２．村上文代　伊藤千賀子、石田さくらこ．2 型糖尿病の一次予防に関する介入研究．日本病態栄養学会誌 2004;7(1):27-34
３．山口満喜子 田中亨　浮田千津子 他．軽度耐糖能異常症例に糖尿病専門外来で早期に介入する意義．京都医学会雑誌 2002;49(2):39-42
４．藤村孝枝　糖尿病集団予防教育の効果　健診成績の推移を評価指標とした検討　山口医学 2003;52(4):125-133

9.　研究対象：

スクリーニングによって見出された 2 型糖尿病発症ハイリスク者

評価モデルの③または④の研究（高血糖状態をエンドポイントとすれば　③、中間状態と考えれば　④となる）

10.　研究の質：

国内外すべて Efficacy 研究と考えられる。

11.　対象者の年齢：

国内外ともにほとんどの研究の主な対象は壮年者であるが、一部、25-39 歳の青年、65 歳-80 歳の老年までを含めている研究もある。

12.　対象者の性別：

国内外ともにほとんどの研究は男女混合だが、国内の 1 研究が男のみを対象としている。

13.　介入の方法：

国外の長期介入研究はいずれも基本的には面接を中心とした個人指導である。一部の研究では集団指導、グループワークなどを個人指導に付加している。

国内の無作為化された研究では面接による個人指導、3 日間の入院と以後 6 ヶ月間の電話によるカウンセリング、対象者からの自己血糖測定結果の送付とそれに対する手紙による返答などが試みられている。

14.　介入の期間：

国外の長期介入研究では糖尿病の罹患率を比較するため介入期間は 3－6 年間としている。

国内の短期介入研究では耐糖能関連指標の比較のため 4-12 ヶ月程度である。

15.　介入の間隔：

国外の長期介入研究 DPP、DPS、DaQing 研究などでは初期の半年から 1 年間には頻回に面接し（DPP、DaQing 研究：最初の半年に 16 回、DPS：最初の 1 年に 7 回）、その後も 1-3 ヶ月毎に個別および集団での介入を継続して行っている。

国内の無作為化された短期介入研究では月に 1 回程度の面接、電話、手紙などの方法が試

みられている。

16. 今後の課題：

費用効果を含む実行の可能性（Effectiveness）が十分に評価されていない。とくに、糖尿病（高血糖状態）が長期間持続した場合に引き起こされる合併症（網膜症・腎症・神経障害・動脈硬化症など）による身体的機能障害への効果が明らかではない。ただし、この効果の検証を科学的に行うことは極めて困難である。今後の課題を列挙する。

1. 生活習慣改善の費用効果に関する研究。一次予防によって糖尿病にともなう疾患の罹患率、死亡率に影響があるか？
2. 前糖尿病状態（ハイリスク者）を同定するもっとも効果的な方法は？
3. 少ない医療資源を用いる介入プログラムの開発
4. 体重減少・身体活動量増加を維持するプログラムの開発
5. 前糖尿病者を同定し生活習慣改善を達成・維持するための、社会的理解・医療関係者の教育・健康保健政策の優れた協力体制の構築に関する研究
6. 地域介入研究の実施によるその有効性等について検証

17. エビデンステーブル：

国外の5研究、国内の8研究（9文献）について概要をまとめた。国外の5研究はすべて無作為割付による長期介入研究である。国内の8研究のうち、4研究は短期ではあるが、無作為割付介入研究である。

論文検索結果一覧：

対象者数と介入研究のデザインで分類した（1群100人以上かどうか、無作為割付かどうか）。

海外論文検索結果　データベース：PubMed (Medline)　　検索年代：制限せず

Ⅰ　1群100人以上の無作為割付介入研究

1) DPP (Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin.　N Engl J Med. 346:393-403, 2002)

2) DPS (Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance.　N Engl J Med 344:1343-50, 2001

3) Da Qing Study　(Pan XR, 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 20:537-44, 1997.)

4) Wein P, Beischer N, Harris C, et al. A trial of simple versus intensified dietary modification for prevention of progression to diabetes mellitus in women with impaired glucose tolerance. Aust N Z J Obstet Gynaecol 39:162-6, 1999

Ⅱ　1群100人未満の無作為割付介入研究

1) Brekke HK, Jansson PA, Mansson JE et al. Lifestyle changes can be achieved through counseling and follow-up in first-degree relatives of patients with type 2 diabetes.　J Am Diet Assoc 2003 ;103(7):835-43.

2) Watanabe M, Yamaoka K, Yokotsuka M, et al. Randomized controlled trial of a new dietary education program to prevent type 2 diabetes in a high-risk group of Japanese male workers. Diabetes Care 2003 ;26(12):3209-14.
3) Mensink M, Corpeleijn E, Feskens EJ et al. Study on lifestyle-intervention and impaired glucose tolerance Maastricht (SLIM): design and screening results. Int J Obes Relat Metab Disord 2003 ;27(3):377-84.
4)Grey M, Berry D, Davidson M, Galasso P, et al. Preliminary testing of a program to prevent type 2 diabetes among high-risk youth. J Sch Health2004 ;74(1):10-5.
5)Mensink M, Blaak EE, Corpeleijn E, et al. Lifestyle intervention according to general recommendations improves glucose tolerance. Obes Res. 2003 ;11(12):1588-96.
6)Tate DF, Jackvony EH, Wing RR. Effects of Internet behavioral counseling on weight loss in adults at risk fortype 2 diabetes: a randomized trial. JAMA. 2003 9;289(14):1833-6
7) Swinburn BA, Metcalf PA, Ley SJ. Long-term (5-year) effects of a reduced-fat diet intervention in individuals with glucose intolerance. Diabetes Care. 2001 ;24(4):619-24
8) Wing RR, Venditti E, Jakicic JM et al. Lifestyle intervention in overweight individuals with a family history of diabetes. Diabetes Care 1998 ;21(3):350-9.
9) Andersen RE, Wadden TA, Bartlett SJ, et al. Effects of lifestyle activity vs structured aerobic exercise in obese women: a randomized trial. JAMA 1999 27;281(4):335-40
10) Samaha FF, Iqbal N, Seshadri P, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. N Engl J Med 2003 22;348(21):2074-81
11)Narayan KM, Hoskin M, Kozak D. Randomized clinical trial of lifestyle interventions in Pima Indians: A pilot study. Diabet Med 1998;15:66-72

Ⅲ 1群100人以上で対照群はあるが無作為割付でない介入研究

1)Simmons D, Voyle JA, Fou F, et al. Tale of two churches: differential impact of a church-based diabetes control programme among Pacific Islands people in New Zealand. Diabet Med. 2004 ;21(2):122-8
2)Swartz AM, Strath SJ, Bassett DR, et al. Increasing daily walking improves glucose tolerance in overweight women. Prev Med. 2003 ;37(4):356-62
3)Eriksson KF, Lindgarde F. Prevention of type 2 (non-insulin-dependent) diabetes mellitus by diet and physical exercise. The 6-year Malmo feasibility study. Diabetologia. 1991 ;34(12):891-8.
4) Eriksson KF, Lindgarde F. No excess 12-year mortality in men with impaired glucose tolerance who participated in the Malmo Preventive Trial with diet and exercise. Diabetologia 1998 ;41(9):1010-6.
4)Long SD, O'Brien K, MacDonald KG Jr, et al. Weight loss in severely obese subjects prevents the progression of impaired glucose tolerance to type II diabetes. A longitudinal interventional study. Diabetes Care. 1994 ;17(5):372-5
5) Holcomb JD, Lira J, Kingery PM et al. Evaluation of jump into action: a program to reduce the risk of non-insulin dependent diabetes mellitus in school children on the Texas-Mexico

border. J Sch Health 1998;68(7):282-8
6)Bjaras G, Harberg LK, Sydhoff J et al. Walking campaign: a model for developing participation in physical activity? Experiences from three campaign periods of the Stockholm Diabetes Prevention Program (SDPP). Patient educ counsel 2001;42:9-14
7)Bjaras G, Ahlbom A, Alvarsson M. Strategies and methods for implementing a community-based diabetes prevention program in Sweden. Promot Internation 1997;12:151-60
8)Daniel M, Green LW, Marion SA. Effectiveness of community-directed diabetes prevention and control in a rural Aboriginal population in British Columbia, Canada. SocSciMed1999;48:815-32
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10)Simmons D, Fleming C, Cameron M et al. A pilot diabetes awareness and exercise programme in a multiethnic workforce. N Z Med J 1996;109(1031):373-6
11)Simmons D, Fleming C, Voyle J et al. A pilot urban church-based programme to reduce risk factors for diabetes among Western Samoans in New Zealand. Diabet Med 1998;15(2):136-42

Ⅳ 1群100人未満で対照群はあるが無作為割付でない介入研究

1) Racette SB, Weiss EP, Obert KA, et al. Modest lifestyle intervention and glucose tolerance in obese African Americans. Obes Res 2001 ;9(6):348-55.

