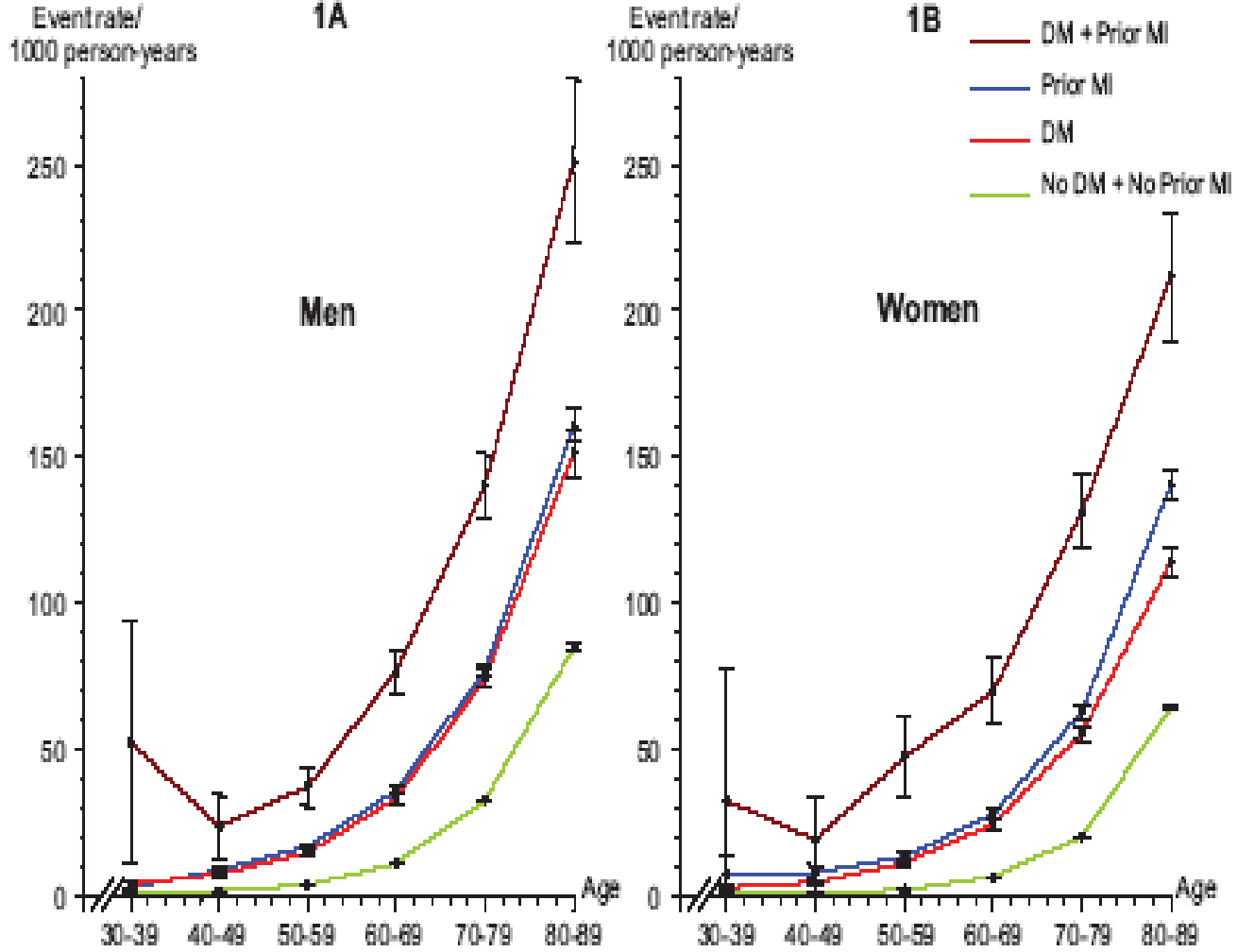
Type 2 diabetes is

a cardiovascular equivalent

and

should be treated aggressively!

Steno



Numbers at risk

No DM + No Prior MI	407 796	374 738	323 089	197 672	134 052	57 626	389 797	368 588	328 918	229 344	183 344	124 858
Prior MI	561	3 289	9 733	14 580	14 769	6 416	149	801	2 585	5 404	7 954	6 905
DM	2 989	4 835	7 985	8 032	6 738	3 102	2 271	3 355	5 101	6 901	8 328	5 685
DM + Prior MI	28	168	735	1 363	1 348	508	13	67	207	502	674	606

Figure 1. Event rates for cardiovascular mortality in men (A) and women (B) stratified by age and sex in relation to diabetes mellitus (DM) and a prior MI.

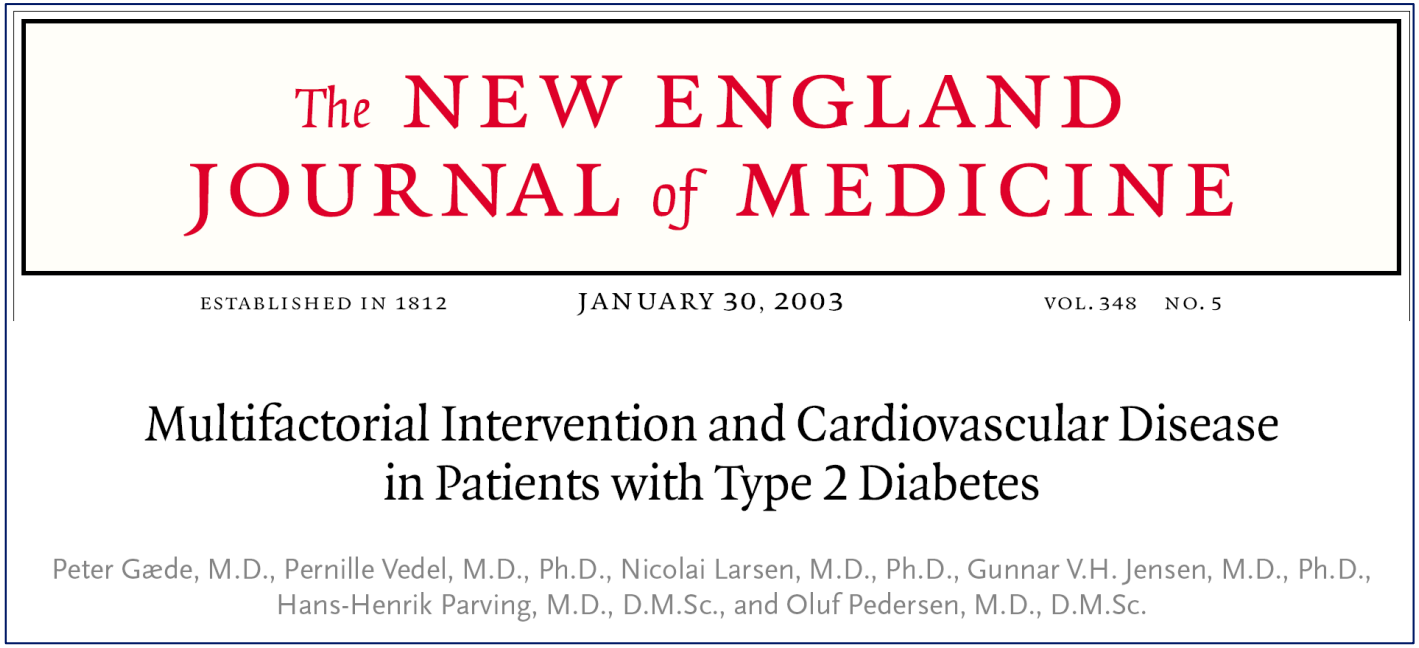
Schramm TK et al, 2008 Circulation 117:1945, 2008

