DKD: Epidemiologia e classificazione

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Roma, 18-19 novembre, 2022

DISCLOSURE

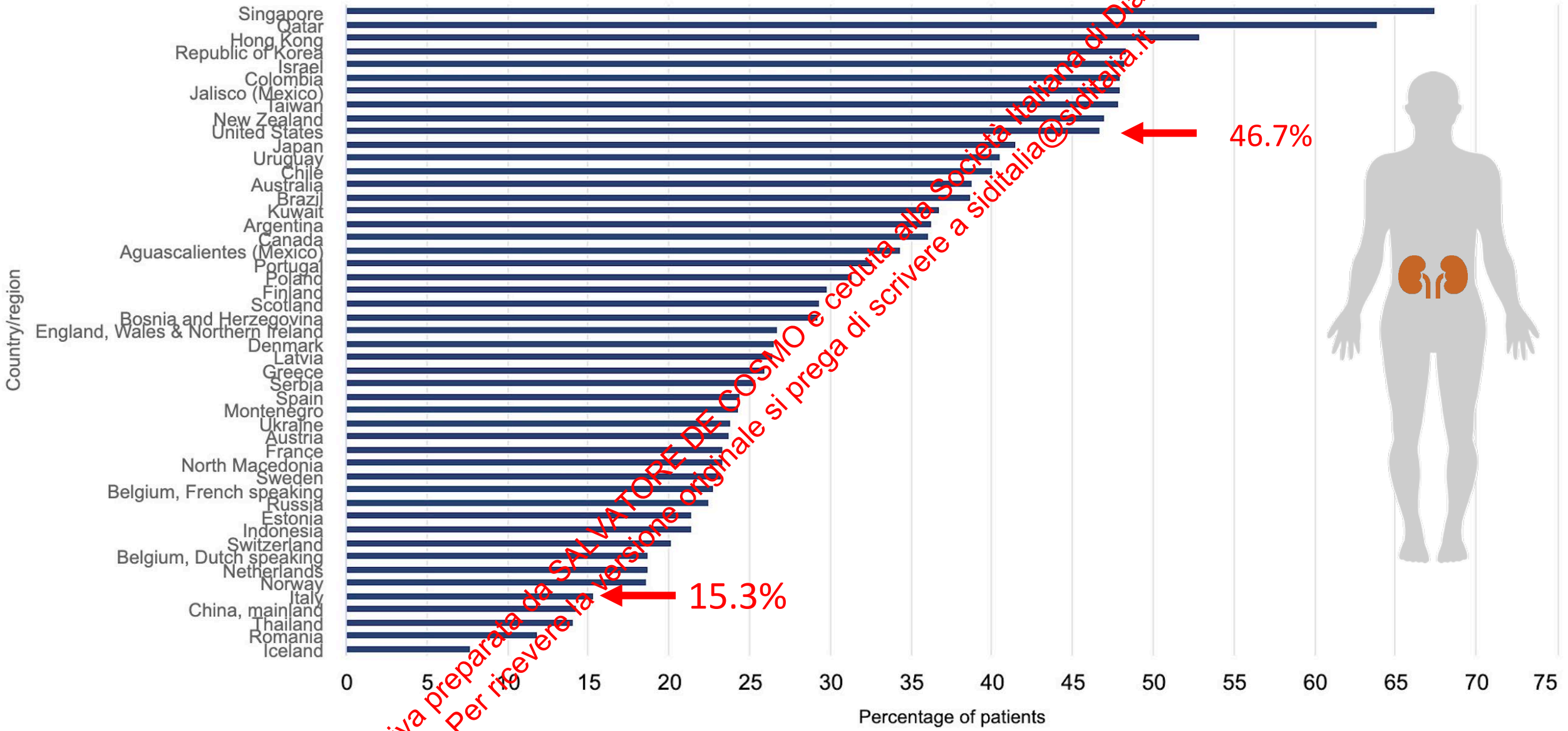
In qualità di RELATORE, ai sensi dell'art.76 sul Conflitto di Interessi dell'Accordo Stato-Regioni del 2 febbraio 2017, dichiaro che negli ultimi due anni ho avuto i seguenti rapporti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

Eli Lilly, Boehringer, Astra-Zeneca, MundiPharma, MSD, Sanofi, Novo-Nordisk, Daiichi Sankyo, Bayer.

Dichiaro, inoltre, che i contenuti formativi esposti sono indipendenti da interessi commerciali.

Percentage of incident cases of treated ESRD attributed to diabetes, by country or region, 2019

Sort by Percentage



Data Source: 2021 United States Renal Data System Annual Data Report

USRDS

RIDT

REGISTRO ITALIANO DI DIALISI E TRAPIANTO

SOCIETÀ ITALIANA DI NEFROLOGIA

REPORT 2018

61° CONGRESSO NAZIONALE SIN

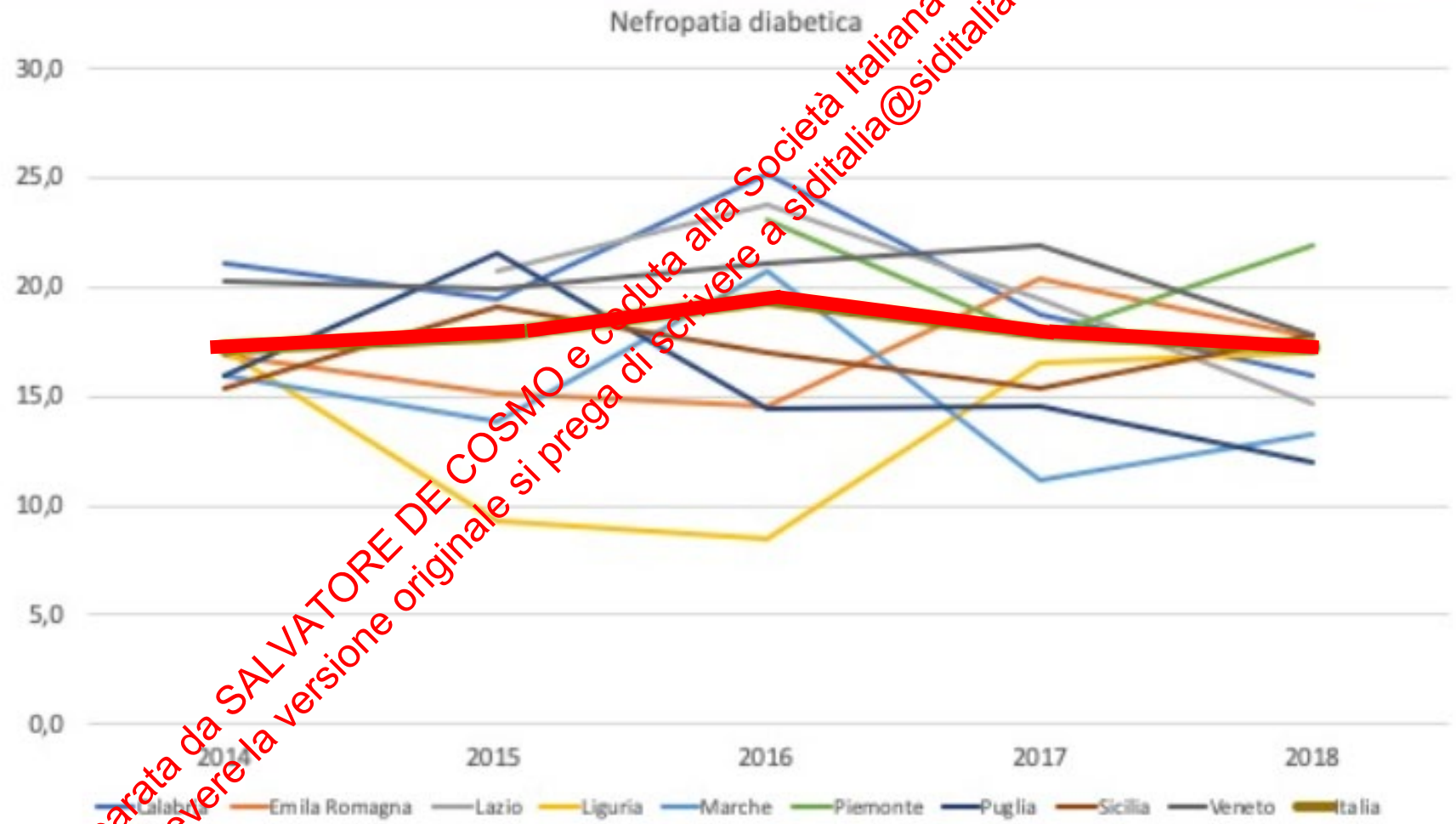
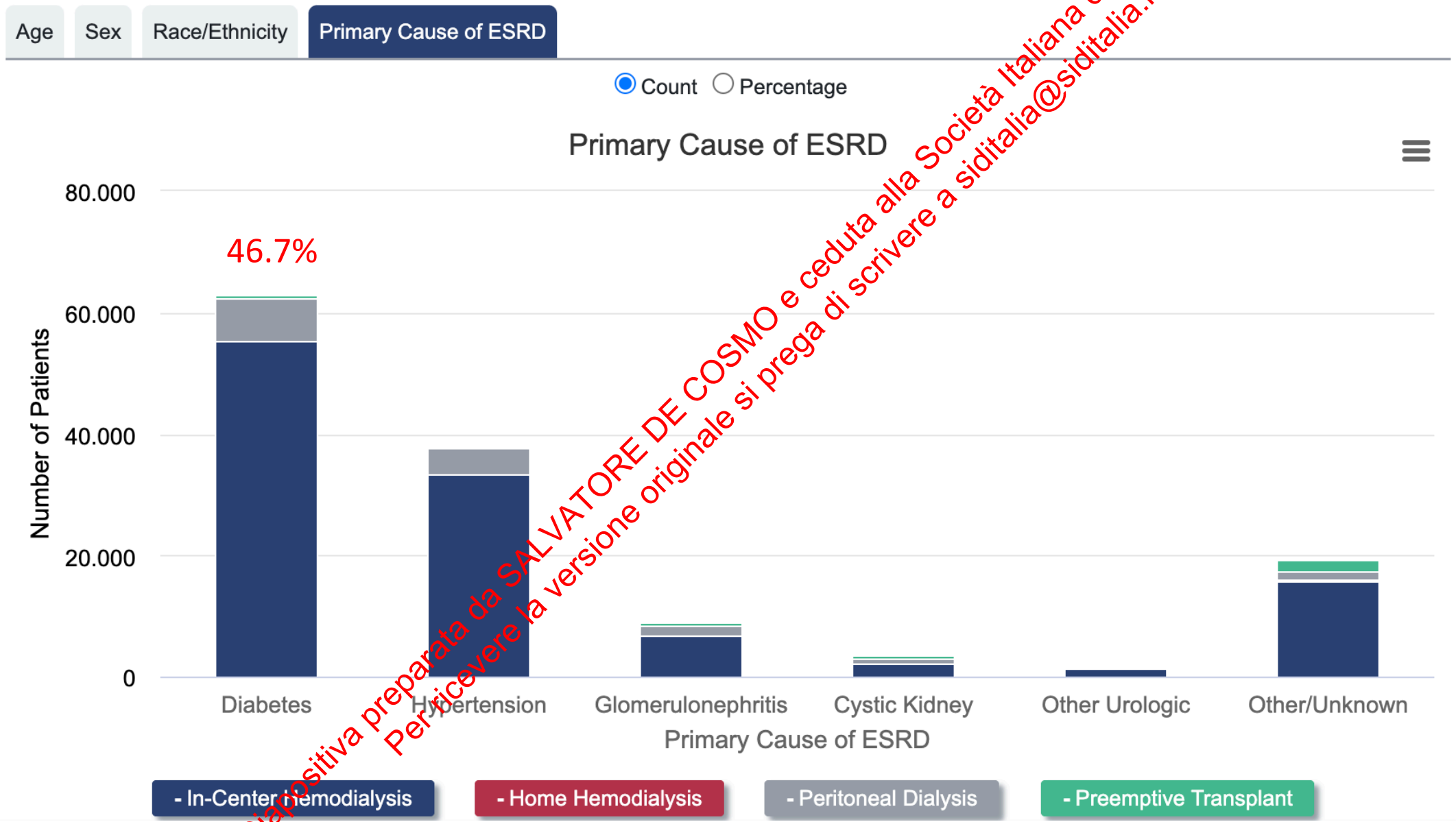
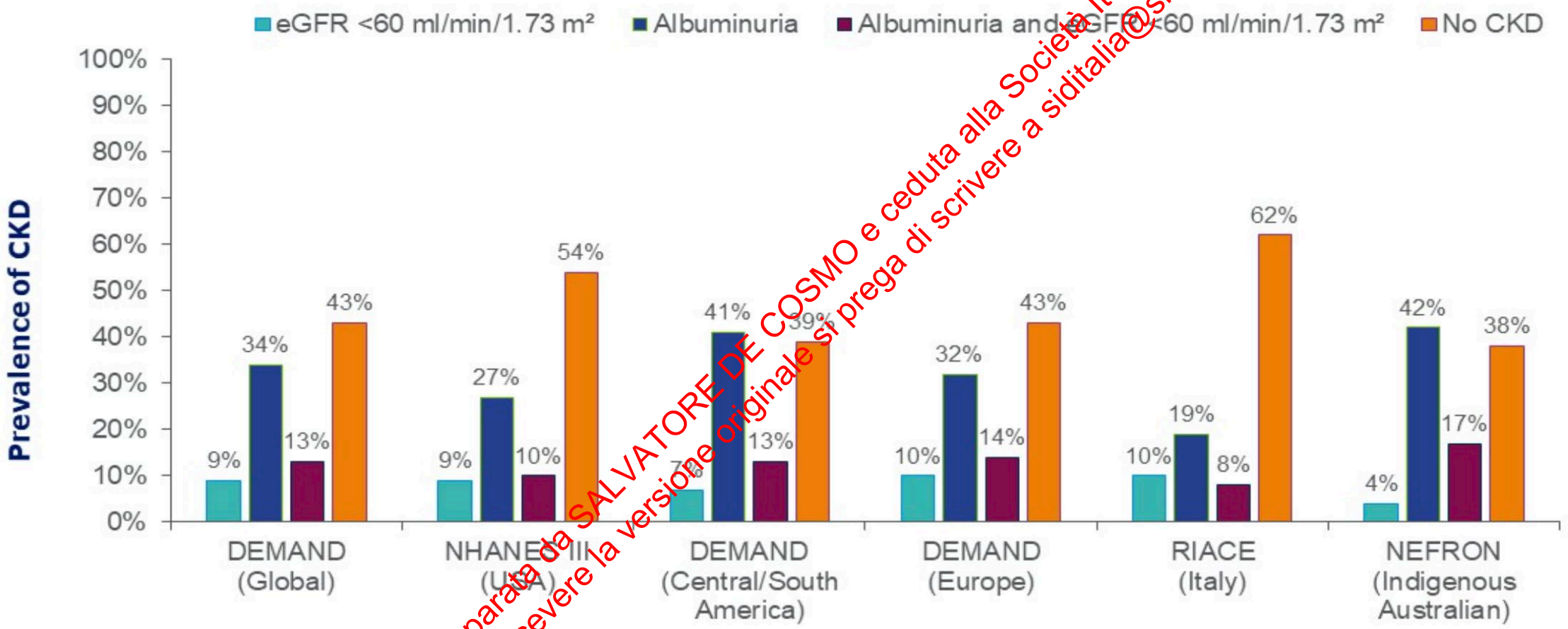


