Drugs for the prevention of diabetes – are there benefits bejond retarding the onset of diabetes

Prague, 06 May 2010

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Diabetes Research Institute,
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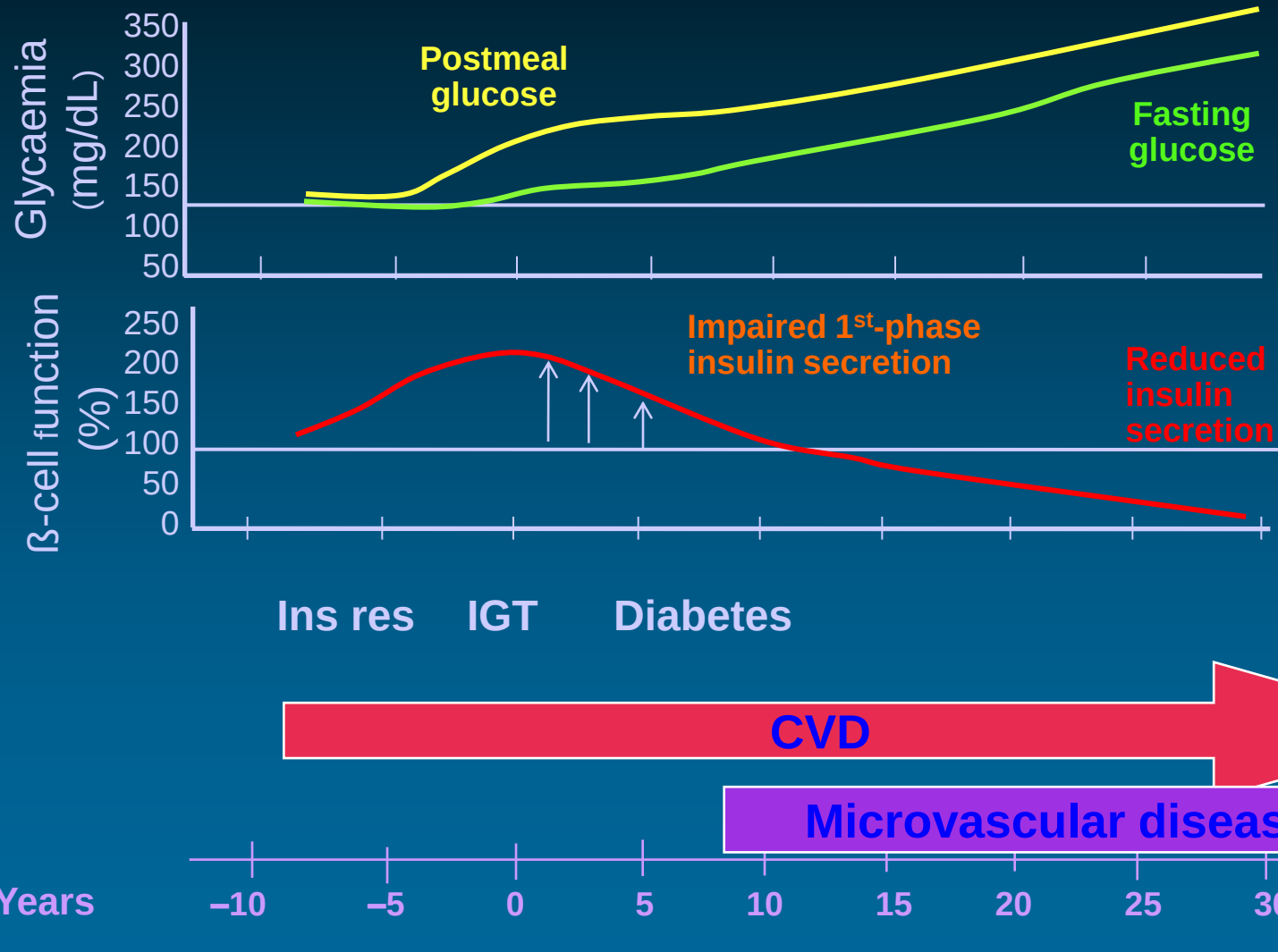
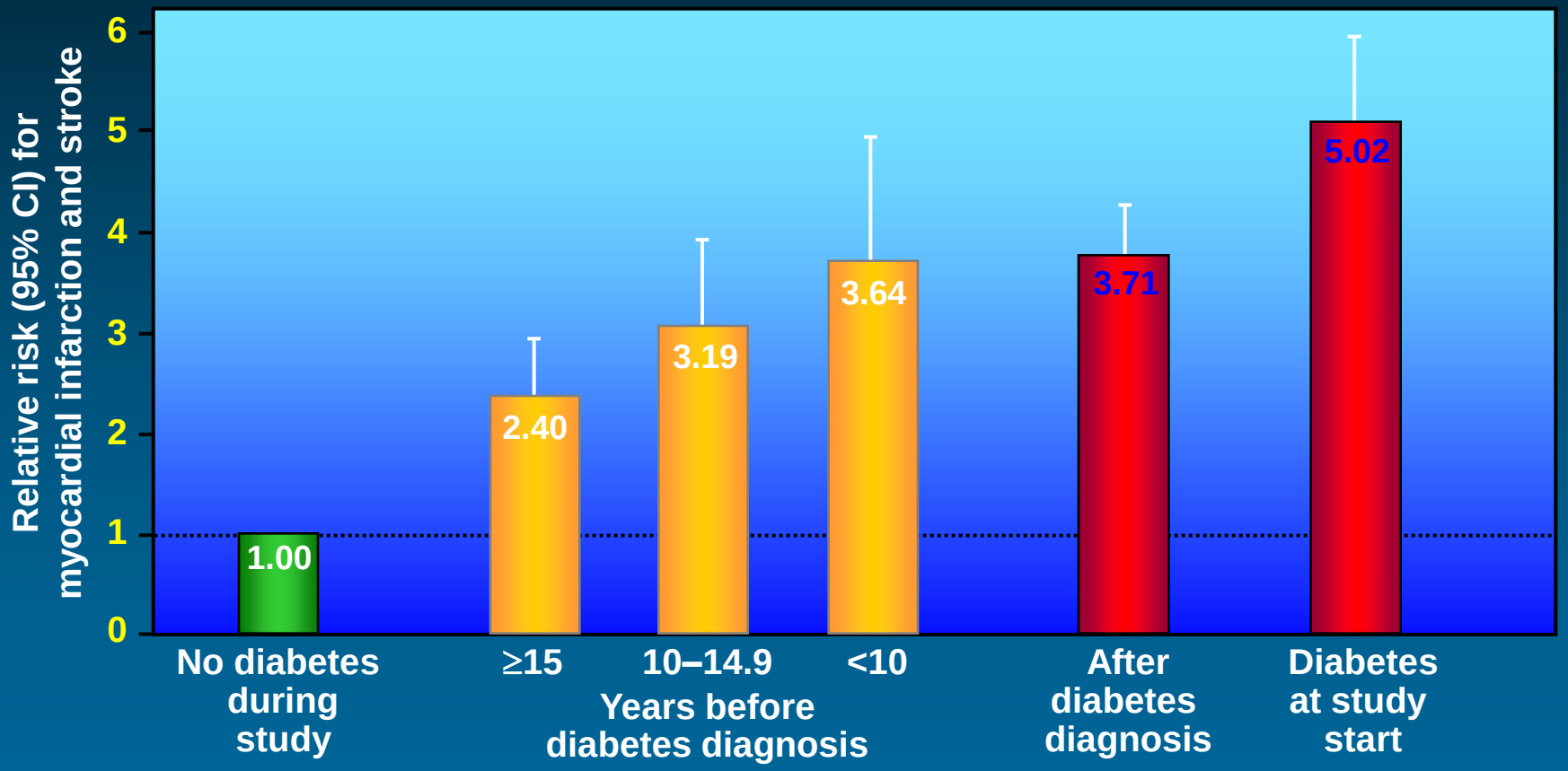
Diabetes and cardiovascular risk

