

Beyond Glycemia 2013

L'approccio terapeutico personalizzato al paziente con diabete tipo 2: efficacia e sicurezza nella complessità

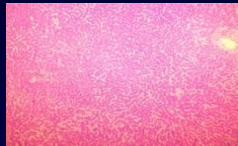
Diabete mellito: la complessità clinica e la complessità nella scelta terapeutica

Enzo Bonora

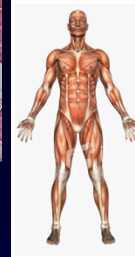
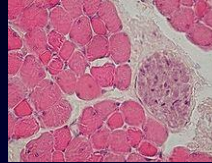
Endocrinologia, Diabetologia e Malattie del Metabolismo
Università e Azienda Ospedaliera Universitaria Integrata
Verona



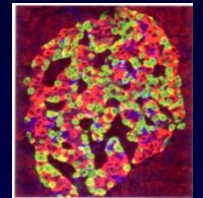
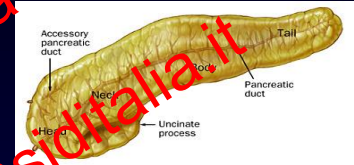
Diabete tipo 2: patogenesi complessa e sistemica



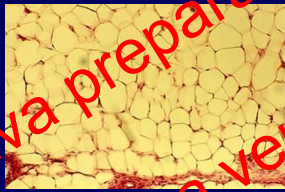
Fegato
Aumentata
produzione di
glucosio



Muscolo scheletrico
Ridotta utilizzazione di glucosio
(trasporto, deposito, ossidazione)



Pancreas endocrino
Ridotta secrezione insulinica
Aumentata secrezione di glucagone



Tessuto adiposo
Rilascio di molecole
diabetogene



Intestino
Ridotto effetto incretinico



Rene
Aumentato riassorbimento
di glucosio



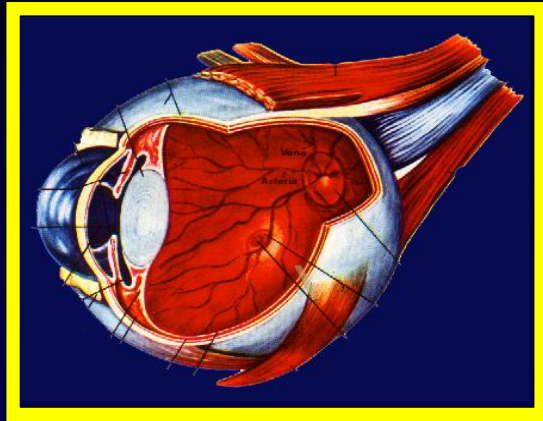
Cervello
Alterato controllo metabolico

Iperglicemia



Diapositiva preparata da Enzo Bonora e condotta alla Società Italiana di Diabetologia.
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Diabete: danno d'organo complesso e sistemico

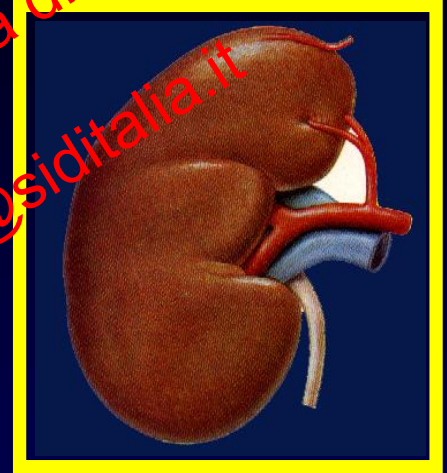


Occhio (retina)

Cute

Gonadi

Apparato
oste articolare



Rene

Iperglicemia

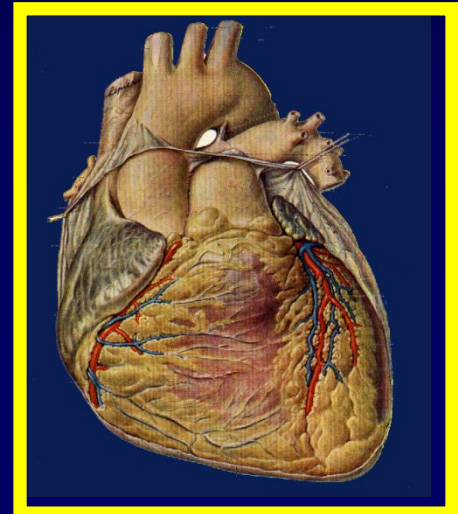
Tubo
digerente

Cervello

Sistema
immune



Nervi



Cuore & Vasi

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Diabete: complicanze gravissime e disabilitanti



Prima causa
di cecità

Causa maggiore
di insufficienza
renale & dialisi

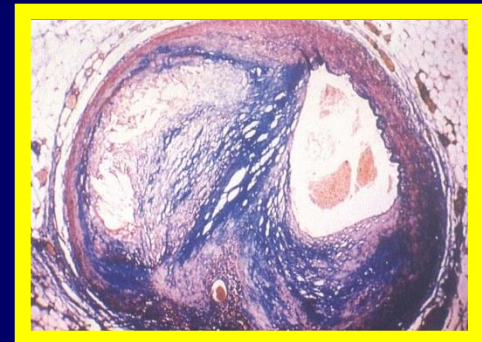


Diabete

Prima causa
di amputazione
non traumatica



Concausa
nel 40-50% di
infarti e ictus



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Incidenza di infarto e ictus nel diabete tipo 2 in Italia

(DAI Study; Avogaro et al, Diabetes Care 2007; Giorda et al, Stroke 2007)

In 10 anni

1 maschio ogni 8 e 1 donna ogni 16

Avranno un infarto (più spesso fatale rispetto ad un non diabetico) o saranno sottoposti ad una rivascolarizzazione coronarica

1 maschio ogni 16 ed 1 donna ogni 16

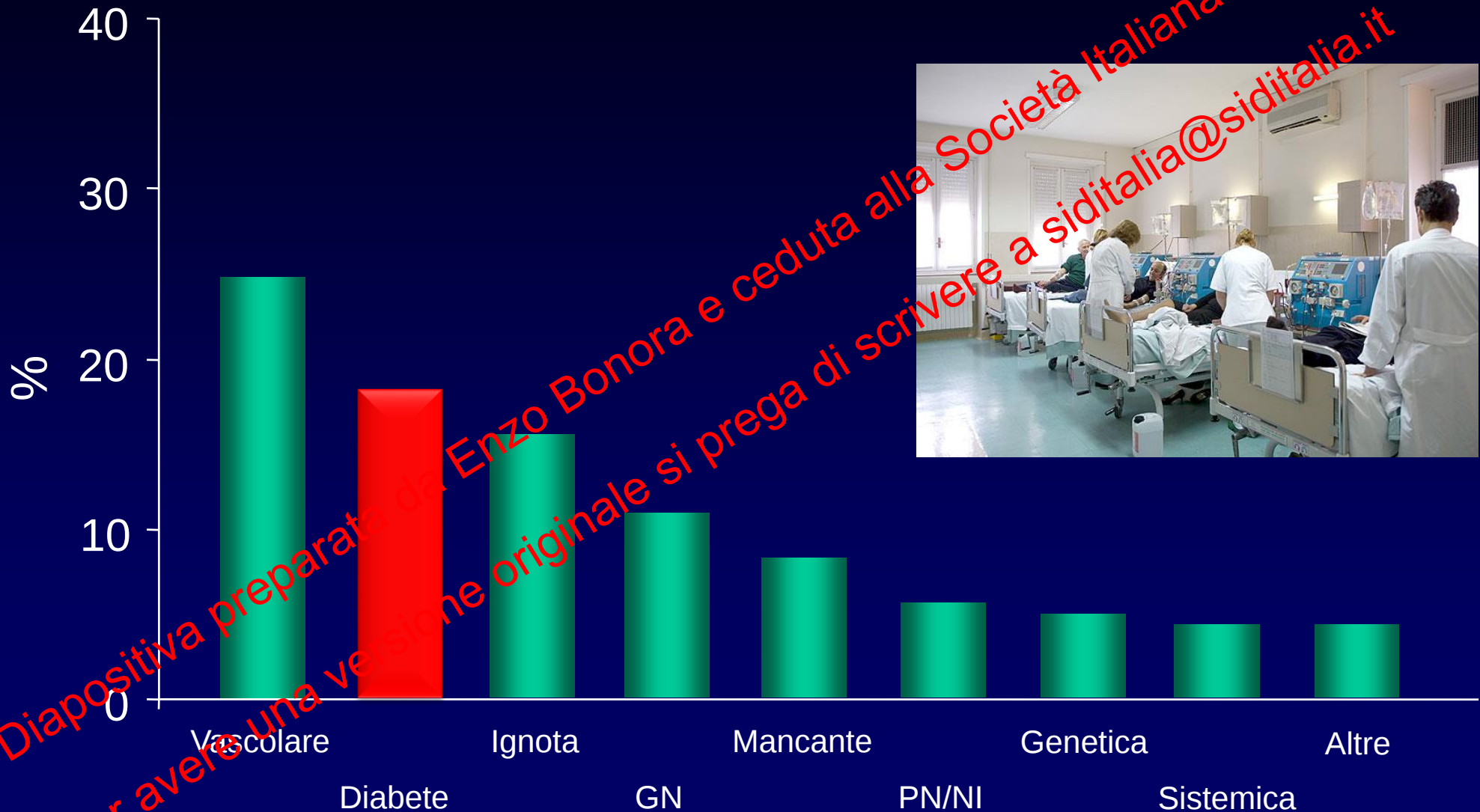
Avranno un ictus (più spesso fatale rispetto ad un non diabetico)



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Casi incidenti di IRC terminale in funzione della causa probabile o accertata

(Registro Italiano di Dialisi e Trapianto, anno 2008)





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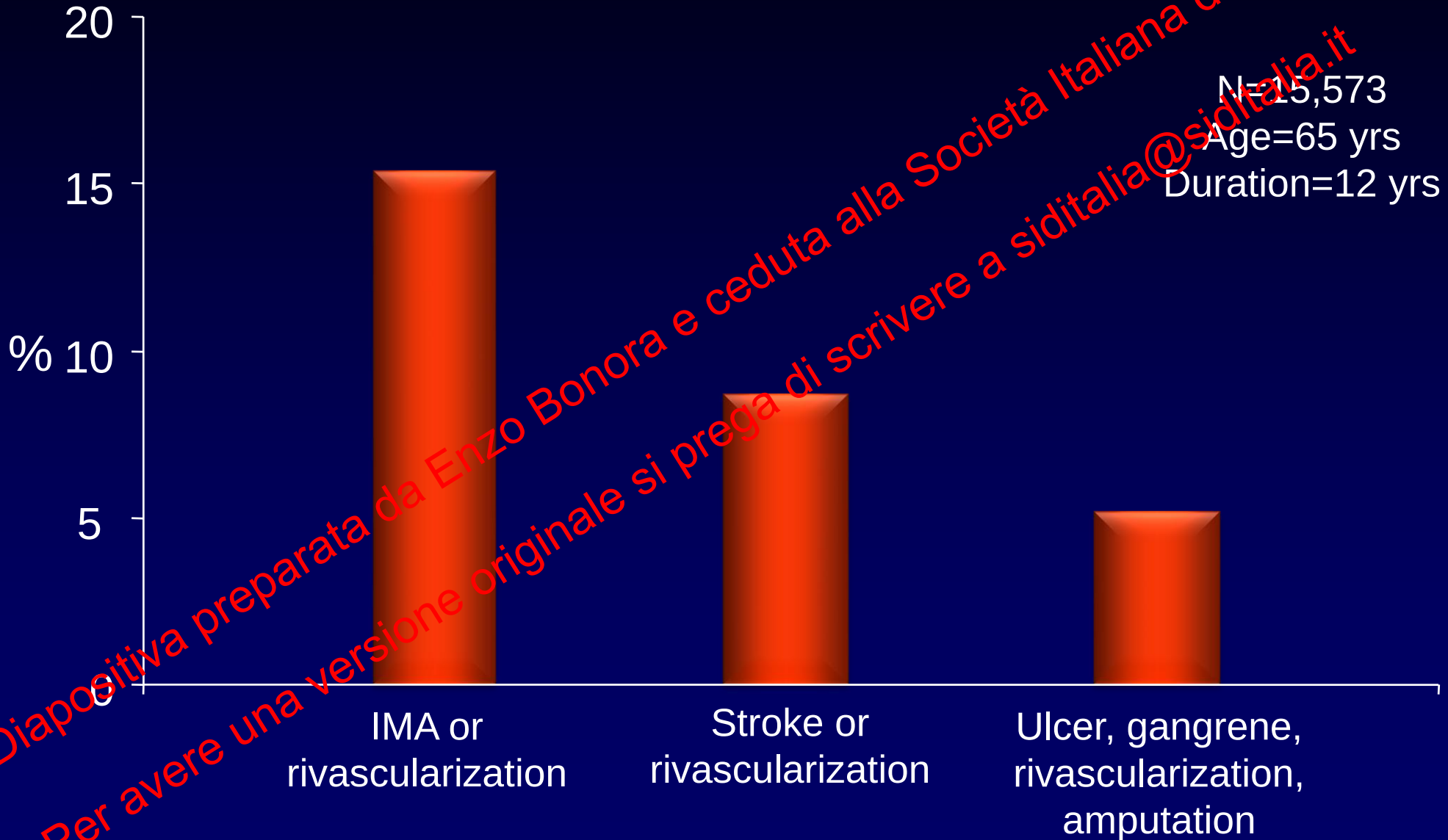
Prevalenza delle complicanze alla diagnosi del diabete tipo 2 a Verona

(Verona Newly Diagnosed Diabetes Study; Bonora et al; dati non pubblicati)