Ⅴ 100人以上で対照群のない介入研究

1)Rowley K, Gault A, McDermott R et al. Reduced prevalence of impaired glucose tolerance and no change in prevalence of diabetes despite increasing BMI among aboriginal people from a group of rwemote homeland communities. Diabetes care 2000;23:898-904
2) Teufel NI. Ritenbaugh CK. Development of a primary prevention program: insight gained in the Zuni Diabetes Prevention Program. Clin Pediatr 1998;37(2):131-141
3) Trevino RP, Pugh JA, Hernandez AE. Bienestar:a diabetes risk factor prevention. J Sch Health 1998;68(2):62-7

Ⅵ 100人未満で対照群のない介入研究

1) Bourn DM, Mann JI, McSkimming BJ, et al. Impaired glucose tolerance and NIDDM: does a lifestyle intervention program have an effect? Diabetes Care 1994 ;17(11):1311-9
2) Marlow E, Melkus G, Bosma A. Stop diabetes! An educational module for Native American adolescents in the prevention of diabetes. Diabetes educ1998;24:441-450

Ⅶ その他 (cluster randomization)

1) Trevino RP, Yin Z, Hernandez A, et al. Impact of the Bienestar school-based diabetes mellitus prevention program on fasting capillary glucose levels: a randomized controlled trial. Arch Pediatr Adolesc Med 2004 ;158(9):911-7

国内の文献検索結果 データベース：医学中央雑誌検索年代：1990-2004年

Ⅰ 1群100人以上の無作為割付介入研究

1)高田康光 西田博，王韜玉． 自己血糖測定を用いた保健指導の血糖改善効果．大阪医学 2002;36:5-9

2)Takata.Y, OuOngyoku, Nishida H et al. Impact of self-monitoring of blood glucose on the lifestyle of subjects with fasting hyperglycemia: A random controlled trial. Journal of occupational health.2002;44:28-33

3)渡邉至 岡山明 島本和明他． 軽症耐糖能異常者に対する個別健康教育による無作為割付介入研究．健康医科学研究助成論文集 2000;15:166-170

Ⅱ 1群100人未満の無作為割付介入研究

1)Fukuda.H, Muto T, Kawanomori R, et al. 軽度2型糖尿病及びIGT（耐糖能障害）に対する3日入院及び電話相談による6ヶ月追跡より成る糖尿病患者教育プログラムの評価(英語). Environmental health and preventive medicine 1999;4(3):122-129

Ⅲ 100人以上で対照群のない介入研究

1)甲斐裕子 熊谷秋三 高柳茂美 他．医療機関と病院外施設の連携モデルと軽症糖尿病患者への健康行動支援プログラムの適用と効果．糖尿病 2003;46(7):533-539

2)勝川史憲．生活習慣病の運動療法 理論から保険診療 若年成人肥満者を対象者とした運動＋食事指導による生活習慣修正の効用．日本臨床スポーツ医学会誌 2003;11(3):454-463

Ⅳ 100人以上で対照群はあるが無作為割付でない介入研究

1) 石田さくらこ、伊藤千賀子、村上文代他．生活習慣介入による糖尿病一次予防（The Diabetes Prevention Program of Hiroshima ; DPPH) -概要および介入1年後の成果-．糖尿病 2004 ; 47 : 707-13

2)村上文代 伊藤千賀子、石田さくらこ．2型糖尿病の一次予防に関する介入研究．日本病態栄養学会誌 2004;7(1):27-34

3)山口満喜子 田中亨 浮田千津子 他．軽度耐糖能異常症例に糖尿病専門外来で早期に介入する意義．京都医学会雑誌 2002;49(2):39-42

4)藤村孝枝 糖尿病集団予防教育の効果 健診成績の推移を評価指標とした検討 山口医学 2003;52(4):125-133

Ⅴ 100人未満で対照群のない介入研究

1)隈元庸夫，伊藤俊一．糖尿病教室への運動療法介入．北海道理学療法 2004;21:17-22

2)伴野祥一，柳川益美， 福村幸仁 他．群馬町での生活習慣予防研究(第一報)．群馬大学医学部保健学科紀要 2002;22:41-45

Ⅵ 100人未満で対照群はあるが無作為割付でない介入研究

1)高田康光．境界型糖尿病症例での自己管理方法と効果的な運動療法．大阪医学 2001;35(1):20-24

Ⅶ人数デザイン等詳細不明（抄録無し）

1)田吹好美．耐糖能異常者への健康教育による生活改善の評価．鉄鋼労働衛生 1993;41(1):91-99

2)友岡裕治，藤洋吐，鳥巣要道 他．耐糖能異常者に対する糖尿病予防教室の効果．公衆衛生 1993;57(6):413-417

海外のレビュー　データベース：PubMed (Medline)　検索年代：2004年

検索式

"diabetes mellitus, type ii"[MeSH Terms] AND ("prevention and control"[Subheading] OR Prevention[Text Word]) AND Review[ptyp] AND English[Lang] AND medline[sb] AND ("human"[MeSH Terms] OR "hominidae"[MeSH Terms]) AND ("2004/01/01"[PDAT] : "3000"[PDAT])　：103件ヒット

主要なもの：

1) ADA: Prevention or Delay of Type 2 Diabetes Diabetes Care. 2004 Jan;27 Suppl 1:S47-54.
2) CDC：　Primary Prevention of Type 2 Diabetes Mellitus by life style Intervention: Implication of Health Policy. Ann Intern Med 140:951-957, 2004
3) Preventing Cancer, Cardiovascular Disease, and Diabetes. A common agenda for the American Cancer Society, the American Diabetes Association, and the American Heart Association Diabetes Care 27:1812-1824, 2004
4) Davies MJ, Tringham JR, Troughton J, Khunti KK. Prevention of Type 2 diabetes mellitus. A review of the evidence and its application in a UK setting. Diabet Med. 2004 May;21(5):403-14.
5) Community-Based Lifestyle Interventions to Prevent Type 2 Diabetes Diabetes Care 26:2643-2652, 2003

1）は、米国糖尿病協会（ADA）の Position Statement。3）は、ACS, ADA, AHA 3学会の共同レビュー。5）は、2003年のものであるが、Community-basedのものであるので加えた。

Randomized Controlled Trial of a New Dietary Education Program to Prevent Type 2 Diabetes in a High-Risk Group of Japanese Male Workers

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OBJECTIVE — The aim of this study was to assess the effectiveness of a new dietary education (NDE) program in reducing plasma glucose (PG) levels in Japanese male workers at high risk for type 2 diabetes through a randomized controlled trial.

RESEARCH DESIGN AND METHODS — We randomly assigned 173 high-risk men (mean age, 55 years) to either the NDE or the control (conventional dietary education) group. Each subject in the NDE group received two individualized interventions especially aimed at reducing total energy intake at dinner by modifying dietary intake. The control group received conventional group counseling. An "overintake/underintake fraction" for total energy intake was used to measure the status of dietary intake. Our hypothesis was that the NDE group would have a 10% decrease in 2-h PG 1 year after the start of the education. Outcome measures were compared with ANCOVA by adjusting for baseline values.

RESULTS — The NDE group had a significantly lower total energy intake at dinner and daily than the control group. The adjusted differences in changes from baseline in the absolute value of the "overintake/underintake fraction" were −15.3% (95% CI −24.6 to −6.0%, $P = 0.002$) for the NDE group and −6.0% (−9.8 to −2.2%, $P = 0.002$) for the control group. The NDE group had a decreased 2-h PG after 1 year, whereas that value was increased in the control group. The adjusted difference in the percent change of 2-h PG was significant (−15.2%, −22.0 to −8.4%, $P < 0.001$).

CONCLUSIONS — The NDE was shown to reduce glucose levels in high-risk subjects for type 2 diabetes.

Diabetes Care 26:3209–3214, 2003

The incidence of type 2 diabetes is increasing worldwide, and its prevalence in adults was estimated to rise to 5.4% by 2025 (1). With the change in recent years from the traditional Japanese lifestyle to a western lifestyle, the prevalence of type 2 diabetes has drastically increased with estimates of no fewer than 6,900,000 cases in Japan (2). This disease leads to vascular complications that result in considerable morbidity and premature mortality (3). Type 2 diabetes incurs serious health problems among the Japanese (4). Dietary education at an early stage may play a key role in preventing diabetes. Considering the poor quality of life that can result from diabetes, effective dietary education that would delay or avoid progression to diabetes in those at high risk is clearly important.