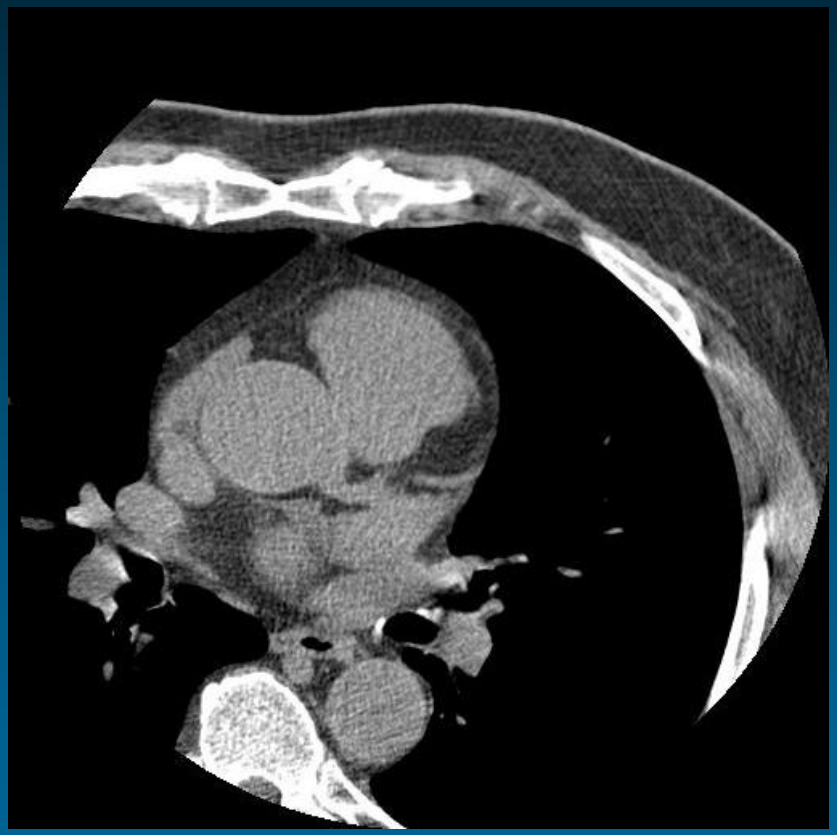


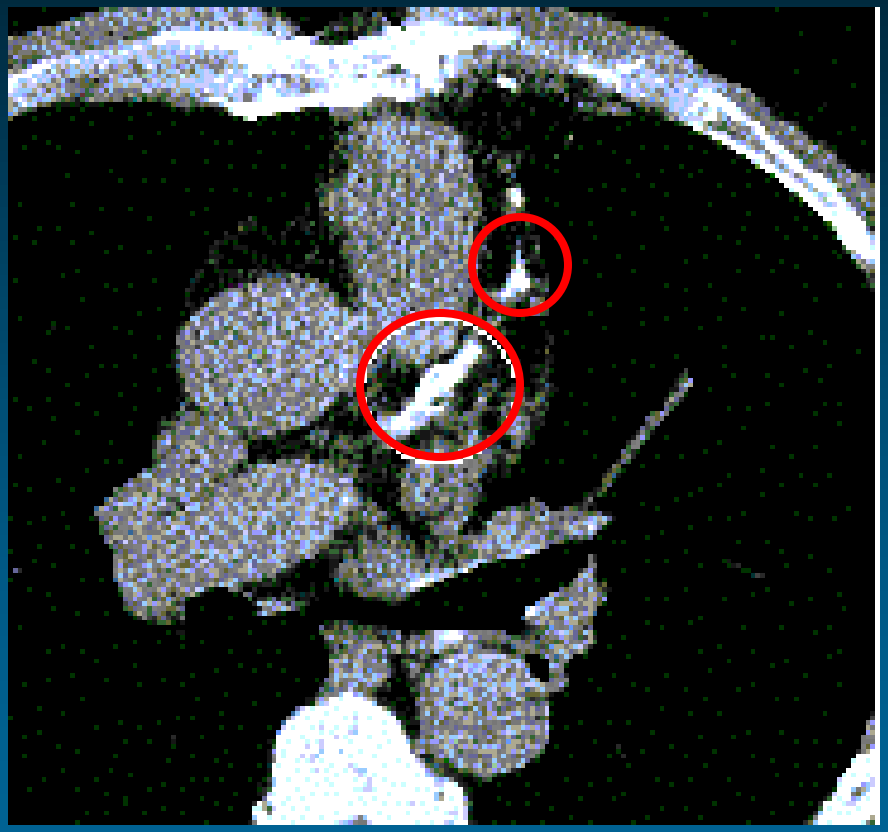
Nurses' Health Study – Risk for myocardial infarction as a function of diabetes development



