

UN ESEMPIO DI PDTA IN NEFROLOGIA

Gaetano La Manna

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Winter School: **LA PROTEZIONE RENALE ALLA LUCE DELLE NUOVE EVIDENZE SCIENTIFICHE**

30 Novembre - 1 Dicembre 2023

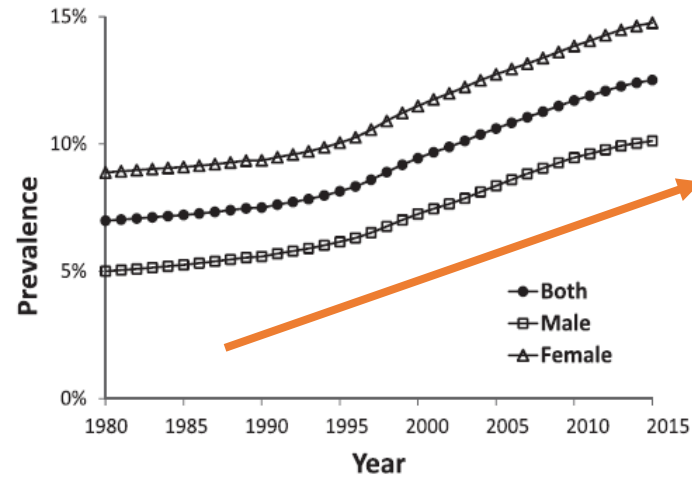
Bologna, Royal Hotel Carlton



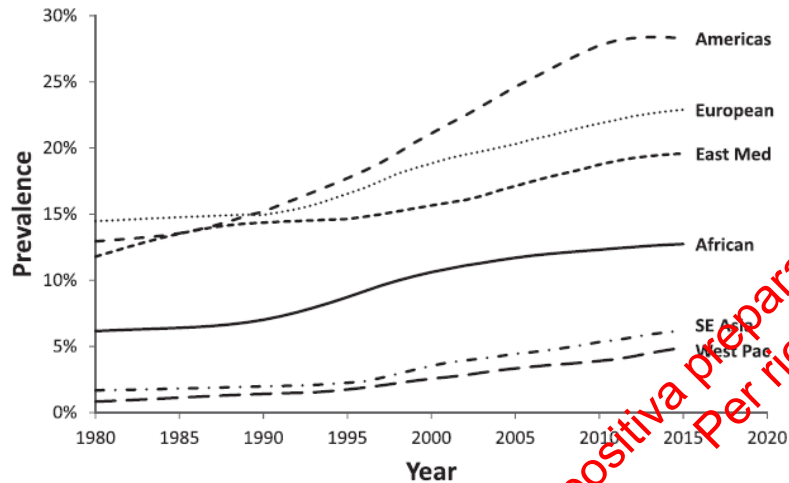
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OBSESITY

Global trends in obesity



Regional trends in obesity



CKD

Extremely common

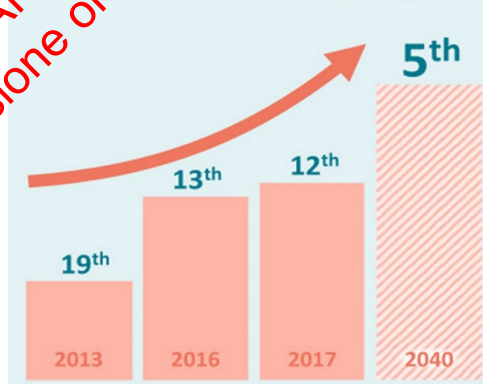
843,6 Million in 2017

Approximately **1 in 10**



Increasing death rate

+41.5% 1990 to 2017

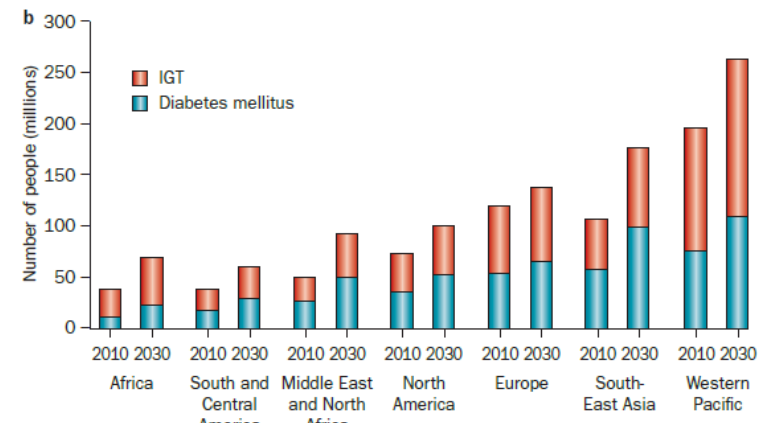
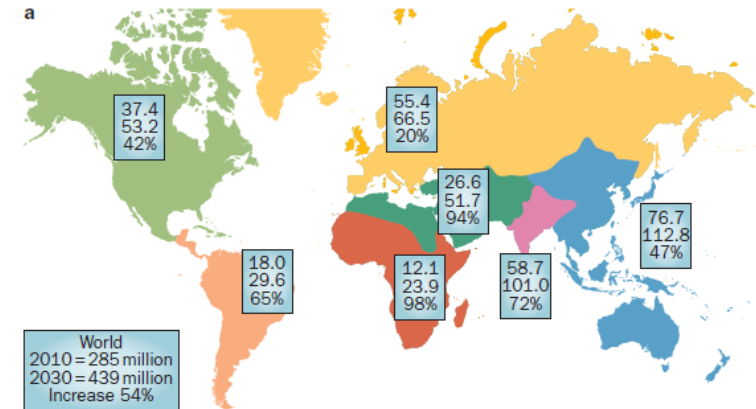


