 0.61	-	-	-
Fasting glucose (mmol/l)	INT	6.01 ± 0.84	5.96 ± 0.88	6.05 ± 1.09	6.30 ± 1.07	0.31	<0.01	0.19
	CON	5.92 ± 0.70	5.94 ± 0.64	6.31 ± 0.84	6.48 ± 0.86	-	-	-
2-Hr Glucose (mmol/l)	INT	8.85 ± 2.01	8.24 ± 2.04	8.50 ± 2.51	8.66 ± 2.38	0.10	<0.01	0.04
	CON	8.80 ± 2.09	8.79 ± 2.25	9.35 ± 2.64	9.38 ± 2.45	-	-	-
Fasting insulin (mU/l)	INT	17.97 ± 8.72	16.03 ± 7.41	12.04 ± 6.61	16.51 ± 8.15	0.84	<0.01	0.68
	CON	17.39 ± 6.89	17.56 ± 8.04	13.31 ± 7.92	16.39 ± 7.26	-	-	-
HBA1c	INT	5.92 ± 0.48	5.69 ± 0.42	5.79 ± 0.59	6.27 ± 0.79	0.85	<0.01	0.91
	CON	5.96 ± 0.51	5.75 ± 0.44	5.85 ± 0.44	6.19 ± 0.72	-	-	-
2-Hr Insulin (mU/l)	INT	96.94 ± 65.96	91.79 ± 80.61	85.18 ± 47.23	118.28 ± 67.46	0.27	<0.01	0.52
	CON	105.91 ± 87.56	103.88 ± 64.25	91.35 ± 65.45	113.36 ± 75.94	-	-	-
HOMA-IR	INT	4.89 ± 2.83	4.32 ± 2.24	3.40 ± 1.94	4.75 ± 2.64	0.44	<0.01	0.54
	CON	4.65 ± 2.09	4.74 ± 2.47	3.74 ± 2.24	4.79 ± 2.39	-	-	-

Glucose lowering Medication	N (%)	INT	0 (0%)	0 (0%)	1 (2%)	5 (9%)	0.98		Chi-square End [†]
		CON	0 (0%)	0 (0%)	0 (0%)	5 (9%)			
Triglycerides	(mmol/l)	INT	1.52 ± 1.18	1.5 ± 1.39	1.24 ± 0.56	1.74 ± 1.87	0.29	<0.01	0.12
		CON	1.44 ± 0.79	1.61 ± 1.19	1.45 ± 1.60	1.53 ± 1.06			
Total cholesterol	(mmol/l)	INT	5.17 ± 0.83	5.14 ± 0.81	5.40 ± 0.85	5.51 ± 0.82	0.58	<0.01	0.43
		CON	5.27 ± 0.85	5.39 ± 0.85	5.55 ± 0.89	5.48 ± 0.97			
HDL cholesterol	(mmol/l)	INT	1.14 ± 0.30	1.14 ± 0.30	1.21 ± 0.33	1.25 ± 0.37	0.25	<0.01	0.41
		CON	1.11 ± 0.28	1.10 ± 0.30	1.16 ± 0.30	1.18 ± 0.31			
LDL cholesterol	(mmol/l)	INT	3.39 ± 0.81	3.35 ± 0.80	3.59 ± 0.81	3.57 ± 0.86	0.30	0.03	0.39
		CON	3.51 ± 0.75	3.60 ± 0.81	3.66 ± 0.81	3.57 ± 0.72			
Blood lipid lowering Medication	N (%)	INT	6 (8%)	5 (8%)	6 (11%)	12 (21%)	0.97		Chi-square End [†]
		CON	5 (7%)	8 (12%)	8 (14%)	12 (21%)			
Diastolic blood pressure	(mm Hg)	INT	89.0 ± 9.4	87.6 ± 7.3	87.6 ± 7.3	83.8 ± 7.9	0.22	<0.01	0.52
		CON	89.1 ± 7.8	88.6 ± 8.0	85.4 ± 8.0	84.9 ± 7.6			
Systolic blood pressure	(mm Hg)	INT	141.6 ± 16.7	138.0 ± 14.7	137.2 ± 14.7	138.6 ± 14.3	0.07	<0.01	0.91
		CON	145.0 ± 14.6	141.0 ± 16.0	139.9 ± 13.5	141.2 ± 13.9			
Blood pressure lowering Medication	N (%)	INT	21 (28%)	21 (33%)	18 (32%)	29 (51%)	0.07		Chi-square End [†]
		CON	18 (25%)	16 (25%)	18 (31%)	19 (33%)			

