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Obiettivi nel paziente con diabete tipo 2: la glicemia non basta

Diapositiva preparata da ANGELO AVOGARO e ceduta alla Società Italiana di Diabetologia.
Per ricevere la versione originale si prega di scrivere a siditalia@siditalia.it

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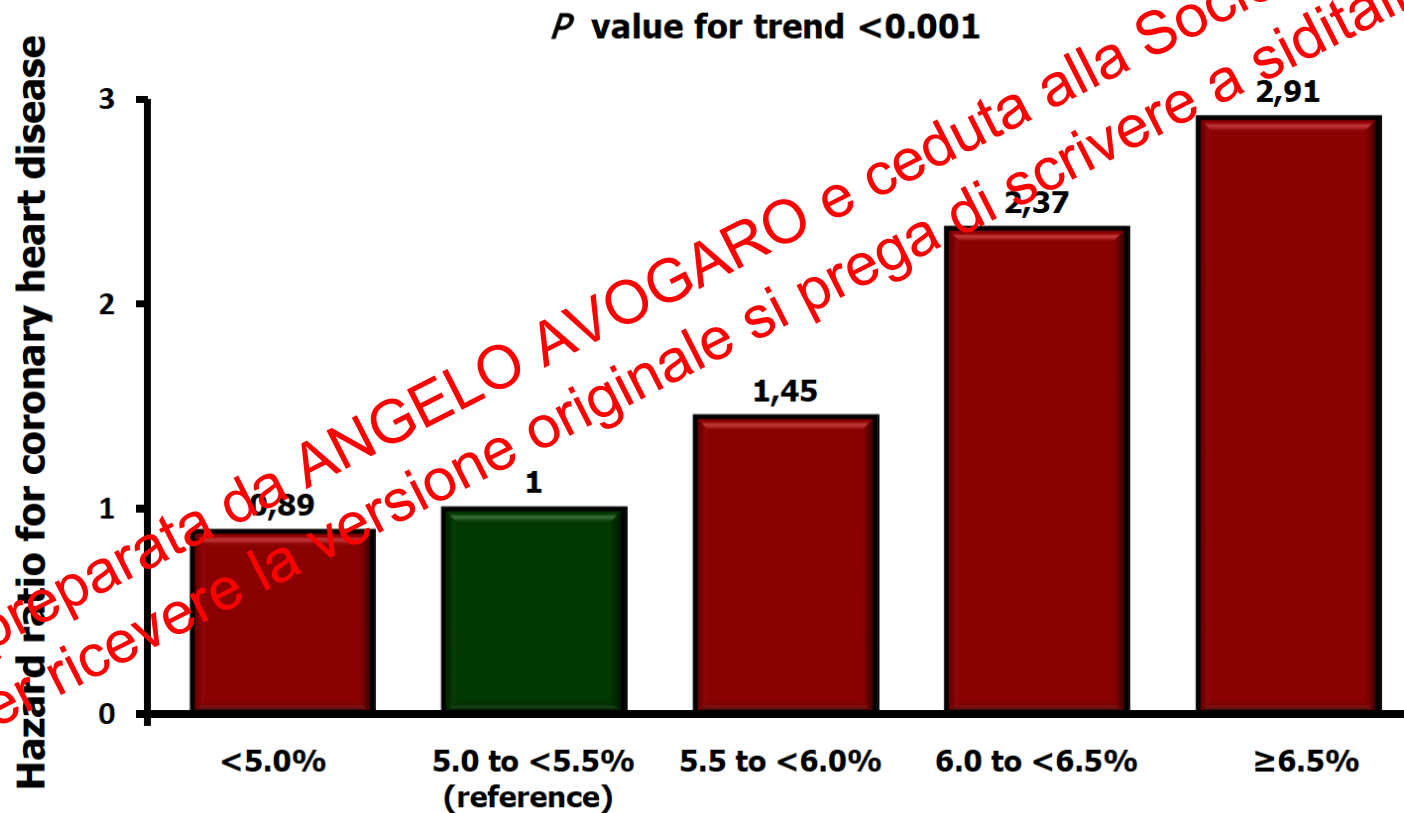
Il sottoscritto Angelo Avogaro dichiara Conflitti di Interesse con le seguenti aziende:

- Novo Nordisk
- Amgen
- Astrazeneca
- Bayer
- Boehringer-Ingelheim
- Servier
- Lilly
- Sanofi
- Takeda
- Mediolanum
- Merck Sharp & Dohme
- Janssen
- Menarini Diagnostici
- Novartis
- Bruno Farmaceutici
- Vifor Pharma
- Allergan

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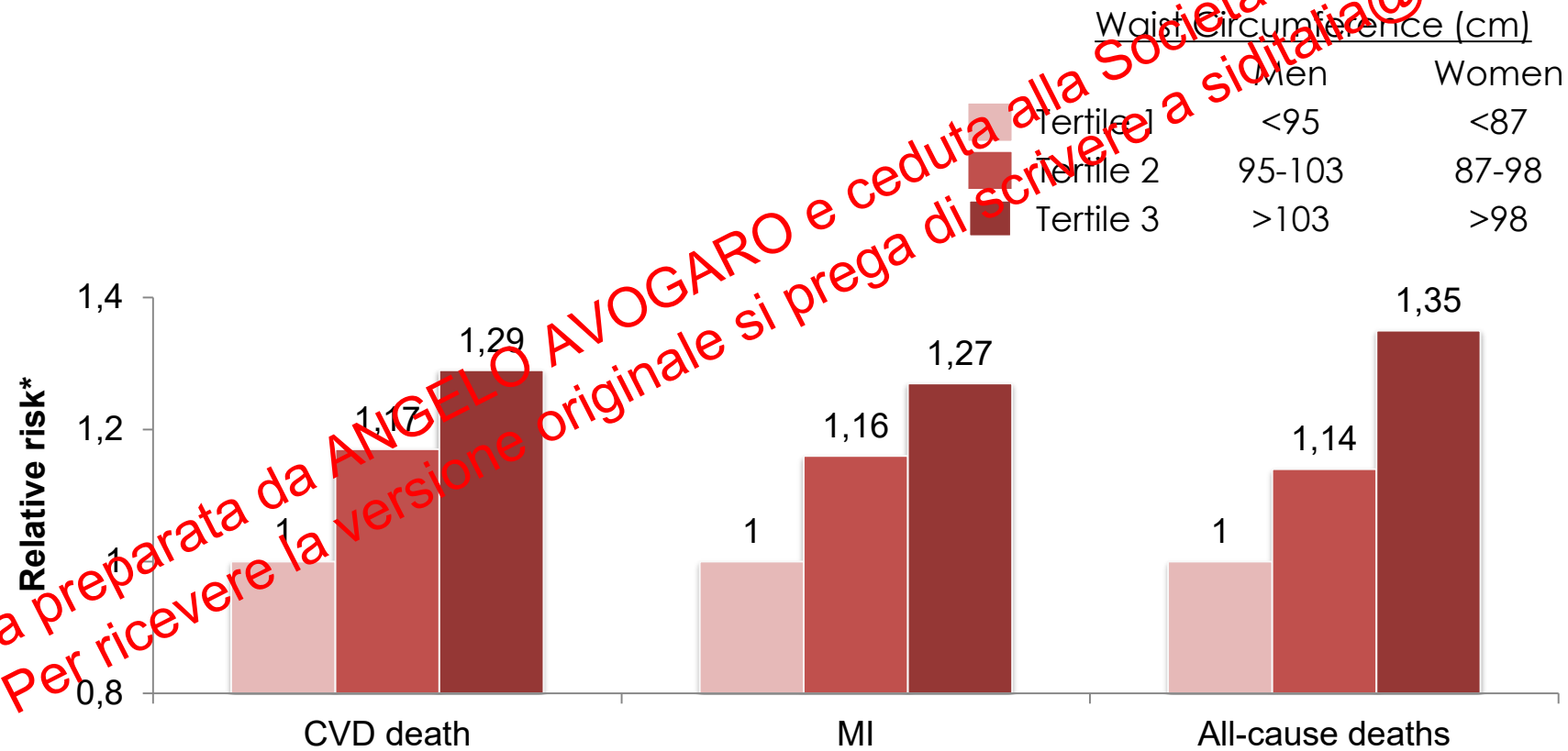
HbA_{1c} levels below the diagnostic threshold for Diabetes associate with an increased risk of cardiovascular disease

Hazard Ratios for coronary heart disease in the Atherosclerosis Risk in Communities (ARIC) population during the 15-Year study period according to HbA_{1c} category at baseline



Abdominal Obesity and Increased Risk of Cardiovascular Events

The HOPE Study

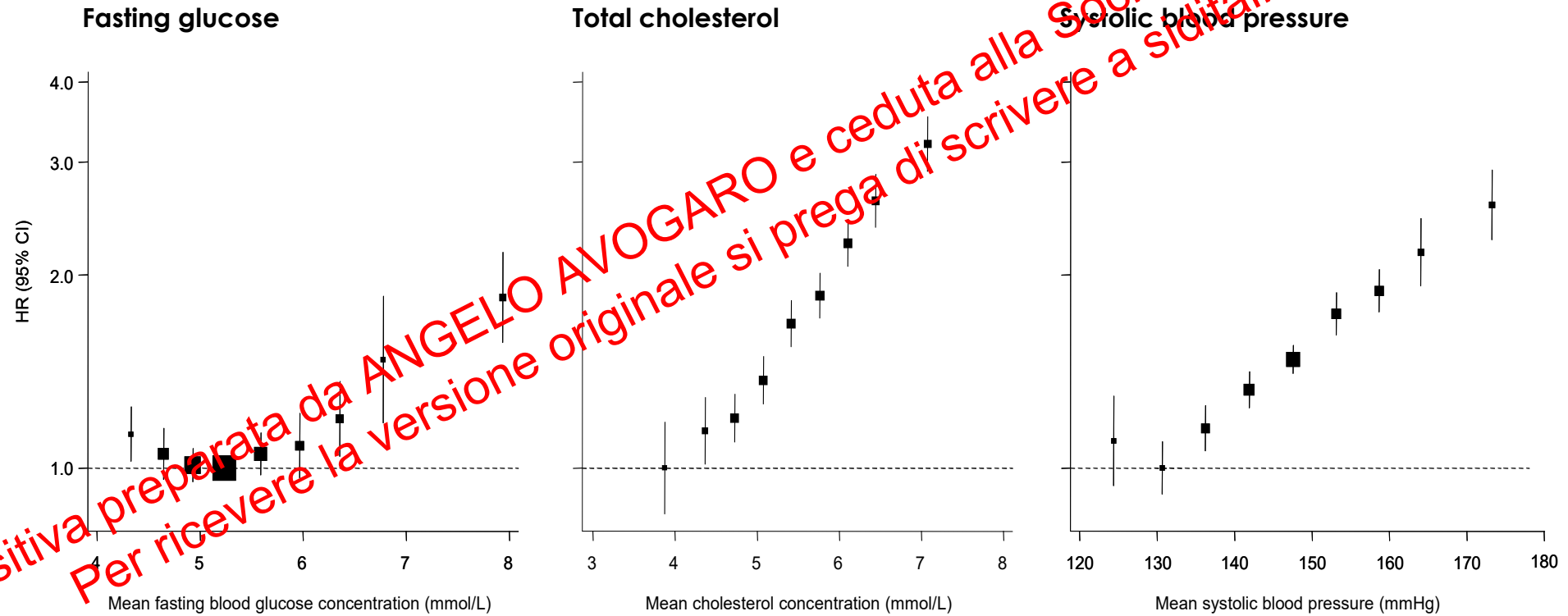


*Adjusted for BMI, age, smoking, sex, CVD disease, DM, HDL-cholesterol, total-C; CVD: cardiovascular disease; MI: myocardial infarction; BMI: body mass index; DM: diabetes mellitus; HDL: high-density lipoprotein cholesterol.