Steno

Steno-2: Major papers

Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study

Peter Gæde, Pernille Vedel, Hans-Henrik Parving, Oluf Pedersen



New Engl J Med 2003; 348: 383-93

Steno

Steno-2: February 7th 2008 paper

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of a Multifactorial Intervention on Mortality in Type 2 Diabetes

Peter Gæde, M.D., D.M.Sc., Henrik Lund-Andersen, M.D., D.M.Sc.,
Hans-Henrik Parving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.

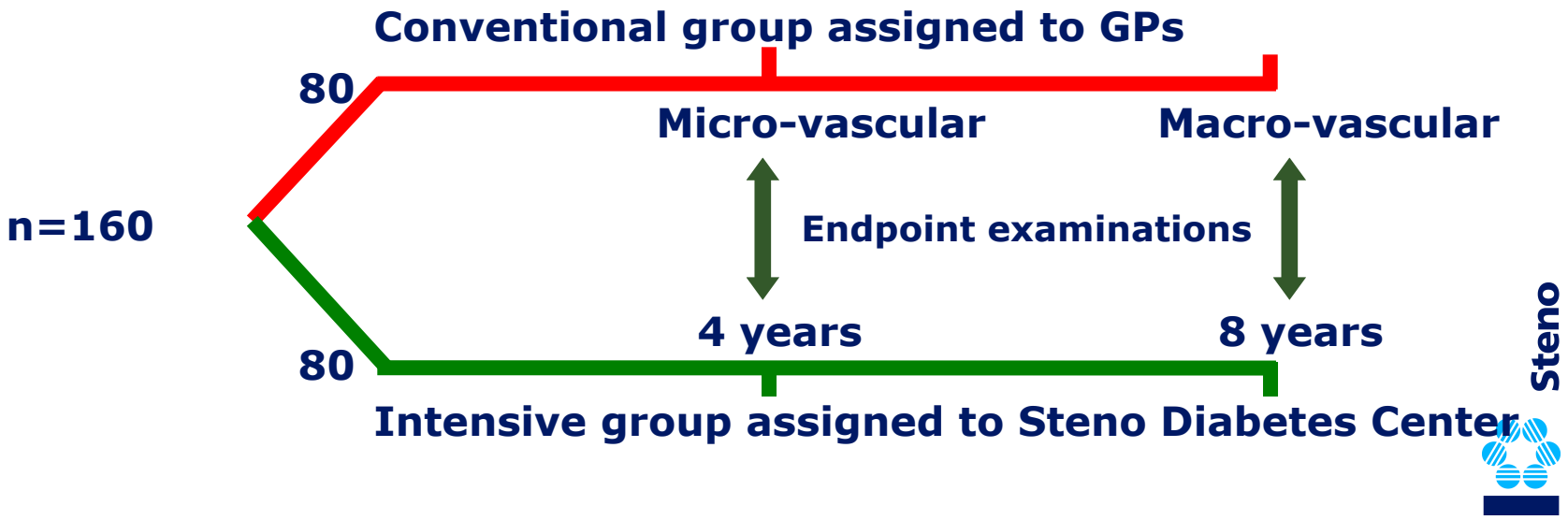
New Engl J Med 2008; 358: 580-91

Steno-2: Design

A PROBE design was applied, i.e.

a Prospective, Randomized, Open, Blinded Endpoint study

160 patients with type 2 diabetes and the metabolic syndrome including micro-albuminuria were with concealed randomization allocated conventional therapy at their GPs or intensive care at Steno Diabetes Center



Steno-2: Baseline Characteristics

	Conventional n=80	Intensive n=80
Gender (M/F)	56/24	63/17
Age (yrs)	55	55
Known DM (yrs)	6	6
Body mass index (kg/m^2)	30	30
Haemoglobin A_{1c} (%)	8.8	8.4
Fasting s -cholesterol (mmol/l)	5.8	5.4
Blood pressure (mm Hg)	149/86	146/85
Albumin excretion rate (mg/24 h)	69	78

Steno

The intensive-therapy group
- what's the difference?