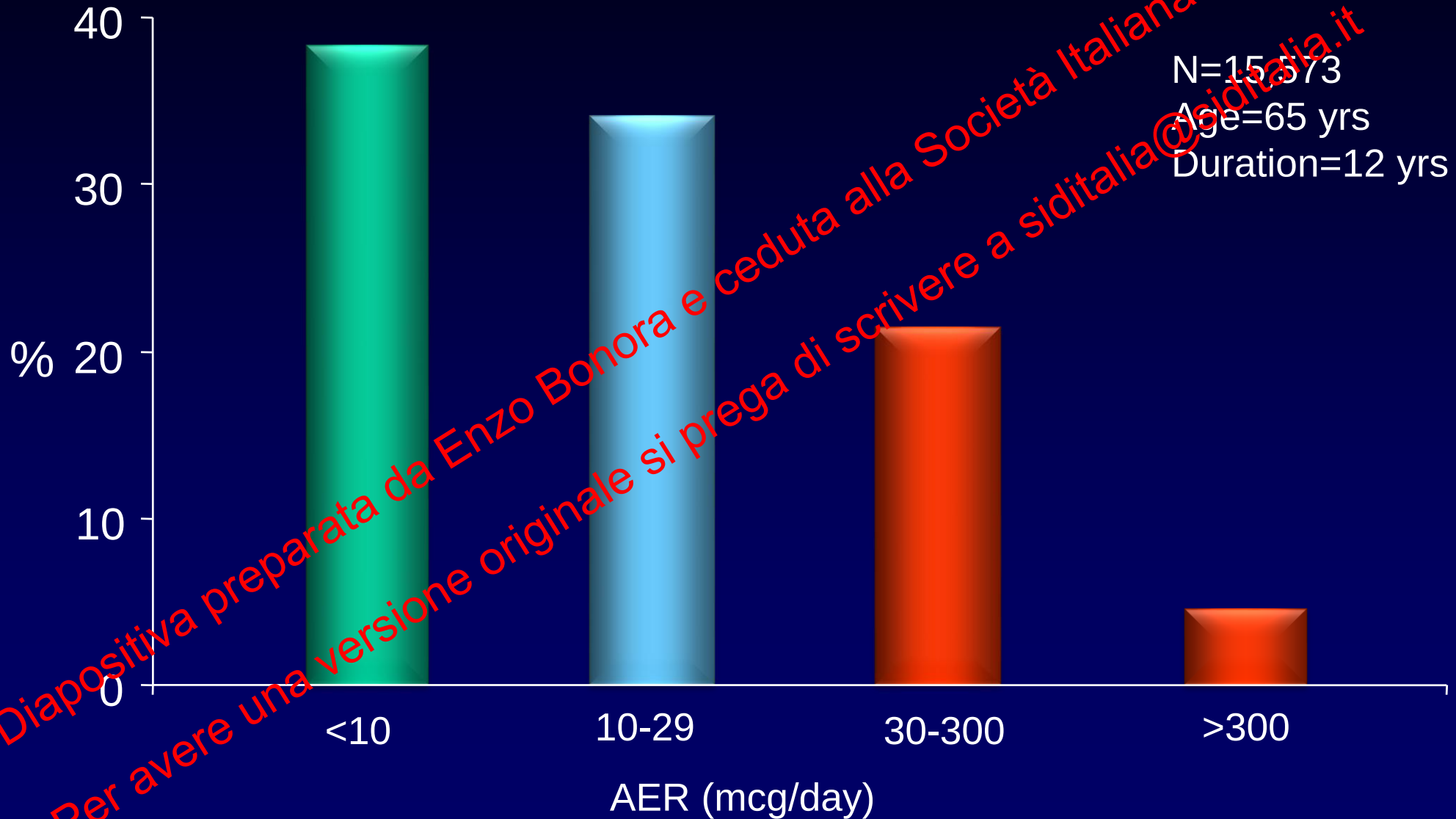
Macrovascular disease in T2DM

Riace – SID Study



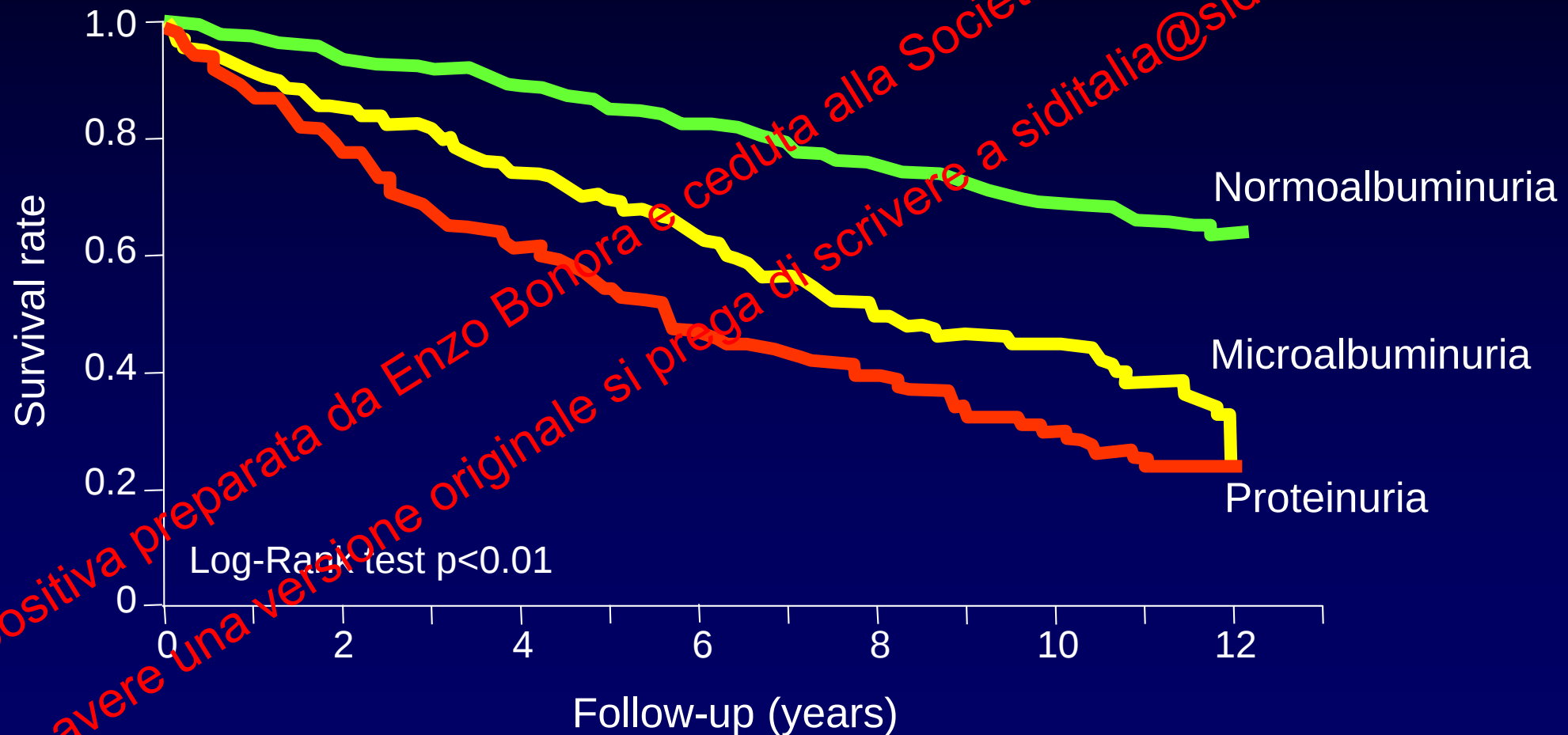
Albuminuria in T2DM

Riace – SID Study



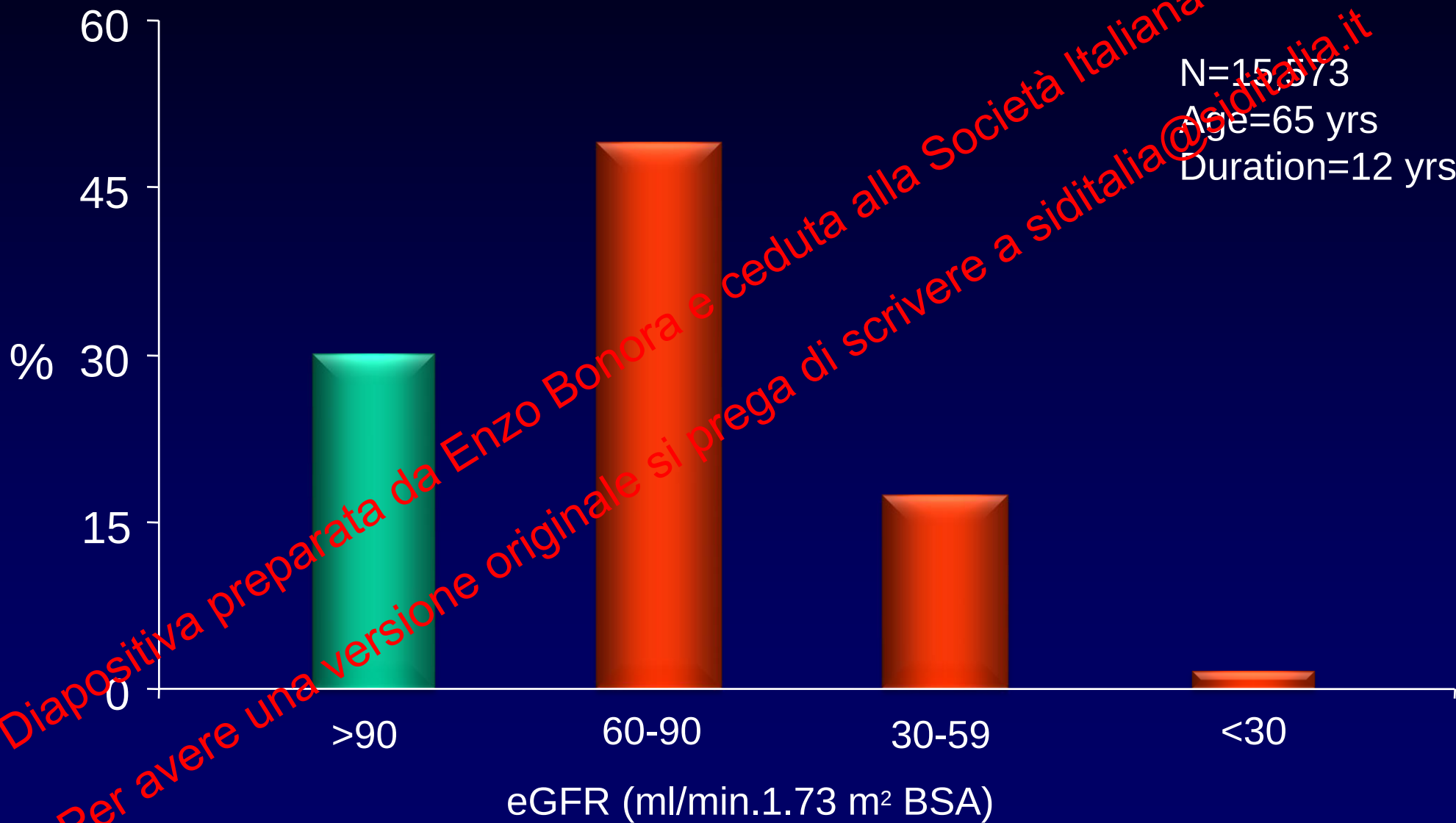
Microalbuminuria and Proteinuria Increase the Risk of Cardiovascular Mortality in T2DM

(Valmadrid CT et al; Arch Intern Med 2000)



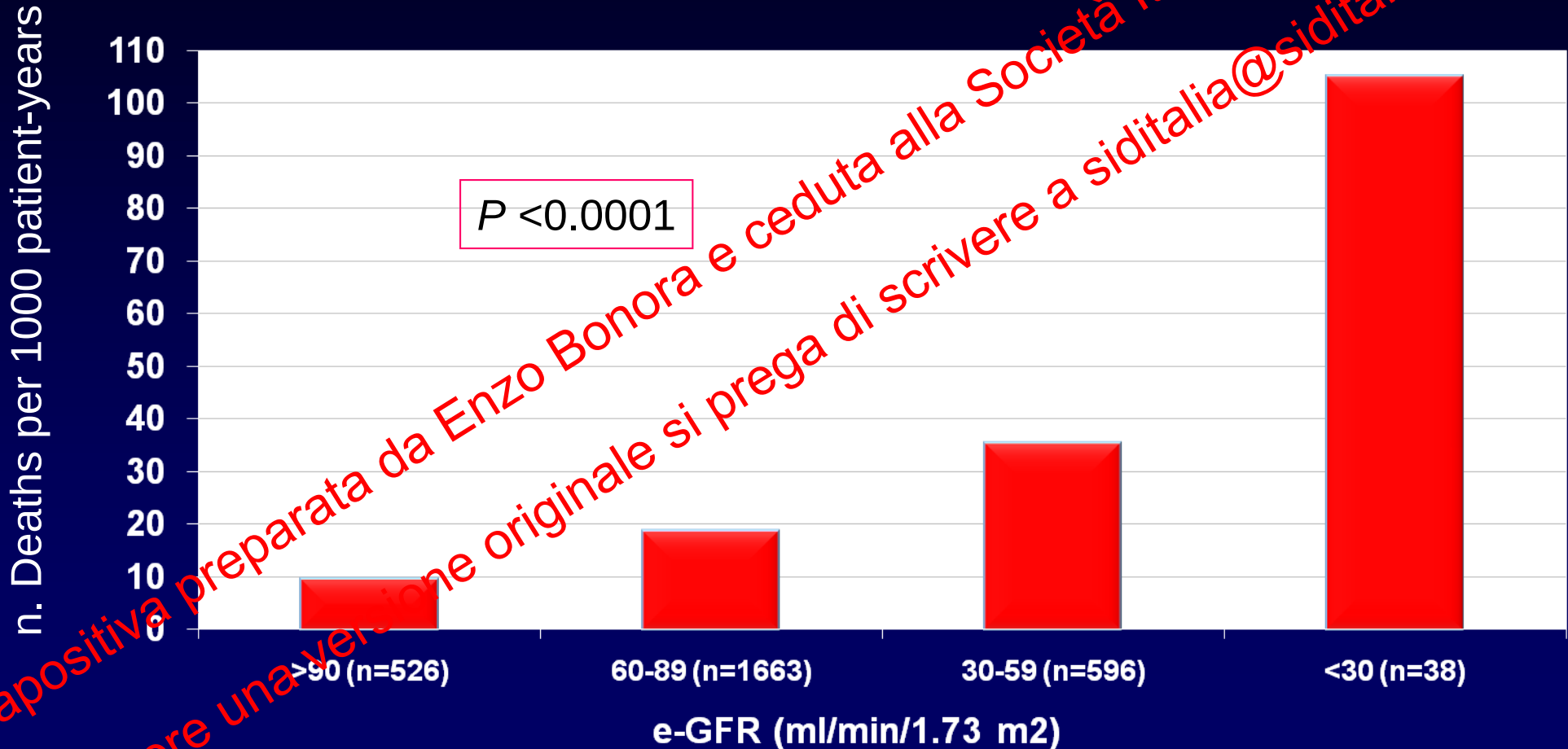
Renal Function in T2DM

Riace – SID Study

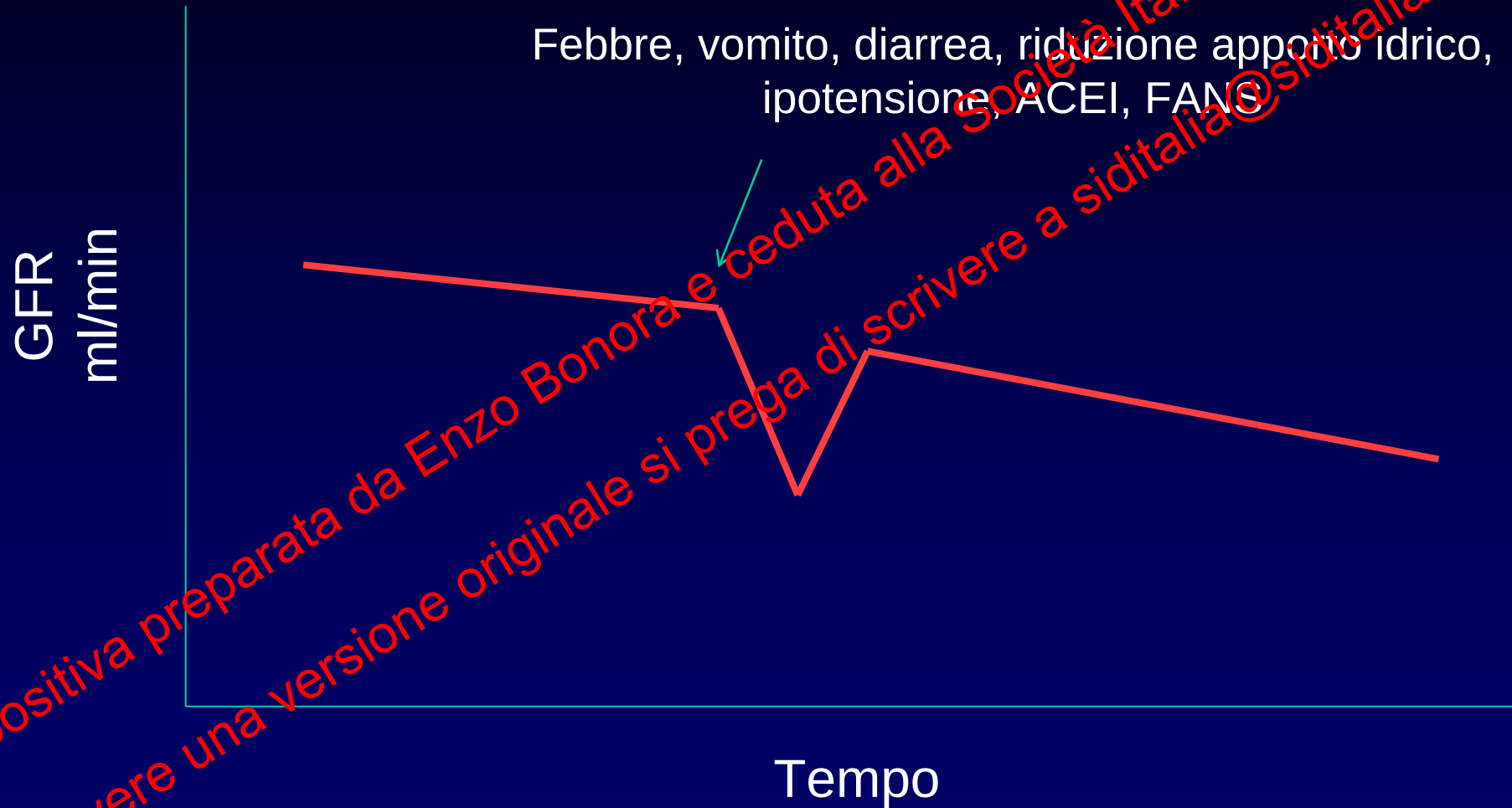


Incidence Rates of All-cause Mortality by eGFR Level in T2DM – Verona Diabetes Study