Dagenais GR, et al. *Am Heart J.* 2005;149:54-60.

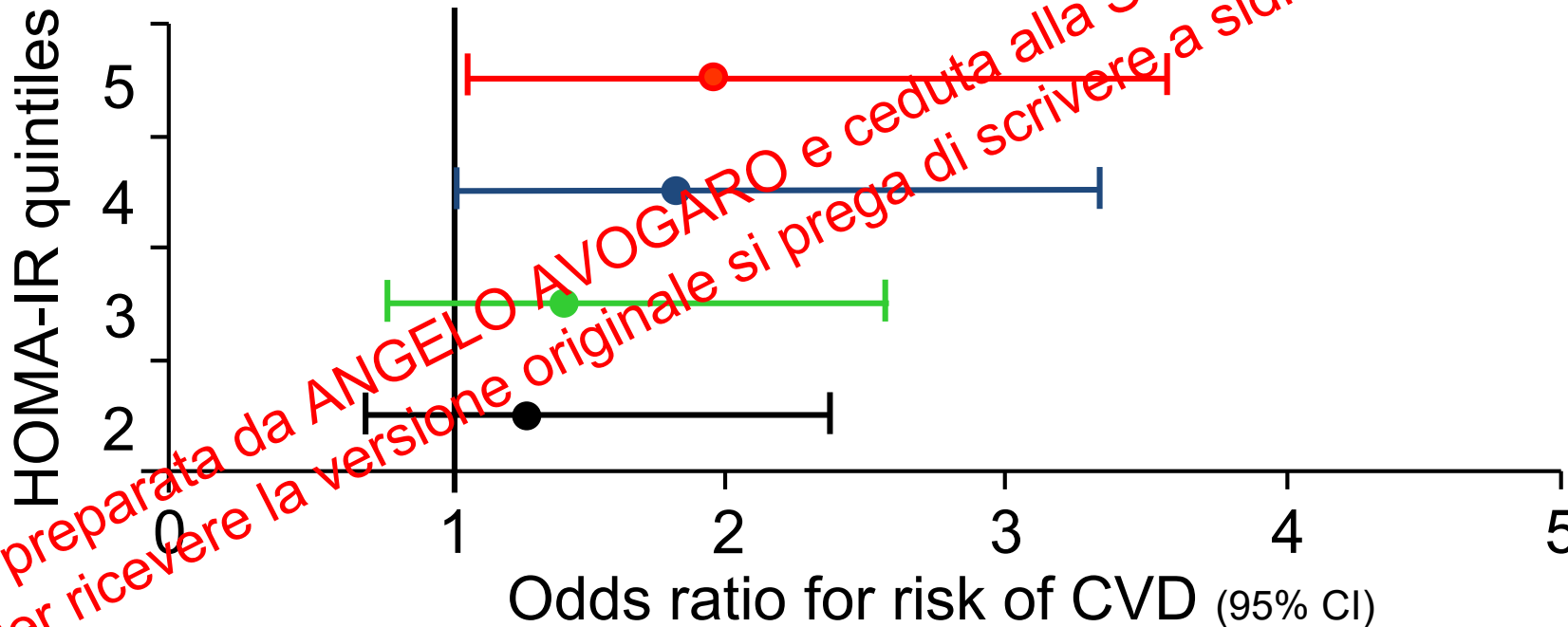
Glucose has different relationship to CVD than do chol / SBP

Meta-analysis of individual data from 102 prospective cohorts



Increased insulin resistance is associated with increased CV risk

San Antonio Heart Study:
HOMA-IR and 8-year risk of CV outcomes

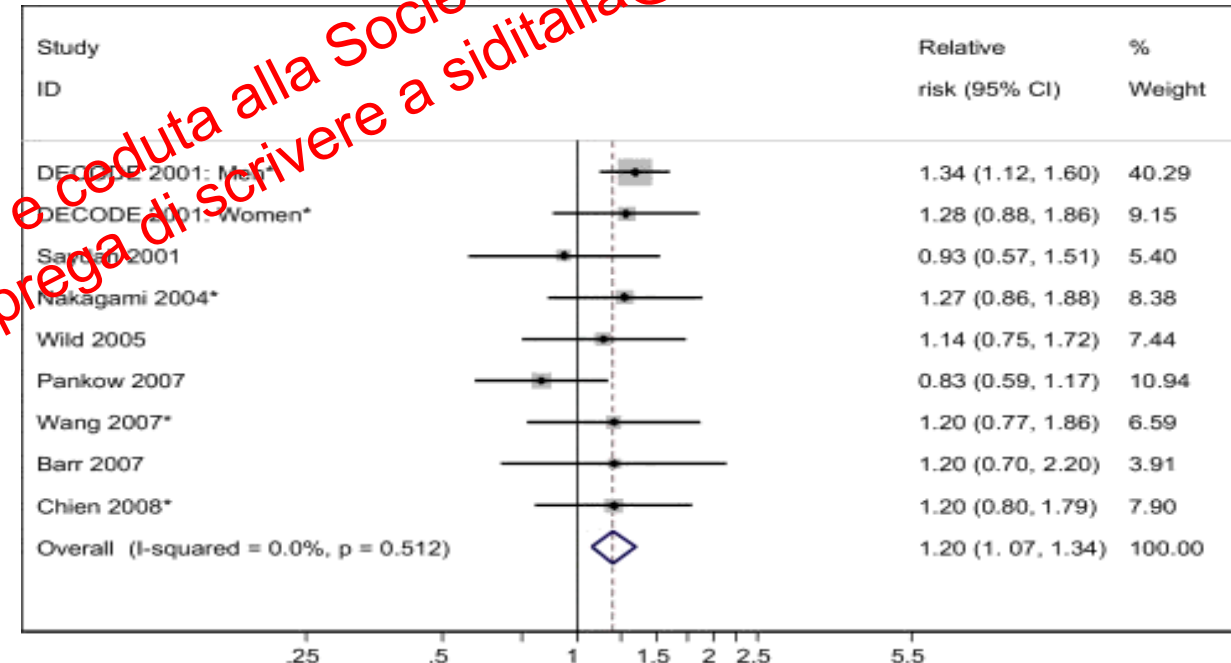
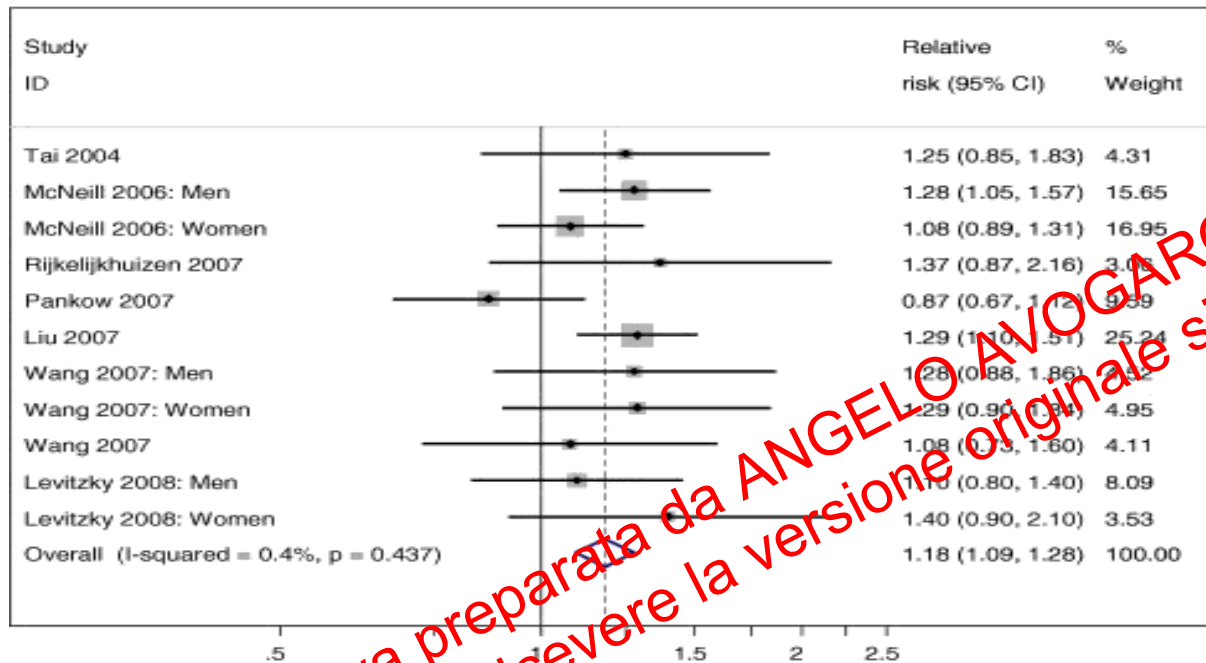


Quintile of HOMA-IR adjusted for age, sex, ethnicity, LDL, triglyceride, HDL, systolic blood pressure, smoking, alcohol consumption, leisure time exercise and waist circumference (median split)

*p=0.0185 for increased CV disease risk across HOMA-IR quintiles

Pre-Diabetic Conditions: Risk of Cardiovascular Disease

Meta-analysis of 18 clinical trials evaluating the risk of CV disease among patients with impaired fasting glucose and/or impaired glucose tolerance



CV=Cardiovascular

Source: Ford ES et al. JACC 2010;55:1310-1317

Association between prediabetes and risk of cardiovascular disease and all cause mortality (Huang et al. BMJ 2016)



