

THERAPEUTICS

An intensive intervention reduced cardiovascular and microvascular events in type 2 diabetes and microalbuminuria

Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med*. 2003;348:383-93.

QUESTION

In patients with type 2 diabetes and microalbuminuria, is a targeted intensive multifactorial intervention more effective than conventional treatment?

DESIGN

Randomized {allocation concealed*}†, blinded {data collectors and outcome assessors}†,* controlled trial with mean follow-up of 7.8 years (the Steno-2 Study).

SETTING

A diabetes center in Denmark.

PATIENTS

160 patients (mean age 55 y) with type 2 diabetes and persistent microalbuminuria. Follow-up was 81%.

INTERVENTION

80 patients were allocated to intensive treatment involving strict treatment goals with a stepwise implementation of behavior modification (diet plan, exercise, and smoking cessation) and pharmacologic therapy that targeted hyperglycemia, hypertension, dyslipidemia, microalbuminuria, and secondary prevention of cardiovascular disease with aspirin. 80 patients were allocated to conventional treatment of multiple risk factors from their general practitioner according to national guidelines.

MAIN OUTCOME MEASURES

The primary outcome was the composite endpoint of death from cardiovascular causes, nonfatal myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, nonfatal stroke, amputation resulting from ischemia, or vascular surgery for peripheral atherosclerotic artery disease. Secondary outcomes were development of diabetic nephropathy, development or progression of diabetic retinopathy, and progression of neuropathy.

MAIN RESULTS

Analysis was by intention to treat. Intensive treatment was associated with a lower risk than conventional treatment for the primary composite outcome, development of diabetic nephropathy, development or progression of retinopathy, and progression of autonomic

neuropathy (Table). Groups did not differ for progression of peripheral neuropathy ($P = 0.66$) or rates of ≥ 1 minor hypoglycemic event ($P = 0.50$) or ≥ 1 major hypoglycemic event ($P = 0.12$).

CONCLUSION

In patients with type 2 diabetes and microalbuminuria, a targeted, long-term, intensified, multifactorial intervention using behavioral modification and polypharmacologic therapy was more effective than conventional treatment for reducing cardiovascular and microvascular events.

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*See Glossary.

†Information provided by author.

Intensive vs conventional treatment in type 2 diabetes and microalbuminuria at mean 7.8 years‡

Outcomes	Intensive	Conventional	Adjusted HR (95% CI)	NNT (CI)
Composite endpoint§	24%	44%	0.47 (0.22 to 0.74)	5 (3 to 19)
			RRR (CI)	NNT (CI)
Diabetic nephropathy	20%	39%	48% (15 to 69)	6 (4 to 22)
Retinopathy	48%	64%	25% (1.5 to 44)	7 (4 to 125)
Autonomic neuropathy	30%	54%	44% (18 to 63)	5 (3 to 12)

‡HR = hazard ratio. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data provided by author. HR adjusted for baseline characteristics.

§Composite endpoint of cardiovascular events.

COMMENTARY

In response to the diabetes epidemic, health systems may consider prioritizing primary prevention, earlier detection, or aggressive intervention in patients with diabetes. National guidelines emphasize the latter approach based on expert opinion and evidence from studies of interventions that target single risk factors and measure process or surrogate endpoints. The impressive risk reduction for the composite cardiovascular endpoint seen in the intensively treated group of the Steno-2 study supports the strict targets in most current guidelines. However, these results may underestimate the true benefit of intensive treatment because the targets in the usual-care group for blood pressure, hemoglobin A_{1c}, lipids, and aspirin use became more intensive over the course of the study, and > 50% of patients in this group were managed in specialist clinics at some point. Although it is unclear which intervention components were responsible for benefit, this study seems to justify widespread use of multiple medications to achieve treatment targets in patients at high risk.

How can we replicate these impressive results? The immediate challenge for health care systems is to identify approaches to assist patients

with adherence to multiple medications. The next is to explore new ways of migrating elements of the specialist function that have traditionally resided in hospital-based clinics into the community to support excellence in primary care-led diabetes care. Examples of such new models of care include use of nurse case managers (1) and electronically linked management systems between primary and secondary care (2). The concept of a Managed Clinical Network has been proposed as part of the National Service Framework for Diabetes in England, and development of these networks may also provide new models for delivering diabetes care.

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References

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2. Montori VM, Dinneen SF, Gorman CA, et al. *Diabetes Care*. 2002;25:1952-7.