Targher G *et al* - NMCD 2011; 21:294-301

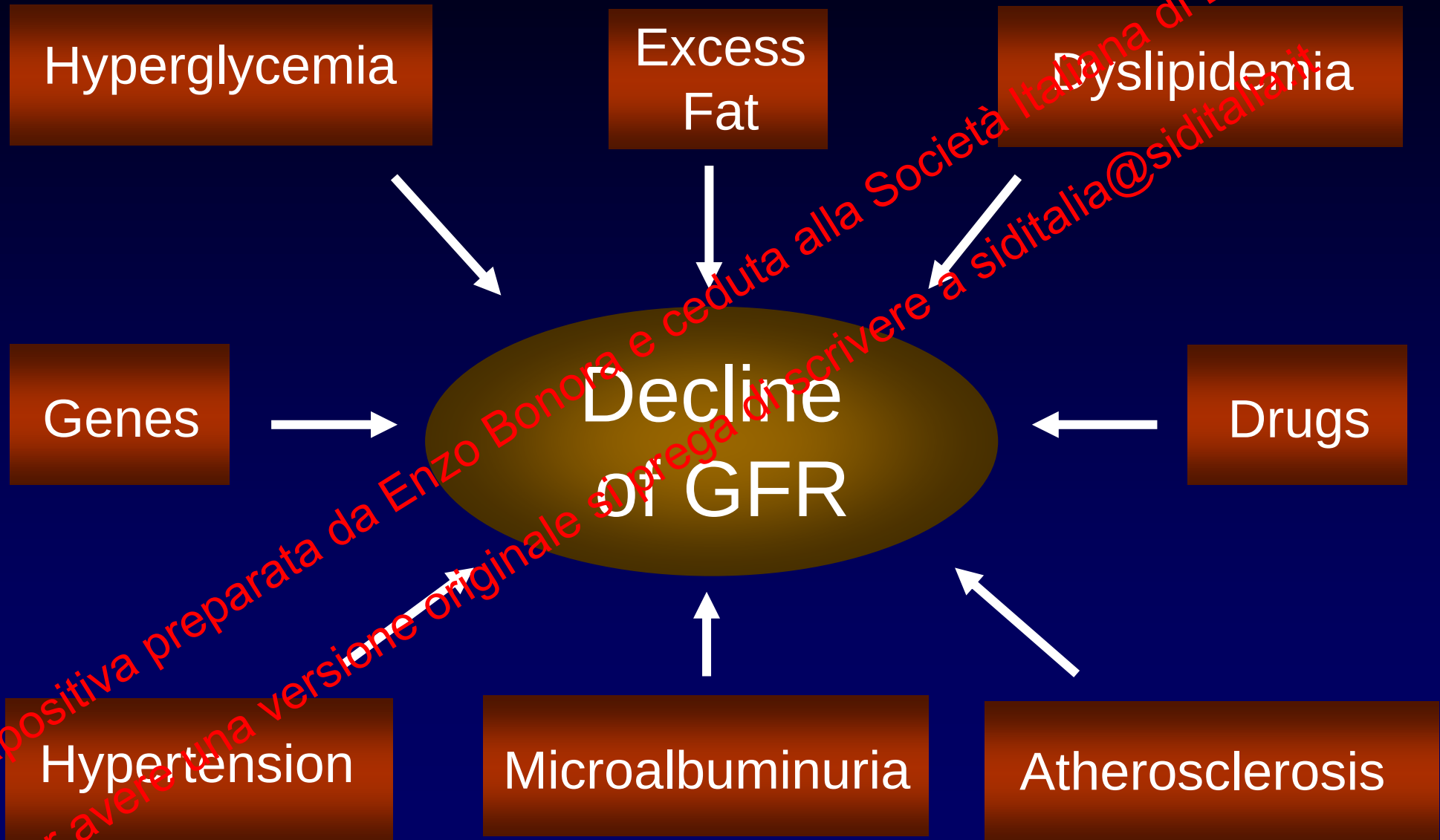


Fluttuazioni nella funzione renale

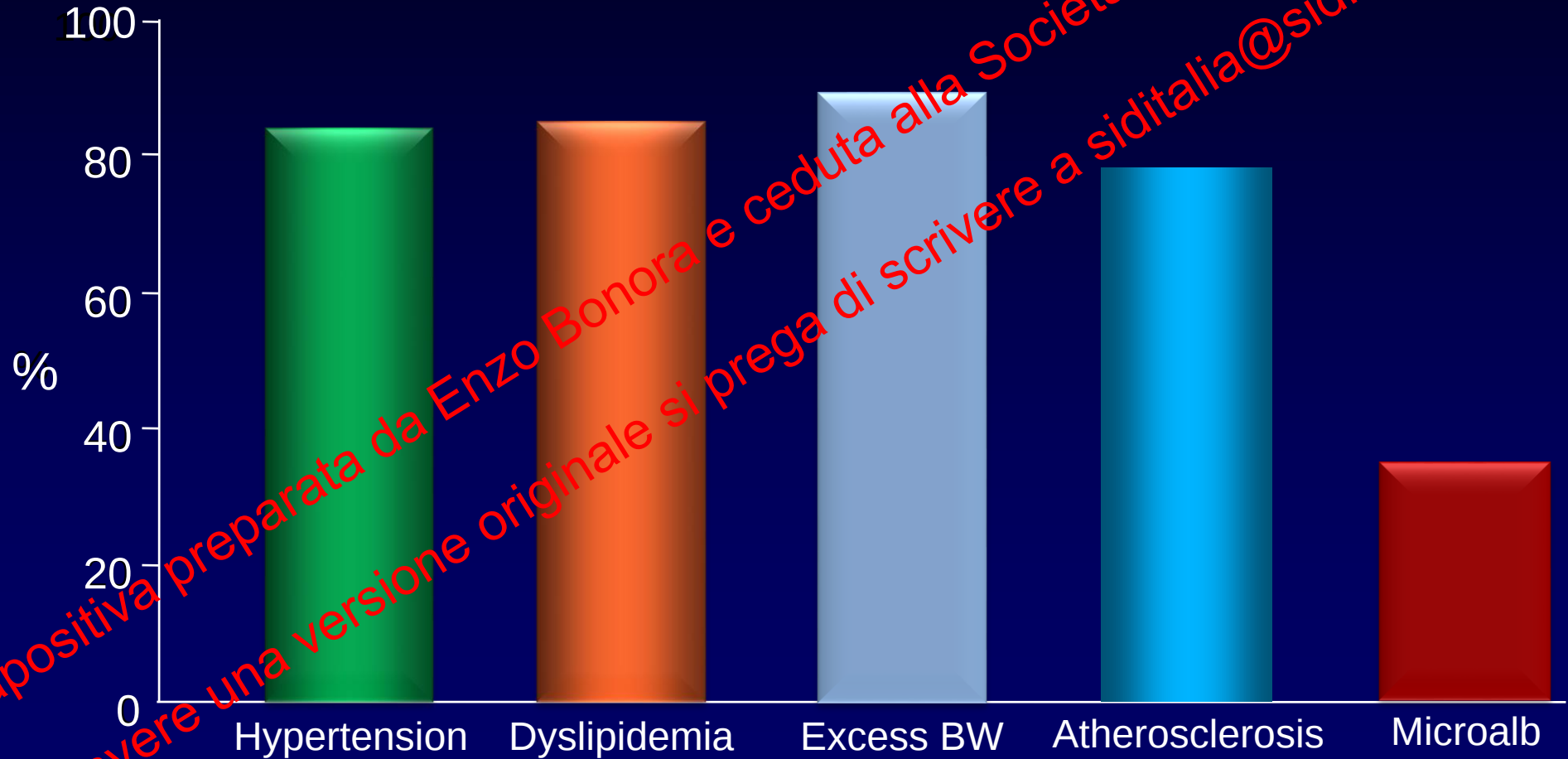


Diapositiva preparata da Enzo Bonora e ceduta alla Società Italiana di Diabetologia.
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Factors involved in the decline of renal function

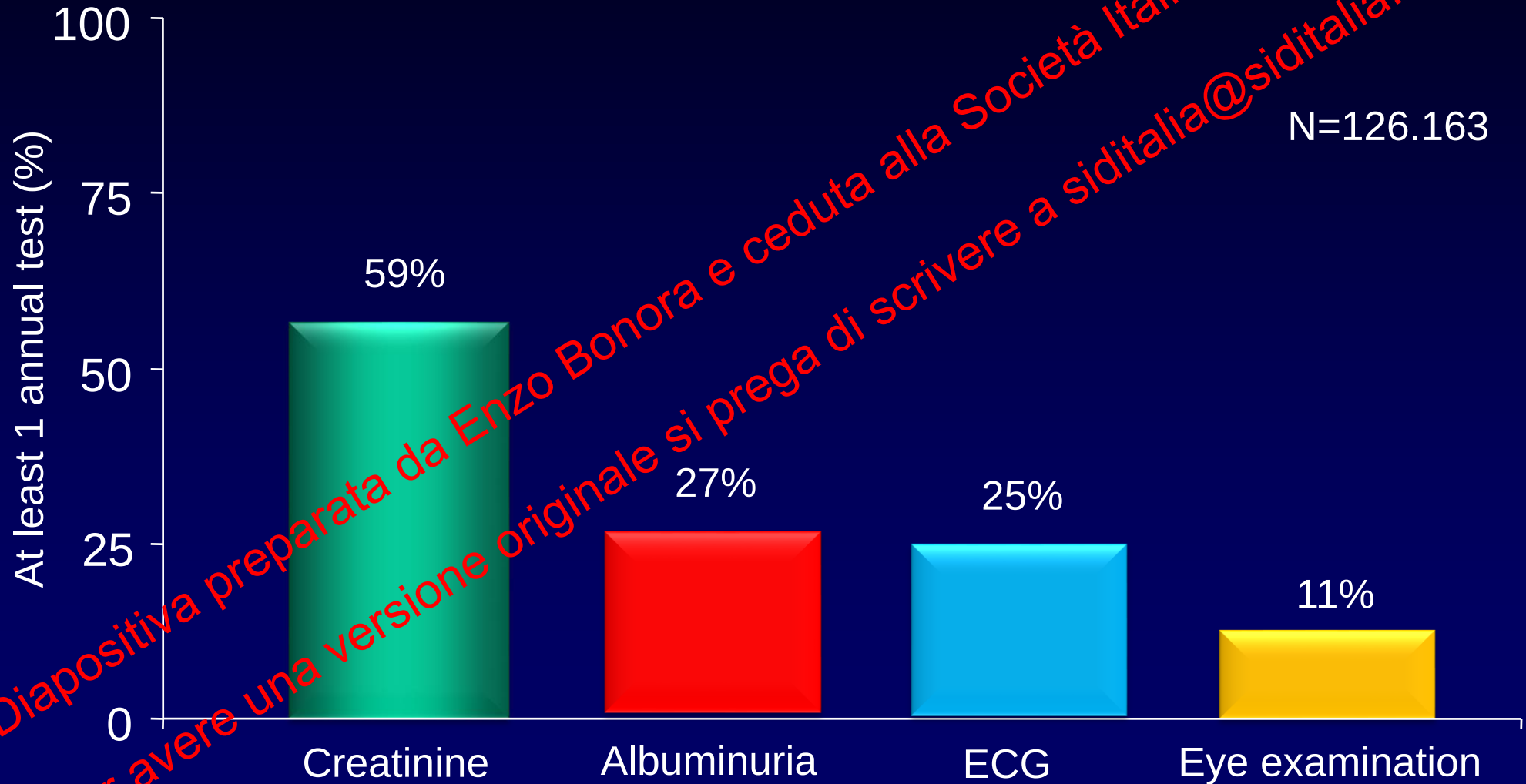


Prevalence of Risk Factors for Decline in GFR in T2DM



Quality of Care Indicators in T2DM Subjects in Italy

CINECA-SID ARNO Database – Bruno et al, Diabetes Care in press



Prevalence of NAFLD in T2DM

Author	Reference	No. subjects Prevalence	Method
Jimba et al	<i>Diabetic Med</i> 2005; 22:1141-1145	N=342 62%	Ultrasound
Targher et al	<i>Diabetes Care</i> 2007; 30: 1212-1218	N=2,839 69%	Ultrasound
Williams et al	<i>Gastroenterology</i> 2011; 140: 124-131	N=64 74%	Liver biopsy

Diapositiva preparata da Enzo Bonora e ceduta alla Societa Italiana di Diabetologia.
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Ultrasonography-Diagnosed NAFLD is an Independent Predictor of CVD in T2DM

Targher G et al – *Diabetes* 2005; 12: 3541-3546

Variable	Model 1	Model 2	Model 3
Age (per 10 yr)	1.13 (1.07-1.14)	1.13 (1.07-1.14)	1.12 (1.06-1.14)
Sex (M vs F)	1.48 (1.1-2.0)	1.46 (1.2-1.9)	1.46 (1.2-1.9)
Smoking (yes vs. no)	1.42 (1.1-2.0)	1.40 (1.1-1.9)	1.40 (1.1-1.9)
NAFLD (yes vs. no)	1.91 (1.4-2.2)	1.84 (1.4-2.1)	1.53 (1.1-1.7)

N=744, follow-up 5 yrs

Model 1: age and sex

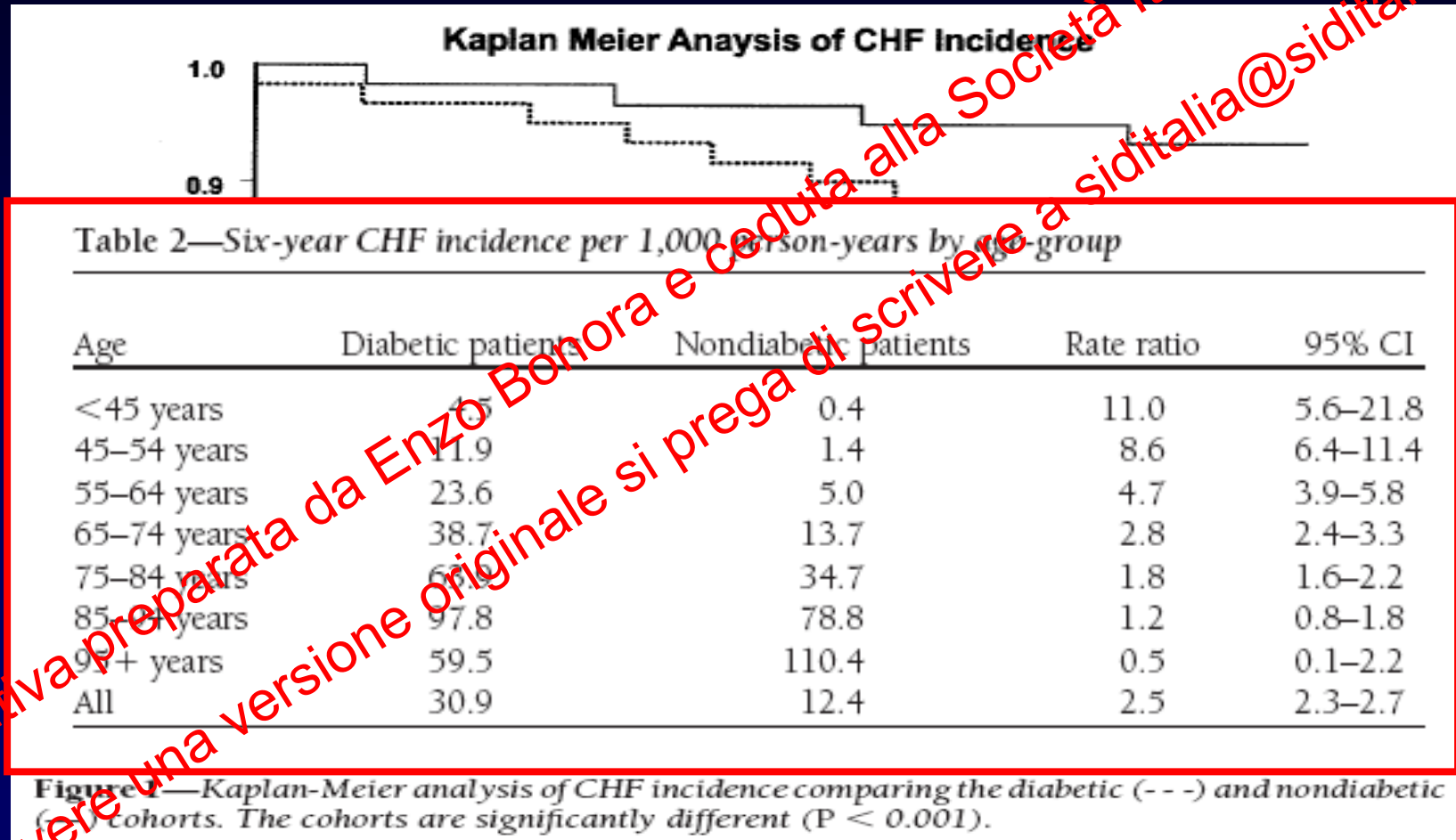
Model 2: + smoking history, diabetes duration, HbA1C, LDL cholesterol, GGT levels, and use of medications (i.e., hypoglycemic, antihypertensive, lipid-lowering, or antiplatelet drugs)

Model 3: + metabolic syndrome

Type 2 Diabetes Increases the Risk of Incident Congestive Heart Failure

The Kaiser Permanente Northwest study

n=8,231 patients with diabetes and 8,845 non-diabetic patients; follow up duration: 6 years



Diabetes Increases Risks for Asthma, Chronic Obstructive Pulmonary Disease, Pulmonary Fibrosis, and Pneumonia

The Kaiser Permanente Medical Care Program cohort
n= 77,637 subjects with diabetes and 51,241 subjects without diabetes; follow up duration: 10 years

Table 2—Age- and sex-adjusted incidence rate (per 1,000 person-years) of each pulmonary outcome in all KPNC members aged ≥ 18 years, by diabetes status

	Full cohort	Survey responder
Pneumonia*		
No diabetes	2.27 (2.24–2.29)	1.96 (1.85–2.08)
Diabetes	5.68 (5.56–6.21)	5.76 (5.40–6.11)
Asthma*		
No diabetes	1.57 (1.54–1.60)	1.48 (1.38–1.58)
Diabetes	2.21 (2.17–2.25)	2.25 (2.14–2.36)
COPD*		
No diabetes	1.64 (1.61–1.67)	1.54 (1.44–1.64)
Diabetes	2.47 (2.42–2.52)	2.48 (2.36–2.60)
Pulmonary fibrosis*		
No diabetes	1.05 (1.02–1.08)	1.05 (1.00–1.10)
Diabetes	1.05 (1.01–1.09)	1.10 (1.04–1.16)

Table 3—HRs and 95% CIs for the association between each pulmonary condition and diabetes status among KPNC survey responder

	Model 1*	Model 2†
Asthma‡	2.21 (1.72–2.85)	1.08 (1.03–1.12)
COPD‡	1.57 (1.40–1.77)	1.22 (1.15–1.28)
Pulmonary fibrosis‡	1.64 (1.23–2.18)	1.54 (1.31–1.81)
Pneumonia‡	2.47 (2.32–2.62)	1.92 (1.84–1.99)
Lung cancer§	1.05 (0.94–1.17)	1.10 (0.96–1.26)

Data are of death. *Adjusted for age, sex, and race/ethnicity. †Adjusted for age, sex, race/ethnicity, smoking, BMI, education, alcohol consumption, and number of outpatient visits. ‡Primary discharge diagnosis or underlying cause of death in the Kaiser Permanente databases. §Identified through the KPNC Cancer Registry.

