Congresso congiunto SIN-SID

I farmaci ipoglicemizzanti nefroprotettivi: SGLT2-I, GLP1-RA

Il punto di vista del Diabetologo

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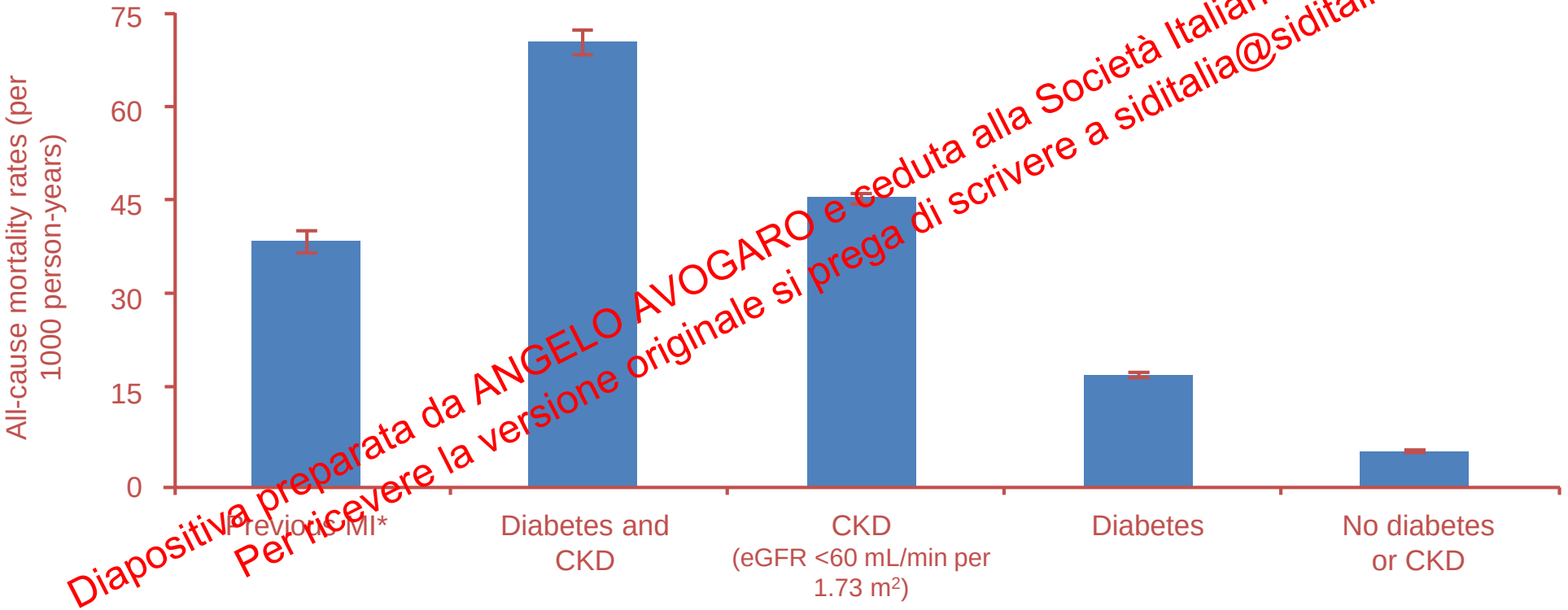
Conflitti di Interesse di Angelo Avogaro

Dichiaro che negli ultimi 5 anni ho ricevuto compensi per advisory board e relazioni dalle seguenti aziende:

AstraZeneca, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly, Bruno Farmaceutici, Mundipharma, Amgen, Servier, Recordati, GlaxoSmithKline, Merck Sharp & Dohme, Novartis, Novo Nordisk, Sanofi, Vifor Pharma, e Takeda.

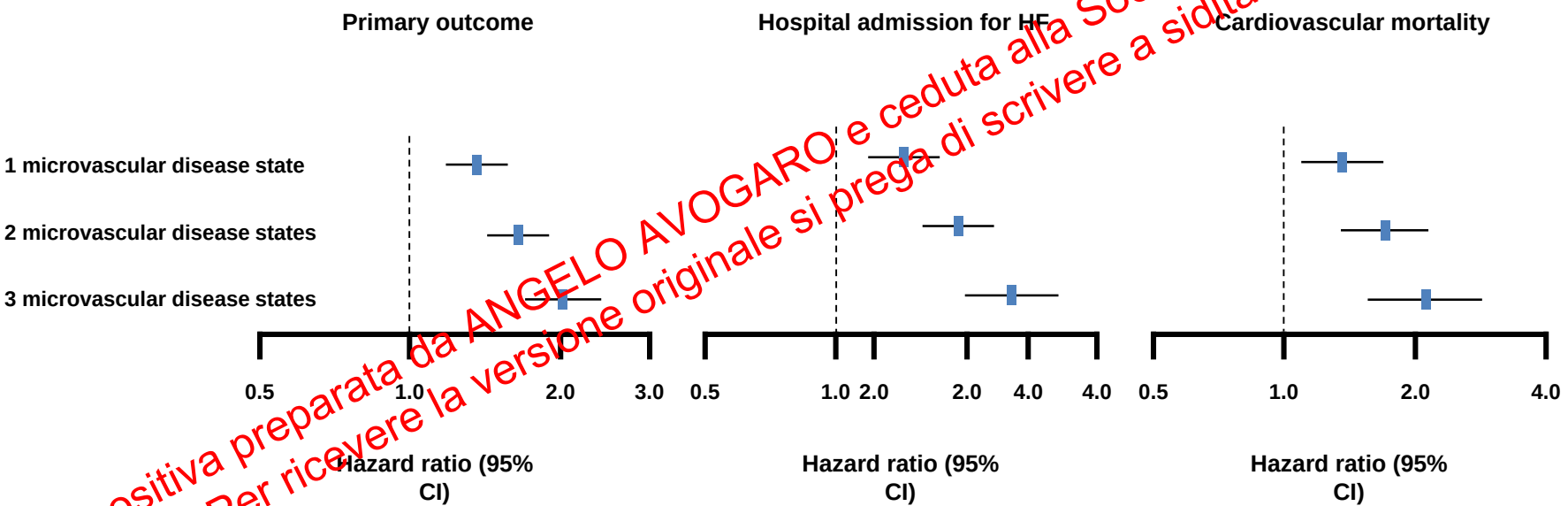
Renal disease is associated with increased all-cause mortality



CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MI, myocardial infarction
*Includes participants with or without diabetes and chronic kidney disease
Tonelli et al. *Lancet* 2012;380(9844):807–14.