Management of diabetes in primary care has been well studied (5–7). In addition, the effects of dietary education as an intervention in high-risk subjects have been the topic of several reports (8–11). Many Japanese male workers tend to eat and drink a great deal late at night, and changing the habit of excess energy intake during this period might reduce the risk for diabetes. For the purpose of attaining and maintaining optimal blood glucose levels and of modifying dietary intake as appropriate for prevention, we developed a new dietary education (NDE) program based on information on an individual's dietary energy intake for breakfast, lunch, and dinner. Information was obtained through use of the semiquantitative food frequency questionnaire that included lists of 65 food items for each meal (FFQW65) (12). Our aim was to assess the effectiveness of the NDE in reducing plasma glucose (PG) levels in Japanese male workers at high risk for type 2 diabetes through a randomized controlled trial and, at the same time, to implement an evidence-based nutritional program.

RESEARCH DESIGN AND METHODS

— The randomized controlled study was designed to assess the effectiveness of the NDE in reducing PG to test the hypothesis that subjects participating in the NDE would have a 10% reduction in the 2-h PG level in the 75-g oral glucose tolerance test (2-h PG, primary end point) 1 year after the start of the education (described in Dietary intervention section) compared with a control group that received conventional dietary education. Enrollment and treatment of

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Received for publication 11 June 2003 and accepted in revised form 28 August 2003

Abbreviations: FFQW65, food frequency questionnaire (65 items); FPG, fasting plasma glucose; ITT, intent to treat; JDS, Japanese Diabetes Society; NDE, new dietary education; PG, plasma glucose; RDA, recommended dietary allowance.

A table elsewhere in this issue shows conventional and Systeme International (SI) units and conversion factors for many substances.

subjects were conducted in accordance with the Helsinki Declaration, and all study subjects gave written informed consent.

Eligibility and exclusion criteria

Study subjects were male workers at high risk for type 2 diabetes, aged 35–70 years, and living in a metropolitan area of Tokyo, Japan. The Japanese Diabetes Society (JDS) Committee has classified the glycemic state into three categories based on fasting plasma glucose (FPG) and 2-h PG (13). Because the JDS strongly recommended considering patients with 1-h PG values of ≥10 mmol/l as borderline, to capture patients at an early stage for risk of diabetes in addition to those above-described definitions, we treated patients with 1-h PG ≥10 mmol/l as borderline in the present study. Our definition was as follows: normal, FPG <6.1 mmol/l, 2-h PG <7.8 mmol/l, and 1-h PG <10 mmol/l; diabetes, FPG ≥7.0 and/or 2-h PG ≥11.1 mmol/l; and borderline, all remaining values between normal and diabetes. Borderline individuals are considered to be high-risk individuals. Subjects were recruited primarily during an annual health checkup in a health examination center located in the center of Tokyo from February 2000 to January 2001. The examination included anthropometrics, blood pressure measurements, and an oral glucose tolerance test. Eligible subjects were those diagnosed as borderline. Subjects taking hypoglycemic agents, cholesterol-lowering drugs, or antihypertensive drugs were excluded. Furthermore, those who refused to participate in the dietary questionnaire survey were excluded. A total of 173 subjects were then randomly assigned to either the NDE group (86 patients) or the control group (87 patients).

Dietary intervention

Each subject in the NDE group received individualized counseling using a booklet explaining the concepts of the NDE. The policies of the NDE were to provide the subject with information on his actual dietary practices as revealed by the FFQW65, to increase his motivation to improve dietary practices, and to help him to recognize his need for behavior modification. The FFQW65, a self-administered semiquantitative food frequency questionnaire, consists of 65 food items for each meal with colored illustrations showing portion sizes. Relatively high validity (correlation coefficient r = 0.64) and reproducibility (r = 0.76) for daily energy intake were obtained (12). From the responses to the FFQW65, energy intake for each meal was estimated according to food groups corresponding to the JDS food exchange book (14). Furthermore, latent problems (e.g., too much eating late at night) could be clarified. The counseling aimed to help individuals reduce total energy intake by modifying dietary intake and to adopt habits appropriate for prevention of diabetes. The dietary education program was comprised of two parts. The first part consisted of an individual dietary counseling session 1 month after the baseline health checkup, and the second part was administered by mail 6 months after the health checkup. Dietary counseling was tailored to each subject on the basis of FFQW65 results with a booklet illustrating "recommendations for meals" corresponding to the recommended dietary allowance (RDA) for total energy intake by the JDS. RDA was calculated based on the individual's height, unit kilocalorie (usually 25–30 kcal), which was defined by physical activity level based on occupation, and age. Then, the following "overintake/underintake fraction" was used to measure the individual's status of dietary intake:

$$\left(\frac{\text{Actual total energy intake}}{\text{RDA}} - 1\right) \times 100(\%)$$

Furthermore, to optimize total energy intake in a day, the NDE aimed to reduce total energy intake at late night. Based on the assessment by the FFQW65, the NDE group knew their actual food intake pattern and recognized how it differed from the recommended pattern. This program also aimed to keep protein energy around 15–20%, fat energy around 20–25%, carbohydrate energy around 55–60% of the total energy intake, and to optimize the intake of whole-grain products, vegetables, fruits, low-fat milk, beans, fish, meat, and eggs and maintain the intake of alcohol at an appropriate level. These standards followed the recommendations of the Japanese Diabetes Society (14) and American Diabetes Association (15). The nutritionist encouraged the subject to recognize latent dietary problems and to set his own goals for improvement and attempted to enhance motivation for dietary improvement.

The importance of education in self-management was emphasized in recommendations for the treatment and prevention of diabetes (16). For the second part of the program, the following four items were mailed to each NDE subject accompanied by a letter encouraging the subject to improve his dietary habits: *1*) self-administered checklist consisting of 10 items that assessed dietary intake; *2*) information related to improving dietary behavior; *3*) examples of menus corresponding to the subject's RDA; and *4*) information to confirm the necessity of blood glucose control. On the other hand, each control group subject was given general oral and written information about results of the health examination and results of the FFQW65 but without a detailed explanation. The control group received only conventional group counseling using a leaflet with general information for prevention of lifestyle-related diseases.

Outcome measures

The primary outcome measure was the percent change from baseline in 2-h PG values 1 year after initiation of dietary education.

The change from baseline in the absolute value of "overintake/underintake fraction" for total energy was used as a secondary outcome measure.

Statistical analyses

Enrolled subjects were randomly assigned to the NDE group or the control group by the study nurse with the use of a randomization list (random permutated blocks with length 4). This process was blinded to other staff members as well as to the subjects. The sample size needed for the study was determined based on information to detect the difference in primary end point with a significance level of 5% and power of 90%. Subjects who withdrew from the study and for whom there were no data on outcome measures were excluded from the main analysis. Difference between groups for baseline characteristics of the subjects who completed the trial were assessed by the Student's t test and Wilcoxon's rank-sum test. Outcome measures were compared using ANCOVA by adjusting for baseline values. The Spearman's correlation coefficient was used for examining the rela-

Table 1—*Baseline characteristics of the subjects who completed the 1-year follow-up*

Parameters	NDE group	Control group
n	79	77
Age (year)	55.2 ± 7.4	54.9 ± 6.7
Body mass index	24.5 ± 3.0	24.2 ± 2.7
PG (mmol/l)		
FPG*	**6.1 ± 0.55**	**5.5 ± 0.55**
1 h after oral glucose challenge	10.7 ± 1.8	10.6 ± 1.6
2 h after oral glucose challenge†	**8.2 ± 1.5**	**7.3 ± 1.7**
Serum lipids (mg/dl)		
Total cholesterol	201.3 ± 32.0	199.5 ± 37.0
HDL cholesterol	52.2 ± 12.2	52.8 ± 15.2
Triglycerides	128.6 ± 64.0	127.1 ± 71.1
Liver function (IU/l)		
Alanine aminotransferase	25.9 ± 7.8	24.0 ± 7.7
Aspartate aminotransferase	31.7 ± 19.9	26.9 ± 14.3
Blood pressure (mmHG)		
Systolic	122.3 ± 14.4	121.1 ± 14.3
Diastolic	77.4 ± 10.2	76.4 ± 10.8
Absolute value of the "overintake/underintake fraction" for total energy intake (%)		
Breakfast	25.4 ± 16.4	23.6 ± 12.9
Lunch	13.8 ± 9.3	12.8 ± 11.6
Dinner	60.5 ± 33.6	62.0 ± 37.1
Daily	21.6 ± 15.0	19.9 ± 14.9
Smoking status (%)		
Yes	22 (28)	30 (39)
No	57 (72)	47 (61)

Data are means ± SD and *n* (%). *$P < 0.05$; †$P < 0.01$ for the comparison with the NDE group by two-tailed Wilcoxon's rank-sum test. Data in bold are statistically significant.

tionship between the percent changes in glucose values (fasting, 1-h PG, and 2-h PG) and the change in the absolute value of the "overintake/underintake fraction" by the NDE group and control group.

