

La ricerca clinica tra cardiologi e diabetologi

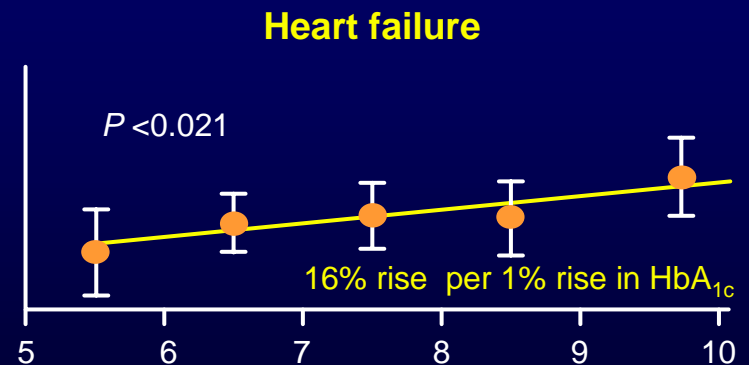
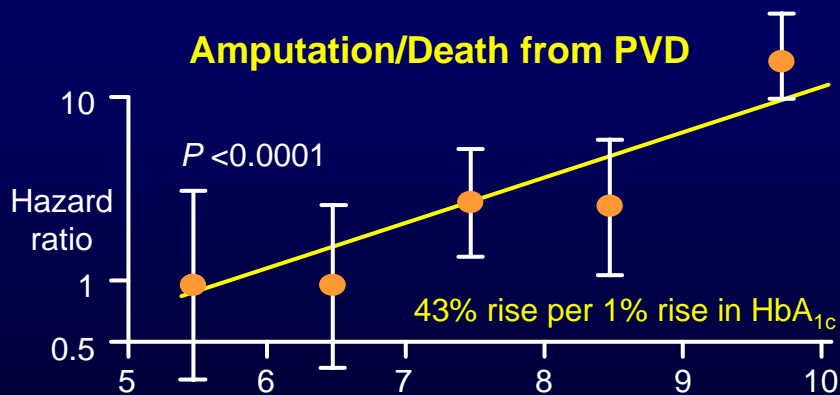
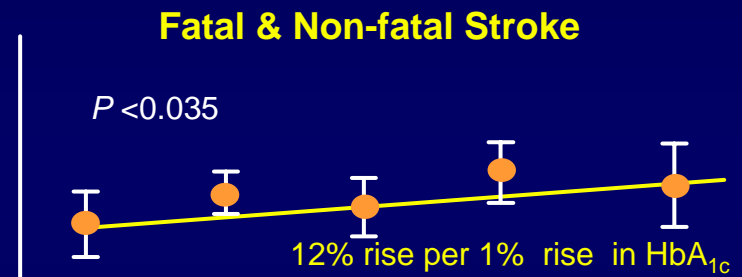
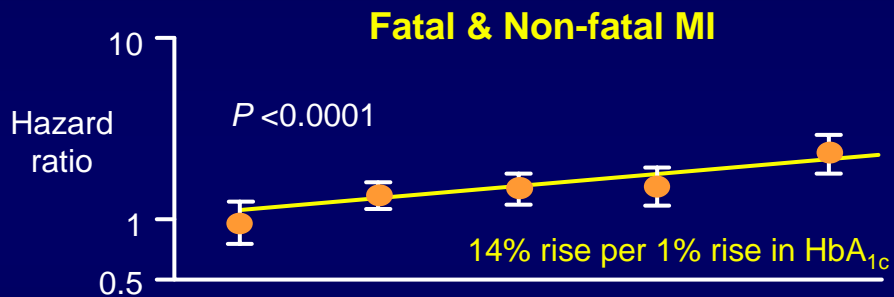
Aldo P Maggioni
Centro Studi ANMCO
Firenze

