An intensive, target driven intervention reduced cardiovascular and microvascular events in patients with type 2 diabetes and microalbuminuria


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For correspondence: Dr O Pedersen, Steno Diabetes Center, Gentofte, Denmark. o.pedersen@steno.dk

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**QUESTION:** In patients with type 2 diabetes and microalbuminuria, what is the effect of a target driven, long term, intensive, multifactorial intervention compared with conventional treatment on cardiovascular and microvascular disease?

**Design**
Randomised [allocation concealed]*, blinded [data collectors and outcome assessors]*, controlled trial with mean follow up of 7.8 years (the Steno-2 Study).

<table>
<thead>
<tr>
<th>Outcomes (mean 7.8 y follow up)</th>
<th>Intensive</th>
<th>Conventional</th>
<th>Adjusted HR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite endpoint†</td>
<td>24%</td>
<td>44%</td>
<td>0.47 (0.22 to 0.74)</td>
<td>5 (3 to 19)</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>20%</td>
<td>39%</td>
<td>0.48 (0.15 to 0.69)</td>
<td>6 (4 to 22)</td>
</tr>
<tr>
<td>Retinopathy (developed or progressed)</td>
<td>48%</td>
<td>64%</td>
<td>0.25 (1.5 to 4.4)</td>
<td>7 (4 to 125)</td>
</tr>
<tr>
<td>Autonomic neuropathy</td>
<td>30%</td>
<td>54%</td>
<td>0.44 (1.8 to 63)</td>
<td>5 (3 to 12)</td>
</tr>
</tbody>
</table>

HRR = 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 various cardiovascular events.

**COMMENTARY**

With the rising incidence of diabetes creating a health and economic burden, research on the prevention of diabetes related morbidity and mortality is applicable to all practitioners.1 The findings of the United Kingdom Prospective Diabetes Study showed that stringent glycaemic control improved outcomes and highlighted the need for interventions to modify the risk of complications.2 In the Steno-2 study, a multifactorial approach (medications and behaviour modification of diet, exercise, and smoking) was used to modify risk factors associated with diabetes. The sustained improvement in the intensive therapy group over 7.8 years of follow up enhances the value of the study findings.

Improvements in fat and carbohydrate intake and reductions in HbA1c, serum triglyceride and cholesterol concentrations, systolic and diastolic blood pressure, and albumin excretion rate were found, but interventions to improve body mass index and increase exercise had little effect. Little information was provided on the behaviourally directed therapies such as the smoking cessation or exercise programme,3 and one is left with the sense that this was a secondary aspect of the management. However, the researchers emphasise that education, motivation, and individualised plans were part of the overall strategy. Patients in the intensive therapy group were seen a mean of 4 times per year at a diabetes centre compared with those in the conventional group who were seen by their general practitioner. However, without a clear understanding of what occurred during these visits, it is difficult to determine the relative importance of interventions directed toward self management of lifestyle versus pharmacological treatments. It is possible that additional gains may result from lifestyle interventions of the same intensity as the pharmacological ones reported in the Steno-2 study. Such investigations are needed.

**Main outcome measures**
The primary outcome was a composite endpoint of death from cardiovascular causes, non-fatal myocardial infarction, revascularisation, non-fatal stroke, amputation resulting from ischaemia, or vascular surgery for peripheral atherosclerotic artery disease. Secondary outcomes were development of diabetic nephropathy and development or progression of diabetic retinopathy or neuropathy.

**Main results**
Analysis was by intention to treat. Intensive treatment was associated with a lower risk than conventional treatment for the primary composite endpoint, development of diabetic nephropathy, development or progression of retinopathy, and progression of autonomic neuropathy (table). Treatment groups did not differ for progression of peripheral neuropathy (p=0.66) or rates of having ≥1 major hypoglycaemia event (p=0.50) or ≥1 major hypoglycaemia event (p=0.12).

**Conclusion**
In patients with type 2 diabetes and microalbuminuria, a target driven, long term, intensive multifactorial intervention using behavioural modification and polypharmacological therapy was more effective than conventional treatment for reducing risk of cardiovascular and microvascular events.

*Information provided by author.

**Patients**
160 patients (mean age 55 v) with persistent microalbuminuria. Follow up was 81%.

**Intervention**
80 patients were allocated to intensive treatment involving strict treatment goals with stepwise implementation of behaviour modification (diet plan, exercise, and smoking cessation) and target driven pharmacological therapy for hyperglycaemia, hypertension, dyslipidaemia, and microalbuminuria. All patients in the intervention group received either an angiotensin converting enzyme inhibitor or angiotensin II receptor antagonist. Aspirin was given for secondary prevention of cardiovascular disease. 80 patients were allocated to conventional treatment of risk factors from their general practitioner according to Danish Medical Association guidelines.