Individualised risk assessment

Ambitious goal setting

Focused behaviour modification

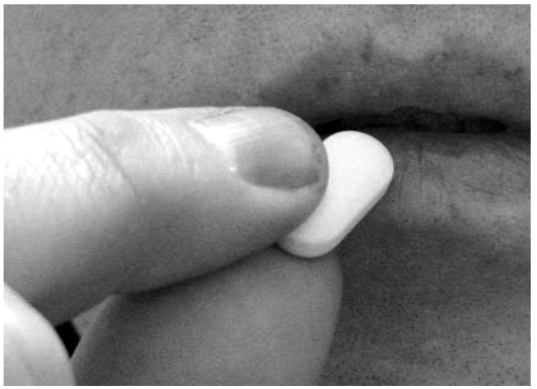
More drugs/higher dose

Continued patient education/motivation

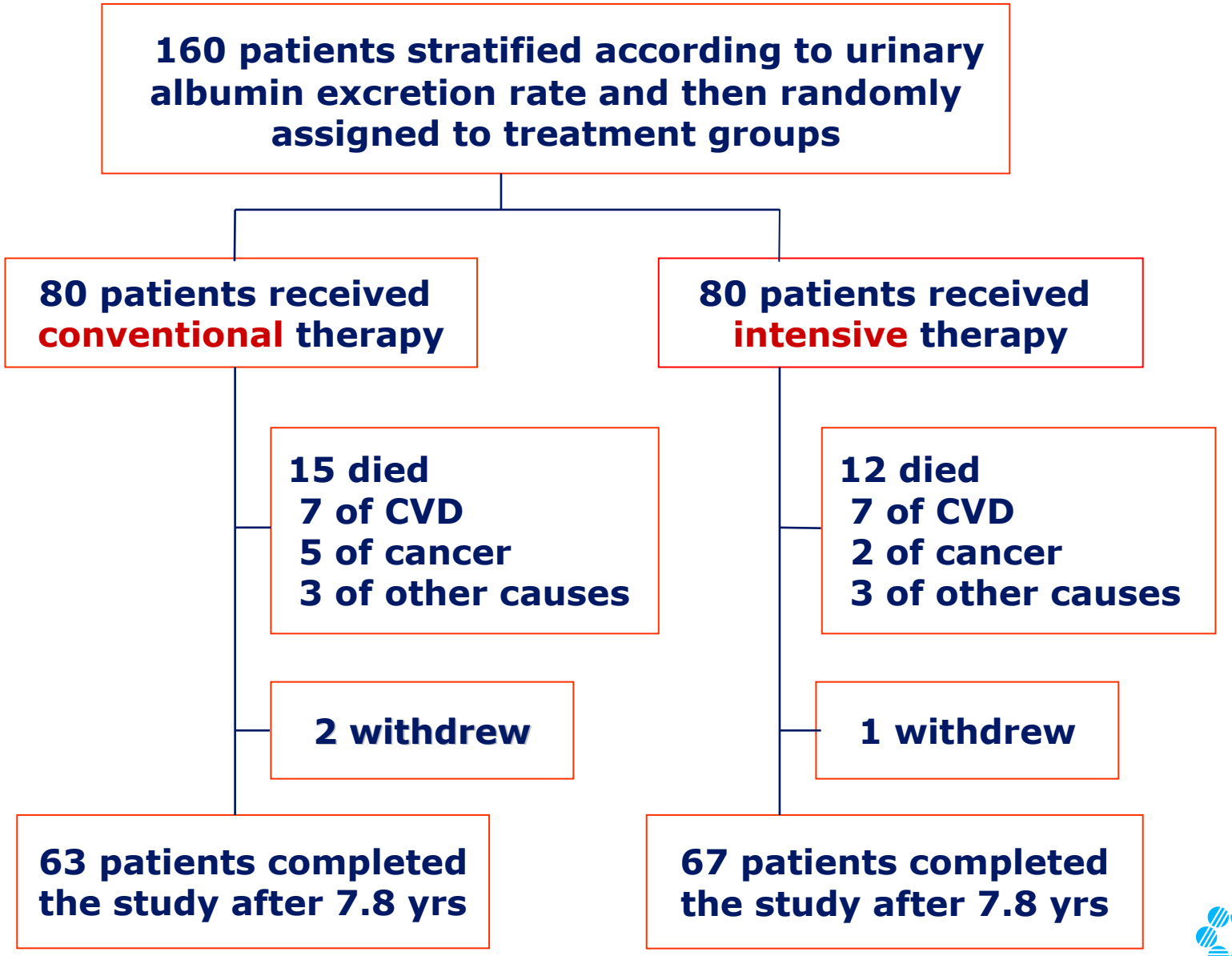
Steno

Drug Treatment: Stepwise and Target Driven

Hyperglycaemia:	**Gliclazide** **Metformin** **Insulin**
Dyslipidaemia:	**Statins** **Fibrates**
Hypertension:	**ACE-inhibitors** **Angiotensin II receptor blockers** **Diuretics** **Calcium antagonists** **Beta-blockers**
Microalbuminuria:	**ACE-inhibitors**
Other CVD prevention:	**Aspirin** **Folic acid**



Steno


160 patients stratified according to urinary albumin excretion rate and then randomly assigned to treatment groups
80 patients received conventional therapy
80 patients received intensive therapy
15 died
7 of CVD
5 of cancer
3 of other causes
12 died
7 of CVD
2 of cancer
3 of other causes
2 withdrew
1 withdrew
63 patients completed the study after 7.8 yrs
67 patients completed the study after 7.8 yrs