Diabetes and CV events

- Diabetes is progressively becoming more common
- In diabetics, the cardiotoxic triad is
 - *coronary artery disease (leading cause of CHF)*
 - *hypertension*
 - *specific diabetic cardiomyopathy*
- Diabetes is an independent risk factor for the development of CV events
- Conversely, the presence of CV diseases is an independent risk factor for the development of diabetes
- The high risk of CV diseases associated with known diabetes must be extended to patients with impaired glucose tolerance

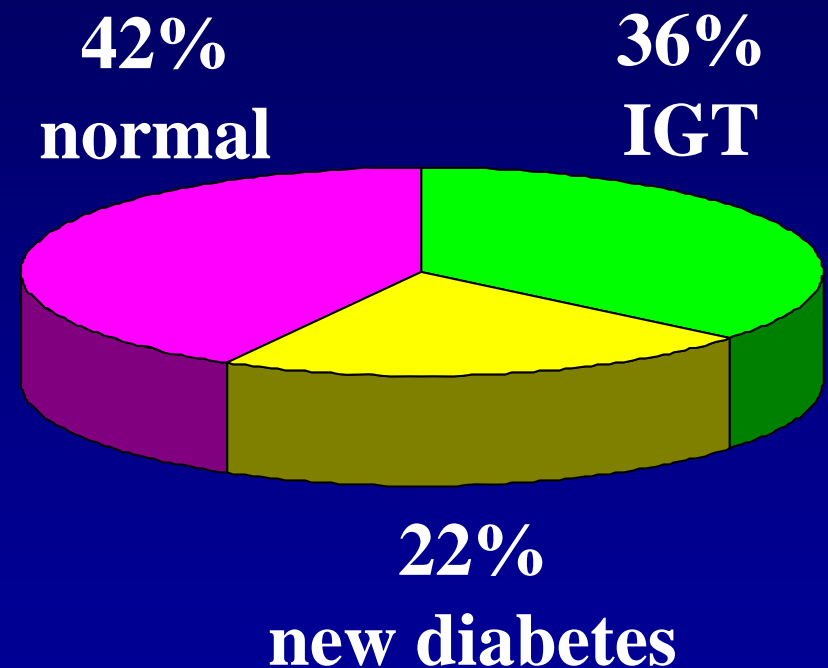
Diabetes, Glucose, and CV Disease

- Diabetes (DM) is an established risk factor for CVD
- In DM, higher glucose levels/HbA_{1c} predict higher CV risk



EURO HEART SURVEY ON DIABETES

- 110 centers in 25 countries
- 2,107 patients admitted for ACS
- OGTT at discharge in non diabetic patients



Glucose metabolism in patients with acute myocardial infarction and no previous diagnosis of diabetes mellitus: a prospective study