Figure 1.9 Modality at incidence of ESRD by patient characteristics



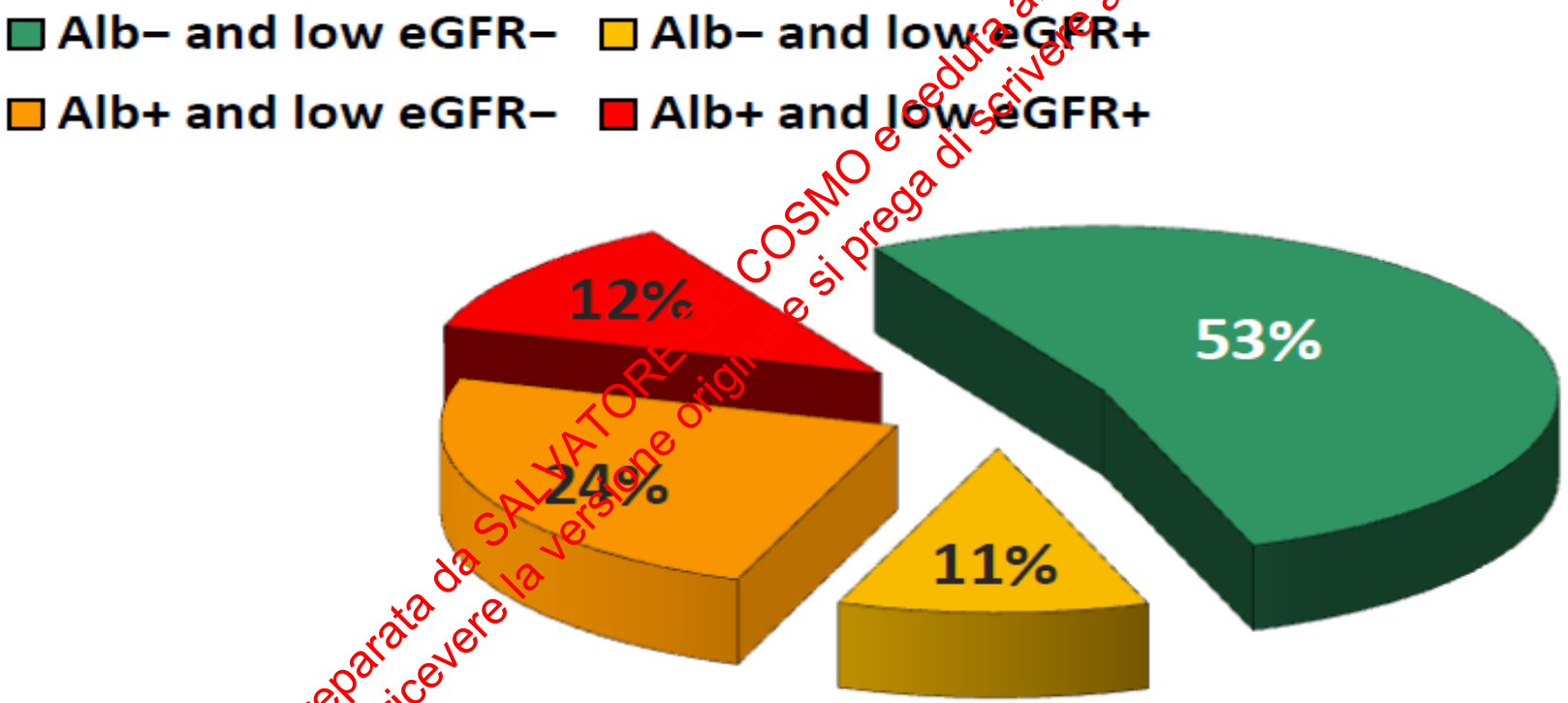
Globally, approximately half of people with T2D present evidence of CKD



Thomas MC, et al. Nat Rev Dis Primers 2015;1:15018

Kidney dysfunction and related cardiovascular risk factors among patients with type 2 diabetes

Large cohort of patients (120.905) with type 2 diabetes mellitus attending 236 Italian Diabetes Clinics in 2009



S. De Cosmo et al. for AMD-Annals Study Group, *NDT* 2014

Stages of CKD are defined according to eGFR and degree of albuminuria

GFR categories, description and range (ml/min/1.73 m²)				Albuminuria stages, description and range (mg/g)		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30	30–300	>300
	G1	Normal or high	≥90	Stage 0 (no CKD) **53%**	Stage 1-2 Albuminuric phenotype **24%**	
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59	Stage 3-5 Non albuminuric CKD phenotype 11%	**Stages 3-5 Albuminuric CKD phenotype 12%**	
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Low risk* Moderately increased risk High risk Very high risk

*Defined as low risk for developing mineral and bone disorders and cardiovascular complications if there are no other markers of kidney disease or CKD

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate Penno G et al. J Hypertens 29: 1802-1809, 2011

Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. *Kidney Int Suppl* 2017;7:1

Diabetic Kidney Disease vs Diabetic Nephropathy

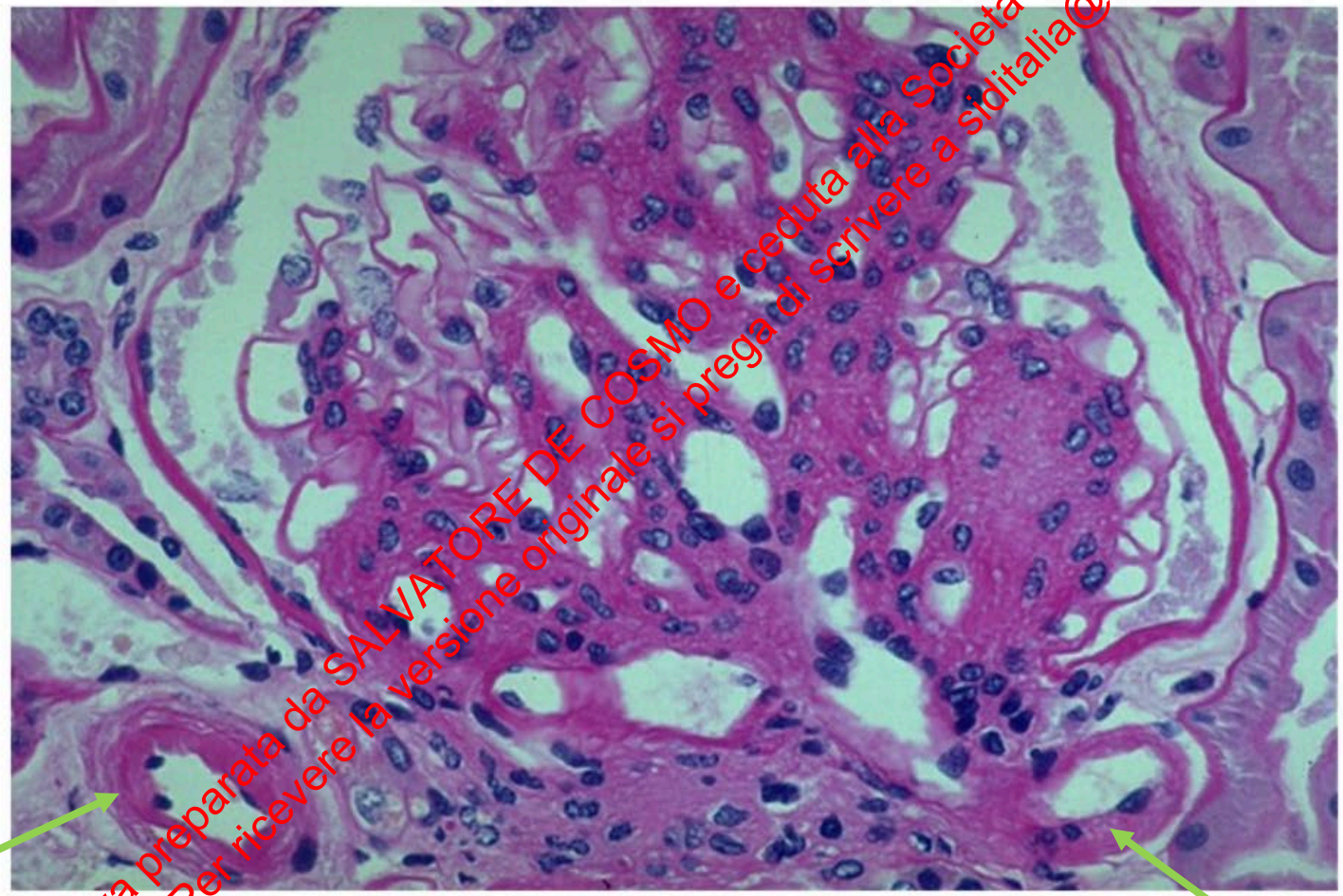
CKD is a clinical diagnosis based upon increased UACR, low eGFR or both

DKD is **chronic kidney disease in diabetes**, not a pathological phenotype

Diabetic Nephropathy is used to specify classic glomerular lesions in diabetes:

- glomerular basement membrane thickening, mesangial expansion and nodules, podocyte loss, endothelial lesions

Classic Diabetic Glomerulopathy



Fioretto P et al, Diabetologia, 2007

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KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

kidney INTERNATIONAL

October 2020

Antihyperglycemic therapies in patients with type 2 diabetes (T2D) and CKD

Diagnostically, CKD occurring among people with diabetes is usually attributed to diabetes, unless other causes are readily evident. Certainly, cases of CKD occurring among people with diabetes are actually heterogeneous, and some are caused by other processes. More work is needed to develop granular approaches to CKD diagnosis and classification in diabetes and to determine the roles of kidney biopsy and biomarkers in this evaluation. Here, we adopt the current clinical approach of treating most presentations of diabetes and CKD similarly, modifying the approach as appropriate according to albuminuria or eGFR category. We avoid the term "diabetic kidney disease" to avoid the connotation that CKD is caused by traditional diabetes pathophysiology in all cases, although this term is entirely appropriate when this limitation is recognized. We also avoid the term "diabetic nephropathy," an outdated term for which there is currently no consensus definition. Prevention, screening, and diagnosis of new-onset diabetes after transplantation are also important topics that were considered out of scope for this guideline.

CJASN Clinical Journal of the American Society of Nephrology

The Modern Spectrum of Renal Biopsy Findings in Patients with Diabetes

Vol 8 October, 2013

Shree G. Sharma, Andrew S. Bomback,† Jai Radhakrishnan,† Leal C. Herlitz,‡ Michael B. Stokes,‡ Glen S. Markowitz,‡ and Vivette D. D'Agati‡*

620 pazienti con Diabete M. Tipo 2 → Biopsie renali afferenti ad un Singolo Centro (2011)

Indicazioni alla Biopsia

- AKI con o senza CKD
- Severità della proteinuria
- Positività test sierologici
- Sedimento urinario attivo

RISULTATI

- **227 (37%) Nefropatia Diabetica (DN) da sola**
- **220 (36%) Nefropatie non Diabetiche (NDRD) da sole**
- **164 (27%) DN + NDRD**

Kidney dysfunction and related cardiovascular risk factors among patients with type 2 diabetes

Clinical features of 120,903 patients with type 2 diabetes: whole sample and division according to the presence/absence of albuminuria or low eGFR

	Whole sample	Alb− and low eGFR−	Alb− and low eGFR+	Alb+ and low eGFR−	Alb+ and low eGFR+
n (%)	120 903	63 639 (52.6%)	13 680 (11.3%)	28 806 (23.8%)	14 684 (12.2%)
Male gender n (%)	70 247 (58.1)	35 822 (56.3)	5076 (42.2)	19 874 (69.0)	8741 (59.5)
Age (years)	66.6 ± 11.0	64.1 ± 10.7	74.0 ± 8.0	65.0 ± 10.8	73.4 ± 8.5
BMI (kg/m^2)	29.7 ± 5.2	29.4 ± 5.2	29.7 ± 5.1	30.2 ± 5.3	30.0 ± 5.2
Serum creatinine (mg/dL)	1.0 ± 0.5	0.8 ± 0.2	1.3 ± 0.5	0.9 ± 0.2	1.6 ± 0.8
eGFR	75.5 ± 1.5	85.1 ± 13.9	48.0 ± 9.8	84.1 ± 14.4	42.8 ± 12.7
Known duration of diabetes (years)	11.1 ± 9.4	9.7 ± 8.6	13.3 ± 10.4	11.0 ± 9.0	15.3 ± 10.5
HbA1c (%)	7.5 ± 1.5	7.4 ± 1.5	7.4 ± 1.4	7.8 ± 1.6	7.7 ± 1.5
Total cholesterol (mg/dL)	186.6 ± 41.0	187.9 ± 40.0	185.7 ± 40.7	185.6 ± 42.3	183.4 ± 42.7
Triglycerides (mg/dL)	148.1 ± 108.2	139.4 ± 99.7	151.1 ± 87.4	157.2 ± 131.0	166.6 ± 108.1
HDL cholesterol (mg/dL)	49.2 ± 13.6	50.4 ± 13.7	49.6 ± 13.8	47.7 ± 13.2	46.5 ± 13.4
LDL cholesterol (mg/dL)	108.2 ± 34.2	110.0 ± 33.8	106.4 ± 34.1	107.1 ± 34.9	103.9 ± 34.4
SBP (mmHg)	139.6 ± 19.1	137.7 ± 18.3	139.5 ± 18.9	141.5 ± 19.5	143. 8 ± 20.5
DBP (mmHg)	79.2 ± 9.8	79.1 ± 9.5	77.3 ± 9.8	80.5 ± 10.0	78.5 ± 10.3
Pulse pressure (mmHg)	60.5 ± 16.5	58.7 ± 15.7	62.3 ± 16.6	61.1 ± 16.6	65.4 ± 18.0
Retinopathy	18.6	14.2	18.5	22.4	30.5
Smokers (%)	17.6	17.5	8.8	23.8	13.4

Alb−, normoalbuminuria; Alb+, albuminuria; eGFR, estimated glomerular filtration rate; BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure All the between-group differences are statistically significant with $P < 0.0001$.

