

# Efficacy of Lifestyle Education to Prevent Type 2 Diabetes

## A meta-analysis of randomized controlled trials

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**OBJECTIVE** — To evaluate the efficacy of lifestyle education for preventing type 2 diabetes in individuals at high risk by meta-analysis of randomized controlled trials, as assessed by incidence and a reduced level of plasma glucose 2 h after a 75-g oral glucose load (2-h plasma glucose).

**RESEARCH DESIGN AND METHODS** — Through an electronic search, 123 studies were identified. A literature search identified eight studies that met strict inclusion criterion of meta-analysis for 2-h plasma glucose and five studies for the incidence of diabetes. All were randomized controlled trials of  $\geq 6$  months with lifestyle education that included a dietary intervention. Subjects were adults diagnosed as being at high risk for type 2 diabetes. The difference in mean reduction of 2-h plasma glucose from baseline to the 1-year follow-up and relative risk (RR) of the incidence of diabetes in the lifestyle education group versus the control group were assessed. Overall estimates were calculated using a random-effects model. Those estimates were confirmed by several models, and the possibility of selection bias was examined using a funnel plot.

**RESULTS** — Lifestyle education intervention reduced 2-h plasma glucose by 0.84 mmol/l (95% CI 0.39–1.29) compared with the control group. The 1-year incidence of diabetes was reduced by  $\sim 50\%$  (RR 0.55, 95% CI 0.44–0.69) compared with the control group. Results were stable and little changed if data were analyzed by subgroups or other statistical models. Funnel plots revealed no selection bias.

**CONCLUSIONS** — Lifestyle education was effective for reducing both 2-h plasma glucose and RR in high-risk individuals and may be a useful tool in preventing diabetes.

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Type 2 diabetes is increasing worldwide largely as a result of increasing obesity and a sedentary lifestyle. Nutritional therapy for diabetic patients was recommended by the American Diabetes Association (1). Considering the severity of the illness and low quality of life among diabetic patients, primary prevention for the development of type 2 diabetes is important. For this purpose, lifestyle education (combined diet and exercise) can be considered a powerful tool. Beginning with the impressive study in Da Qing, China (2), the benefits of lifestyle modification have been assessed. Some

recent studies based on randomized controlled trials for high-risk subjects revealed the potential for prevention of type 2 diabetes. In a previous study, we conducted a randomized controlled trial of a new dietary education program to reduce plasma glucose levels in Japanese male workers, and we showed that the new dietary education could reduce glucose levels by effecting changes in the total energy intake of individuals at high risk for type 2 diabetes (3). Most current lifestyle education interventions are based on a combination of dietary education with exercise. However, the effects are still controver-

sial. The aim of the present study was to evaluate the efficacy of lifestyle education for preventing type 2 diabetes in individuals at high risk, using a meta-analysis of randomized controlled trials.

## RESEARCH DESIGN AND METHODS

### Study selection and data extraction

The study question was whether a lifestyle education program compared with conventional education improved the overall glucose level or incidence of diabetes in individuals at high risk for type 2 diabetes. Examples of “conventional education” would be usual exercise with or without general information about diet or general dietary advice about healthy food choices on entering the trial.

**Outcome measures.** To reduce the risk of development of type 2 diabetes, reduction of blood glucose level is necessary. Therefore, the present study considered two outcome measures: the glucose level and incidence of type 2 diabetes. As to the glucose level, the difference in the plasma glucose value 2 h after a 75-g oral glucose load (2-h plasma glucose) between baseline and  $\geq 6$  months (mainly 1 year) later was used as an outcome measure. The difference in means of those measures from baseline to 1 year between the lifestyle education intervention and control groups were the effect size of this study. Relative risk (RR), or hazard ratio, for incidence of type 2 diabetes in the lifestyle education intervention group over the control group was another effect size.