Data are mean ± SD. *P-value using intention-to-treat analysis using all available data regarding the difference between the groups over a mean follow-up of 4.1 (3-6) years. P-value for fasting glucose, 2-hr glucose, triglycerides, total cholesterol, HDL cholesterol, LDL cholesterol, diastolic and systolic blood pressure were adjusted for medication use. [†]Data on medication use are analysed using a chi-square test, presenting the p-value at the end of intervention for differences between study groups.

Table 2. Baseline characteristics of those who completed the full study protocol (completers) compared to those who discontinued participation previous to the end of the study (dropouts).

		Completers	Dropouts	P
n		115	32	-
INT (male/female)		57 (30/27)	16 (7/9)	0.49
CON (male/female)		58 (32/26)	16 (6/10)	0.13
Age	(years)	56.2 ± 7.1	58.3 ± 6.7	0.16
Low Social Economic Status	N (% of total)	47 (41%)	23 (72%)	<0.01
Smoking status	N (% of total)	15 (13%)	3 (9%)	0.62
Weight	(kg)	85.1 ± 13.0	87.0 ± 11.4	0.46
BMI	(kg/m ²)	29.4 ± 3.5	31.3 ± 4.4	<0.01
Waist	(cm)	102.8 ± 10.2	106.6 ± 11.3	0.07
Bodyfat percentage	%	38.1 ± 6.3	40.4 ± 6.4	0.07
Diastolic blood pressure	(mm Hg)	89.3 ± 8.4	88.2 ± 9.6	0.52
Systolic blood pressure	(mm Hg)	142.8 ± 15.7	145.1 ± 16.0	0.47
VO ₂ max	(l/min)	2.2 ± 0.6	1.9 ± 0.6	0.04
Fasting glucose	(mmol/l)	5.9 ± 0.8	6.1 ± 0.7	0.23
2h glucose	(mmol/l)	8.6 ± 1.7	9.8 ± 2.8	<0.01
HBA1c	(%)	5.9 ± 0.5	6.1 ± 0.5	0.15
Fasting insulin	(mU/l)	17.4 ± 6.6	18.8 ± 11.5	0.94
2h insulin	(mU/l)	99.12 ± 78.9	110.6 ± 72.9	0.42
HOMA-IR		4.6 ± 2.0	5.2 ± 3.8	0.79
Triglycerides	(mmol/l)	1.4 ± 0.7	1.4 ± 0.6	0.91
Total Cholesterol	(mmol/l)	5.2 ± 0.8	5.3 ± 1.0	0.73
HDL cholesterol	(mmol/l)	1.1 ± 0.3	1.1 ± 0.3	0.95
LDL cholesterol	(mmol/l)	3.4 ± 0.7	3.5 ± 0.9	0.56
Total energy intake	(MJ/day)	8.8 ± 2.4	8.2 ± 2.1	0.18
Total fat intake	(En%)	35.6 ± 6.7	35.5 ± 6.4	0.94
Saturated fat intake	(En%)	13.6 ± 3.2	13.4 ± 3.2	0.74
Total carbohydrate intake	(En%)	42.2 ± 7.5	43.8 ± 6.0	0.31
Fibre intake	(mg/MJ)	2.7 ± 0.8	2.9 ± 0.9	0.17
Alcohol consumption	(En%)	5.8 ± 6.3	4.2 ± 7.6	0.24

Data are Mean ± SD.