De Cosmo S, et al., The AMD-Annals Study Group. Nephrol Dial Transplant, 29: 657-662, **2014**

Baseline clinical characteristics by renal outcomes in 27,029 patients with T2DM

S. De Cosmo et al. for AMD-Annals Study Group, *Medicine*, 2016

	Overall	Alb-/eGFR-	Alb-/eGFR+	Alb+/eGFR-	Alb+/eGFR+	
					n=1,207 (5%)	p
Male gender (n,%)					651 (53.9%)	<.001
Age (years)					**69±8**	<.001
Duration of diabetes (years)					**12±9**	<.001
BMI (Kg/m^2)					29.9±5	<.001
Serum creatinine (mg/dL)					0.94±0.16	<.001
eGFR (mL/min/1.73 m2)					74±10	<.001
eGFR >90 mL/min/1.73 m^2 (n,%)					104 (8.6%)	<.001
HbA1c (%)					**7.6±1.4**	<.001
HbA1c ≥7% (53 mmol/mol)(n, %)	14,194 (52.9%)	9,156(51.1%)	1,559 (56.4%)	2,751(55.7%)	728 (61%)	<.001
Total cholesterol (mg/dL)						<.001
Triglycerides (mg/dL)						<.001
Triglycerides ≥150 mg/dl (n			%)		%)	<.001
HDL-c (mg/dL)						<.001
HDL-c <40 mg/dL if male, <50 mg/dL if female (n, %)			%)		%)	<.001
LDL-c (mg/dL)	111±32	112±32				<.001
LDL-c ≥100 mg/dL (n, %)	15,523 (61.9%)	10,585 (63.3%)	1,547 (60.2%)	2,759 (59.3%)	632 (56.8%)	<.001
Systolic BP (mmHg)	139±18	**138±18**	**142±18**	**139±18**	**143±18**	<.001
Diastolic BP (mmHg)	80±9	80±9	80±9	80±9	80±9	.91
Systolic/Diastolic BP ≥140/85 mmHg (n, %)	1,3702 (59.1%)	8,828 (57.4%)	1,489 (64.4%)	2,670 (60.2%)	715 (69.2%)	<.001
Retinopathy (n, %)	2,510 (9.3%)	**1,499 (8.3%)**	**318 (11.4%)**	**541 (10.9%)**	**152 (12.6%)**	<.001

Low eGFR & Albuminuria

- Age
- BMI
- Dyslipidemia
- Antihypertensive and antihyperglycemic intensity of treatment

Low eGFR

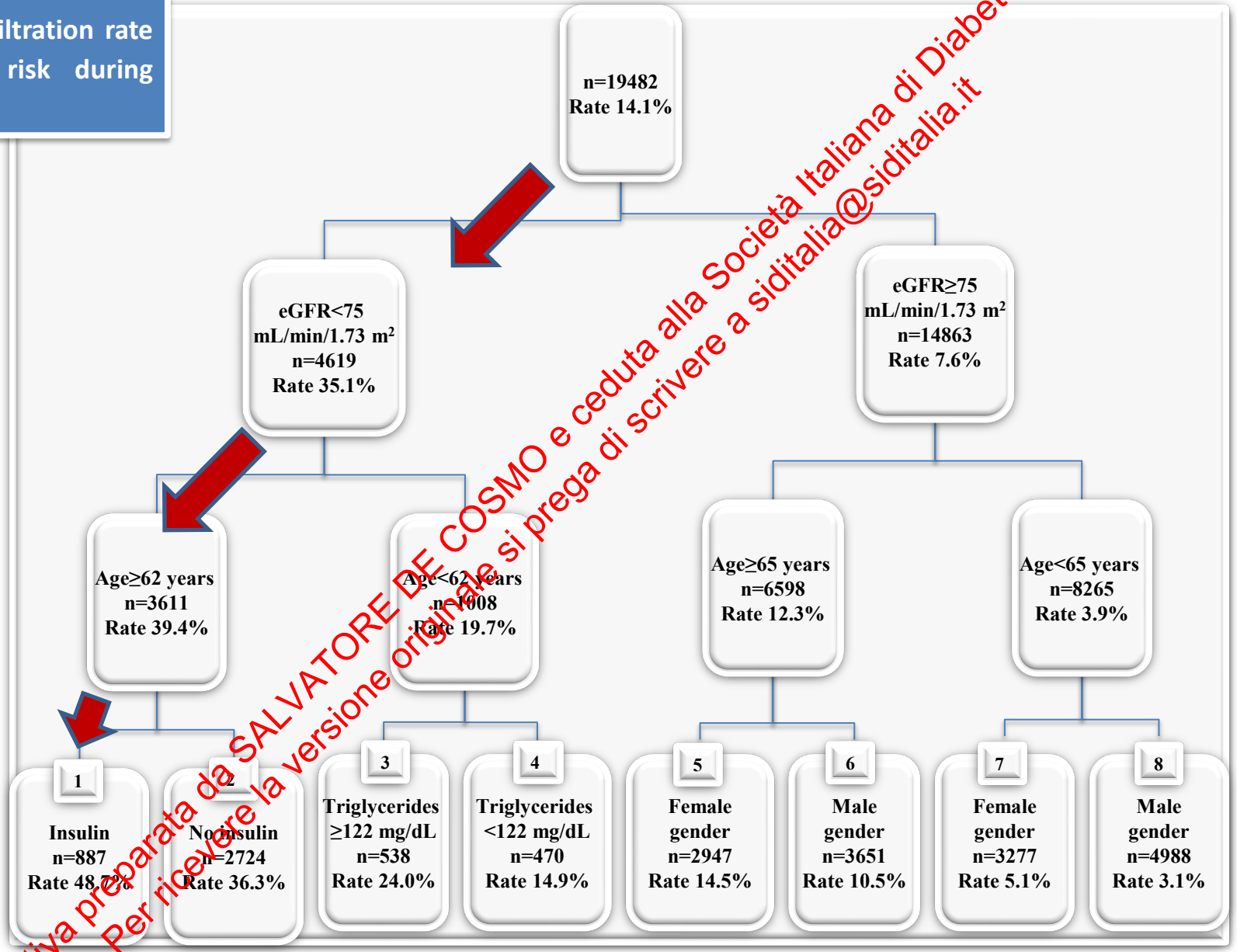
- Female
- Triglycerides

Albuminuria

- Male
- HbA1c
- Low HDL-C

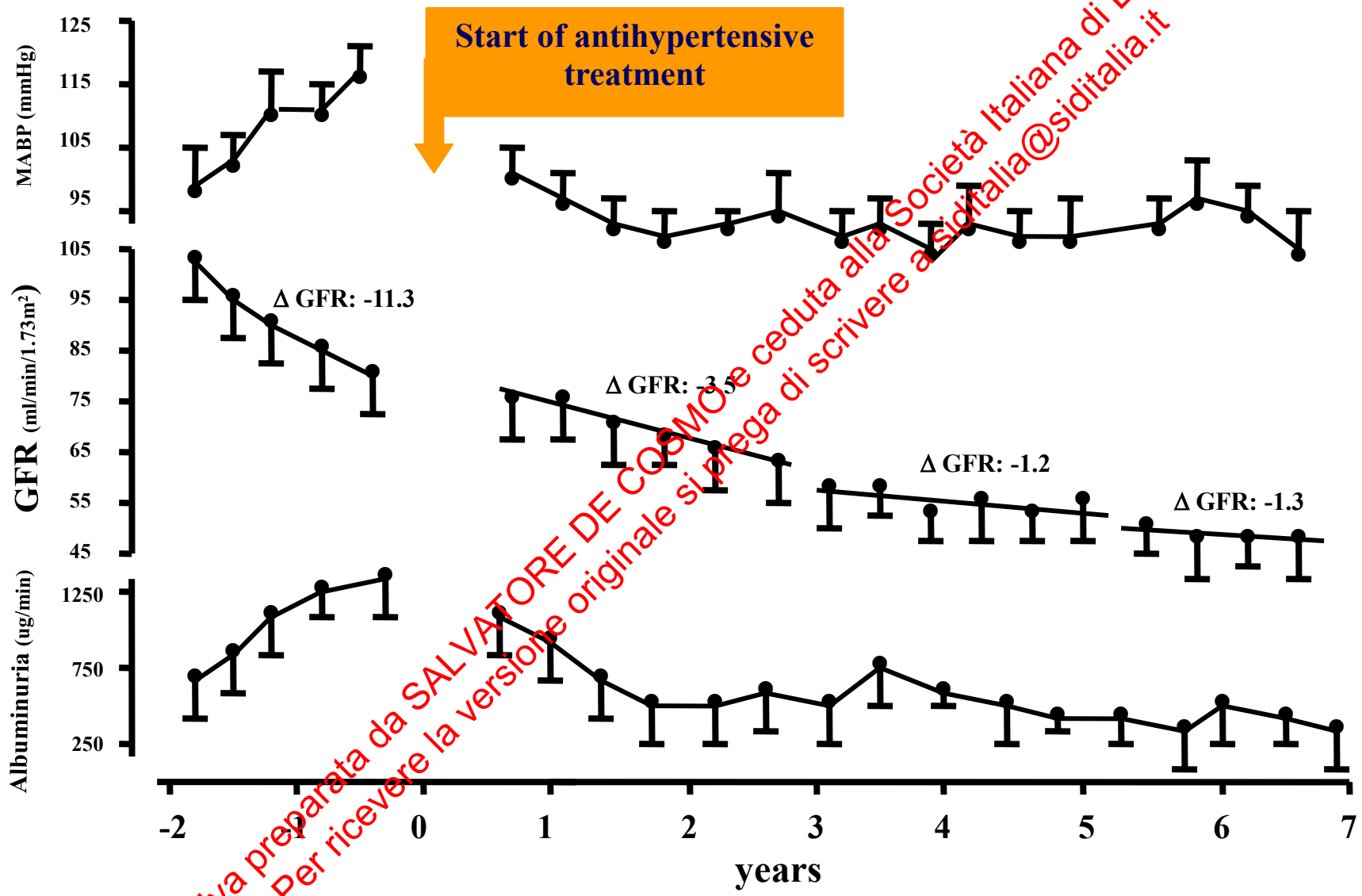
RECPAM analysis

Hierarchical tree of glomerular filtration rate (eGFR) <60 mL/min/1.73 m² risk during follow-up