Hu FB, et al. Diabetes Care 2002;25:1129–34

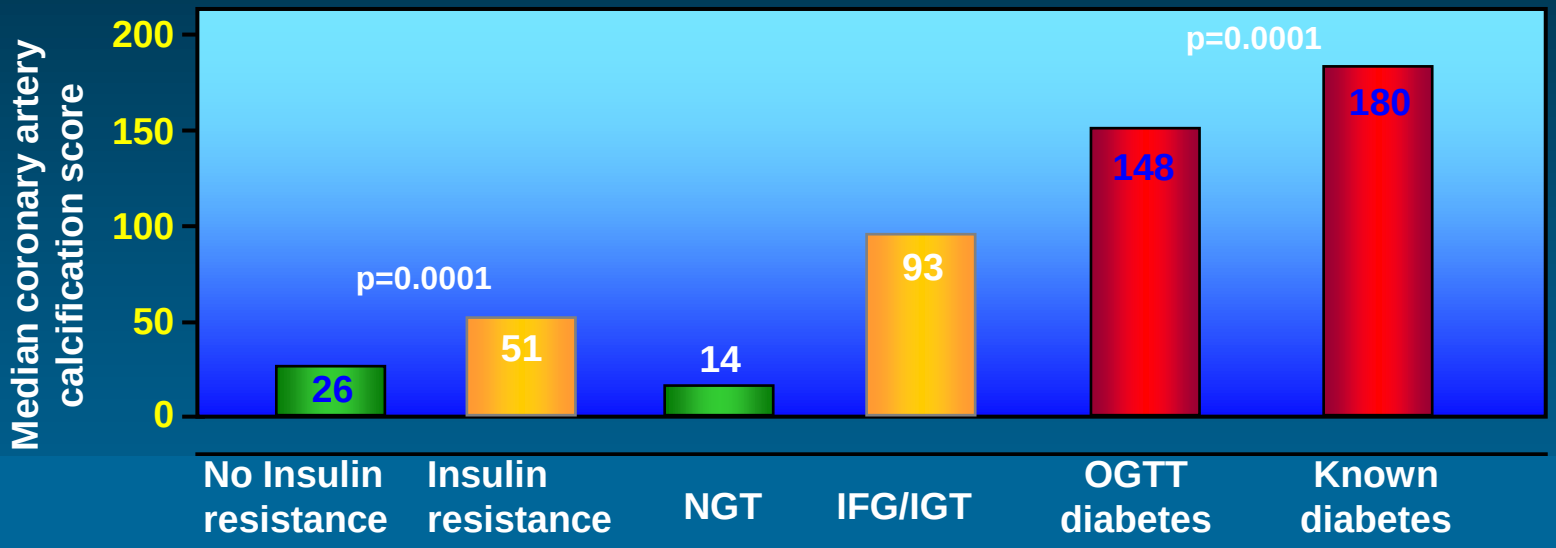
Coronary calcifications in diabetes





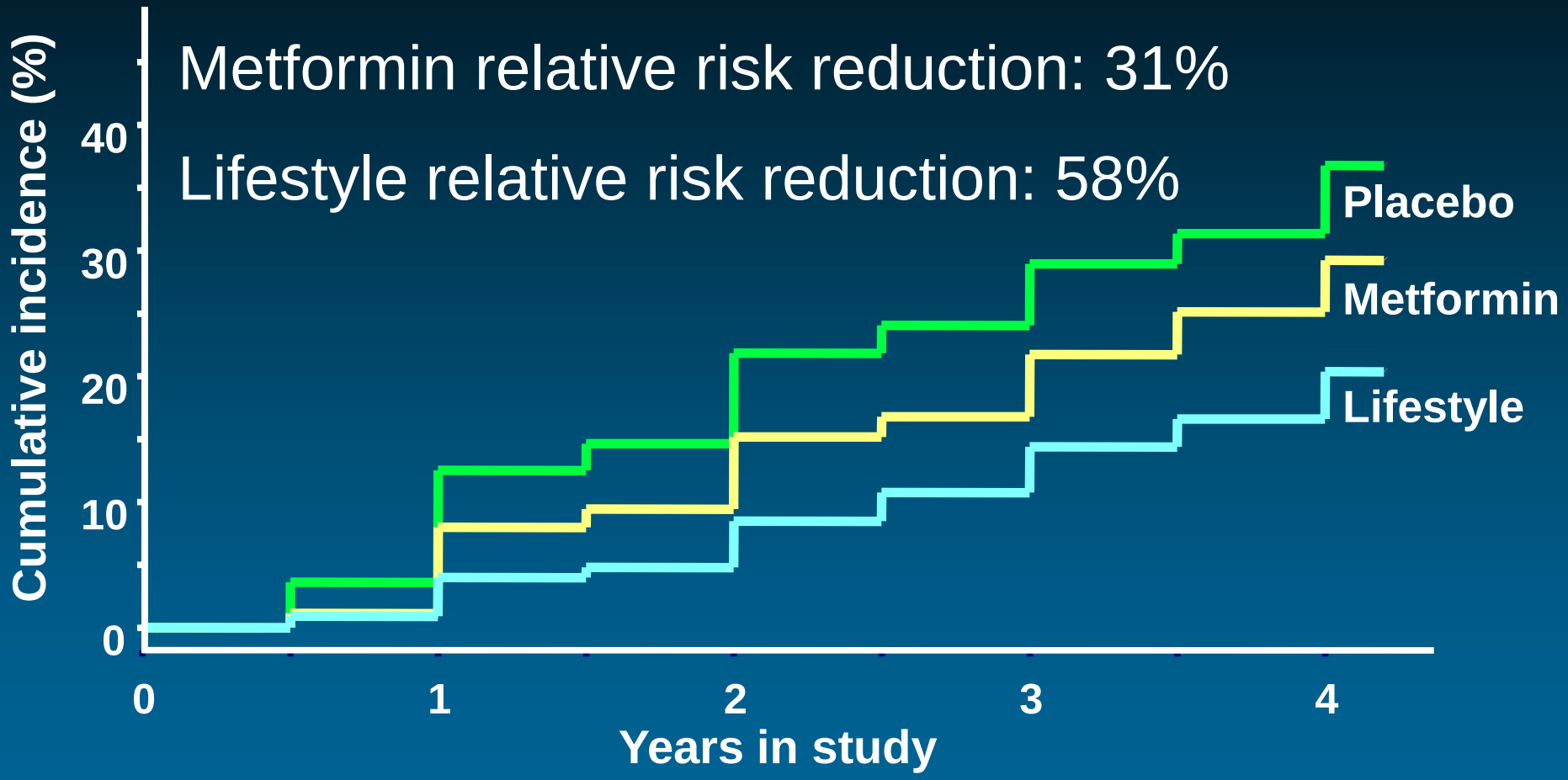
Schnell O et al, Exp Clin Endocrinol Diabetes (2004); 27:324-332

Framingham Offspring Study – Insulin resistance and coronary artery calcification



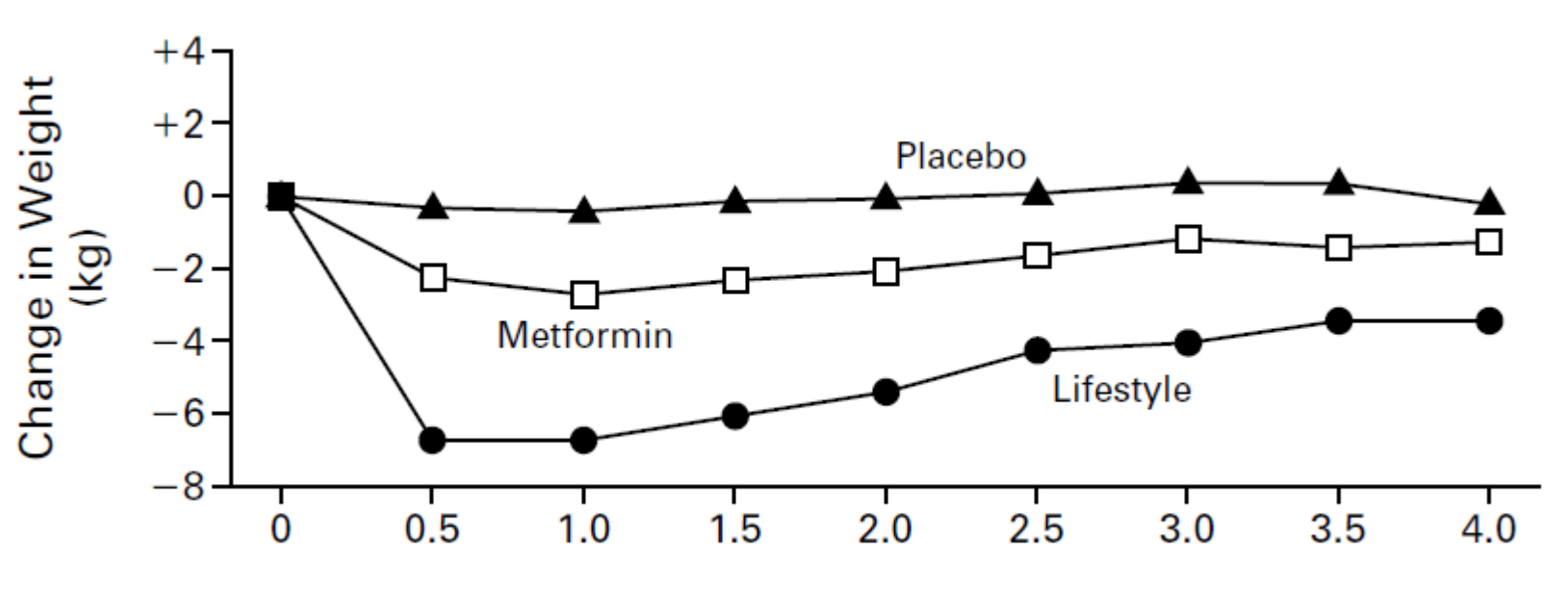
Meigs JB. Diabetes Care 2002;25:1313–19.

Diabetes Prevention Programme (DPP)



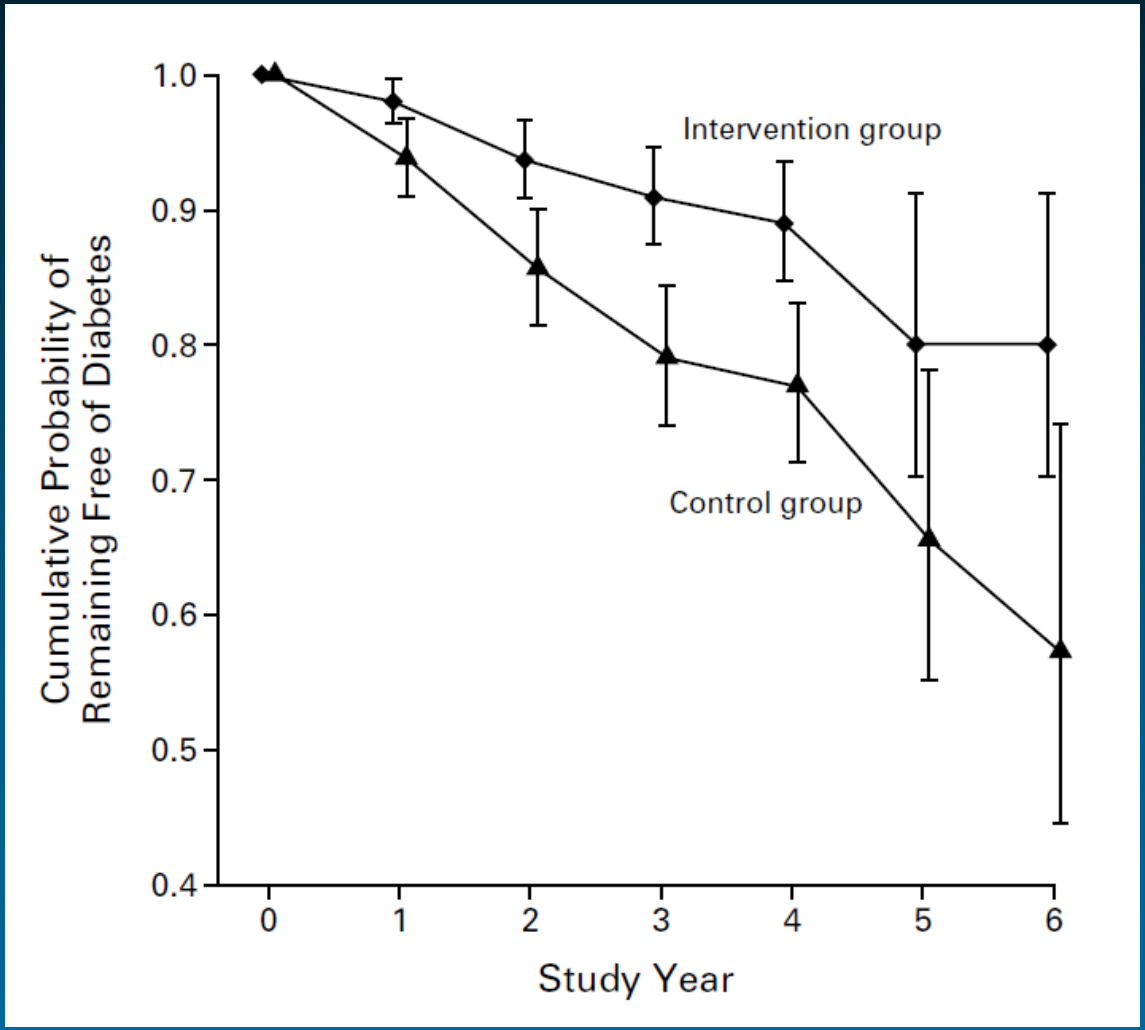
New Engl J Med 2002; ***346****: 393-346*