DIABETES

REVIEWS

The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives

Lei Chen, Dianna J. Magliano and Paul Z. Zimmet

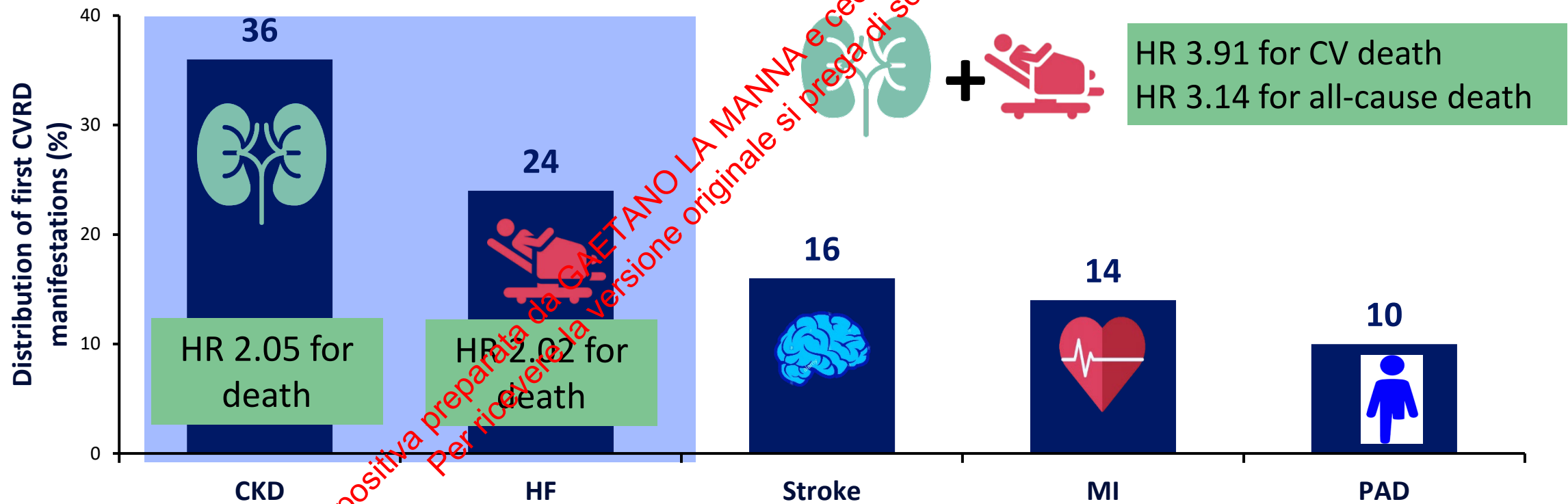


Heart failure and chronic kidney disease manifestation and mortality risk associations in type 2 diabetes: A large multinational cohort study

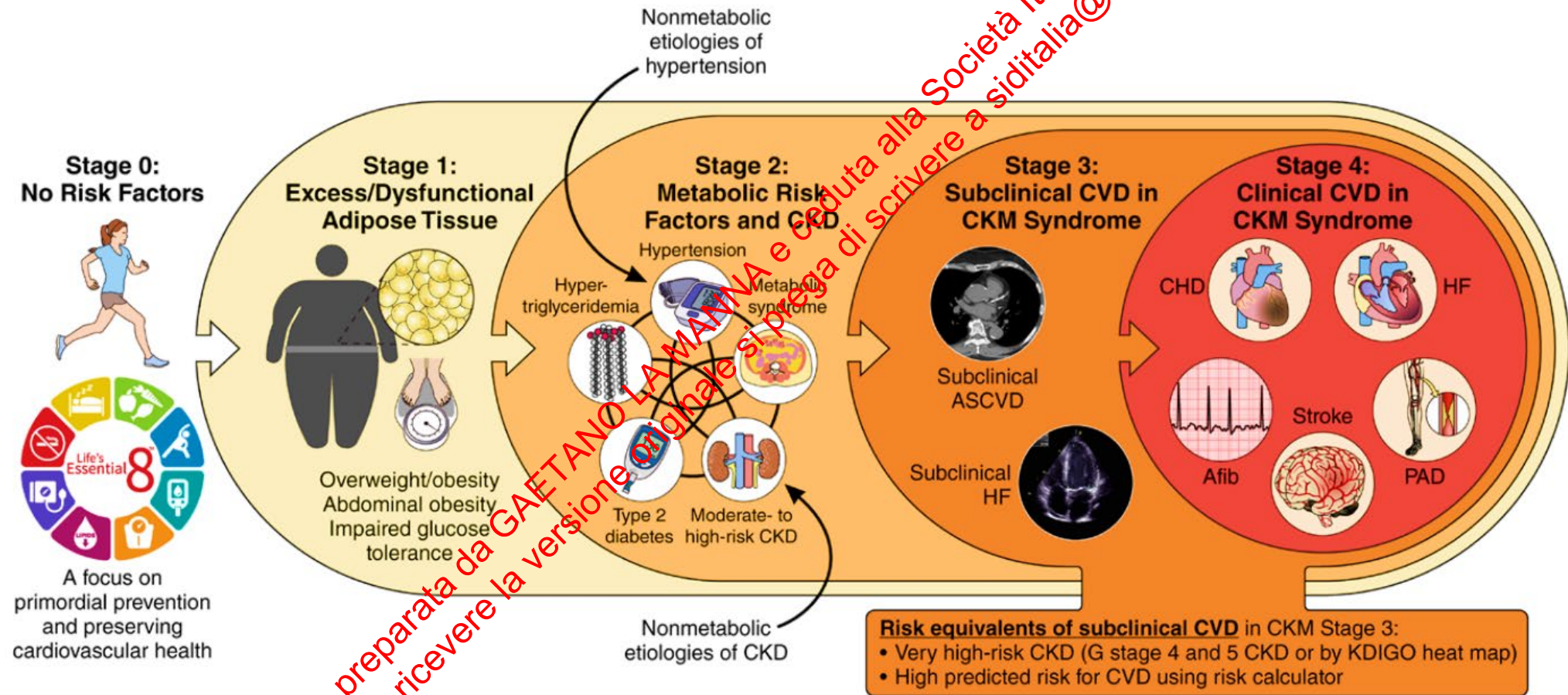
Diabetes Obes Metab. 2020 Sep;22(9)