**Types of participants.** Subjects were adults who were diagnosed to be at high risk for type 2 diabetes: impaired glucose tolerance (IGT) (4), impaired fasting glucose (IFG) (5), and borderline (6). The definition of borderline was according to the Japan Diabetes Society (JDS) as follows: normal: fasting plasma glucose  $< 6.1$  mmol/l, 2-h plasma glucose  $< 7.8$  mmol/l, and 1-h plasma glucose  $< 10$  mmol/l; diabetes: fasting plasma glucose  $\geq 7.0$  and/or 2-h plasma glucose  $\geq 11.1$  mmol/l; and borderline: all remaining values between normal and diabetes. The

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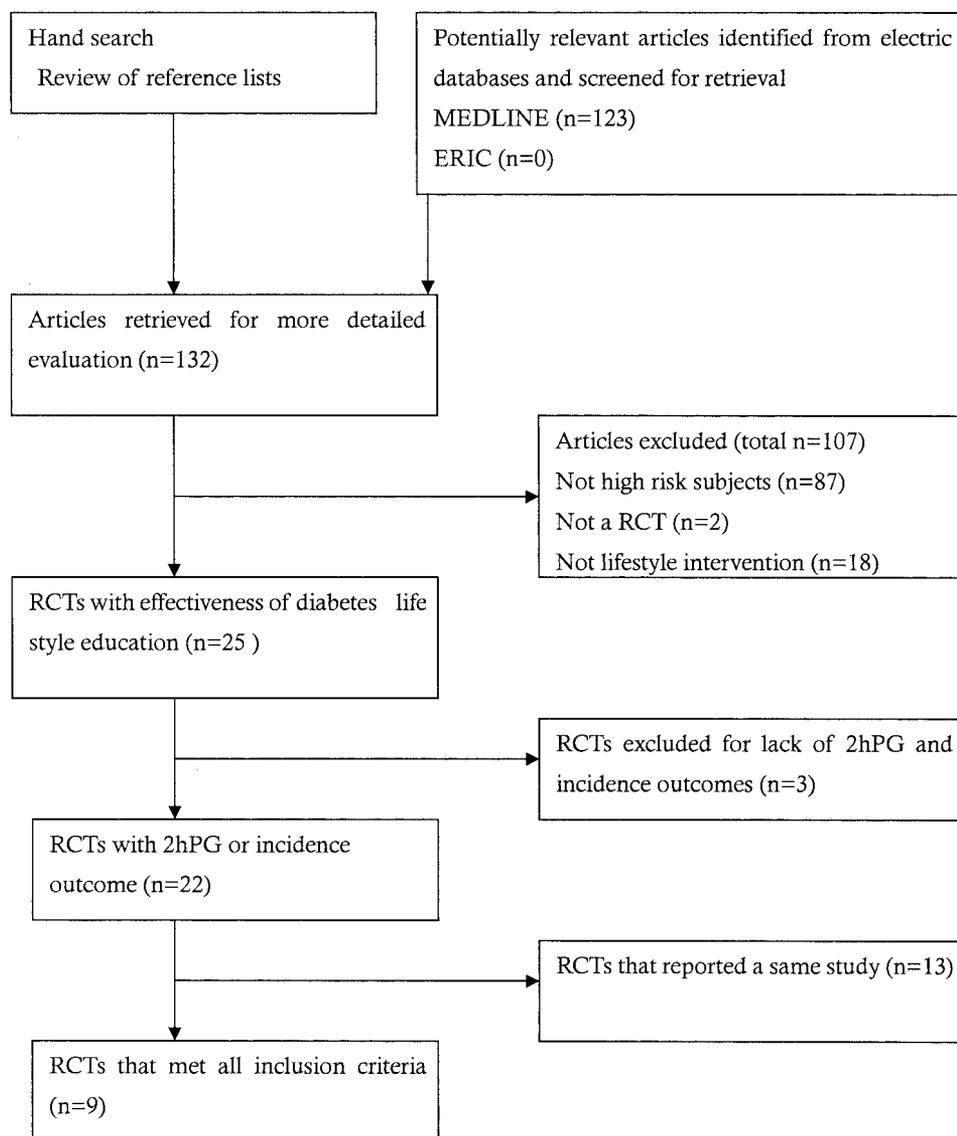
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**Abbreviations:** DPPRG, Diabetes Prevention Program Research Group; IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

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

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**Figure 1**—Systematic review flow diagram. n = number of articles. ERIC, Educational Resources Information Center database; 2hPG, 2-h plasma glucose; RCT, randomized controlled trial.

borderline type corresponds to the sum of IFG plus IGT (6).

**Types of studies.** Randomized controlled trials that followed patients for  $\geq 6$  months were included. Randomization of individuals or clusters of individuals was accepted.

