III SESSIONE • **Non solo cuore e diabete**

Moderatori: Giuseppe Grandaliano, Anna Solini

Non scordiamoci del rene - **Loreto Gesualdo**

Disclosures

Dichiaro di aver ricevuto negli ultimi due anni compensi o finanziamenti dalle seguenti Aziende Farmaceutiche e/o Diagnostiche:

- **Research funding**: ABIONYX, SANOFI
- **Speaker activity**: FRESENIUS, ESTOR, WERFEN, ASTELLAS, ASTRAZENECA, TRAVERE
- **Consulting activity**: SANDOZ, SANOFI, BAXTER, MUNDIPHARMA, ESTOR, PHARMADOC, RETROPHIN, TRAVERE, ASTRAZENECA, GSK, NOVARTIS, CHINOOK

Dichiara altresì il proprio impegno ad astenersi, nell'ambito dell'evento, dal nominare, in qualsivoglia modo o forma, aziende farmaceutiche e/o denominazione commerciale e di non fare pubblicità di qualsiasi tipo relativamente a specifici prodotti di interesse sanitario (farmaci, strumenti dispositivi medico-chirurgici, ecc.).

850,000,000+

People world wide have kidney diseases

10.4% men and 11.8% women

Kidney Diseases 850 M

Diabetes Mellitus 422 M

Cancer 42 M

HIV/AIDS 37 M

Mark D. Okusa,
President ASN 2018

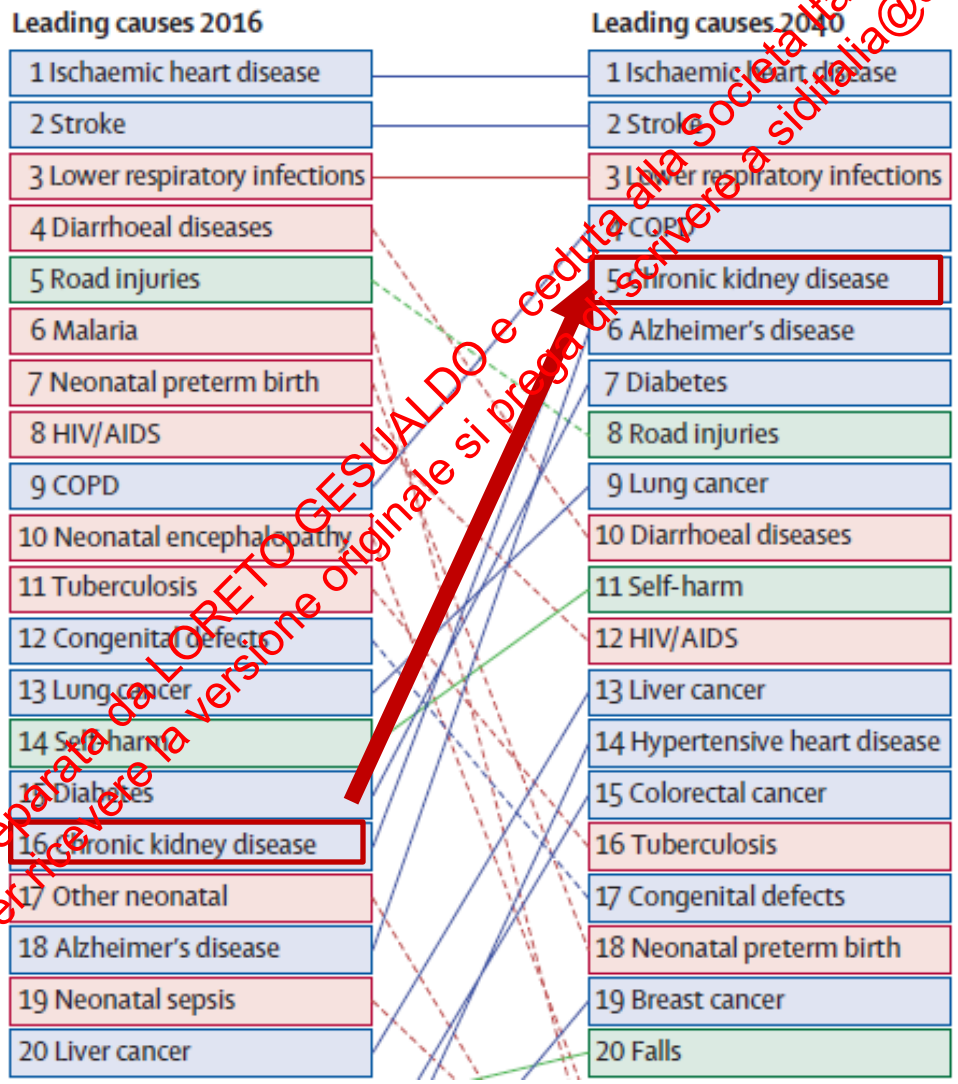
ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

ISN

Jager, Kidney Int, 30 Sept 2019

Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories

GBD Chronic Kidney Disease Collaboration



Lancet 2018; 392: 2052–90

Review

Journal of INTERNAL MEDICINE

doi: 10.1111/j.1365-2796.2010.02269.x

Chronic kidney disease: a public health priority and harbinger of premature cardiovascular disease

P. Stenvinkel

Division of Renal Medicine, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden

Abstract. Stenvinkel P (Division of Renal Medicine, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden). Chronic kidney disease: a public health priority and harbinger of premature cardiovascular disease (Review). *J Intern Med* 2010; **268**: 456–467.

The epidemics of cardiovascular disease, obesity, diabetes, HIV and cancer have all received much attention from the public, media and policymakers. By contrast, chronic kidney disease (CKD) has remained largely a 'silent' epidemic. This is unfortunate because early diagnosis of renal disease based on proteinuria and/or reduced estimated glomerular filtration rate could enable early intervention to reduce the high risks of cardiovascular events, end-stage renal disease (ESRD) and death that are associated with CKD. Given the global increase in the incidence of the leading causes of CKD – hypertension, obesity and diabetes mellitus – better disease management and prevention planning are needed, as effective strategies are available to slow the progression of CKD and reduce cardiovascular risk. CKD may be regarded as a clinical model of accelerated vascular disease and premature ageing, and the risk-factor profile changes during the progression from mild/moderate CKD to ESRD. Although many randomized controlled trials in patients with mild to moderate CKD have shown beneficial effects of interventions aimed at preventing the progression of CKD, most trials have been unable to demonstrate a beneficial effect of interventions aimed at improving outcome in ESRD. Thus, novel treatment strategies are needed in this high-risk patient group.

Keywords: cardiovascular disease, chronic kidney disease, dialysis, inflammation.

P. Stenvinkel Journal of Internal Medicine 2010

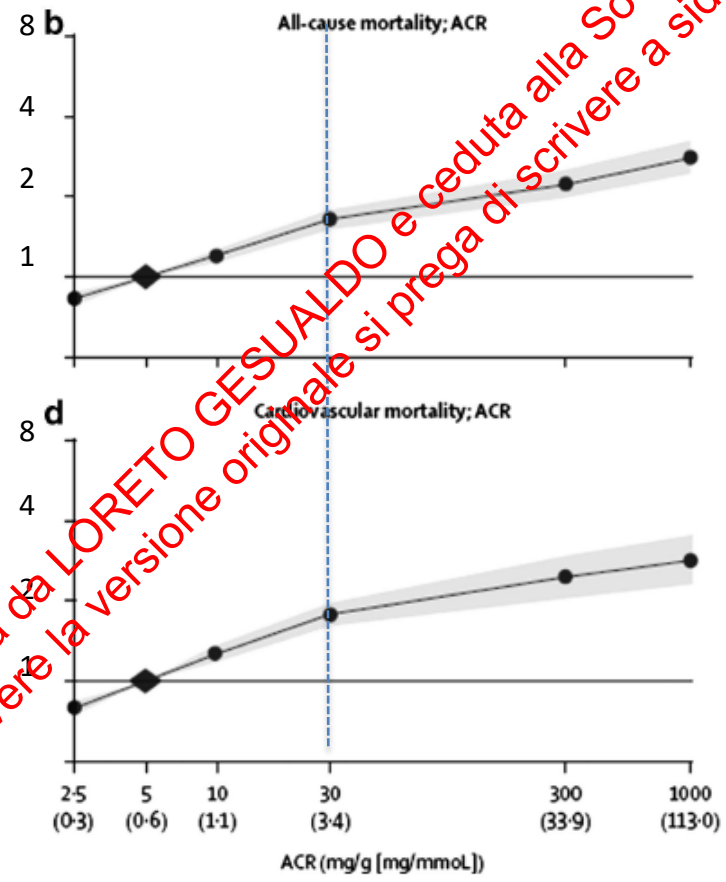
The reduction in GFR and the increase in albuminuria are independently associated with mortality and end-stage chronic renal failure

MRC should be regarded as relevant risk factor for mortality and ESRD in **independently from hypertension**

The relative risks of mortality and ESRD by eGFR and ACR are the same **irrespective of the presence or absence of diabetes**

Both low eGFR and high albuminuria were independently associated with mortality and ESRD **independently from age** of patients

Albuminuria and cardiovascular or all-cause mortality



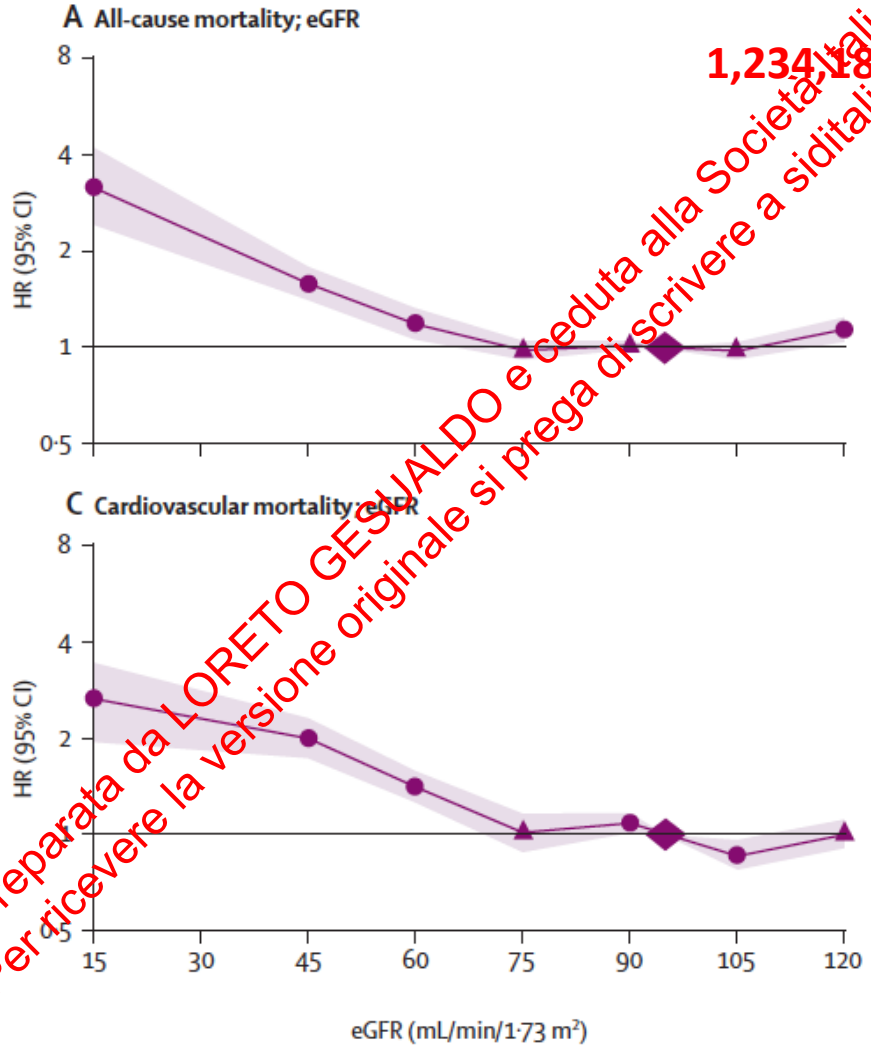
21 studies
N. 105,872 pts.

NS

Significant

Matsushita K et al; Lancet 2010; 375: 2073-81

eGFR e mortality



1,234,182 pts from 21 studies

NS

Significant

Matsushita K et al; Lancet 2010; 375: 2073-81

eGFR-Albuminuria e renal outcome

http://www.kidney-international.org original article

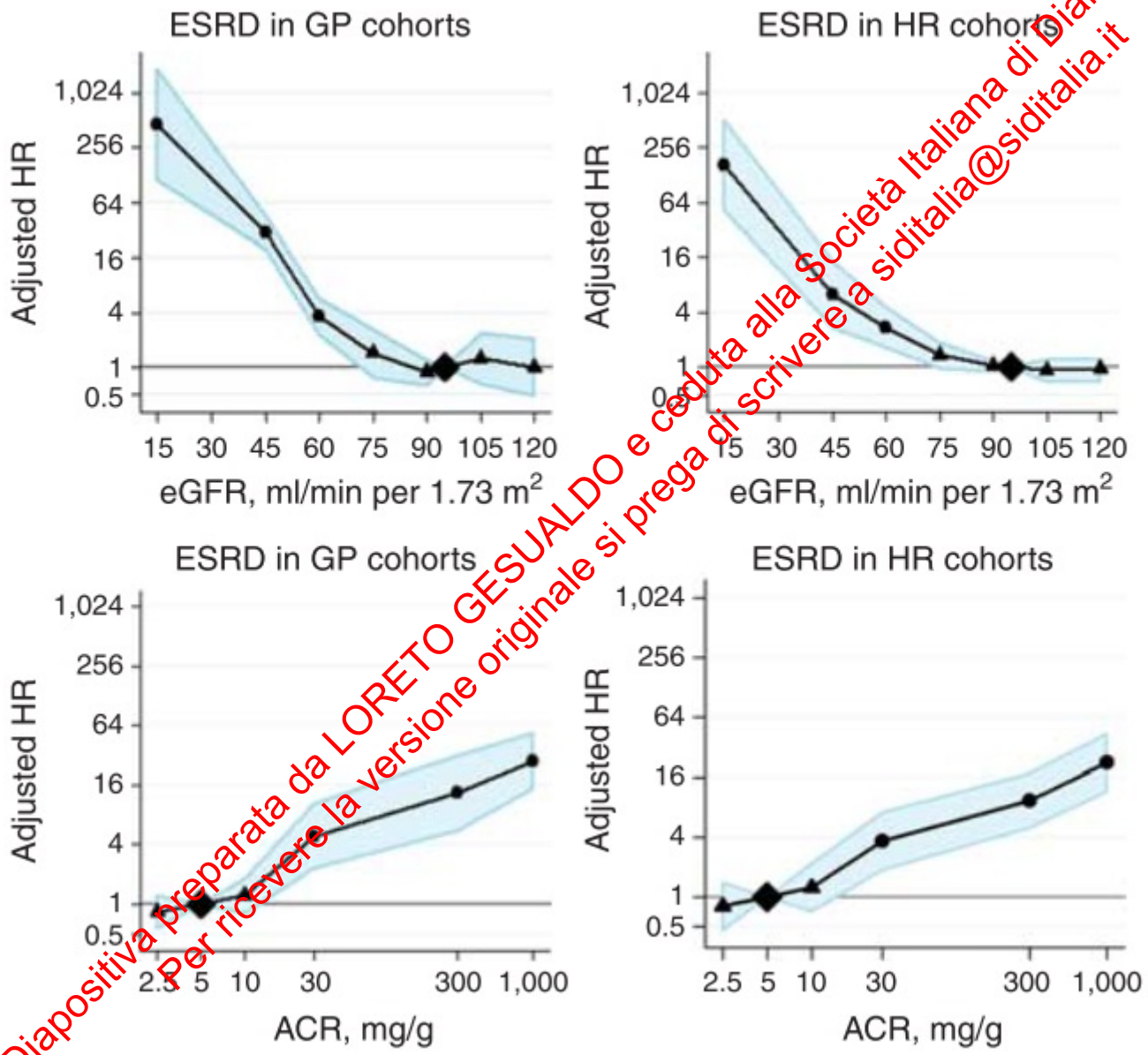
Lower estimated GFR and higher albuminuria are associated with adverse kidney outcomes. A collaborative meta-analysis of general and high-risk population cohorts