Steno

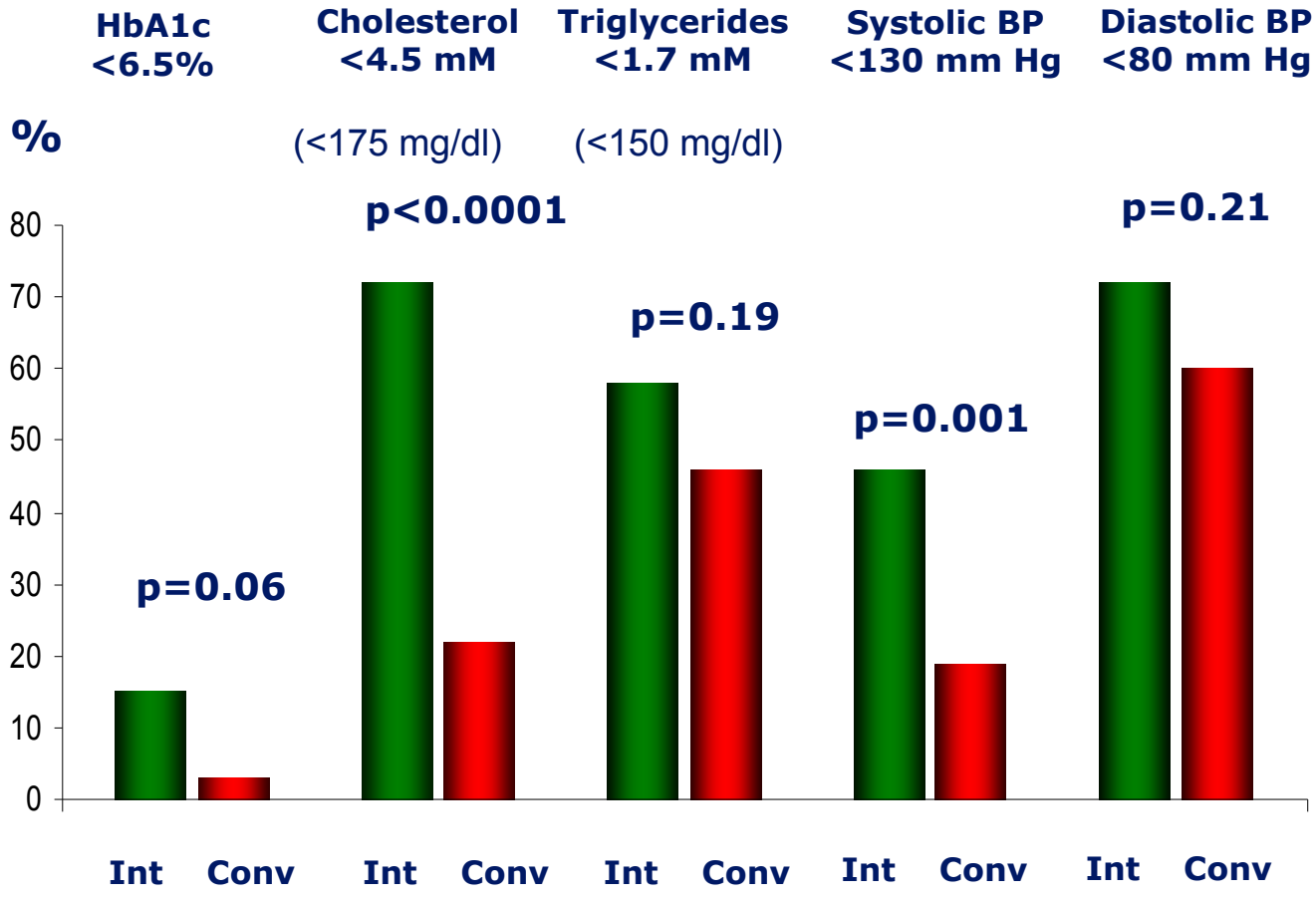
Risk factors at 8 years

	Conventional n=63	Intensive n=67
Haemoglobin A1c (%)	9.0	7.9
F-s-total-cholesterol (mmol/l)	5.7	4.1
F-s-LDL-cholesterol (mmol/l)	3.1	2.1
F-s-triglycerides (mmol/l)	3.1	1.7
Systolic BP (mm Hg)	146	132
Diastolic BP (mm Hg)	78	73
Albumin excretion rate (mg/24h)*	99	58

Values are mean

* median

Percentage of patients achieving treatment goals set for the intensive-therapy group at 8 years



Steno

Steno-2: Endpoints at 8 Yrs

Primary: Cardiovascular disease

Cardiovascular mortality
Non-fatal myocardial infarction
Coronary artery bypass graft
Non-fatal stroke
Revascularization
Amputation

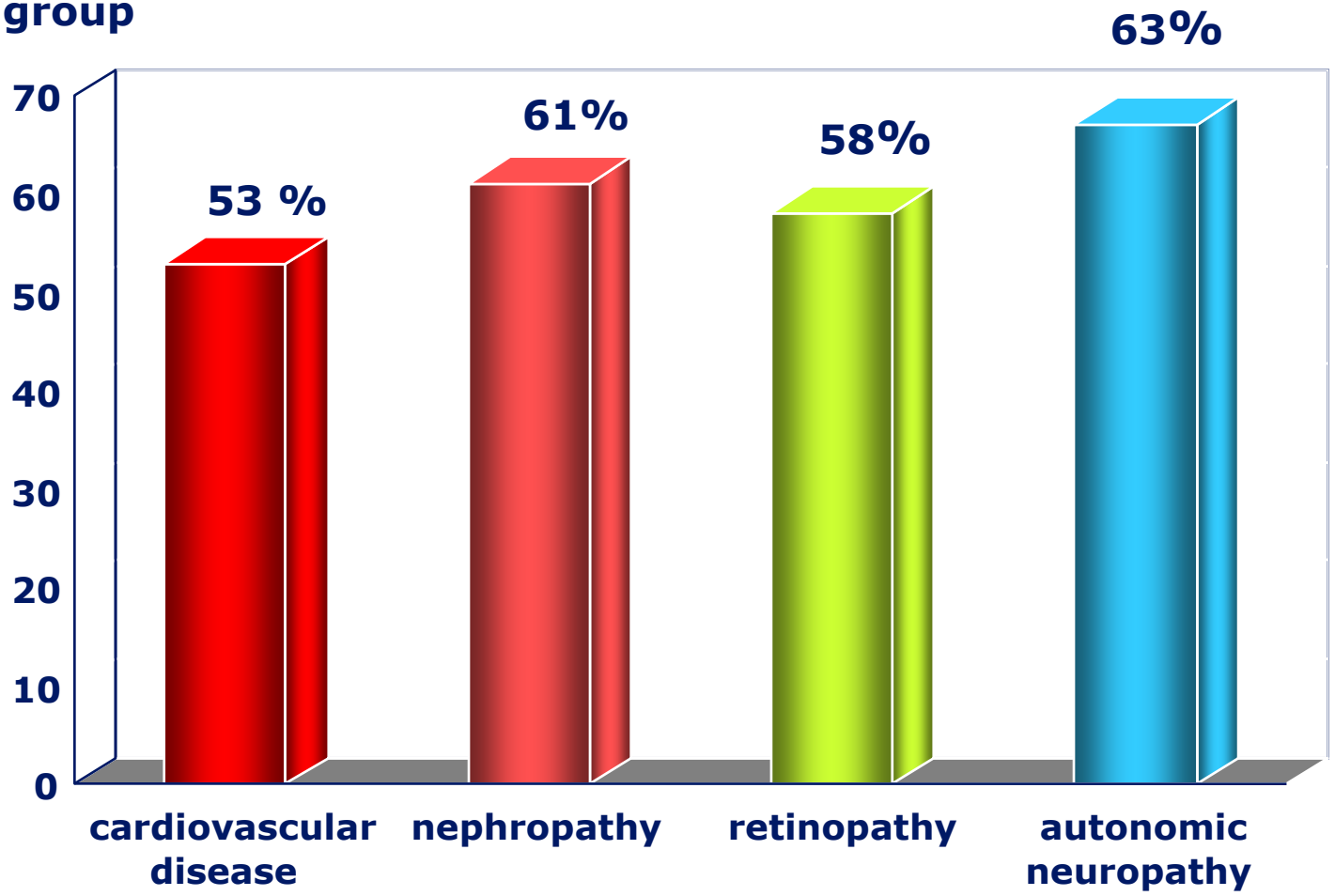
Secondary: Microvascular disease

Progression to nephropathy
Development of/progression in retinopathy
Development of/progression in neuropathy