**Types of intervention.** Lifestyle (combined diet and exercise) or solely dietary education interventions were selected. Control interventions were those described above.

**Search strategy for identification of studies.** Medline and ERIC (Educational Resources Information Center) databases (January 1966 to November 2004) were searched to identify relevant literature (restricted to the English language). Search terms were free text terms, MeSH (Medical subject heading), and Medline medical index terms. For instance, diabetes, IGT, IFG, borderline, etc. for type 2

diabetes and related conditions; exercise, physical fitness, nutrition, diet, etc., for lifestyle interventions; and prevention and randomized controlled trials were used as search terms.

#### Statistical analysis

Overall estimates were examined using a fixed-effects model (general variance-based method), a random-effects model (DerSimonian-Laird method) (7), and a Bayesian model with noninformative priors (Monte Carlo Markov chain) (8). A  $\chi^2$  test was used to assess heterogeneity among trials. Considering that the fixed-effects model is useful only under conditions of homogeneity and that the power of statistical tests of heterogeneity is low, we planned to use the random-effects model as the primary method irrespective of the test result of heterogeneity. We used the other models for sensitivity anal-

yses. S-plus (9) was used for estimation of the random-effects model and the fixed-effects model, and WinBUGS (10) was used for the Bayesian model (burn-in sample = 1,000, number of Gibbs sampling = 10,000).

The measure of effect size for 2-h plasma glucose is given by the difference between the lifestyle education intervention group and control group ( $\Delta$ ) for each individual study, which is equal to  $\Delta_i - \Delta_c$ , where  $\Delta_i$  and  $\Delta_c$  are mean differences from baseline to end point (basically at 1 year) in 2-h plasma glucose between, respectively, the lifestyle education intervention and control groups. When the SD of the difference from baseline to end point was not given in the literature, it was calculated using  $SD_{pre}$  (SD of the baseline 2-h plasma glucose) and  $SD_{post}$  (SD of the end point) for each group, using the formula  $SD^2 = SD_{pre}^2 + SD_{post}^2 -$

Table 1—Characteristics of the nine randomized controlled trials\*

Study (ref. no.)	Randomized subjects	Inclusion criteria	Follow-up duration (years)	Diabetes incidence (r/n)†		2hPG (mmol/l)	
				Control	Intervention	Baseline (means ± SD)	Difference from baseline at 1 year (means ± SD) (n)‡
Pan et al. (2)	577§	M&F, IGT	6	90/133	58/130	C: 9.03 ± 0.89 L: 9.11 ± 0.93	C: 3.96 ± 3.82 (133)   L: 1.65 ± 3.16 (130)
Wein et al. (13)	200	Female, IGT	4.25	7/100	6/100	C: 9.8 ± 0.74   L: 9.9 ± 0.74	C: 0.1 ± 1.94 (96)   L: -0.1 ± 2.19 (97)
Lindhahl et al. (14)	186	M&F, BMI >27, age 30–60, IGT	1	NA	NA	C: 8.0 ± 11.09¶ L: 7.5 ± 6.99	C: -0.30 ± 2.75 (93)¶ L: -0.68 ± 1.95 (93)
Oldroyd et al. (15)	78	M&F, age 24–75, IGT	0.5	NA	NA	C: 9.2 ± 0.9 L: 9.1 ± 0.9	C: -0.5 ± 1.8 (32)# L: -0.7 ± 1.9 (35)
Tuomilehto et al. (16)	522	M&F, BMI >25, age 40–64, IGT	6**	51/257	22/265	C: 8.9 ± 1.5 L: 8.9 ± 1.5	C: -0.3 ± 2.2 (250) L: -0.9 ± 1.9 (256)
Swinburn et al. (17)	176	M&F, age ≥40, IGT + (2hPG 7.0–7.8 mmol/l)	1	NA	NA	C: 7.5 ± 2.4 D: 7.9 ± 2.5	C: 0.74 ± 2.76 (70) D: 0.01 ± 2.68 (66)
Mensink et al. (18)	114	M&F, BMI >25, age ≥40, IGT	3	NA	NA	C: 8.6 ± 1.48 D: 8.8 ± 2.06	C: 0.2 ± 2.23 (55) L: -0.8 ± 2.06 (47)
Watanabe et al. (3)	173	Male, age 35–70, borderline	1	6/87	3/86	C: 7.3 ± 1.7 D: 8.2 ± 1.5	C: 0.67 ± 1.74 (77) D: -0.76 ± 1.36 (79)
DPPRG (19)	3,234§	M&F, age ≥25, BMI >24 (Asian >22), 27 centers, IFG	2.8	313/1,082‡	155/1,079‡	C: 9.1 ± 0.9 L: 9.1 ± 0.9	NA