Ron T. Gansevoort[1], Kunihiro Matsushita[2], Marije van der Velde[1], Brad C. Astor[2], Mark Woodward[3], Andrew S. Levey[4], Paul E. de Jong[1], Josef Coresh[2] and the Chronic Kidney Disease Prognosis Consortium

[1]Department of Nephrology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands; [2]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA; [3]George Institute, University of Sydney, Sydney, New South Wales, Australia and [4]Division of Nephrology, Tufts Medical Center, Boston, Massachusetts, USA

***Kidney International* 2011; 80: 93–104**

eGFR-Albuminuria and renal outcome



Gansevoort RT et al. Kidney International 2011; 80:93–104

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10.4% men and 11.8% women

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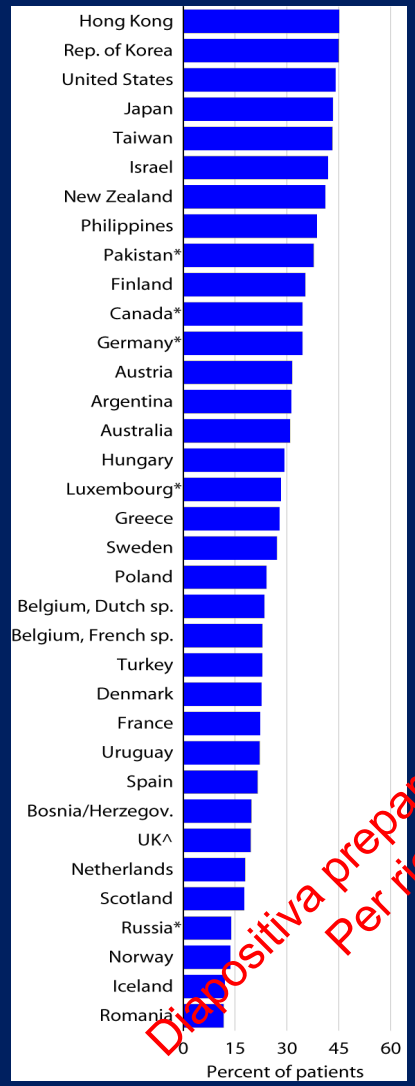
ISN

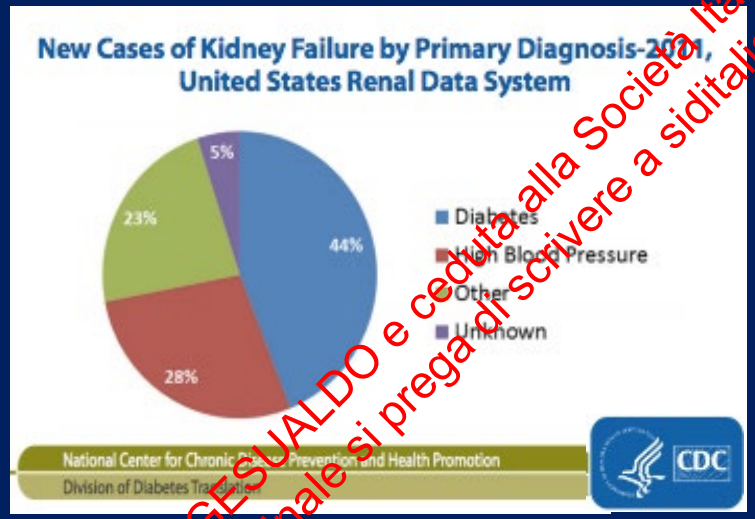
Jager, Kidney Int, 30 Sept 2019

Diabetes and End Stage Renal Disease (ESRD)

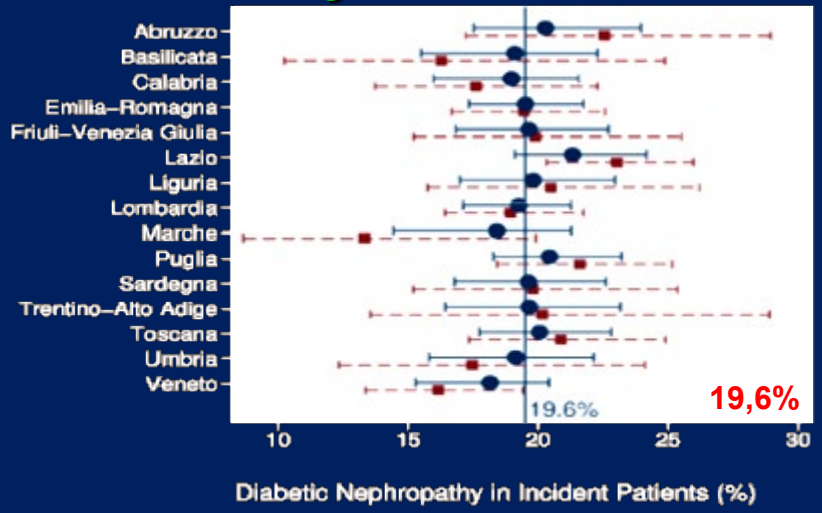
INCIDENCE

World…





Italy…



Renal Damage in a diabetic patient = diabetic nephropathy

- **Most nephrologists do not advocate renal biopsy in diabetic subjects, arguing that this procedure would simply confirm the presence of DN in the majority of patients**

- **There is no overall consensus on timing and indications, the decision to perform RB is usually based on personal opinions or single-center policies**

- **RB is an invasive procedure that is not completely free from complications.**

Histopatological Characteristics of renal damage in Diabetes

CLASSIFICATION	HISTOLOGY	PREVALENCE
• Class 1	Diabetic glomerulosclerosis	(39,6%)
• Class 2	Vascular (arterioarteriolosclerotic) and ischemic glomerular changes	(15,2%)
• Class 3a	Glomerular diseases superimposed on diabetic glomerulosclerosis	(45,03%)
• Class 3b	Other glomerulonephritis without the presence of diabetic lesions	

Mazzucco G et al, *Am J Kidney Dis* 2002; 39: 713-716

NDT Advance Access published May 4, 2016

Nephrol Dial Transplant (2016) 0: 1–14
doi: 10.1093/ndt/gfw070

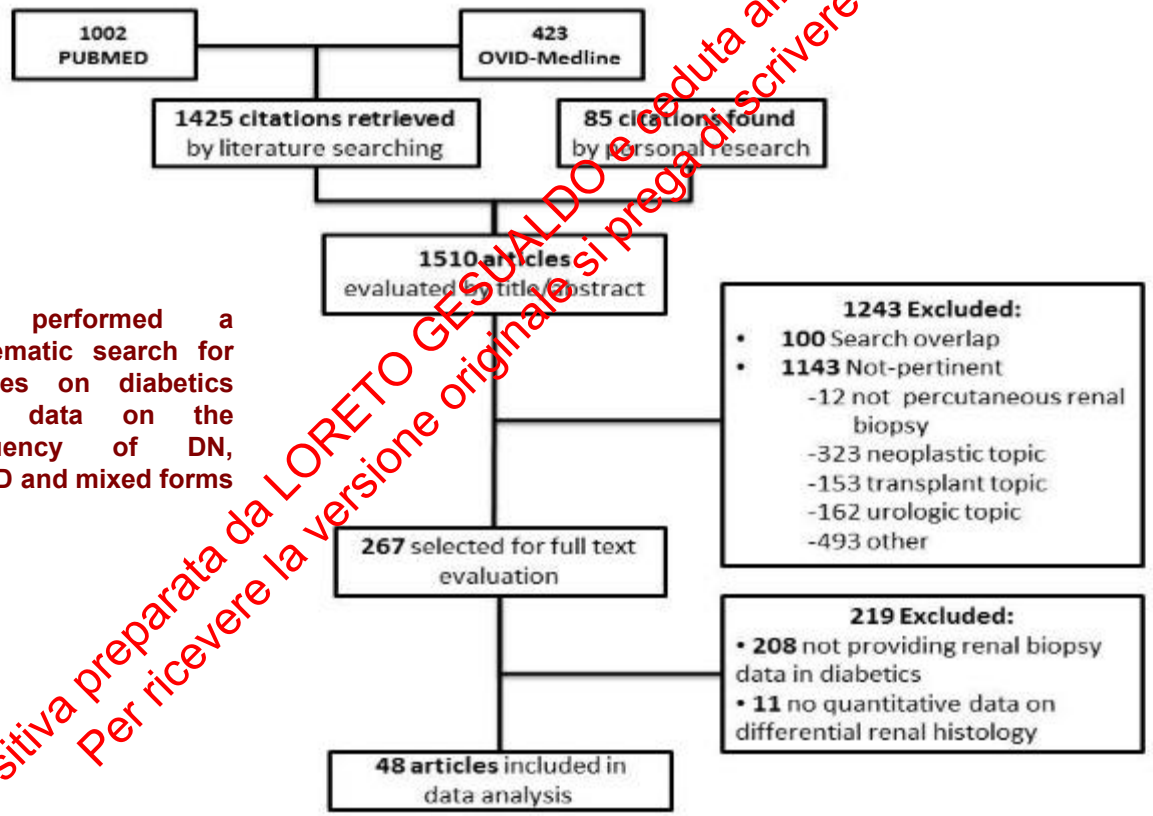
Original Article

Renal biopsy in patients with diabetes: a pooled meta-analysis of 48 studies

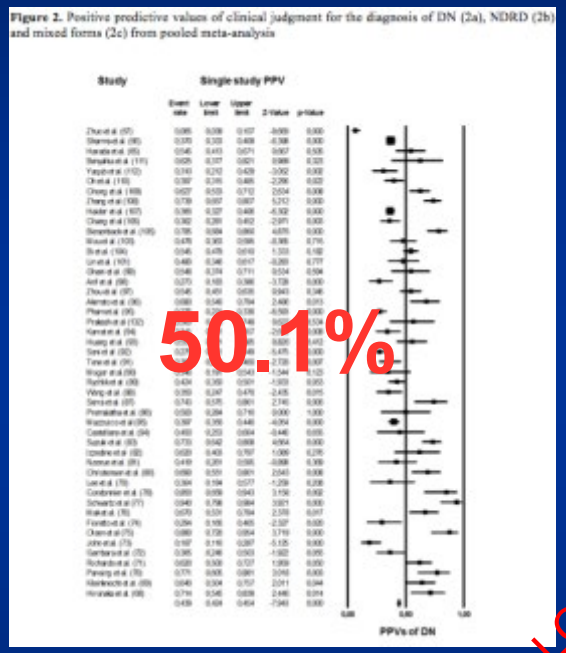
Marco Fiorentino[1], Davide Bolignano[2,3], Vladimir Tesar[4], Anna Pisano[2], Winfried van Biesen[3], Giovanni Tripepi[2], Graziella D'Arrigo[2] and Loreto Gesualdo[1] on behalf of the ERA-EDTA Immunonephrology Working Group

Flow of the study selection process

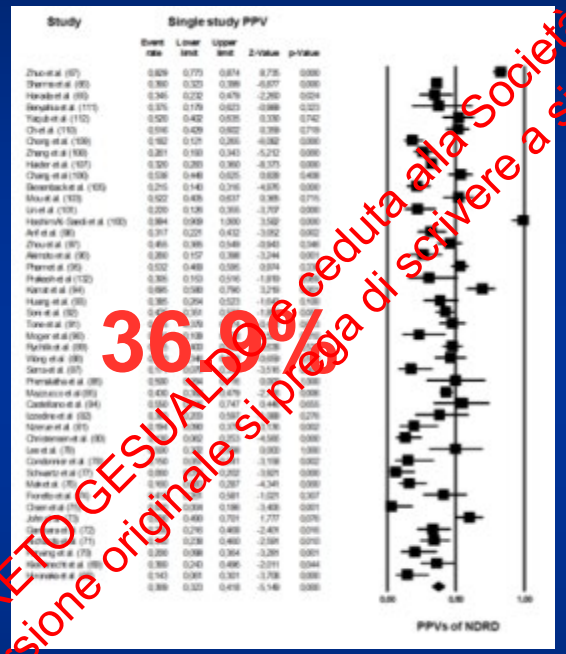
We performed a systematic search for studies on diabetics with data on the frequency of DN, NDRD and mixed forms