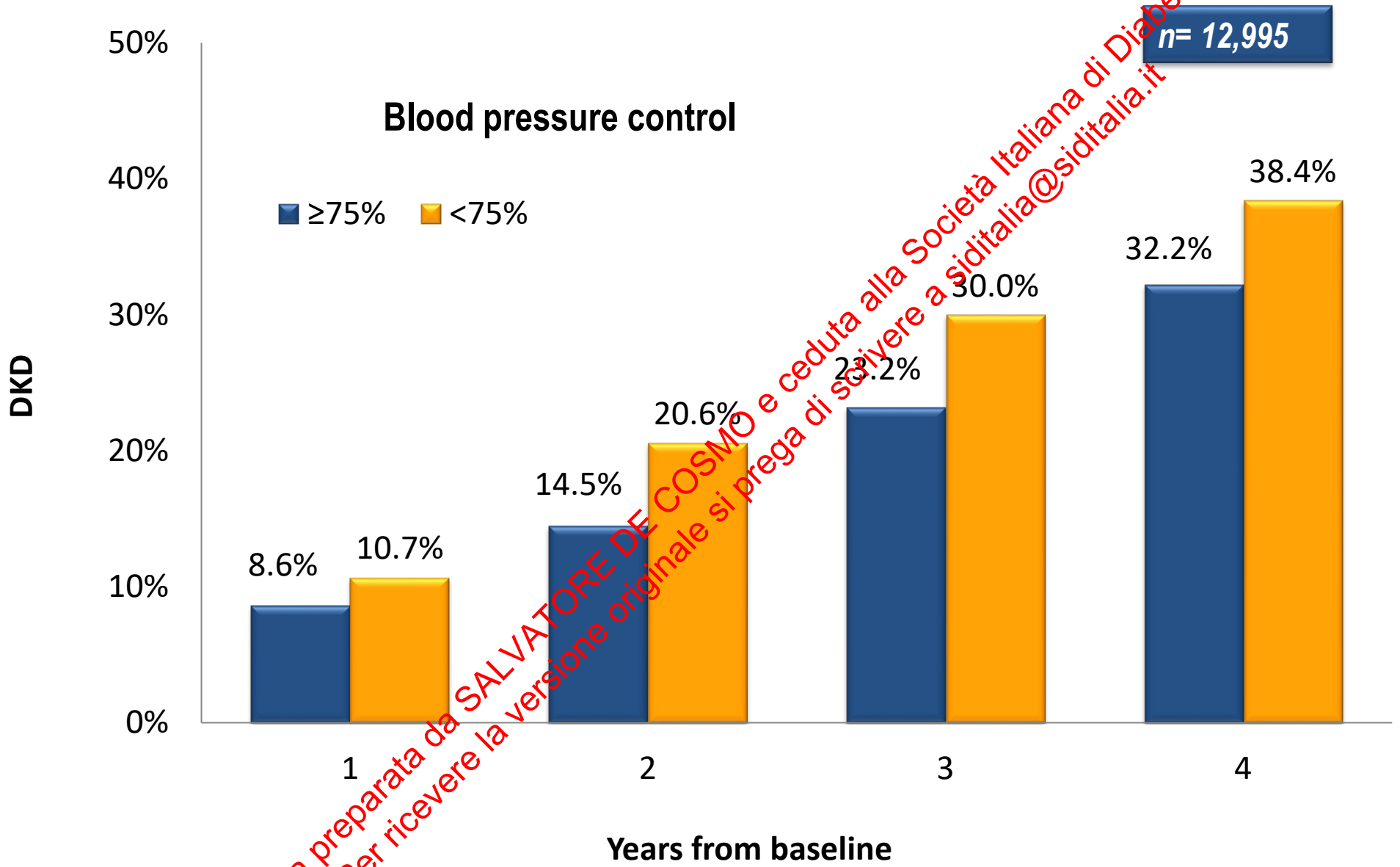


S. De Cosmo et al. for AMD-Annals Study Group, *Medicine,* 2016

Blood Pressure reduction *conveys* renal protection

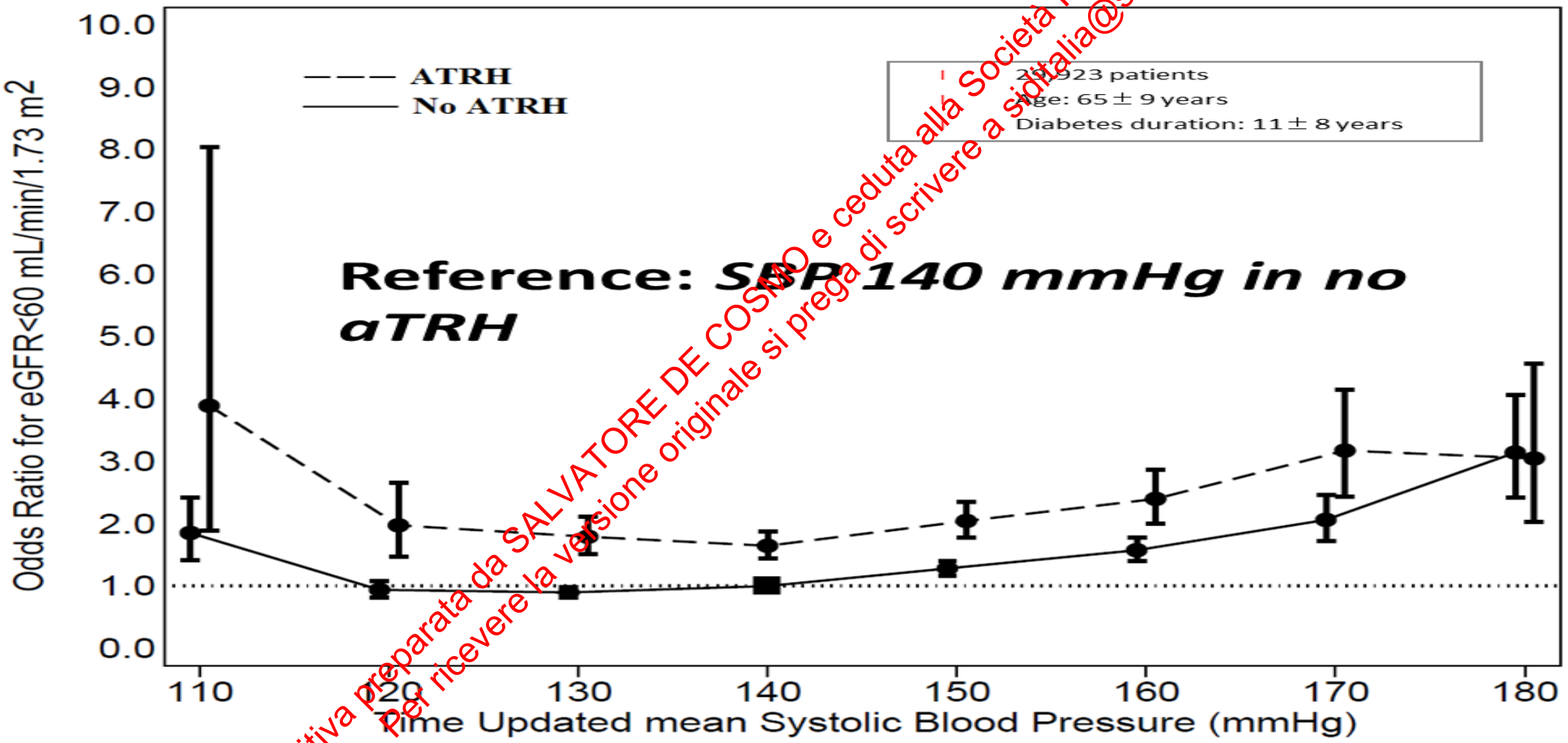


From Parving H-H, Am J Kidney Dis 1993



De Cosmo S & Pontremoli R et al. Hypertension, 2016

Resistant hypertension and renal outcome in T2DM
The J curve relationship between BP and renal function



Viazzi F, Pontremoli R et al. J Am Heart Assoc 2017

Serum Uric Acid and Risk of CKD in Type 2 Diabetes

Salvatore De Cosmo, Francesca Viazzi, Antonio Pacilli, Carlo Giorda, Antonio Ceriello, Sandro Gentile, Giuseppina Russo, Maria C. Rossi, Antonio Nicolucci, Pietro Guida, Daniel Feig, Richard J. Johnson, Roberto Pontremoli, and the AMD-Annals Study Group

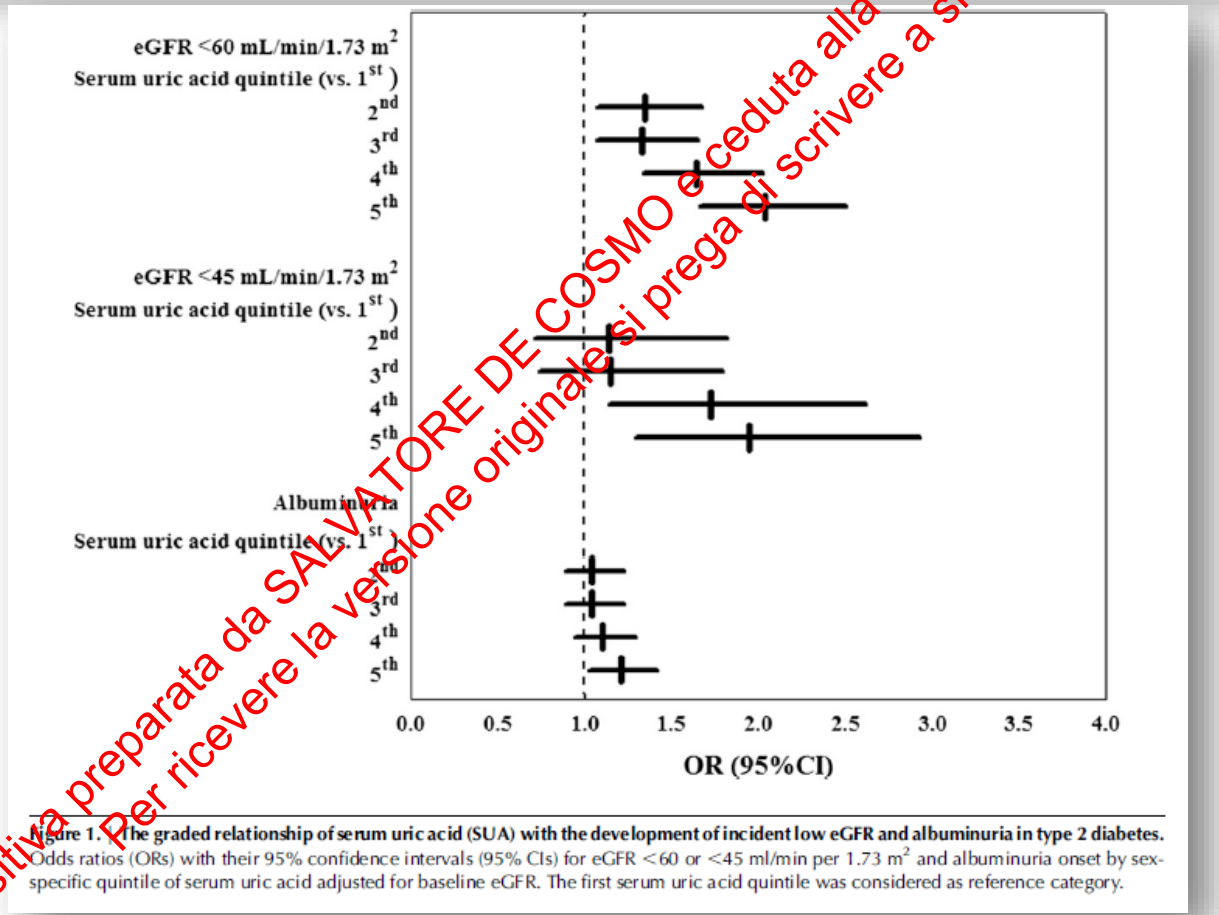


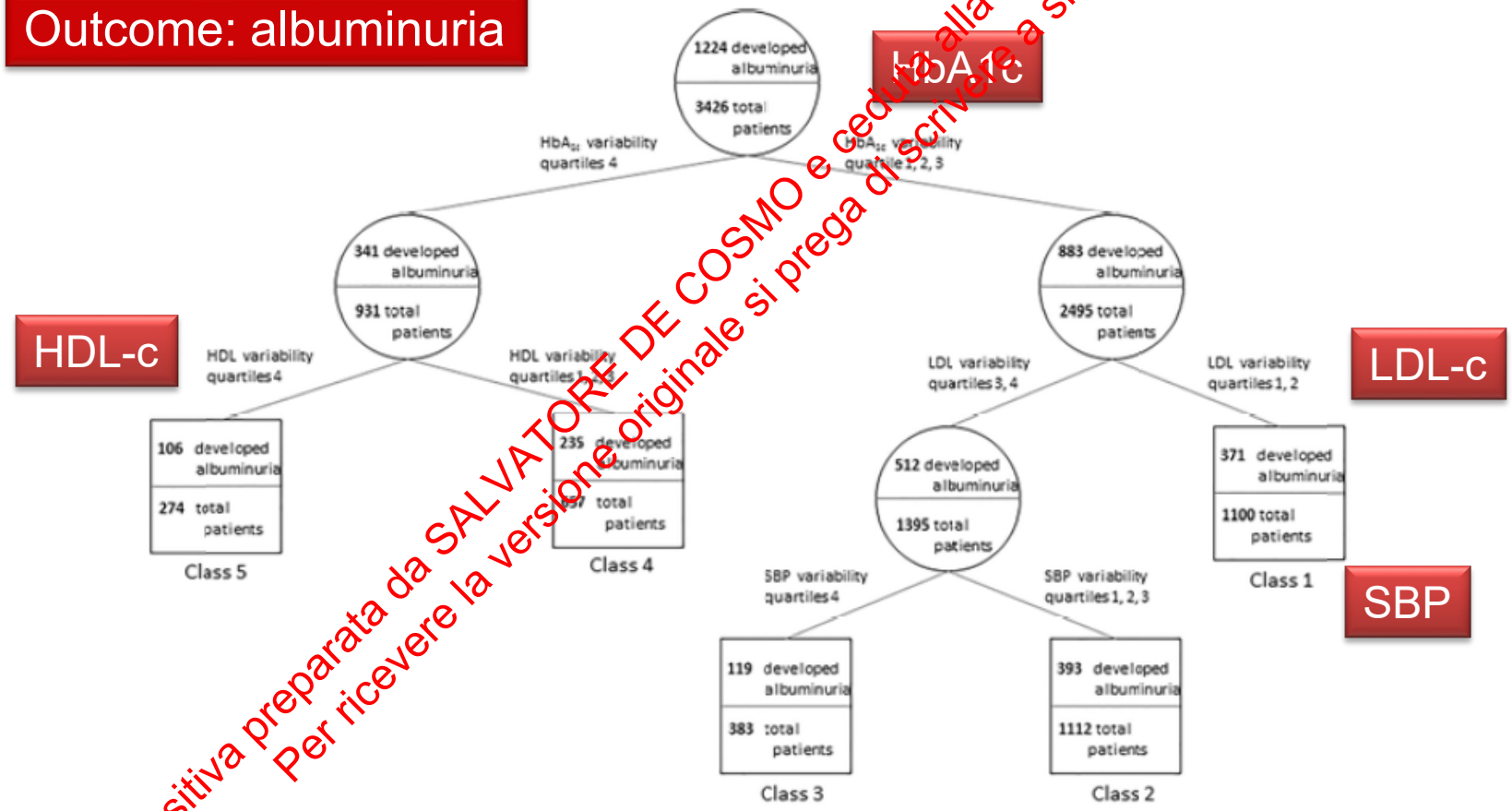
Figure 1. The graded relationship of serum uric acid (SUA) with the development of incident low eGFR and albuminuria in type 2 diabetes. Odds ratios (ORs) with their 95% confidence intervals (95% CIs) for eGFR <60 or <45 ml/min per 1.73 m^2 and albuminuria onset by sex-specific quintile of serum uric acid adjusted for baseline eGFR. The first serum uric acid quintile was considered as reference category.

Clin J Am Soc Nephrol, 2015.

DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

Variability in HbA1c, blood pressure, lipid parameters and serum uric acid and risk of development of chronic kidney disease in type 2 diabetes

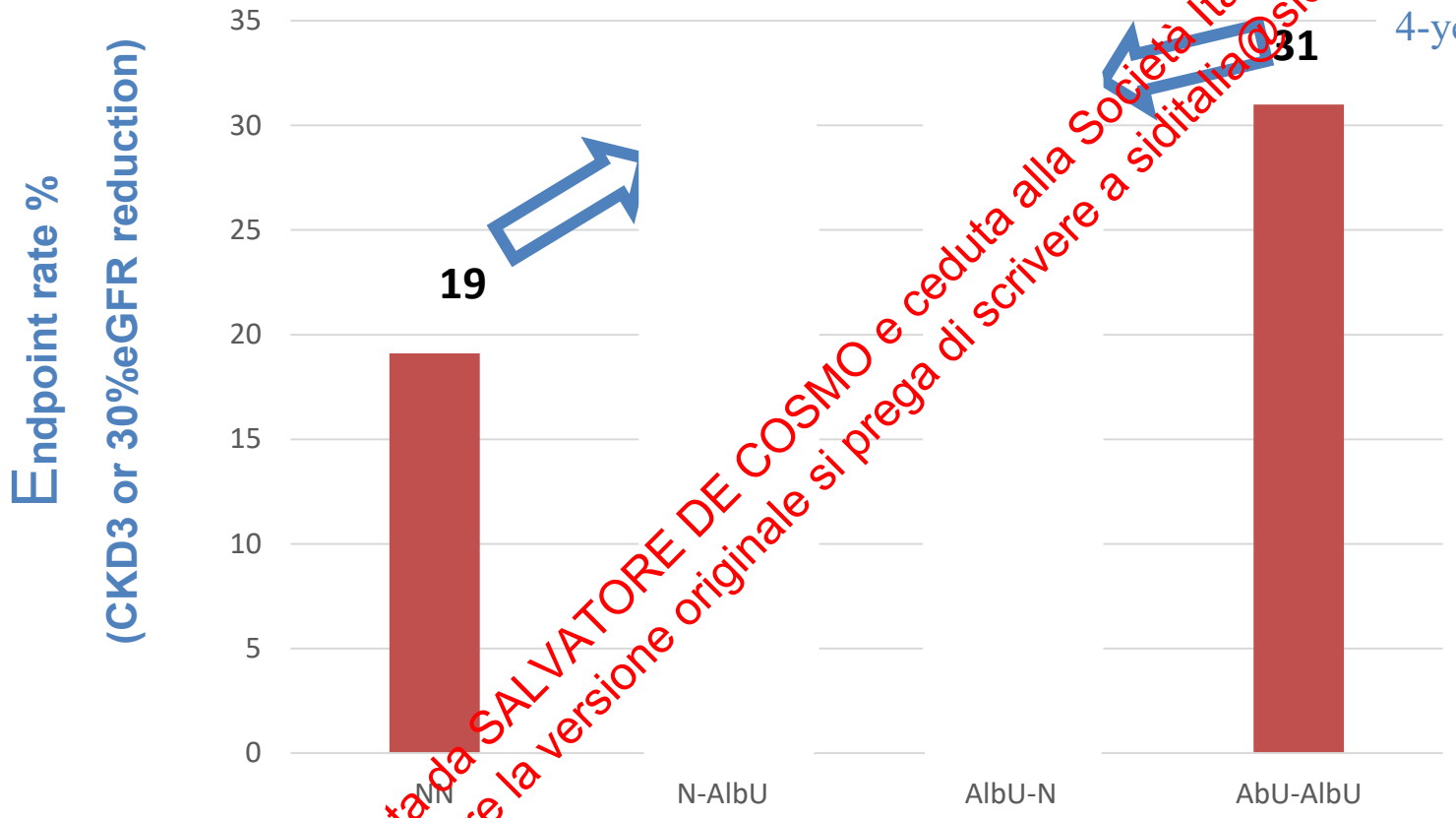
Outcome: albuminuria



A.Ceriello et a. for AMD-Annals Study Group, DOM, 2017

Changes in albuminuria and renal outcome in patients with hypertension and T2D

12,611 ptz with T2D and HT
eGFR >60 ml/min independently by albuminuria
4-years f-up



"[…] changes in albuminuria translate to changes in risk."

