

A lifestyle intervention or metformin prevented or delayed the onset of type 2 diabetes in persons at risk

Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002 Feb 7;346:393-403.

QUESTION

In overweight persons with elevated fasting and postload plasma glucose levels, does an intensive lifestyle intervention or treatment with metformin plus standard lifestyle recommendations prevent or delay the onset of type 2 diabetes mellitus?

DESIGN

Randomized (allocation concealed*), blinded (clinicians and participants for metformin and placebo),* placebo-controlled trial with mean follow-up of 2.8 years.

SETTING

27 centers in the United States.

PARTICIPANTS

3234 participants (mean age 51 y, 68% women) without diabetes who had a body mass index ≥ 24 kg/m² (≥ 22 kg/m² for Asians) and a plasma glucose level 5.3 to 6.9 mmol/L in the fasting state and 7.8 to 11.0 mmol/L 2 hours after a 75-g oral glucose load. Exclusion criteria included medications known to alter glucose tolerance and illnesses that could seriously reduce life expectancy or ability to participate in the trial. Follow-up was 93%.

INTERVENTION

Participants were allocated to an intensive program of lifestyle modification ($n = 1079$), standard lifestyle recommendations plus glucose control with metformin (850 mg twice daily) ($n = 1073$), or placebo ($n = 1082$). The intensive-lifestyle intervention consisted of a 16-lesson curriculum aimed at achieving and maintaining a weight reduction of $\geq 7\%$ of initial body weight through a low-calorie, low-fat diet and physical activity of moderate intensity. Standard lifestyle recommendations emphasized the importance of reducing weight and increasing physical activity.

MAIN OUTCOME MEASURES

Incidence of type 2 diabetes mellitus.

MAIN RESULTS

Analysis was by intention to treat. At 3 years, the cumulative incidence of diabetes was lower in the intensive lifestyle-intervention and metformin groups than in the placebo

group (Table). The incidence rates of diabetes were 4.8, 7.8, and 11.0 patients per 100 person-years for the intensive lifestyle-intervention, metformin, and placebo groups, respectively.

CONCLUSION

In overweight persons with elevated fasting and postload plasma glucose concentrations, an intensive lifestyle intervention or treatment with metformin plus standard lifestyle recommendations was more effective than standard lifestyle recommendations alone for preventing or delaying the onset of type 2 diabetes mellitus.

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*See Glossary.

Intensive lifestyle intervention (ILI) or metformin plus standard lifestyle vs placebo plus standard lifestyle for prevention of type 2 diabetes at 3 years†

Outcome	Comparisons	Event rates	RRR (95% CI)	NNT (CI)
Incidence of diabetes	ILI vs placebo	14% vs 29%	50% (41 to 58)	7 (6 to 10)
	Metformin vs placebo	22% vs 29%	25% (13 to 35)	14% (9 to 34)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The onset of type 2 diabetes can be delayed and perhaps prevented. In this trial by the Diabetes Prevention Program Research Group, patients received an intensive lifestyle-modification intervention or metformin. Both interventions lowered glucose levels during the first year; thereafter, the rate of increase in the fasting glucose level for both interventions was similar to that in the control group. This similarity can be explained partly by a decrease in patients' adherence to the program over time. The costs are unclear, but both interventions seemed safe. Other trials have shown that intensive lifestyle modification delays the onset of diabetes (1, 2).

Is it desirable to prevent diabetes? Preventing diabetes may avert loss of quality of life and insurability. It may also delay the development of cardiovascular disease, although direct evidence for this benefit is not yet available. Hypothetically, how diabetes prevention affects cardiovascular outcomes could depend on the preventive modality. Several observations link physical fitness and healthy diet to a lower risk for cardiovascular disease. Furthermore, a healthier lifestyle can modify obesity, hypertension, dyslipidemia, and other risk factors for cardiovascular disease. Metformin may also lower the risk for cardiovascular disease (3).

Is it feasible to prevent diabetes? Although lifestyle modification may be more effective and perhaps less expensive, metformin treatment

may be easier to implement and sustain. Lifestyle modification requires expertise in behavior modification and the effective mobilization of community resources to support the patient. Financial and logistical barriers may limit the implementation of an intensive lifestyle-modification intervention in clinical practice. However, this evidence justifies efforts to remove these barriers and, on a broader scale, to promote a healthier lifestyle to control the diabetes epidemic.

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