Prevention or delay of progression of microvascular complications may help reduce CV risks

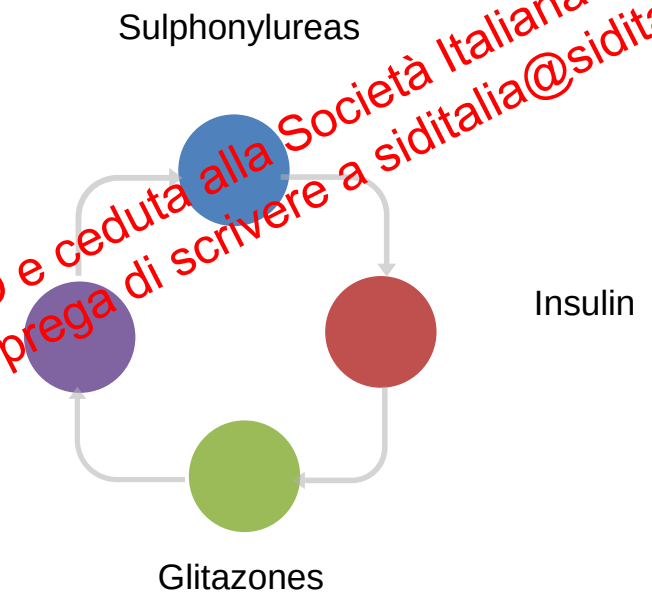
The burden of microvascular disease is a determinant of **future CV risk**[1]



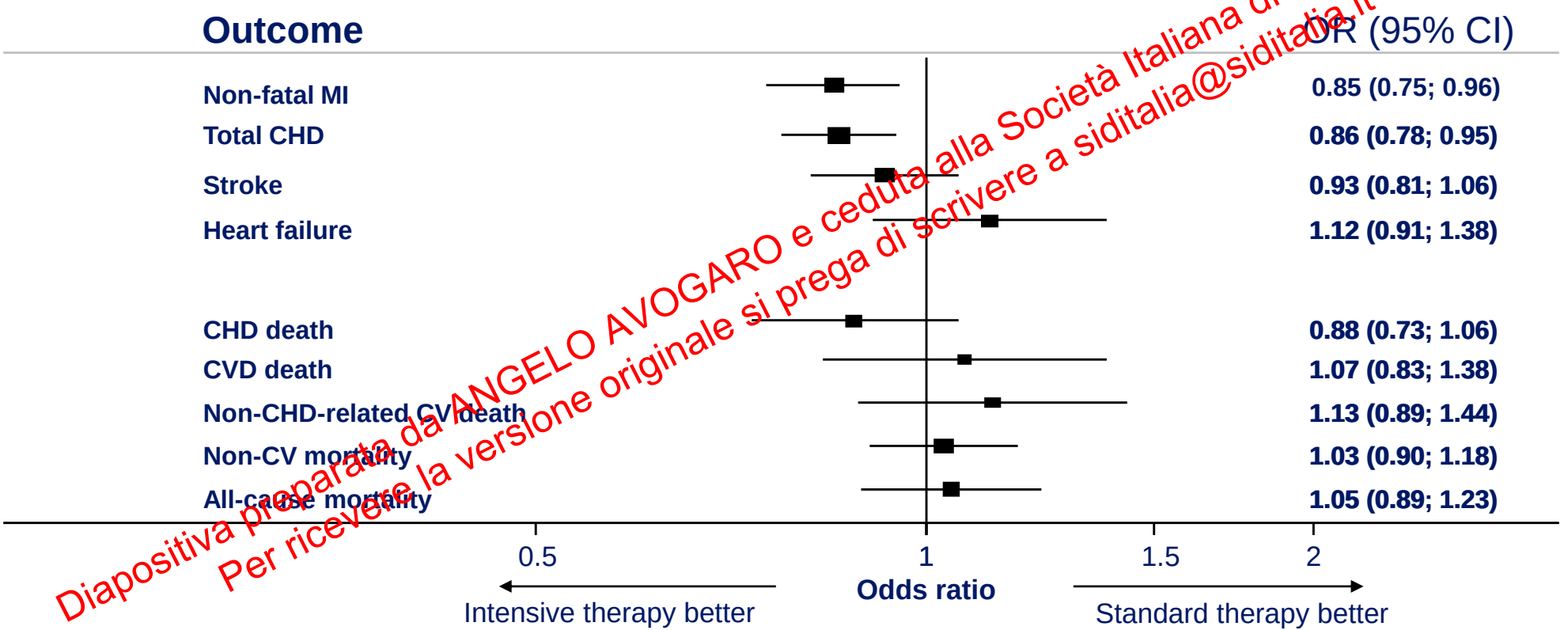
CV, cardiovascular; RCT, randomized control trial