England, Germany, Japan, the Netherlands, Norway and Sweden

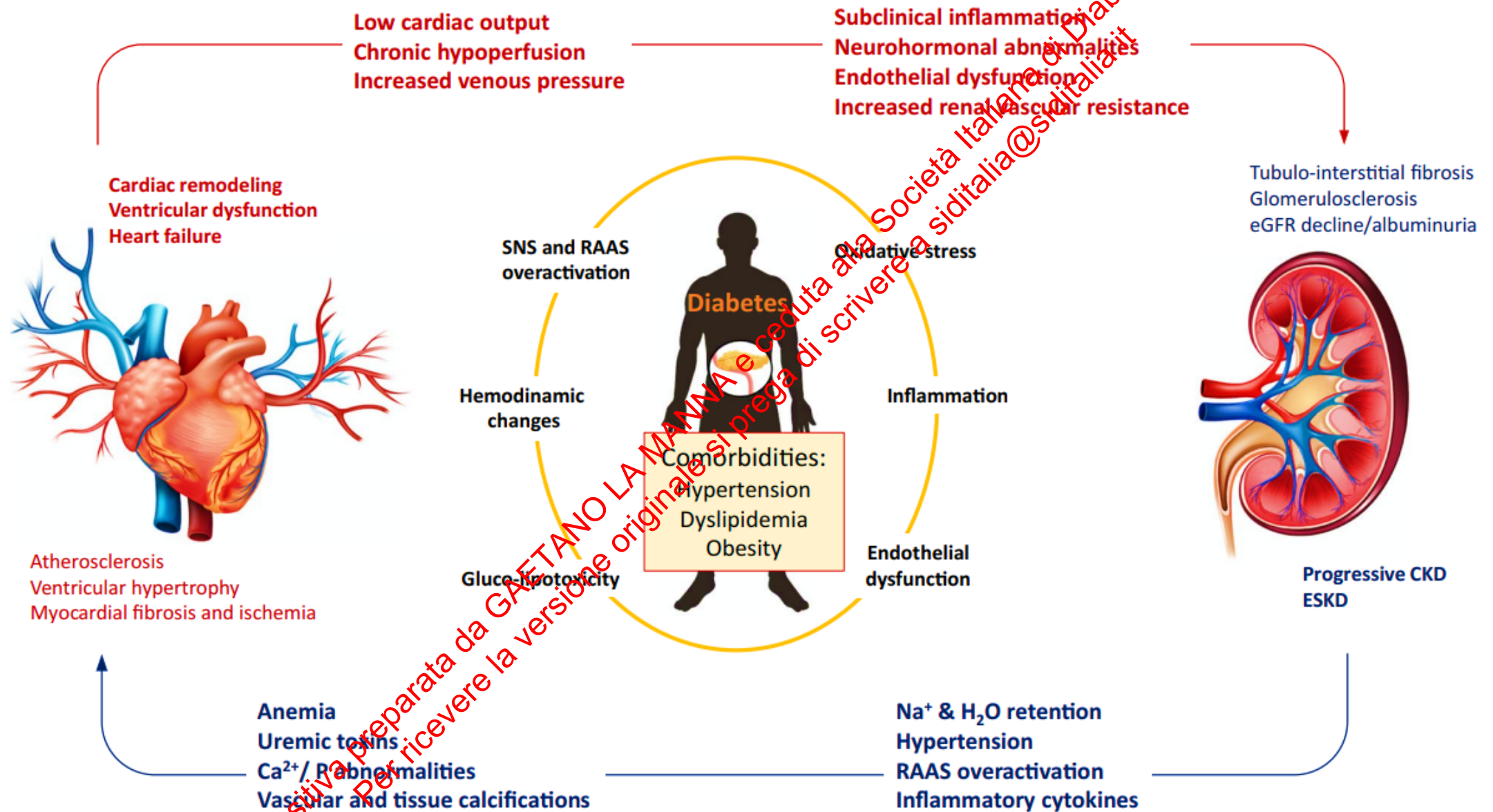
Development of first CVRD manifestation in patients with T2D (18%) in a large multinational cohort study (N=772,336). Follow-up: 4.5 years