CVD



CHD



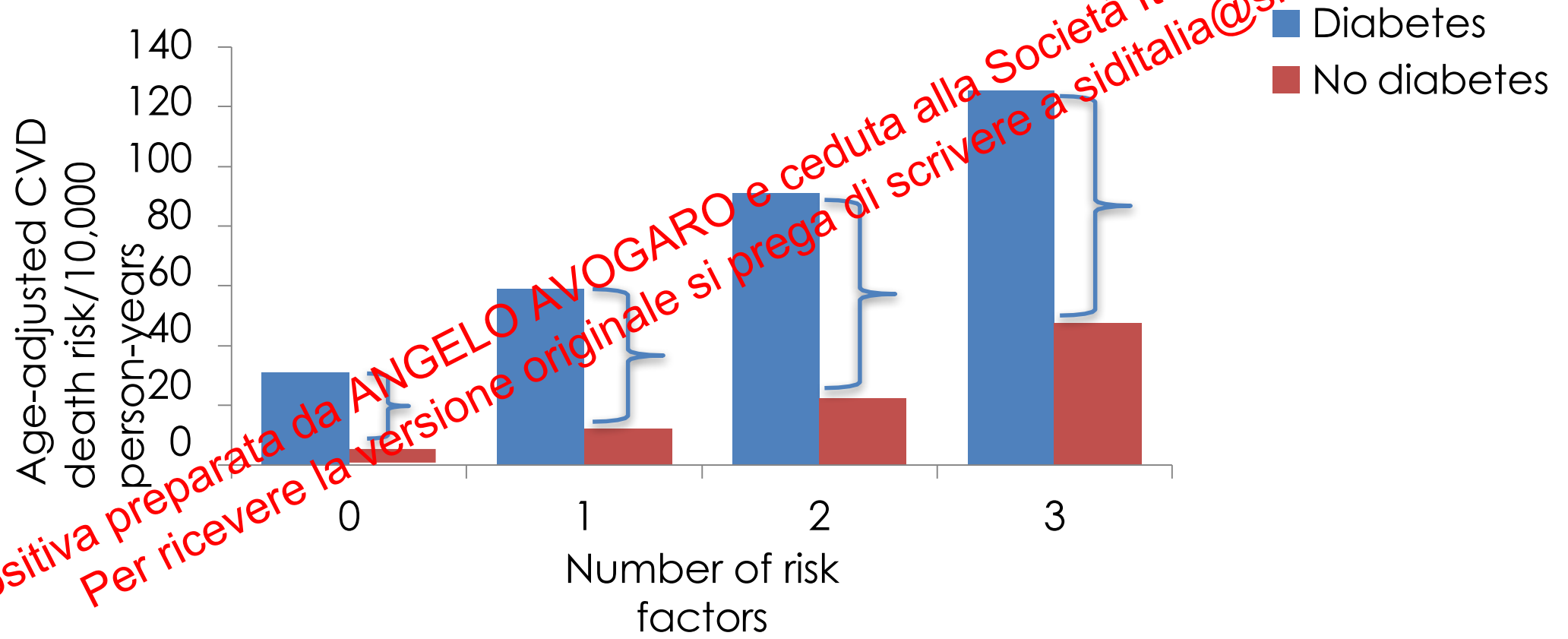
STROKE



ALL CAUSE DEATH

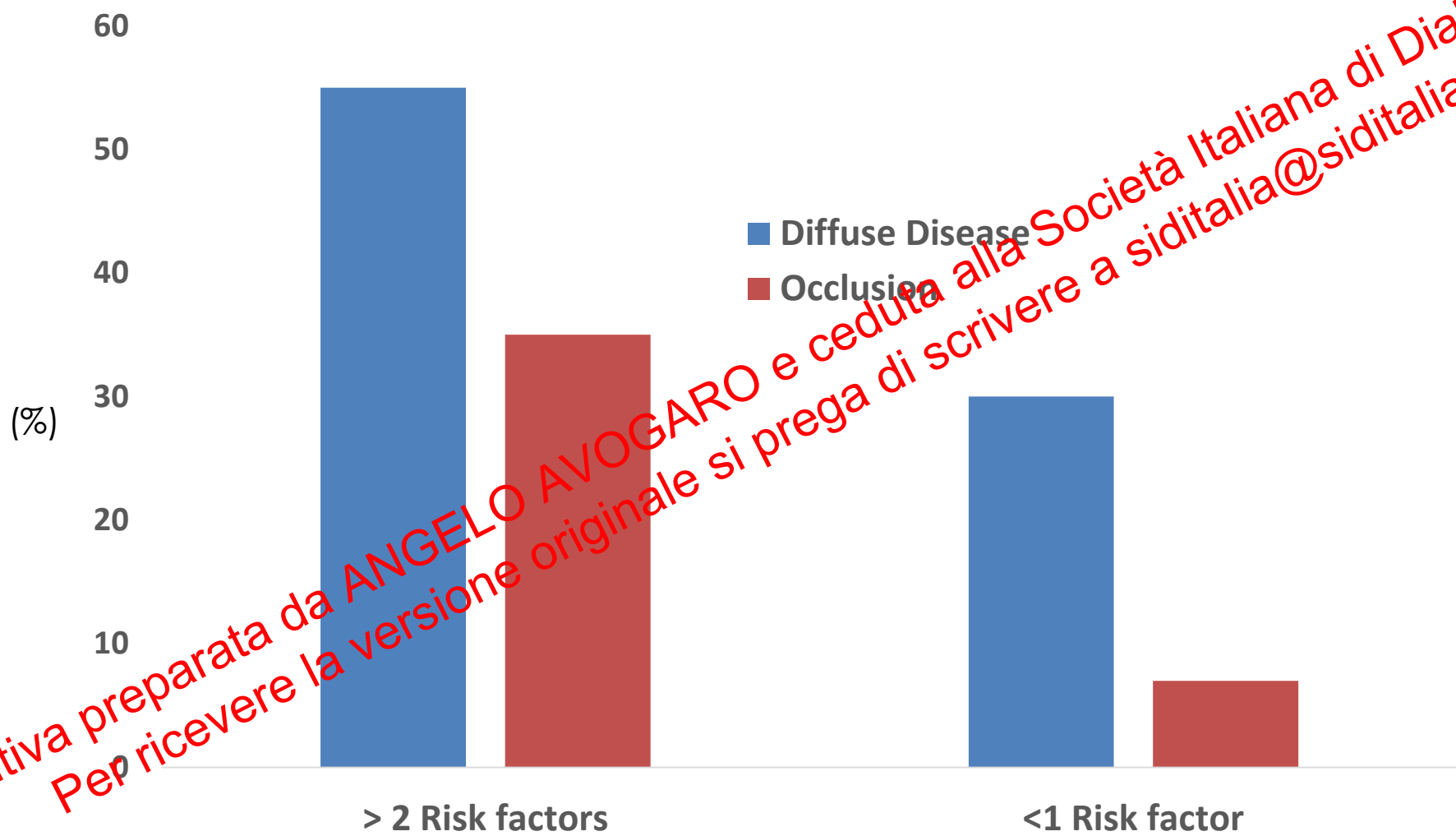
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The Study MRFIT showed that Glucose multiplies the negative effects of associated Risk factors



Risk factors were serum cholesterol ≥ 200 mg/dL, current smoker, SBP ≥ 120 mmHg
Stamler et al. Diabetes Care 1993;16:434.

Prevalence of a “diffuse” coronary disease (defined by the presence of significant stenosis in two or more coronary vessels involving two or more segments of each artery) and of total occlusion in at least one epicardial vessel



Risk Factor for CHD in UKPDS Study

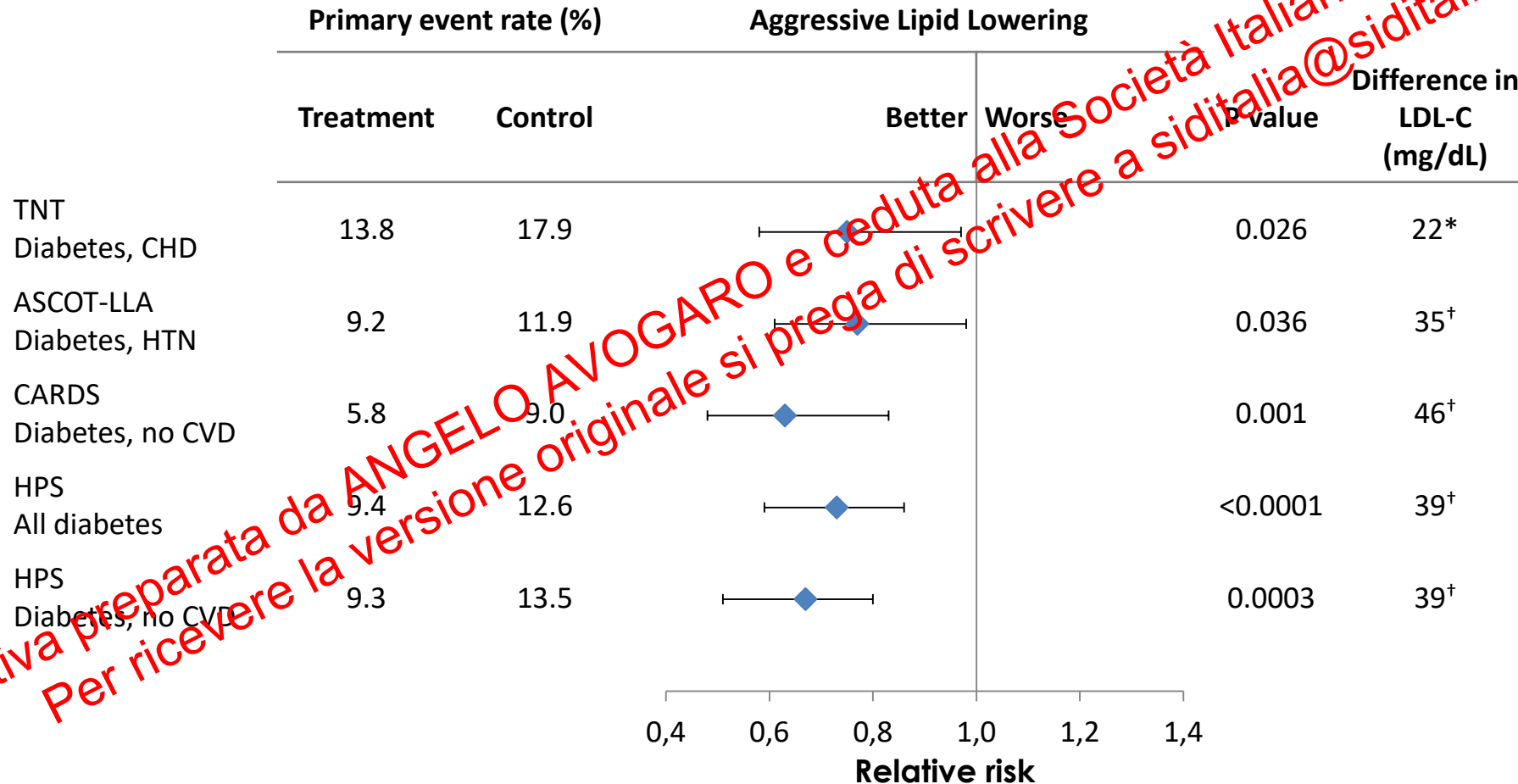
Coronary Artery Disease (n=280)

Position in Model	Variable	p Value
First	LDL Cholesterol	<0.0001
Second	HDL Cholesterol	0.0001
Third	Hemoglobin A _{1c}	0.0022
Fourth	Systolic Blood Pressure	0.0065
Fifth	Smoking	0.056

*Adjusted for age and sex.

Turner RC et al. *BMJ* 1998;316:823-828.

Benefits of Aggressive LDL-C Lowering in Diabetes



*Atorvastatin 10 vs 80 mg/day.