1. Adapted from Brownrigg JR et al., Lancet Diabetes Endocrinol 2016;4:588–597

UKPDS	7.5% > 7%
ACCORD	8.3% > 6.6%
ADVANCE	7.5% > 6.5%
VADT	9.4% > 6.9%

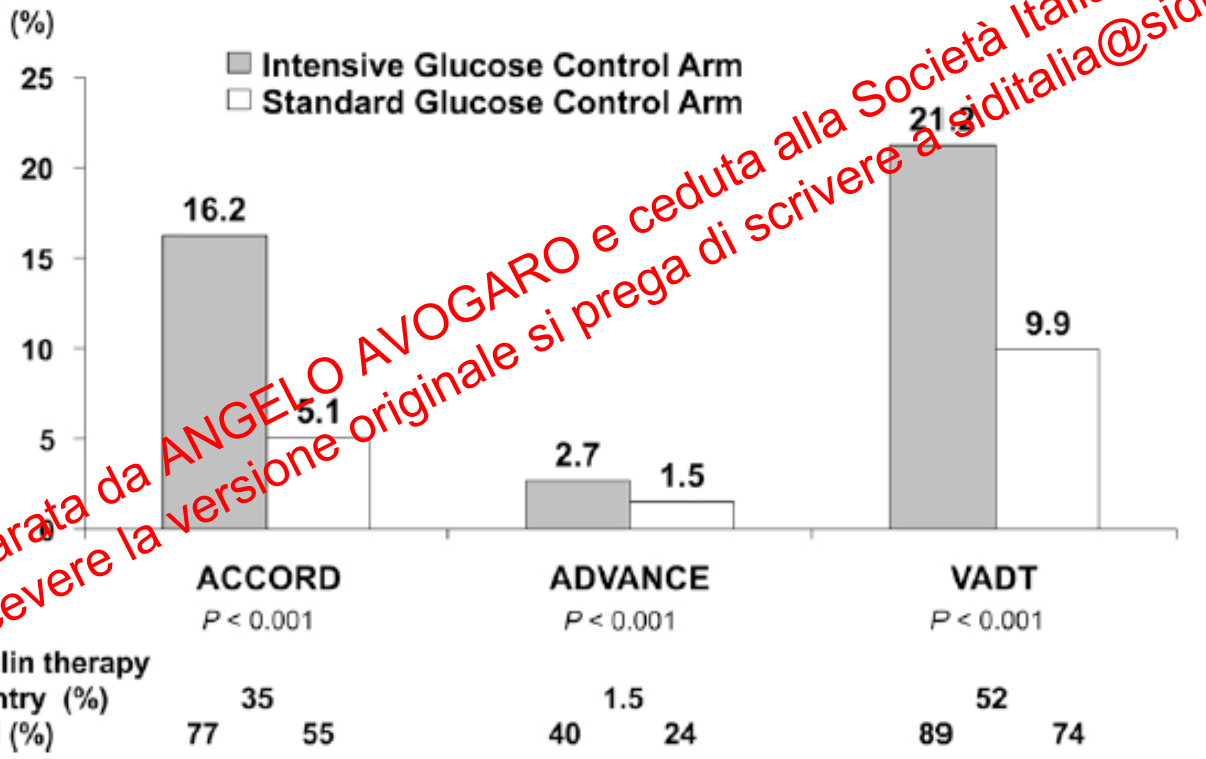


Meta-analysis: Comparison of effect of more intensive glycaemic control on clinical outcomes*

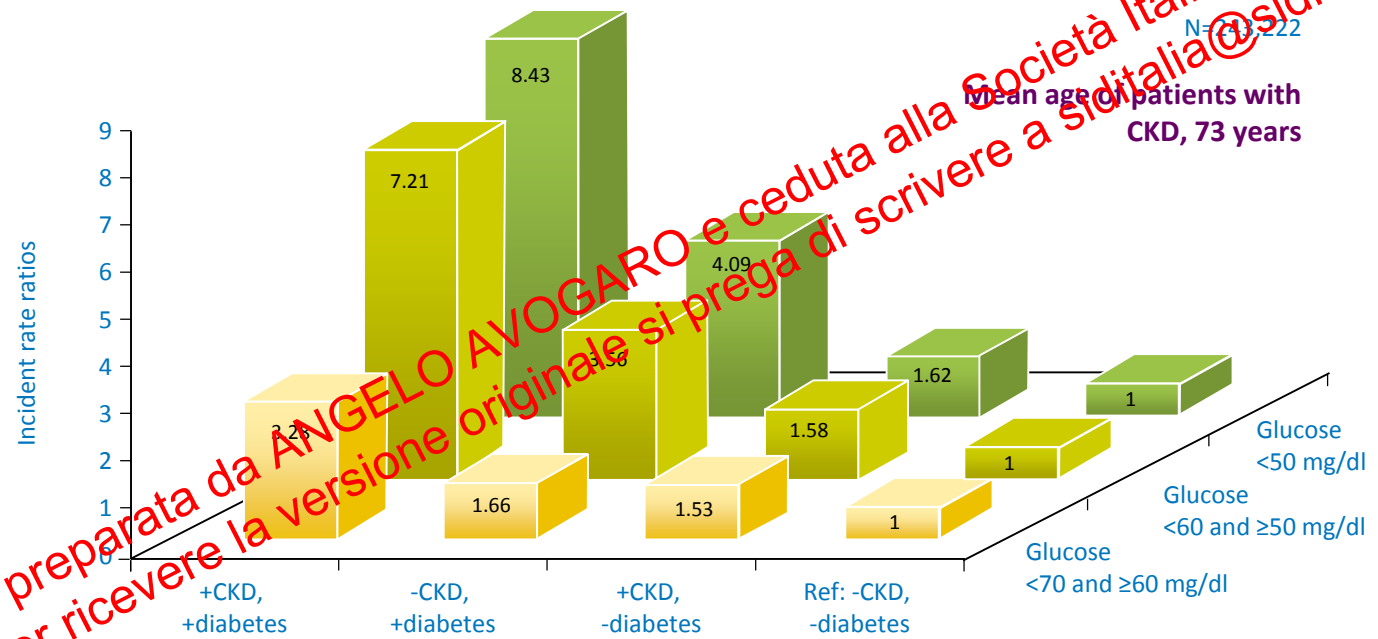


*Contributing studies include: PROactive, ADVANCE, VADT & ACCORD
CI, confidence interval; CHD, chronic heart disease; CVD, cardiovascular death; MI, myocardial infarction; OR, odds ratio.
Ray KK. *Lancet* 2009;373:1765–1772, supplementary figure 4.