\*Nine studies were reported in 22 published articles. One article is listed as a representative of the relevant study. †Incidence of type 2 diabetes: r/n = (number of cases divided by total number of analyzed subjects). ‡Except for the studies by Pan (2) = 6 years, Wein (13) = average 4.25 years, and Oldroyd (15) = 6 months. §Including other intervention types. ||SD for the mean difference was calculated using SDs in each point. ¶SD was calculated using 95% CIs. #Difference from baseline at 6 months. \*\*Strong intervention was performed during the 1st year. ††Calculated from incidence. C, control; D, solely dietary education intervention; L, lifestyle education (combined diet and exercise) intervention; M&F, male and female.

$2rSD_{pre}SD_{post}$ , where  $r$  is the correlation between the baseline and end point groups. Because no study reported  $r$ , and its true value is unknown, we consulted our past study data and used  $r = 0.5$ . For this, a sensitivity analysis was performed, using  $r = 0.3$  and  $r = 0.7$ . If the 95% CI was shown instead of SD, SD was calculated using the formula  $SD = (\sqrt{n}) (95\% CI_{upper} - 95\% CI_{lower}) \div 4$ , where  $n$  denotes sample size of a group.

Net change in 2-h plasma glucose or RR is shown for each individual study, with lines extending from circles representing 95% CIs in the Forest plot. A cumulative meta-analysis by the random-effects model (11) was also performed to determine at which point (when sufficient evidence was available) to demonstrate a beneficial lifestyle education intervention effect. Subgroup analysis by intervention type, i.e., diet versus lifestyle (combined

diet and exercise) and follow-up duration (<1 vs. ≥2 years), was conducted as a sensitivity analysis. The selection bias was visually examined using the funnel plot.

**RESULTS**— Following the QUOROM guidelines (12), Fig. 1 depicts the flow diagram for this review. Eight studies (2,3,13–18) met strict inclusion criteria for the analysis of 2-h plasma glucose and five studies (2,3,13,16,19) for the analysis

Table 1—Continued

Age (years)	BMI (kg/m <sup>2</sup> )	Type of intervention	Dietary education	Exercise education	Control
45	26	Dietary + exercise	Reducing energy intake	Increase leisure physical exercise at least 1 unit/day	General instructions for diet and/or increased leisure physical activities
39	25	Dietary + exercise	Standard diet advice sheet with telephone contact (three per month)	Emphasizing need for regular exercise	Regular exercise and standard diet advice
55	31	Dietary + exercise	Low-fat, high-fiber diet	Regular exercise with a program implemented during a 1-month stay at a wellness center that included intense dietary learning sessions	Standard program including counseling session for 30–60 min conducted by a specially trained nurse
58	30	Dietary + exercise	Regular diet counseling from a dietician	Physical activity counseling from a physiotherapist	General instructions for diet and/or increased leisure physical activities
55	31	Dietary + exercise	Individualized dietary counseling from a nutritionist	Circuit-type resistance training sessions and advice on increasing overall physical activity	General dietary and exercise advice at baseline and an annual physician's examination
52	29	Dietary alone	Reduced-fat diet and participation in monthly small-group education session for 1 year	None	General dietary advice about health food choices
57	29	Dietary + exercise	Regular dietary advice	Stimulated to lose weight and increase physical activity with visits scheduled at regular intervals	Brief information about the beneficial effects of a healthy diet and increased physical activity
55	24	Dietary alone	Reducing energy intake, especially at dinner	None	Conventional group counseling
50	34	Dietary + exercise	Weight reduction through a healthy low-calorie, low-fat diet	Engage in physical activity of moderate intensity by individualized curriculum by case managers	Written information for standard lifestyle recommendation and an annual 20- to 30-min individual session emphasizing importance of a healthy lifestyle

of RR. In this process, one study was selected among studies that published results from the same trial, and one intervention (having priority on lifestyle intervention over the diet-alone intervention) was selected from a study. The general characteristics and outcomes of the studies are shown in Table 1.