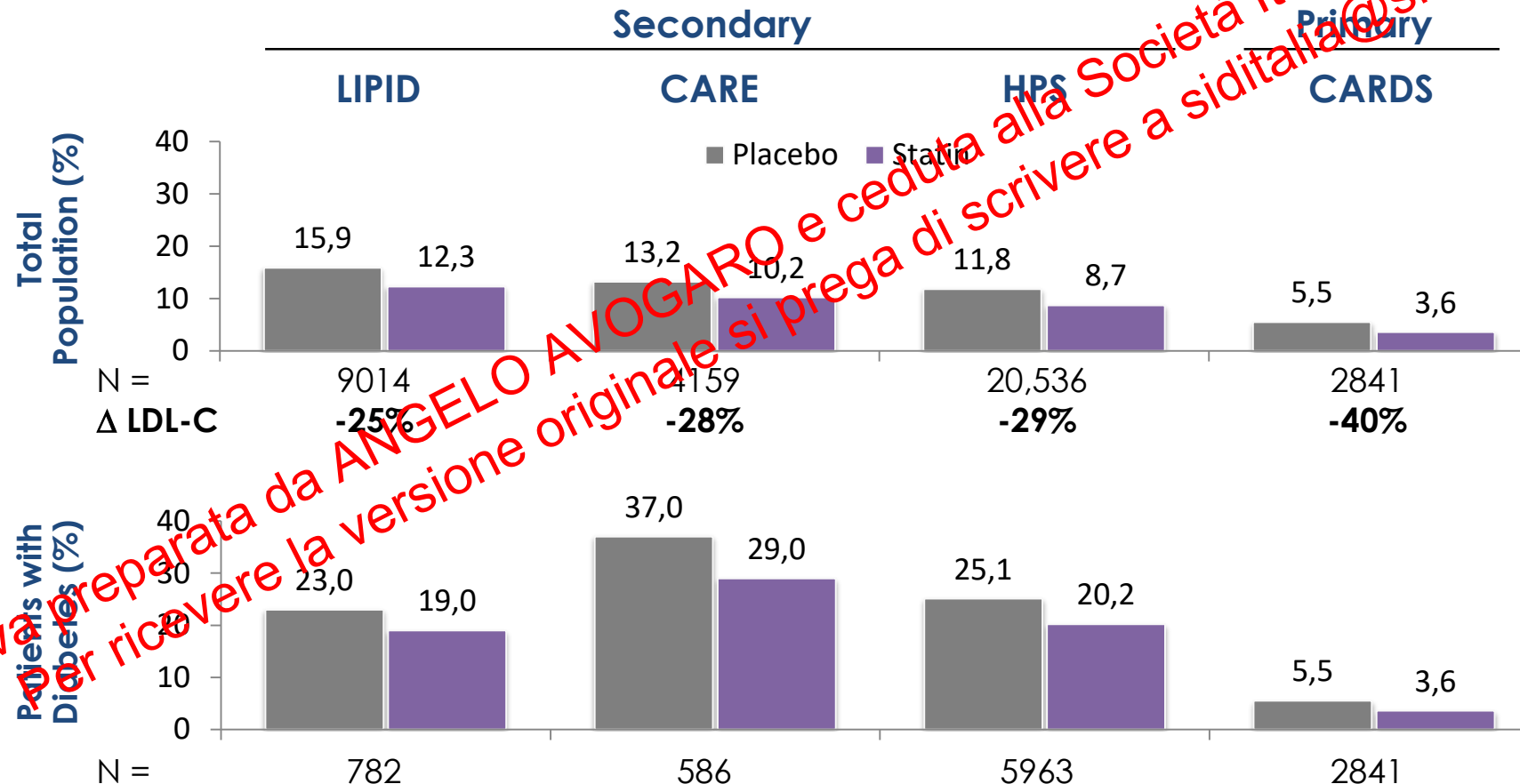
†Statin vs placebo.

Shepherd J, et al. *Diabetes Care*. 2006;29:1220-1226. Sever PS, et al. *Diabetes Care*. 2005;28:1151-1157.

Colhoun HM, et al. *Lancet*. 2004;364:685-696. HPS Collaborative Group. *Lancet*. 2003;361:2005-2016.

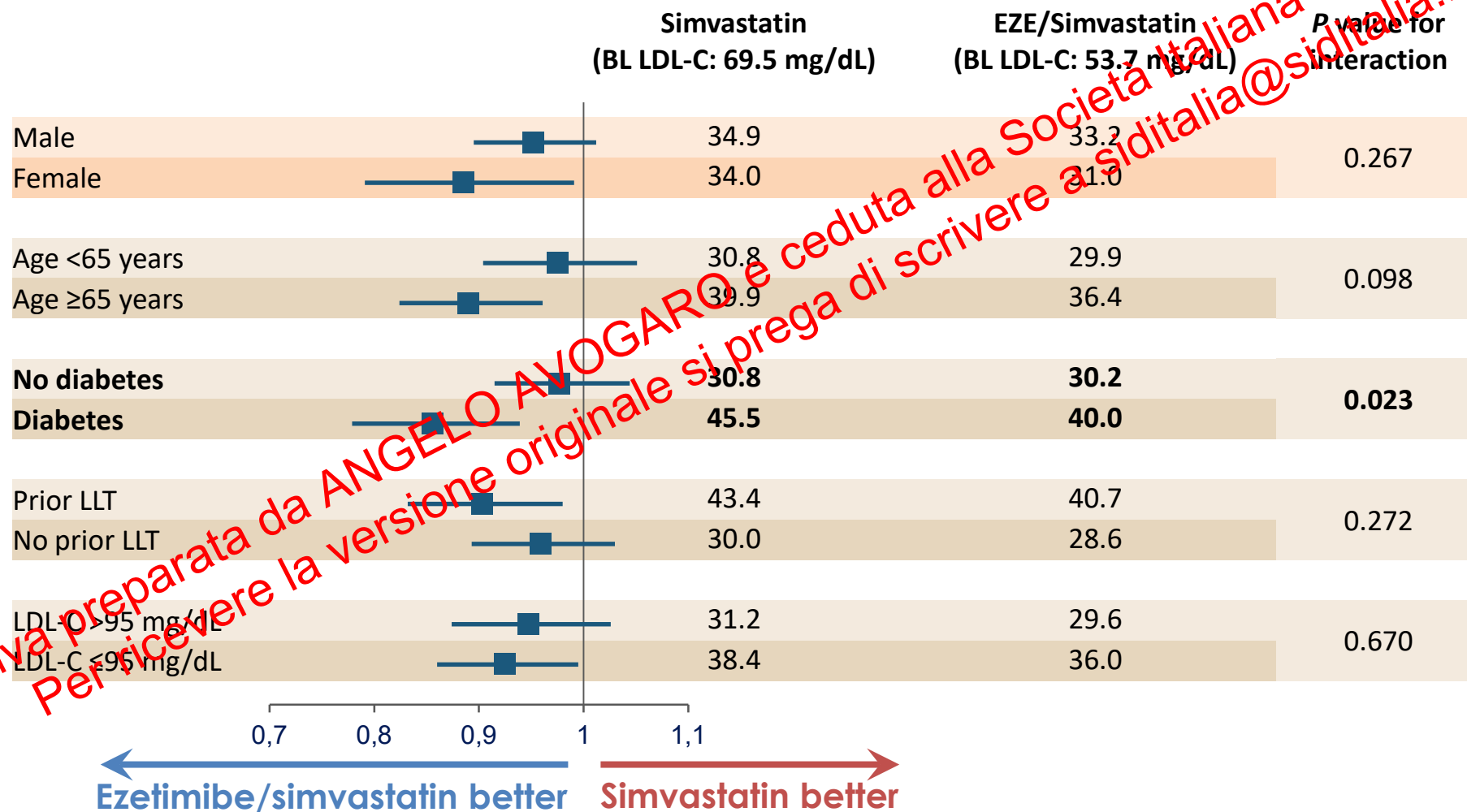
Residual Cardiovascular Risk in Major Statin Trials