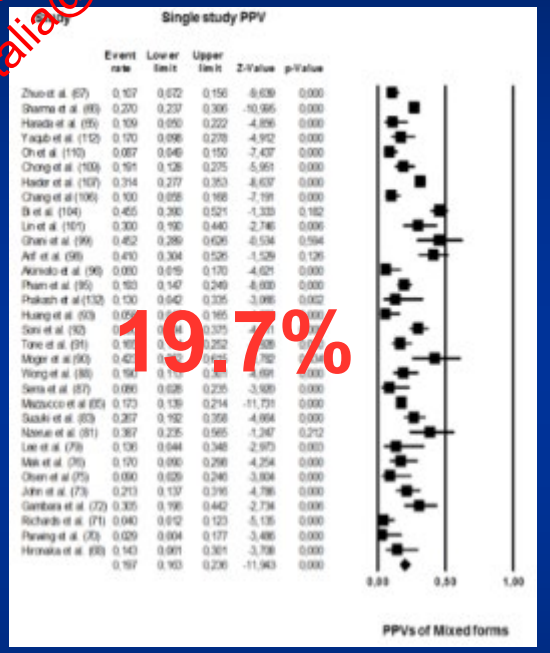
Positive predictive values of clinical judgment for the diagnosis of DN (2a), NDRD (2b) and mixed forms (2c) from pooled meta-analysis



50.1%



36.9%

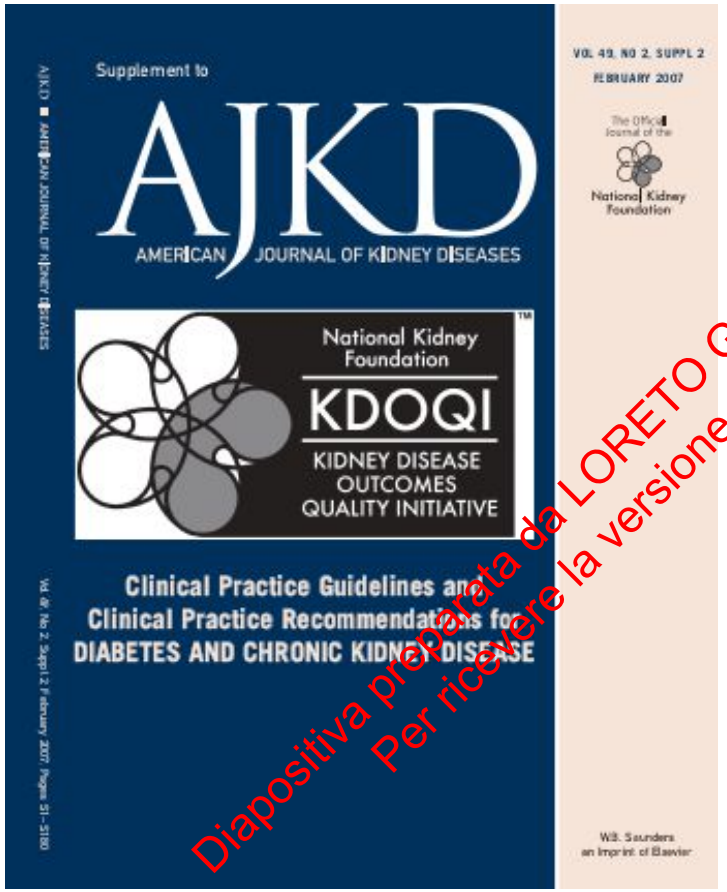


19.7%

Positive predictive values (PPVs) (pooled data) of clinical judgment for identifying DN, NDRD and mixed forms (as assessed by renal biopsy) were 50.1% (95% CI: 44.9 -55.3), 36.9% (95% CI: 32.3-41.8) and 19.7% (95% CI: 16.3-23.6), respectively

Meta-regression identified systolic pressure, HbA1c, diabetes duration and retinopathy as factors explaining heterogeneity for NDRD, creatinine and GFR for mixed forms and only serum creatinine for DN.

DIABETES AND RENAL DAMAGE



Terminology for the Kidney Disease of Diabetes

«The term diabetic nephropathy has been replaced by diabetic kidney disease (DKD). The term diabetic nephropathy should be reserved to biopsy-proven kidney disease caused by diabetes».

1. Il danno renale nel paziente diabetico è sempre causato dal diabete?

SI

NO

NON SO

Lo screening e la stadiazione del rischio di MRC deve basarsi sulla valutazione del volume di filtrazione glomerulare stimato (eGFR) e della albuminuria (uACR)

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min per 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.

Patients stratification

		Cases			
N		A1	A2	A3	Total
G1	>90	62% 9900			4,662 (29.6)
G2	60-90				8,152 (51.7)
G3a	45-60	11% 1638	22% 3,497	5% 738	1,951 (12.4)
G3b	30-45				750 (4.8)
G4	15-30				229 (1.5)
G5	<15				29 (0.2)
Total		11,538 (73.2)	3,497 (22.2)	738 (4.7)	15,773 (100.0)

eGFR ml/min

<30 mg/g >30 <300 mg/g >300 mg/g

ALBUMINURIA

Patients stratification

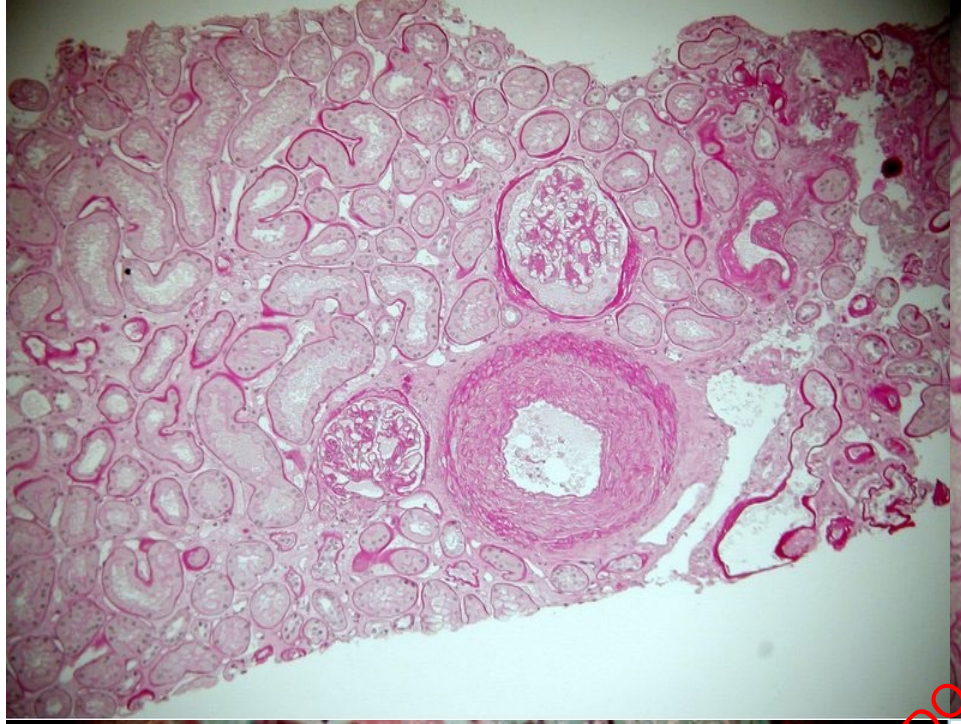
	Cases			
N	A1	A2	A3	Total
G1	3,610 (22.9)		120 (0.8)	4,662 (29.6)
G2	6,255 (39.7)		244 (1.6)	8,152 (51.7)
G3a			136 (0.9)	1,951 (12.4)
G3b			136 (0.9)	750 (4.8)
G4			87 (0.6)	229 (1.5)
G5			15 (0.1)	29 (0.2)
Total	11,538 (73.2)	3,497 (22.2)	738 (4.7)	15,773 (100.0)

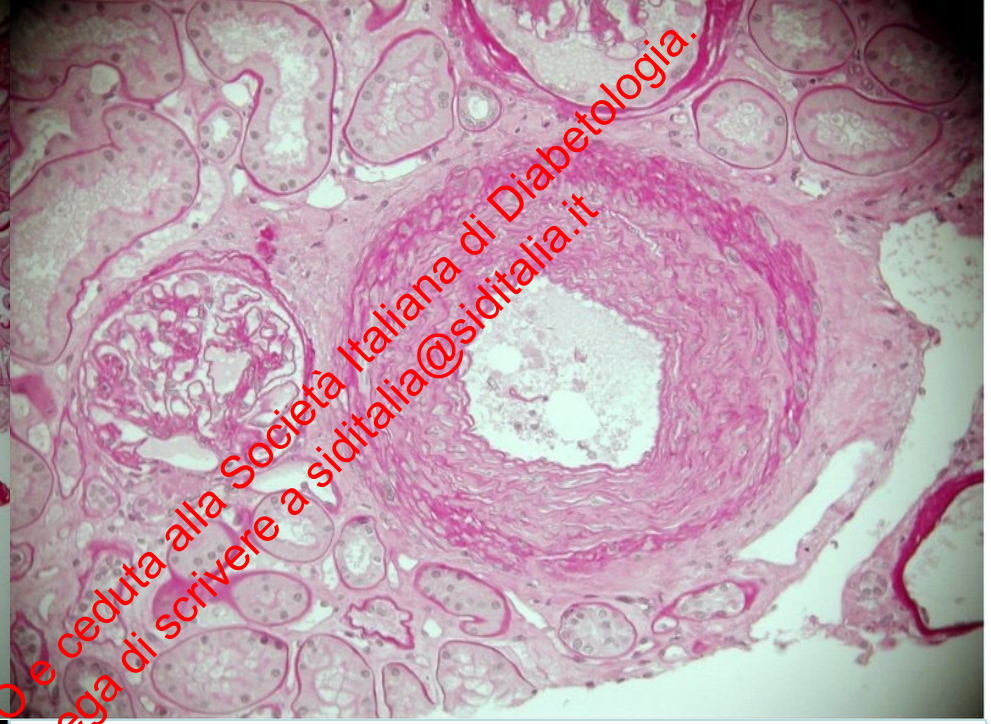
11%
1638

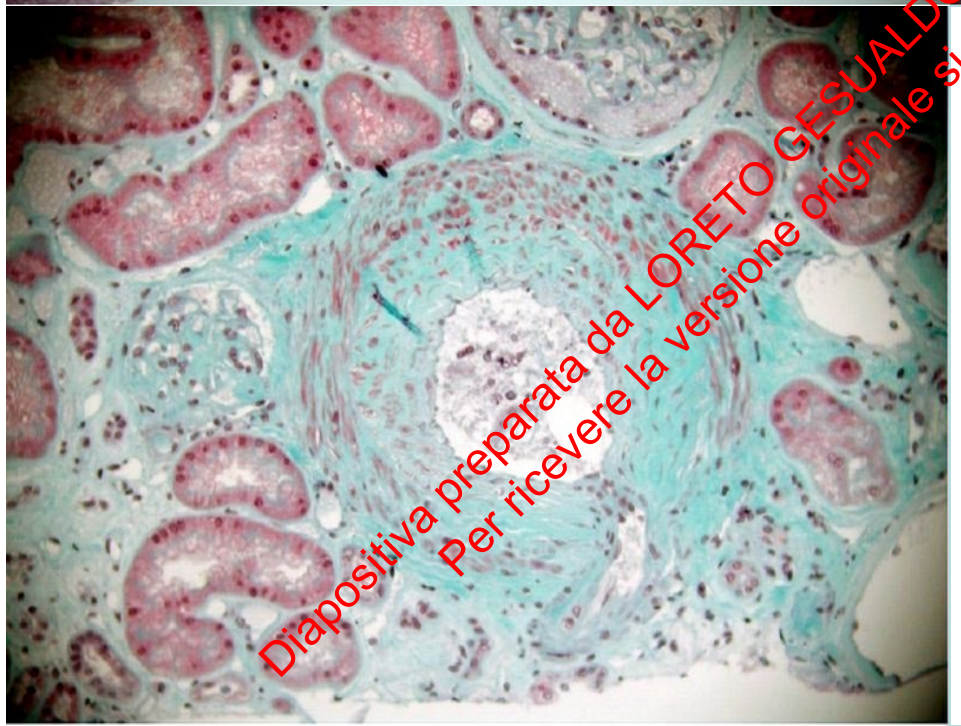
22%
3,497

<30 mg/g >30 <300 mg/g >300 mg/g

ALBUMINURIA







Class 2

- ✓ Vascular disease with macroangiopathic lesions
- ✓ Glomeruli small and ischemic
- ✓ Marked arteriosclerosis
- ✓ Chronic tubulointerstitial damage