### Type of intervention

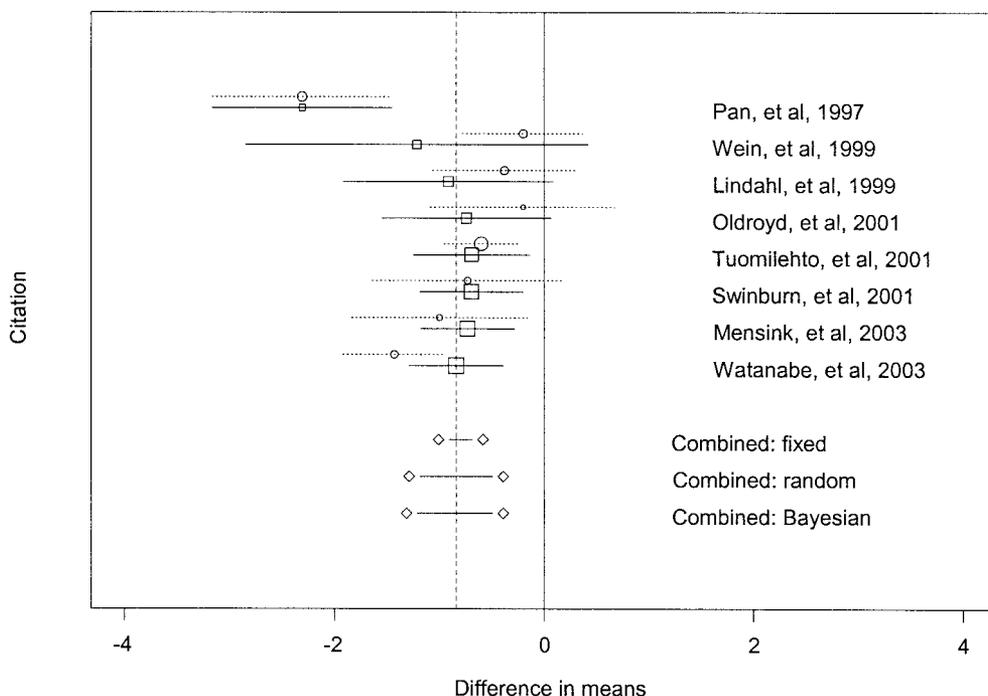
Lifestyle education interventions of the selected studies varied widely. Lifestyle education (combined diet and exercise) was conducted in seven studies (2,13–16,18,19), and a solely lifestyle education intervention was carried out in two stud-

ies (3,17). Details of the type of intervention are summarized in Table 1.

### 2-h plasma glucose

Two studies (2,13) did not report the SD of the differences from baseline to end point, so the SD was calculated from  $SD_{pre}$  and  $SD_{post}$ . Two studies (13,14) showed the 95% CI instead of SD; thus, SD was calculated from 95%  $CI_{upper}$  and 95%  $CI_{lower}$ . In the eight studies (2,3,13–18) in which the 2-h plasma glucose level was determined, evidence of heterogeneity among the studies was shown ( $P < 0.001$ ). Figure 2 shows the net change in 2-h plasma glucose, results of cumulative

meta-analysis, and overall estimates for 2-h plasma glucose by several models. The estimates from the random-effects model are shown, with lines extending from quadrangular symbols representing 95% CIs. The ranges of 95% CIs of the overall estimates for several models are shown with the solid line between the diamond symbols in the figure. In calculating overall estimates for 2-h plasma glucose, the results were insensitive to  $r$  in the range we expected (0.3–0.7); therefore, data are presented with the value of  $r = 0.5$ . Cumulative analysis indicated that from the last four studies, overall estimates became significant. Overall, a



**Figure 2**—Forest plot for the net change in 2-h plasma glucose in eight randomized controlled trials of the effects of lifestyle education, with their 95% CIs (individual and cumulative meta-analysis). Net change in 2-h plasma glucose is shown for each individual study, with dotted lines extending from circles representing 95% CIs. Cumulative meta-analysis by the random-effects model in 2-h plasma glucose is shown by each individual study (sequentially cumulated), with solid lines extending from quadrangles representing 95% CIs. The ranges of 95% CIs of the overall estimates are shown for several models with solid lines between the diamonds.