Because the subjects who dropped out before the end of the 1-year intervention period were not included in the main analysis, an "intent-to-treat" (ITT) approach (17) was used. Specifically, we introduced a binary outcome measure of "reduced/not reduced" that could apply to all randomized subjects, where reduction was defined as "percent change of glucose level >10%," and the subjects without data on the outcome measure were assigned to "not reduced." Then, for each of the glucose values, the odds ratio (crude and adjusted for baseline value) of reduction in the NDE group compared with the control group was estimated by logistic regression models for the subjects used in the main analysis and for all randomized subjects. Incidence of type 2 diabetes during the first year of intervention adjusted for the baseline 2-h PG value was also examined for ITT.

All tests for significance were two-sided with a 5% significance level. All statistical analyses were performed using SAS version 8.12 for Windows (SAS Institute, Cary, NC).

RESULTS— Of the 173 randomized subjects (86 NDE group, 87 control group), 156 (90.2%) completed the 1-year follow-up, and their data were analyzed. Of the remaining 17 subjects, 1 changed his job (NDE group), 5 retired (1, NDE group; 4, control group), 1 canceled his follow-up checkup for financial reasons (control group), and 10 could not be located (6, NDE group; 4, control group). All subjects were asked to complete the FFQW65 before the health checkup, and all subjects cooperated.

The baseline characteristics of NDE and control group subjects who completed the 1-year follow-up are presented in Table 1. At baseline, characteristics did not differ statistically between groups except for FPG ($P < 0.05$) and 2-h PG ($P < 0.01$).

For dietary intake, as shown in Table 2, the adjusted difference in the change from baseline in the absolute value of "overintake/underintake fraction" for total energy intake was significant for dinner (−15.3%, 95% CI −24.6 to −6.0%, $P = 0.002$) and daily (−6.0%, −9.8 to −2.2%, $P = 0.002$). The Spearman correlation coefficient between the percent change in 2-h PG and the change from baseline in the absolute value of the "overintake/underintake fraction" was significant at dinner in the NDE group ($r = 0.36$, $P = 0.001$).

Although the baseline level of 2-h PG was significantly different between the two groups, the adjusted difference in the percent change of 2-h PG was also significantly different (−15.2%, 95% CI −22.0 to −8.4%, $P < 0.001$) (Table 2, Fig. 1).

As described above, the 17 withdrawn subjects were excluded from the main analysis. Therefore, to check their potential influence on trial results, we conducted ITT analysis (17). The crude and adjusted odds ratios of reduction in the NDE group compared with the control group and their 95% CI estimated using logistic regression models were similar; only the difference in the 2-h PG was statistically significant. The proportion of subjects showing significant reduction in the main analysis in the NDE group for 2-h PG was 48% (38 of 79) vs. 16% (12 of 77) for the control group. In the analysis that included all randomized subjects, on the other hand, the proportion of subjects showing reduction in the NDE group was 44% (38 of 86) vs. 14% (12 of 87) in the control group. Adjusted odds ratio was 4.1 (95% CI 1.9–9.0, $P < 0.001$) in the main analysis and 5.0 (2.4–10.8, $P < 0.001$) in the analysis for all randomized subjects. These results did not exhibit any statistical evidence of bias due to exclusion of the withdrawn subjects.

CONCLUSIONS— This study provides evidence that an increase in 2-h PG can be prevented by an individualized counseling and diabetes education program using the FFQW65 for male workers at high risk for type 2 diabetes. The 2-h PG was reduced by ~15% (adjusted) compared with the control group. The ef-

Table 2—*Percent changes in 2-h PG and changes from baseline in the absolute value of "overintake/underintake fraction" for total energy intake 1 year after initiation of dietary education in the NDE group and the control group*

Variable	NDE group	Control group	Adjusted* difference between the groups		
			Mean	95% CI	Two-tailed *P* value
n	79	77			
Percent changes in plasma glucose (%)					
Fasting	−0.5 ± 0.9	2.2 ± 0.9	−1.8	−4.2 to 0.6	0.153
1-h PG	−5.2 ± 2.6	−3.3 ± 2.3	−3.7	−9.9 to 2.5	0.242
2-h PG	−8.2 ± 1.9	11.2 ± 3.0	−15.2	−8.4 to −22.0	<0.001
Change from baseline in the absolute value of "overintake/underintake fraction" for total energy intake (%)					
Breakfast	0.4 ± 1.5	−2.1 ± 0.9	2.6	−0.7 to 5.8	0.126
Lunch	0.4 ± 1.1	1.0 ± 1.2	−0.5	−3.8 to 2.7	0.746
Dinner	−3.0 ± 4.1	11.7 ± 3.7	−15.3	−24.6 to −6.0	0.002
Daily	−1.8 ± 1.5	4.0 ± 1.4	−6.0	−9.8 to −2.2	0.002

Data are mean ± SD unless otherwise indicated. *Adjusted for baseline value by ANCOVA.

fect was confirmed by analysis according to the ITT principle (17), even though some NDE group subjects did not follow dietary recommendations.

To prevent diabetes, early detection of risk and care to maintain normal PG levels might be effective. Improvement in lifestyle relative to diet and exercise (8–10) or lifestyle and drugs (11) plays an important role. Studies in China (8), Finland (9), New Zealand (10), and the U.S. (11) provide evidence that changes in lifestyle, including dietary intake, can be effective in preventing diabetes. In the Chinese study (8), an attempt to determine whether a change in diet or a change in exercise habits was the more effective showed no difference in outcome between the two interventions. In the Finnish study (9), they did not separate the effects by diet and exercise but assessed changes in lifestyle that were as extensive as possible for each subject. In the New Zealand study (10), the effects on body weight and glucose tolerance of a 1-year intervention for reducing dietary fat were examined. In the U.S. study (11), the effectiveness of a lifestyle intervention and treatment with metformin for subjects at high risk for diabetes was discussed. In our intervention study, we concentrated on assessing the effect of NDE on glucose tolerance based on a randomized controlled trial. Our results were similar to those of the above-mentioned studies. Specifically, as for 1-year changes in 2-h PG from baseline, there was an ~6% reduction (baseline and change in 1 year were 8.8 and −0.83 mmol/l for the intervention group and 8.8 and −0.28 mmol/l for the control group, respectively) in Finland, a 9% reduction (baseline and change in 1 year were 7.5 and 0.01 mmol/l for the intervention group and 7.9 and 0.74 mmol/l for the control group, respectively) in New Zealand, an ~27% reduction in China (baseline and change in 6 year were 9.03 and 3.96 mmol/l for the dietary intervention group and 9.03 and 1.48 mmol/l for the control group, respectively), and a 15.2% reduction (adjusted, Table 2) in our study. Because our study was designed to verify the primary end point of 2-h PG, the fact that the difference in the incidence of diabetes between the two groups was not significant is not of concern. Also, the time frame of 1 year was very short to show such a difference in incidence.