STAGES OF CARDIOVASCULAR-KIDNEY-METABOLIC SYNDROME



CARDIOVASCULAR-KIDNEY-METABOLIC (CKM) SYNDROME

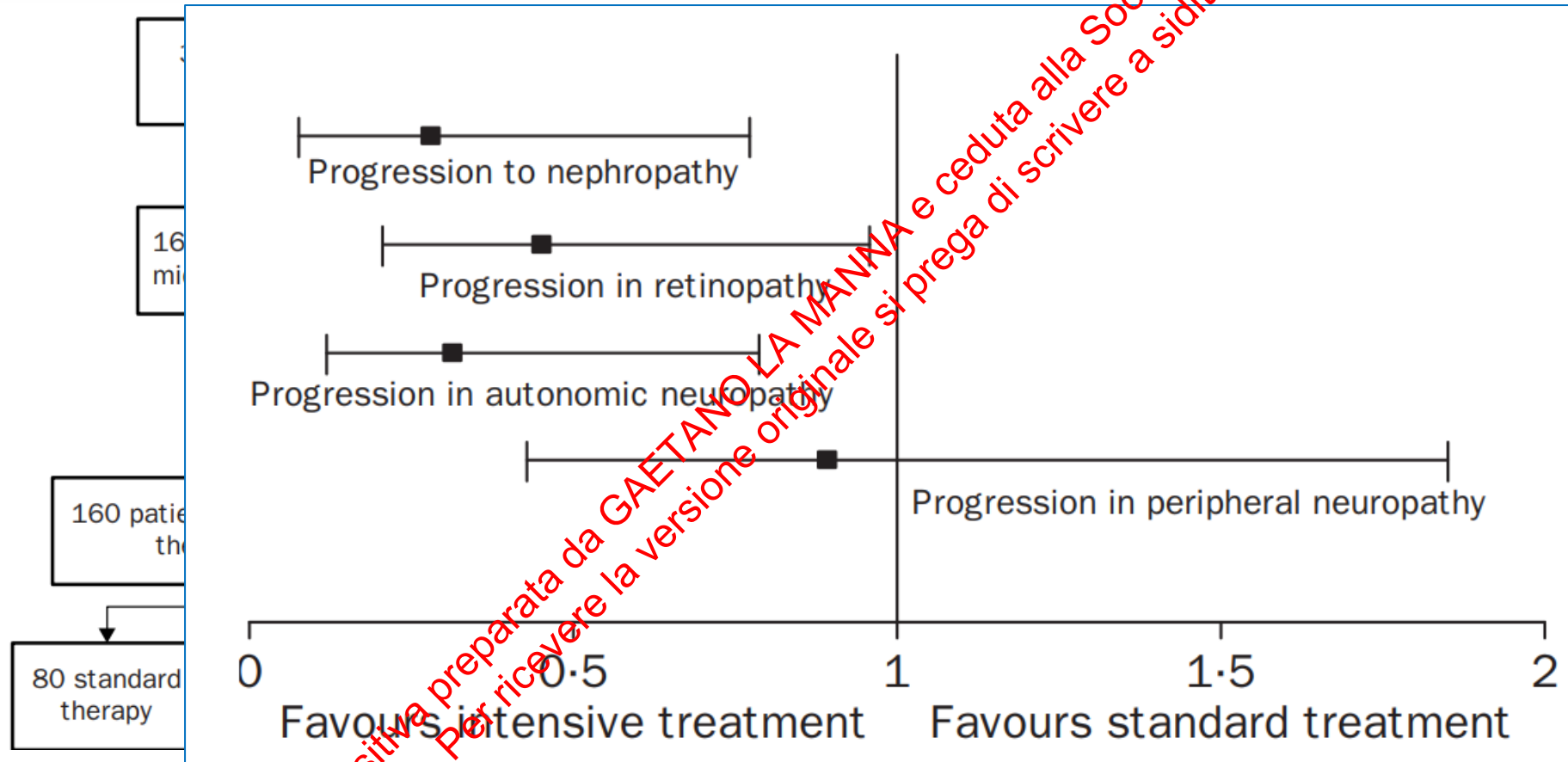


INTENSIVE TREATMENT IS THE KEY

Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study

Peter Gæde MD^o, Pernille Vedel PhD^o, Prof Hans-Henrik Parving DMSc^o, Prof Oluf Pedersen DMSc^o

THE LANCET
1999; **353**: 617–22



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hypertension,

Summary of benefits elucidated in diabetes CVOTs in the cardiovascular–metabolic axis

CV benefits



3P/4P-MACE

- Empagliflozin
- Liraglutide
- Semaglutide
- Canagliflozin
- Albiglutide*
- Dulaglutide
- Sotagliflozin*
- Efpeglenatide*

HHF
SGLT2 inhibitors and GLP-1 RAs



EASD, ADA, ACC and ESC guidelines recommend GLP-1 RAs & SGLT2i in T2D with CVD



EASD, ADA and ESC guidelines recommend SGLT2i to prevent HF risk in patients with T2D

Metabolic benefits



All GLDs improved HbA1c levels

Other metabolic benefits were also recorded in many CVOTs, such as **reductions in weight**



EASD guidelines recommend GLP-1 RAs & SGLT2i with a proven benefit for weight control in patients with T2D



EASD guidelines recommend GLP-1 RAs, SGLT2i, DPP-4i or TZDs to minimise hypoglycaemia risk

Renal benefits



Renal impairment

- All SGLT2 inhibitors, except sotagliflozin*
- Dulaglutide

Albuminuria

- All SGLT2 inhibitors, except sotagliflozin*
- All GLP-1 RAs



EASD, KDIGO and ERA-EDTA guidelines recommend SGLT2i in patients with T2D and CKD if eGFR adequate