Viazzi F, Pontremoli R et al. J Hypertens 2018.

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journal homepage: WWW.JDCJOURNAL.COM

Association of kidney disease measures with risk of renal function worsening in patients with hypertension and type 2 diabetes

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Chronic kidney disease

ABSTRACT

Aims: To assess the role of kidney disease measures on the development of chronic kidney disease (CKD) in patients with type 2 diabetes (T2D) and hypertension (HT).
Methods: Clinical records from a total of 17,160 patients with T2D and HT, a baseline estimated glomerular filtration rate (eGFR) values ≥60 mL/min/1.73 m², evaluation for albuminuria and regular visit during a four-year follow-up were retrieved and analyzed. The incidence of eGFR <60 mL/min/1.73 m² and/or a reduction >30% from baseline was evaluated.
Results: At baseline 23% of patients (n = 3873) had albuminuria. Over the 4-year follow-up 20% (n = 3480) developed a renal endpoint 28% (n = 1074) of those with albuminuria and 17% (n = 2406) of those without albuminuria. The presence of baseline albuminuria entailed a 1.8 independent, greater risk of reaching stage 3 CKD. Patients with normal albuminuria showed a 1.54 ($p < 0.001$) greater risk for each 5 mL reduction (below 90 mL/min) in baseline GFR.
Conclusions: In T2D patients with HT, eGFR reduction and albuminuria are independently associated with a greater risk of developing stage 3 CKD. While baseline albuminuria entails a greater renal risk, due to a larger occurrence of the non-albuminuric phenotype, renal function worsening is more likely to be observed in patients without albuminuria.

1. Introduction

The prevalence of chronic kidney disease (CKD) has been steadily growing in recent years mainly as a consequence of improvements in the prevention and management of cardiovascular complications and the subsequent increase in life expectancy of patients with type 2 diabetes (T2D) (Gregg, Williams, & Geiss, 2014). Yet, the development of renal disease carries an unfavorable impact on patients' quality of life and greatly reduces their life expectancy mainly by raising the incidence of cardiovascular events (Tancredi et al., 2015). Due to its direct and indirect costs, diabetic kidney disease (DKD) is rapidly becoming a major concern for public health systems worldwide.

Albuminuria and glomerular filtration rate (GFR) reduction are well known independent predictors of cardiovascular and renal events (Fox et al., 2012). At variance with the traditional clinical presentation of renal disease in type 1 diabetes, wherein the development of albuminuria is known to precede and predict renal function worsening, in patients with T2D the presence of increased albuminuria carries a somewhat less specific predictive power with respect to renal function deterioration (Penno et al., 2011). Furthermore, it has recently been reported that a significant portion of diabetic patients progressing to ESRD do not show albuminuria or proteinuria (Soetal, 2006).

Hypertension (HT) is an exceedingly common feature of patients with T2D (Hypertension in Diabetes Study, 1993). While an increase in blood pressure (BP) may results from diabetes itself or accompany the development of diabetic renal impairment, it more often precedes the onset of diabetes (Ritz, 2013) and represents a well known risk factor for the development of albuminuria as well as for progression

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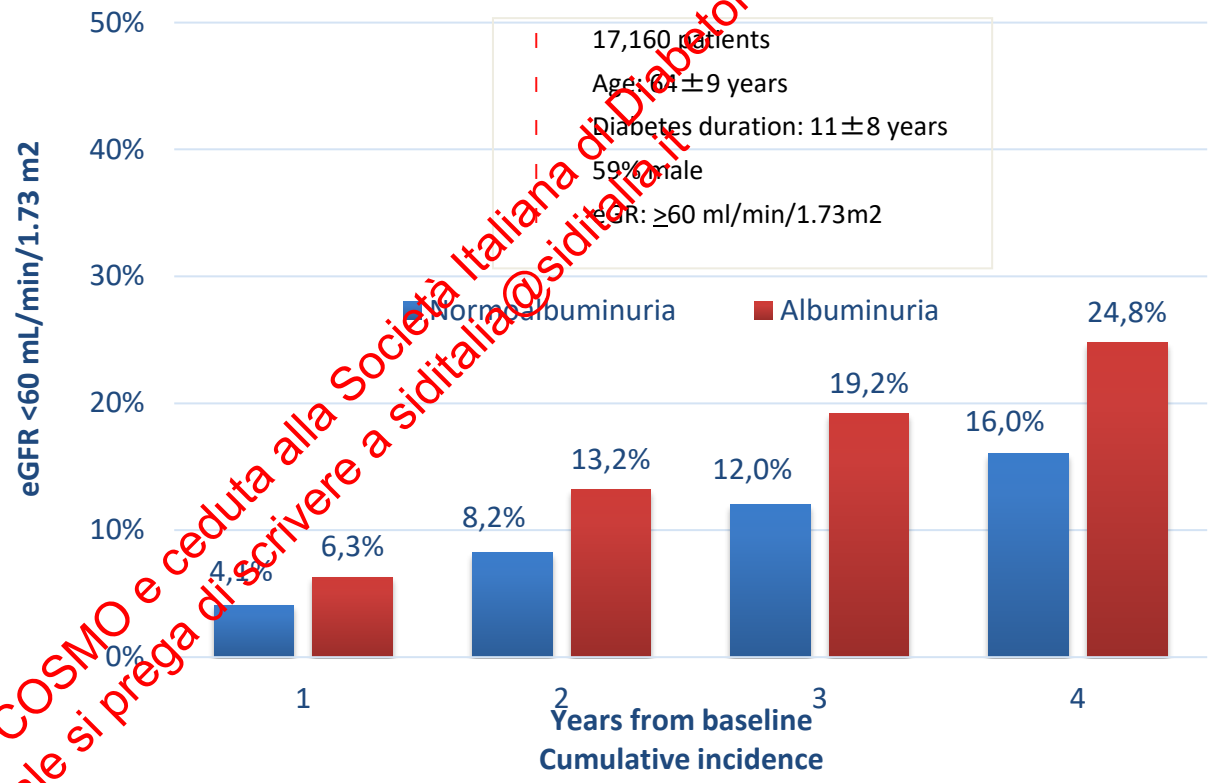
http://dx.doi.org/10.1016/j.jdiacomp.2016.10.030
1056-8727/

The presence of albuminuria entails a greater renal risk at any given GFR value. However, due to a greater occurrence of the non-albuminuric phenotype at baseline, progression to CKD stage 3 is more likely to be observed in patients without albuminuria.



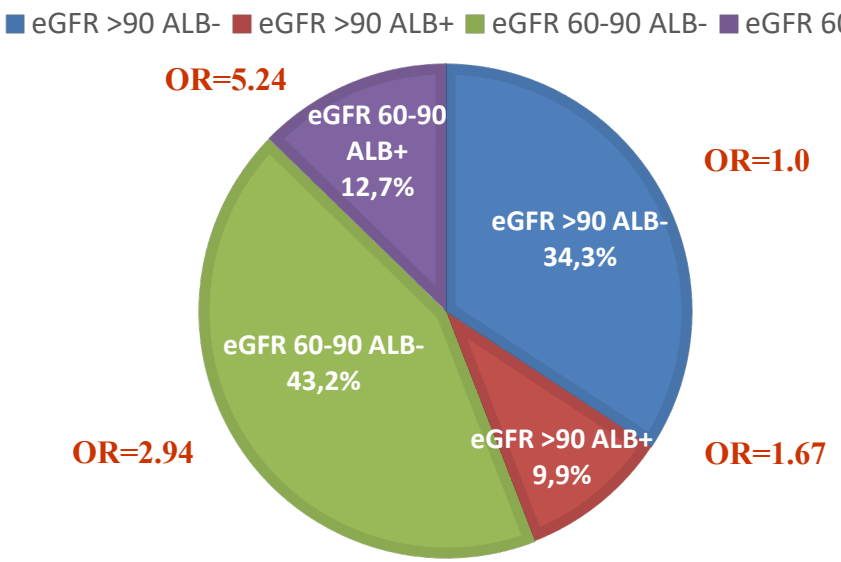


Table 3

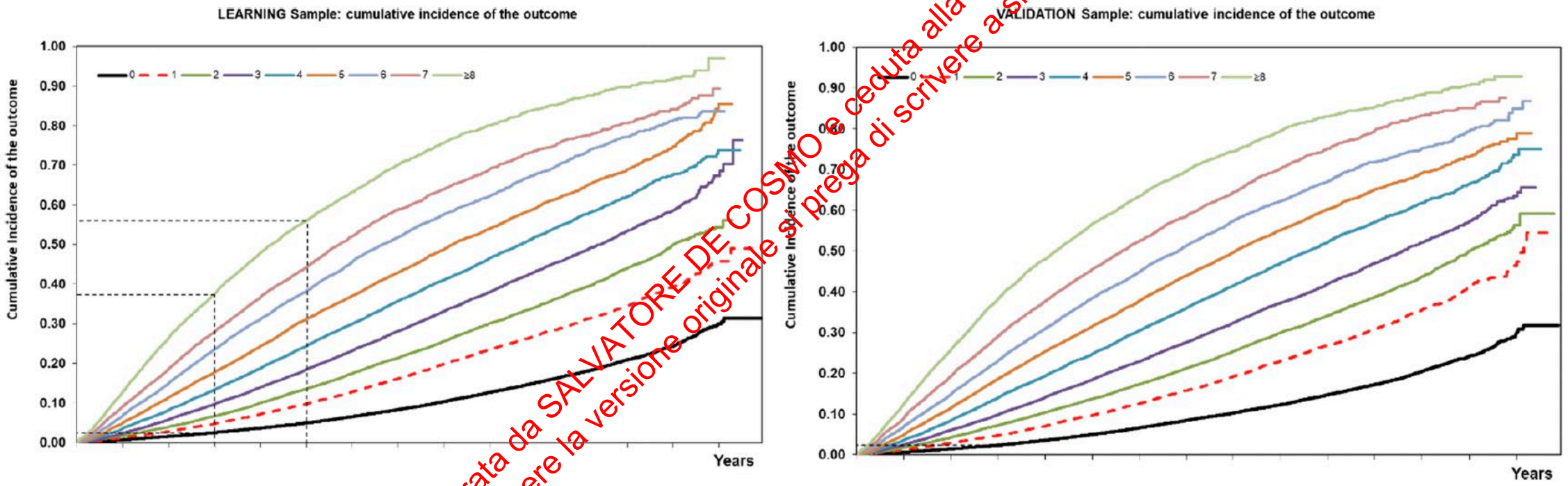


Fig. 2. Survival Curves derived from Learning (left) and Validation (right) sample. 3-years and 5-years risk of developing the primary renal outcome according to eGFR loss score (LEARNING Sample).

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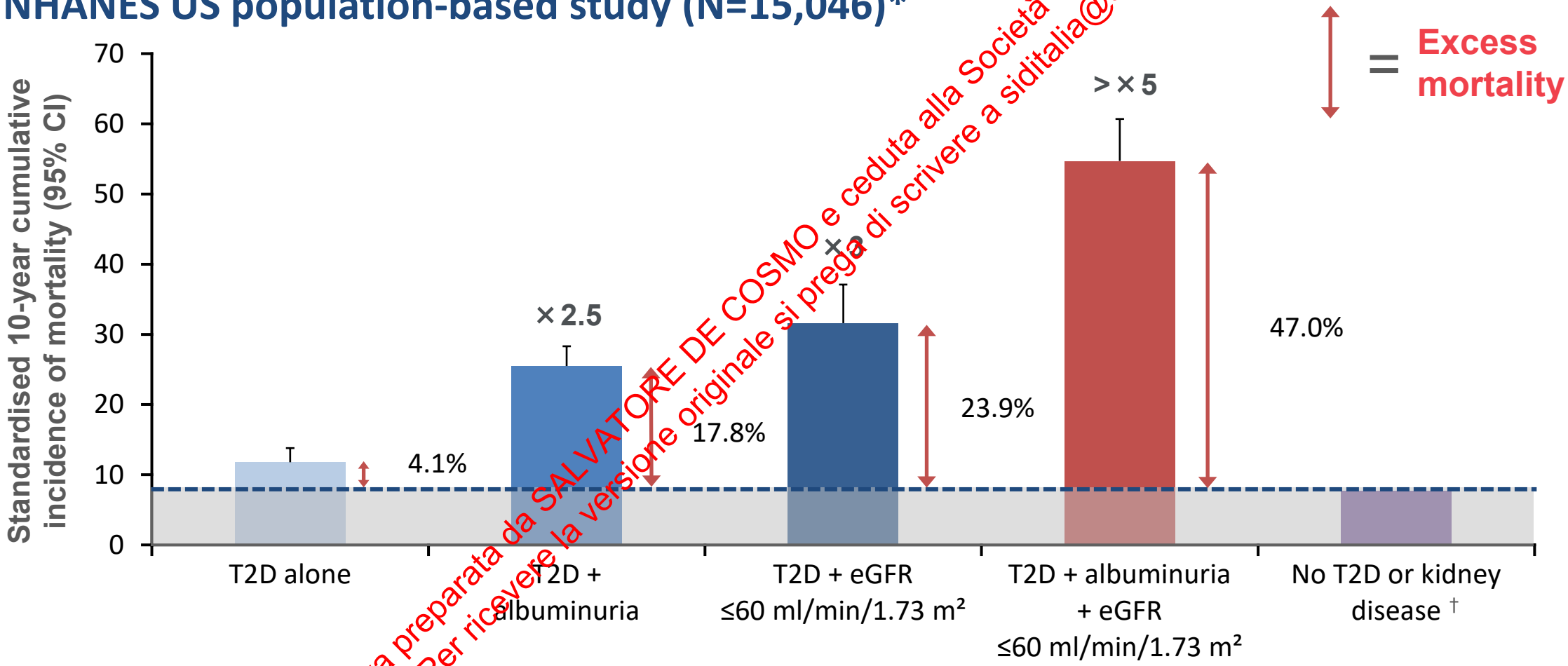
DKD is associated with increased mortality