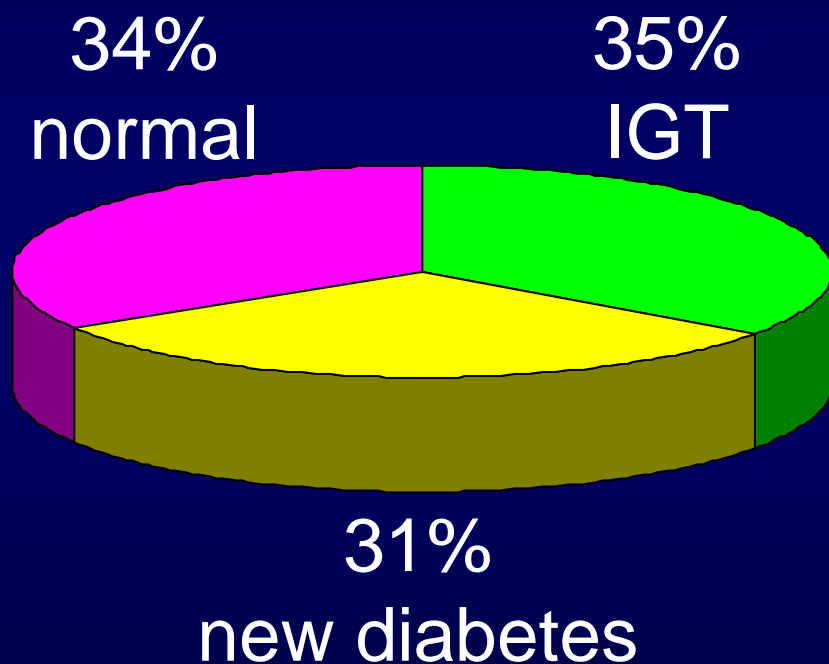
Lancet 2002, 359:2140

Anna Norhammar, Åke Tenerz, Göran Nilsson, Anders Hamsten, Suad Efendic, Lars Rydén, Klas Malmberg

31 August 2004

GAMI: Glucose abnormalities in patients with myocardial infarction - prevalence and prognostic implications

ESC 2004



- **A shift of paradigm in clinical practice seems to be warranted**
- **Abnormal glycemia must be excluded in all patients with AMI by means of an OGTT test before discharge**
- **Patients with IGT are at high risk for further CV events**

Prevention of CV events in diabetic patients

- What we already know