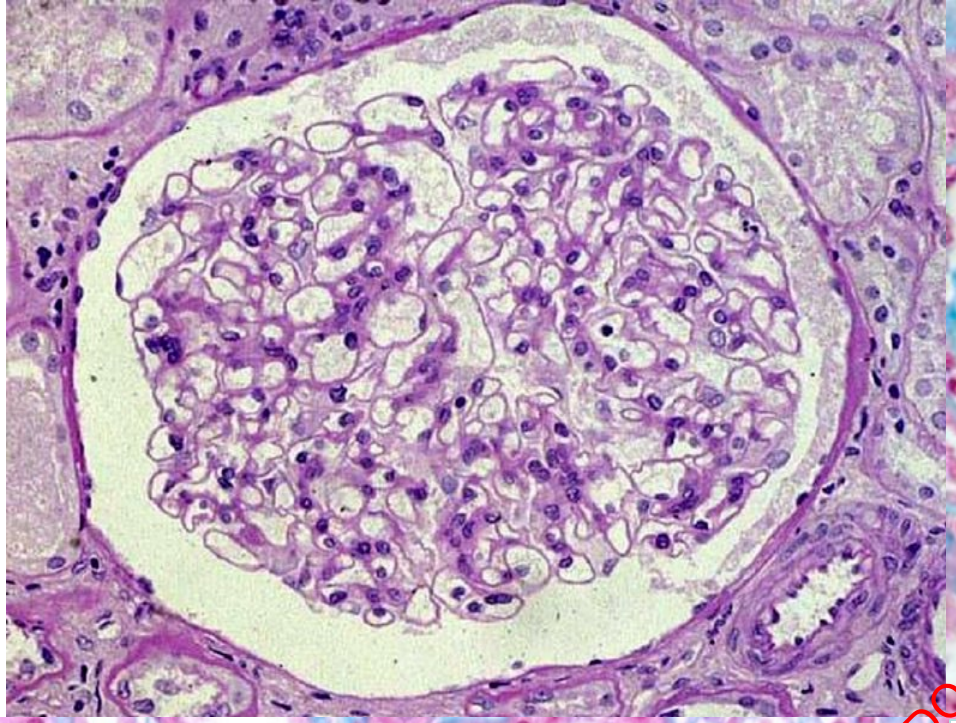
Patients stratification

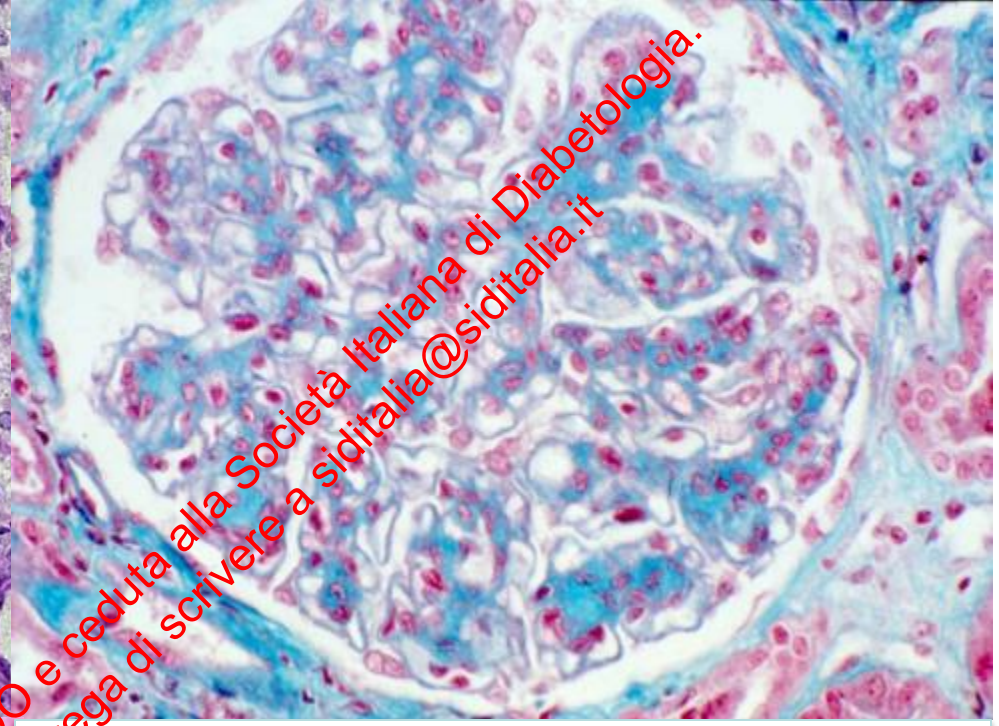
	Cases			
N	A1	A2	A3	Total
G1 >90	3,610 (22.9)			4,662 (29.6)
G2 60-90	6,255 (39.7)			8,152 (51.7)
G3a 45-60	1,253 (7.9)	22% 3,497	5% 738	1,951 (12.4)
G3b 30-45	351 (2.2)			750 (4.8)
G4 15-30	60 (0.4)			229 (1.5)
G5 <15	9 (0.06)			29 (0.2)
Total	11,538 (73.2)	3,497 (22.2)	738 (4.7)	15,773 (100.0)

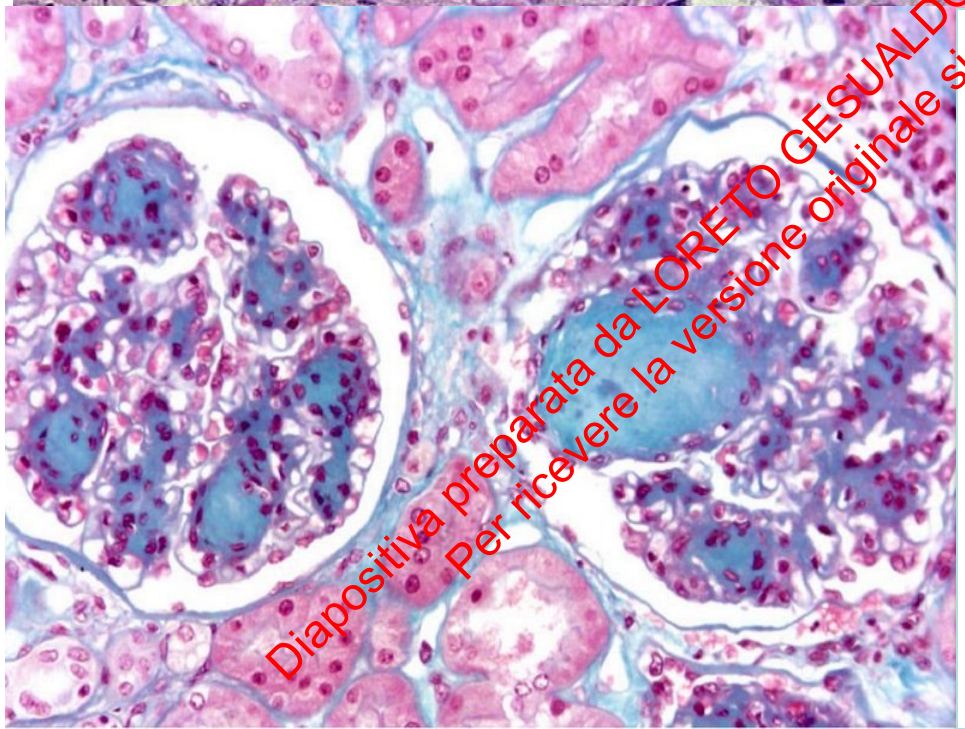
eGFR ml/min

<30 mg/g | >30 <300 mg/g | >300 mg/g

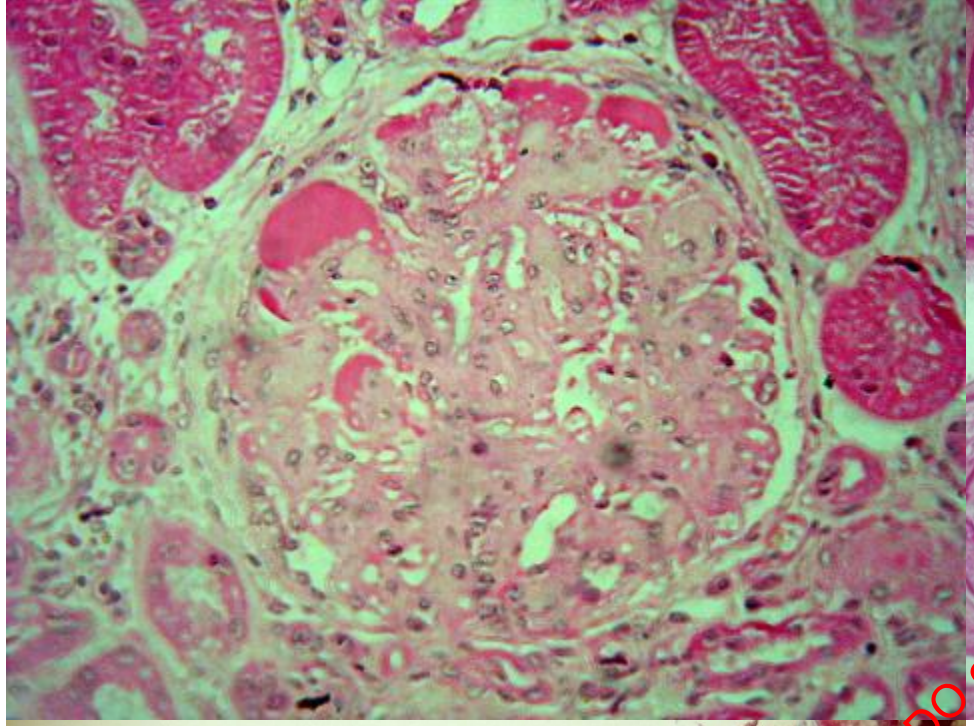
ALBUMINURIA

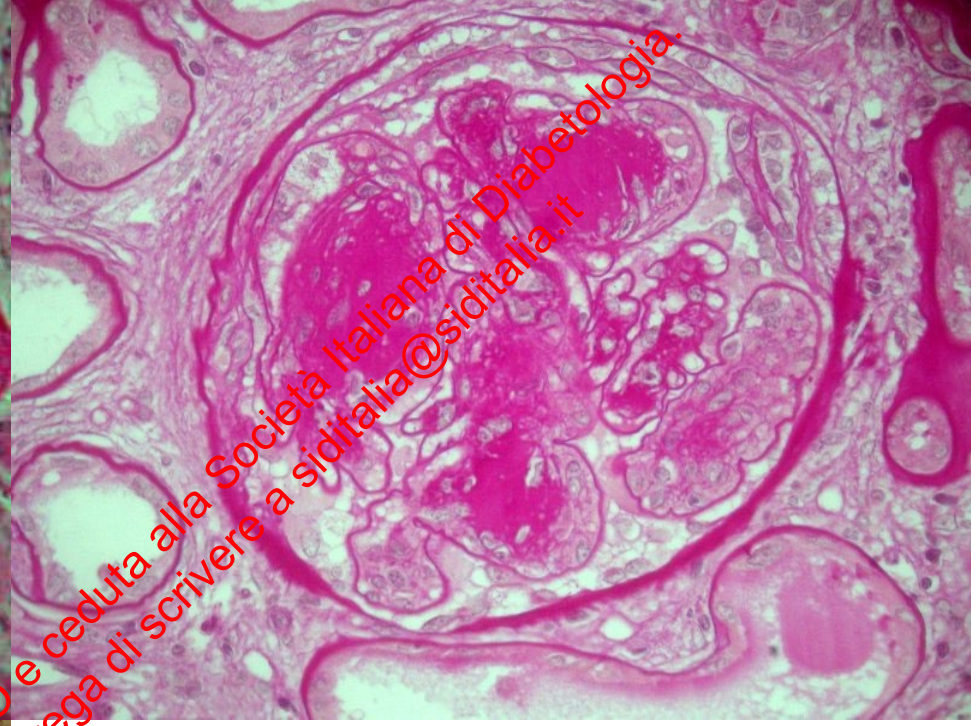


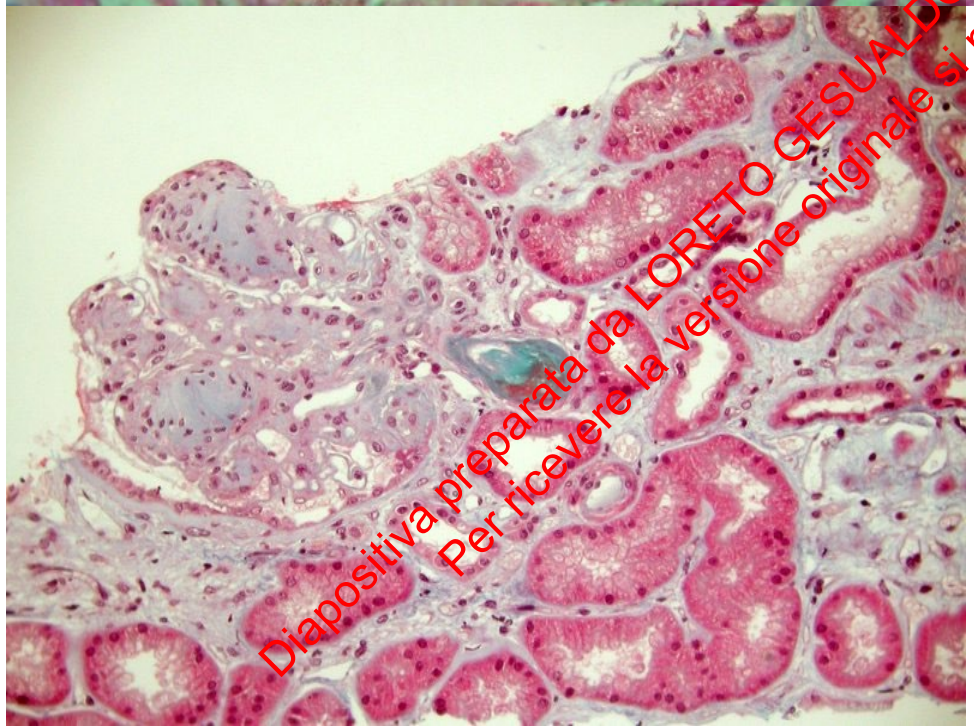




Class 1
(Kimmelstiel
Wilson lesions)







Class 1

- ✓ Glomerular hypertrophy
- ✓ Mesangial expansion (fibrosis)
- ✓ Mesangiolysis
- ✓ Sclerosis
- ✓ Nodular appearance
- ✓ Fibrin caps
- ✓ Fibrin necrosis on the afferent artheriola
- ✓ IFTA

Patients stratification

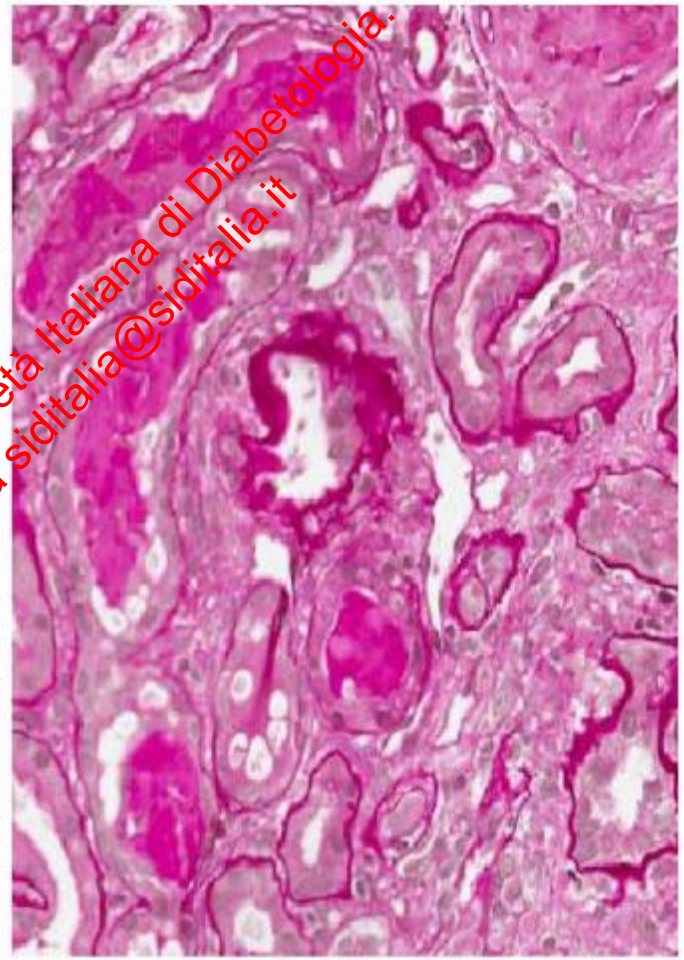
		Cases			
N		A1	A2	A3	Total
G1	>90	3,610 (22.9)	932 (5.9)		4,662 (29.6)
G2	60-90	6,255 (39.7)	1,653 (10.5)		8,152 (51.7)
G3a	45-60	1,253 (7.9)	562 (3.6)		1,951 (12.4)
G3b	30-45	351 (2.2)	253 (1.7)		750 (4.8)
G4	15-30	60 (0.4)	82 (0.5)		229 (1.5)
G5	<15	9 (0.06)	5 (0.03)		29 (0.2)
Total		11,538 (73.2)	3,497 (22.2)	738 (4.7)	15,773 (100.0)