Empagliflozin in Heart Failure

Diuretic and Cardiorenal Effects

Matthew Griffin, MD*

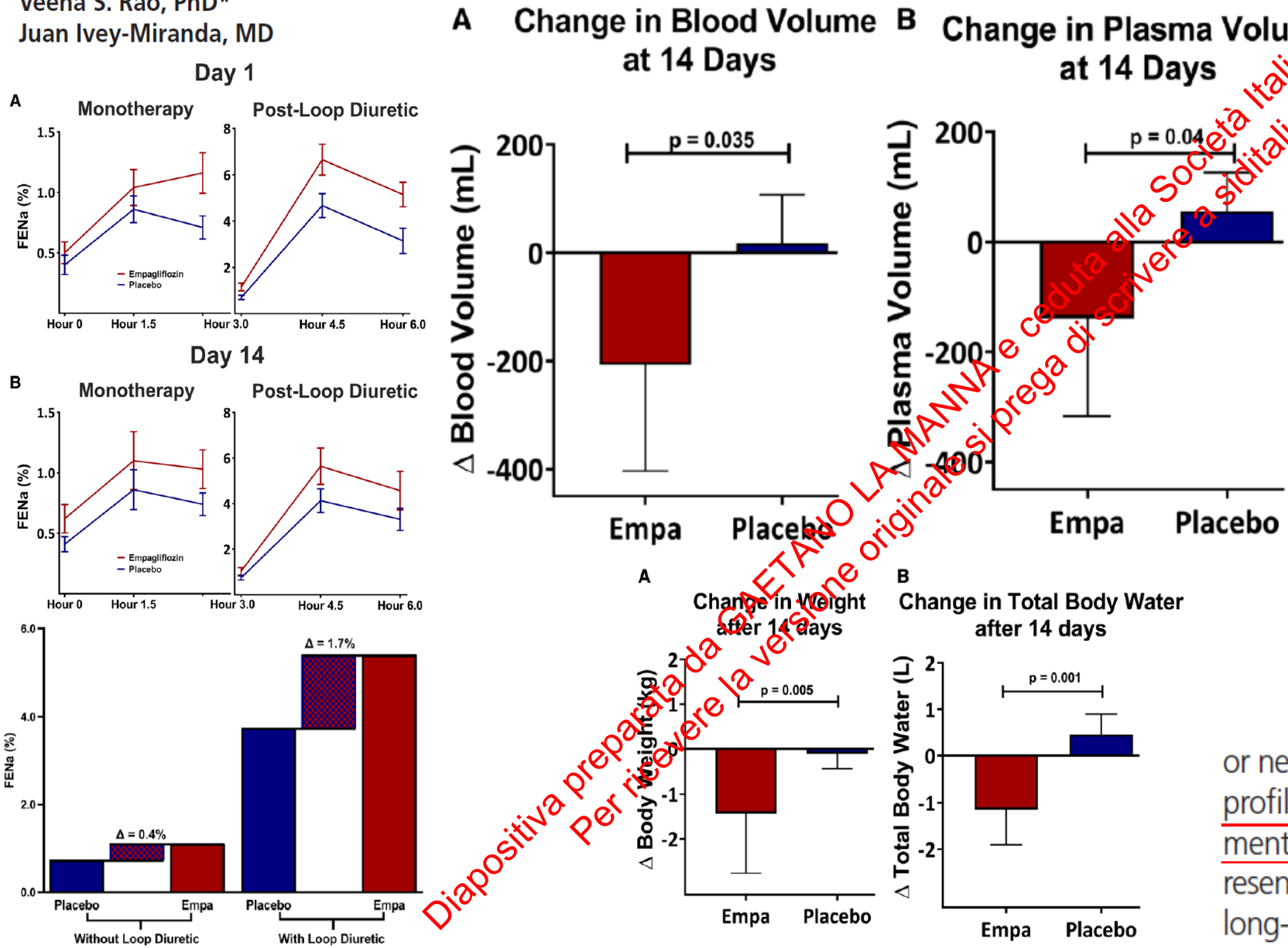
Veena S. Rao, PhD*

Juan Ivey-Miranda, MD

Circulation. 2020;142:1028–1039. DOI: 10.1161/CIRCULATIONAHA.120.045691

Study Design

The study was a randomized, double-blind, placebo-controlled crossover study consisting of treatment with either 10 mg of empagliflozin or matched placebo daily for 14 days followed by a 2-week washout period and crossover to 14 days of treatment



Characteristic	Cohort (n=20)
Age, y	60±12
Female sex, n (%)	5 (25)
Body mass index, kg/m ²	37±7
Race, n (%)	
Black	8 (40)
NYHA functional classification, n (%)	
3	6 (30)
4	0 (0)
Heart rate, bpm	74±12
Systolic blood pressure, mmHg	126±18
Left ventricular ejection fraction, %	42.9±15.0
HFrEF, n (%)*	9 (45)