To prevent the continuation of the recent increase in the prevalence of diabetes

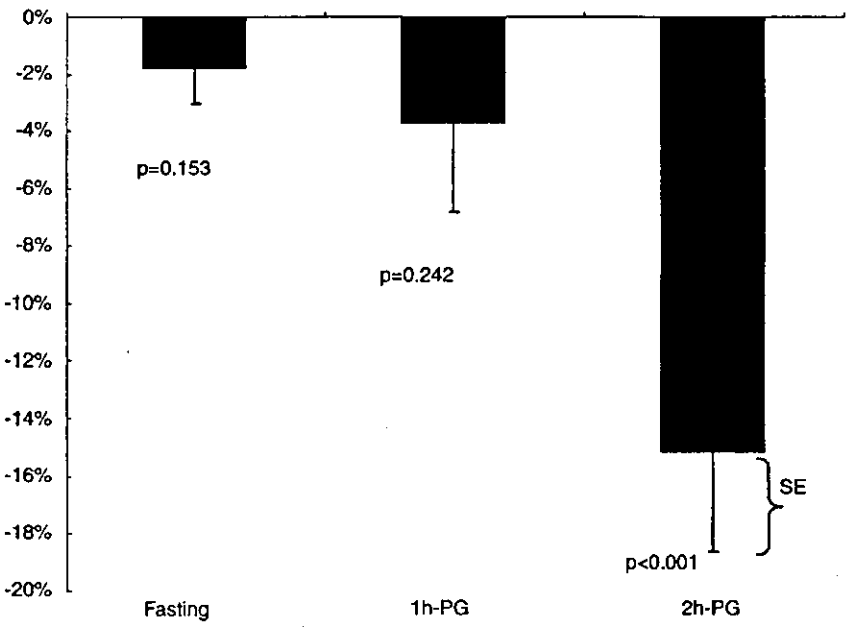

Figure 1—*Difference in the mean percent changes from baseline in 2-h PG after 1 year between the NDE group and the conventional dietary education (control) group (adjusted for baseline value).*

(2,13), an effective dietary education measure is warranted. Our study was directed toward assessing the effectiveness of the NDE in reducing PG levels in high-risk subjects for type 2 diabetes among Japanese men by correcting total energy intake through adequate instruction. Compared with the control group, total energy intake both at dinner and daily was relatively lower in the NDE group, although the magnitude of these reductions was not significant. Furthermore, dietary changes were correlated with changes in PG in the NDE group. These results indicated the effect of the NDE in reducing the blood glucose level. To optimize total energy intake each day, the NDE aimed to reduce total energy intake late at night. The intake of energy during the day rather than at night improves insulin resistance, resulting in a reduced blood glucose level. The rationale for this can be explained by the study of Lindsay et al. (18), which indicated that when a fasting blood glucose level reaches 7.8 mmol/l or more, the total amount of insulin secretion after a meal begins to decrease.

One may wonder why only two education events could result in a reduction of 2-h PG. Three reasons can be cited. Namely, the subject was given specific information about his actual dietary habits through use of the FFQW65 and could manage to maintain the current level rather than experience an increase as shown in the control group. Furthermore, the program focused on increasing motivation and encouraging the subject to recognize the need for behavior modification through his own efforts. The rader chart of "ratio of actual-to-RDA" for total energy intake by meals and illustrations of portions might have helped the subjects modify their food intake pattern through recognition of their own dietary problems. In fact, many subjects successfully managed to maintain a balance of total energy intake. For instance, energy intake for oil and alcohol was decreased in the NDE group ($P > 0.05$), and those differences were significantly correlated to the percent change of 2-h PG. Spearman correlation coefficients for oil were as follows: dinner, $r = 0.33$, $P = 0.003$ and daily $r = 0.23$, $P = 0.044$. For alcohol daily, the Spearman correlation coefficient was $r = 0.28$, $P = 0.013$. These provide evidence for the effect of the NDE on dietary intake.

Our study has a limitation in that the subjects were all Japanese male workers. The value of this dietary intervention for specific populations or in countries other than Japan is likely but unknown, especially when different risk factors for diabetes may exist in various areas. However, the strategy of our program, particularly the focus on maintaining balance in dietary intake among the three meals daily, could reasonably be extended to countries other than Japan. Furthermore, although our definition of the high-risk group was less stringent than that of the IGT because we used 2-h PG as the outcome measure and examined the effect of the NDE by a randomized controlled trial, the same result may apply using the IGT definition. The effect of the interventions was assessed after 1 year because an earlier assessment could be biased as a result of changes made only because subjects were conscious of being studied. As for the influence of other risk factors such as smoking, we did an additional analysis that included smoking as a covariate. The distribution of smokers at baseline was not different between the NDE and control groups. However, the adjusted difference in the percent change of 2-h PG was still significant (−14.9%, 95% CI −8.1 to −21.7%, $P < 0.001$). However, three subjects stopped smoking within 1 year in the NDE group. Therefore, we excluded them and confirmed the result. The adjusted difference was almost concordant (−14.9%, −8.0 to −21.8%, $P < 0.001$). Although our study design was a randomized controlled trial, we cannot deny the influence of unknown factors, such as physical exercise.

In conclusion, the NDE can reduce glucose levels by effecting changes in the total energy intake of subjects at high risk for type 2 diabetes. The NDE with the strategy for maintenance of balance in dietary intake among the three daily meals and using the FFQW65 may play an important role in the prevention of diabetes for high-risk groups in the early stages.

Acknowledgments— This study was financially supported by the Ministry of Education, Science, Sports and Technology in Japan Grant-in-Aid for Scientific Research Grant C (2) in 2001–2002 and Grant 13680169.

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The New England
Journal of Medicine

VOLUME 344 MAY 3, 2001 NUMBER 18

PREVENTION OF TYPE 2 DIABETES MELLITUS BY CHANGES IN LIFESTYLE AMONG SUBJECTS WITH IMPAIRED GLUCOSE TOLERANCE

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ABSTRACT

Background Type 2 diabetes mellitus is increasingly common, primarily because of increases in the prevalence of a sedentary lifestyle and obesity. Whether type 2 diabetes can be prevented by interventions that affect the lifestyles of subjects at high risk for the disease is not known.

Methods We randomly assigned 522 middle-aged, overweight subjects (172 men and 350 women; mean age, 55 years; mean body-mass index [weight in kilograms divided by the square of the height in meters], 31) with impaired glucose tolerance to either the intervention group or the control group. Each subject in the intervention group received individualized counseling aimed at reducing weight, total intake of fat, and intake of saturated fat and increasing intake of fiber and physical activity. An oral glucose-tolerance test was performed annually; the diagnosis of diabetes was confirmed by a second test. The mean duration of follow-up was 3.2 years.

Results The mean (±SD) amount of weight lost between base line and the end of year 1 was 4.2±5.1 kg in the intervention group and 0.8±3.7 kg in the control group; the net loss by the end of year 2 was 3.5±5.5 kg in the intervention group and 0.8±4.4 kg in the control group ($P<0.001$ for both comparisons between the groups). The cumulative incidence of diabetes after four years was 11 percent (95 percent confidence interval, 6 to 15 percent) in the intervention group and 23 percent (95 percent confidence interval, 17 to 29 percent) in the control group. During the trial, the risk of diabetes was reduced by 58 percent ($P<0.001$) in the intervention group. The reduction in the incidence of diabetes was directly associated with changes in lifestyle.

Conclusions Type 2 diabetes can be prevented by changes in the lifestyles of high-risk subjects. (N Engl J Med 2001;344:1343-50.)

THE incidence of type 2 diabetes mellitus is increasing worldwide. Type 2 diabetes results from the interaction between a genetic predisposition and behavioral and environmental risk factors.[1] Although the genetic basis of type 2 diabetes has yet to be identified, there is strong evidence that such modifiable risk factors as obesity and physical inactivity are the main nongenetic determinants of the disease.[2-9]

Impaired glucose tolerance is an intermediate category between normal glucose tolerance and overt diabetes,[10,11] and it can be identified by an oral glucose-tolerance test. Subjects with impaired glucose tolerance have an increased risk of type 2 diabetes[12] and therefore form an important target group for interventions aimed at preventing diabetes.[2-5] The Finnish Diabetes Prevention Study was conducted to determine the feasibility and effects of a program of chang-

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es in lifestyle designed to prevent or delay the onset of type 2 diabetes in subjects with impaired glucose tolerance.

METHODS

Study Design

The design of the Diabetes Prevention Study has been described in detail elsewhere.[13] The study was designed on the assumptions of a 35 percent cumulative incidence of diabetes and a 35 percent reduction in incidence in the intervention group, as compared with the control group, during a six-year period. The study protocol was approved by the ethics committee of the National Public Health Institute in Helsinki, Finland, and all the study subjects gave written informed consent.

Study subjects were recruited primarily through the screening of members of high-risk groups, such as first-degree relatives of patients with type 2 diabetes. Overweight persons (defined as those with a body-mass index [the weight in kilograms divided by the square of the height in meters] of 25 or higher) who were 40 to 65 years old and had impaired glucose tolerance were eligible for the study. Impaired glucose tolerance was defined as a plasma glucose concentration of 140 to 200 mg per deciliter (7.8 to 11.0 mmol per liter) two hours after the oral administration of 75 g of glucose in subjects whose plasma glucose concentration after an overnight fast was less than 140 mg per deciliter.[14] The test was repeated in subjects in whom the first result was abnormal, and the mean of the two values was used to determine eligibility. Criteria for exclusion were a diagnosis of diabetes mellitus, the presence of chronic disease rendering survival for six years unlikely, and other characteristics (psychological or physical disabilities) deemed likely to interfere with participation in the study.