Type 2 Diabetes Increases the Risk of Hip Fracture

The Nurses' Health Study

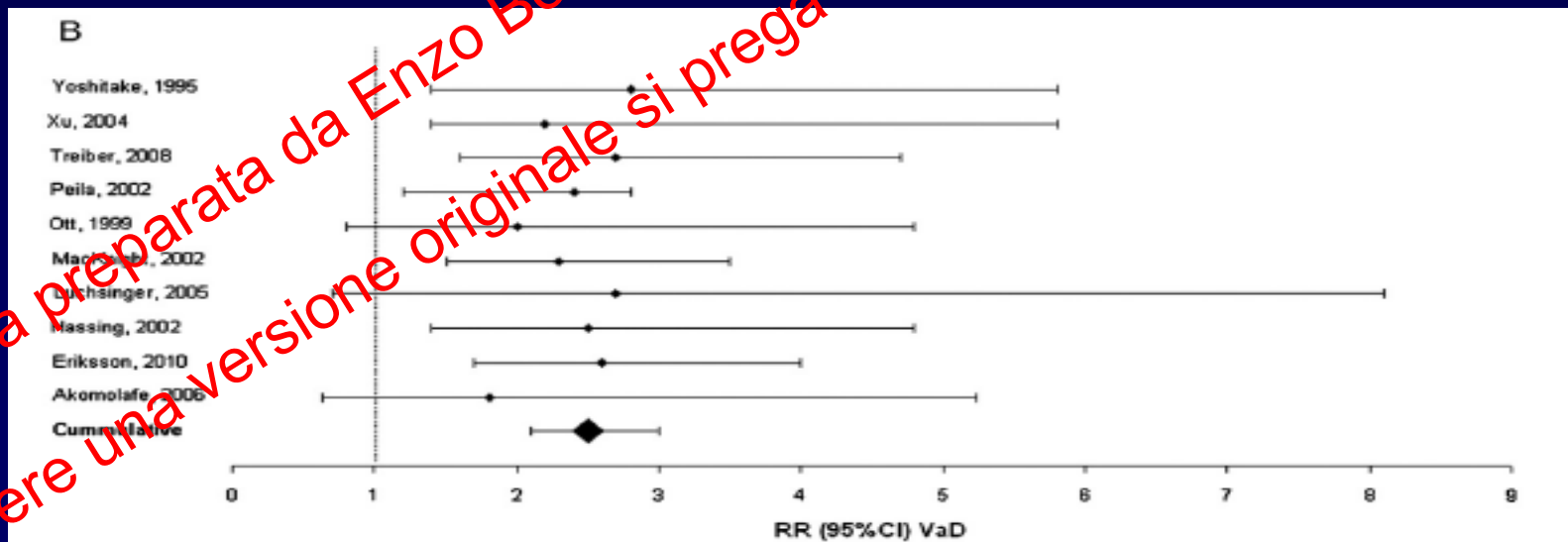
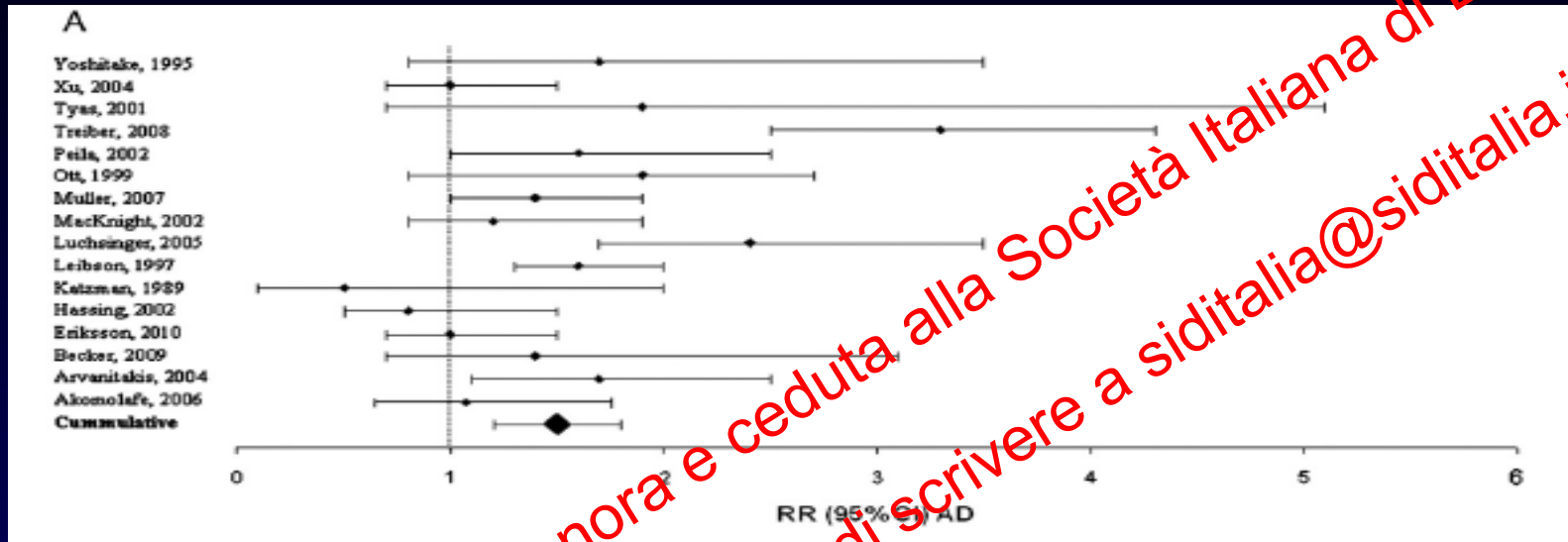
n= 8,348 women with type 2 diabetes and 101,343 nondiabetic patients;
follow up duration: 22 years

Table 2—Incidence rates and RRs of hip fracture by diabetes status, duration of diabetes, and treatment in the NHS, 1980–2002

Variables	n	Incidence/100,000 person-years	Age-adjusted RR	Age and BMI-adjusted RR	Multivariate-adjusted RR
Nondiabetes	1,255	59	1.0	1.0	1.0
Type 1 diabetes	18	383	7.1 (4.4–11.5)	6.4 (4.0–10.3)*	6.4 (3.9–10.3)*
Type 2 diabetes	125	153	1.7 (1.4–2.0)*	2.3 (1.9–2.7)*	2.2 (1.8–2.7)*
Type 2 diabetes <5 years	34	107	1.3 (0.9–1.9)	1.8 (1.3–2.6)*	1.7 (1.2–2.4)*
Type 2 diabetes 5–11 years	34	127	1.4 (1.0–1.9)	1.9 (1.3–2.7)*	1.8 (1.3–2.6)*
Type 2 diabetes ≥12 years	57	248	2.4 (1.8–3.1)*	3.1 (2.3–4.1)*	3.1 (2.3–4.0)*
Type 2 diabetes treatment					
Nondiabetes	1,255	59	1.0	1.0	1.0
Never used insulin	83	283	1.4 (1.1–1.8)*	1.9 (1.5–2.4)*	1.9 (1.5–2.3)*
Ever used insulin	36	209	2.4 (1.8–3.5)*	3.4 (2.4–4.8)*	3.4 (2.4–4.7)*

Total number of cases is not the same for each variable because of missing values. RRs (95% CI) were calculated by the Cox proportional hazard model, adjusted for age, BMI, physical activity, menopausal status and estrogen use, smoking and daily intake of calcium, vitamin D, and protein. *P < 0.001.

Diabetes Increases Risk of Alzheimer's disease (A) and Vascular Dementia (B): Meta-analysis



Diabetes and Cancer Risk: Meta-analysis

Table 1 Meta-analyses on the relative risk (RR) of cancer in different organs of diabetic patients

Cancer		RR (95% CI)
Liver (El-Serag <i>et al.</i> 2006)	13 case-control studies	2.50 (1.8–3.5)
	7 cohort studies	2.51 (1.9–3.2)
Pancreas (Huxley <i>et al.</i> 2005)	17 case-control studies	1.94 (1.53–2.46)
	19 cohort studies	1.73 (1.59–1.88)
Kidney ^a (Lindblad <i>et al.</i> 1999, Washio <i>et al.</i> 2007)	1 cohort study	1.50 (1.30–1.70)
	1 cohort study	2.22 (1.04–4.70)
Endometrium (Friberg <i>et al.</i> 2007)	13 case-control studies	2.22 (1.80–2.74)
	3 cohort studies	1.62 (1.21–2.16)
Colon-rectum (Larsson <i>et al.</i> 2005)	6 case-control studies	1.36 (1.23–1.50)
	6 cohort studies	1.29 (1.16–1.43)
Bladder (Larsson <i>et al.</i> 2006)	7 case-control studies	1.37 (1.04–1.80)
	3 cohort studies	1.43 (1.18–1.74)
Non-Hodgkin's lymphoma (Mitri <i>et al.</i> 2008)	5 cohort studies	1.41 (1.07–1.88)
	11 case-control studies	1.12 (0.95–1.31)
Breast (Larsson <i>et al.</i> 2004)	5 case-control studies	1.18 (1.05–1.32)
	15 cohort studies	1.20 (1.11–1.30)
Prostate (Kasper & Giovannucci 2006)	9 case-control studies	0.89 (0.72–1.11)
	10 cohort studies	0.81 (0.71–0.92)

^aData on kidney cancer were not obtained from meta-analysis.

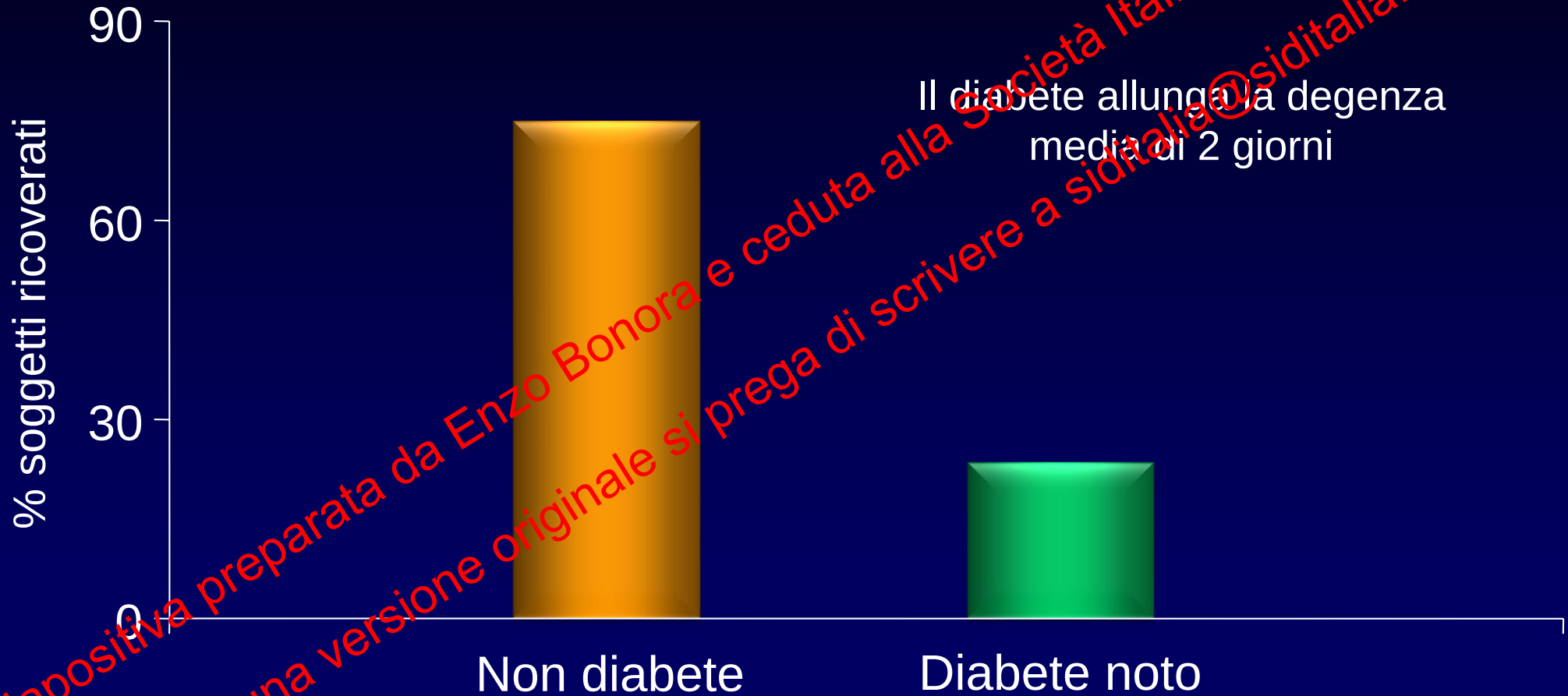
Il diabete aumenta il rischio di tutte le patologie che generano ricoveri ospedalieri

Nutr Metab Cardiovasc Dis 2011

Complicanze e patologie concomitanti	OR (IC 95%)
IMA	1,85 (1,77-1,92)
Cardiopatia ischemica	2,47 (2,41-2,53)
Scompenso cardiaco	2,48 (2,40-2,56)
Aritmie	2,49 (1,45-1,53)
Complicanze cerebrovascolari	2,02 (1,97-2,07)
Ictus ischemico	2,07 (1,96-2,18)
Ictus emorragico	1,26 (1,12-1,40)
Complicanze renali	2,82 (2,73-2,91)
Neuropatia	3,77 (3,55-4,00)
Complicanze oculari	1,74 (1,70-1,79)
Complicanze arti inferiori	6,01 (5,44-6,64)
Vasculopatia periferica	4,09 (3,94-4,24)
Amputazioni	8,77 (7,16-10,75)
Amputazioni maggiori	4,31 (3,29-5,65)
Amputazioni minori	15,04 (11,12-20,34)
Malattie infettive	1,87 (1,83-1,90)

Presenza di diabete fra i soggetti degenti in Ospedale a Verona (anno 2010)

(Bonora et al; dati non pubblicati)



HbA1c Targets in Diabetes Care

(AMD-SID Standards of Care, 2009-2010)

Obiettivo generale

<7%

Nuova diagnosi o breve durata,
discreto compenso pregresso

<6.5%

Lunga durata, CVD o comorbidità/fragilità,
cattivo compenso pregresso

7-8%

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Obiettivi glicemici per il diabetico anziano

(Standard di Cura AMD/SID 2009-2010)

Nei diabetici anziani gli obiettivi glicemici dovrebbero essere individualizzati. Se le condizioni generali sono relativamente buone, il valore di HbA1c potrà essere compreso fra 6.5 e 7.5%.

Livello della prova VI, forza della raccomandazione B.

Negli anziani fragili (con complicanze, affetti da demenza, con pluripatologia, nei quali il rischio di ipoglicemia è alto e nei quali il rischio di un controllo glicemico intensivo supera i benefici attesi) è appropriato un obiettivo meno restrittivo, con valori di HbA1c compresi fra 7.5 e 8.5%.

Livello della prova VI, forza della raccomandazione B.

Personalization of Glycemic Targets by ADA/EASD Consensus Statement 2012

Approach to management of hyperglycaemia:

More stringent

Less stringent

Patient attitude and expected treatment efforts

Highly motivated, adherent, excellent self-care capacities

Less motivated, non-adherent, poor self-care capacities

Risks potentially associated with hypoglycaemia, other adverse events

Low

High

Disease duration

Newly diagnosed

Long-standing

Life expectancy

Long

Short

Important comorbidities

Absent

Few / mild

Severe

Established vascular complications

Absent

Few / mild

Severe

Resources, support system

Readily available

Limited

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Anti-Diabetic Agents Available in Year 2013

Classes	Molecules
α -Glycosidase Inhibitors	Acarbose
AMPK Activators	Metformin
SUR Agonists	Glibenclamide, Gliclazide, Glimepiride Repaglinide
DPP-4 Inhibitors	Saxagliptin, Sitagliptin, Vildagliptin, Linagliptin
GLP-1R Agonists	Exenatide, Liraglutide
SGLT-2 Inhibitors	Dapagliflozin
Insulin Receptors Agonists	Insulin and its analogs

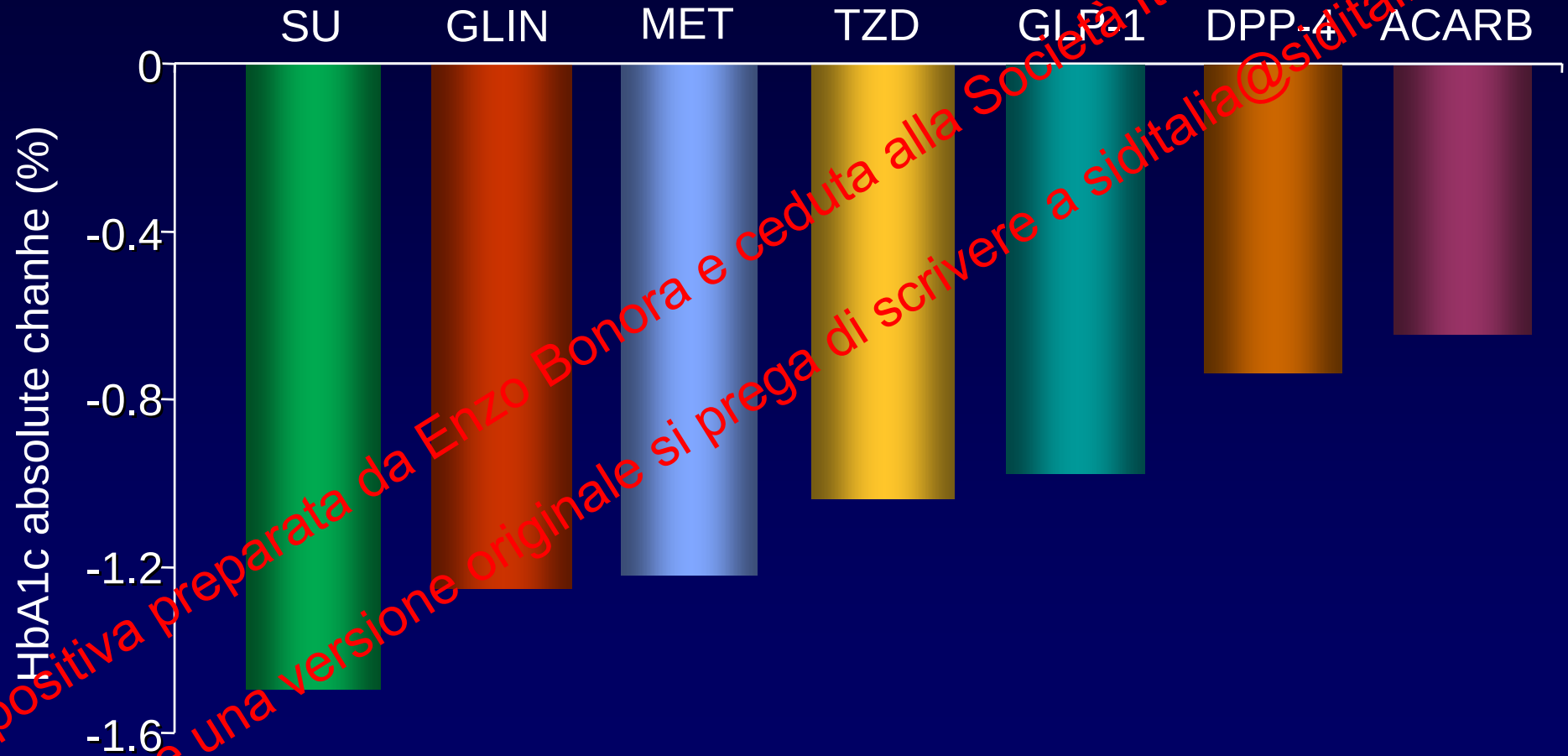
Targeting Pathogenetic Defects in T2DM

Year 2013

Defect	Agent
Insulin resistance	Biguanides, TZD
Impaired insulin secretion	SU, Glinides, Insulin Incretin mimetics & enhancers
Reduced beta-cell mass	Biguanides, TZD Incretin mimetics & enhancers
Increased glucagon levels	Incretin mimetics & enhancers
Reduced incretin levels	Incretin mimetics & enhancers
Increased glucose reabsorption	SGLT2 inhibitors
CNS dysfunction	Bromocriptine

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Mean Reduction of HbA1c During 6-Month Therapy with Anti-Diabetic Agents vs. Placebo in RCTs