 - *Meticulous metabolic control*
 - *BP control*
 - *Lipid control*
 - *The role of blockers of the RAS system*
- What we are investigating
 - *LV function assessment in diabetics without clinically apparent CV disease (DYDA study)*
 - *The role of insulin and N-3 PUFA (ORIGIN study)*
 - *The role of ARBs and nateglinide (NAVIGATOR trial)*

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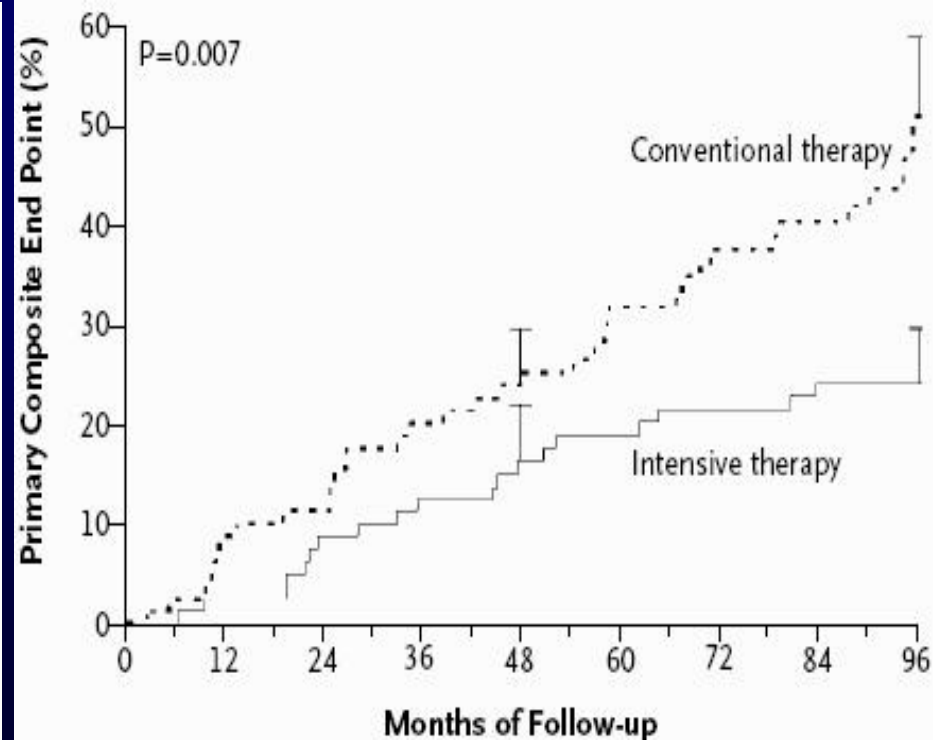
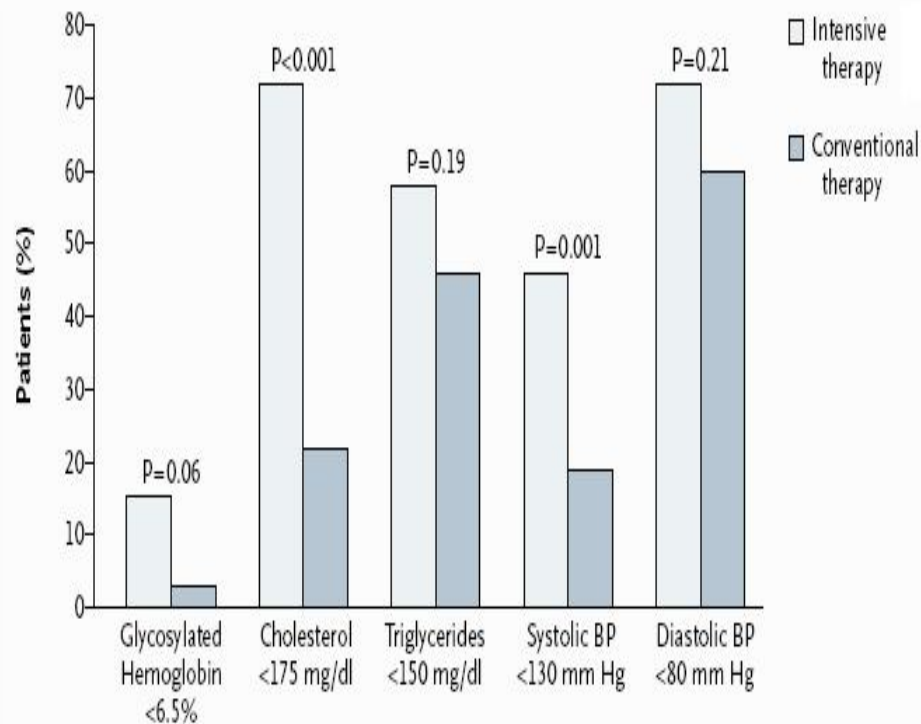
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Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes