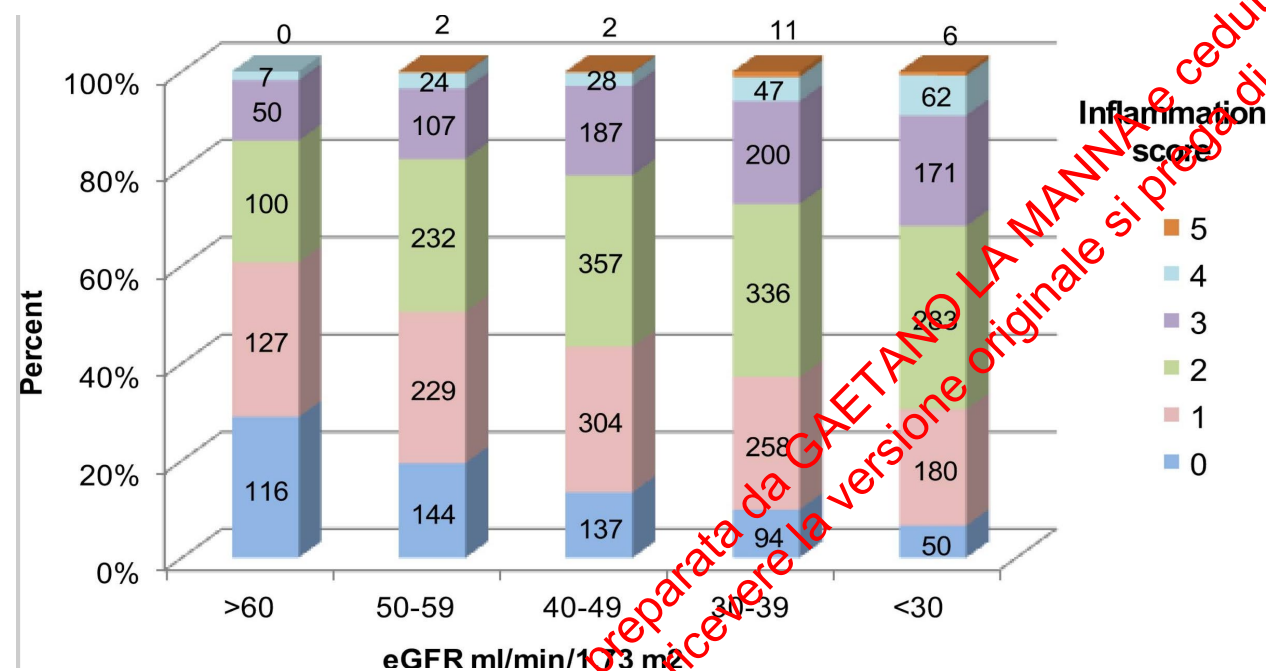
or neurohormonal activation. This seemingly ideal diuretic profile may offer significant advantages in the management of volume status in patients with HF and may represent an important mechanism underlying the superior long-term HF outcomes observed with these agents.

Relation between CKD and inflammation

Association between Albuminuria, Kidney Function, and Inflammatory Biomarker Profile in CKD in CRIC

Jayanta Gupta,* Nandita Mitra,* Peter A. Kanetsky,* Joe Devaney,† Maria R. Wing,† Muredach Reilly,* Vallabh O. Shah,‡ Vaidyanathapura S. Balakrishnan,§ Nicolas J. Guzman,† Matthias Girndt,|| Brian G. Periera,§ Harold I. Feldman,* John W. Kusek,|| Marshall M. Joffe,* Dominic S. Raj,✉† and for the CRIC Study Investigators

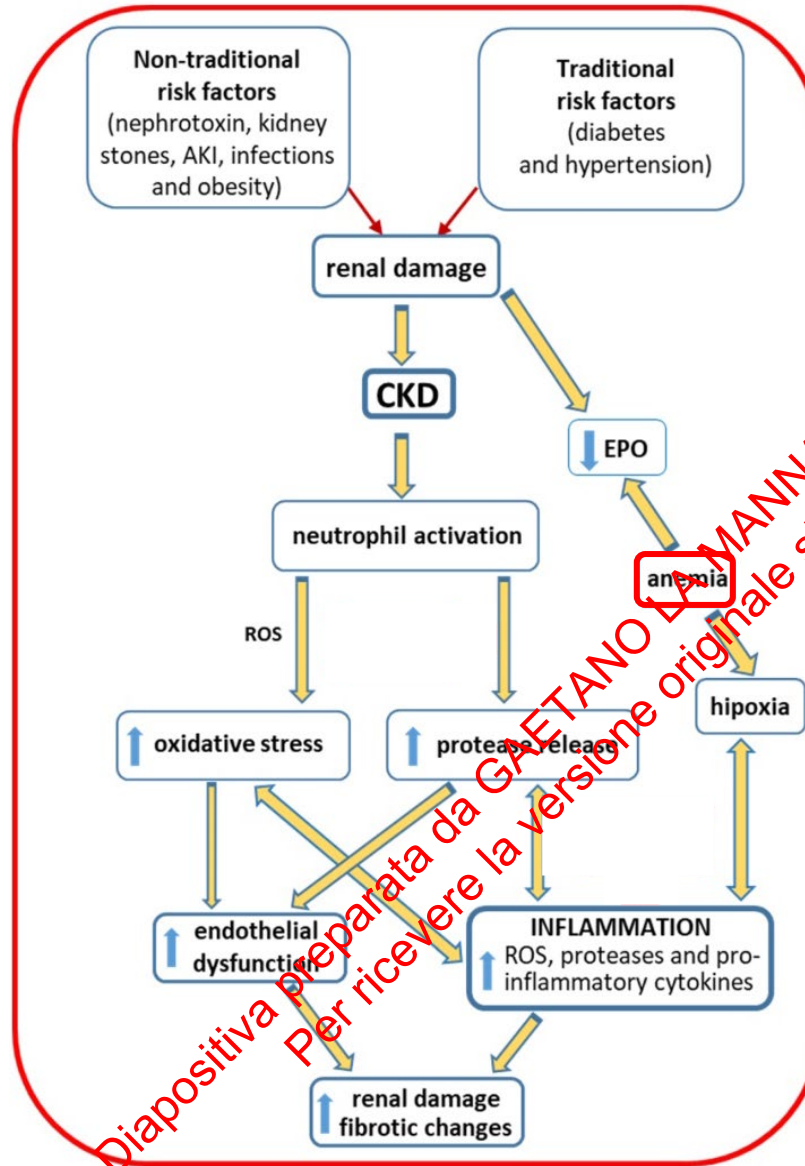
The CRIC study is a prospective observational cohort study of 3939 participants with established CKD. The organization, design, and methods of the CRIC study have been previously reported ([15](#)).