5%
738

eGFR ml/min

<30 mg/g | >30 <300 mg/g | >300 mg/g

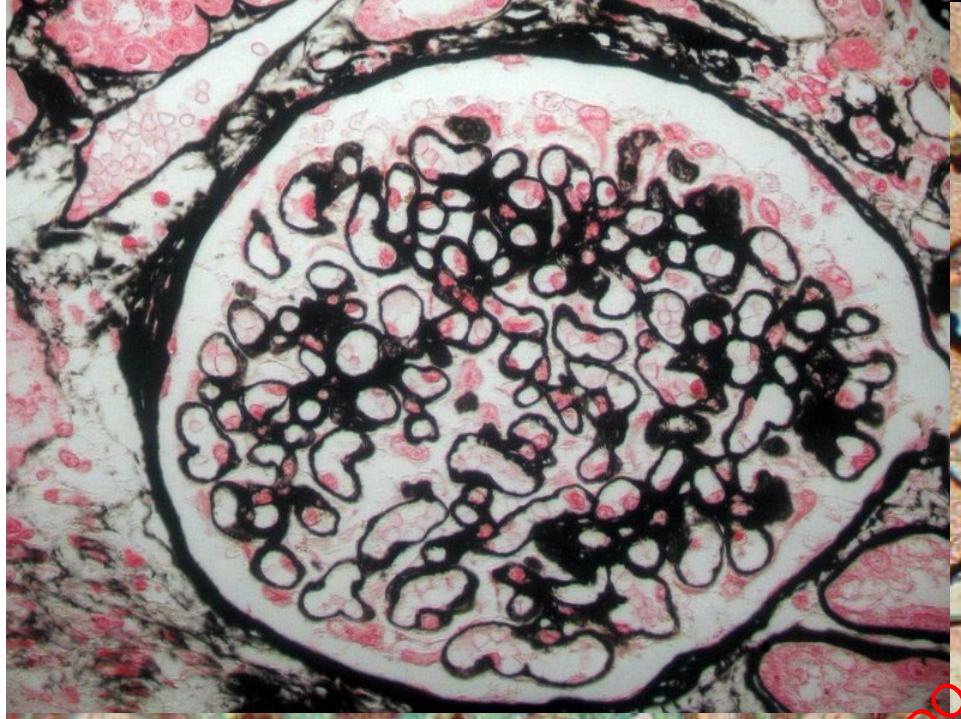
ALBUMINURIA

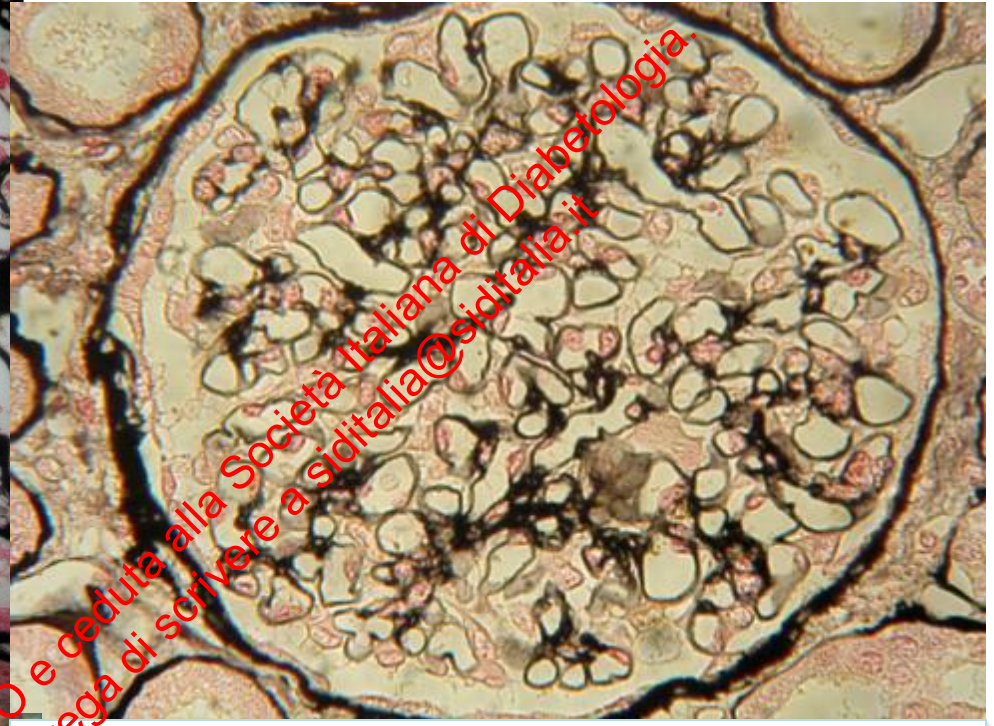


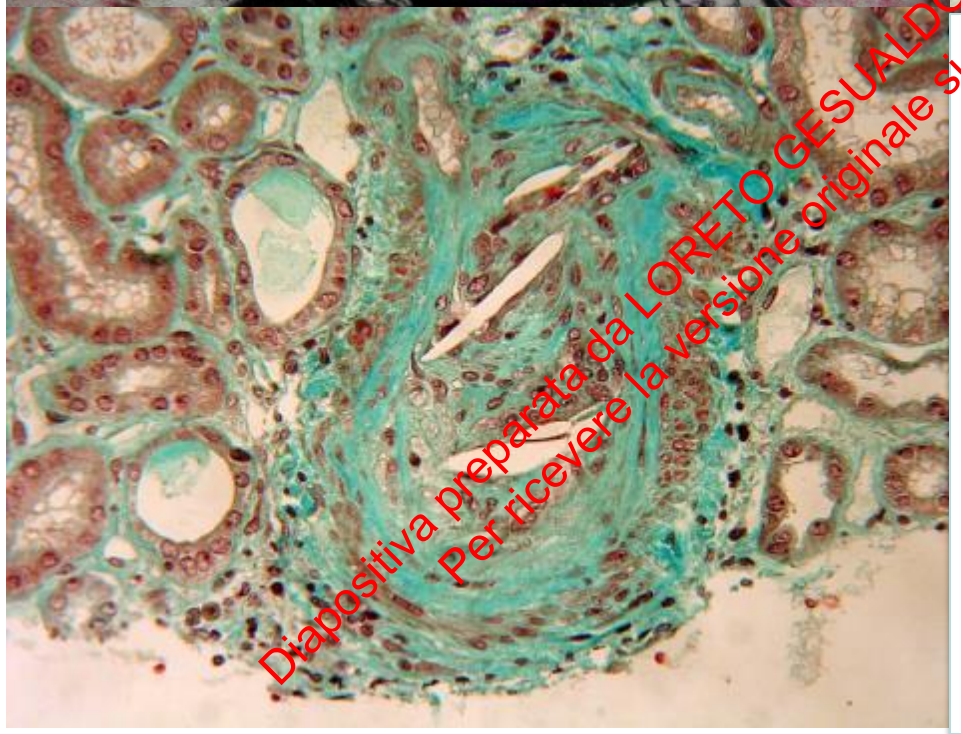
Classe 3

Another glomerular disease superimposed on well-developed diabetic glomerulo-sclerosis

DN + Cast Nephropathy







Class 3b

Glomerular disease without clearly detectable or minimal lesions of diabetic nephropathy (membranous nephropathy, IgA nephropathy….)

2. Quanti fenotipi clinici renali è possibile riconoscere?

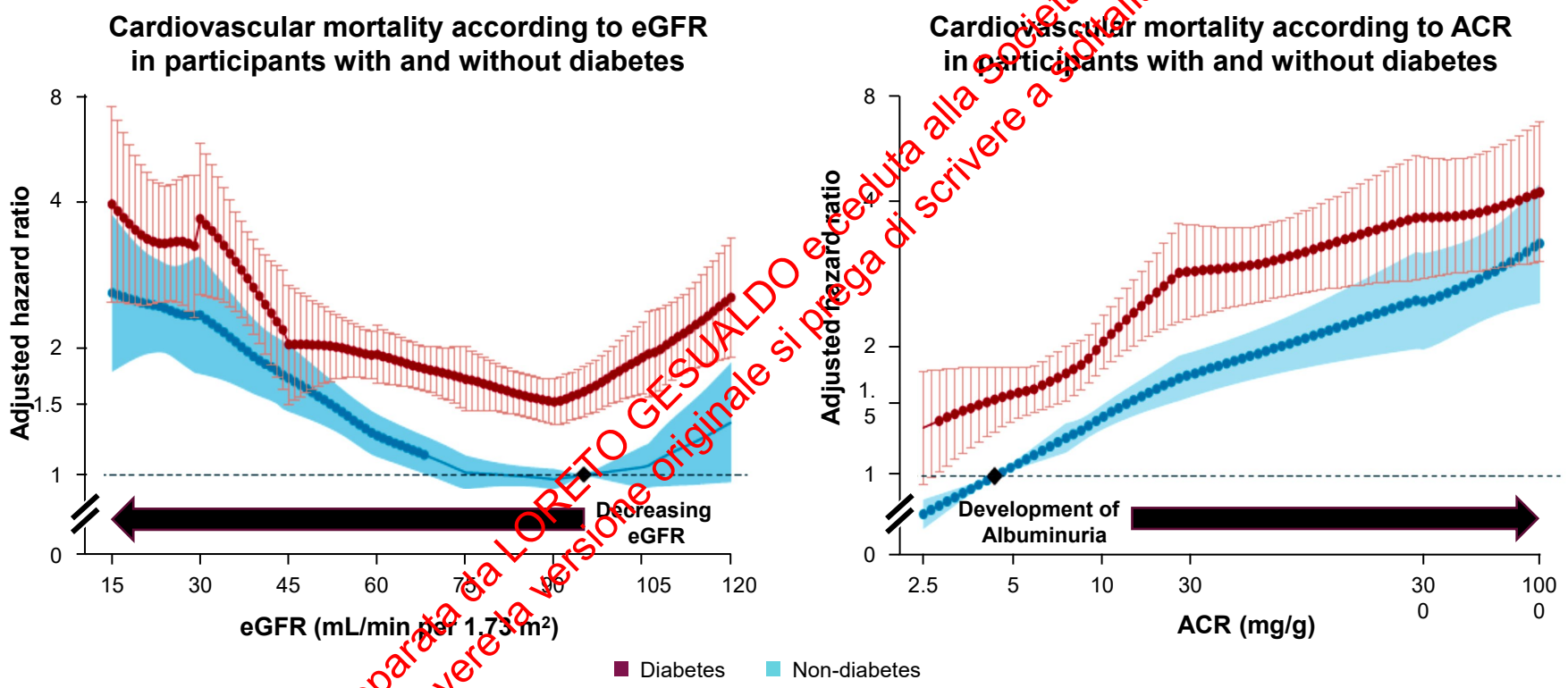
A: 1

B: 2

C: 3

D: >3

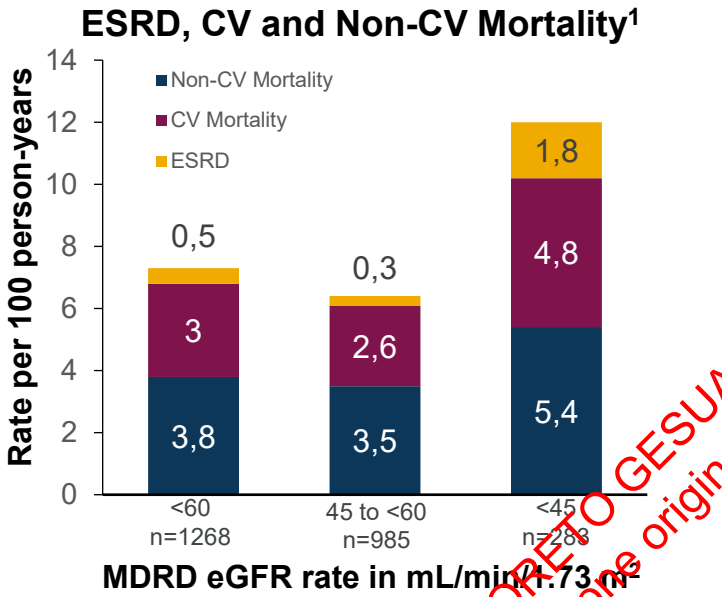
In diabetes, both lower eGFR and development of albuminuria are associated with increased risk of CV mortality



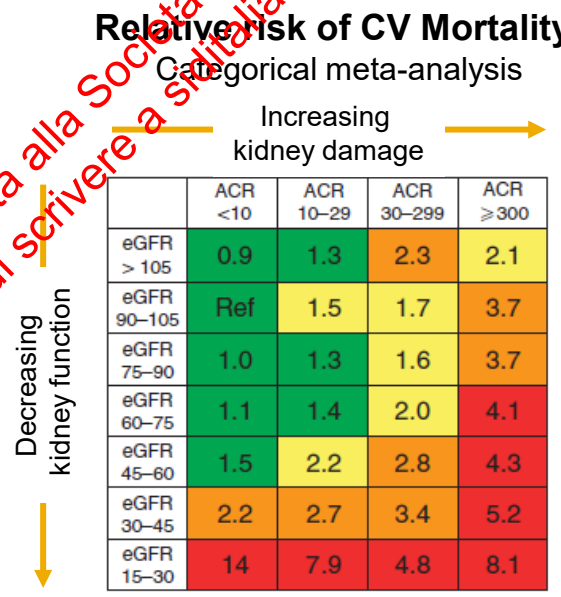
ACR = albumin:creatinine ratio; CKD = chronic kidney disease; CV = cardiovascular; DKD = diabetic kidney disease; eGFR = estimated glomerular filtration rate.