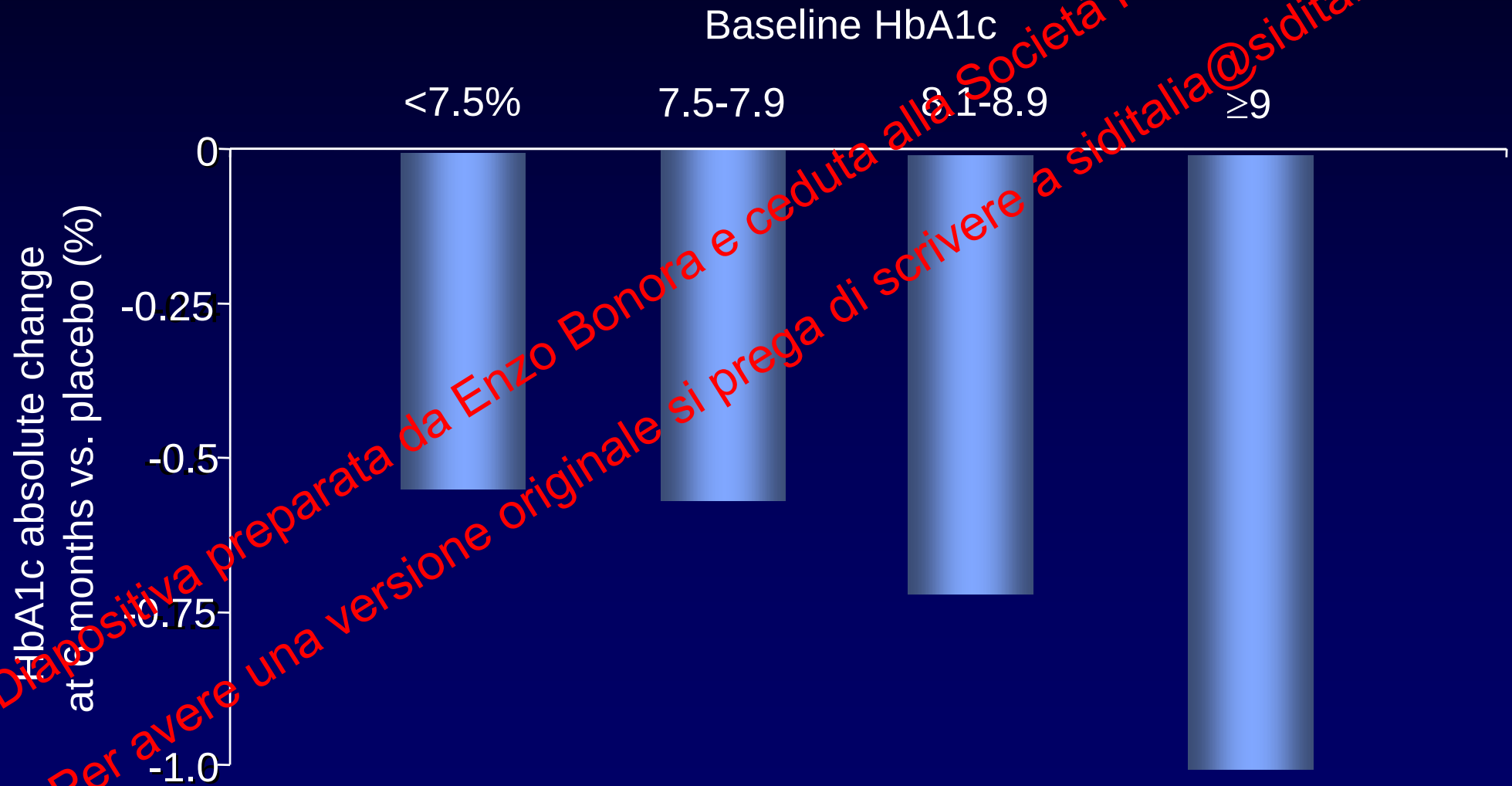


The Efficacy of a Given Hypoglycemic Agent is not the Same in All Subjects

Category of patients	Decrease in HbA1c
Very good responders	>1.8%
Good responders	1.2-1.8%
Average responders	0.6-1.1%
Poor responders	0.3-0.5%
No responders	<0.3%

Glucose lowering effect of linagliptin is greater in subjects with higher baseline HbA1c (pool of data from RCTs)

Del Prato et al - Diabetes Obes Metab 2011;13: 258-267



The Efficacy of Anti-Diabetic Agents Changes over Years According to Mechanism of Action

Durability is not the same

Class of OHA	Durability
Insulin receptor agonists	Unlimited
SUR agonists	Limited
AMPK activators	Fair
Alpha-glycosidase inhibitors	Poorly known
PPAR gamma agonists	Good
GLP-1 receptor agonists	Promisingly good
DPP-4 inhibitors	Promisingly good

Criteria in the selection of an anti-diabetic drug

- Efficacy (glucose lowering effect)
- Additional benefits (BW, lipids, blood pressure, CVD, etc.)
- Hypoglycemia risk
- Tolerability and safety
- Interactions with other drugs
- Contraindications (temporary/permanent)
- Oral or injectable
- Number of pills/injections per day (adherence)
- Need to titrate the dose
- SMBG required (mainly to unveil hypoglycemia)
- Capability to modify the natural history of the disease (disease modifier)

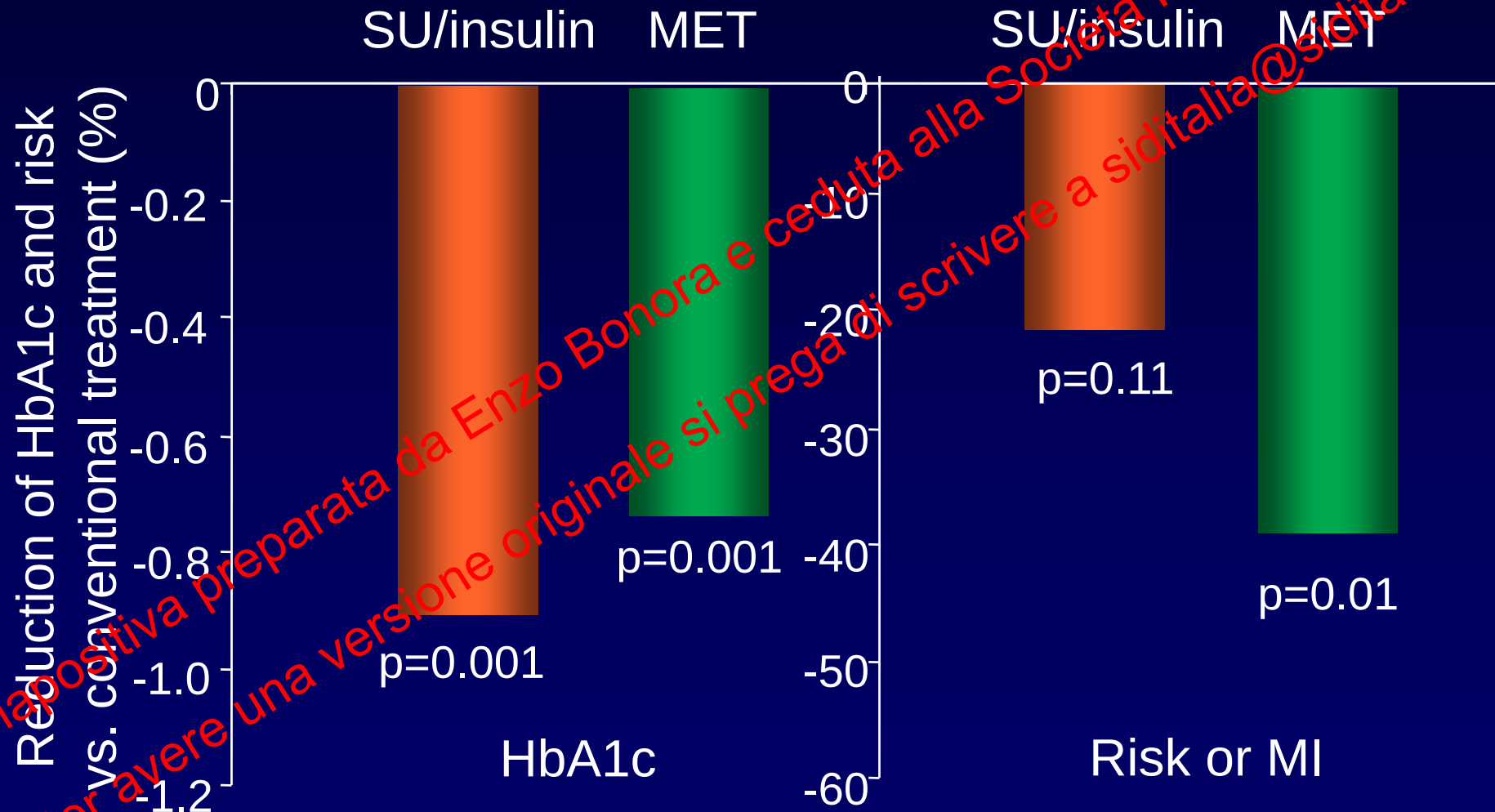
Cardiovascular Events in Insulin-Treated T2DM Patients in whom Metformin vs. Placebo was Added

(Kooy A et al. - Arch Intern Med 6:616, 2009)



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Effects of Intensive Treatment on HbA1c and the Risk of Myocardial Infarction in Overweight (mean BMI=31) Type 2 Diabetic Patients of the UKPDS



Ischemic Preconditioning and Sulphonylureas

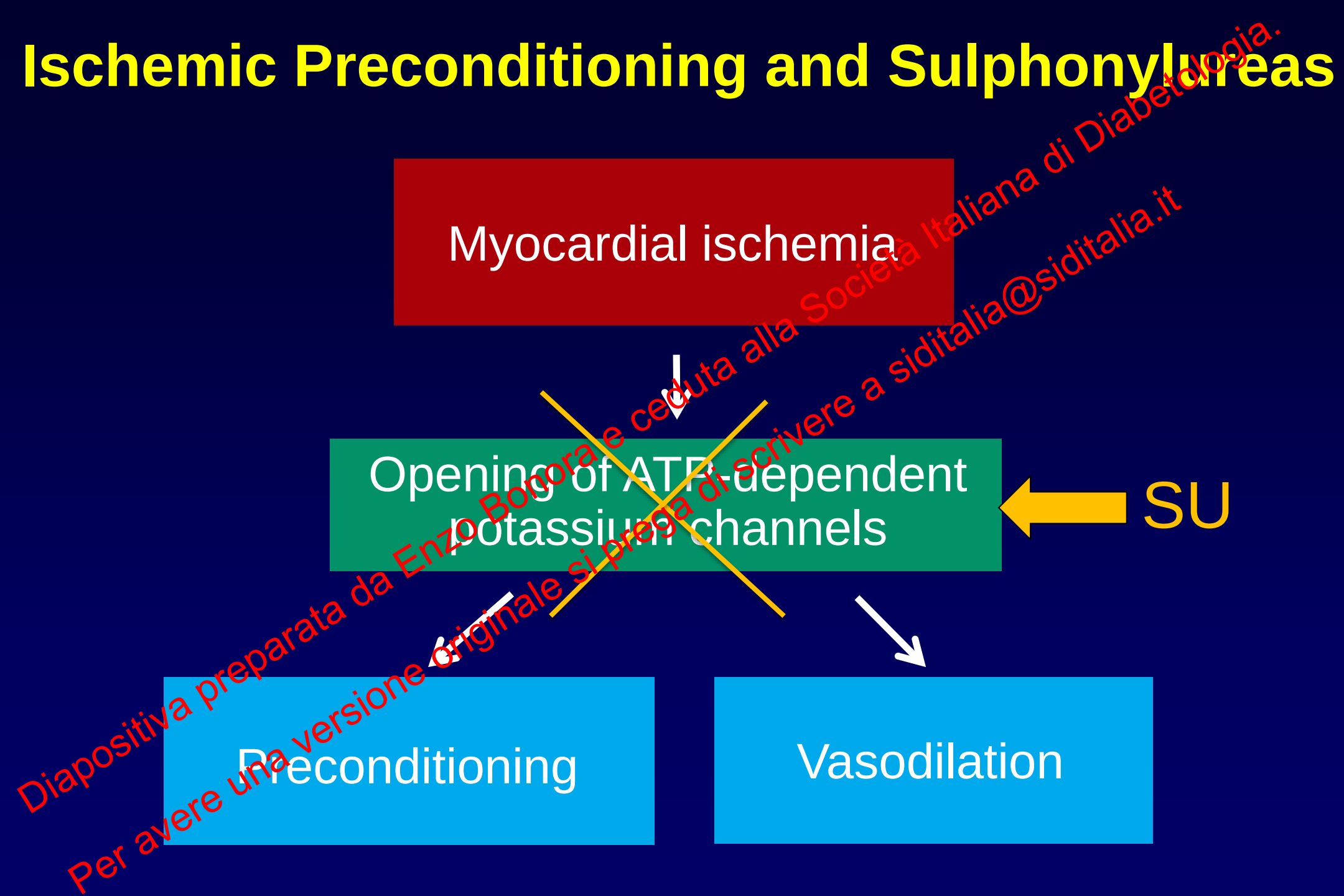
Myocardial ischemia

Opening of ATP-dependent
potassium channels

SU

Preconditioning

Vasodilation

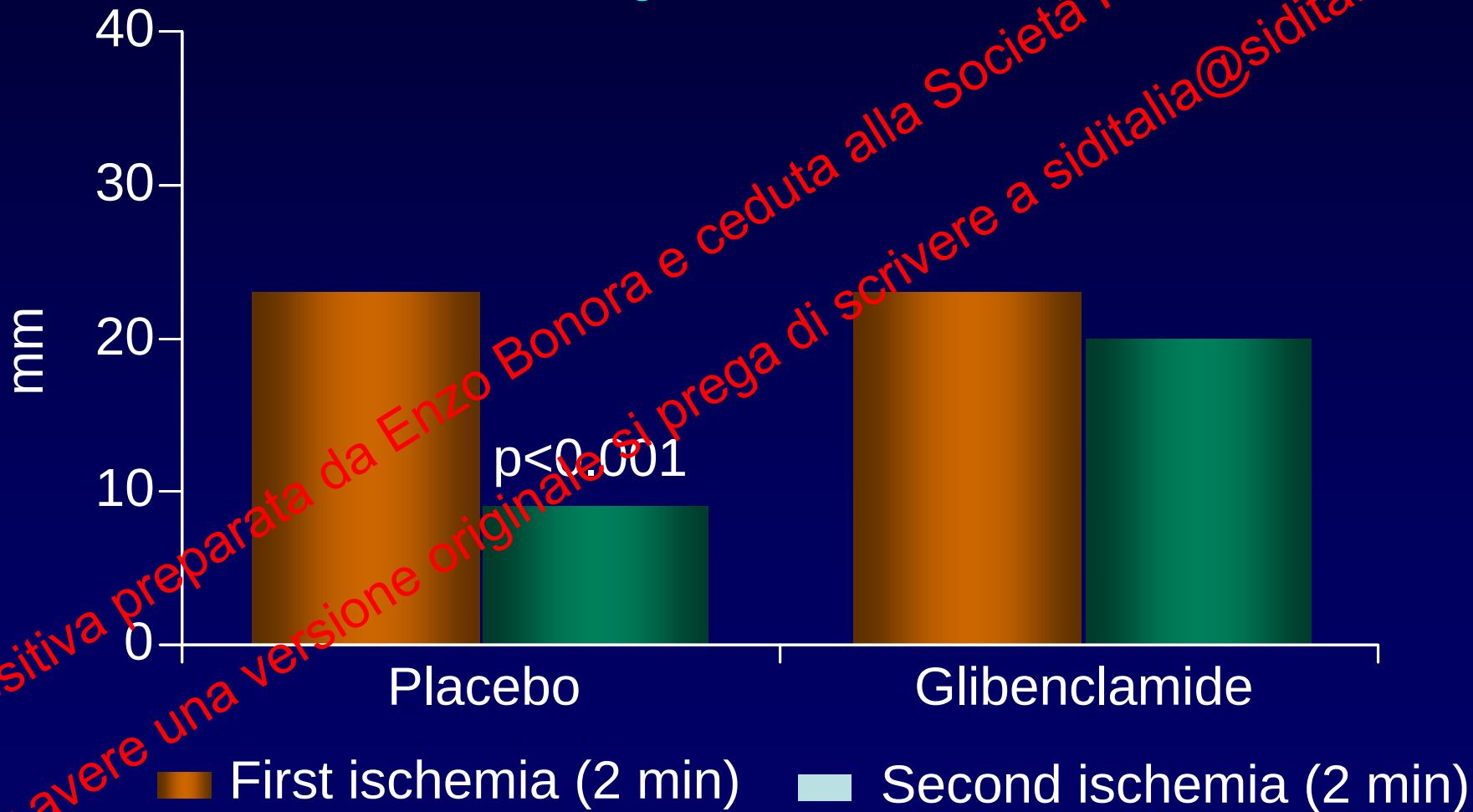


Ischemic preconditioning during PTCA

Effect of Glibenclamide

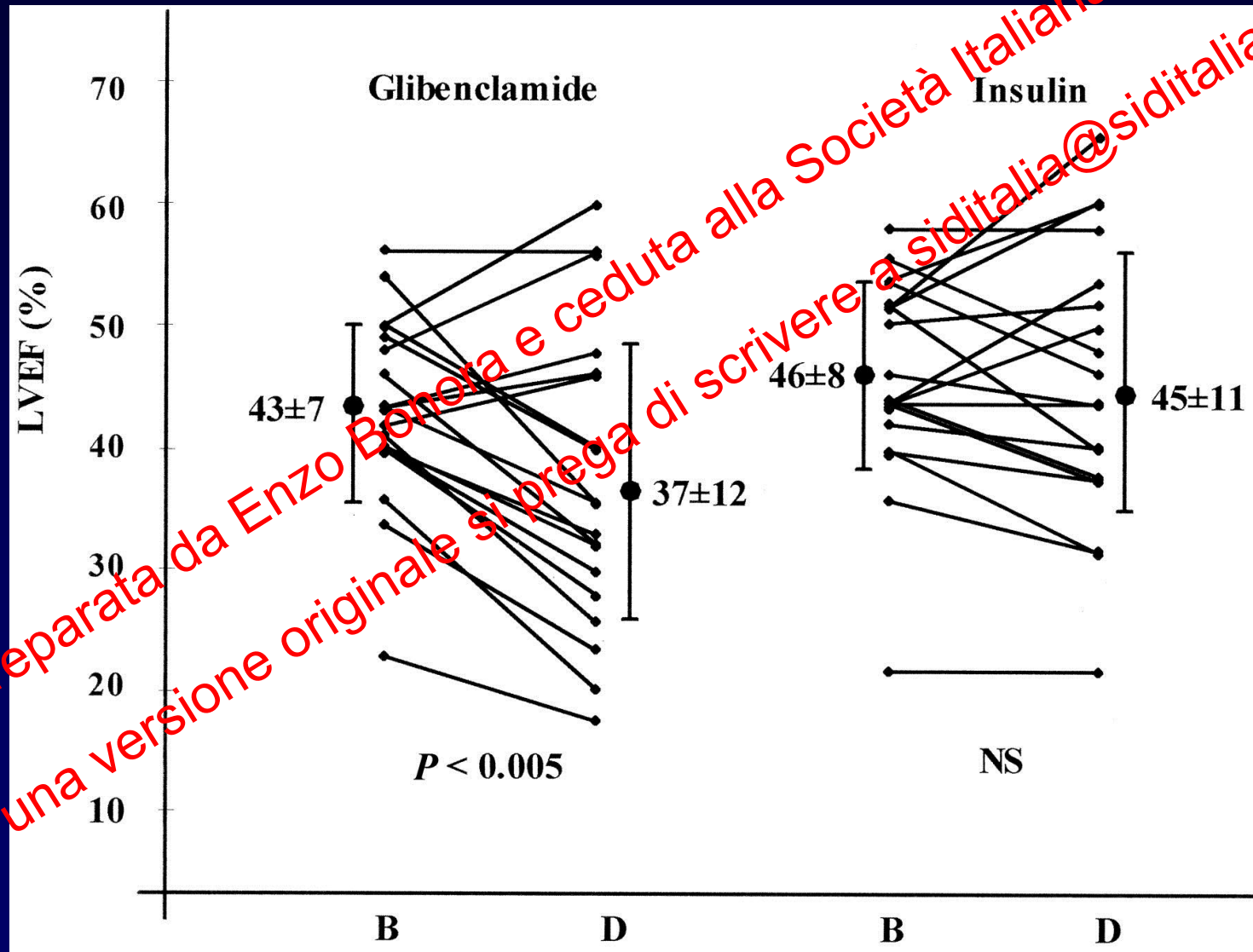
(Tomai et al – Circulation 90: 700-705, 1994)