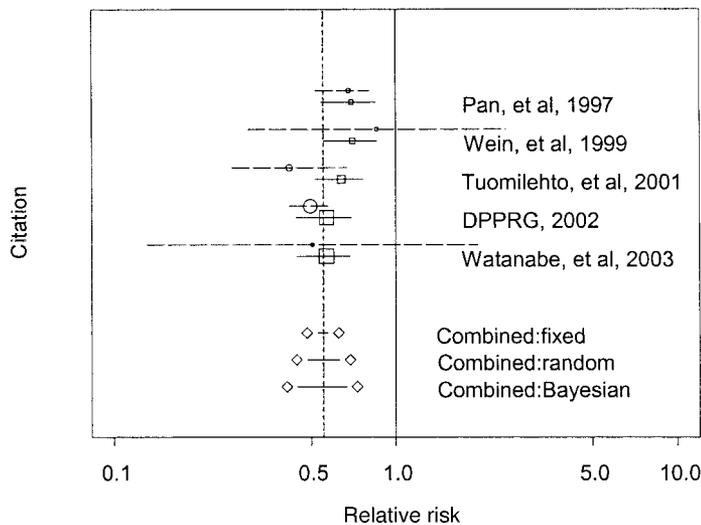
1-year lifestyle education intervention reduced 2-h plasma glucose by 0.84 mmol/l (95% CI 0.39–1.29) compared with the control intervention, as determined by the random-effects model. Concordant results were obtained by other models, i.e., a 0.80 mmol/l (0.58–1.01) reduction was estimated by the fixed-effects model and a 0.84 mmol/l (0.39–1.32) reduction by the Bayesian model. All of the overall estimates denoted a significant reduction of 2-h plasma glucose in the lifestyle education intervention groups compared with control groups.

Because there was evidence of heterogeneity in this combined analysis, subgroup analyses were conducted to analyze sensitivity. Overall estimates of 2-h plasma glucose were obtained according to the length of the study (1 year for five studies and >1 year [6 and 4.25 years] for two studies) and by the types of intervention (lifestyle education for six studies and solely dietary education for two studies.) Excluding studies that exceeded 1 year (two studies), the results still showed a significant reduction in 2-h plasma glucose, except those for the Bayesian model.

A funnel plot of sample size against the effect size was examined (figure not shown). From observations of data, selection bias did not largely affect the results of the present study. In addition, the related factors of mean age, study publication year, baseline value of 2-h plasma glucose, and BMI varied, and these factors were visually examined. From an observational point of view, the results detected no bias (figures not shown).

**RR**

In the five studies (2,3,13,16,19) in which the incidence was obtained, analysis showed no evidence of heterogeneity among studies ( $P = 0.145$ ). Figure 3 shows RRs of each study, the result of cumulative meta-analysis, and overall RRs by several models. The cumulative meta-analysis indicated significant effects in all cases. All of the results indicated that lifestyle education groups had a relatively lower incidence than control groups. The risk of incidence of type 2 diabetes in the lifestyle education intervention group was reduced by ~50% (RR = 0.55 [95% CI 0.44–0.69]) compared with the control intervention group by the random-effects model. The results from other models were similar. Specifically, RR was estimated as 0.55 (0.48–0.63) by the fixed-effects model and 0.55 (0.41–0.74) by the Bayesian model. Because there was one mega-study conducted by the Diabetes Prevention Program Research Group



**Figure 3**—Forest plot for RR in five randomized controlled trials of the effects of lifestyle education, with their 95% CIs (individual and cumulative meta-analysis). For explanation of the figure, see the legend to Fig. 2.

(DPPRG) (19), we excluded it from analysis. Although the number of subjects was small except for the mega-study, meta-analysis of small trials was shown to be concordant with the results of the mega-study when we examined the fixed-effects model, the random-effects model, and Bayesian model.