Fox CS et al. *Lancet*. 2012;380:1662-1673.

Risk of death more likely than progression to ESRD



Leading causes of death in CKD[2]:
- CV events
- non-CV causes: cancer, infection



	ACR <10	ACR 10–29	ACR 30–299	ACR ⩾300
eGFR > 105	0.9	1.3	2.3	2.1
eGFR 90–105	Ref	1.5	1.7	3.7
eGFR 75–90	1.0	1.3	1.6	3.7
eGFR 60–75	1.1	1.4	2.0	4.1
eGFR 45–60	1.5	2.2	2.8	4.3
eGFR 30–45	2.2	2.7	3.4	5.2
eGFR 15–30	14	7.9	4.8	8.1

Renal decline is associated with increased risk of CV mortality

CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; ESRD = end stage renal disease; MDRD = Modified Diet in Renal Disease; REF = reference;

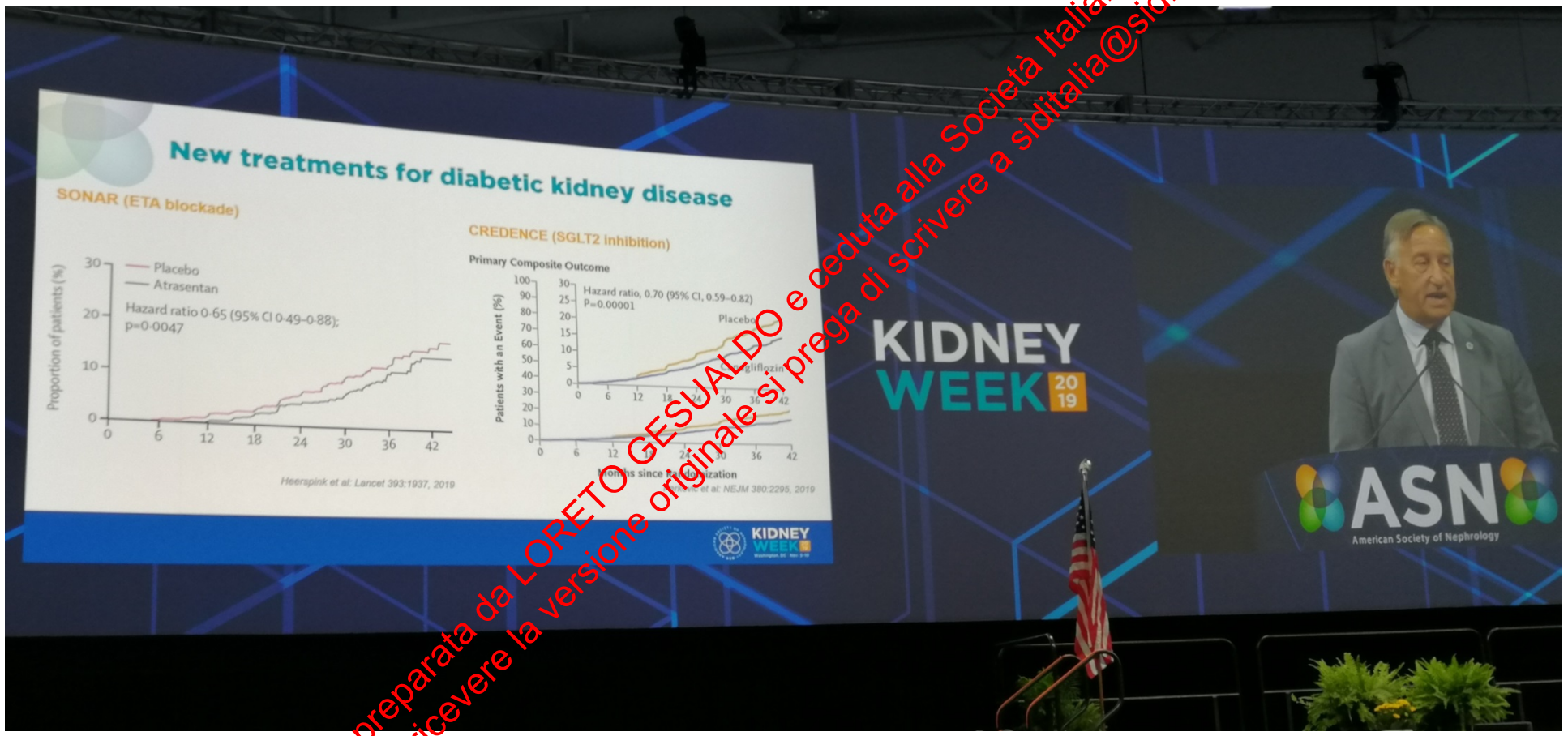
1. Dalrymple L et al. J *Gen Intern Med*. 2011;26:379-385; 2. Thompson S et al. *J Am Soc Nephrol*. 2015;26:2504-2511; 3. KDIGO CKD Work Group. *Kidney Int Suppl*. 2013;3:1-150

Options to prevent new onset or worsening renal function are limited

Drug/Class	Study Name	Patient Population	Year	Effect on CKD progression
ACE				
Ramipril	REIN[2]	Non-DM Nephropathy (eGFR 20-70 mL/min/1.73 m^2 ; UPE >1g/24h)	1997	✓
ARBs				
Irbesartan	IDNT[3]	T2D; CKD (UPE ≥900mg/24h; SCr 1-3 mg/dL)	2001	✓
Losartan	RENAAL[4]	T2D; CKD (UACR ≥300; SCr 1.3-3mg/dL)	2001	
Olmesartan	ROADMAP[5]	T2D; normoalbuminuria	2011	
ACE/ARB Combo				⊖
Telmisartan/ramipril	ONTARGET[6]	ASCVD or diabetes with end-organ damage	2008	
Losartan/lisinopril	VA NEPHRON-D[7]	T2D; CKD (eGFR ≥30 to <90mL/min/1.73 m^2; UACR ≥300)	2013	
DRI				⊖
Aliskiren	ALTITUDE[8]	T2D; CKD (eGFR ≥30 and <60ml/min/1.73 m^2) or CVD	2012	
Glycosaminoglycan				⊖
Sulodexide	SUN MACRO[9,10]	T2D; CKD (UPE>900mg/24h)	2012	
Anti-inflammatory				⊖
Bardoxolone methyl	BEACON[11]	T2D; CKD (eGFR 15 to <30 mL/min/1.73 m^2)	2013	

NUOVE EVIDENZE

Farmaci innovativi per la prevenzione del danno d'organo



Rosemberg, Presidential Address ASN 2019

Washington, 6 November 2019

THE TRIALS

SGLT-2 INHIBITOR TRIALS

Empagliflozin EMPA-REG OUTCOME

- All with CVD, none with eGFR <30

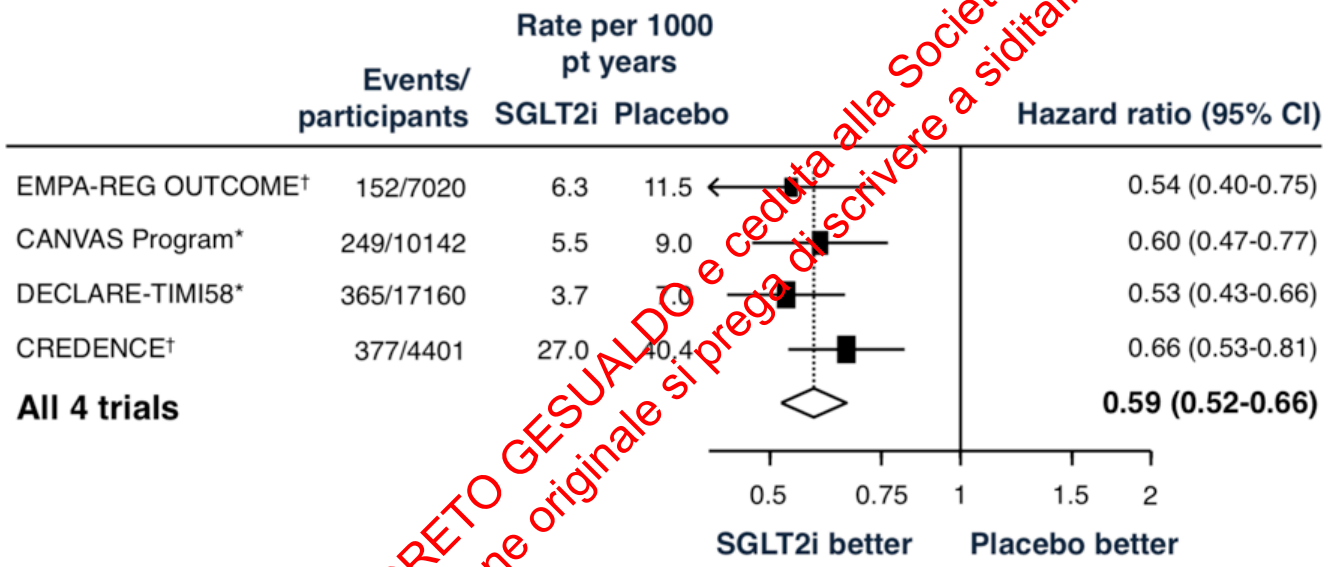
Canagliflozin CANVAS

- 2 CV risk factors + age 50+, exclude eGFR <30

Dapagliflozin DECLARE–TIMI 58

- renal composite: ≥40% decrease in eGFR, ESKD, death

SGLT2 INHIBITORS IN TYPE 2 DIABETES:
KIDNEY DISEASE PROGRESSION

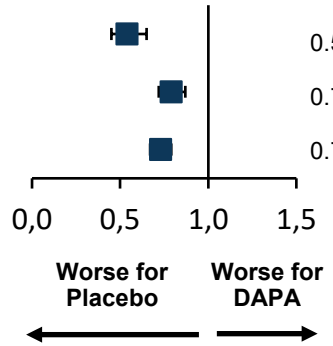


Outcomes
† = Doubling of creatinine or ESRD
* = 40% decline in eGFR or ESRD

Wanner NEJM 2016: 375: 323-334; Neal NEJM 2017; 377: 644-57; Wiviott NEJM 2018; Nov 10; Perkovic NEJM 2019; Apr 14.

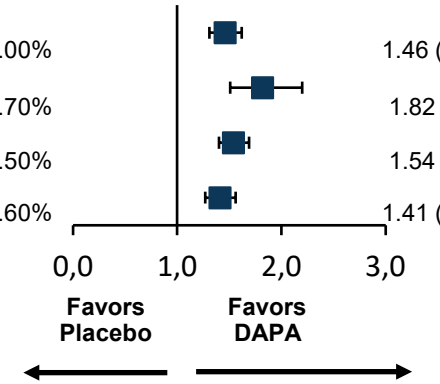
Dapagliflozin decreased the likelihood of patients deteriorating to a worse albuminuria category

	Dapagliflozin		Placebo				
	n/N (%)	KM Event Rate	n/N (%)	KM Event Rate		Hazard Ratio (95% CI)	Cox p-value
Endpoints							
Deterioration from baseline							
Normo/Micro to Macro	181/7836 (2..3)	2.30%	330/7838 (4.2)	4.2%		0.54 (0.45, 0.65)	<0.0001
Normo to Micro/Macro	772/5819 (13.3)	13.30%	958/5825 (16.5)	16.3%		0.79 (0.72, 0.87)	<0.0001
Normo to Micro/Macro or Micro to Macro	928/7836 (11.8)	11.90%	1243/7838 (15.9)	15.8%		0.73 (0.67, 0.79)	<0.0001



Dapagliflozin increased the likelihood of patients improving in albuminuria category, regardless of baseline UACR

	Dapagliflozin		Placebo			
	n/N (%)	KM Event Rate	n/N (%)	KM Event Rate	Hazard Ratio (95% CI)	Cox p-value
Endpoints						
Improvement from baseline						
Micro to Normo	774/2017 (38.4)	38.90%	576/2013 (28.6)	29.00%	1.46 (1.31, 1.62)	<0.0001
Macro to Normo/Micro	282/594 (47.5)	48.10%	175/575 (30.4)	31.70%	1.82 (1.51, 2.2)	<0.0001
Macro to Normo/Micro or Micro to Normo	1056/2611 (40.4)	41.00%	751/2588 (29.0)	29.50%	1.54 (1.4, 1.69)	<0.0001
Micro/Macro to Normo	809/2611 (31.0)	31.50%	604/2588 (23.3)	23.60%	1.41 (1.27, 1.56)	<0.0001