ST-segment shift on ECG



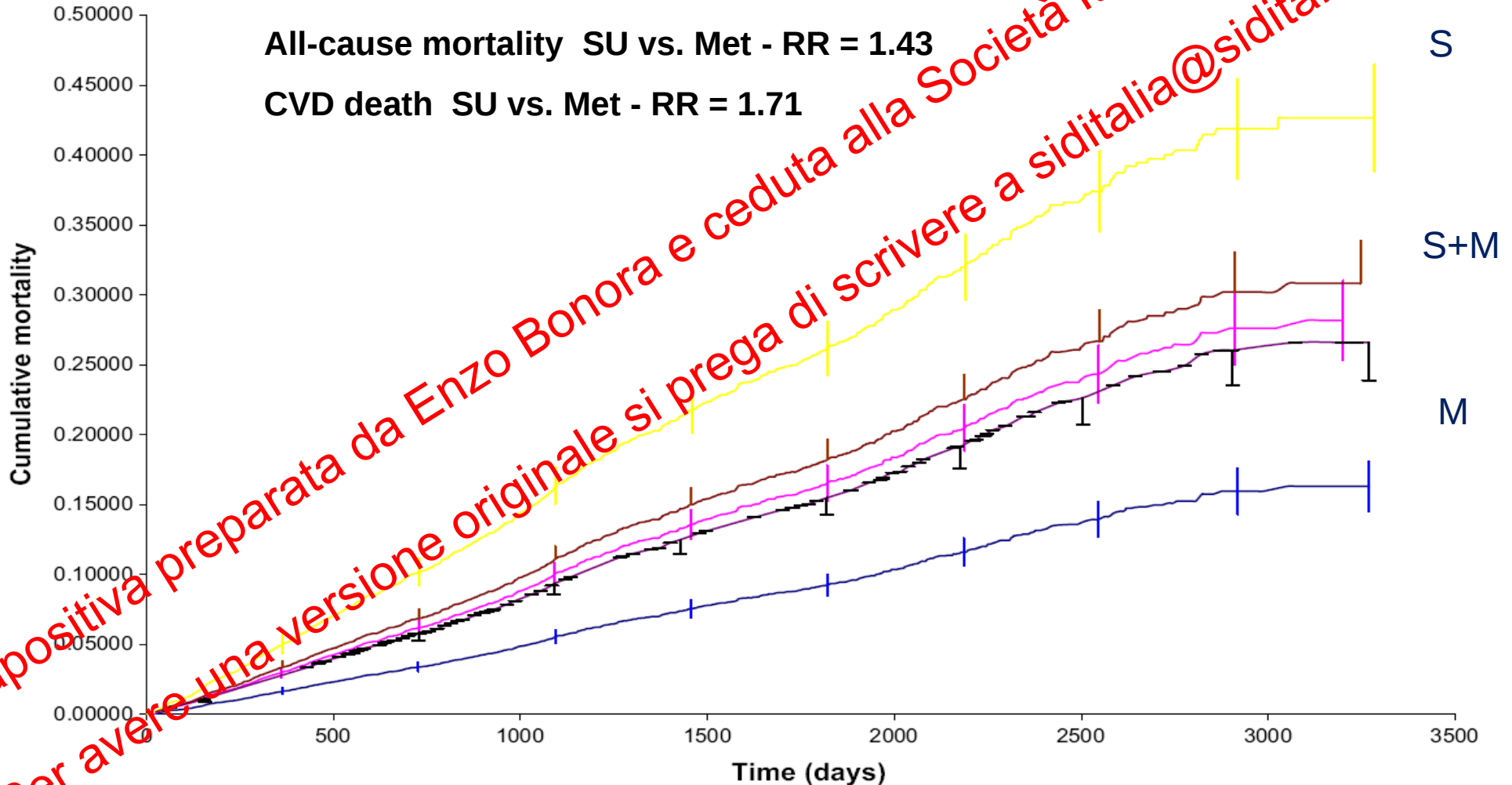
Effects of treatment with sulfonylurea and insulin drugs on left ventricular function during echostress with dipyridamole in T2DM

(Sognamiglio et al – Diabetes 2002)



All-cause mortality in 5 Cohorts of T2DM Patients Treated with Sulphonylurea and/or Metformin

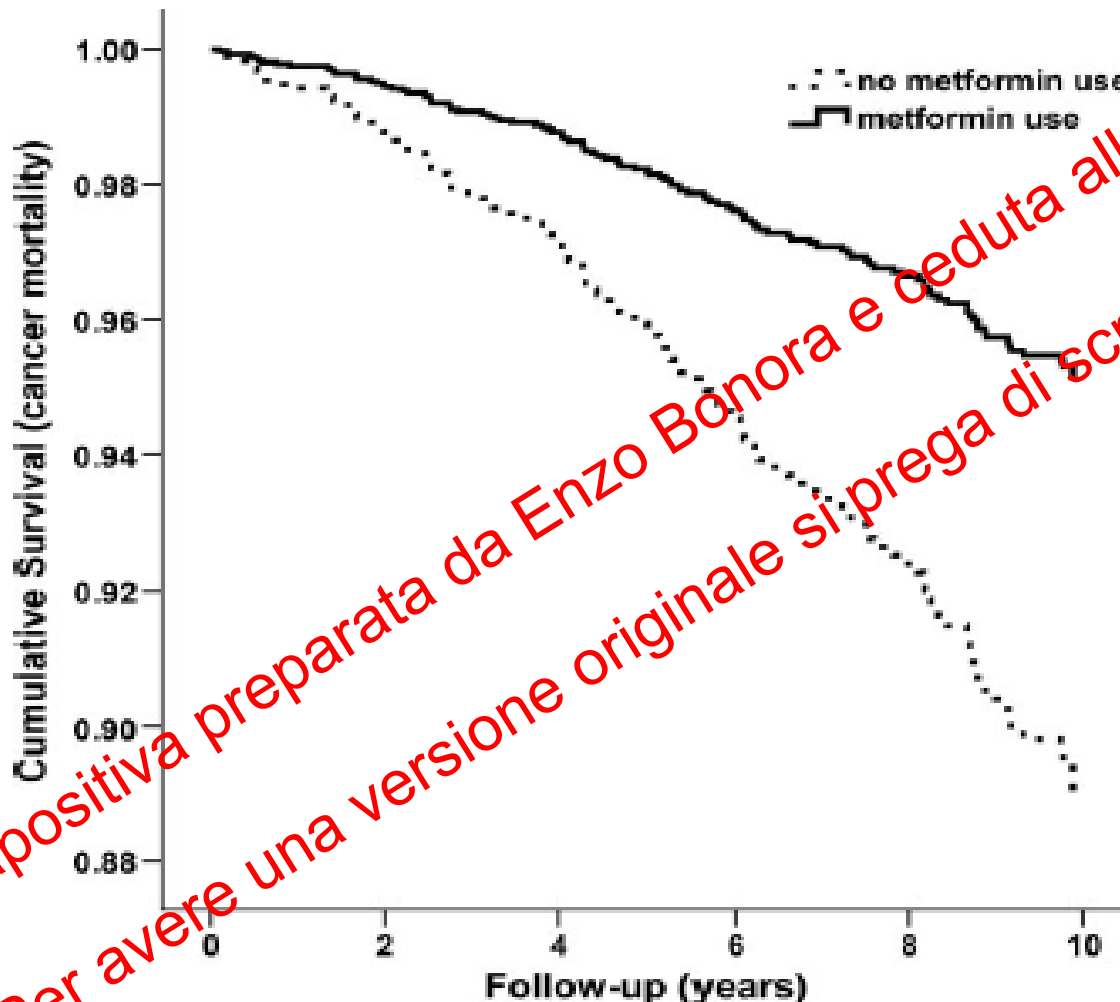
(Evans JMM - *Diabetologia* 2006)



Use of metformin and cancer mortality in T2DM

(Landman GDW et al - Diabetes Care 33: 322, 2010)

Metformin and cancer mortality in type 2 diabetes



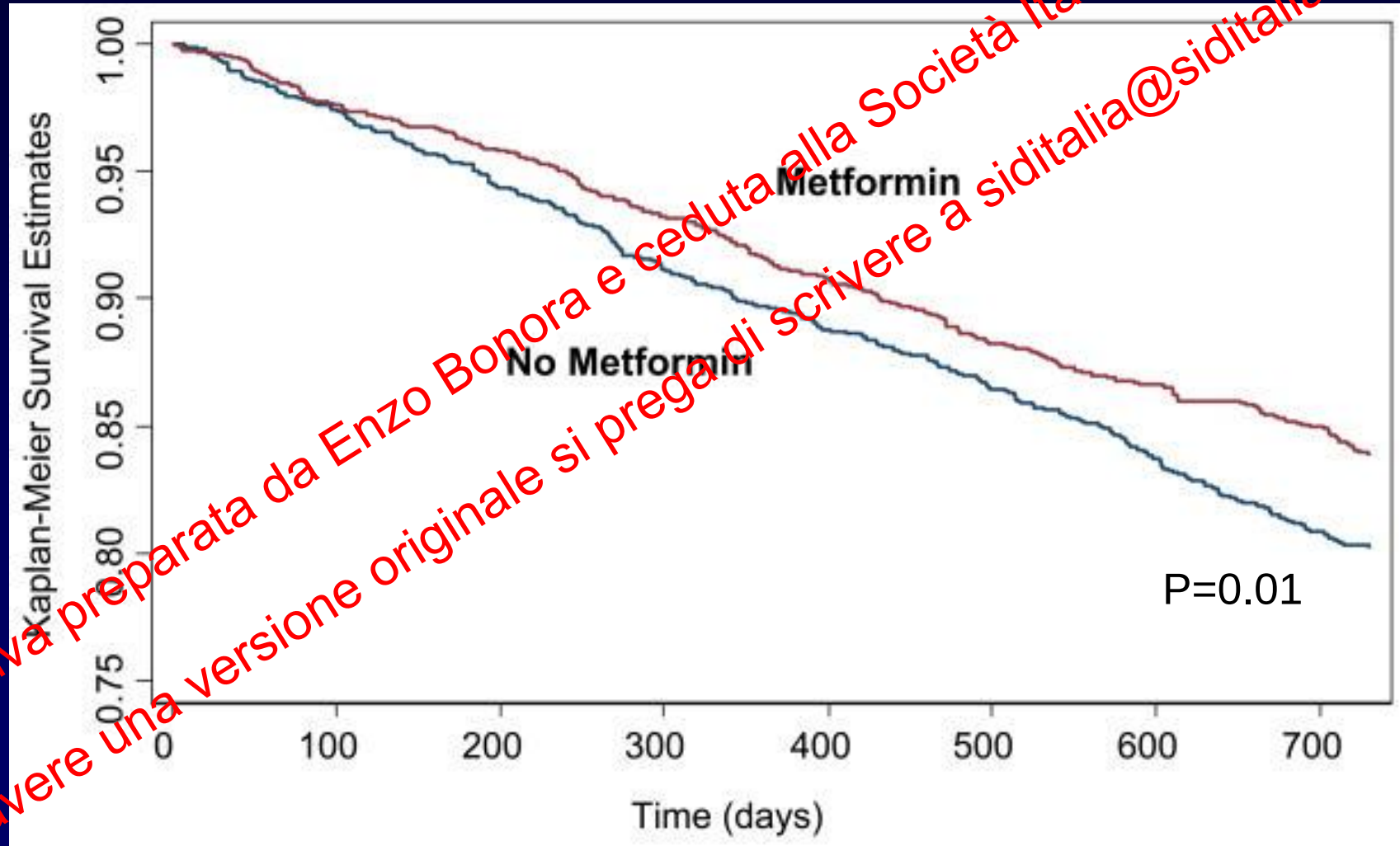
ZODIAC, n=1353,
Follow-up 9.6 yrs

Metformin vs. no metformin
HR 0.43 (0.23-0.80)

After adjustment for age, sex,
smoking, duration, HbA1c,
creatinine, albuminuria,
blood pressure,
total/HDLcholesterol, insulin
use, SU use, CVD

Metformin Use and Survival in patients with T2DM and Heart Failure

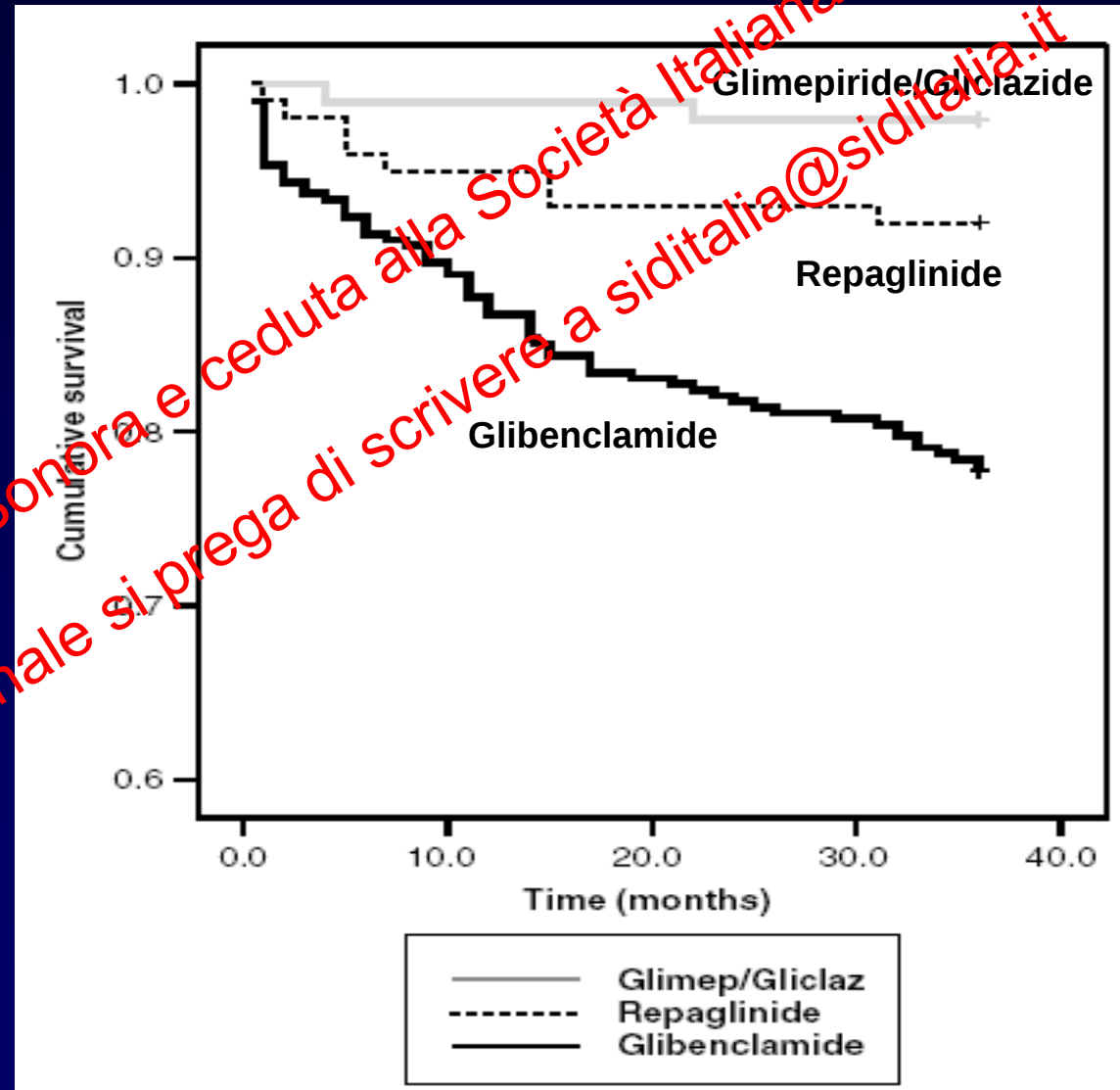
(Aquilar et al - Circ Heart Fail 2011; 4: 53–58)



Three-Year Mortality in T2DM Treated with Different Agonists to SUR

(Monami et al – Diab Metab Res Rev 22: 477-482, 2006)