Figure 1. Trial profile. Participants who dropped out of the program were were treated as censored observations in the intention-to-treat analyses.

Figure 2 A-D. Changes in lifestyle parameters and 2-hr glucose concentrations, presented as mean \pm SEM, during a combined diet-and-exercise lifestyle intervention to prevent type 2 diabetes. Total fat intake (A), Body weight (B), VO₂ max (C), and 2-hr plasma glucose levels (D) for the intervention group (black squares) and control group (open triangles) at baseline, after 1 year, 2 years and at the end of the lifestyle intervention (mean 4.1 years). Dashed lines between year 2 and endpoint represents estimate progression in between.

Figure 3. Proportion of subjects with diabetes during the lifestyle intervention. Cumulative diabetes incidence in the intervention group and control group. The relative risk of diabetes for subjects in the intervention group, as compared with those in the control group, was 0.53 (P=0.04 for the comparison between the groups).

March 1999-May 2000

114 randomized

May 2002-November 2000

33 randomized

Baseline

74 intervention

73 control

End of intervention
june 2006

52 intervention

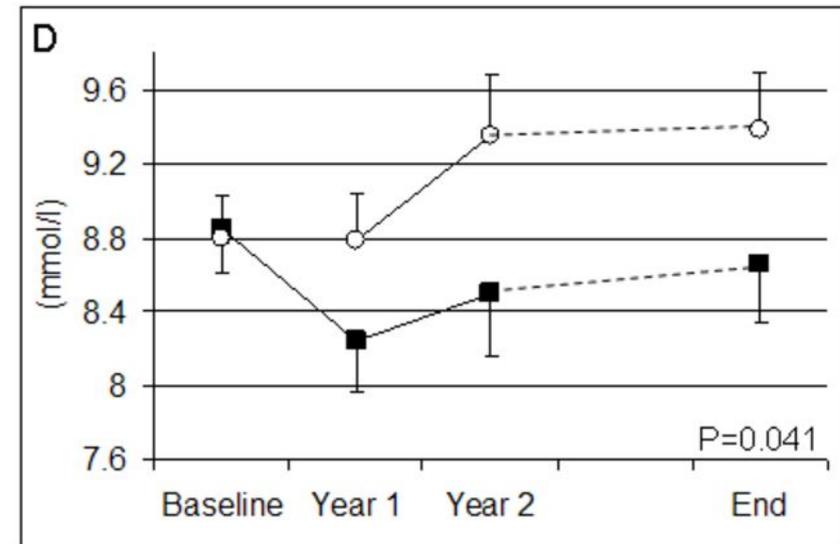
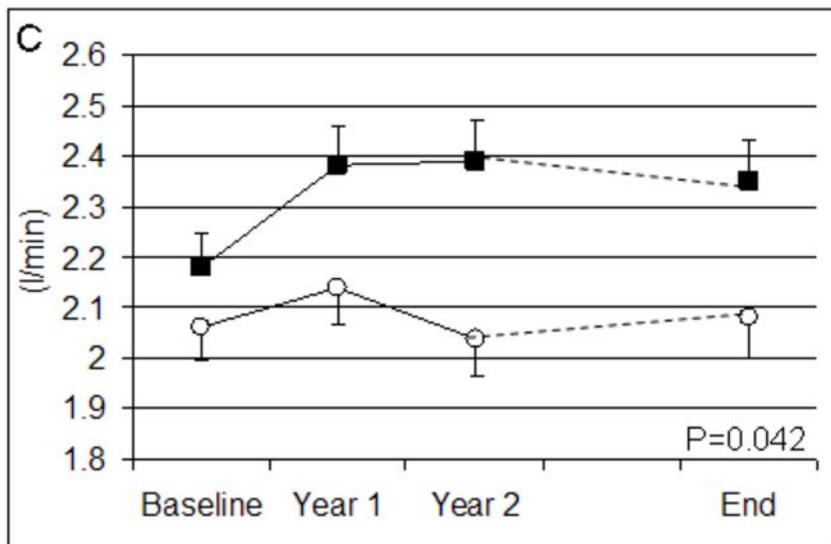
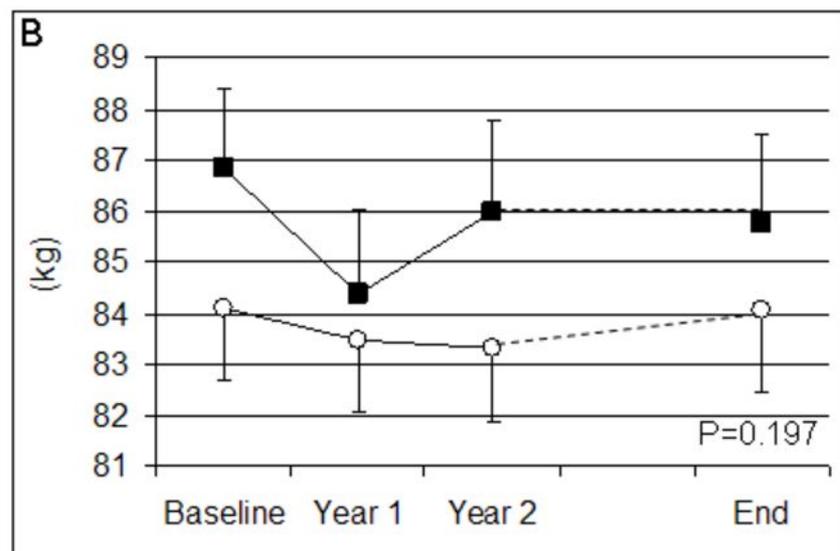
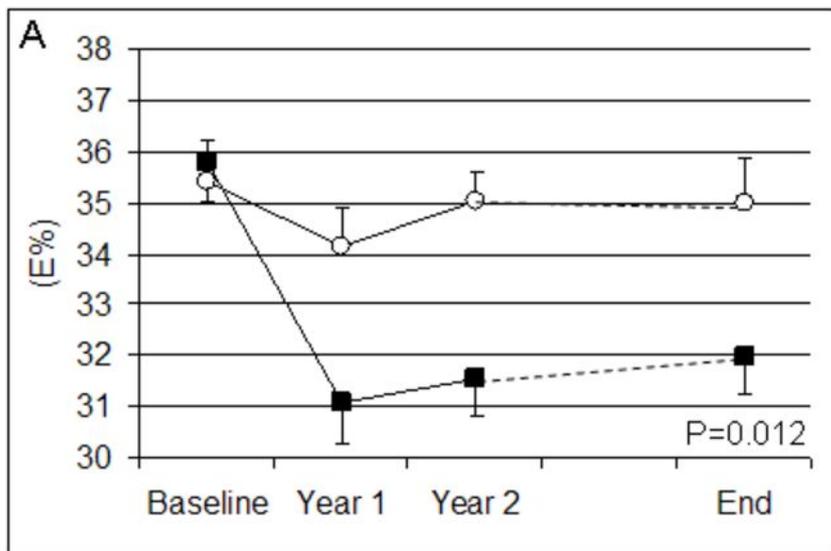
6 not all years
16 dropout:
6 medical reasons
5 lack of time
2 lack of motivation
1 no response
1 no transportation
1 unknown

54 control

3 not all years
16 dropout:
4 medical reasons
2 lack of time
5 lack of motivation
3 dissatisfied
1 deceased
1 unknown

Of 52 intervention:
52 completed 3 yrs
51 completed 4 yrs
34 completed 5 yrs
1 missed yr 5, but
attended yr 6
35 completed 6yrs

Of 54 control:
54 completed 3 yrs
43 completed 4 yrs
29 completed 5 yrs
6 missed yr 5, but
attended yr 6
35 completed 6yrs



Kaplan-meier estimate of probability of developing diabetes