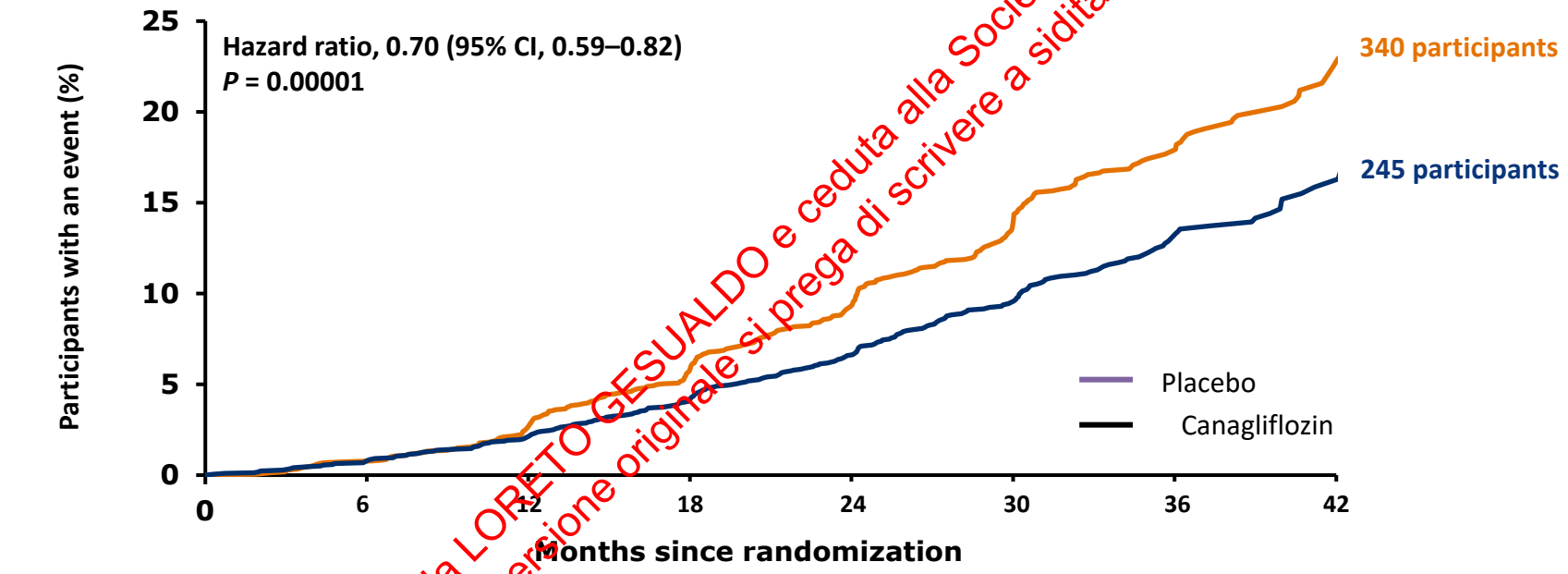


Randomised controlled trials of SGLT2 inhibitors in CKD

	CREDENCE[1–4]	Dapa-CKD[5-6]	EMPA-KIDNEY[8]
Population	**PROTEINURIC DIABETIC KIDNEY DISEASE** ✓ T2D x Non-DM x Non-Albuminuric	**PROTEINURIC CHRONIC KIDNEY DISEASE** ✓ T2D ✓ Non-DM ✓ Non-Albuminuric	**CHRONIC KIDNEY DISEASE** T2D ✓ Non-DM ✓ Non-Albuminuric
No. of patients	4401	4304	~6000
Key inclusion criteria	eGFR ≥30 to <90 **and** UACR >300 mg/g	eGFR ≥25 to ≤75 **and** UACR ≥200 mg/g	eGFR ≥20 to <45 **or** eGFR ≥45 to <90 and UACR ≥200 mg/g
Primary composite outcome	ESKD, doubling of creatinine, or renal/CV death	ESKD, ≥50% sustained eGFR decline, or renal/CV death	ESKD, or ≥40% sustained eGFR decline, or renal/CV death
Study start and stop date (announced or planned)	February 2014 July 2018[3]	February 2017 March 2020[7]	November 2018 ~June 2022
No. of countries	34	21	8

1. Jardine MJ et al. AJN 2017;46:462; 2. Clin.Trials.gov. NCT02065791; 3. Janssen Pharm., Inc. Press release 2018; 4. Perkovic V et al. NEJM 2019;380:2295-

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

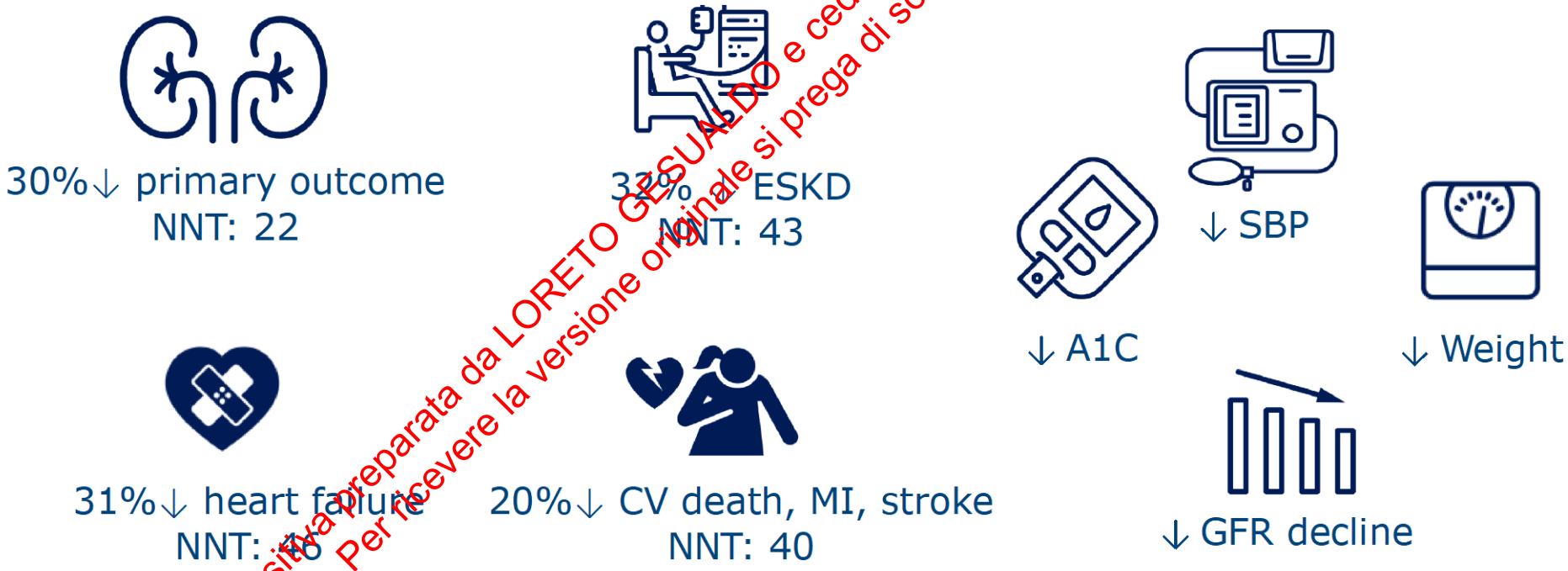


No. at risk								
Placebo	2199	2178	2132	2047	1725	1129	621	170
Canagliflozin	2202	2181	2145	2081	1786	1211	646	196

Perkovic et al, NEJM April 14, 2019; DOI: 10.1056/NEJMoa1811744

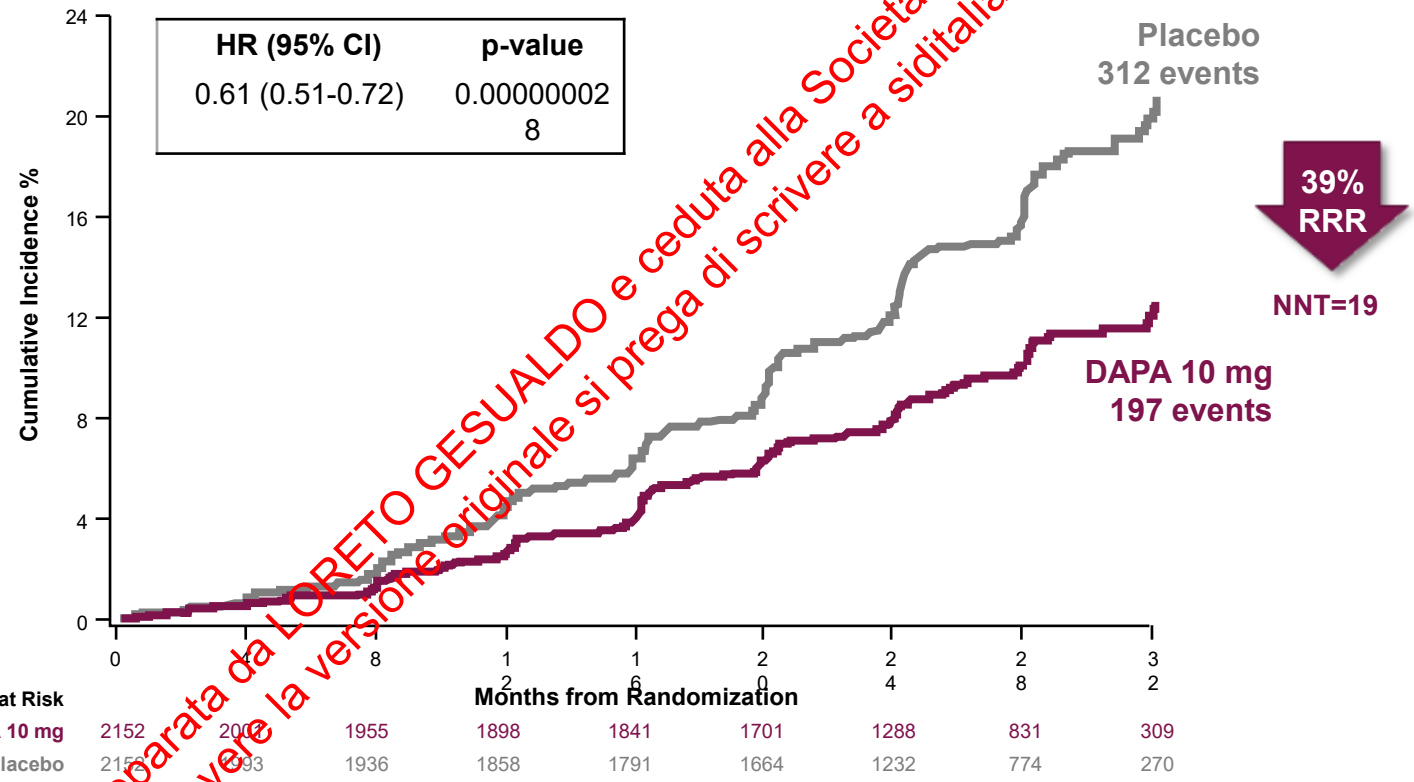
Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

V. Perkovic, M.J. Jardine, B. Neal, S. Bompoint, H.J.L. Heerspink, D.M. Charytan, R. Edwards, R. Agarwal, G. Bakris, S. Bull, C.P. Cannon, G. Capuano, P.-L. Chu, D. de Zeeuw, T. Greene, A. Levin, C. Pollock, D.C. Wheeler, K. Yavin, H. Zhang, B. Zinman, G. Meininger, B.M. Brenner, and K.W. Mahaffey, for the CREDENCE Trial Investigators*



N ENGL J MED April 14, 2019.

Primary Composite Outcome: Sustained ≥50% eGFR Decline, ESKD, Renal or CV Death[a]



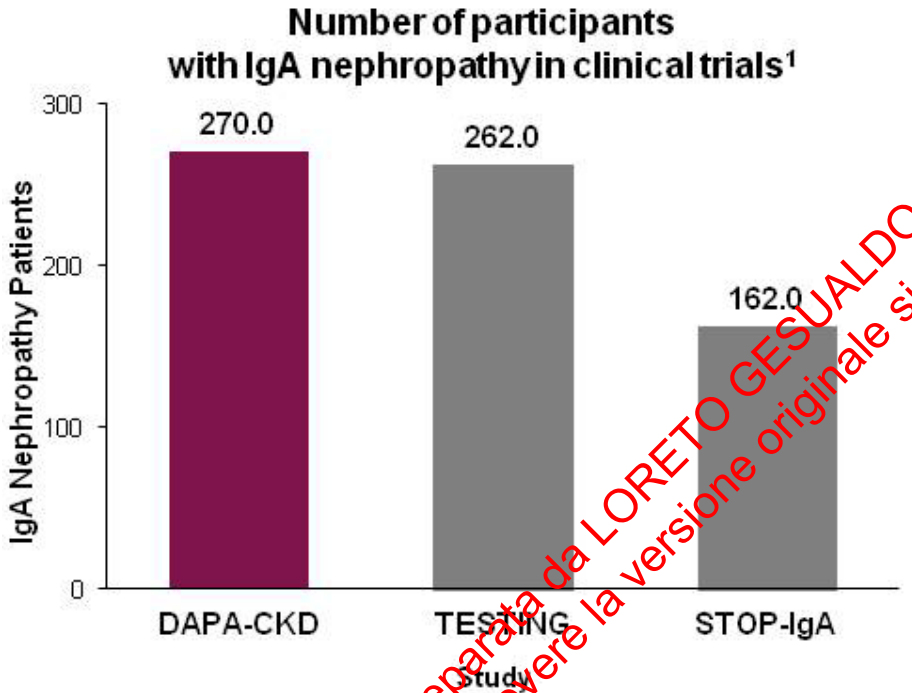
[a]ESKD defined as the need for maintenance dialysis (peritoneal or hemodialysis) for at least 28 days and renal transplantation or sustained eGFR <15mL/min/1.73m^2 for at least 28 days. Renal death was defined as death due to ESKD when dialysis treatment was deliberately withheld for any reason.[2] CV = cardiovascular; DAPA = dapagliflozin; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; HR = hazard ratio; ; NNT = number needed to treat; RRR = relative risk reduction.

1. Heerspink HJL. Presented at: ESC Congress - The Digital Experience; August 29 - September 1, 2020. 2. Heerspink HJL et al. *Nephrol Dial Transplant*. 2020;35:274–282.