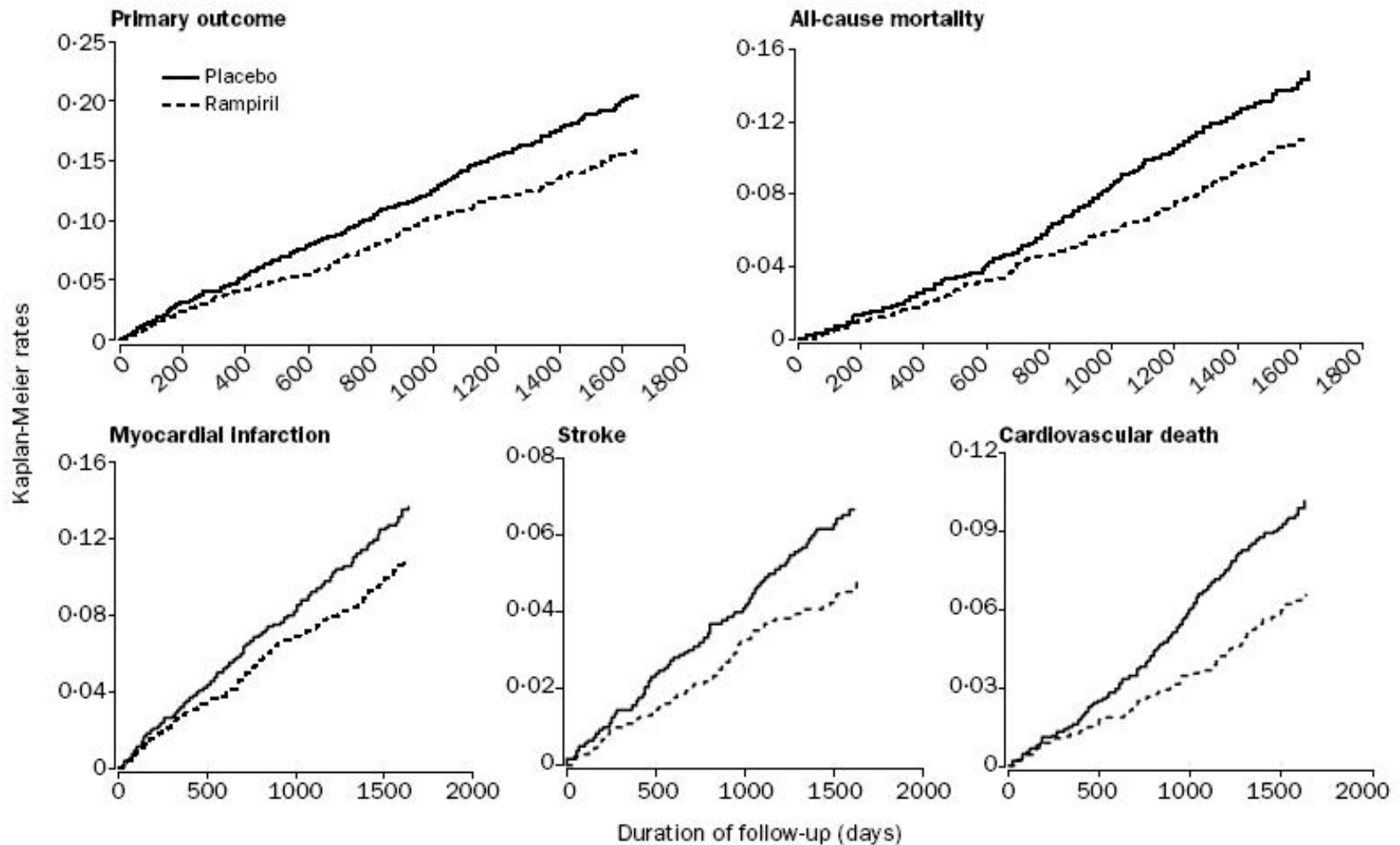
Peter Gæde, M.D., Pernille Vedel, M.D., Ph.D., Nicolai Larsen, M.D., Ph.D., Gunnar V.H. Jensen, M.D., Ph.D., Hans-Henrik Parving, M.D., D.M.Sc., and Oluf Pedersen, M.D., D.M.Sc.



Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy

Heart Outcomes Prevention Evaluation (HOPE) Study Investigators*

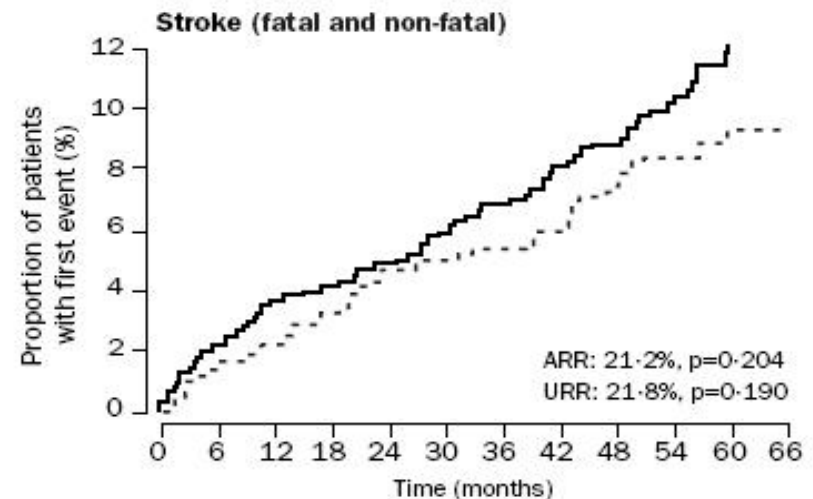
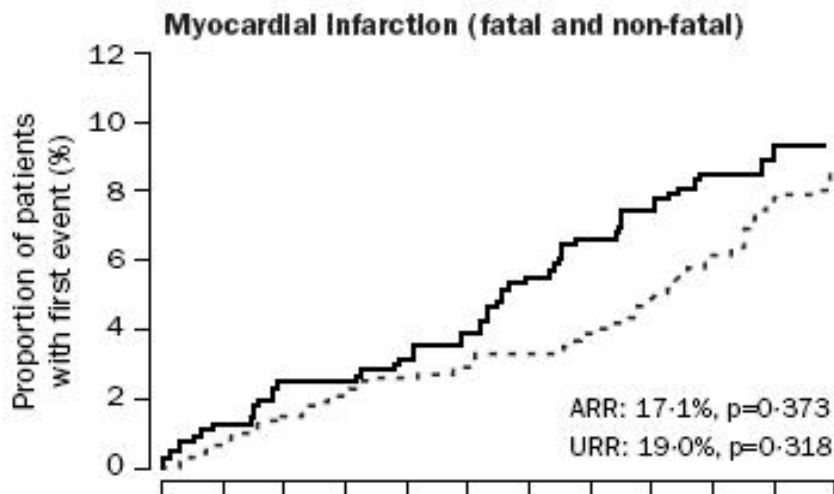
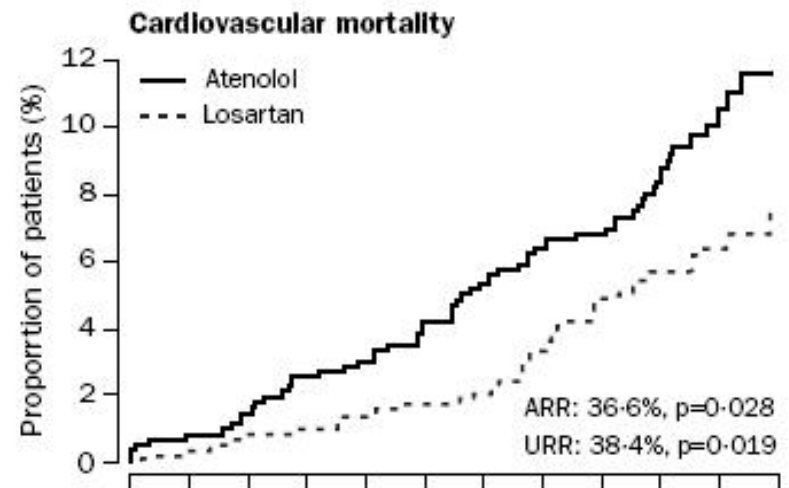
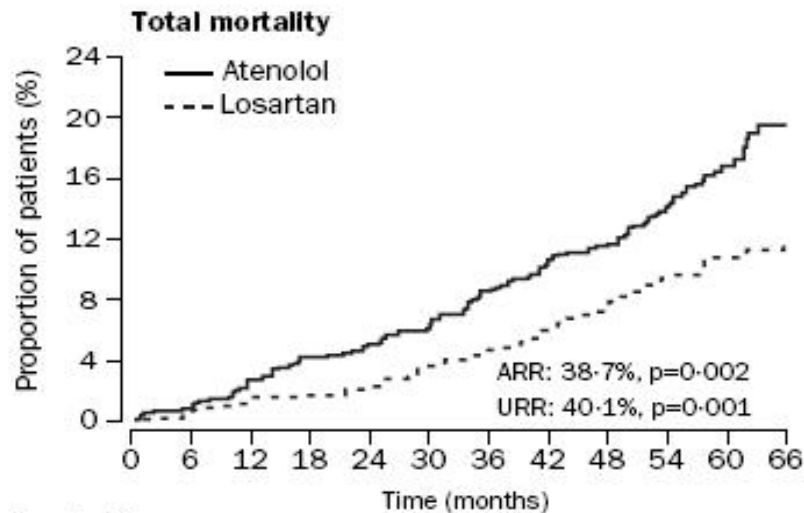
Lancet 2000; 355: 253–59



Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol

Lars H Lindholm, Hans Ibsen, Björn Dahlöf, Richard B Devereux, Gareth Beevers, Ulf de Faire, Frej Fyhrquist, Stevo Julius, Sverre E Kjeldsen, Krister Kristiansson, Ole Lederballe-Pedersen, Markku S Nieminen, Per Omvik, Suzanne Oparil, Hans Wedel, Peter Aarup, Jonathan Edelman, Steven Snapinn, for the LIFE study group*

Lancet 2002; 359: 1004-10



Prevention of HF in diabetic patients

- What we already know
 - *Meticulous metabolic control*
 - *BP control*
 - *Lipid control*
 - *The role of blockers of the RAS system*
- **What we are investigating**
 - ***LV function assessment in diabetics without clinically apparent CV disease (DYDA study)***
 - ***The role of insulin and N-3 PUFA (ORIGIN study)***
 - ***The role of ARBs and nateglinide (NAVIGATOR trial)***

left ventricular **DY**sfunction in **DiA**betes (**DYDA** study)

- **Purposes**

- to identify the rate of LV dysfunction in diabetic patients without clinically documented CV disease
- to identify the independent predictors of LV dysfunction

- **Method**

- echocardiographic assessment and BNP measure

- **Setting**

- 50 Italian diabetology/cardiology centers
- 1000 diabetics without clinical signs of CV disease



**Outcome Reduction with an
Initial Glargine INtervention**

NAVIGATOR

Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research

- Multinational trial in 9524 IGT patients randomized to either placebo or:
 - *Nateglinide 60 mg tid ac*
 - *Valsartan 160 mg/d*
 - *Combination of nateglinide (60 mg tid ac) and valsartan (160 mg/d)*
- Study duration of 5-6 years
- Represents the largest diabetes prevention study to date and the only one powered to assess CVD

NAVIGATOR: Primary Objectives

- Evaluate the effect of nateglinide, valsartan or the combination on progression to diabetes in patients with IGT
- Evaluate the effect of nateglinide, valsartan or the combination on the composite CV end point (CV mortality, non-fatal MI, stroke, unstable angina, revascularization)

NAVIGATOR 2 x 2 Factorial Design


Valsartan comparison

Valsartan/Nateglinide (n = 2381)	Placebo/Nateglinide (n = 2381)
Valsartan/Placebo (n = 2381)	Placebo/Placebo (n = 2381)


Nateglinide comparison

- Dosages
 - Nateglinide 60 mg tid ac
 - Valsartan 160 mg/d

All subjects will receive a lifestyle advice program

Treatment of patients with diabetes and CHD/CHF

- **Targeting diabetes**
 - *DIGAMI trial in AMI, intensive care patients*
 - *no trials in CHF*
- **Effects in diabetics of the treatments generally used in CHD/CHF**
 - *ACE-inhibitors*
 - *betablockers*
 - *ARBs*
 - *aldosterone blockers*

Diabetics patients with CHF

Neither evidences from RCTs are available nor studies are ongoing with the aim to demonstrate that more intensive metabolic control of diabetes can improve the outcome of patients with HF

Diabetes and cardiovascular diseases

- A meticulous control of diabetes, blood pressure and lipid levels does prevent the occurrence of CV diseases
- To prevent the occurrence of CV events, including HF, in type 2 diabetic or IFG/IGT patients, new studies are ongoing trying to evaluate
 - *the prevalence of asymptomatic LV dysfunction in patients without clinical signs of CV disease*
 - *the role of insulin glargine, N-3 PUFA, ARBs, sibutramine*

Diabetes and cardiovascular diseases

- No evidences are available on the effects of a more stringent metabolic control on prognosis of patients with type 2 diabetes and HF
- RCTs aimed to test this hypothesis are warranted
- Recommended treatments for CHD/CHF seem to provide similar benefits in diabetic and non diabetics patients
- More adherence to guidelines in diabetic patients is needed