Proportion reporting major hypoglycaemia in recent trials



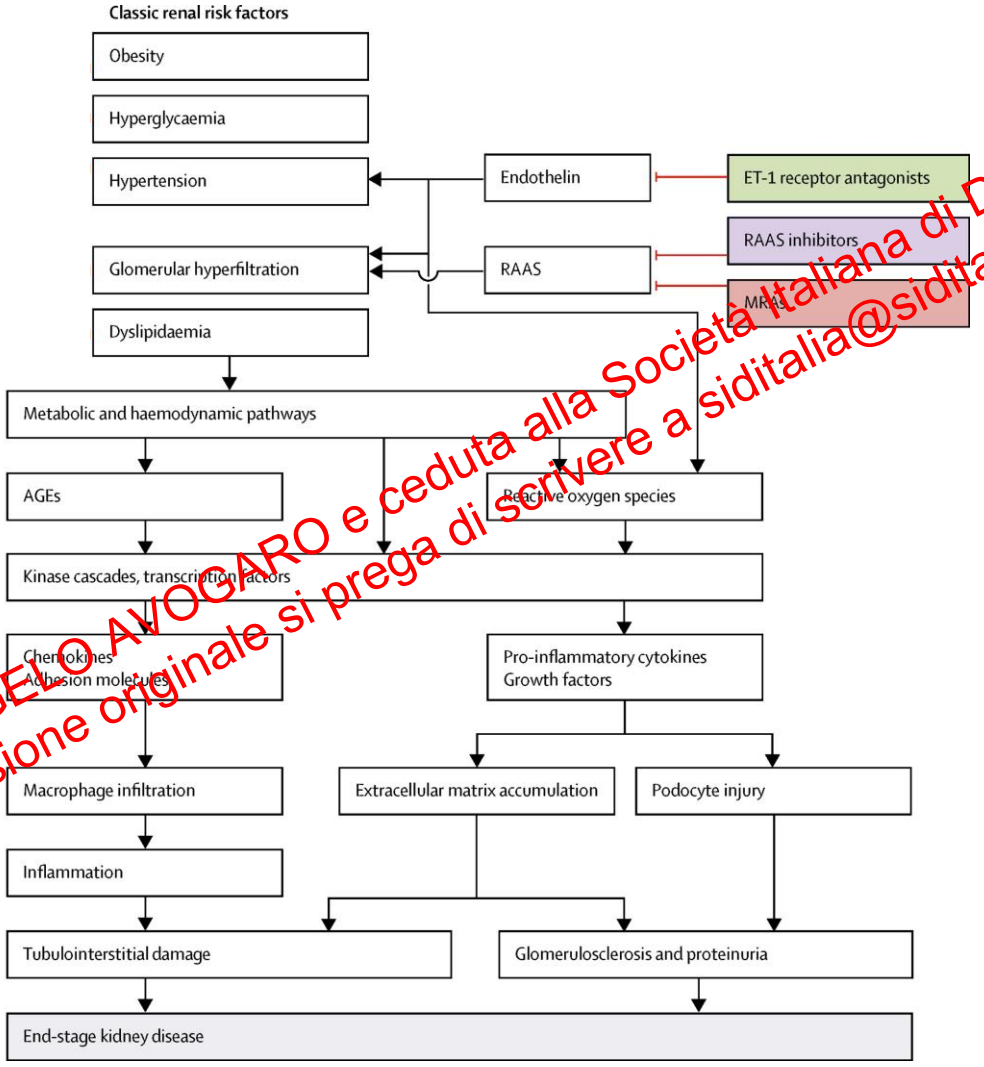
Diabetes increases the risk of hypoglycaemia in patients with chronic kidney disease



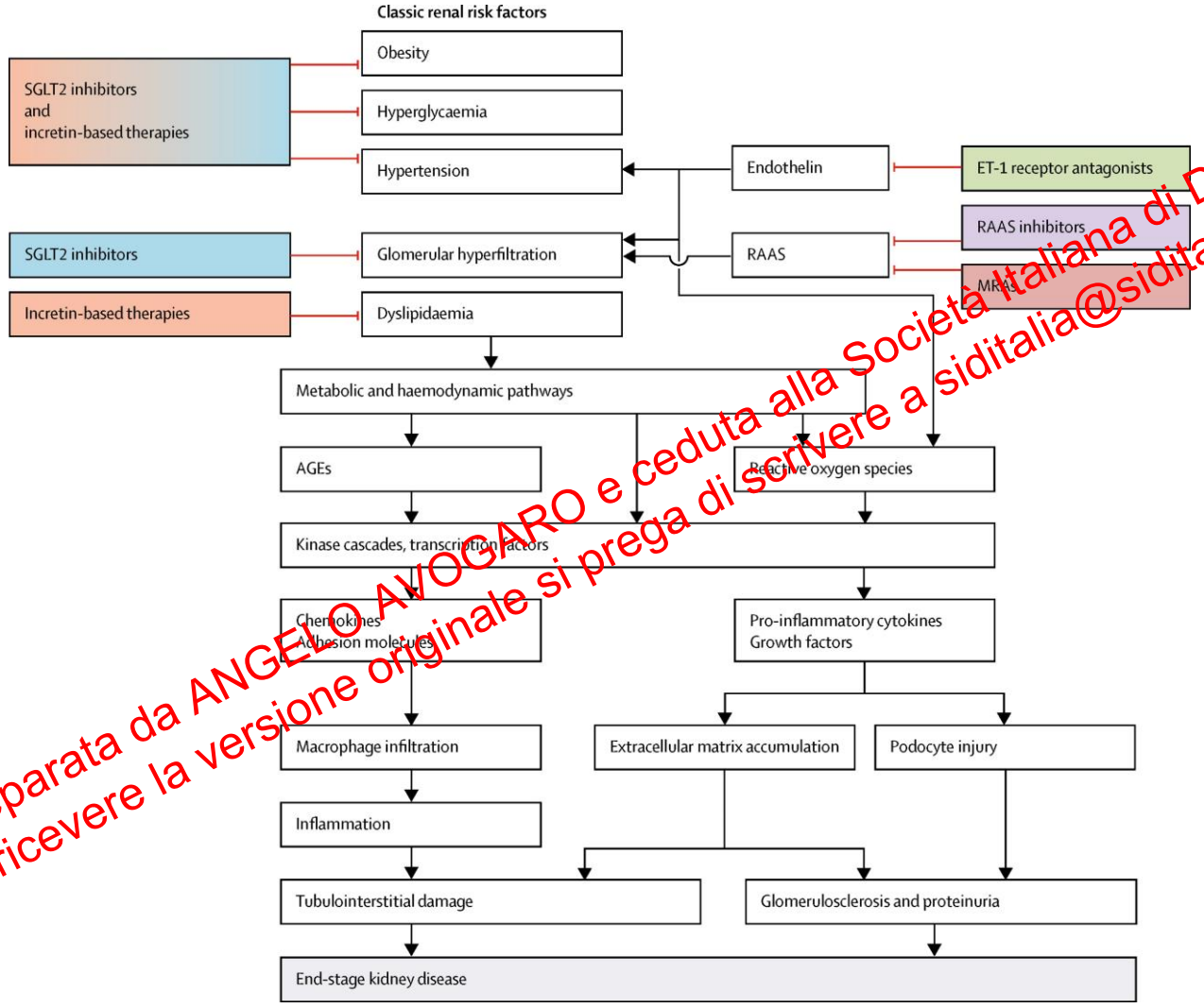
Moef MF, et al. Clin J Am Soc Nephrol. 2009;4:1121-7.