NHANES US population-based study (N=15,046)*



Percentages indicate absolute excess mortality above the reference group (individuals with no diabetes or kidney disease)
*Adults aged ≥20 years with diabetes mellitus participating in National Health and Nutrition Examination Surveys from 1988 to 2014; †Kidney disease defined as albuminuria, impaired glomerular filtration or both. DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; T2D, type 2 diabetes. Afkarian M *et al. J Am Soc Nephrol* 2013;24:302

Albuminuria

eGFR

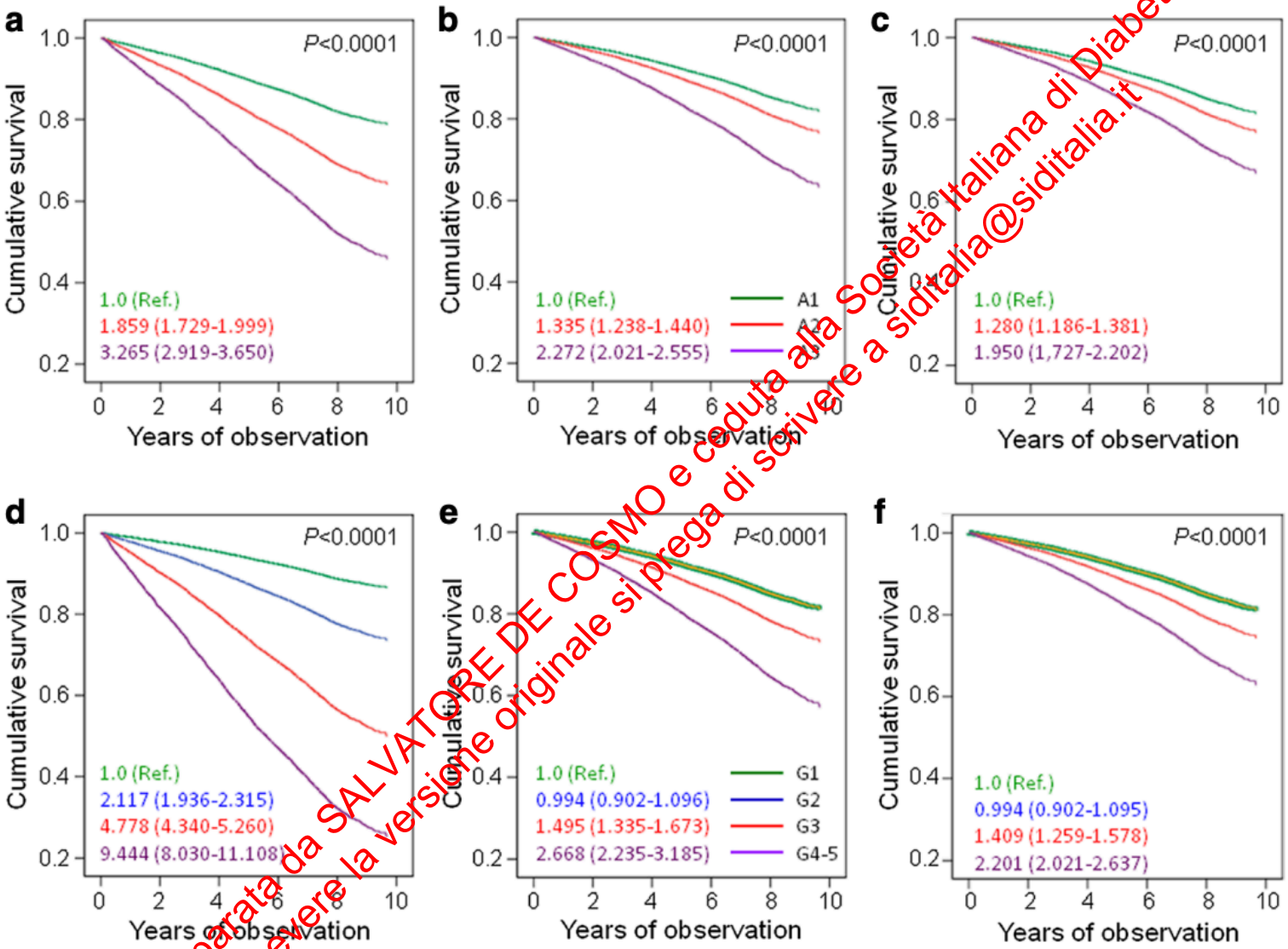
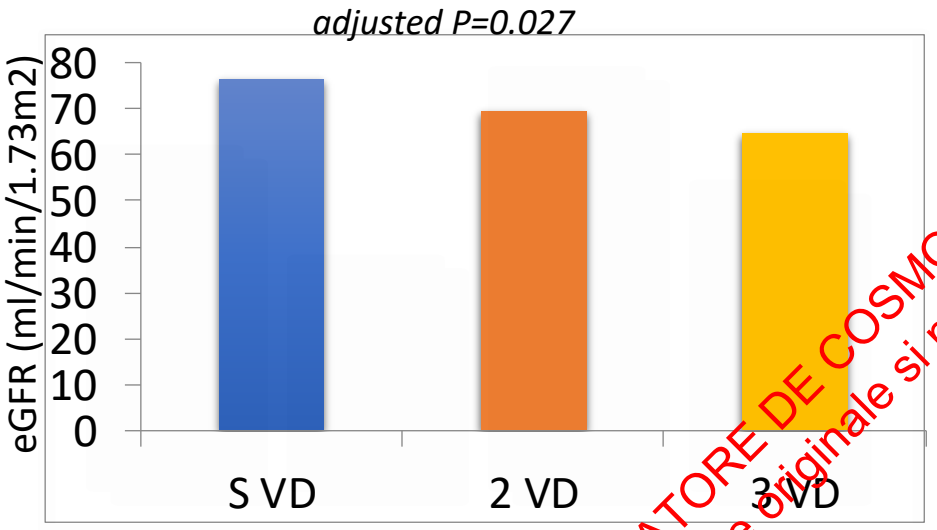


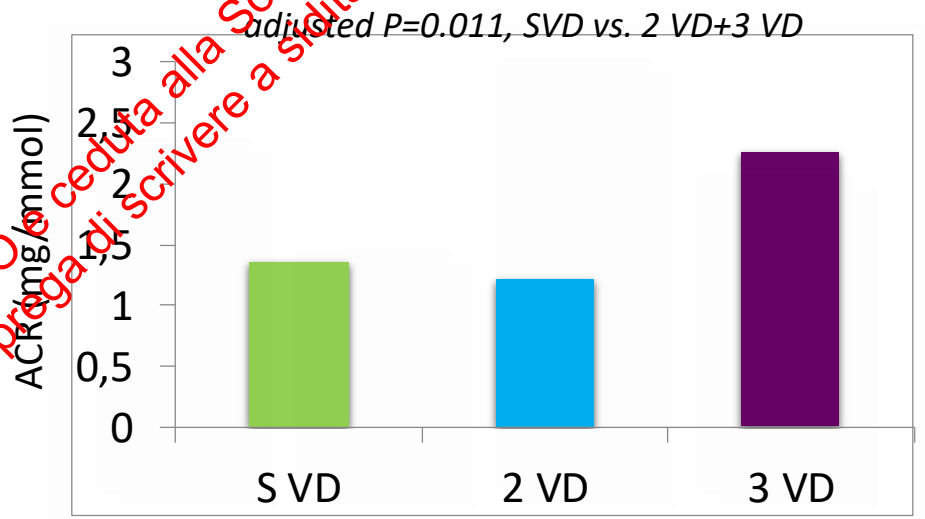
Fig. 1 Cumulative survival by Cox proportional hazards regression, unadjusted (**a**, **d**), adjusted for multiple confounders (**b**, **e**) and further adjusted for each other (**c**, **f**), according to albuminuria (A1, A2, and A3, **a**–**c**) and eGFR (G1, G2, G3, and G4-5, **d**–**f**) categories. HRs (95% CI) for mortality are shown for each category. *HR* hazard ratio, *CI* confidence interval

Penno G. et al. Acta Diabetologica https://doi.org/10.1007/s00592-018-1133-z

EGFR and ACR values according to the burden of coronary atherosclerosis.

N=208 patients, 69.3+13 yrs, N=97 T2DM





Atherosclerotic burden

M. D'Errico et al., Acta Diabetol. 2017

ASSESSMENT DEL RISCHIO CV NEL DIABETE SECONDO ESC 2021

Patients with type 2 diabetes mellitus

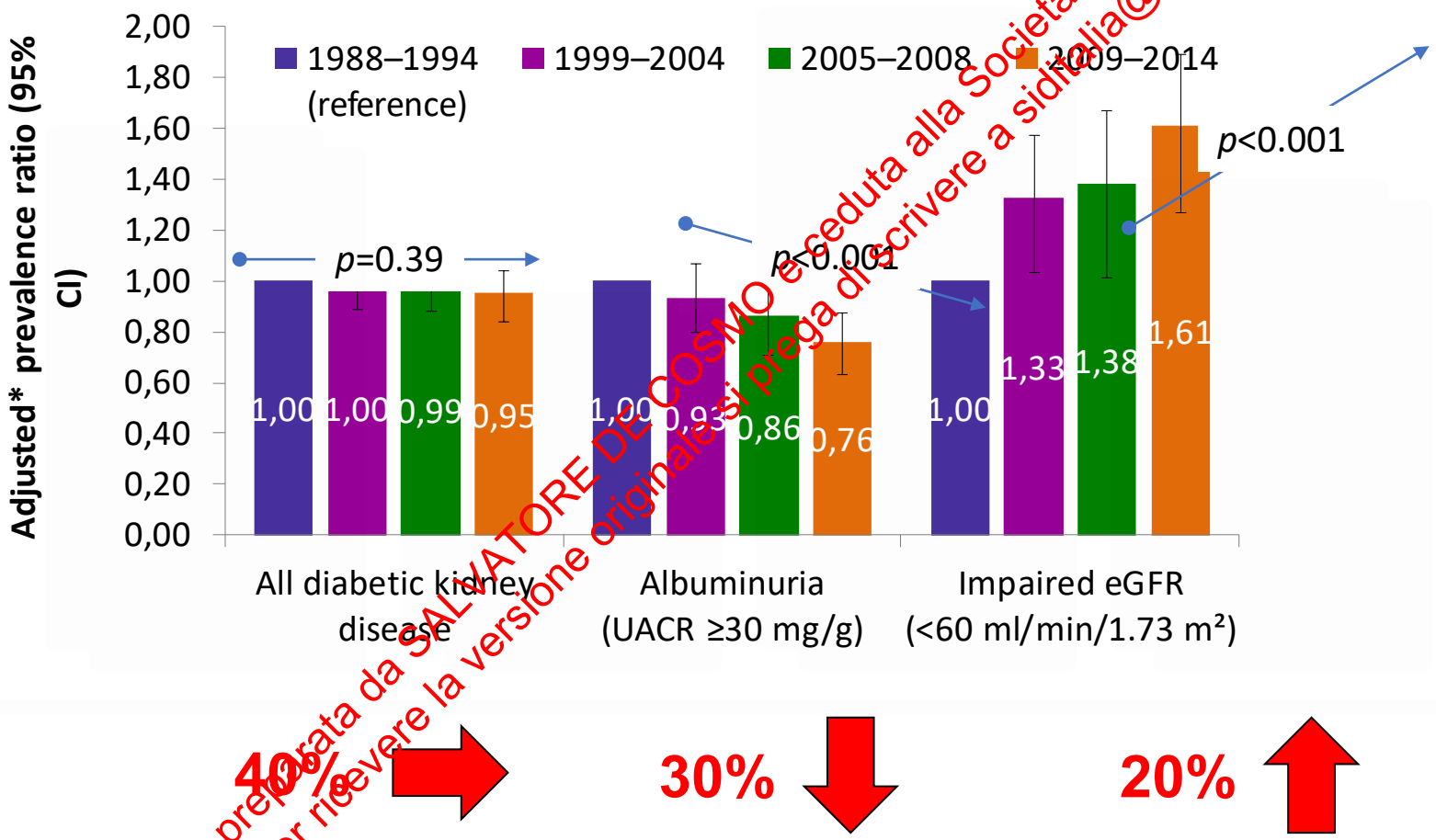
Patients with type 1 DM above 40 years of age may also be classified according to these criteria	Patients with well controlled short-standing DM (e.g. <10 years), no evidence of TOD and no additional ASCVD risk factors	Moderate-risk
	Patients with DM without ASCVD and/or severe TOD, and not fulfilling the moderate risk criteria.	High-risk
	Patients with DM with established ASCVD and/or severe TOD:[87, 93-95] • eGFR <45 mL/min/1.73 m^2 irrespective of albuminuria • eGFR 45-59 mL/min/1.73 m^2 and microalbuminuria (ACR 30 -300 mg/g) • Proteinuria (ACR >300 mg/g) • Presence of microvascular disease in at least 3 different sites (e.g. microalbuminuria plus retinopathy plus neuropathy)	Very high-risk

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Visseren LFJ et al. Eur Heart J 2021

Clinical manifestations of Kidney Disease among US Adults with DM 1988-2014

Prevalent cases of diabetic kidney disease in the United States accounting for persistence