“An inverse association between the inflammation score and eGFR was seen ($P < 0.001$). Biomarkers of inflammation were inversely associated with measures of kidney function”

This study measured the plasma levels of IL-18, IL-1 receptor antagonist (IL-1RA), IL-6, TNF- α , TGF- β , high-sensitivity C-reactive protein (hs-CRP), fibrinogen, and serum albumin in 3939 participants enrolled in the Chronic Renal Insufficiency Cohort study between June 2003 and September 2008.

Risk factors effects in CKD



1. In CKD the release of ROS and proteases, leads to **oxidative stress and renal cell damage**, contributing to **endothelial dysfunction and to inflammation** that will be further enhanced by the release of pro-inflammatory cytokines.
2. These changes **favor worsening of renal damage and the development of fibrotic alterations**. Anemia, resulting from the reduced production of erythropoietin by the injured kidneys, leads to hypoxia, favoring inflammation.

The joint diabetic-renal clinic in clinical practice: 10 years of data from a District General Hospital

M.K. Jayapaul, R. Messersmith, D.N. Bennett-Jones, P.A. Mead, D.M. Large

Diabetic nephropathy: an observational study on patients attending a joint diabetes renal clinic.

B S Liew, C Perry, J M Boulton-Jones, K Simpson, K Paterson

A combined diabetes renal clinic improves risk factor management and progression of renal disease in a district general hospital

Manish Patel BSc(Hons) PhD, Ilona G. Barclay MD MRCP, Gerard A. McKay BSc(Hons) FRCPGlasg

Influence of Referral to a Combined Diabetology and Nephrology Clinic on Renal Functional Trends and Metabolic Parameters in Adults With Diabetic Kidney Disease

William P. Martin MB BCh, MSc, Tomás P. Griffin MB BCh, MSc, David W. Loppin MB BCh, PhD, Damian G. Griffin MB BCh, DM, John P. Ferguson PhD, Timothy O'Brien MD, PhD, Matthew D. Griffin MB BCh, DMed

A co-designed integrated kidney and diabetes model of care improves mortality, glycaemic control and self-care

Edward Zimbudzi, Clement L. Sanjeena, Anasinha, Arul Earnest, Helena Teede, Tim Usherwood, Kevan R. Polkinghorne, Gregory Fulcher, Martin Gallagher, Stephen Jan, Alan Cass, Rowan Walker, Grant Russell, Greg Johnson, Peter G. Kerr and Sophia Zoungas

High-risk diabetic nephropathy patients: The outcome of evidence-based clinical practice in an outpatient clinic

Helen Slade, Sheila M. Williams, Patrick J. Manning, Robert J. Walker

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A co-designed integrated kidney and diabetes model of care improves mortality, glycaemic control and self-care

Edward Zimbudzi^{1,2,*}, Clement Lo^{1,3,*}, Sanjeeva Ranasinha¹, Arul Earnest¹, Helena Teede^{1,3}, Tim Usherwood^{4,5}, Kevan R. Polkinghorne^{1,2,6}, Gregory Fulcher^{7,8}, Martin Gallagher^{4,9}, Stephen Jan^{4,10}, Alan Cass^{4,11}, Rowan Walker¹², Grant Russell¹³, Greg Johnson¹⁴, Peter G. Kerr^{2,6} and Sophia Zoungas^{1,3,4}



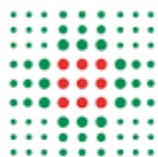
(2022) 37: 1472–1481

Background	Hospitalization indicators	Intervention (n = 196; person-years = 484)	Non-intervention (n = 7513; person-years = 13 252)	IRR (95% CI)	P-value	of care for abetes and tcomes
	Frequency of admissions/participant, n (%)					
	1	56 (28.6)	4222 (56.2)	–	–	
	2	40 (20.4)	1298 (17.3)	–	–	
	>3	100 (51.0)	1991 (26.5)	–	<0.00001	
	Rate of hospital admission/100 person-years (95% CI)					
	All-cause admissions	166.3 (155.0–178.2)	137.6 (135.6–139.6)	1.2 (1.13–1.30)	<0.0001	
	Major coronary events ^a	3.3 (1.89–5.37)	6.6 (6.13–7.01)	0.5 (0.29–0.82)	0.003	
	Heart failure	6.8 (4.69–9.58)	8.2 (7.75–8.74)	0.8 (0.57–1.17)	0.285	
	Ischaemic stroke	0.4 (0.05–1.49)	0.3 (0.23–0.44)	1.3 (0.15–4.89)	0.685	
	Hypertension	12 (0.45–2.70)	0.5 (0.43–0.68)	2.3 (0.81–5.21)	0.078	
	Diabetes events ^b					
	Short-term complications	4.5 (1.89–5.37)	3.0 (2.54–3.12)	1.2 (0.66–1.93)	0.522	
	Long-term complications	12.8 (9.82–16.42)	5.6 (5.17–5.98)	2.3 (1.75–2.99)	<0.0001	
	Rate of death/100 person-years (95% CI)	5.6 (3.7–8.1)	12.7 (12.1–13.4)	0.4 (0.29–0.64)	<0.0001	
	LOS, median (IQR)					
	LOS for all admissions	2 (6–1)	4 (9–1)	–	<0.0001	
	LOS for first admission only	5.5 (14.5–1)	7 (14–3)	–	0.004	

^aMajor coronary events included admissions due to cardiac death, non-fatal acute myocardial infarction and unstable angina requiring hospitalization. ^bThese are defined in [Supplementary data, Table S1](#); ambulatory sensitive conditions included hypertension, diabetes short-term complications, diabetes long-term complications and uncontrolled diabetes.

