

Can we prevent high-risk patients from getting type 2 diabetes?

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Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen HH, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001;344:1343-50.

Research question

Can a lifestyle intervention prevent those at high risk (eg, overweight people and people with high fasting glucose levels) from progressing to type 2 diabetes?

Type of article and design

Randomized controlled trial.

Relevance to family physicians

We seem to spend a good deal of our time providing reactive care and prescribing pills to our patients at risk of diabetes and coronary artery disease (CAD). We discuss lifestyle issues with our patients, but we seldom bring about changes in behaviour. Reasons for this include lack of training and knowledge, the insidious effects of diabetes, and health system factors, but one concern has always been the lack of evidence. It is, therefore, refreshing to review a paper that looks at whether lifestyle changes make a difference.

Type 2 diabetes is becoming epidemic in Canada. Risk of developing type 2 diabetes increases with age, obesity, and lack of physical activity.¹ Researchers predict that 3 million Canadians will be suffering from type 2 diabetes in 2010.² Increased screening has certainly contributed to these numbers and has uncovered many patients with high fasting glucose levels (fasting blood sugar between 6 and 7; >7 indicates diabetes). These patients are often obese and at about a threefold risk for all the cardiovascular diseases inherent in type 2 diabetes.^{3,4} Most current evidence informs us about people who already have diabetes, but can we prevent it among people who are clearly on the path to getting it?

Critical Appraisal reviews important articles in the literature relevant to family physicians. Reviews are by family physicians, not experts on the topics. They assess not only the strength of the studies but the "bottom line" clinical importance for family practice. We invite you to comment on the reviews, suggest articles for review, or become a reviewer. Contact Coordinator Michael Evans by e-mail michael.evans@utoronto.ca or by fax (416) 603-5821.

Overview of study and outcomes

This Finnish trial randomly assigned 522 middle-aged, overweight subjects (172 men and 350 women; mean age 55 years; mean body mass index 31) with impaired glucose tolerance to an intervention group or a control group. Subjects in the intervention group met with a nutritionist seven times during the first year and every 3 months thereafter.

Counseling focused on five issues: reducing weight by 5% or more, reducing total intake of fat (<30% of energy intake), reducing intake of saturated fat (<10% of energy intake), increasing fibre intake (at least 15 g/1000 kcal), and increasing exercise (to at least 30 min/d). Participants completed 3-day food records four times a year to individualize feedback. Aerobic and supervised resistance training sessions were offered. An oral glucose-tolerance test was performed annually; diagnosis of diabetes was confirmed by a second test. Mean duration of follow up was 3.2 years.

Results

Mean weight loss between baseline and end of year 1 was 4.2 (± 5.1) kg in the intervention group and 0.8 ± 3.7 kg in the control group. Net loss by end of year 2 was 3.5 (± 5.5) kg in the intervention group and 0.8 (± 4.4) kg in the control group ($P < .001$ for both comparisons between groups). Rate of participation in the guided exercises during the first year varied from 50% to 85%, depending on centre. Cumulative incidence of diabetes after 4 years was 11% (95% confidence interval [CI] 6% to 15%) in the intervention group and 23% (95% CI 17% to 29%) in the control group.

Absolute risk reduction, therefore, was 12%; relative risk of diabetes was reduced by 58% ($P < .001$) in the intervention group. At the 1-year examination, subjects were ranked according to their success in achieving the goals of the intervention on a scale of 0 to 5, with 5 representing success. There was a strong inverse relationship between success score and risk

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of diabetes. Reduction in the incidence of diabetes was directly associated with changes in lifestyle. **Table 1** shows participants' success in achieving the five lifestyle goals.

Table 1. Participants' success in achieving the five goals: *P* value .001

GOAL	% OF INTERVENTION GROUP ACHIEVING GOAL	% OF CONTROL GROUP ACHIEVING GOAL
To reduce weight > 5%	43	13
To lower fat intake to < 30% of energy intake	47	26
To lower saturated fat intake to < 10% of energy intake	26	11
To increase fibre intake to >15g/1000 kcal	25	12
To exercise > 30 min/d	86	71

During the study, 40 patients (8%) withdrew: 23 in the intervention group and 17 in the control group. Of these, 27 withdrew for personal reasons, nine could not be contacted, three had severe illnesses, and one died.