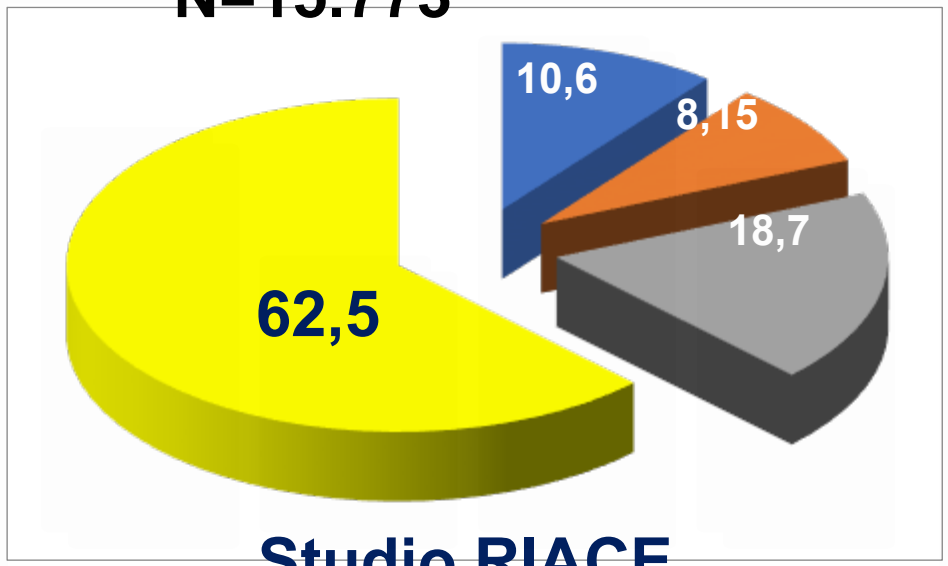


*Adjusted for age, sex, and race/ethnicity. p-values are for trend
UACR, urine albumin-to-creatinine ratio

Afkarian M et al., JAMA, 2016 *USRDS*

DMT2 e FUNZIONE RENALE

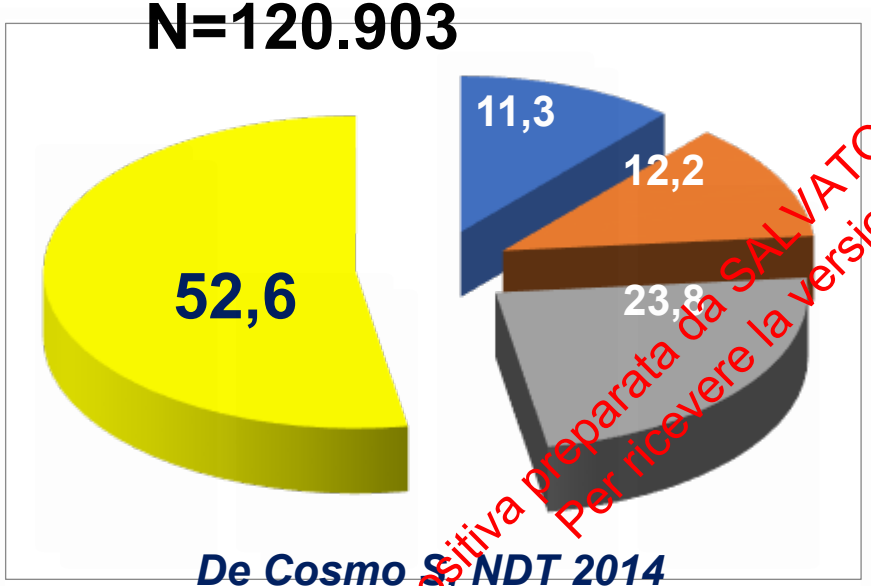
N=15.773



Studio RIACE

(Penno G, J Hypertens 2011)

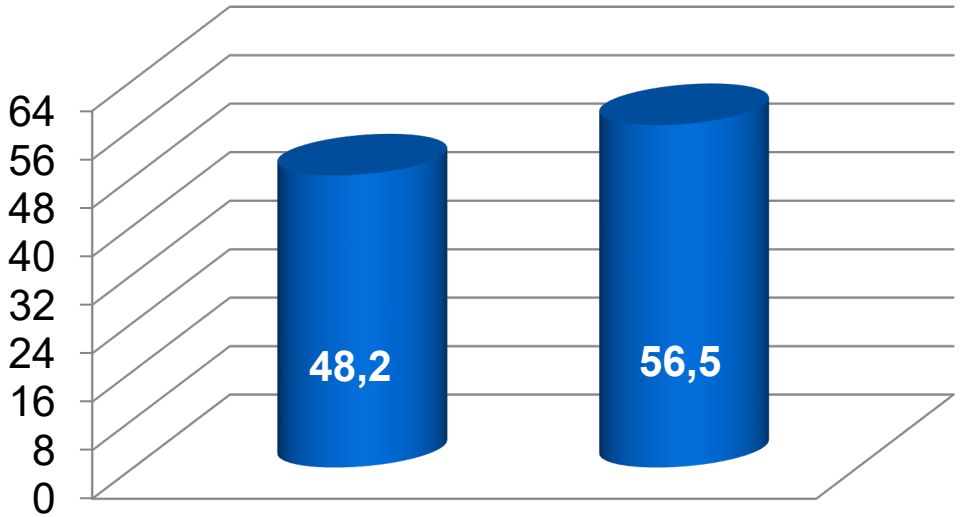
N=120.903



De Cosmo S, NDT 2014

- eGFR>60 ml/min. Normoalb.
- eGFR<60 ml/min. Normoalb.
- eGFR<60 ml/min. Alb.
- eGFR>60 ml/min. Alb.

Pazienti con CKD Normoalbuminurica (%)



De Cosmo S NDT 2014

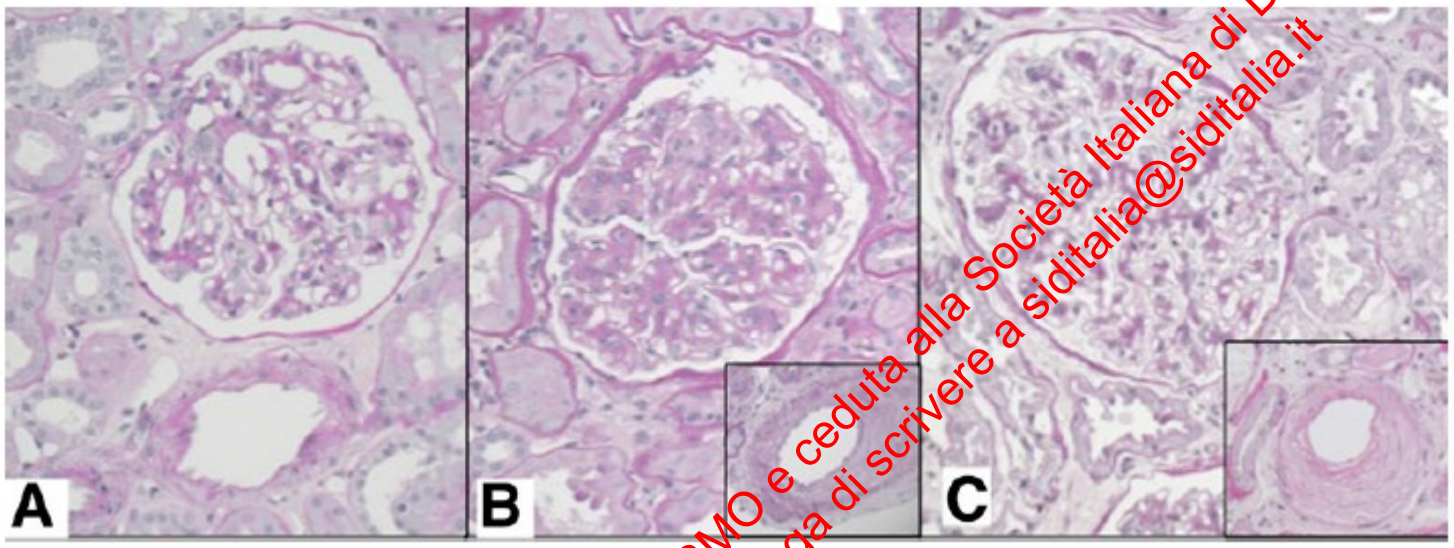
Penno G J Hypertens 2011

Albuminuria is not a prerequisite for DKD

	Patients n.	DM %	Follow-up years	Renal impairment	Non-albuminuric renal impairment
UKPDS *Diabetes 55: 1832-1839, 2006*	4,006	100	15	28%	67% (51%)
DCCT/EDIC *Diabetes Care 33: 1536-1543, 2010*	1,439	100 (T1DM)	19	6.2%	24%
AMD Annals **Diabetes Metab Res Rev 2017**	**20,464**	100 (T1DM)	19	23.5%	**49%**

MacIsaac RJ et al., *Diabetes Care 27: 195-200, 2004*	301	100	---	36%	39%
Kramer HJ et al., NHANES III *JAMA 289: 3273-3277, 2003*	1,197	100	---	13%	36%
Thomas MC et al., NEFRON *Diabetes Care 32: 1497-1502, 2009*	3,893	100	---	23%	55%
Ninomiya T et al., ADVANCE *J Am Soc Nephrol 20: 1813-1821, 2009*	10,640	100	---	19%	62%
Bakris GL et al., ACCOMPLISH *Lancet 375: 1173-1181, 2010*	11,482	60	---	9.5%	47%
Tube SW et al., ONTARGET/ TRASCEND *Circulation 123: 1098-1107, 2011*	23,422	37	---	24%	68%
Drury PL et al., FIELD *Diabetologia 54: 32-43, 2011*	9,765	100	---	5.3%	59%
RIACE Study Group, RIACE *J Hypertens 29: 1802-1809, 2011*	15,773	100	---	18.8%	57%
AMD ANNALS **NDT 2015**	**116,777**	**100**	**---**	**21%**	**48%**

Danno renale in T2DM con CKD Normoalbuminurica

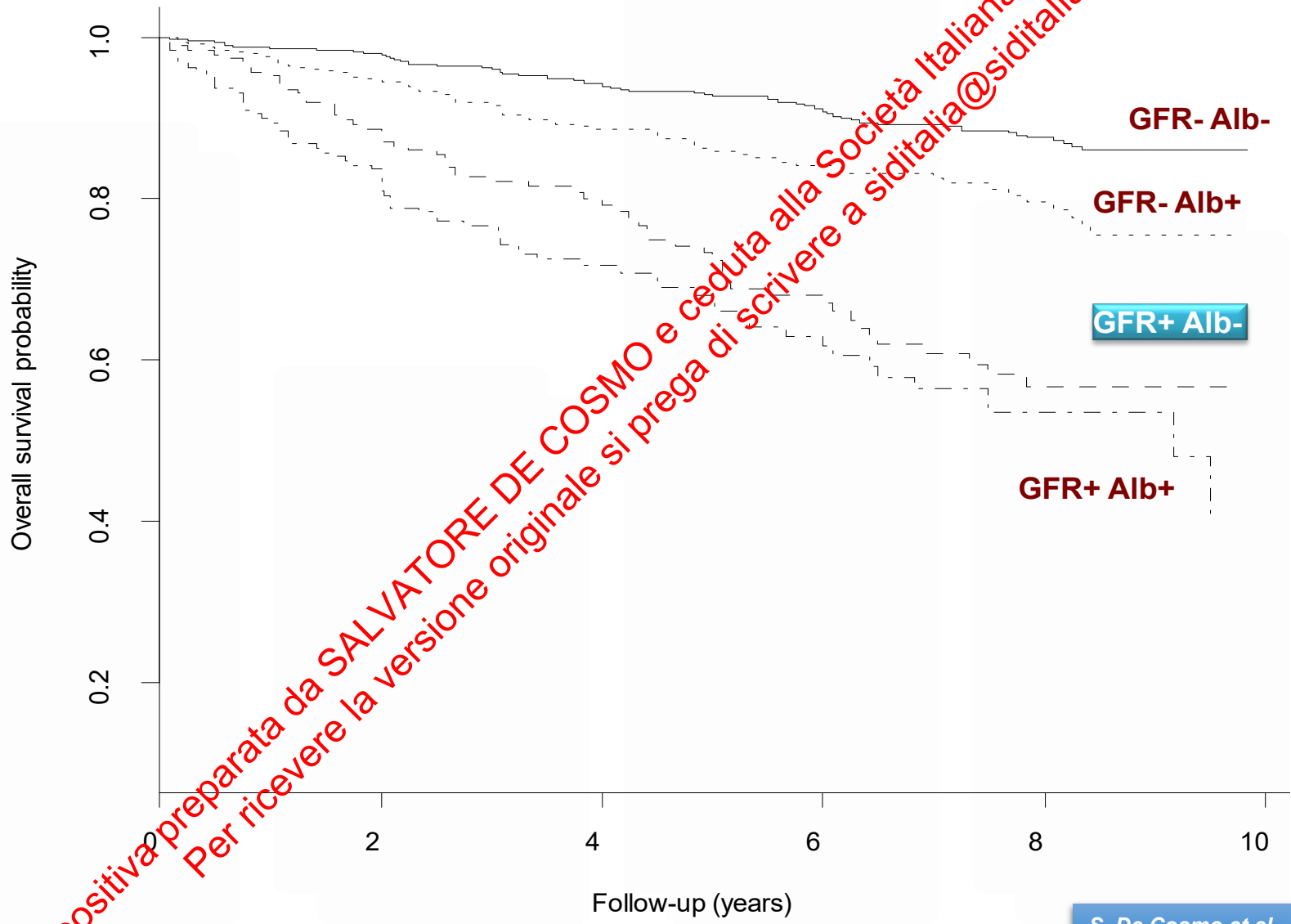


Normale (paz. 1) | **GS e arteriosclerosi (Paz.3)** | **Arteriosclerosi severa (Paz.8)**

Patient study number	Fioretto category	GS score (0–3)	Mesangial expansion (0–3)	IF/IF (0–3)	Arteriolar hyalinosis (0–3)	Arterioscleros (0–3)	Summary
1	C1	1	0	0	0	0	Not DN, mild IgA nephropathy, no cause for renal impairment found
2	C1	2	0	1	1	1	Mild nonspecific changes, not DN
3	C2	1	3	2	3	2	Typical advanced DN
4	C2	1	1	1	1	1	Typical early DN
5	C2	1	1	0	1	2	Typical early DN
6	C3	1	0	1	2	1	Renovascular, not DN
7	C3	1	0	1	0	2	Renovascular, not DN
8	C3	3	1	3	1	3	Atypical DN, mild glomerular changes + severe vascular and tubulointerstitial disease

Ekinci EI, Diabetes Care 2013

Survival curves for all-cause mortality in T2DM patients according to presence/absence of albuminuria and low eGFR.