CHD events still occur in patients treated with statins

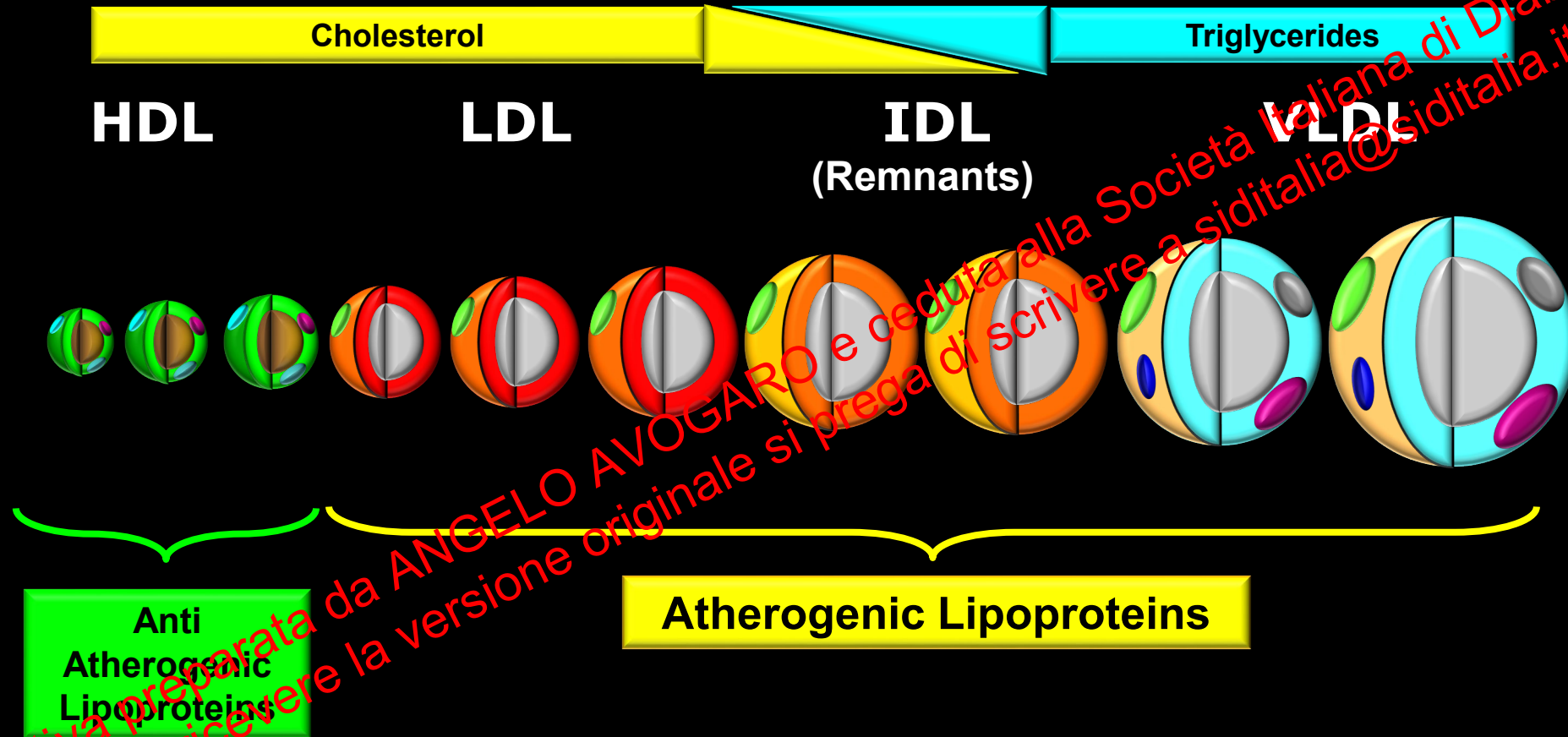


IMPROVE-IT

Major Prespecified Subgroups

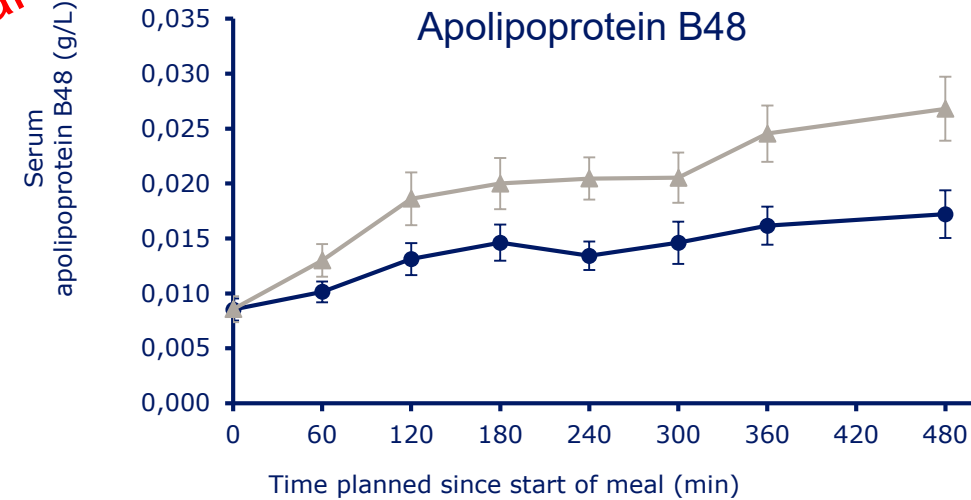
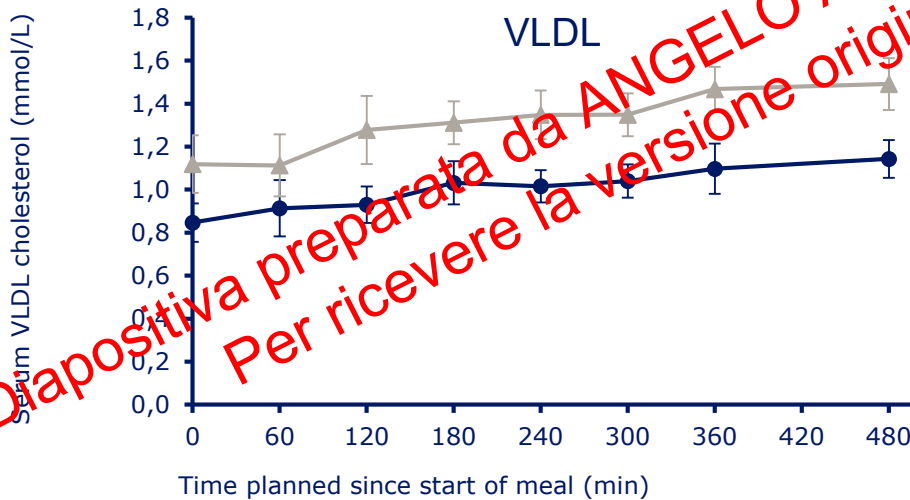
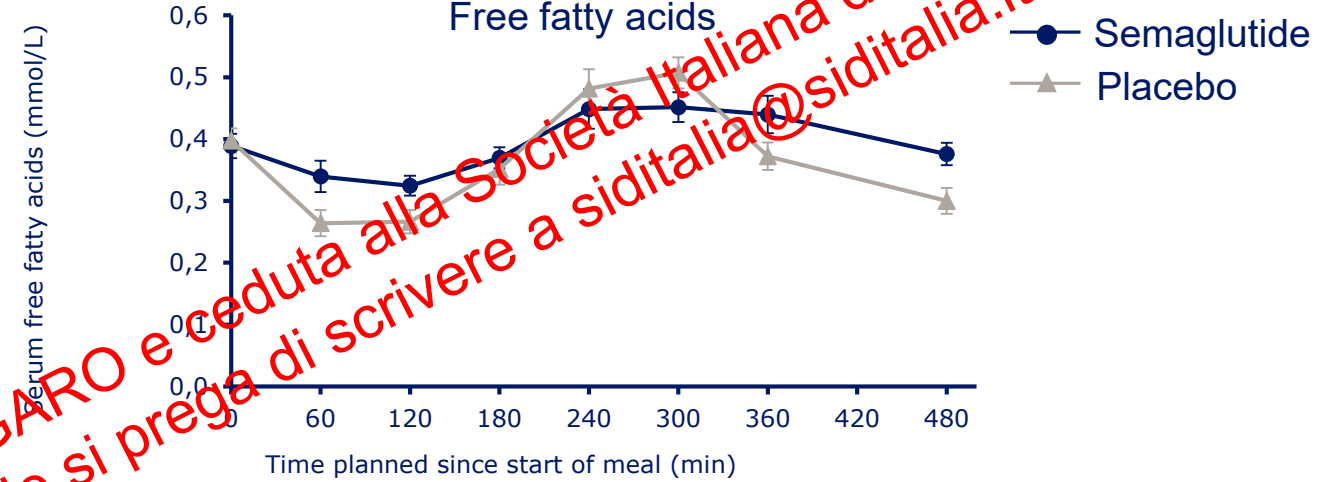
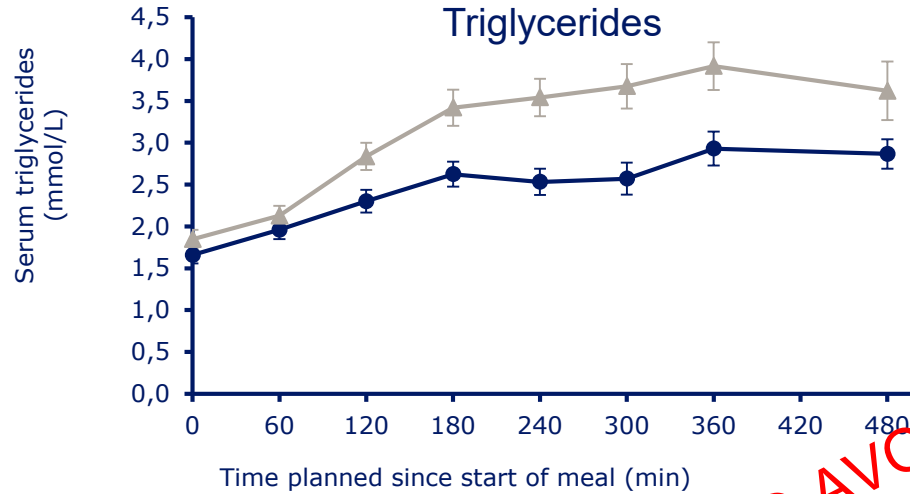


Plasma Lipoproteins

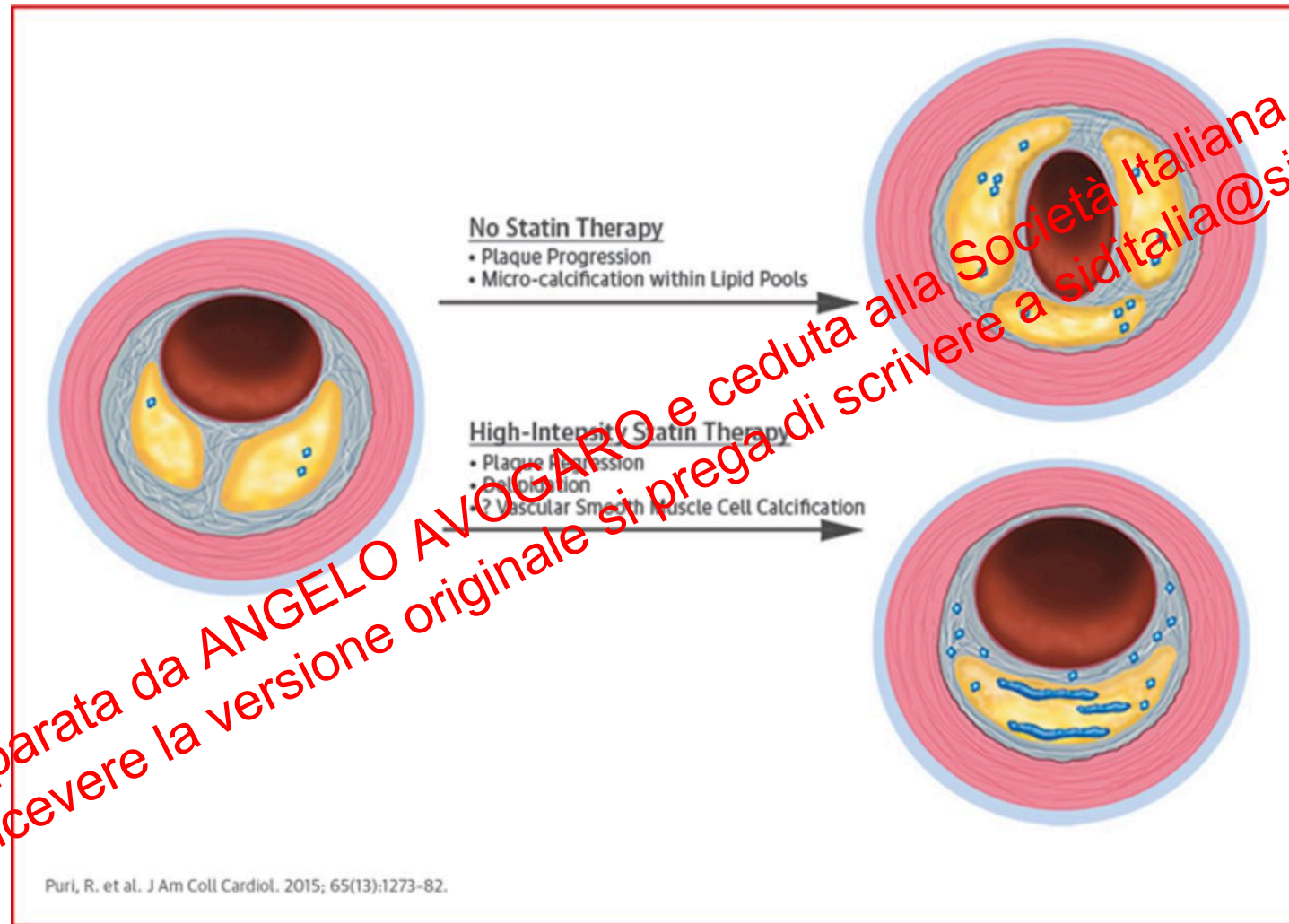


Mean lipid profiles

AFTER STANDARDISED, FAT-RICH BREAKFAST



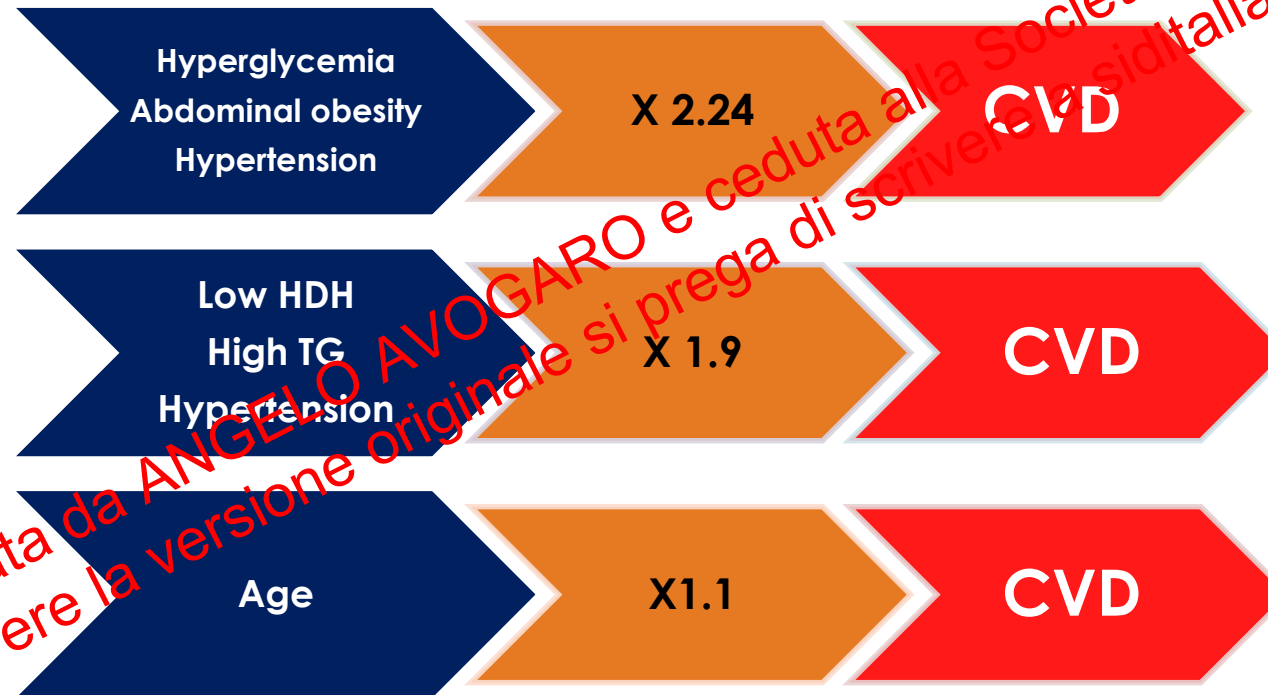
The importance of regression: aim less than 70!