The authors calculated that 22 people would have to be treated for 1 year (or five people for 5 years) to prevent one case of diabetes. This is looking at the outcome of diabetes only, however, and does not include all the other likely advantages of this type of lifestyle intervention.

Analysis of methodology

This well executed trial had intention-to-treat analysis. The control group got general health advice at baseline and annual follow-up visits, so the benefit does not appear to have been overestimated. The main question with this trial is whether it can be replicated. Were the Finnish people enrolled in this trial somehow more amenable to lifestyle changes than my patients? Could I arrange, and would my patients attend, seven visits with a nutritionist in the first year and every 3 months thereafter? The drop-out rate in this trial was quite low (9% in the intervention group, 7% in the control group).

Application to clinical practice

It was not a foregone conclusion that reduction of risk factors would translate into reduced risk of diabetes. Therefore, this trial is groundbreaking in making the connection. Interestingly, the advice for patients was not to cut down on sugar, but rather to adopt a healthy lifestyle. As well, the

trial achieved significant results without dramatic weight loss, which is encouraging for both me and my patients. The advice given in this trial is straightforward and can be replicated in my clinic. Having patients see a nutritionist so frequently likely cannot. Clearly, this trial has set the stage for replication in a North American setting with a pathway to achieving lifestyle goals that my patients and I could follow.

Author's note: Since submission of the review, results from the Diabetes Prevention Program have been posted on the National Institutes of Health website.⁵ Essentially they reinforce the findings of the Finnish trial and augment those data with some important features.

- A much larger ($N = 3234$) and more heterogeneous population was involved.
- They had more success with participants older than 60 years (71% relative risk reduction).
- Metformin (850 mg twice daily) was given to patients in one arm of the study and was found to be effective for all participants, but was relatively ineffective for older people who were less overweight than the standard. A fourth arm of the study assessed troglitazone; that part of the trial was stopped because of concerns about liver toxicity. The trial lasted 3 years and was ended early because of its success.

Bottom line

- Diabetes can be prevented in high-risk (glucose intolerant and obese) patients through lifestyle changes. After 3.2 years, this trial showed an impressive 58% reduction in the number of patients progressing to a diagnosis of type 2 diabetes.
- Lifestyle changes had five specific goals: to reduce weight (>5%), to lower total fat intake and saturated fat intake, and to increase fibre intake and exercise. Weight loss was relatively small (4.2 ± 5.1 kg in the intervention group and 0.8 ± 3.7 kg in the control group at 1 year), given the outcome.
- Study subjects saw a nutritionist seven times in the first year and every 3 months thereafter. This would be difficult to replicate in most practices. This trial showed that prevention is possible; now we need to define which changes have the most effect and to delineate a pathway that we and our patients can follow.
- A recent large US study confirmed these results and showed that metformin (850 mg twice daily) was successful in delaying type 2 diabetes in all but less overweight elderly participants. ❖

Points saillants

- Il est possible de prévenir le diabète chez les patients à risque élevé (l'intolérance au glucose et l'obésité) grâce à des modifications au mode de vie. Après 3,2 ans, cette étude a fait valoir une impressionnante réduction de 58% dans le nombre de patients qui progressent vers un diagnostic de diabète de type 2.
- Les modifications au mode de vie avaient cinq objectifs précis: réduire le poids (>5%), réduire la consommation totale de gras et de gras saturés, et accroître la consommation de fibres et l'activité physique. La perte de poids a été relativement faible compte tenu des résultats ($4,2 \pm 5,1$ kg dans le groupe d'intervention et $0,8 \pm 3,7$ kg dans le groupe de contrôle après un an).
- Les sujets consultaient un diététiste sept fois durant la première année et chaque trimestre par la suite. Il serait difficile de faire de même dans la plupart des pratiques. L'étude a démontré que la prévention était possible; il faut maintenant définir quels changements ont le plus de résultats et établir un cheminement que nos patients et nous-mêmes pouvons suivre.
- Une récente étude d'envergure aux États-Unis a confirmé ces résultats et démontré que la metformine (850 mg deux fois par jour) était efficace pour retarder l'apparition du diabète de type 2 chez tous les participants sauf les moins obèses.

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