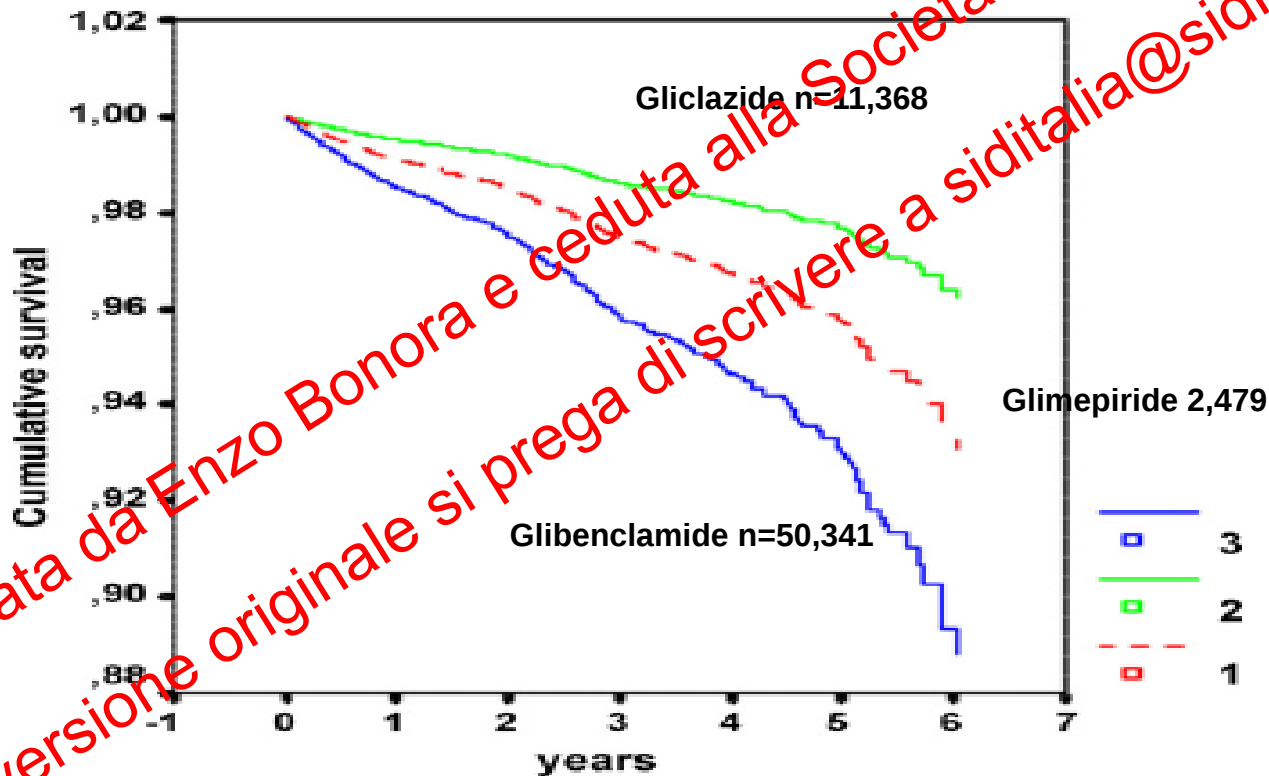
Selectivity
for B-cell SUR



N= 2002
Follow-up: 3 yrs

All-Cause Mortality According to Treatment with Different Sulphonylureas

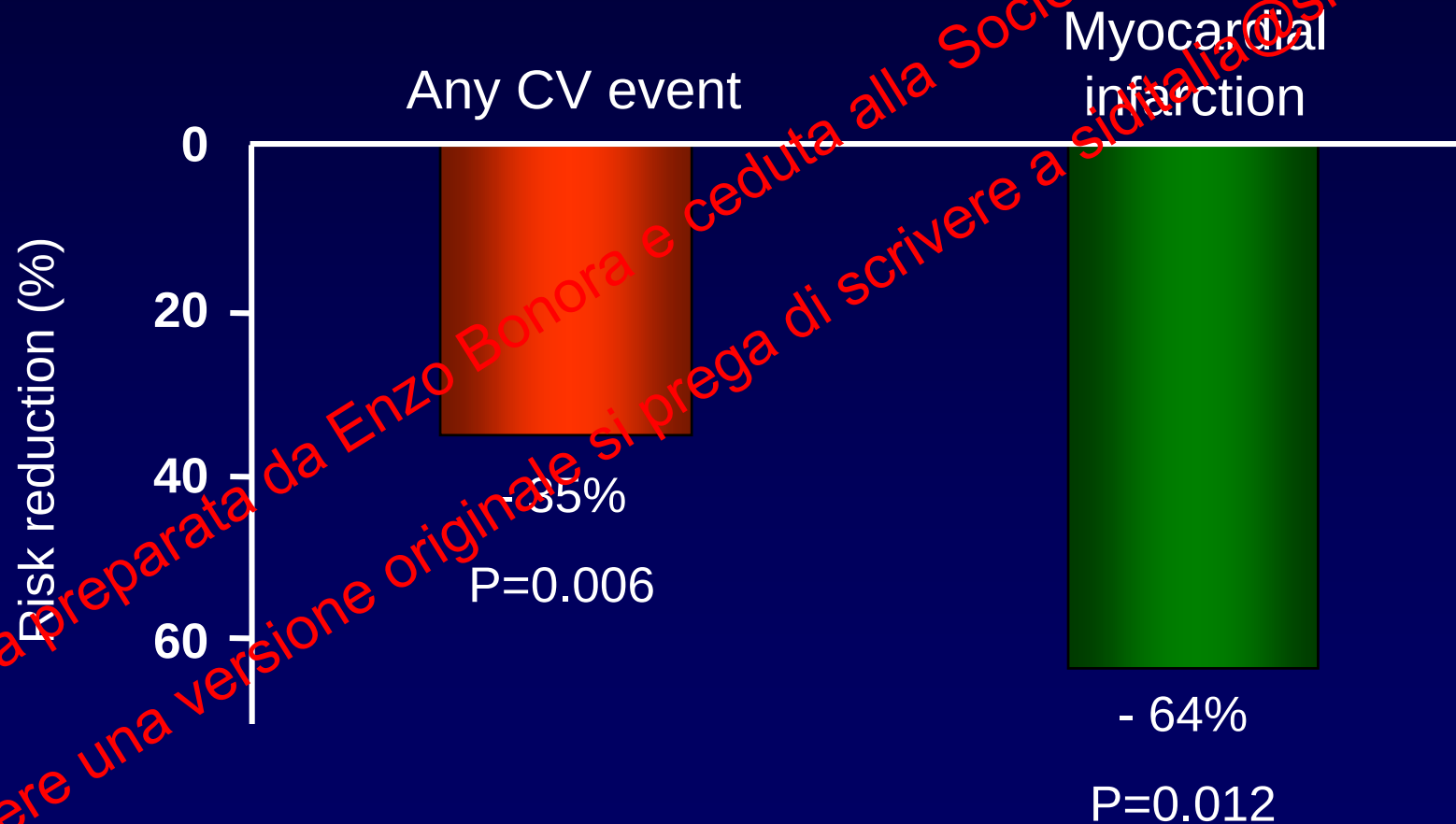
(Khalangot et al – Diab Res Clin Pract 86: 247-253, 2009)



CVD mortality Gliclazide vs. Glibenclamide
HR 0.29 [0.21-0.38], $p < 0.001$

Cardiovascular risk reduction by acarbose in patients with established type 2 diabetes

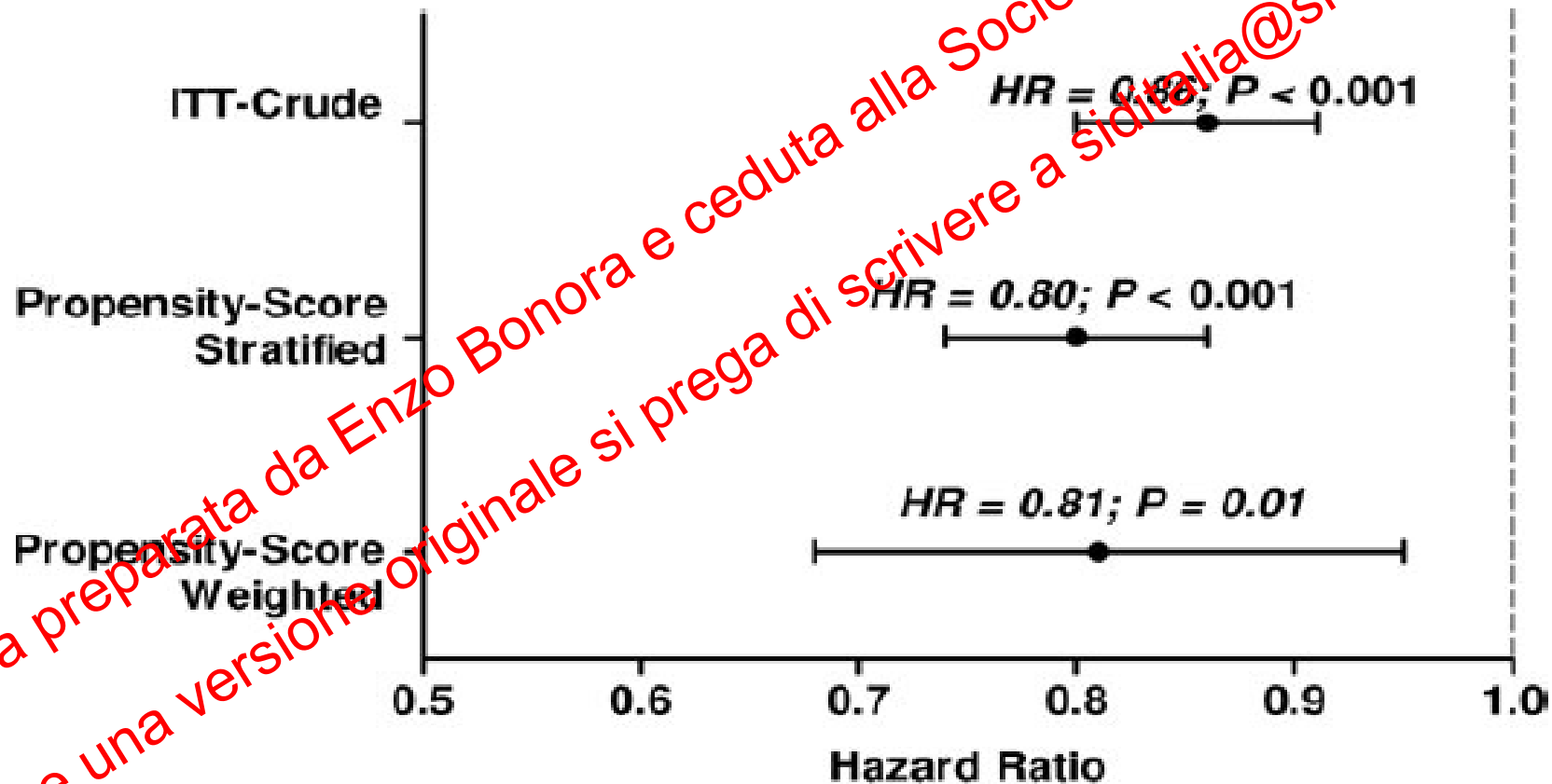
(Hanefeld M et al, Eur Heart J 25: 10-16, 2004)



Risk of CVD in T2DM Treated with Exenatide vs. Other Anti-Diabetic Agents

A retrospective analysis of the LifeLink database

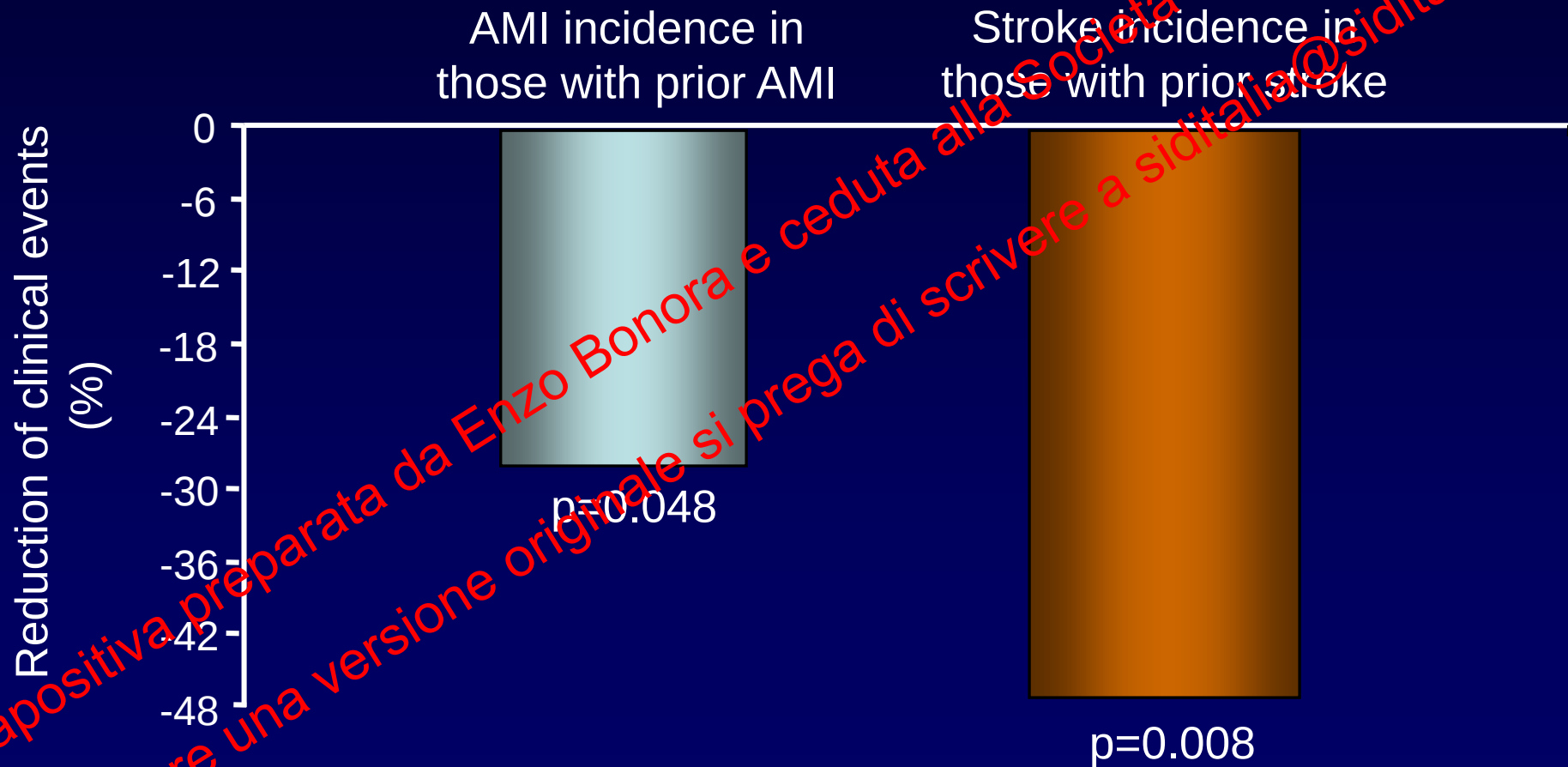
(Best et al – Diabetes Care 2011)



First new prescription: Exenatide (n=21,754) - Other agents (n=361,771)

Secondary Prevention of CVD by Pioglitazone in T2DM: Secondary Analyses

(PROactive Study; Erdmann, JACC 2007; Wilcox, Stroke 2007)

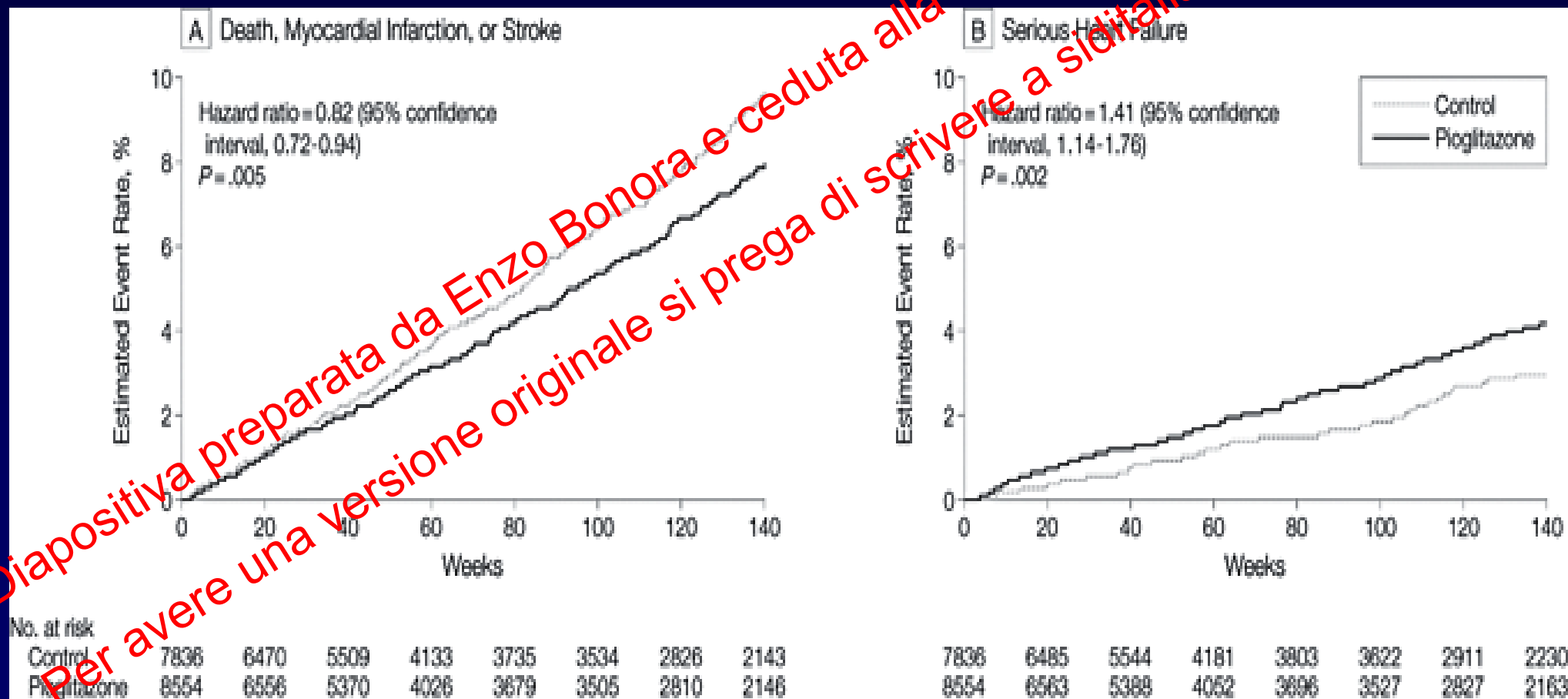


Risk of CVD During Treatment with Pioglitazone: a Meta-analysis

(Lincoff AM et al - JAMA 298:1180, 2007)