Steno

Steno-2: Relative risk reduction at 8 years

Relative risk reduction in intensive therapy group

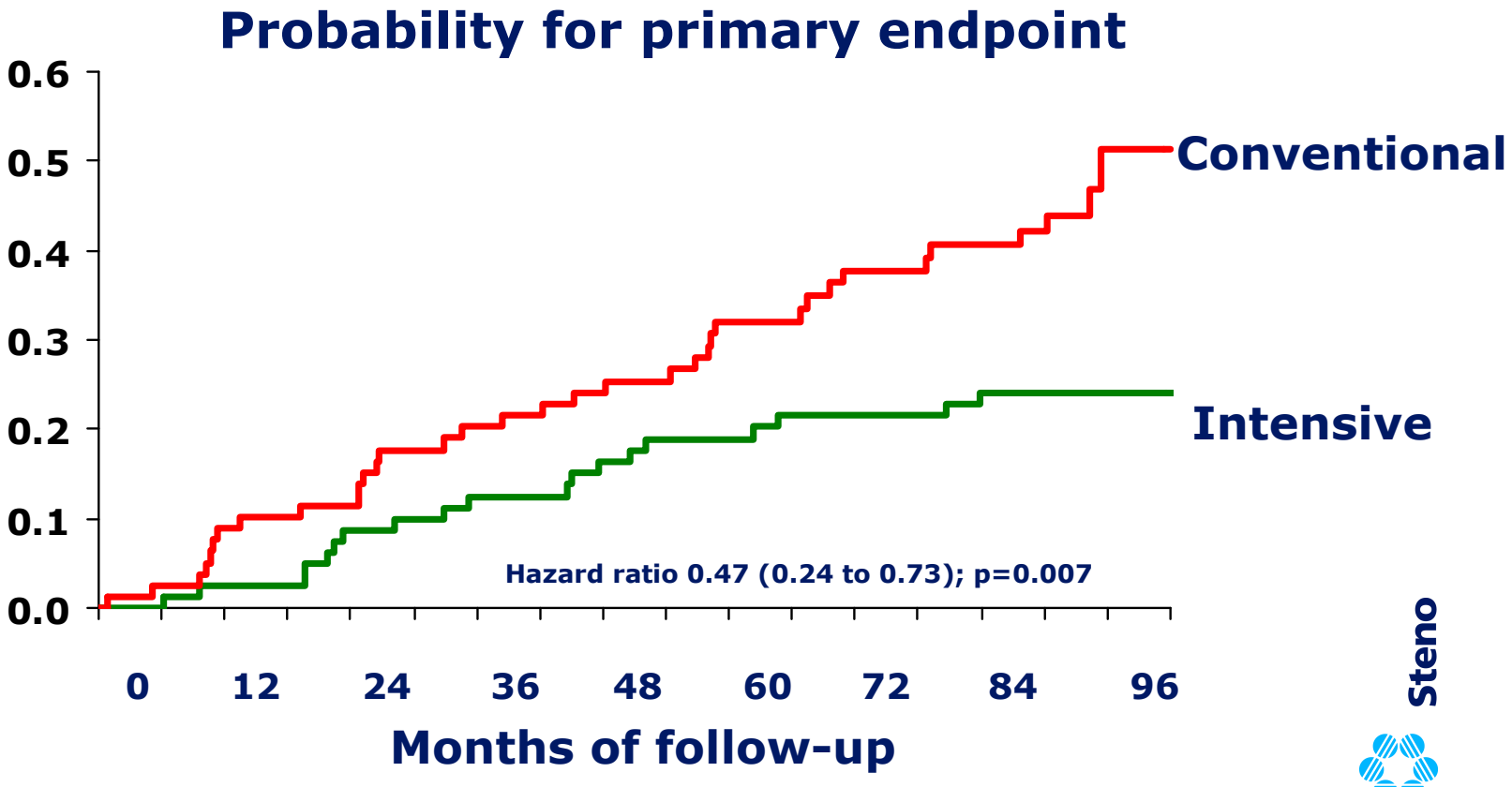


Steno

N Engl J Med 348:383-93, 2003

Primary Composite Cardiovascular Endpoint

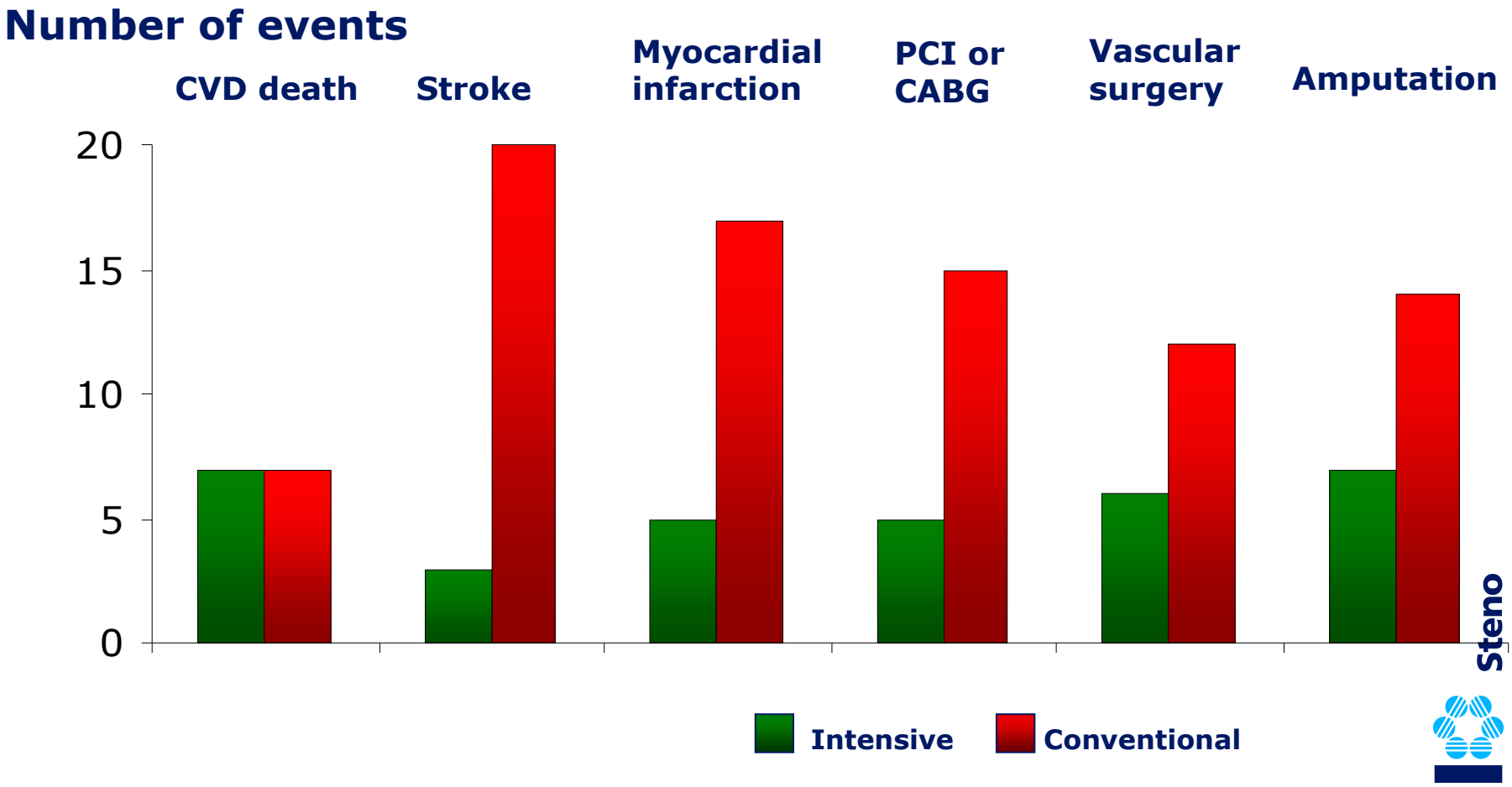
85 CVD events in 35 'conventional' patients (44%)
33 CVD events in 19 'intensive' patients (24%)