Diabetes Prevention Programme (DPP)
Change in weight



New Engl J Med 2002; ***346****: 393-346*

The Finnish Diabetes Prevention Study
Development of diabetes



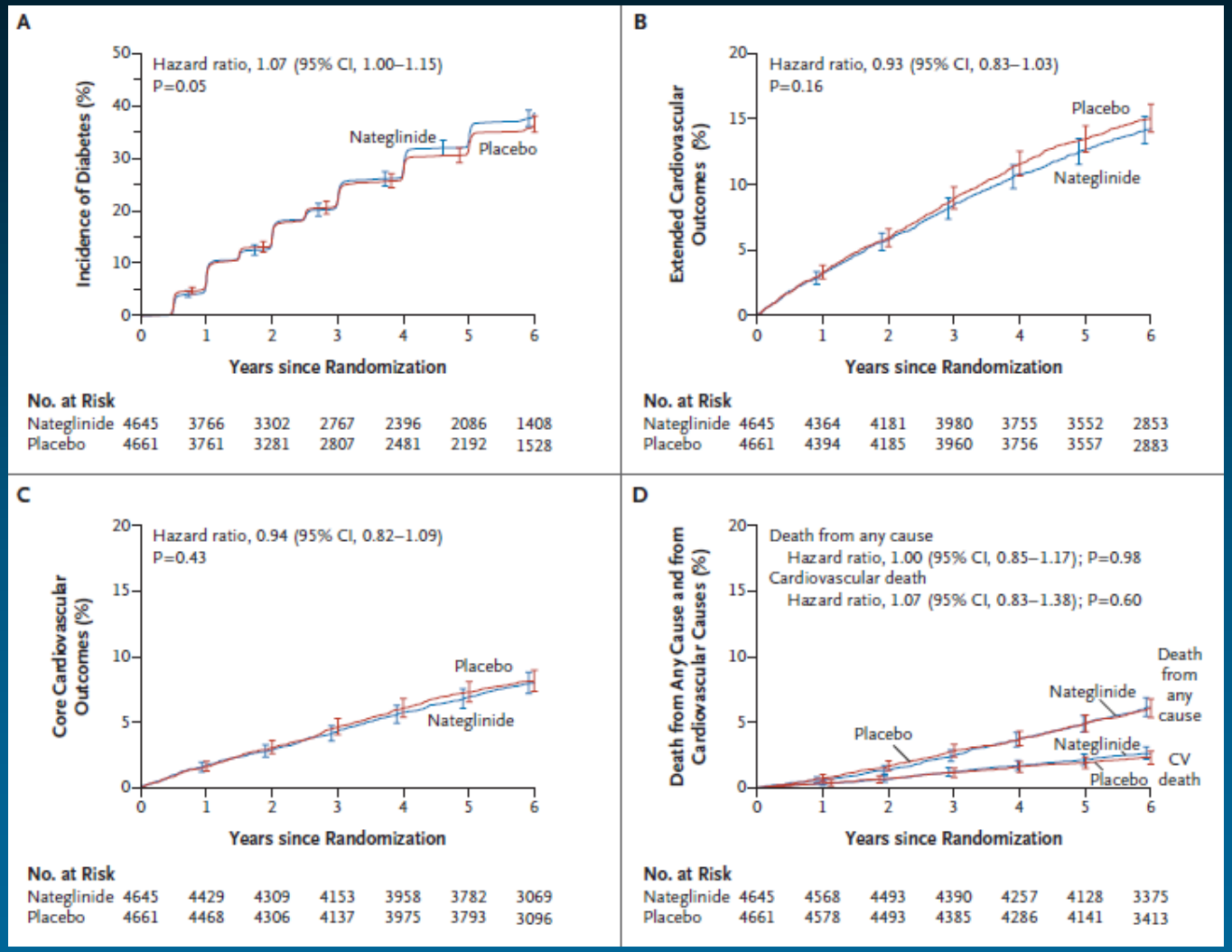
Tuomilehto J et al, New Engl J Med 2001; 344: 1343-1350

The Finnish Diabetes Prevention Study
Clinical and metabolic variables

Variable	Intervention Group (N=256)		Control Group (N=250)		P Value†
	mean ±SD	95% CI	mean ±SD	95% CI	
Change in weight					
In kilograms	−4.2±5.1	−4.8 to −3.6	−0.8±3.7	−1.3 to −0.3	<0.001
Percent change	−4.7±5.4	−5.0 to −4.4	−0.9±4.2	−1.0 to −0.8	<0.001
Change in waist circumference (cm)	−4.4±5.2	−5.1 to −3.9	−1.3±4.8	−1.9 to −0.7	<0.001
Change in plasma glucose (mg/dl)					
Fasting	−4±12	−6 to −2	1±12	0 to 2	<0.001
2 Hr after oral glucose challenge	−15±34	−19 to −11	−5±40	−8 to −2	0.003
Change in serum insulin (μg/ml)					
Fasting	−2±9	−3 to −1	−1±7	−2 to 0	0.14
2 Hr after oral glucose challenge	−29±64	−37 to −21	−11±51	−18 to −4	0.001
Change in serum lipids (mg/dl)‡					
Total cholesterol	−5±28	−8 to −2	−4±28	−7 to −1	0.62
High-density lipoprotein cholesterol	2±7	1 to 3	1±6	0 to 2	0.06
Triglycerides	−18±51	−24 to −12	−1±60	−8 to 6	0.001
Change in blood pressure (mm Hg)§					
Systolic	−5±14	−7 to −3	−1±15	−3 to 1	0.007
Diastolic	−5±9	−6 to −4	−3±9	−4 to −2	0.02

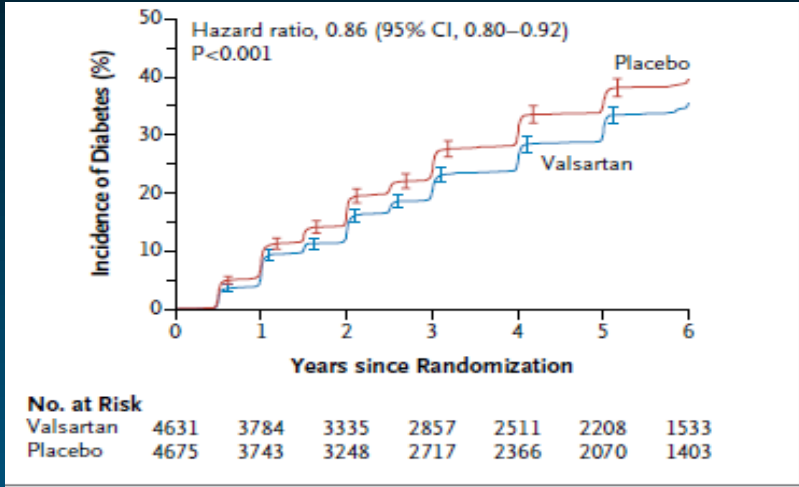
Tuomilehto J et al, New Engl J Med 2001; 344: 1343-1350