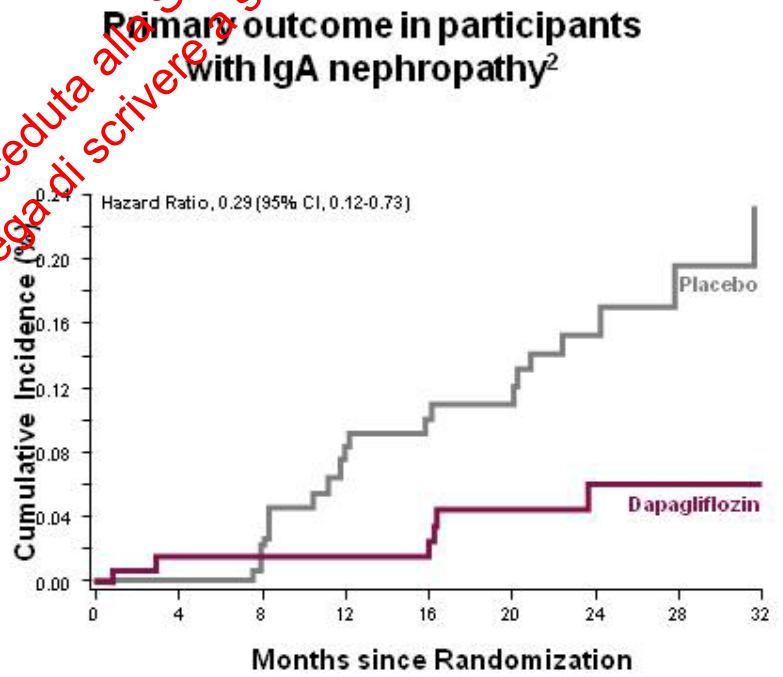
DAPA-CKD primary outcome result, by diabetes and renal subgroups

	Dapagliflozin	Placebo	HR (95% CI)	Het. test
Primary outcome	**197**	**312**	**0.61 (0.51-0.72)**	
Type 2 diabetes	152	229	0.64 (0.52-0.79)	0.24
No diabetes	45	83	0.50 (0.35-0.72)	
uACR ≤1000 mg/g	44	64	0.54 (0.37-0.77)	0.52
uACR >1000 mg/g	153	228	0.62 (0.50-0.76)	
eGFR ≤45	152	217	0.63 (0.51-0.78)	0.22
eGFR >45	45	95	0.49 (0.34-0.69)	

IgAN subgroup

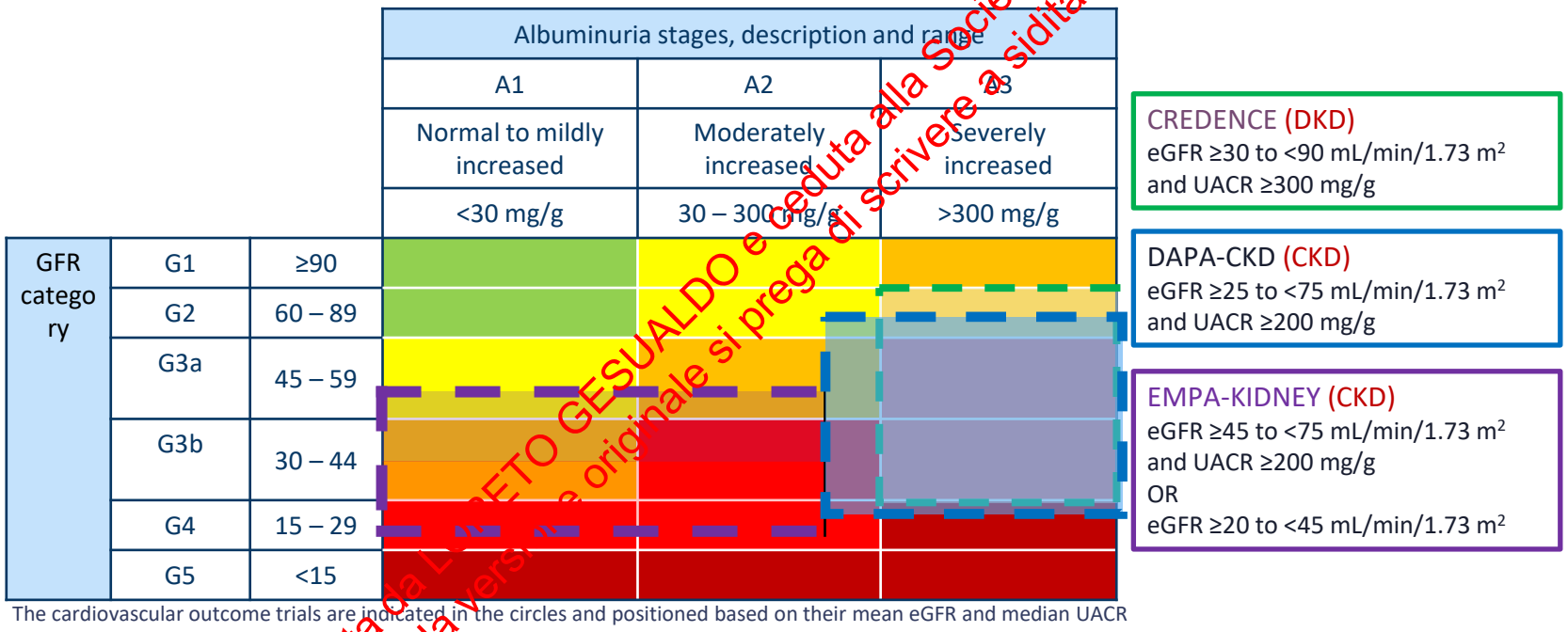


Wheeler DC et al. Nephrol Dial Transplant. 2020



Wheeler DC. Presented at: ASN – Kidney Week 2020

SGLT2 Inhibitors: Primary Kidney Outcome Trials

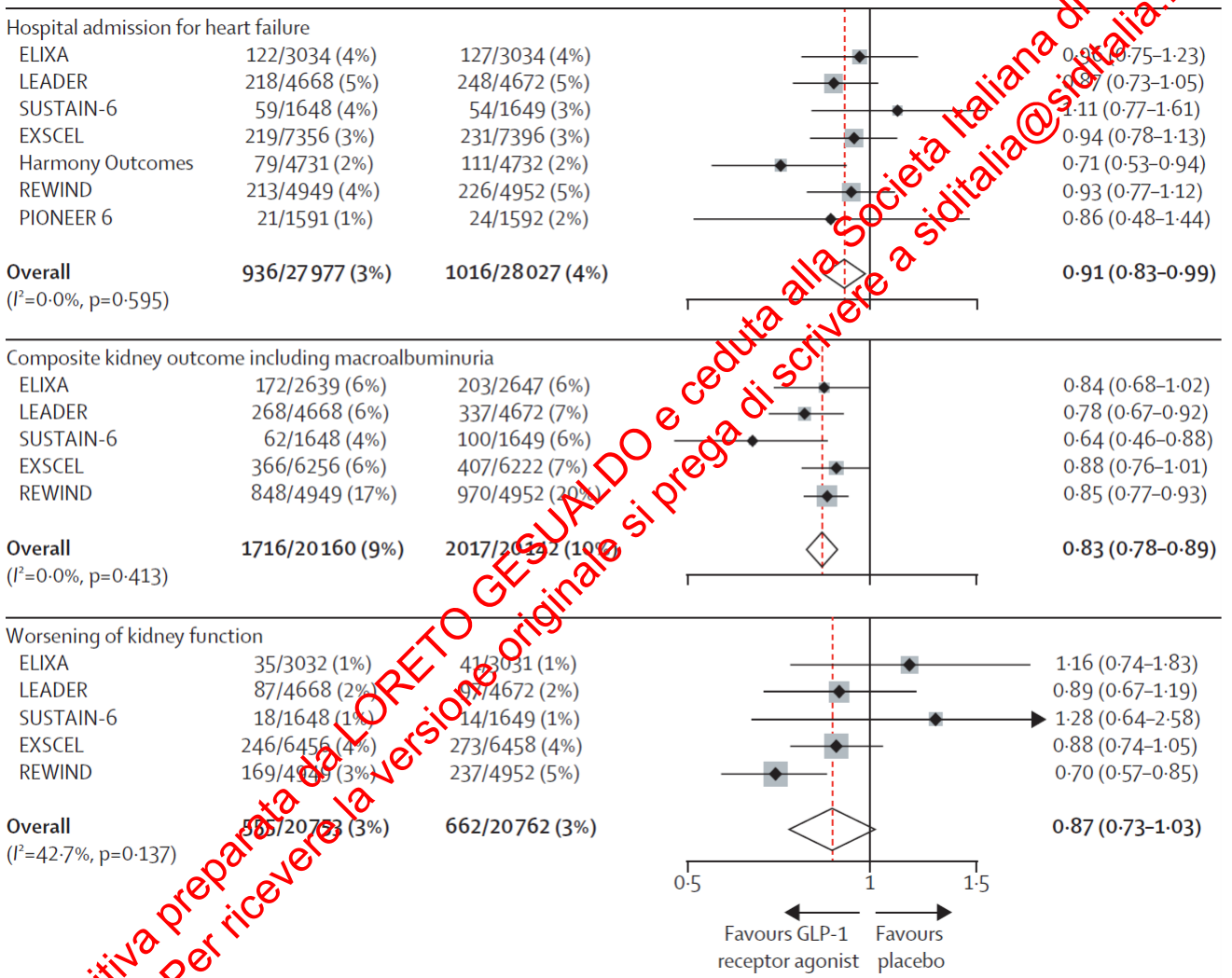


The cardiovascular outcome trials are indicated in the circles and positioned based on their mean eGFR and median UACR

CREDENCE: Perkovic et al. *N Engl J Med* 2019; 380: 2295-2306
DAPA-CKD: Heerspink et al. *N Engl J Med* 2020; 383: 1436-1446
EMPA-KIDNEY: Ongoing; Herrington WG, et al. *Clin Kidney J*. 2018; 11:749-761.

Courtesy of Dr. Peter Rossing

Effetti di GLP-1RA su Outcomes renali ed insufficienza cardiaca*

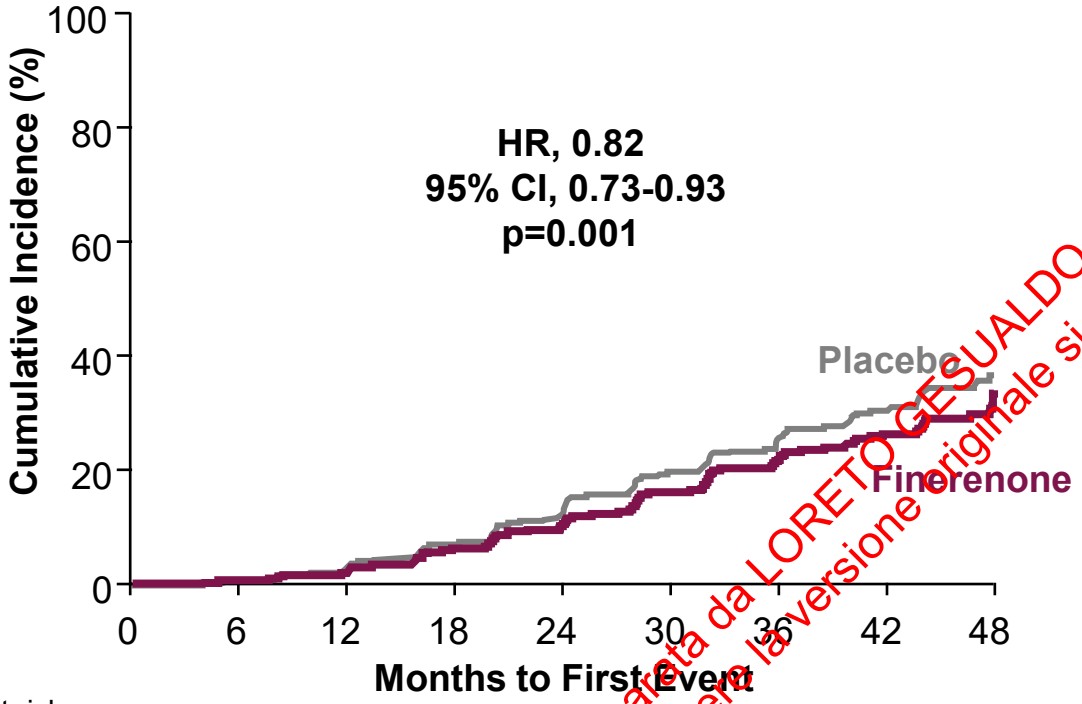


*based on ELIXA, EXSCEL, HARMONY, LEADER, PIONEER 6, REWIND, SUSTAIN-6

Kristensen SL et al. *Lancet Diabetes Endocrinol*. 7: 776-785, 2019

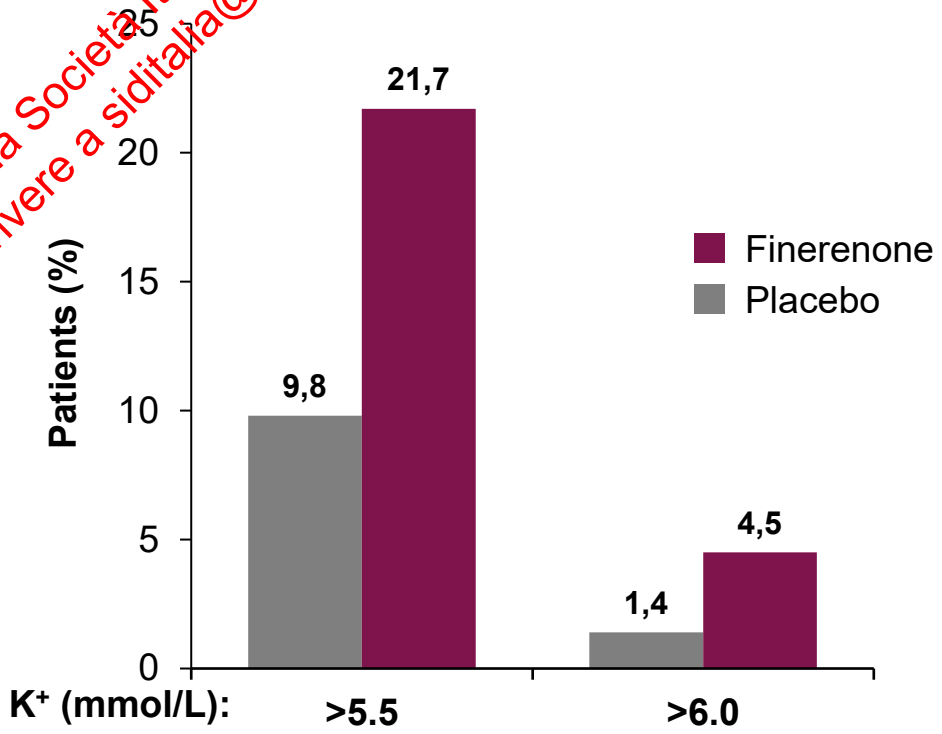
FIDELIO-DKD: Finerenone decreased the risk of CKD progression in patients with T2DM but was associated with hyperkalemia

Time to first event of kidney failure, sustained decrease in eGFR[a], or death from renal causes
(Primary composite endpoint)



No. at risk									
Placebo	2841	2724	2586	2379	1756	1348	792	453	82
Finerenone	2833	2705	2607	2397	1808	1274	787	441	83

Incidence of Hyperkalemia



Treatment discontinued due to hyperkalemia:
Finerenone, 2.3% (n=64) vs. placebo, 0.9% (n=25)

[a]Sustained decrease in eGFR defined as at least 40% reduction in eGFR from baseline over a period of at least 4 weeks.

CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; FIDELIO-DKD = Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease; HR = hazard ratio; T2DM = Type 2 diabetes mellitus.

Bakris GL et al. *N Engl J Med*. 2020.

3. Dobbiamo offrire a tutti i fenotipi clinici renali la stessa protezione cardio-renale?

SI

NO

NON SO

GRAZIE PER L'ATTENZIONE

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min per 1.73 m²) Description and range			Persistent albuminuria categories Description and range		
			A1	**A2**	**A3**
			Normal to mildly increased	Moderately increased	Severely increased
			<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
G1	Normal or high	≥90			
G2	Mildly decreased	60–89			
G3a	Mildly to moderately decreased	45–59			
G3b	Moderately to severely decreased	30–44			
G4	Severely decreased	15–29			
G5	Kidney failure	<15			

Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red, very high risk.