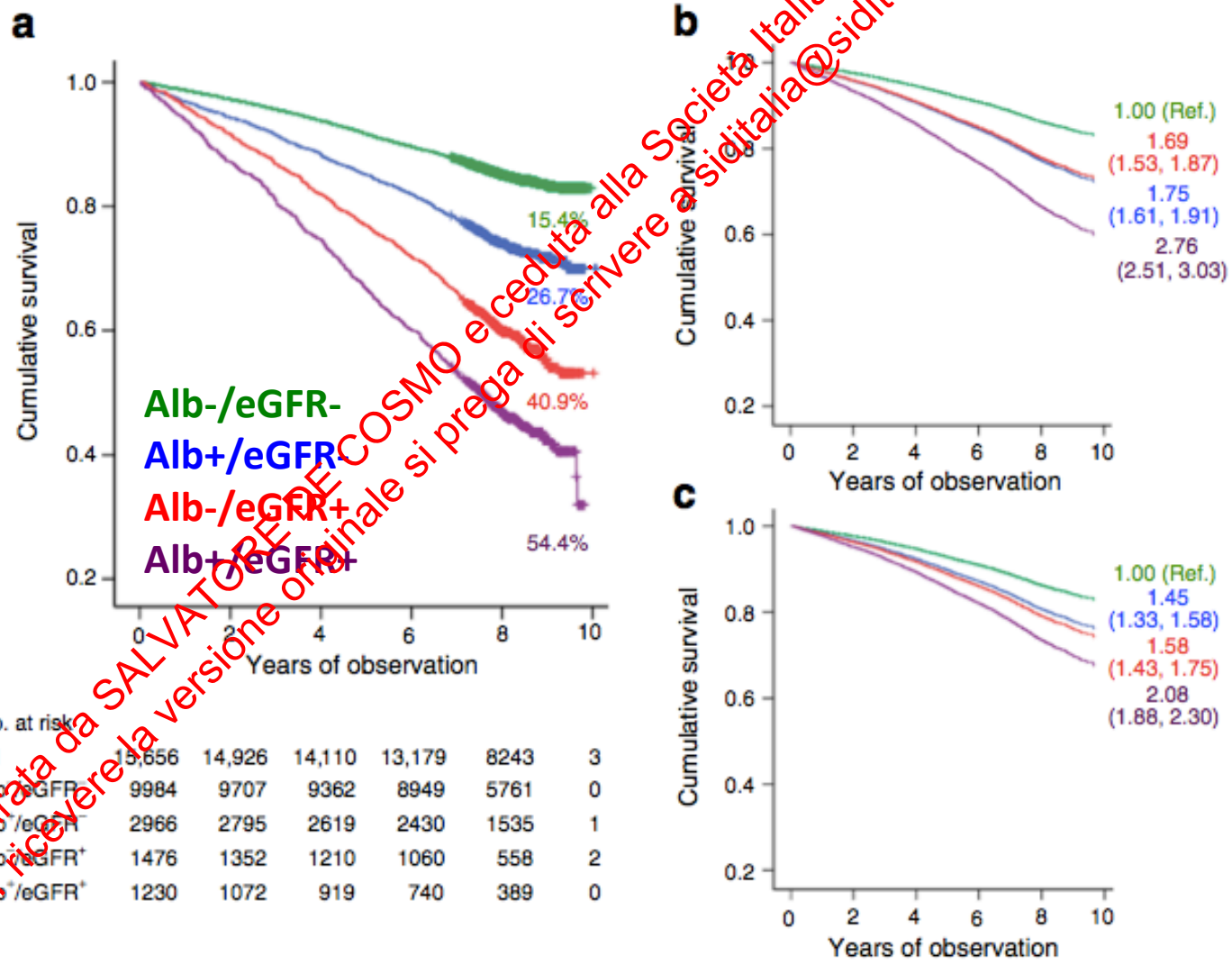
S. De Cosmo et al., Acta Diabetol. 2014

Renal impairment is a strong predictor of mortality in individuals with type 2 diabetes: the Renal Insufficiency And Cardiovascular Events (RIACE) Italian multicentre study

MEAN FOLLOW-UP 7.4±2.1 years

Kaplan–Meier analysis (a) and Cox proportional hazards regression, adjusted for age (b) and multiple confounders (c), according to DKD phenotype.

Percentages for death (a) or HRs (95% CI) for mortality (b, c) are shown for each phenotype; p<0.0001 across the phenotypes.



Penno G. et al, RIACE. Diabetologia 61: 2277-2289, **2018**

Grazie per l’attenzione

Internal and Eme
https://doi.org/1

IM - ORIGI

Low eGF
in high-r

Maria Madda
Mauro Salvat
Salvatore A. I

	Whole population $n=1017$	eGFR ≥ 60 $n=721$ (70.9%)	eGFR <60 $n=296$ (29.1%)	p value
Male n (%)	759 (74.6%)	563 (78.1%)	196 (66.2%)	<0.001
Age (years)	68.4 ± 10.8	65.9 ± 10.4	74.6 ± 9.2	<0.001
Smokers/ex n (%)	225/119 (22.1%/11.7%)	184/85 (26.0%/12.0%)	41/34 (13.8%/11.5%)	<0.001
Dyslipidemia n (%)	727 (71.5%)	506 (70.2%)	221 (74.9%)	0.129
Arterial hypertension n (%)	883 (86.8%)	601 (83.4%)	282 (95.3%)	<0.001
Type 2 Diabetes n (%)	410 (40.3%)	249 (34.5%)	161 (54.4%)	<0.001
Previous CVE n (%)	466 (45.8%)	295 (40.9%)	171 (57.8%)	<0.001
BMI (kg/m^2)	28.4 ± 5.0	28.3 ± 4.9	28.5 ± 5.5	0.693
SBP (mmHg)	132.6 ± 16.6	132.4 ± 16.2	132.9 ± 17.6	0.669
DBP (mmHg)	75.3 ± 9.6	75.2 ± 9.2	75.5 ± 10.5	0.654
Triglycerides (mg/dl)	140 (33–855)	138 (33– 855)	150 (40 – 514)	0.071
HDL-c (mg/dl)	47.1 ± 13.8	48.0 ± 13.9	44.8 ± 13.5	0.002
LDL-c (mg/dl)	97.6 ± 34.4	99.5 ± 34.5	93.1 ± 33.8	0.015
HbA1c (%)	6.7 ± 1.5	6.6 ± 1.4	6.9 ± 1.5	0.021
Uric acid (mg/dl)	5.3 ± 1.6	5.0 ± 1.4	6.0 ± 1.8	<0.001
eGFR (mL/min/1,73 m^2)	73.2 ± 25.6	85.0 ± 19.5	44.5 ± 13.0	<0.001
ACR (mg/mmol)	1.41 (0.27–1471)	1.22 (0.34–831)	2.81 (0.27–1471)	<0.001
Normoalbuminuria n (%)	507 (68.8%)	395 (76.0%)	112 (51.6%)	<0.001
Microalbuminuria n (%)	177 (24.0%)	105 (20.2%)	72 (33.2%)	
Macroalbuminuria n (%)	53 (7.2%)	20 (3.8%)	33 (15.2%)	
3-VD n (%)	260 (25.6%)	165 (22.9%)	95 (32.1%)	0.006
Cumulative mortality n (%)	114 (11.2%)	45 (6.2%)	69 (23.3%)	<0.001

Mean ± SD, absolute frequency (percentage) and media n (range)

Internal and Emergency Medicine
https://doi.org/10.1007/s11739-021-02851-4

IM - ORIGINAL

Low eGFR and albuminuria independently predict all-cause mortality in high-risk subjects undergoing coronary arteriography

Maria Maddalena D'Errico[1] · Pamela Piscitelli[1] · Antonio Mirijello[1] · Mariateresa Santoliquido[1,2] · Valentina Massa[1] · Mauro Salvatori[3] · Carlo Vigna[3] · Gianluigi Vendemiale[4] · Filippo Aucella[5] · Roberto Pontremoli[6] · Salvatore A. De Cosmo[1]

Subjects N. 1.017 Events N. 114

Fig. 1 Kaplan–Meier cur
depicting the survival cur
for all-cause mortality in
pooled sample divided in
two groups according to e
below (dashed line) or eq
above (continuous line) 6
min/1.73 m^2

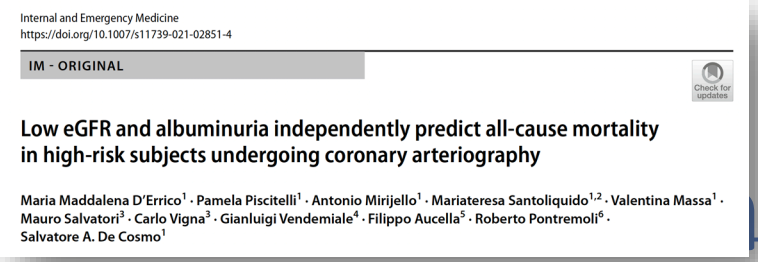
R ≥60 ml/min/1.73m2
R <60 ml/min/1.73m2

cidence rates (n events per 100 py) in the whole sam-
ided according to eGFR equal or above or below 60 ml/
min/1.73m^2

	Model	IR	95% CI	
			LB	UB
Whole sample ($n=1017$)	Unadjusted	3.2	2.7	3.8
	Adjusted for sex and age	2.4	1.9	3.1
Subjects with eGFR ≥ 60 ml/min/1.73m^2 ($n=721$)	Unadjusted	1.7	1.3	2.3
	Adjusted for sex and age	1.1	0.7	1.8
Subjects with eGFR < 60 ml/min/1.73m^2 ($n=296$)	Unadjusted	7.1	5.6	9.0
	Adjusted for sex and age	6.7	5.1	8.7

py, person-year; *IR*, incidence rate; *95% CI*, 95% confidence intervals; *LB, lower bound; UB, upper bound; eGFR*, estimated glomerular filtration rate

M. et al., 2021



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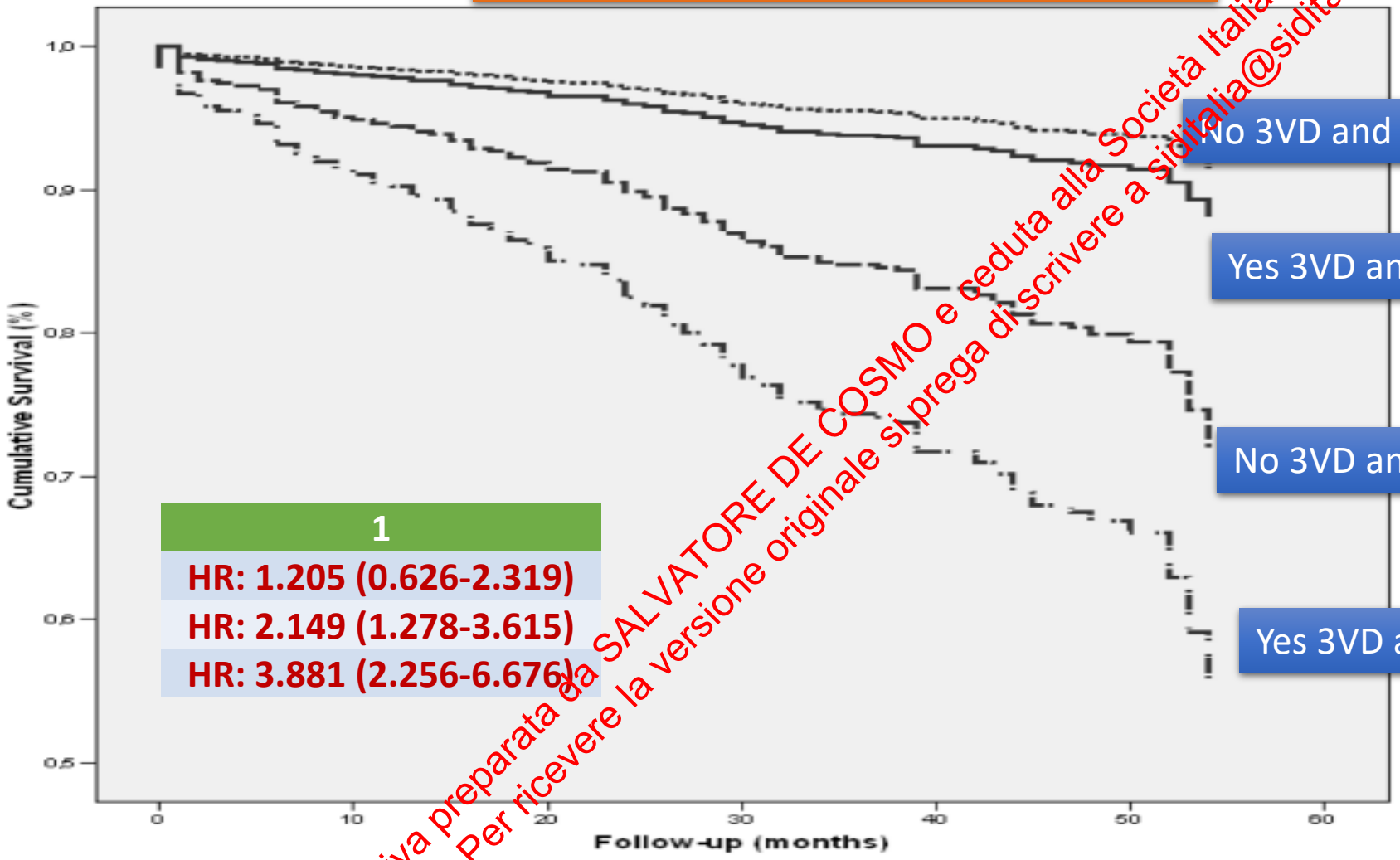
- In the subset of subjects in whom albuminuria was available (n = 737), the presence at baseline of microalbuminuria or macroalbuminuria significantly increased the risk of death.
- Compared to subjects with normoalbuminuria, which were the reference category, subjects with **microalbuminuria** showed a twofold greater risk of death: **HR 2.58 (95% CI 1.58–4.20**; p < 0.001), adjusted HR 2.61 (95% CI 1.48–4.60; p = 0.001), fully adjusted HR 2.09 (95% CI 1.17–3.73; p = 0.012).
- This risk of death further increased in subjects with **macroalbuminuria**: **HR 5.65 (95% CI 3.20–9.98; p < 0.001),** adjusted HR 6.21 (95% CI 3.26–11.82; p < 0.001), fully adjusted HR 4.26 (95% CI 2.18–8.33; p < 0.00

Low eGFR amplifies the risk of all-cause mortality associated to coronary 3-vessel disease

Subjects N=1,017; Events N= 114



1
HR: 1.205 (0.626-2.319)
HR: 2.149 (1.278-3.615)
HR: 3.881 (2.256-6.676)

No 3VD and eGFR ≥60 ml/min/1.73m^2

Yes 3VD and eGFR ≥60 ml/min/1.73m^2

No 3VD and eGFR <60 ml/min/1.73m^2

Yes 3VD and eGFR <60 ml/min/1.73m^2

Piscitelli P. et al. NMCVD, 2021