Subjects who enrolled in the study were randomly assigned to the intervention group or the control group by the study physician, with the use of a randomization list, with stratification according to center, sex, and the mean plasma glucose concentration two hours after oral glucose challenge (140 to 169 mg per deciliter or 170 to 200 mg per deciliter [7.8 to 9.4 mmol per liter or 9.5 to 11.0 mmol per liter]). The nurses who scheduled the study visits did not have access to the randomization list. However, the staff members involved in the intervention had to be aware of the group assignment; thus, the study was only partly blinded. Laboratory staff did not know the subjects' group assignments, and the subjects were not informed of their plasma glucose concentrations during follow-up unless diabetes was diagnosed.

A total of 523 subjects in five study centers were randomly assigned to one of the two treatment groups. The end-points committee excluded one subject who had diabetes at base line whose diagnosis of diabetes was confirmed at her two-year visit. The subjects in the control group were given general oral and written information about diet (a two-page leaflet) and exercise at base line and at subsequent annual visits, but no specific individualized programs were offered to them. They completed a three-day food diary at base line and at each annual visit, using a booklet illustrating the sizes of portions of food.[15] Nutrient intakes were computed with the use of a program developed at the National Public Health Institute.[16]

The subjects in the intervention group were given detailed advice about how to achieve the goals of the intervention, which were a reduction in weight of 5 percent or more, in total intake of fat to less than 30 percent of energy consumed, and in intake of saturated fat to less than 10 percent of energy consumed; an increase in fiber intake to at least 15 g per 1000 kcal; and moderate exercise for at least 30 minutes per day. Frequent ingestion of whole-grain products, vegetables, fruits, low-fat milk and meat products, soft margarines, and vegetable oils rich in monounsaturated fatty acids was recommended. The dietary advice was tailored to each subject on the basis of three-day food records completed four times per year. Each subject in the intervention group had seven sessions with a nutritionist during the first year of the study and one session every three months thereafter. These subjects also received individual guidance on increasing their level of physical activity. Endurance exercise (such as walking, jogging, swimming, aerobic ball games, or skiing) was recommended as a way to increase aerobic capacity and improve cardiorespiratory fitness. Supervised, progressive, individually tailored, circuit-type resistance-training sessions were also offered with the aim of improving the functional capacity and strength of the large muscle groups; subjects were instructed to perform a moderate to high number of repetitions and to take a break of 15 to 60 seconds between the stations on the circuit. During the first year, the rate of participation in these sessions varied from 50 percent to 85 percent at different centers.

If, at an annual visit, the study physician discovered a clinical condition that required attention, such as a high serum cholesterol concentration or hypertension, the subject was advised to contact his or her own physician for treatment and follow-up.

Clinical Studies

At base line and at each annual visit, all study subjects completed a medical-history questionnaire and underwent a physical examination that included anthropometric and blood-pressure measurements and an oral glucose-tolerance test, as described elsewhere.[13]

Biochemical Assessments

Plasma glucose was measured at each center by means of standard methods. The glucose measurements were standardized by the central laboratory in Helsinki, whose staff analyzed 60 to 80 plasma samples from each center in duplicate. A linear-regression equation was calculated for each center, with the use of the plasma glucose measurement determined at the Helsinki laboratory as the standard. These equations were used to correct the locally measured plasma glucose values. The result of the second oral glucose-tolerance test was considered the base-line value for comparison with values obtained later; in some subjects whose entry into the study was delayed, a third oral glucose-tolerance test was performed whose result was considered the base-line value. The serum insulin concentration was measured by a radioimmunoassay (Pharmacia, Uppsala, Sweden), and serum levels of total cholesterol, high-density lipoprotein cholesterol, and triglycerides were measured by enzymatic assay in the central laboratory in Helsinki.

Assessment of the End Points

Diabetes was defined according to the 1985 criteria of the World Health Organization[14] as either a fasting plasma glucose concentration of 140 mg per deciliter or higher or a plasma glucose concentration of 200 mg per deciliter or higher two hours after an oral glucose challenge. We required confirmation of the diagnosis of diabetes by a second oral glucose-tolerance test; if the diagnosis was not confirmed by the second test, the subject followed the program according to the original random assignment. The diagnosis of diabetes was based on the locally measured plasma glucose values, since these were used for the inclusion of subjects in the study. In the statistical analysis, corrected plasma glucose values were used. The independent end-points committee confirmed all newly diagnosed cases of diabetes. The study centers did not exchange information concerning the number of subjects who reached the end point, and the end-point data were linked to the group assignment at the study center only after a total of 80 subjects had reached the end point, as stated in the study plan.

Statistical Analysis

In March 2000, an independent statistician completed the first analysis of data, which included all cases of diabetes diagnosed before that date. On the basis of the results of this analysis, the end-points committee recommended that the trial be ended.

Two-sided t-tests and chi-square tests were used to analyze the differences between the groups at base line and during follow-up. Survival curves were calculated to estimate the cumulative incidence of diabetes. The difference between the groups in the incidence of

diabetes was tested by means of the two-sided log-rank test. All analyses of end points were based on the intention-to-treat principle. The SAS PHREG procedure was used to derive the basic estimates, such as the survival functions and the 95 percent confidence limits of the estimates (SAS/STAT software, version 6.12, SAS Institute, Cary, N.C.). Subjects who withdrew from the study were considered to be at risk for diabetes until their last oral glucose-tolerance test, at which point data were censored. To estimate the extent of the dependence of the incidence of diabetes on the changes in lifestyle that were achieved, subjects were given a grade for each goal of the intervention at the one-year visit (with 0 indicating that it was not achieved or 1 indicating that it was achieved), and a success score was computed as the sum of these grades. For each subgroup defined according to success score, the proportion of subjects in whom diabetes had developed was calculated. To test for a statistical association between this proportion and the success score, logistic-regression analysis was performed with the use of the SAS GENMOD procedure. The expected proportion was modeled as a linear function of the success score.

RESULTS

The first subject was assigned to a group in November 1993 and the last in June 1998. At that time, 90 percent of the study subjects had been enrolled in the trial for at least 2 years, and the mean duration of follow-up was 3.2 years. The base-line characteristics of the two groups were similar (Table 1). During the first year, the mean (±SD) body weight decreased by 4.2±5.1 kg (4.7±5.4 percent) in the intervention group and by 0.8±3.7 kg (0.9±4.2 percent) in the control group ($P<0.001$) (Table 2). Waist circumference, the fasting plasma glucose concentration, the plasma glucose concentration two hours after oral glucose challenge, and the serum insulin concentration two hours after glucose challenge decreased significantly more among subjects in the intervention group than among those in the control group. At two years, the decrease in weight remained significantly greater in the intervention group (3.5±5.5 kg) than in the control group (0.8±4.4 kg) ($P<0.001$). At this time, the mean change from base line in the fasting plasma glucose concentration was −2±12 mg per deciliter (−0.1±0.7 mmol per liter) in the intervention group and +3±14 mg per deciliter (+0.2±0.8 mmol per liter) in the control group ($P<0.001$); the change in the plasma glucose concentrations measured two hours after oral glucose challenge was −14±37 mg per deciliter (−0.8±2.1 mmol per liter) in the intervention group and +0±44 mg per deciliter (+0±2.5 mmol per liter) in the control group ($P<0.001$). There were also significantly greater decreases in the intervention group than in the control group in the serum insulin concentration two hours after oral glucose challenge, as well as in the triglyceride concentration and blood pressure (data not shown).

The study subjects were asked about their health-related behavior at base line and subsequently at each annual follow-up examination (Table 3). The subjects in the intervention group were more likely to report changes in dietary and exercise habits. Success in achieving the goals of the intervention was estimated on the basis of the food records and exercise questionnaires collected at the one-year examination (Table 4). The proportion of subjects in the intervention group who succeeded in achieving a particular goal varied from 25 percent (fiber intake) to 86 percent (exercise).

TABLE 1. BASE-LINE CHARACTERISTICS OF THE SUBJECTS IN THE INTERVENTION AND CONTROL GROUPS.*

CHARACTERISTIC	INTERVENTION GROUP (N=265)	CONTROL GROUP (N=257)
Sex (no.)		
Male	91	81
Female	174	176
Age (yr)	55±7	55±7
Body-mass index	31.3±4.6	31.0±4.5
Waist circumference (cm)	102.0±11.0	100.5±10.9
Hip circumference (cm)	110.4±10.5	109.4±9.7
Plasma glucose (mg/dl)		
Fasting	109±14	110±13
2 Hr after oral glucose challenge	159±27	159±26
Serum insulin (μU/ml)		
Fasting	15±7	15±8
2 Hr after oral glucose challenge	98±74	93±54
Serum lipids (mg/dl)†		
Total cholesterol	215±37	215±35
High-density lipoprotein cholesterol	46±12	47±11
Triglycerides	154±72	158±69
Blood pressure (mm Hg)‡		
Systolic	140±18	136±17§
Diastolic	86±9	86±10

*Plus–minus values are means ±SD. To convert values for glucose to millimoles per liter, multiply by 0.056. To convert values for insulin to picomoles per liter, multiply by 6. To convert values for cholesterol to millimoles per liter, multiply by 0.026. To convert values for triglycerides to millimoles per liter, multiply by 0.011.