**CONCLUSIONS**— This meta-analysis provided evidence of the efficacy of lifestyle education for individuals at high-risk of type 2 diabetes in reducing 2-h plasma glucose and RR. It reduced 2-h plasma glucose by  $\sim 0.84$  mmol/l (95% CI 0.39–1.29) and also the incidence of type 2 diabetes by  $\sim 50\%$  (RR 0.55 [0.44–0.69]) compared with the control group, as determined by the random-effects model. Significant effects were also obtained by other models. Although the interventions and methods of lifestyle education varied in these studies, these results indicate that lifestyle education as well as a solely dietary education improved 2-h plasma glucose and reduced the risk of type 2 diabetes in high-risk individuals.

Although lifestyle education for high-risk subjects is an accepted cornerstone of prevention of type 2 diabetes as well as treatment of type 2 diabetes, a formal and systematic overview of its efficacy and method of delivery has not been available. Our study provides evidence of a relationship between lifestyle education in high-risk subjects and the prevention of type 2 diabetes.

Several meta-analyses have been published on the effects of lifestyle education on GHb for diabetic patients (20), low-glycemic index diets in the management of diabetes (21), and glucose and insulin responses to dietary chromium supplements (22). Although the purpose, methods, and types of subjects differed, there was evidence that not only clinical care but also lifestyle education is effective. Our study aimed at examining lifestyle education for those at high risk of type 2 diabetes. Considering the poor quality of life of diabetic patients, preventing the development of this disease is important, and much more attention should be paid to lifestyle education.

Many individuals at high risk for diabetes are designated as having what is now called metabolic syndrome, and, recently, considerable attention has been paid to this syndrome. The primary end points of the randomized controlled trials analyzed in the present study were de-

signed as 2-h plasma glucose and/or incidence of type 2 diabetes. Therefore, we cannot examine the effects of lifestyle education on the metabolic syndrome. Obesity is one component of the metabolic syndrome. Many studies examined BMI as one of the secondary end points. Some of the individual studies (13–15,17) did not find a significant effect of lifestyle education on 2-h plasma glucose, but they did find that it affected BMI. This means that a weak effect of lifestyle intervention on weight loss may exist. Further study of the metabolic syndrome is needed to define effective interventions for this condition.

Many of the studies included in this meta-analysis involve only a small number of subjects, with the exception of one mega-trial (19), which was used for analysis of RR in this report. The results, when excluding the mega-study, were also significant. The findings suggest the clinical benefits of lifestyle education. There has been extensive discussion of the differences between meta-analyses and mega-trials (23). Selective nonpublication of negative trials seems to be a likely explanation for that. Our results suggest that the meta-analyses of small trials is concordant with the results of the DPPRG, for which we examined the random-effects model as well as the fixed-effects model and Bayesian model.

The strengths and limitations of this meta-analysis should be considered. Our study has several strengths. As far as we know, this is the first study to examine the effects of lifestyle education for individuals at high risk of type 2 diabetes by meta-analysis, although the education reported in the studies was not uniform. We also focused attention on two types of viewpoints: 2-h plasma glucose and incidence. Considering that those with higher values for 2-h plasma glucose are more likely to develop diabetes, it is meaningful that both glucose level and incidence indicated the effect of lifestyle education when compared with control subjects.

This study has several important limitations. This analysis was confined to English-language articles, which could introduce bias. Furthermore, only randomized controlled trials were included, which could also introduce bias. However, considering that the quality of studies of lifestyle education as well as solely dietary education may be affected by many confounding biases, these limitations may be acceptable. From the visual observations by plots on the effect of life-

style education against the factors on the effect size, the results were not greatly affected by those factors. Publication bias is always a concern in meta-analyses. We performed electronic searches, including a hand search, and examined by funnel plot sample size against effect size. The funnel plot suggested little influence from publication bias on the effect size. Although it may be small, we cannot deny the possibility of selection bias. Our study has a limitation in that the follow-up period extended for  $\geq 6$  months; however, this may be acceptable because an earlier assessment could be biased as a result of changes made only because subjects were conscious of being studied. In the prevention of diabetes, maintaining long-term control is warranted. Another limitation, which was the variability of lifestyle education, was examined by subgroup analyses. Although the quality of lifestyle education varied, the results indicated that it was effective.

Taking these limitations into account, the meta-analysis provided objective evidence that lifestyle education for reducing 2-h plasma glucose and the incidence of type 2 diabetes in groups of high-risk individuals is effective and may be a useful tool for preventing type 2 diabetes. Approaches that include lifestyle education with the goal of preventing the development of type 2 diabetes should be given more attention.

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