La riduzione dell'HbA1c a target con strategie non innovative:

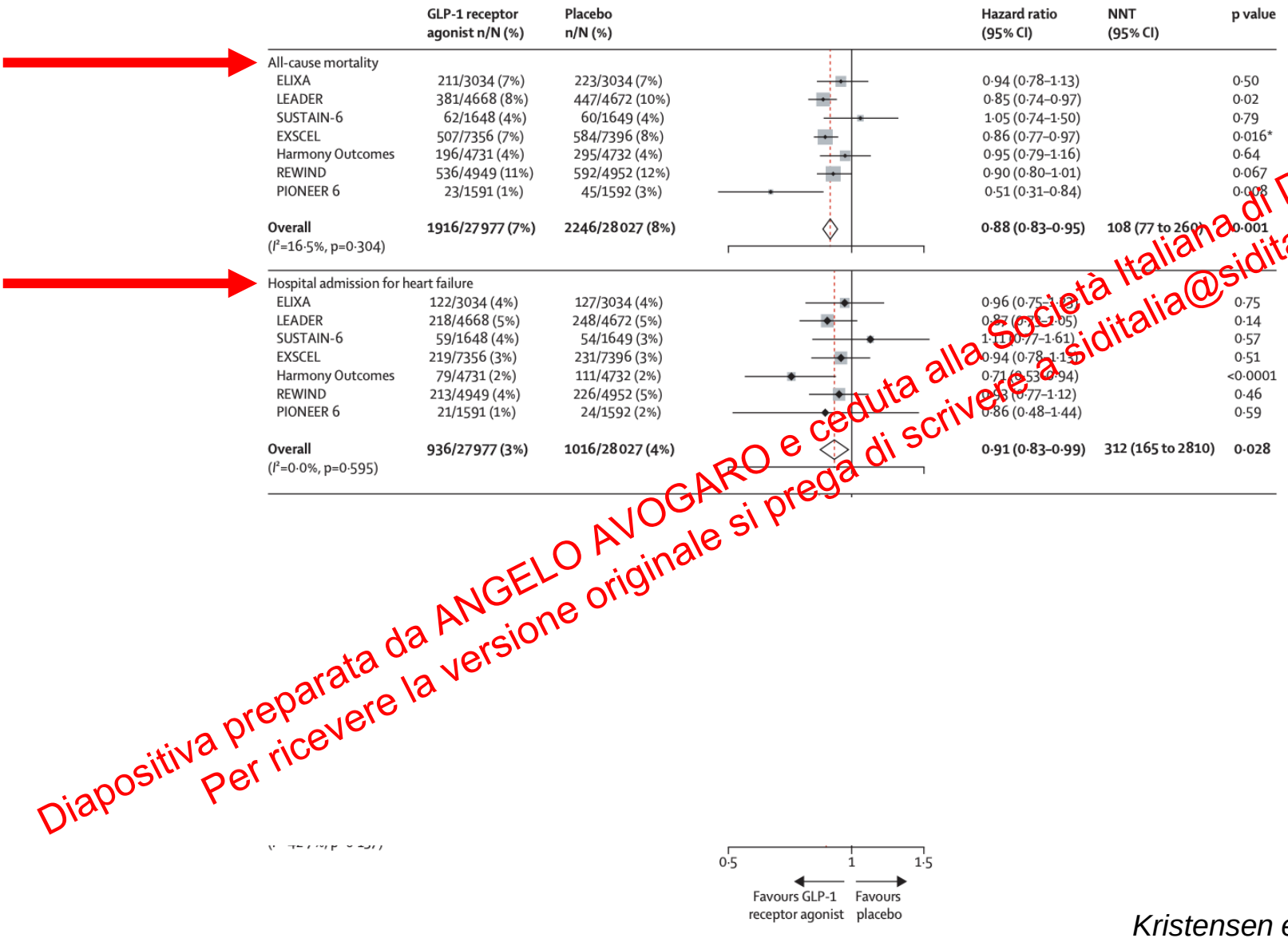
1. Espone al rischio di ipoglicemie severe
2. Non conferisce nefro-protezione indipendentemente dalla riduzione della glicemia