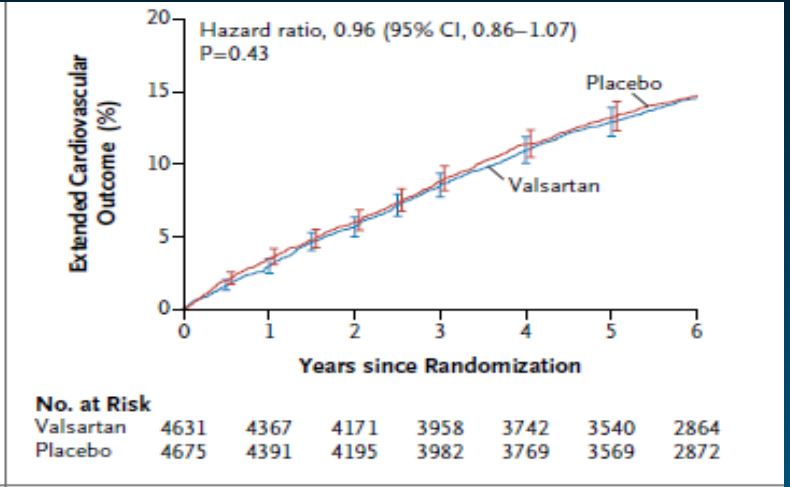
NAVIGATOR: No reduction of incident DM and cardiovascular outcomes with nateglinide

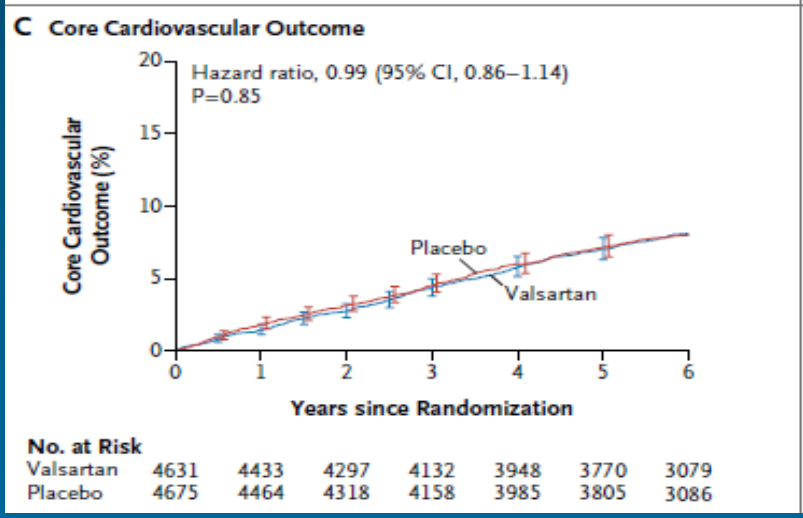


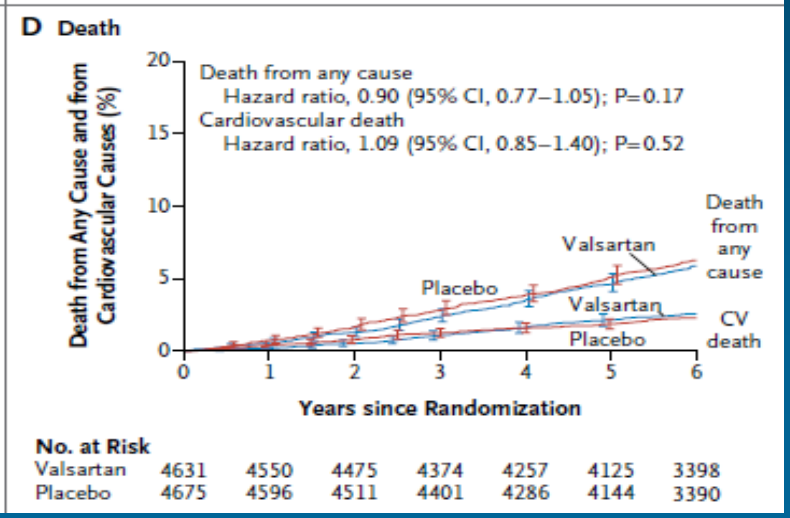
The Navigator Study Group; NEJM 2010, published online on March 14

NAVIGATOR: Reduction of incident DM, but no effect on cardiovascular outcomes and death on valsartan