Trajectories of Entering the Metabolic Syndrome

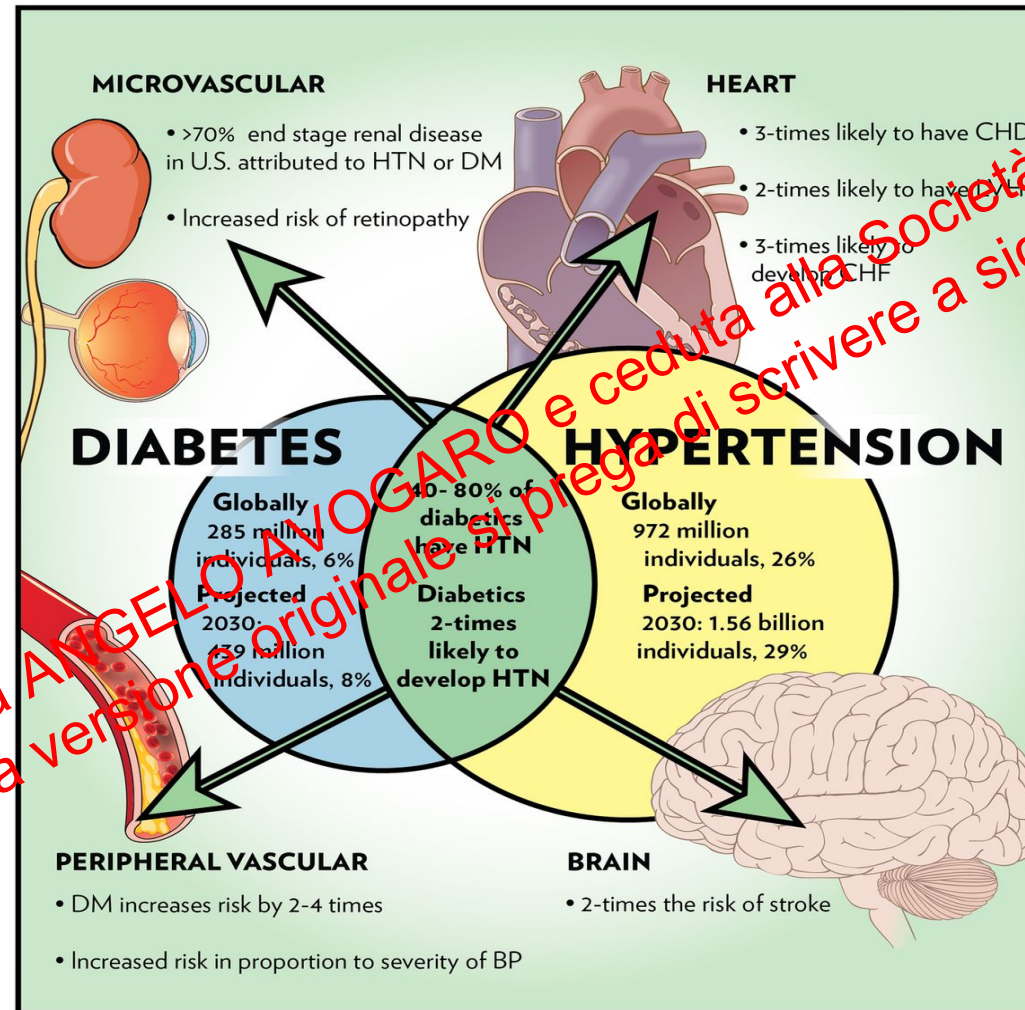
The Framingham Heart Study

Oscar H. Franco, MD, DSc, PhD; Joseph M. Massaro, PhD; Jacky Civil, PhD; Mark R. Cobain, PhD;
Brendan O'Malley, PhD; Ralph B. D'Agostino, Sr, PhD



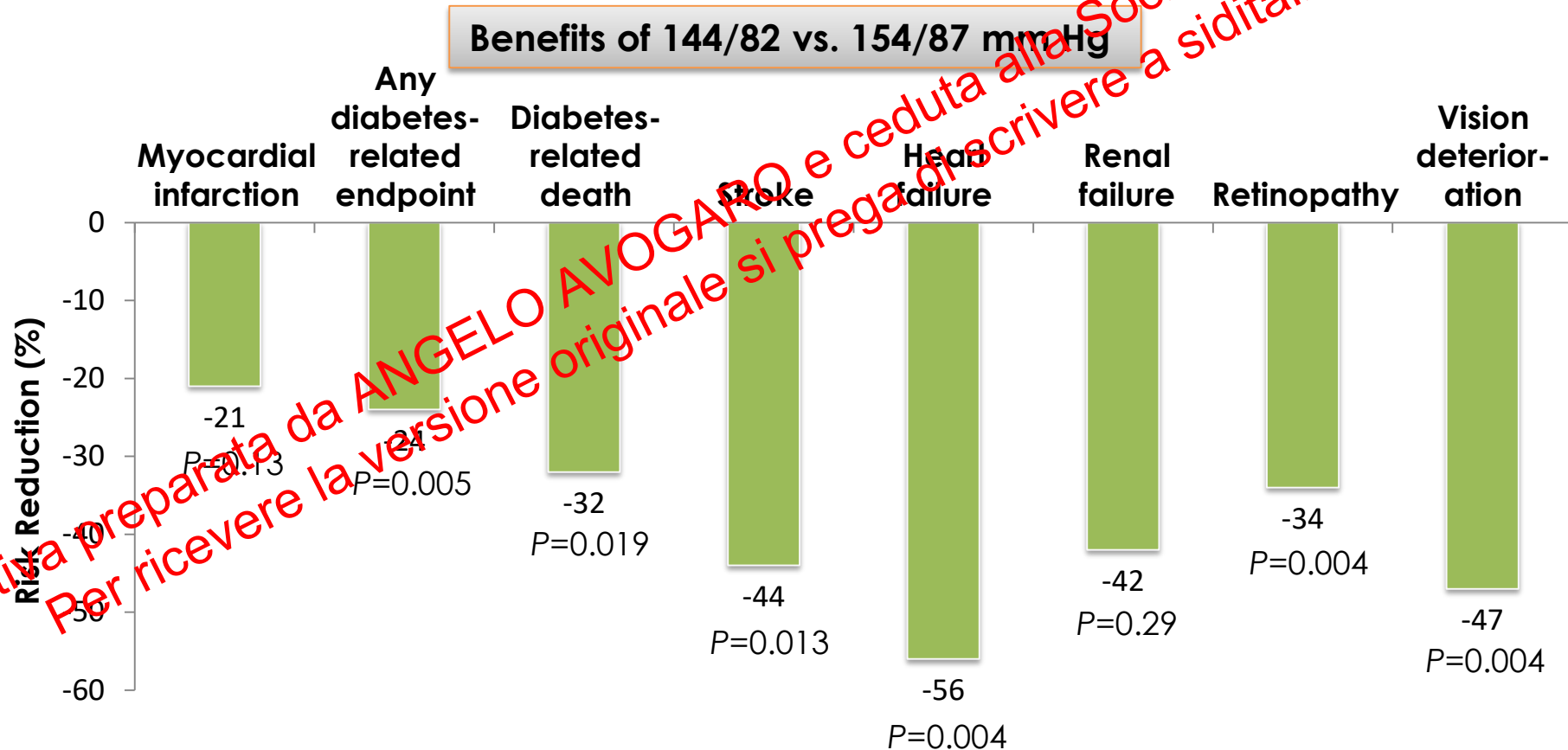
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A summary of the incidence of diabetes, hypertension, and clinical manifestations.

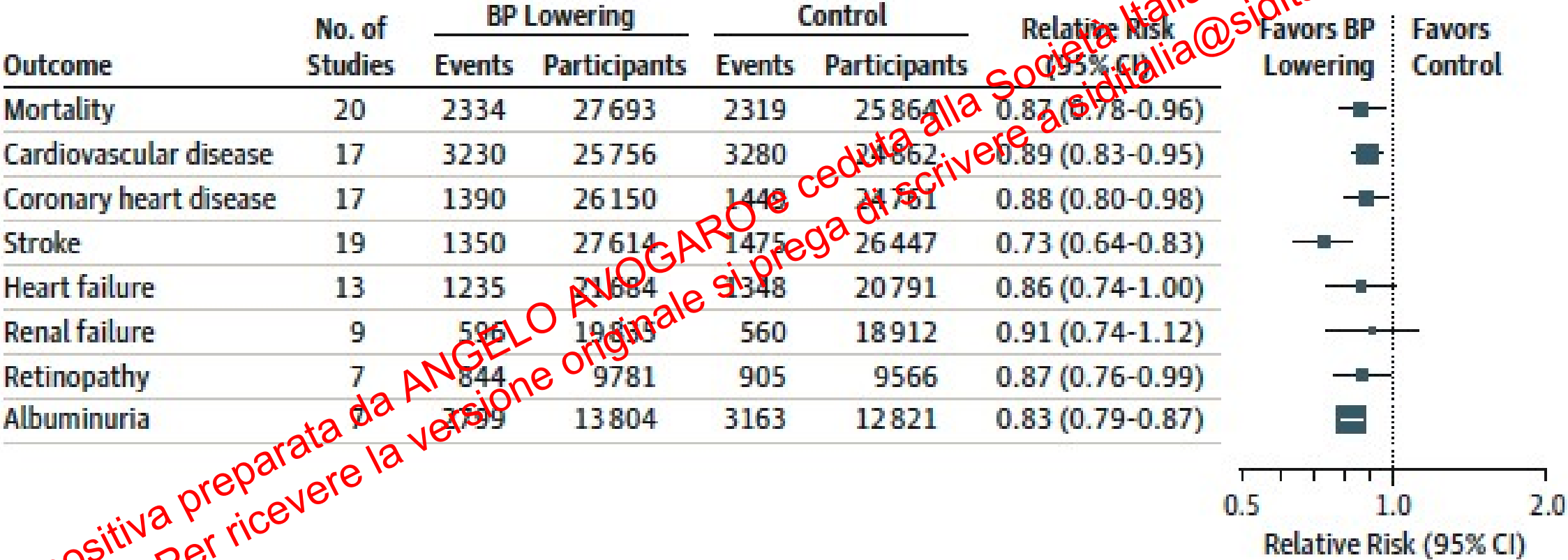


BP Reductions and Risk of Microvascular and Macrovascular Complications in T2D

United Kingdom Prospective Diabetes Study
(N=1148)