†Cholesterol-lowering drugs were being taken by 5 percent of the subjects in the intervention group and 6 percent of the subjects in the control group at base line.

‡Antihypertensive drugs were being taken by 30 percent of the subjects in the intervention group and 31 percent of the subjects in the control group at base line.

§$P=0.03$ for the comparison with the intervention group by two-tailed t-test.

Diabetes was diagnosed in a total of 86 subjects — 27 in the intervention group and 59 in the control group. The average proportion of subjects in whom impaired glucose tolerance progressed to diabetes was 3 percent per year in the intervention group and 6 percent per year in the control group. The absolute incidence of diabetes was 32 cases per 1000 person-years in the intervention group and 78 per 1000 person-years in the control group.

The cumulative incidence of diabetes was lower in the intervention group than in the control group (Fig. 1). The difference was statistically significant after two years: 6 percent in the intervention group (95 per-

TABLE 2. CHANGES IN SELECTED CLINICAL AND METABOLIC VARIABLES FROM BASE-LINE TO THE END OF YEAR 1 IN THE SUBJECTS IN THE INTERVENTION AND CONTROL GROUPS.*

VARIABLE	INTERVENTION GROUP (N=256)		CONTROL GROUP (N=250)		P VALUE†
	mean ±SD	95% CI	mean ±SD	95% CI	
Change in weight					
In kilograms	−4.2±5.1	−4.8 to −3.6	−0.8±3.7	−1.3 to −0.3	<0.001
Percent change	−4.7±5.4	−5.0 to −4.4	−0.9±4.2	−1.0 to −0.8	<0.001
Change in waist circumference (cm)	−4.4±5.2	−5.1 to −3.9	−1.3±4.8	−1.9 to −0.7	<0.001
Change in plasma glucose (mg/dl)					
Fasting	−4±12	−6 to −2	1±12	0 to 2	<0.001
2 Hr after oral glucose challenge	−15±34	−19 to −11	−5±40	−8 to −2	0.003
Change in serum insulin (μg/ml)					
Fasting	−2±9	−3 to −1	−1±7	−2 to 0	0.14
2 Hr after oral glucose challenge	−29±64	−37 to −21	−11±51	−18 to −4	0.001
Change in serum lipids (mg/dl)‡					
Total cholesterol	−5±28	−8 to −2	−4±28	−7 to −1	0.62
High-density lipoprotein cholesterol	2±7	1 to 3	1±6	0 to 2	0.06
Triglycerides	−18±51	−24 to −12	−1±60	−8 to 6	0.001
Change in blood pressure (mm Hg)§					
Systolic	−5±14	−7 to −3	−1±15	−3 to 1	0.007
Diastolic	−5±9	−6 to −4	−3±9	−4 to −2	0.02

*A total of 15 subjects withdrew from the study within the first year; 1 additional subject did not undergo testing at one year, although she remained in the study. To convert values for glucose to millimoles per liter, multiply by 0.056. To convert values for insulin to picomoles per liter, multiply by 6. To convert values for cholesterol to millimoles per liter, multiply by 0.026. To convert values for triglycerides to millimoles per liter, multiply by 0.011. CI denotes confidence interval.

†P values were determined by a two-tailed t-test for the difference between the groups.

‡Cholesterol-lowering drugs were being taken by 6 percent of the subjects in the intervention group and 8 percent of those in the control group by the end of year 1.

§Antihypertensive drugs were being taken by 30 percent of the subjects in the intervention group and 31 percent of those in the control group by the end of year 1.

TABLE 3. SELF-REPORTED CHANGE IN DIETARY AND EXERCISE HABITS DURING THE FIRST YEAR OF THE INTERVENTION, ACCORDING TO TREATMENT GROUP.*

VARIABLE	INTERVENTION GROUP (N=253)	CONTROL GROUP (N=247)	P VALUE†
	% of subjects		
Decreased consumption of fat	87	70	0.001
Changed the quality of fat	70	39	0.001
Increased consumption of vegetables	72	62	0.01
Decreased consumption of sugar	55	40	0.001
Decreased consumption of salt	59	50	0.03
Decreased consumption of alcohol	26	23	0.43
Increased exercise‡	36	16	0.001

*Seven subjects of 507 who remained in the study at one year had some missing data and are not included in this table.

†P values were determined by the chi-square test for the difference between the groups.

‡Subjects reported the frequency of exercise in terms of a shift to a higher category of the following four categories: (1) "I read, watch television, and work in the household at tasks that don't strain me physically"; (2) "I walk, cycle, or exercise lightly in other ways at least four hours per week"; (3) "I exercise to maintain my physical condition by running, jogging, skiing, doing gymnastics, swimming, playing ball games, etc., for at least 3 hours per week"; or (4) "I exercise competitively several times a week by running, orienteering, skiing, playing ball games, or engaging in other sports involving heavy exertion."

cent confidence interval, 3 to 9 percent) and 14 percent in the control group (95 percent confidence interval, 10 to 19 percent). At four years, the cumulative incidence was 11 percent (95 percent confidence interval, 6 to 15 percent) in the intervention group and 23 percent (95 percent confidence interval, 17 to 29 percent) in the control group. According to the Cox regression analysis of all person-years accumulated, the cumulative incidence of diabetes was 58 percent lower in the intervention group than in the control group (hazard ratio, 0.4; 95 percent confidence interval, 0.3 to 0.7; $P<0.001$). The incidence of diabetes was 63 percent lower among men in the intervention group (95 percent confidence interval, 18 to 79 percent; $P=0.01$) and 54 percent lower among women (95 percent confidence interval, 26 to 81 percent; $P=0.008$).

The study subjects were ranked according to their success in achieving the goals of the intervention (and given a success score between 0 and 5) at the one-year examination, with higher scores indicating more goals met (Fig. 2). There was a strong inverse correlation between the success score and the incidence of diabetes. Thirteen subjects in the intervention group and 48 subjects in the control group did not achieve any of the goals; diabetes developed in 38 percent and 31

TABLE 4. SUCCESS IN ACHIEVING THE GOALS OF THE INTERVENTION BY ONE YEAR, ACCORDING TO TREATMENT GROUP.*

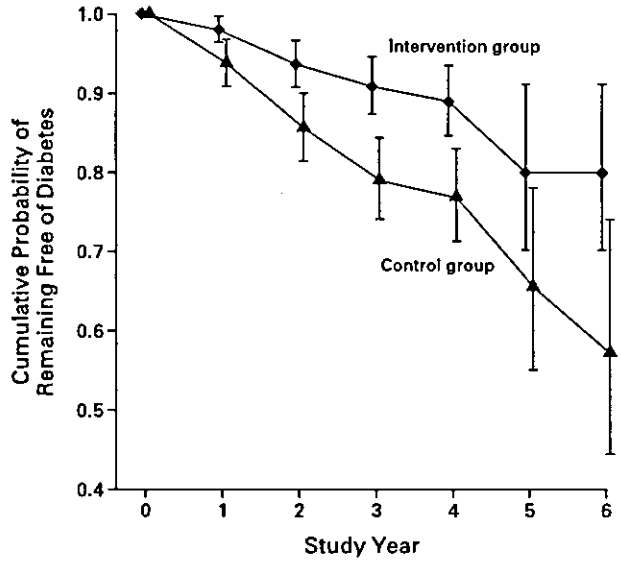
GOAL	INTERVENTION GROUP	CONTROL GROUP	P VALUE†
	% of subjects		
Weight reduction >5%	43	13	0.001
Fat intake <30% of energy intake	47	26	0.001
Saturated-fat intake <10% of energy intake	26	11	0.001
Fiber intake ≥15 g/1000 kcal	25	12	0.001
Exercise >4 hr/wk‡	86	71	0.001

*Nutrient intakes were calculated from three-day food records.

†P values were determined by the chi-square test for the difference between the groups.

‡Exercise frequency was reported by the subjects who chose one of the four categories described in Table 3. The goal identified here was a frequency in category 2 or higher.