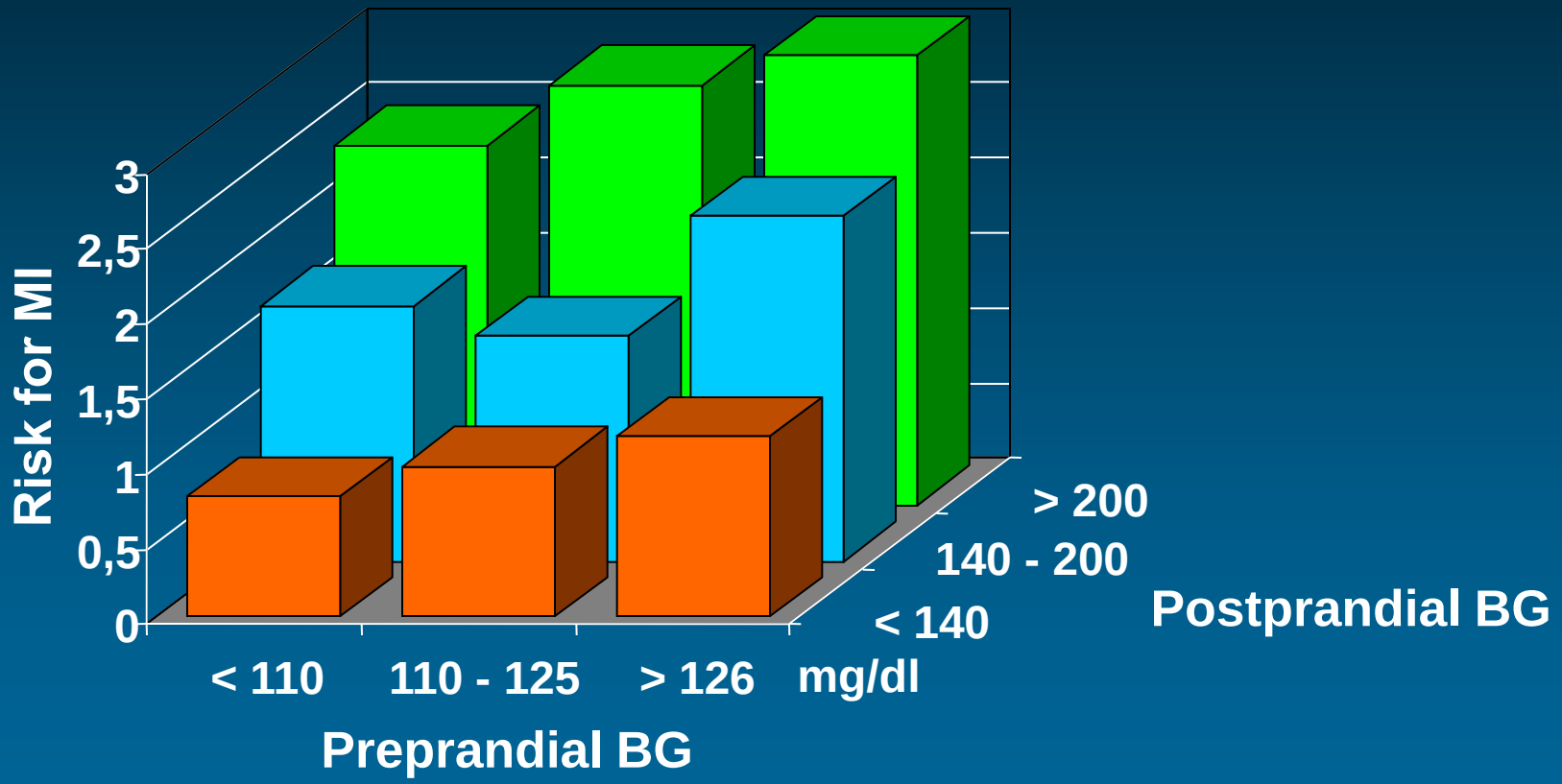






The Navigator Study Group; NEJM 2010, published online on March 14

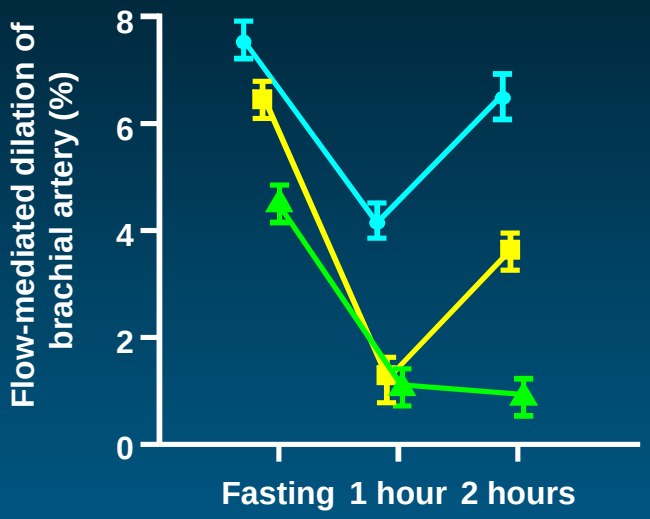
Postprandial glucose and CV risk - DECODE-Study

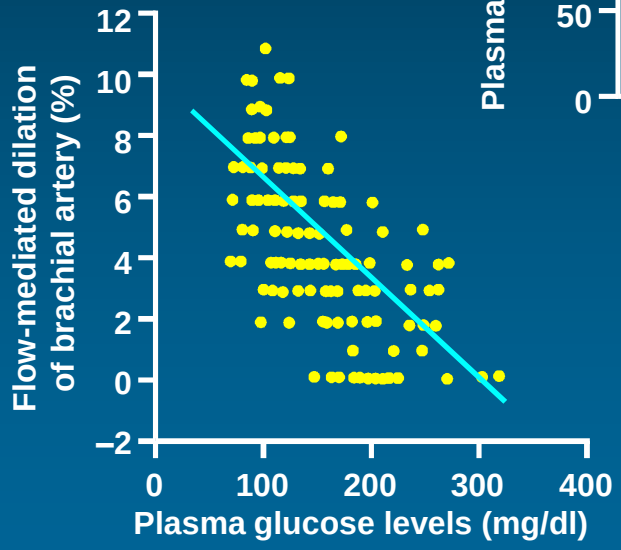


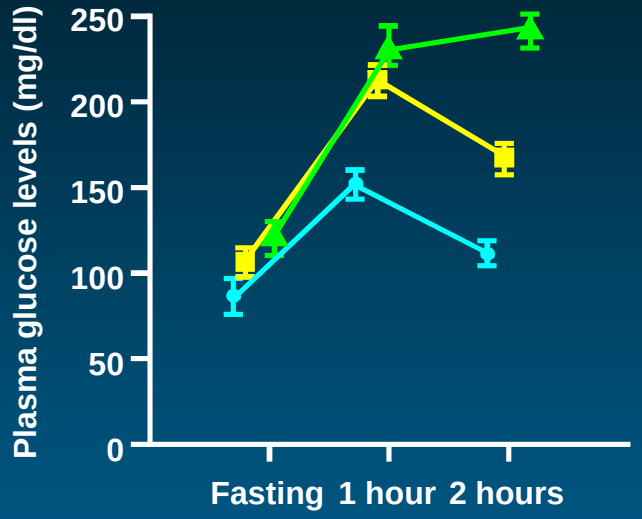
Tuomilehto.J., Lancet 1999, 354:617

The DECODE Study Group, Diabetologia 42:647-654

Endothelial dysfunction and hyperglycemia







NGT = normal glucose tolerance; IGT = impaired glucose tolerance; DM = diabetes mellitus

Kawano H et al. J Am Coll Cardiol 1999

STOP-NIDDM: Effect of acarbose on glucose tolerance in individuals with IGT

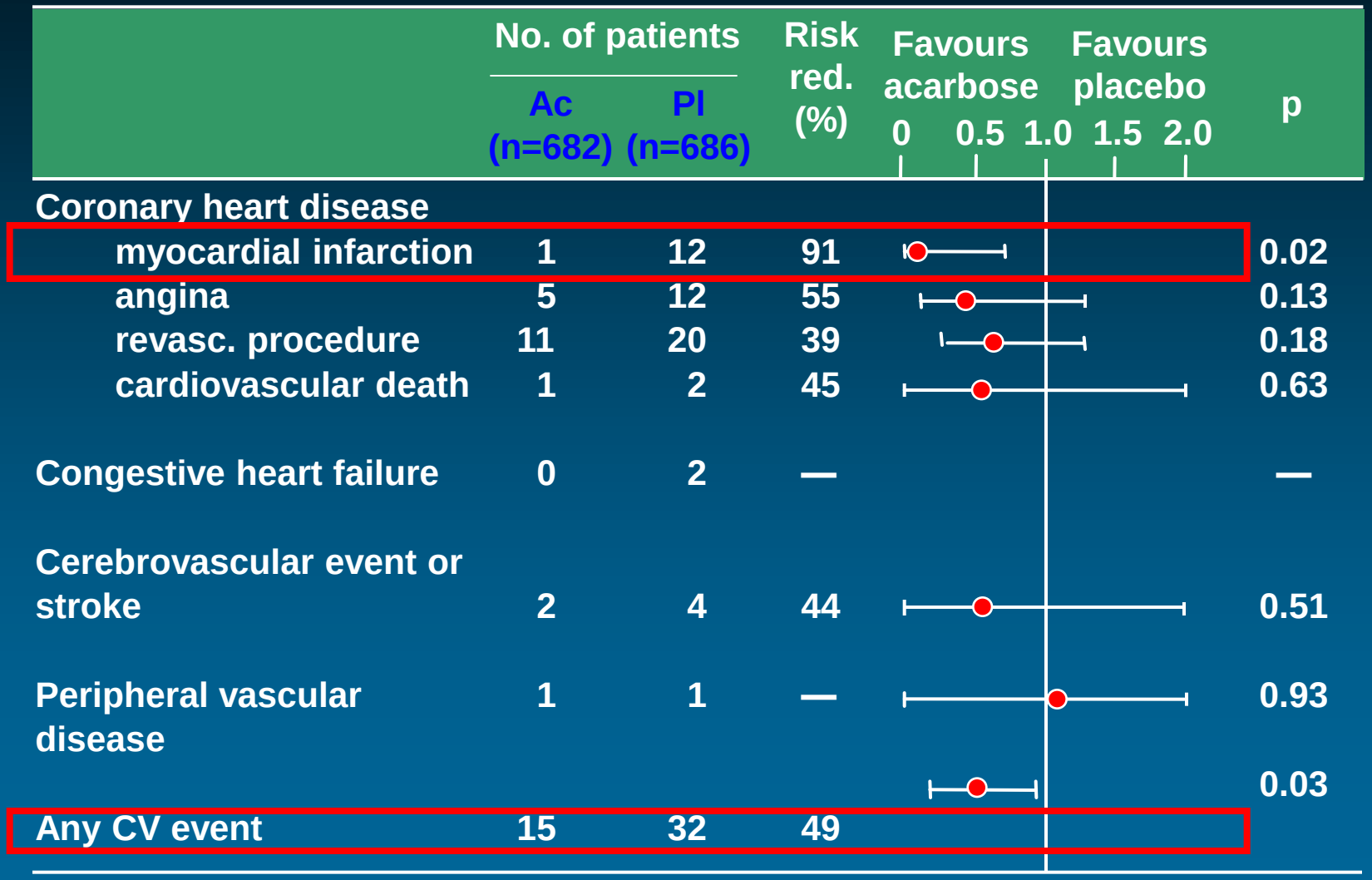
Glucose tolerance at end of treatment (%)