Death, MI, stroke: RR 0.82

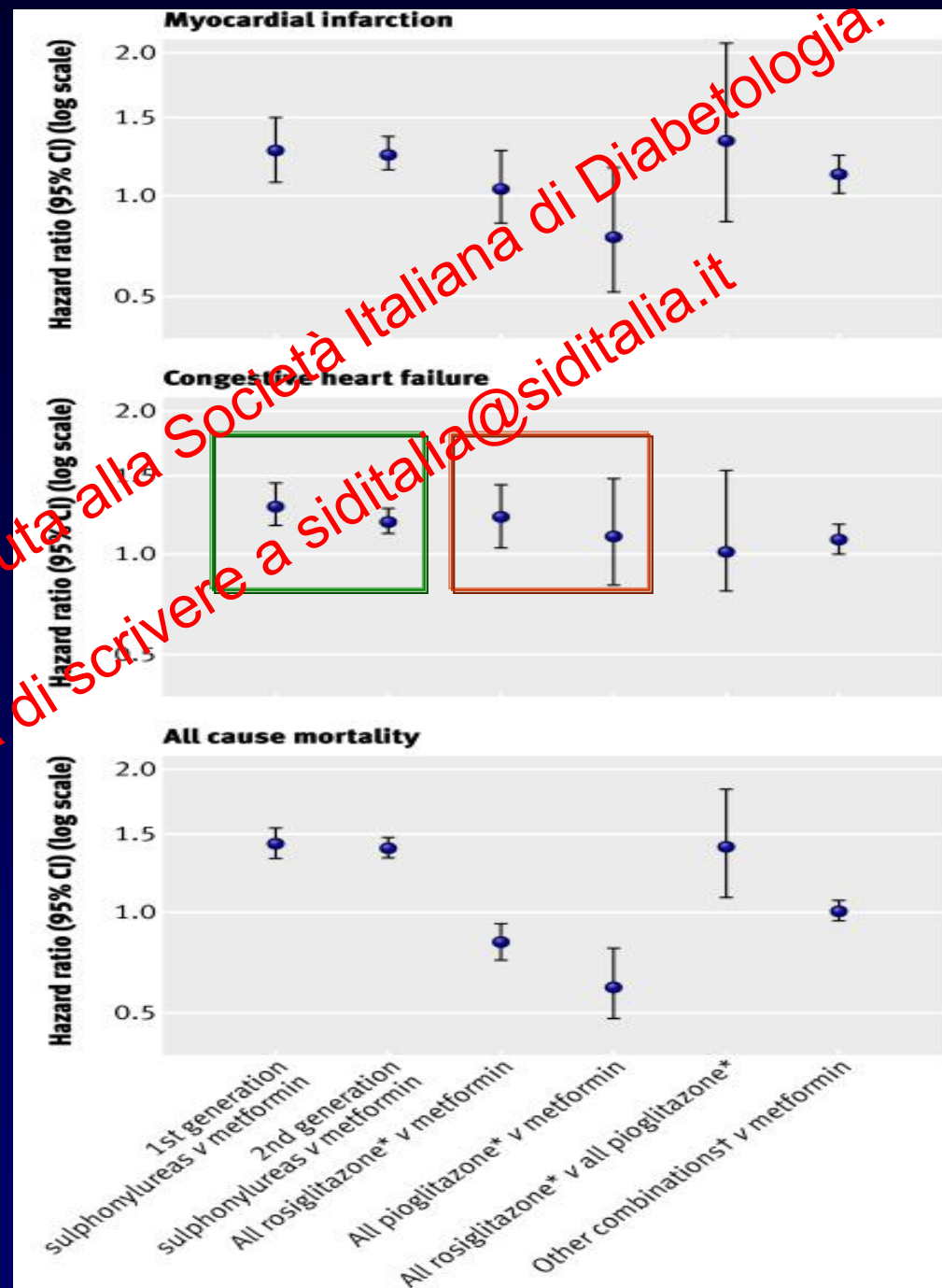
Serious HF: RR 1.41



Risk of CVD disease and all cause mortality in T2DM as a function of OHA prescribed: a retrospective observational study vs. metformin

(Tzoulaki I et al - BMJ 339: b4731, 2009)

N=91,521; age 65; follow-up 7.1



RECORD Study: Bone fractures

	Rosiglitazone n=2220	Control n=2227
All	185 (225)	118 (132)
Upper limb	86 (101)	55 (58)
Distal lower limb	70 (73)	27 (28)
Femur/hip	10 (11)	8 (8)
Spine	14 (14)	9 (9)
Pelvis	0 (0)	4 (4)
Other	25 (26)	25 (25)

Number of participants (fractures)

Some people had more than one fracture and in different territories

The Use of Pioglitazone and the Risk of Bladder Cancer in Type 2 Diabetes: Nested Case-Control Study

(Azoulay et al - BMJ 344 :e3645, 2012)

Patients with at least one prescription of an antidiabetic agent between 1 January 1988 and 31 December 2009 (n=241 111)

Excluded (n=124 779):
 <1 year of medical history in general practice research database before cohort entry (n=107 857)
 Insulin prescription as first prescription (n=5135)
 <40 years of age at cohort entry (n=11 787)

Cohort with type 2 diabetes (n=116 332)

Bladder cancer before cohort entry (n=605)

Study cohort (n=115 727)

Cases of incident bladder cancer with at least one year of follow-up (n=376)

Ever use of pioglitazone
Adjusted RR 1.83 (1.10-3.05)

Treatment >24 months
Adjusted RR 1.99 (1.14-3.45)

Cumulative dose >28.000 mg
Adjusted RR 2.54 (1.05-6.14)

Increased risk not observed with rosiglitazone

Adjusted for excessive alcohol use, obesity, smoking status, HbA_{1c}, previous bladder conditions, previous cancer (other than non-melanoma skin cancer), Charlson comorbidity score, and ever use of other antidiabetic agents (metformin, sulfonylureas, insulin, and other oral hypoglycaemic agents)

rate 89.4 per 100,000 person years (less than 1 out of 1000 per year)

Hypoglycemia in T2DM patients randomized and maintained on monotherapy in the UKPDS

(J Diabetic Compl 20: 395, 2006)



Diapositiva preparata da Enzo Bonora e ceduta alla Società Italiana di Diabetologia.
Per avere una versione originale si prega di scrivere a siditalia@siditalia.it

Hypoglycemia in T2DM patients treated in monotherapy with the “new anti-diabetic agents”

(data from RCT)



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Main Untoward Effects of Anti-Diabetic Agents

	Hypos	GI Discomfort	Weight Gain	Edema	Bone Fracture
Metformin		Yes			
Sulphonylurea	Yes		Yes	(Yes)	
Acarbose					
Repaglinide	Yes		Yes		
Pioglitazone			Yes	Yes	Yes
GLP-1 RA		Yes			
DPP-4 inhibitor					

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Main Interactions of Anti-Diabetic Agents

	Warfarin	FANS	Antibiotics Antifungins	Fibrates	Digoxin	Others
Metformin						
Sulphonylurea	Yes	Yes	Yes	Yes		Yes
Acarbose					Yes	Yes
Repaglinide			Yes	Yes		
Pioglitazone						Yes
GLP-1 RA	(Yes)	(Yes)	(Yes)	(Yes)	(Yes)	Yes
DPF-4 Inhibitor			(Yes)			(Yes)

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Warning or Contraindication of Anti-Diabetic Agents According to Organ Failure

	Heart Failure	Respiratory Failure	Liver Failure	Kidney Failure
Metformin	Yes	Yes	Yes	Yes
Sulphonylurea			Yes	Yes
Acarbose			Yes	Yes
Repaglinide			Yes	
Pioglitazone	Yes		Yes	
GLP-1 RA			Yes	Yes
DPP-4 inhibitor			Yes but...	Yes but...

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Main Limitations of Oral Anti-Diabetic Agents

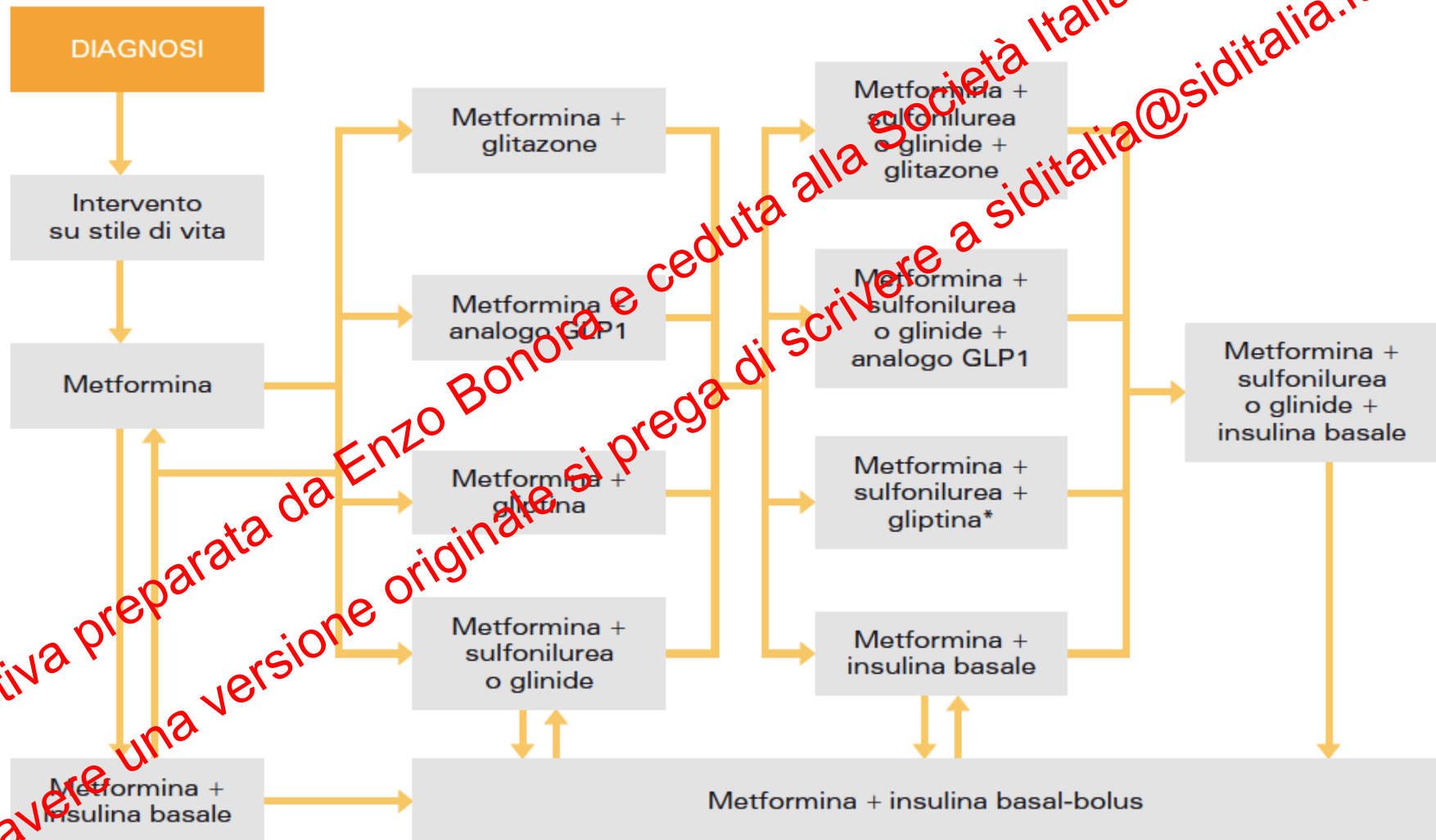
	MET	SU	AGI	REP	PIO	DPP-4	GLP-1
Loss of efficacy	++	+++		+++			
Need to titrate	++	+++	+++	+++			+
Need of lab exam monitoring	++	+		+		(+)	+
Need of SMBG		+++		+++			
Injections							+
Interactions		+++	+	+++	+		
Contraindications	+	++	+	++	++	(+)	+
Warnings	+	+		+++	+++	(+)	
Side effects	+	++	+++		++		++
Hypoglycemia		+++		++			

Dispositiva preparata da Enzo Bonora e ceduta alla Società Italiana di Diabetologia.
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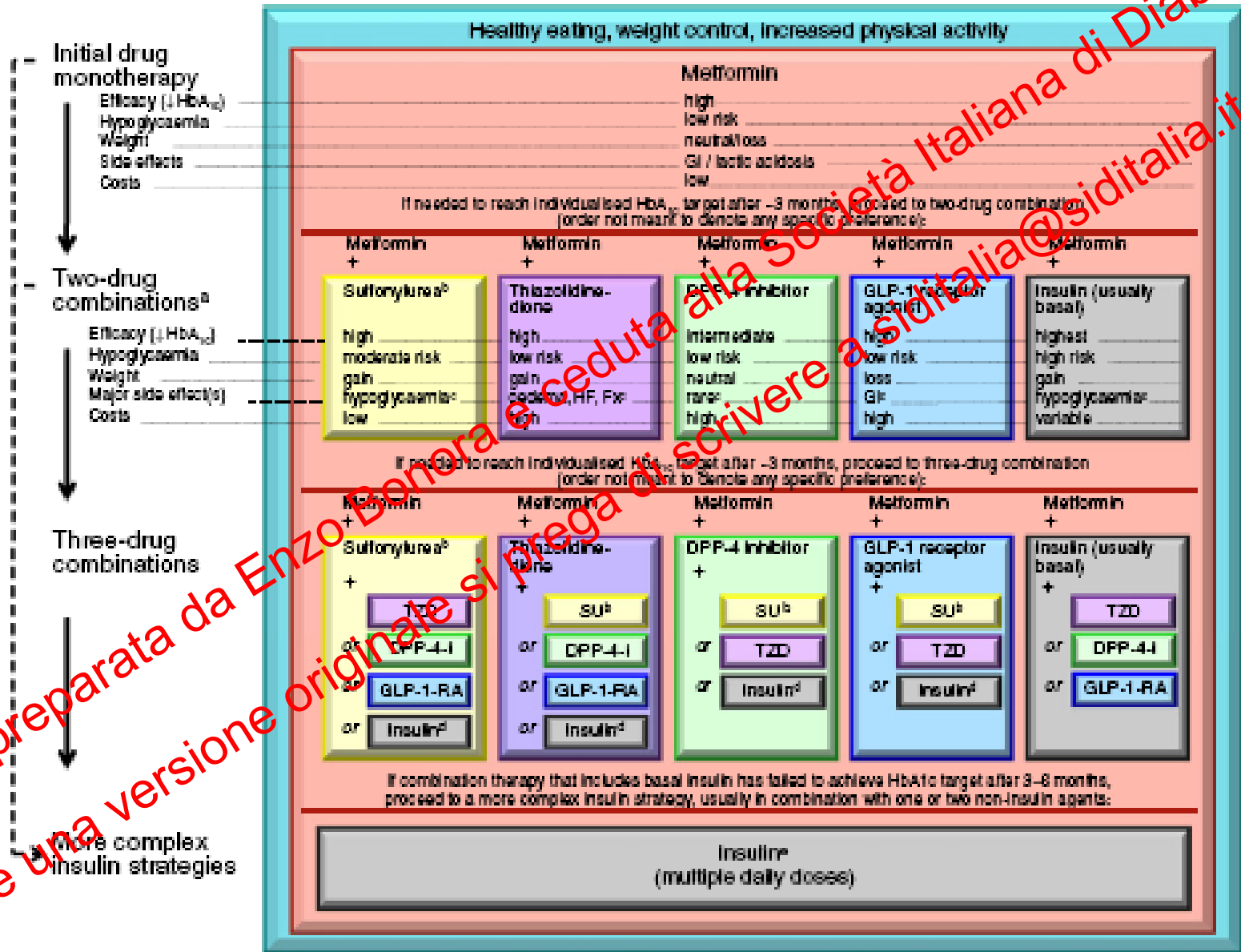
Standard di Cura SID-AMD 2010

Algoritmo terapeutico per il diabete tipo 2

Flow-chart per la terapia del diabete mellito di tipo 2.



Algorithm of anti-diabetic treatment by ADA/EASD Consensus Statement 2012



Step 1

Metformin

If contraindicated
or not tolerated:

Acarbose

or

Gliptin

or

Glitazone

or

Repaglinide

or

Sulphonylurea

or

GLP-1 Analog

Insulin

1-4 injections/day
(temporary
or permanent)

Step 2*

Metformin
+
Acarbose

Metformin
+
Gliptin

Metformine
+
Glitazone

Metformin
+
Repaglinide

Metformin
+
Sulphonylurea

Metformin
+
GLP-1 Analog

Metformin
+
Basal Insulin

Step 3**

3 OHAs

2 OHAs
+
GLP-1 Analog

2 OHAs
+
Basal insulin

Metformin
+
2-4 insulin
injections/day

Insulin
2-4 injections/day

Step 4**

4 OHAs

3 OHAs
+
GLP-1 Analog

3 OHAs
+
Basal insulin

Insulin
2-4
injections/day

*Other associations might be necessary in case of contraindication or intolerance to metformin (e.g., sulphonylurea or repaglinide or gliptin + glitazone; sulphonylurea o repaglinide + GLP-1 analog). **Some associations are off label

Terapia ipoglicemizzante nel diabete tipo 2

Insuline rapide

Insuline lente

Biguanidi

Sulfoniluree

Inibitori alfa-glucosidasi

Glinidi

Glitazoni

Gliptine

Incretine

Glifozine

>100 possibili combinazioni di farmaci!

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Indicated associations of anti-diabetic agents (from RCP)

	Met	SU	Acarb	Rep	Pio	GLP-1 RA	DDP-4	INS
Met	-	Yes	Yes	Yes	Yes	Yes	Yes	Yes
SU	Yes	-	Yes	Yes	Yes	Yes	Yes	Yes
Acarb	Yes	Yes		Yes	Yes	Yes	Yes	Yes
Rep	Yes			-				
Pio	Yes	Yes			-			Yes
GLP-1 RA	Yes	Yes			Yes	-		Yes
DDP-4	Yes	Yes			Yes		-	Yes

Fine

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