Steno

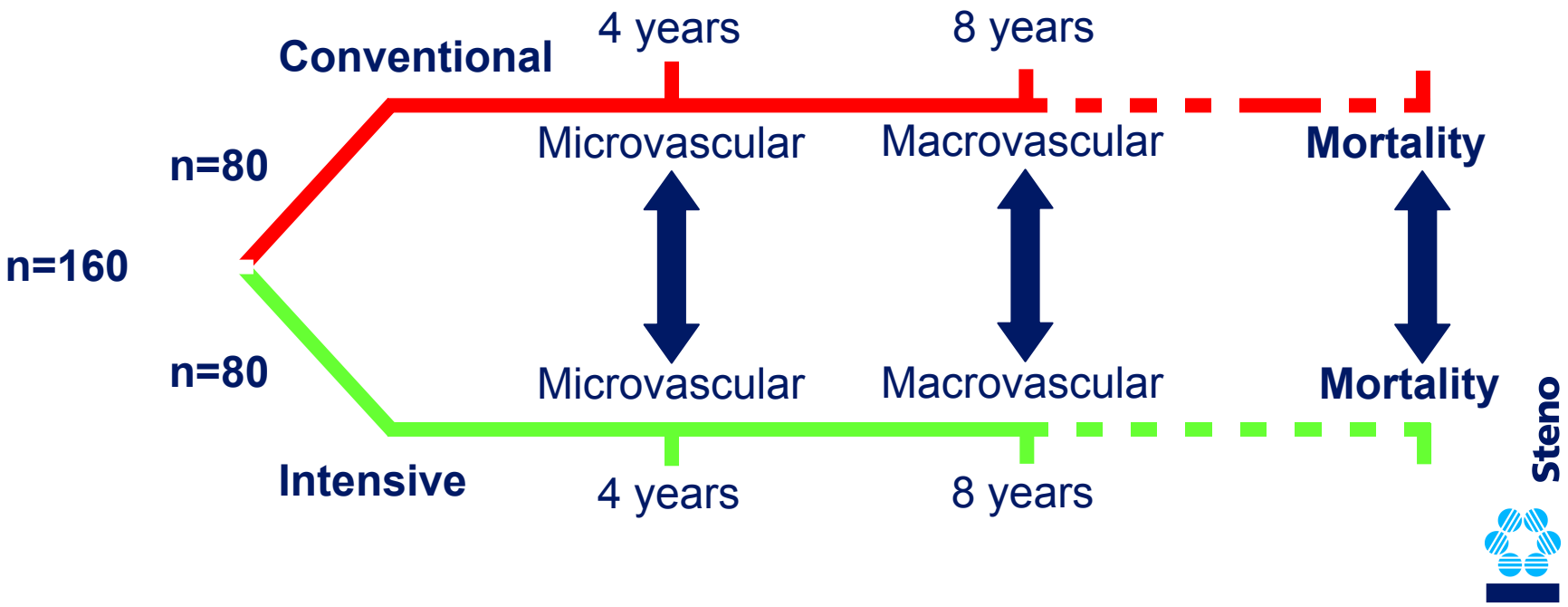
Steno-2: CVD

85 CVD events in 35 'conventional' patients
33 CVD events in 19 'intensive' patients

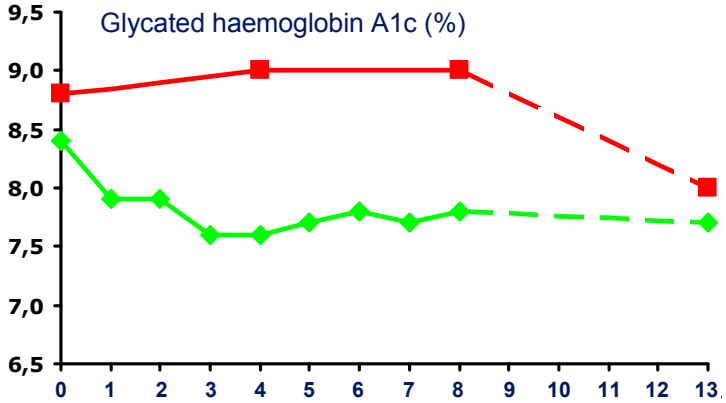


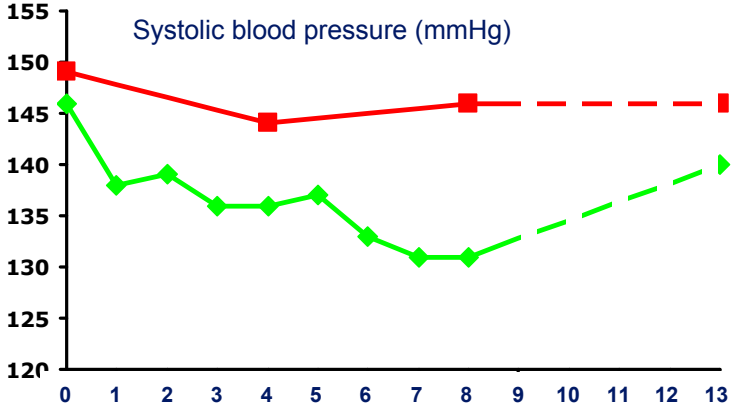
Steno-2: Design

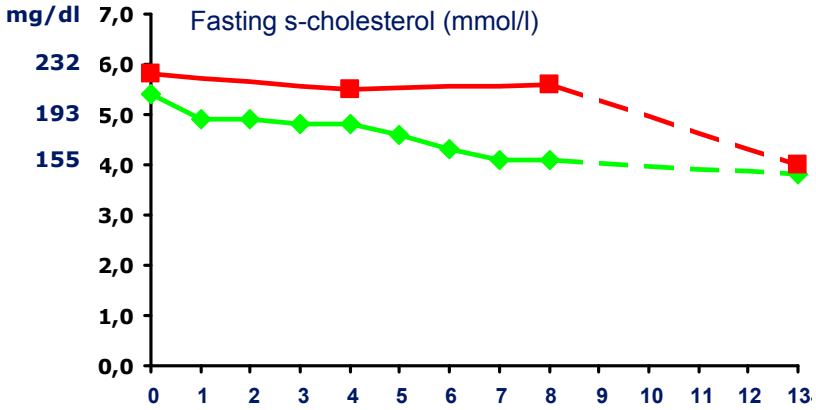
- **Pre-planned endpoint examinations at 4, 8 years after randomization and after 60 cases of mortality**
- **Interventional part of study ended after 8 years**