	NGT	IGT	Diabetes
Acarbose (n=682)	35.3*	28.4	32.4*
Placebo (n=686)	30.9	24.9	41.5

*p<0.001

Chiasson JL et al. Lancet (2002); 359: 2072-77

Time to develop first CV event



Chiasson JL et al. JAMA 2003;290:486–94

STOP-NIDDM: Effect of acarbose on myocardial infarction

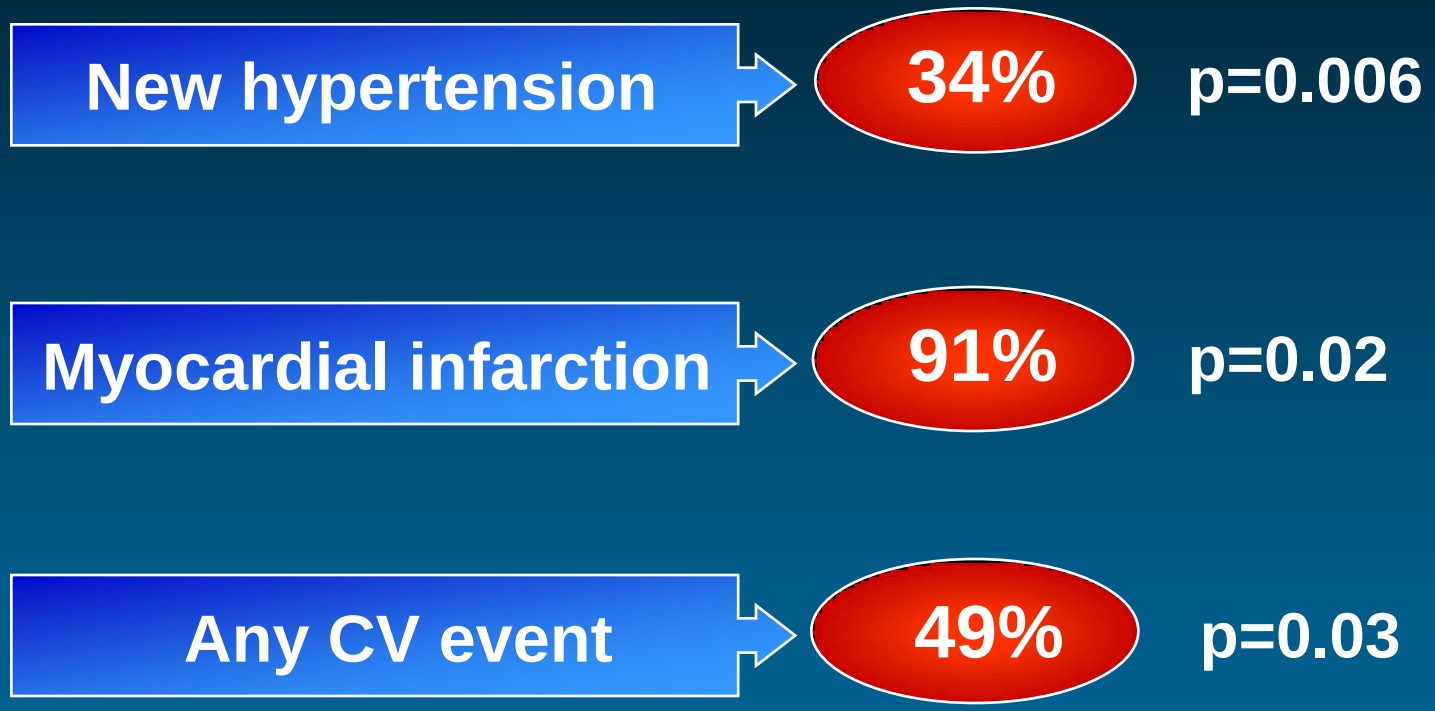
	Acarbose (n=682)	Placebo (n=686)	p
No. of clinical MIs	1	12	0.02*
No. of silent MIs	1	7	
Total	2	19	0.001**

Acarbose treatment resulted in a statistically significant reduction in incidence of MI

***Cox proportional hazards analysis**
****Fisher exact test**

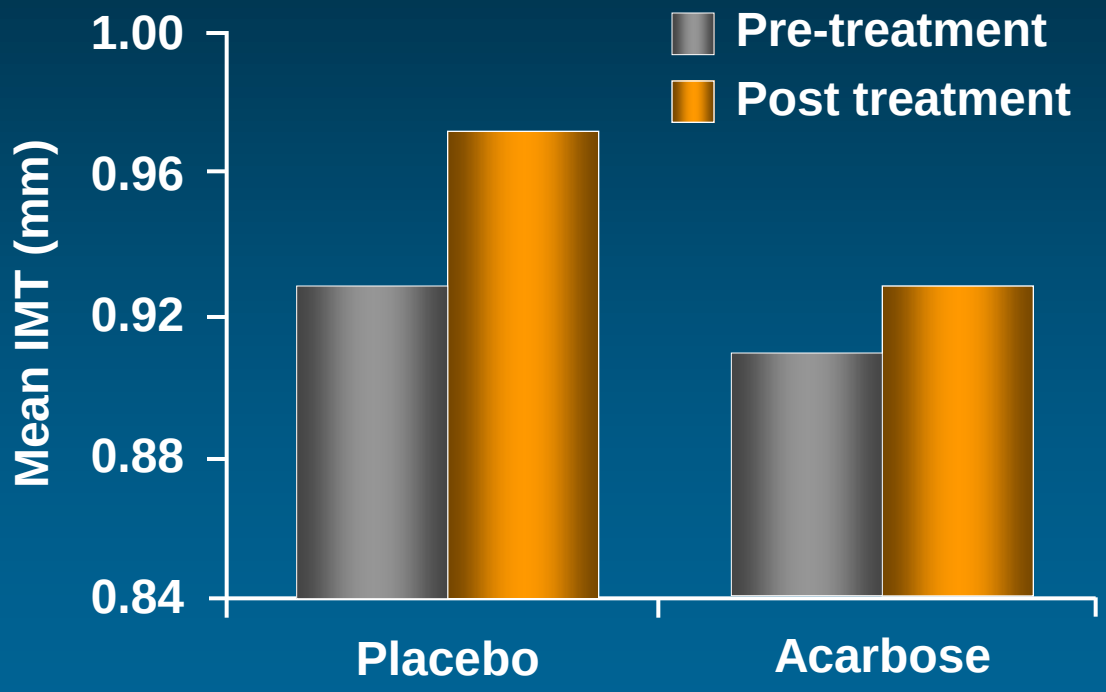
Chiasson JL et al. JAMA 2003;290:486–94

STOP-NIDDM: Risk reduction with acarbose



Chiasson JL et al. JAMA 2003;290:486–94

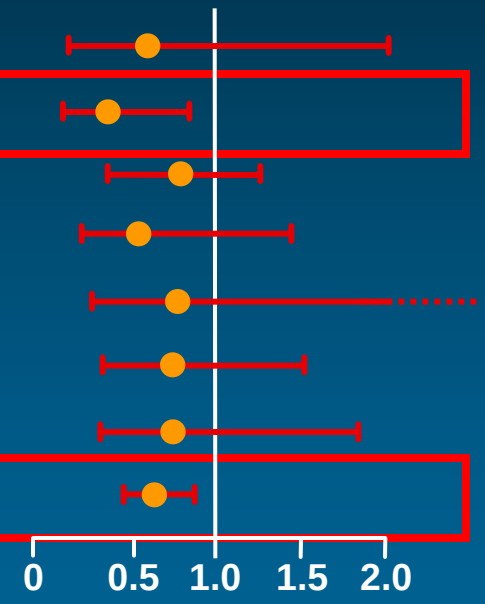
Acarbose slows progression of intima-media thickness of carotid arteries in subjects with IGT (3.9 yr follow-up)