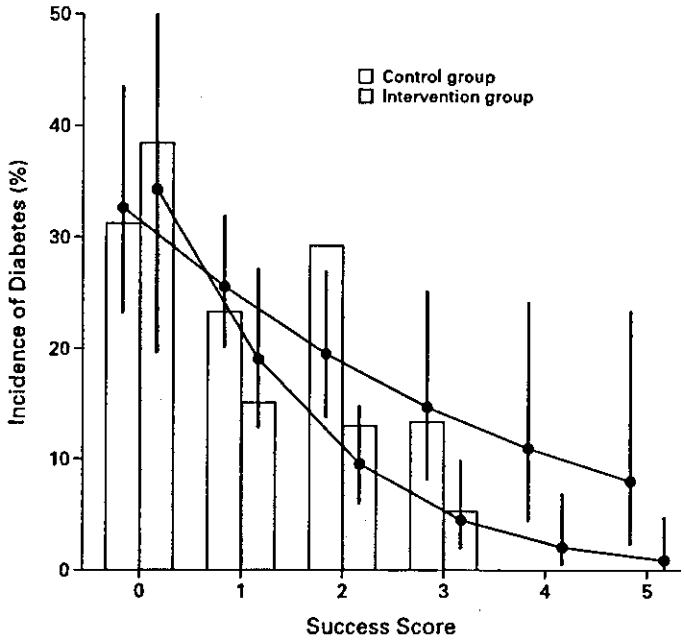
percent of these subjects, respectively, during follow-up. Diabetes had not developed in any of the subjects who reached four or five of the goals (49 subjects in the intervention group and 15 in the control group). According to a univariate analysis, the odds ratio for diabetes in subjects in the intervention group who had lost more than 5 percent of their initial weight by the one-year follow-up visit was 0.3 (95 percent confidence interval, 0.1 to 0.7) as compared with those in the intervention group who had lost less weight or none at all; the corresponding odds ratio in the control group was 0.4 (95 percent confidence interval, 0.1 to 1.2). Among the subjects in the intervention group who did not reach the goal of losing 5 percent of their initial weight, the odds ratio for diabetes in those who had achieved the goal with respect to exercise (more than four hours per week) during the first year was 0.2 (95 percent confidence interval, 0.1 to 0.6) as compared with those in the intervention group who maintained a sedentary lifestyle; the corresponding odds ratio in the control group was 0.6 (95 percent confidence interval, 0.3 to 1.1). After adjustment



SUBJECTS AT RISK						
Total no.	507	471	374	167	53	27
Cumulative no. with diabetes:						
Intervention group	5	15	22	24	27	27
Control group	16	37	51	53	57	59

Figure 1. Proportion of Subjects without Diabetes during the Trial.

The vertical bars show the 95 percent confidence intervals for the cumulative probability of remaining free of diabetes. The relative risk of diabetes for subjects in the intervention group, as compared with those in the control group, was 0.4 (P<0.001 for the comparison between the groups).



No. with Diabetes/Total No.						
Intervention group	5/13	10/66	9/69	2/38	0/25	0/24
Control group	15/48	25/107	14/48	2/15	0/11	0/4

Figure 2. Incidence of Diabetes during Follow-up, According to the Success Score.

At the one-year visit, each subject received a grade of 0 for each intervention goal that had not been achieved and a grade of 1 for each goal that had been achieved; the success score was computed as the sum of the grades. Forty subjects who withdrew from the study when their diabetes status was unknown and 14 subjects with incomplete data were excluded from this analysis. The association between the success score and the risk of diabetes, with 95 percent confidence intervals, was estimated by means of logistic-regression analysis of the observed data. The curves show the model-based incidence of diabetes according to the success score as a continuous variable; the curve whose data points align with the open bars represents the model-based incidence for the control group, and the curve whose data points align with the shaded bars represents the model-based incidence for the intervention group.

for base-line body-mass index, the odds ratio for diabetes in those in the intervention group who had achieved the exercise goal was still statistically significant (odds ratio, 0.3; 95 percent confidence interval, 0.1 to 0.7).

During the study, 40 subjects (8 percent) withdrew — 23 in the intervention group and 17 in the control group. Of these subjects, 9 could not be contacted, 3 withdrew due to severe illness, 1 died, and 27 withdrew for personal reasons.

DISCUSSION

This study provides evidence that type 2 diabetes can be prevented by changes in the lifestyles of both women and men at high risk for the disease. The overall incidence of diabetes was reduced by 58 percent. Our estimate of the effect of the intervention can be considered conservative for two reasons. First, the data were analyzed according to the intention-to-treat principle, even though some subjects in the intervention group did not follow the recommendations about diet and exercise. Second, for ethical reasons, all subjects assigned to the control group also received general health advice at base line and at annual follow-up visits and may have benefited from this advice.

The results from previous studies in Sweden[17] and China[18] also provide evidence that changes in lifestyle are effective in preventing diabetes, and the magnitude of the benefit in these studies was similar to that in our study. In those two studies, the subjects were not randomly assigned to the intervention and control groups. The randomization in our study was stratified according to clinic, sex, and base-line plasma glucose concentration two hours after oral glucose challenge in order to obtain the best possible comparability between groups. In the Chinese study,[18] an attempt to

determine whether a change in diet or a change in exercise habits was more effective found no difference in outcome between the two interventions. We did not try to separate these changes but, rather, tried to achieve changes in lifestyle that were as extensive as possible for each subject.

The effect of the interventions was assessed after one year because earlier assessment may be biased as a result of changes made only because subjects are conscious of being studied. The effect of the intervention on the incidence of diabetes was most pronounced among subjects who made comprehensive changes in lifestyle; on the other hand, the failure to make any changes resulted in an incidence of diabetes that was close to the estimate of 35 percent for this high-risk population. The average amount of weight lost was not large, yet the difference between the incidence of diabetes in the intervention group and that in the control group was substantial. The low odds ratio for diabetes among those who lost at least 5 percent of their initial weight reveals the importance of even a relatively small reduction in weight in the prevention of diabetes.

Our counseling regarding physical exercise included components designed to improve both cardiorespiratory fitness and muscle strength. Achieving a relatively conservative target of more than four hours of exercise per week was associated with a significant reduction in the risk of diabetes in the subjects who did not lose weight. It is likely that any type of physical activity — whether sports, household work, gardening, or work-related physical activity — is similarly beneficial in preventing diabetes. Many subjects with impaired glucose tolerance are both obese and inactive, and therefore we would expect to find a dose–response relation between the correction of these multiple risk factors and reductions in the risk of diabetes.

The main justification for the type of intervention used in the high-risk subjects in this study is that it may prevent or postpone the onset of type 2 diabetes and the complications related to the disease. Patients with diabetes — with or without symptoms — have an increased prevalence of both macrovascular and microvascular complications at the time when diabetes is diagnosed. Many also have hypertension and an atherogenic serum lipid profile.[19-22] The changes in lifestyle in our study not only improved glucose tolerance but also reduced the magnitude of several other cardiovascular risk factors.[13] It is commonly argued that it is difficult to change the lifestyle of obese and sedentary people, but such pessimism may not be justified. The reasonably low dropout rate in our study also indicates that subjects with impaired glucose tolerance are willing and able to participate in a demanding intervention program if it is made available to them.

It is possible to achieve primary prevention of type 2 diabetes by means of a nonpharmacologic intervention that can be implemented in a primary health care setting. According to our results, 22 subjects with impaired glucose tolerance must be treated in this way for one year — or 5 subjects for five years — to prevent one case of diabetes.

Supported by the Finnish Academy (grants 8473/2298, 40758/5767, and 38387/54175), the Ministry of Education, the Novo Nordisk Foundation, the Yrjö Jahnsson Foundation, and the Finnish Diabetes Research Foundation.

We are indebted to Ms. Kirsi Frantsi, Mr. Olli Heinonen, Ms. Katri Hemiö, Ms. Pirjo Härkönen, Ms. Pia Högström, Ms. Anja Ilmanen, Ms. Kaija Kettunen, Ms. Paivi Kleemola, Ms. Anna Korhonen, Ms. Marjukka Lauhkonen, Ms. Pirjo Lehto, Ms. Liisa Mikkola, Ms. Paula Nyholm, and Ms. Arja Putila for their skillful assistance in performing the study; to Dr. Timo Lakka and Professor Jukka T. Salonen for their expert advice concerning the assessment of exercise; to Professor Marja-Riitta Taskinen and Professor Antti Aro for their participation on the end-points committee; and to Dr. William C. Knowler for his important contribution to the planning of our study.

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