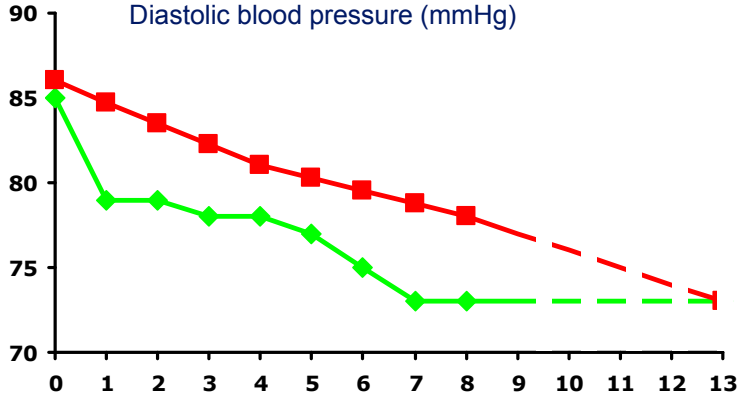


Risk markers during follow-up









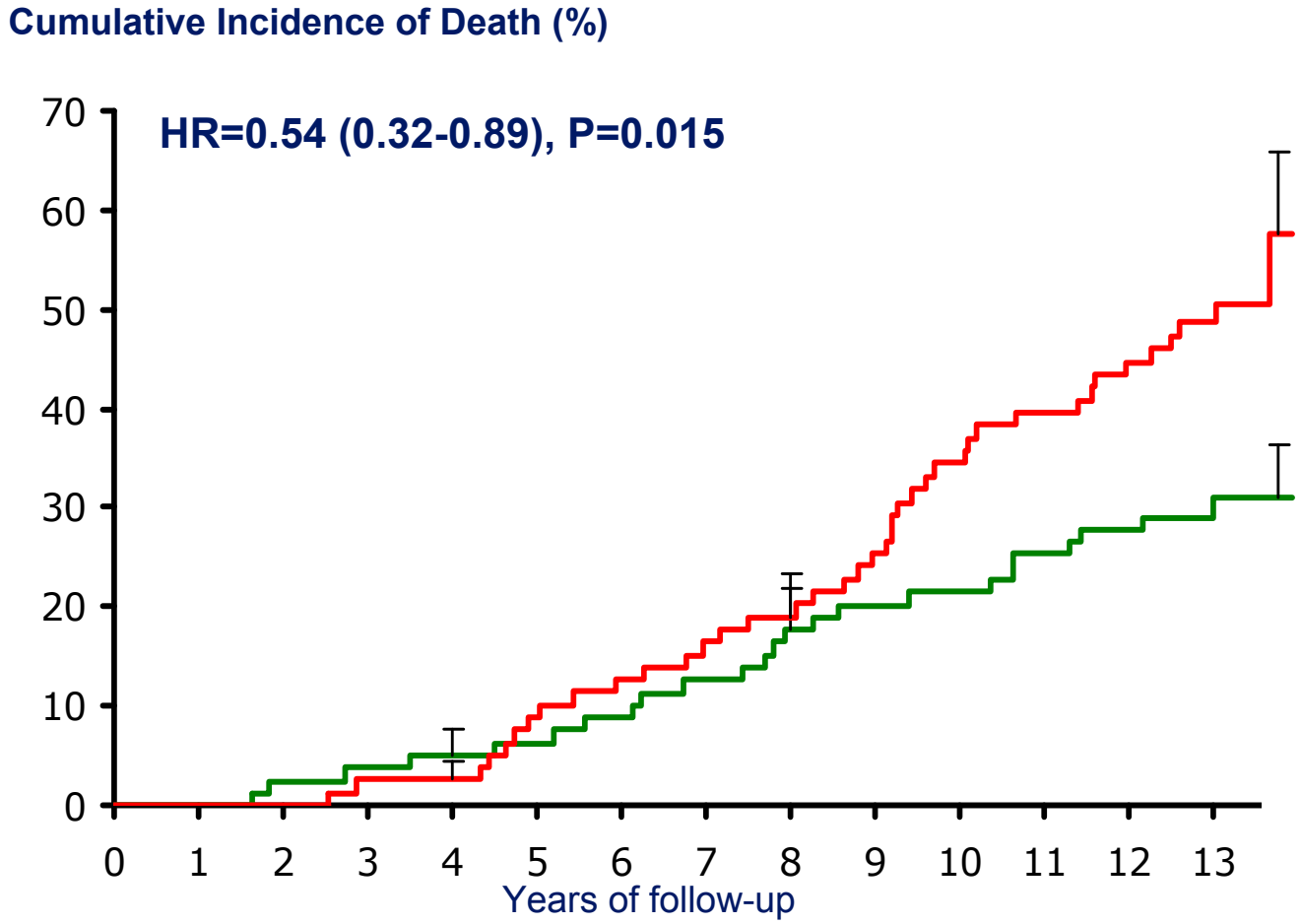
Steno

Risk markers at end of Steno-2 Post Trial at 13 years

	Intensive N=55	Standard N=38
HbA_{1c} (%)	7.7	8.0
Cholesterol (mmol/l)	3.8	4.0
LDL-cholesterol (mmol/l)	1.8	2.0
HDL-cholesterol (mmol/l)	1.32	1.22
Triglycerides (mmol/l)	1.12	1.67
Systolic BP (mmHg)	140	146
Diastolic BT (mmHg)	74	73
Albumin excretion rate (mg/24h)*	69	75

*median

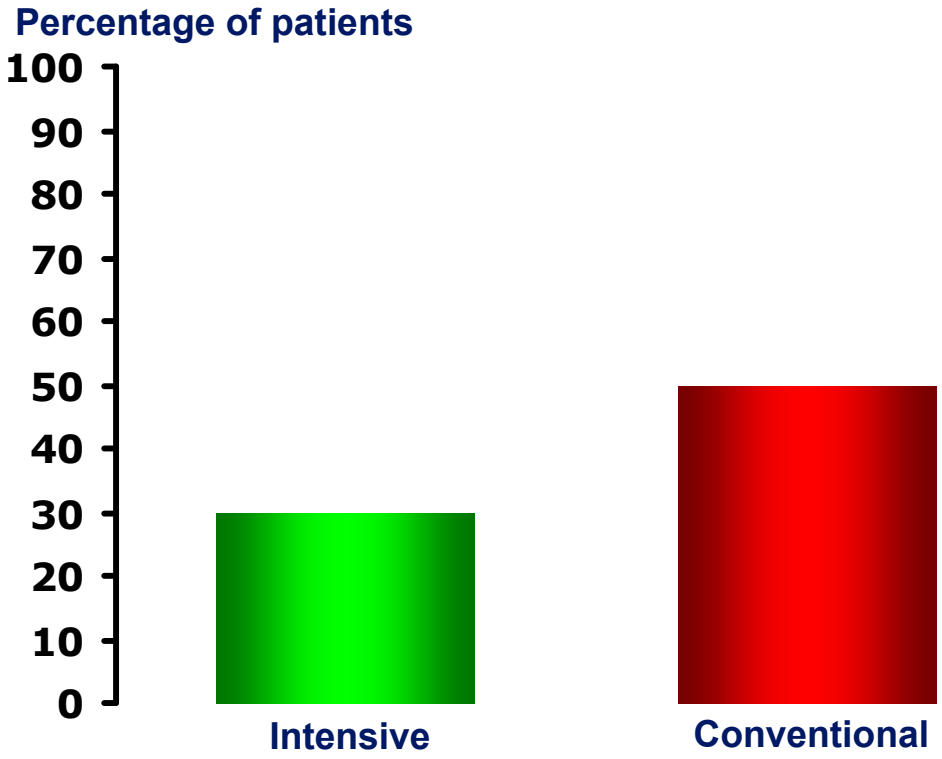
Steno-2 Post Trial: Mortality



Numbers at risk								
Conventional	80	80	77	69	63	51	43	30
Intensive	80	78	75	72	65	62	57	39