Hanefeld M, et al. Stroke 2004;35:1073–78

Effect of acarbose on developing cardiovascular events during treatment

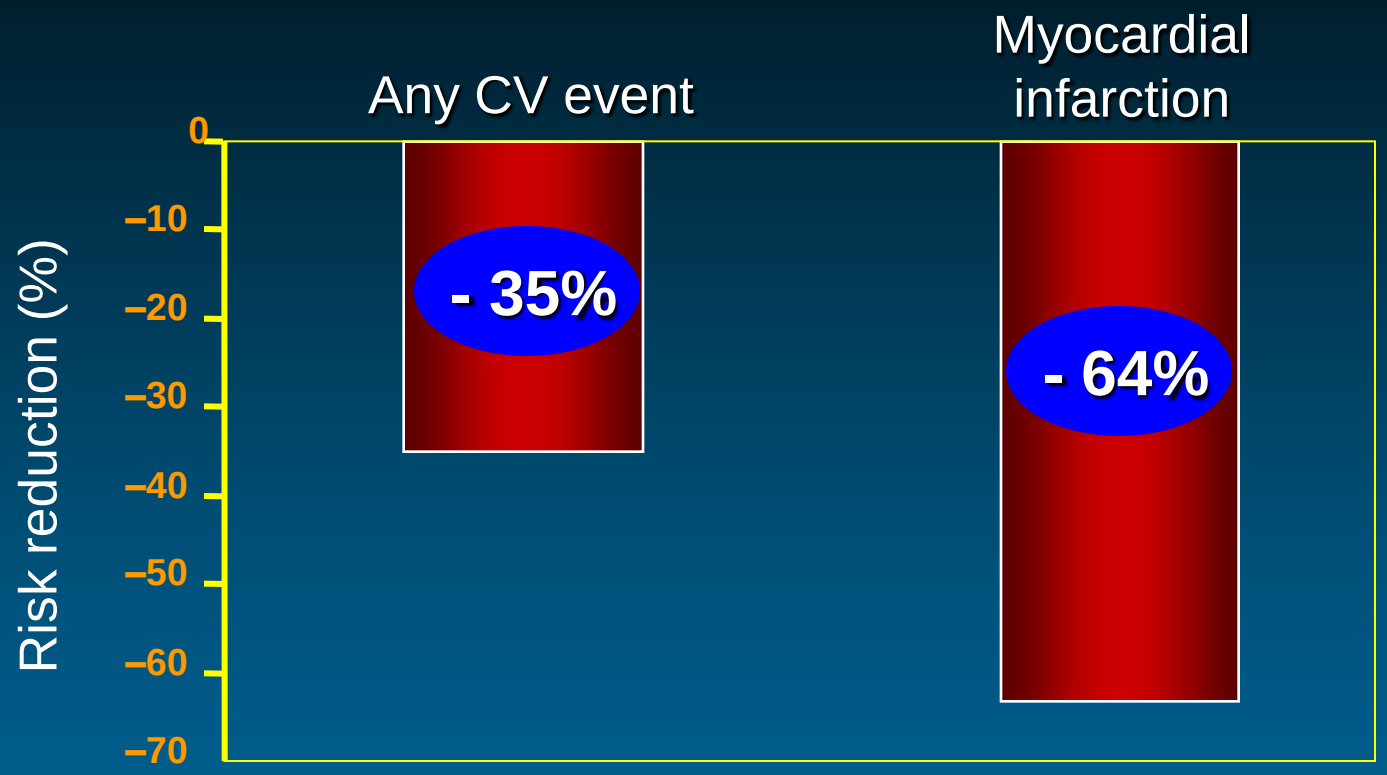
CV event	p
Coronary death	0.4368
Myocardial infarction	0.0120
Angina	0.3883
Heart failure	0.2251
Revascularisation procedure	0.6784
Peripheral vascular disorder	0.4558
Stroke/cerebrovascular accident	0.5269
Any CV event	0.0061



Cox proportional hazards model

Hanefeld M et al. Eur Heart J (2004) 25:10-16

Cardiovascular risk reduction in patients with Type 2 diabetes



Hanefeld M et al. Eur Heart J (2004) 25:10-16

New ESC/EASD Guidelines

On hyperglycemia

Eur Heart J (2007) 28, 88-136

ESC & EASD GUIDELINES Executive summary

Recommendation	Class	Level
People at high risk for type 2 diabetes should receive life style counselling, and if needed, drugs to reduce or delay their risk of diabetes. This may decrease their risk to develop cardiovascular disease	I	A
In people with impaired glucose tolerance the onset of diabetes can be delayed by certain drugs (such as **acarbose**, metformin).	I	A

Sweden; Markku Laakso, Finland; Klas Malmberg, Sweden; Silvia Priori, Italy; Jan Östergren, Sweden; Jaakko Tuomilehto, Finland; Inga Thrainsdottir, Iceland

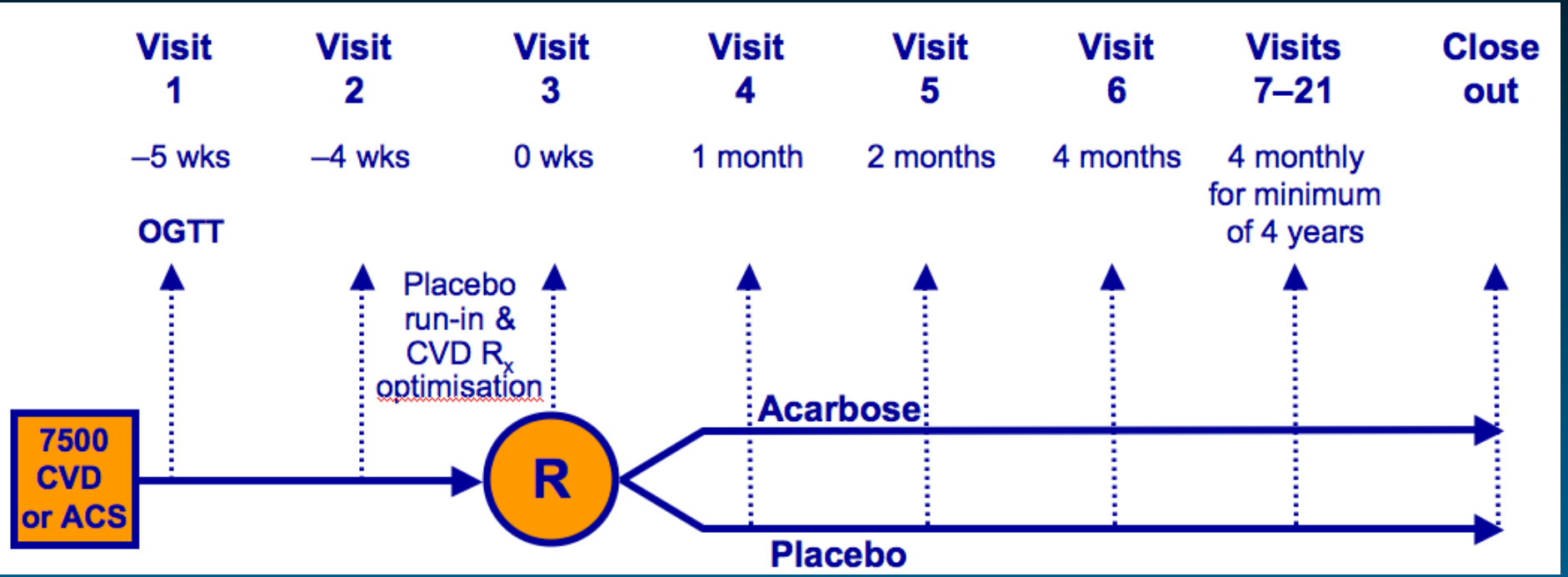
Other Contributors: Ilse Vanhorebeek (Belgium); Marco Stramba-Badiale (Italy); Peter Lindgren (Sweden); Qing Qiao (Finland).

ACE - Major Inclusion Criteria

- Male or female, aged 50 years or more
- CVD
  - Prior MI
  - Prior unstable angina
  - Current stable angina
- Impaired glucose tolerance (IGT) when screened with an oral glucose tolerance test:
  - FPG <7.0 mmol/l
  - 2-hour plasma glucose ≥7.8 and ≤11.1 mmol/l
- Optimized CVD drug therapy with no planned revascularisation procedures
- Written informed consent

ACE Study Flow Chart

A minimum of 904 adjudicated primary events are required



Acarbose, 50 mg (three times daily) or matching placebo (three times daily)

Tablets will be taken with meals using a ‘Start low, go slow’ dose titration