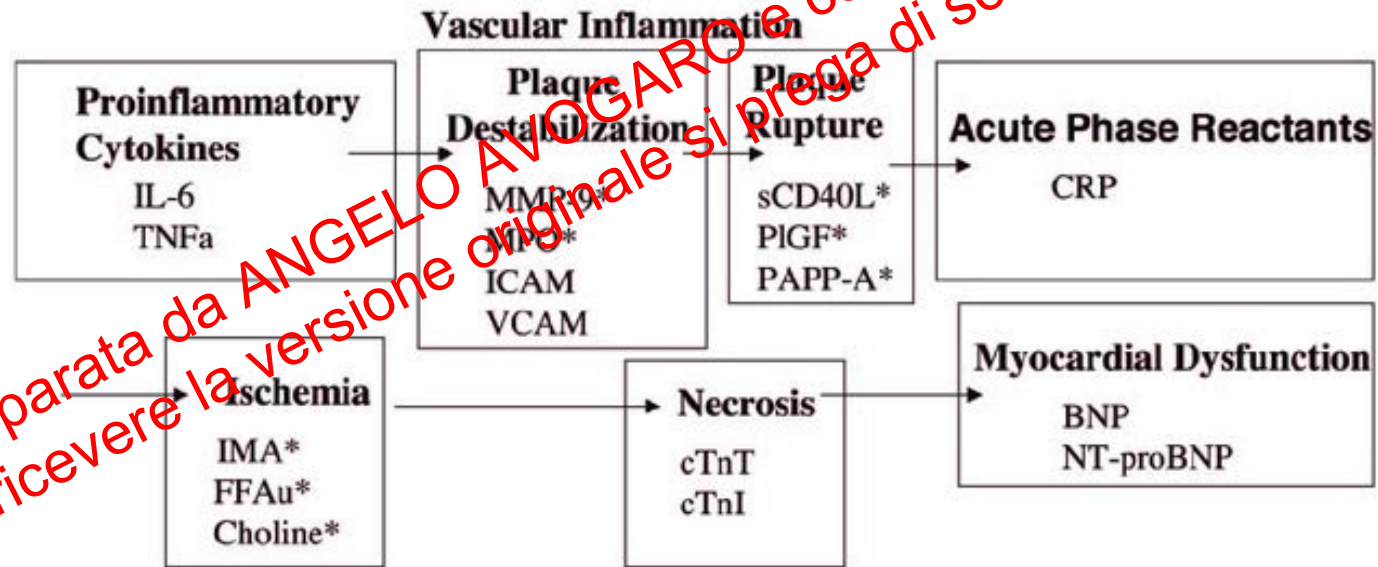
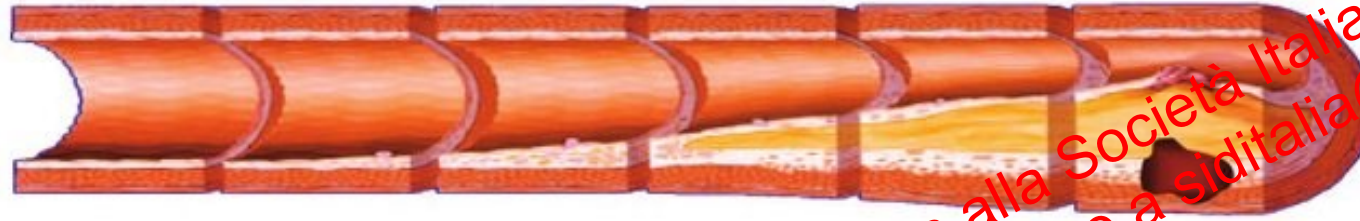


Standardized Associations between 10-mmHg Lower Systolic BP and All- Cause Mortality Macrovascular Outcomes, and Microvascular Outcomes in Diabetic Patients



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L'infiammazione è una componente importante della placca aterosclerotica



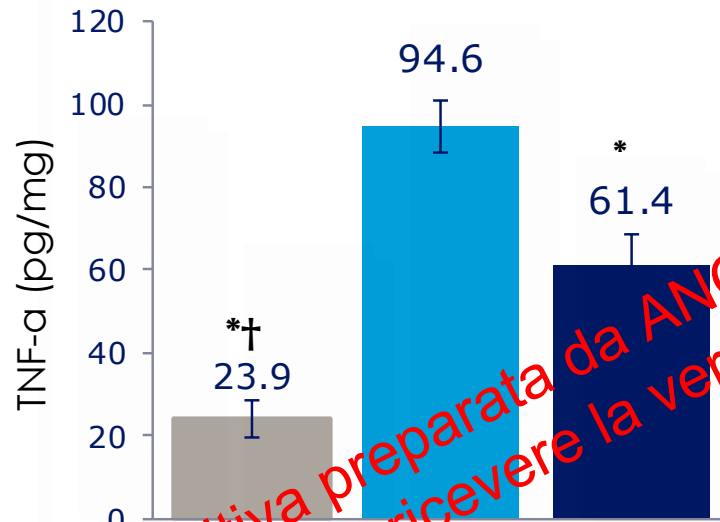
Incretin therapy improves indicators of plaque stability in patients with T2DM

■ Non-diabetes control N=30

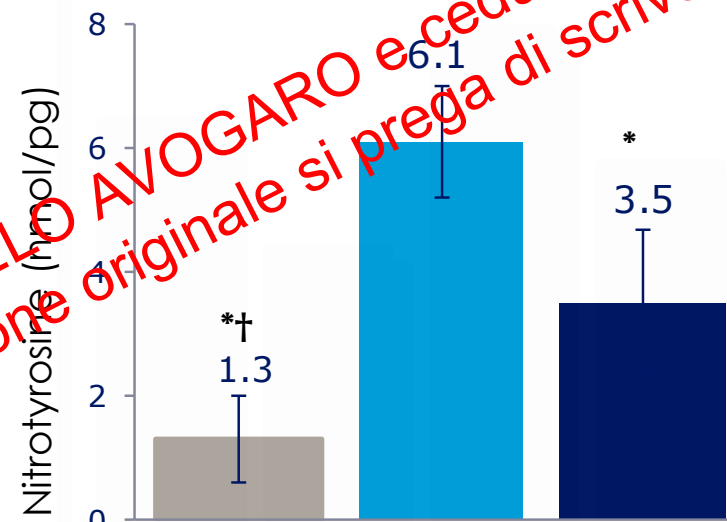
■ Never incretin users N=28

■ Current incretin users N=24

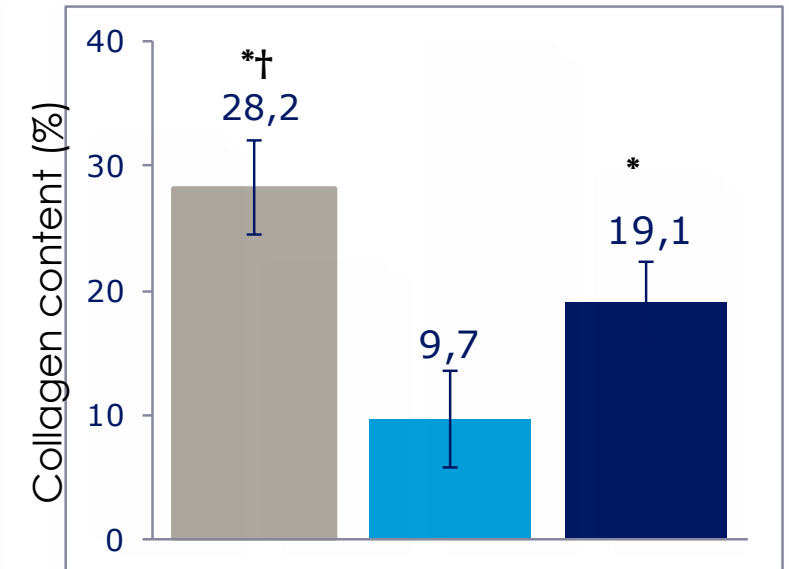
Inflammation



Oxidative stress



Collagen content



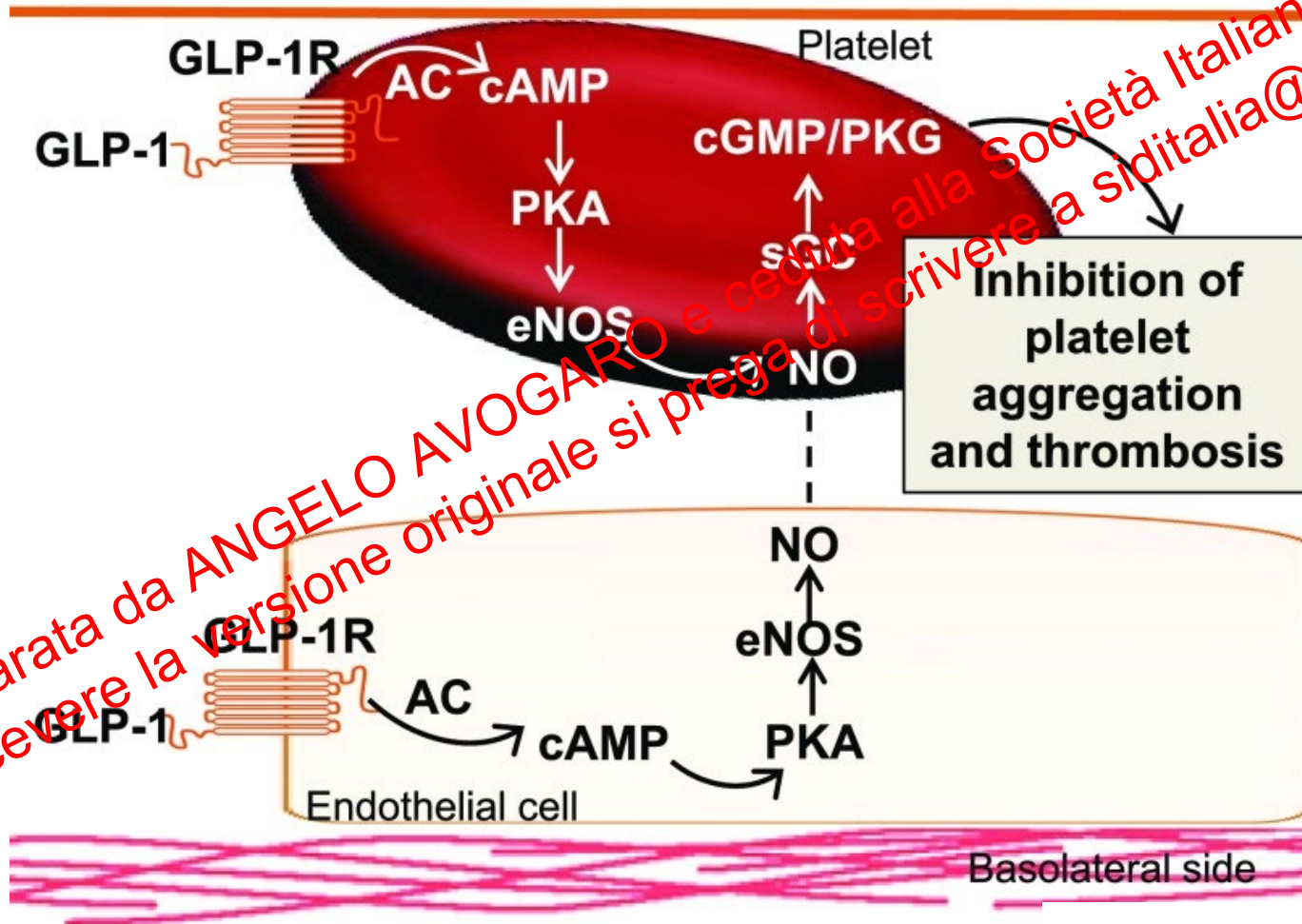
* $p < 0.05$ vs. never users group; † $p < 0.05$ vs. current users group.

Atherosclerotic plaques from patients undergoing carotid endarterectomy; patients included patients without diabetes and patients with T2DM ± incretin therapy.