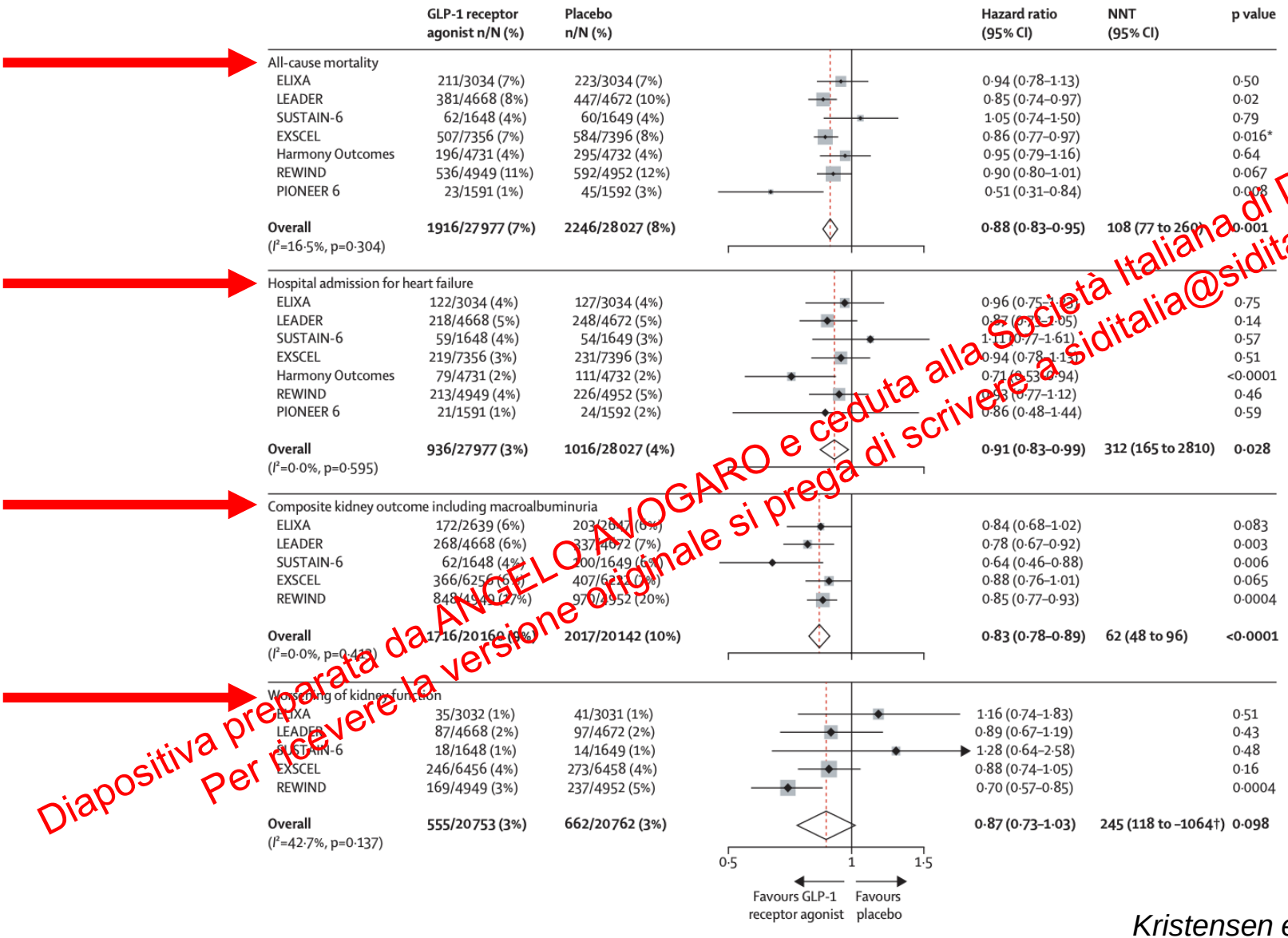
The Lancet Diabetes & Endocrinology 2019 7, 397-412DOI: (10.1016/S2213-8587(18)30263-8)



The Lancet Diabetes & Endocrinology 2019 7, 397-412DOI: (10.1016/S2213-8587(18)30263-8)



Kristensen et al. Lancet DE 2019



Kristensen et al. Lancet DE 2019

SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials

Thomas A Zelniker, Stephen D Wiviott, Itamar Raz, Kyungah Im, Erica L Goodrich, Marc P Bonaca, Ofri Mosenzon, Eri T Kato, Avivit Cahn, Remo H M Furtado, Deepak L Bhatt, Lawrence A Leiter, Darren K McGuire, John P H Wilding, Marc S Sabatine