Steno

Steno-2 Post Trial: Mortality



30% of patients (n=24) died in the intensive group compared to 50% of patients (n=40) in the conventional group

Absolute risk reduction = 20%

Steno

Steno-2: Major clinical results

- A 50 % relative risk reduction in microvascular disease after 4 years of intervention maintained throughout the rest of follow-up
- A 50 % relative risk reduction in major cardiovascular events after 8 years of intervention maintained throughout the rest of follow-up
- A 50 % relative reduction in mortality after 13 years of follow-up

Steno

Steno-2: Number Needed to Treat for 13 Years to Prevent One ---

Death	5 patients
Cardiovascular death	8 patients
Major cardiovascular event	3 patients
Progression of nephropathy	5 patients
Dialysis	16 patients
Laser treatment	7 patients

Steno

Dagens situation

- Alle med type 2 diabetes skal have statin
- Alle med type 2 diabetes skal ha farmakologisk behandling
- Alle skal holde op med at ryge
- Lavere blodtryk
- Mange skal have magnyl
- Hurtigere til undersøgelse for CVD

Steno

Curr Rheumatol Rep (2012) 14:455–462
DOI 10.1007/s11926-012-0271-5

RHEUMATOID ARTHRITIS (LW MORELAND, SECTION EDITOR)

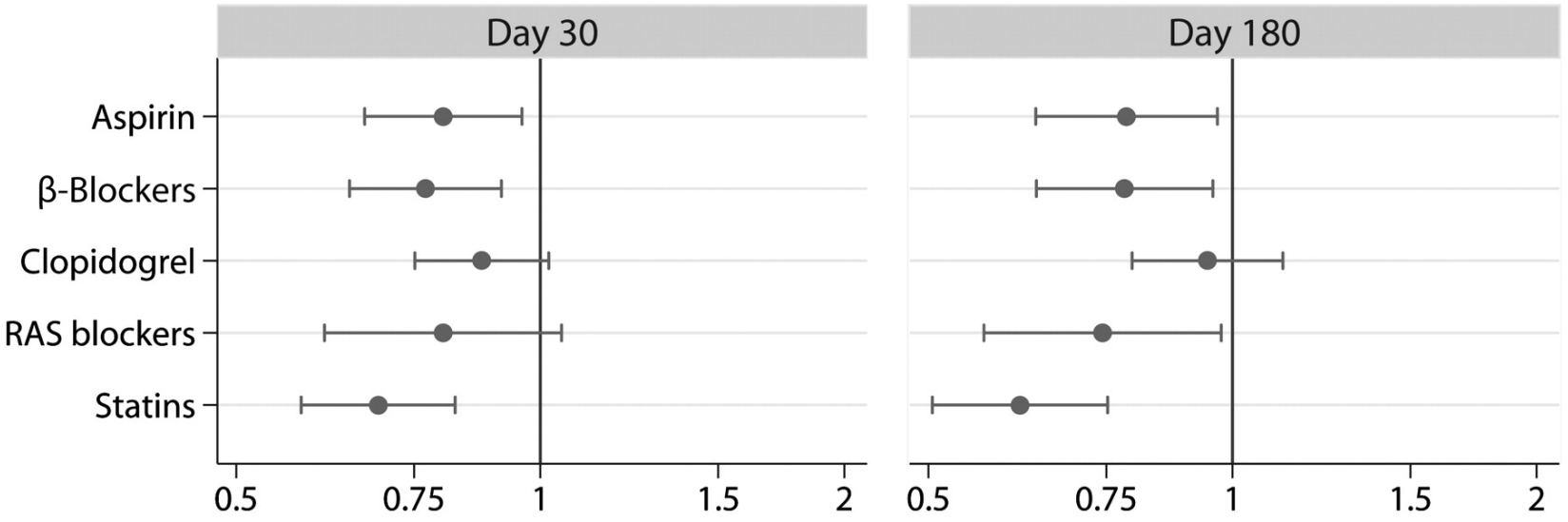
Cardiovascular Disease and Rheumatoid Arthritis: An Update

Christina Charles-Schoeman

Steno

Recommendations	Level of evidence	Strength of recommendation
1. RA should be regarded as a condition associated with higher risk for CV disease. This may also apply to AS and PsA, although the evidence base is less. The increased risk appears to be due to both an increased prevalence of traditional risk factors and the inflammatory burden	2b–3	B
1. Adequate control of disease activity is necessary to lower the CV risk	2b–3	B
1. CV risk assessment using national guidelines is recommended for all patients with RA and should be considered annually for all patients with AS and PsA. Risk assessments should be repeated when antirheumatic treatment has been changed	3–4	C
1. Risk score models should be adapted for patients with RA by introducing a 1.5 multiplication factor. This multiplication factor should be used when the patient with RA meets two of the following three criteria:	3–4	C
1. Disease duration of more than 10 years		
1. RF or anti-CCP positivity		
1. Presence of certain extra-articular manifestations		
1. TC/HDL cholesterol ratio should be used when the SCORE model is used	3	C
1. Intervention should be carried out according to national guidelines	3	C
1. Statins, ACE inhibitors and/or AT-II blockers are preferred treatment options	2a–3	C-D
1. The role of coxibs and most NSAIDs in CV risk is not well established and needs further investigation. Hence, we should be very cautious about prescribing them, especially for patients with a documented CV disease or in the presence of CV risk factors	2a–3	C
1. Corticosteroids: use the lowest dose possible	3	C
1. Recommend smoking cessation	3	C

Adjusted OR for treatment initiation with secondary prevention drugs after myocardial infarction on days 30 and 180 after discharge associated with rheumatoid arthritis (RA).



Lindhardsen J et al. Ann Rheum Dis 2012;71:1496-1501

RA is

a cardiovascular equivalent

and

should be treated aggressively!

Steno