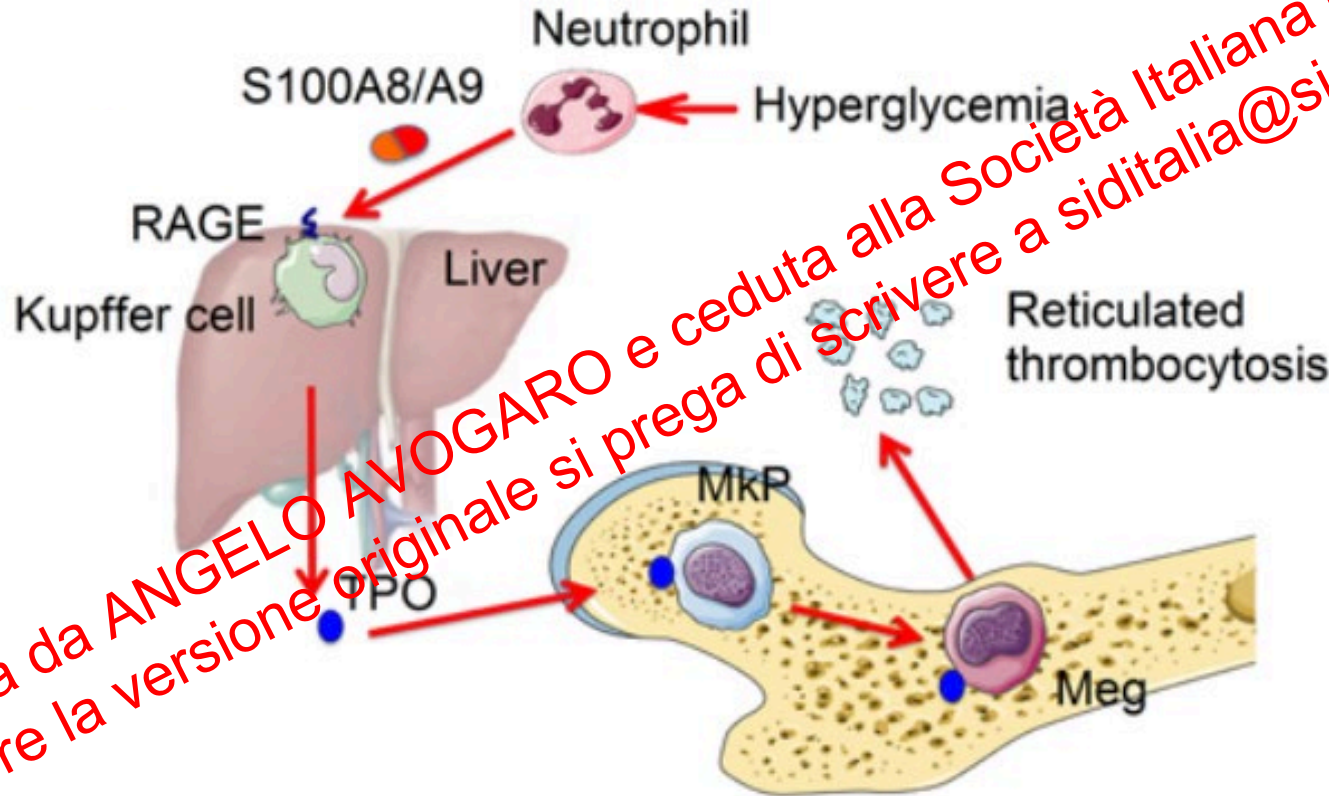
TNF-α, tumour necrosis factor-α; T2DM, type 2 diabetes mellitus.

Balestrieri ML et al. *Diabetes* 2015;64:1395–1406.

Proposed mechanisms of GLP-1R activation in the prevention of platelet aggregation and thrombosis



Diabetes, Neutrophil, and reticulated platelets

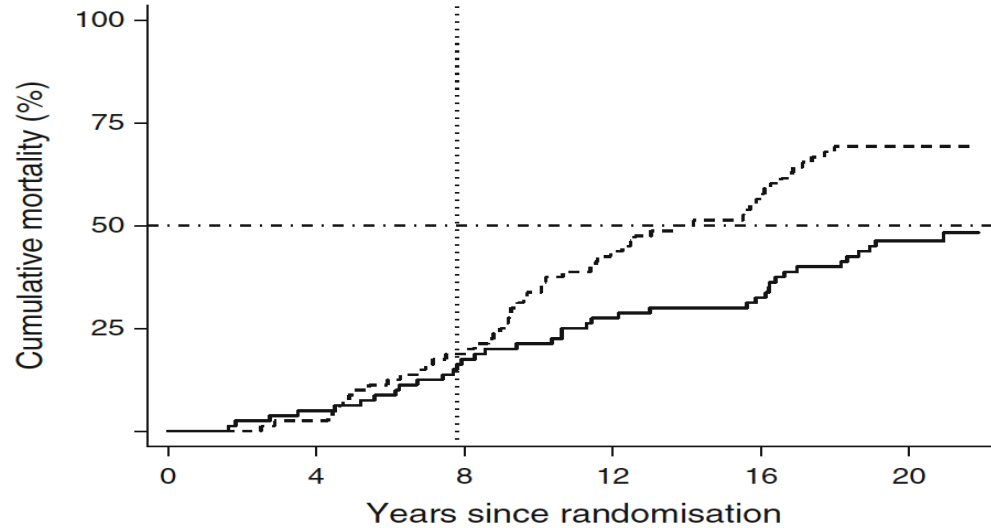


TPO: Thrombopoietin
MkP: megakaryocyte progenitors

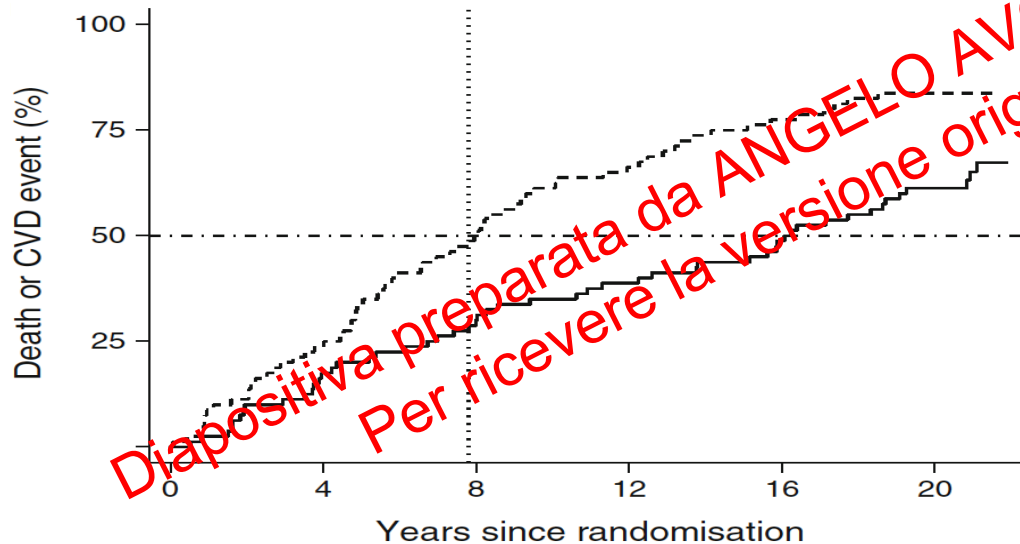
Kraakman et al. JCI 2017

Years of life gained by multifactorial intervention

21 years follow-up on the Steno-2 randomized trial

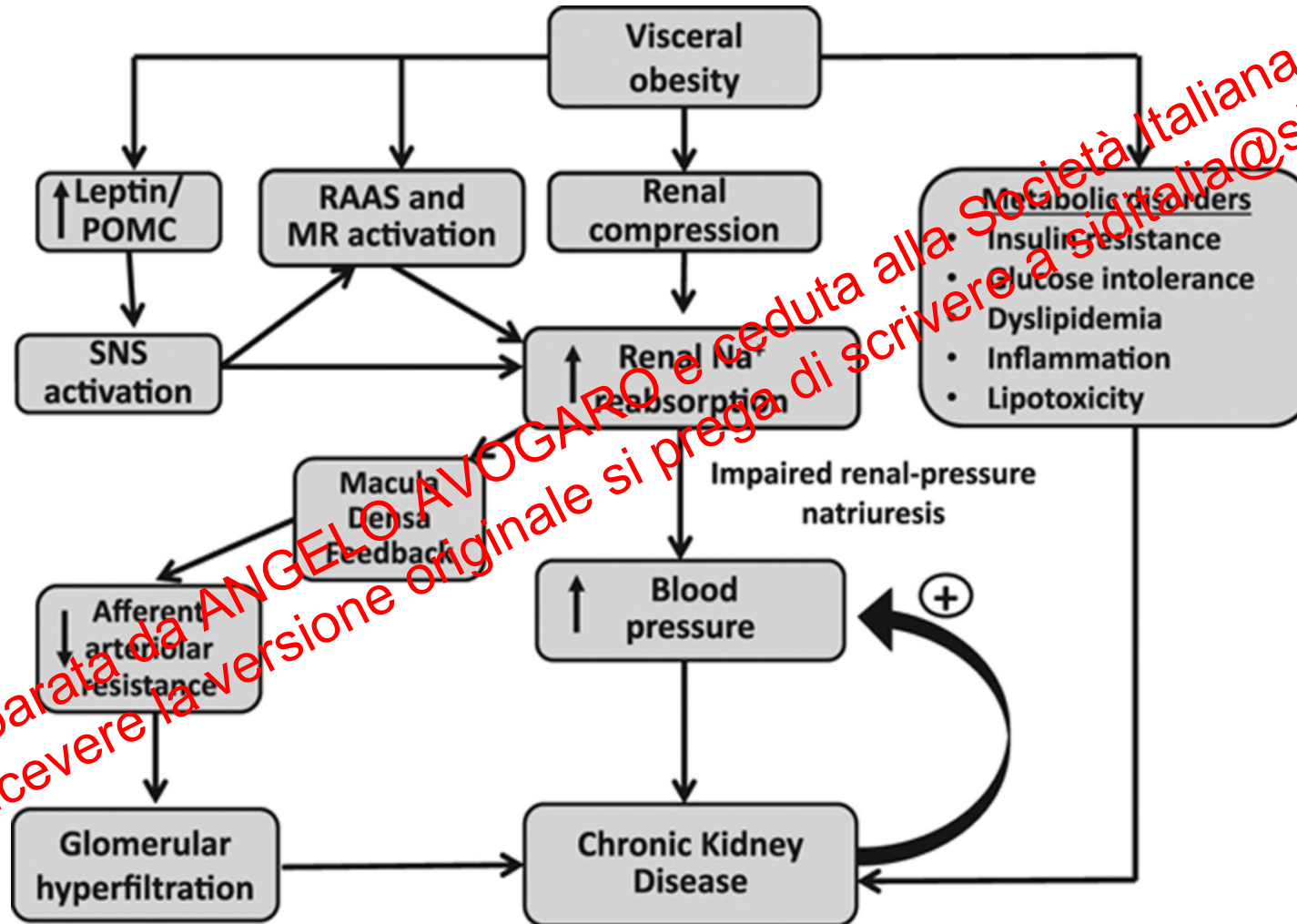


Median survival time in original intensive-therapy group was 7.9 years longer than in the conventional-therapy group



Median difference in survival before first CVD event was 8.1 years in favor of the original intensive-therapy group

Summary of mechanisms by which obesity initiates development of hypertension and renal injury



Holistic Treatment approach beyond glycemia in a patients with type 2 diabetes



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