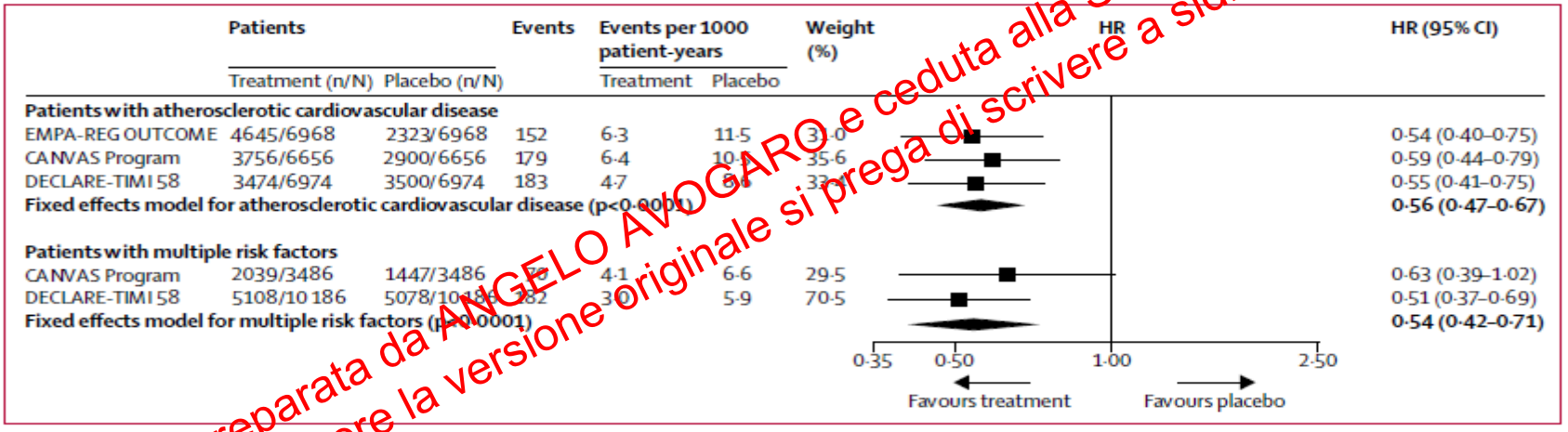
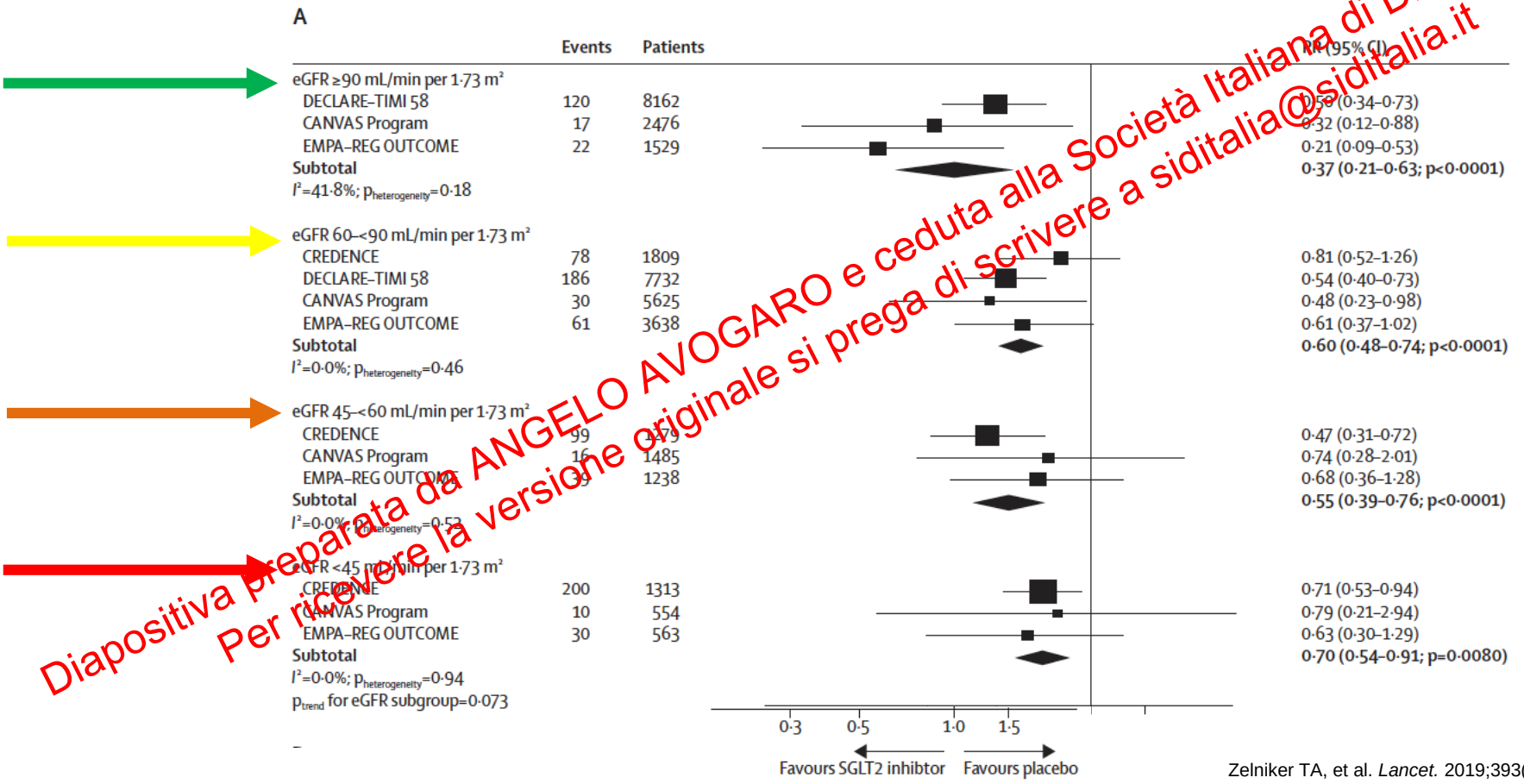


Figure 4: **Meta-analysis of SGLT2 trials on the composite of renal worsening, end-stage renal disease, or renal death stratified by the presence of established atherosclerotic cardiovascular disease**

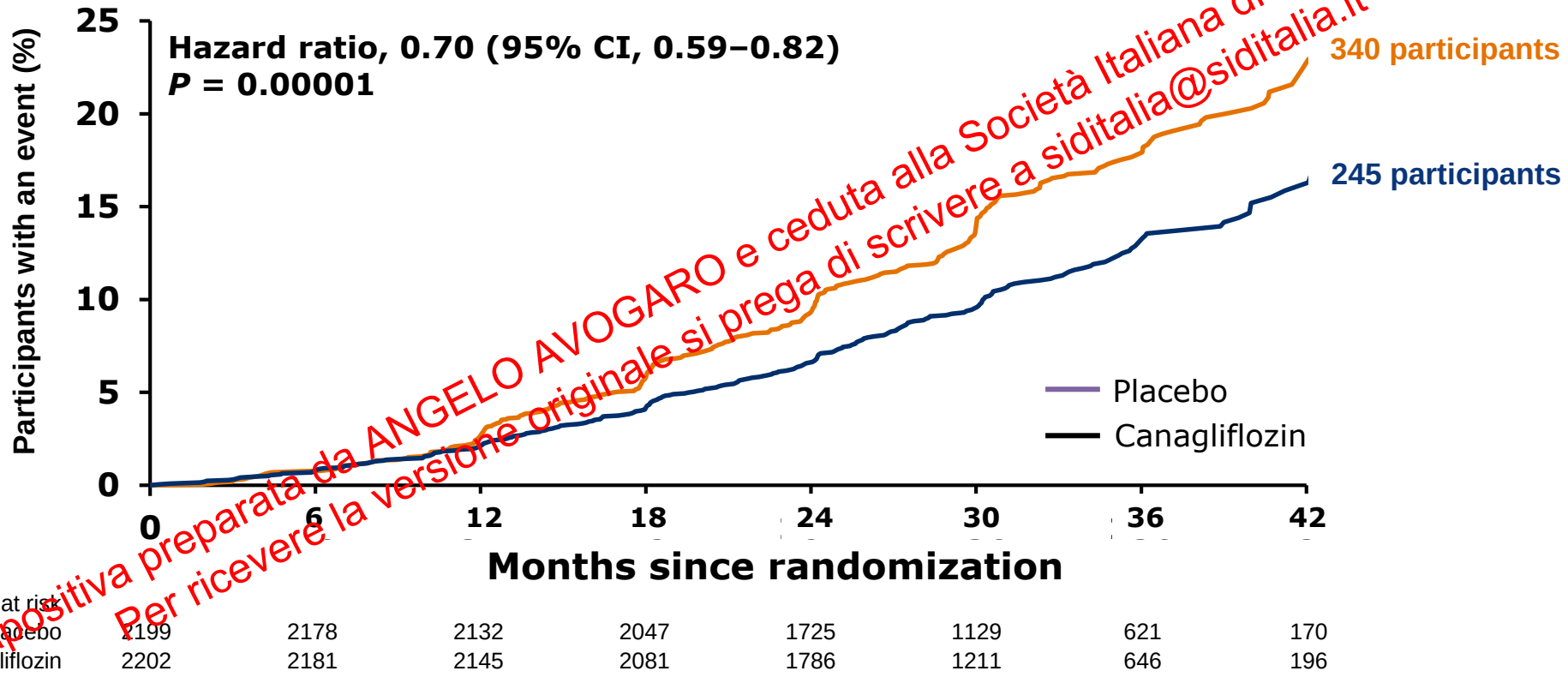
Atherosclerotic cardiovascular disease: Q statistic=0·19, p=0·91, I^2=0%; multiple risk factors: Q statistic=0·52, p=0·47, I^2=0% The p value for subgroup differences was 0·71. Tests for subgroup differences were based on F tests in a random effect meta-regression estimated using restricted maximum likelihood and Hartung Knapp adjustment. HR=hazard ratio. SGLT2i=sodium-glucose cotransporter-2 inhibitors.

Effect of SGLT2 inhibitors on substantial loss of kidney function, ESKD, death due kidney disease stratified by baseline eGFR

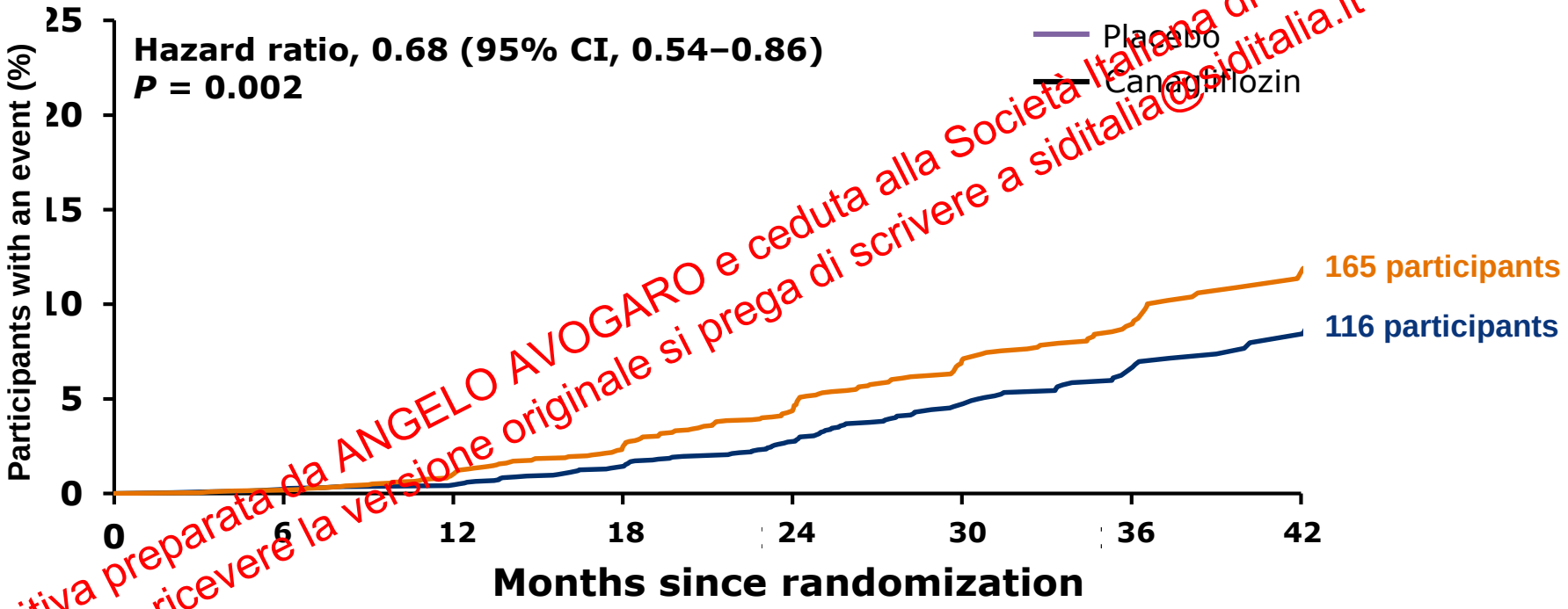


Zelniker TA, et al. *Lancet.* 2019;393(10166):31-39.

Primary Outcome:
ESKD, Doubling of Serum Creatinine, or Renal or CV Death



End-stage Kidney Disease



Primary or secondary prevention?

Risk enhancers in Diabetes

Long duration (≥10 years for type 2 diabetes mellitus[S4.3-20] or ≥20 years for type 1 diabetes mellitus[S4.3-6]
Albuminuria ≥30 mcg of albumin/mg creatinine[S4.3-25]
eGFR <60 mL/min/1.73 m^2[S4.3-25]
Retinopathy[S4.3-19]
Neuropathy[S4.3-16]
ABI <0.9[S4.3-22,S4.3-24]

Conclusioni

1. La malattia renale cronica è una complicanza molto frequente che il diabetologo deve saper prevenire utilizzando farmaci innovativi
2. La distinzione tra prevenzione primaria e secondaria è fuorviante: vi sono pazienti ad altissimi rischio Cv senza precedente evento, specie coloro con malattia renale cronica
3. Diabetologo e nefrologo devono condividere il follow-up del paziente con diabete e malattia renale cronica avanzata