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n baseline)
2.26
0.83 to 3.69)
p <0.001
1.3
4.17 to 1.67)
p = 0.397
0.23%



**SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA**
Azienda Ospedaliero - Universitaria di Bologna
IRCCS Istituto di Ricovero e Cura a Carattere Scientifico



ALMA MATER STUDIORUM
UNIVERSITÀ BOLOGNA

**U.O. Nefrologia, Dialisi e
Trapianto**

**U.O. Endocrinologia e Cura e
Prevenzione del Diabete**

**Invio a PDTA o ambulatori congiunti già
esistenti:**

- Multidisciplinare Bariatria
- Congiunto Nefro-Osteometabolico
- Congiunto Nefro-Genetica Med
- Congiunto Diabete-Cardiologia

**Ambulatorio Congiunto
Nefro-Diabetologico**

Prestazioni richiedibili:

- esami biochimici
- Indagini strumentali (eco, TC)
- Ricovero ospedaliero
- Biopsia renale
- Visite specialistiche
- Visita dietologica

**U.O. Nefrologia, Dialisi e
Trapianto**

**U.O. Endocrinologia e Cura e
Prevenzione del Diabete**

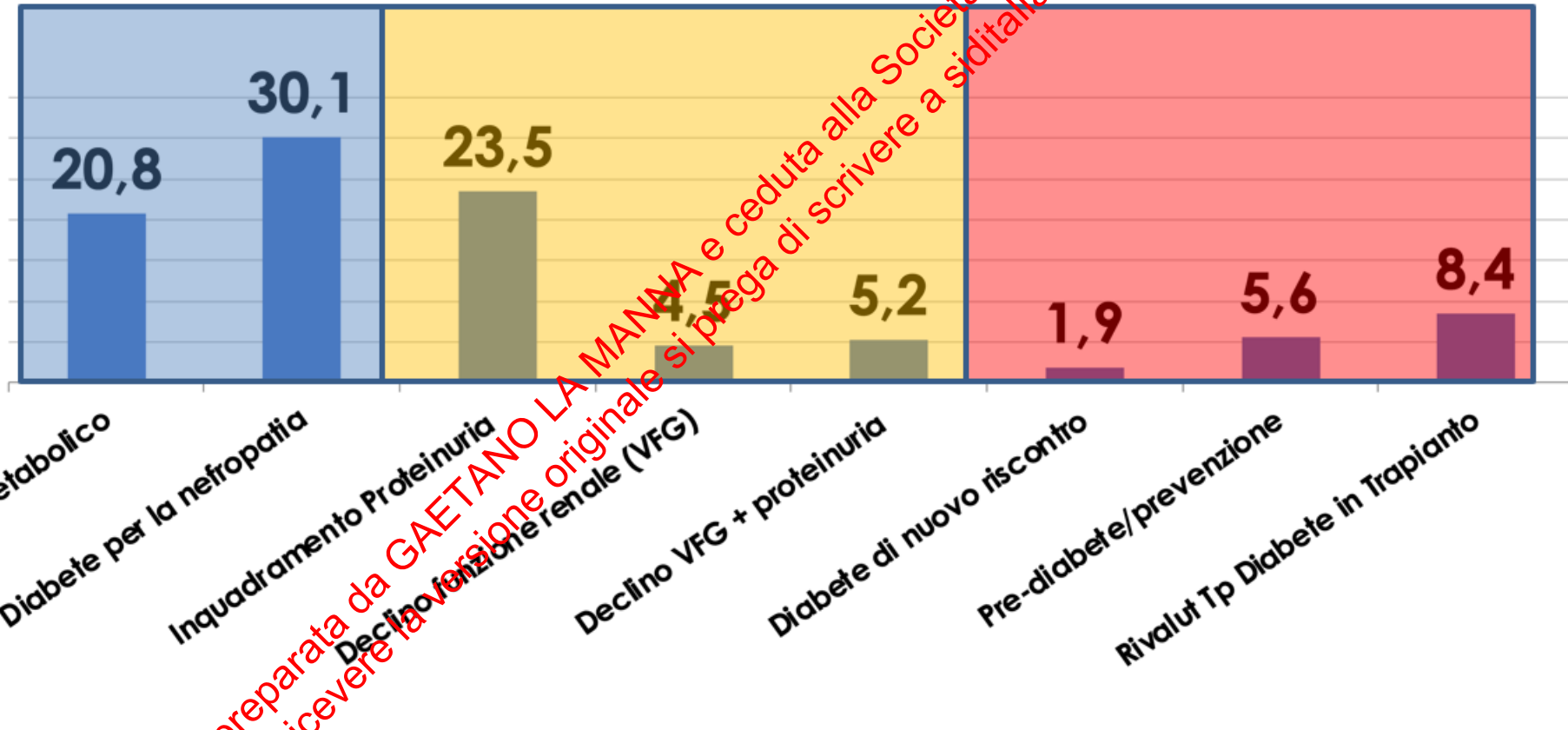
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PERIODO DI ATTIVITA'	INIZIO FEBBRAIO 2020 STOP MARZO-GIUGNO 2020 (EMERGENZA COVID) RIPRESA GIUGNO 2020	37 MESI DI ATTIVITA'
PRESTAZIONI ESEGUITE	7 VISITE SETTIMANALI	780 TOTALI 345 PRIME VISITE 435 CONTROLLI
AGENDA PRENOTAZIONE	Visita ambulatoriale congiunta «Nefro-Diabetologica» Prenotazione su Centro di Costo Unico per entrambe le UO	
PAZIENTI INVIATI	35.2 % da UO Endocr. Prev.Cura Diabete 66.8 % Nefrologia, dialisi e Trapianto	345

Nefrologia

Diabetologia

Trapianto Renale

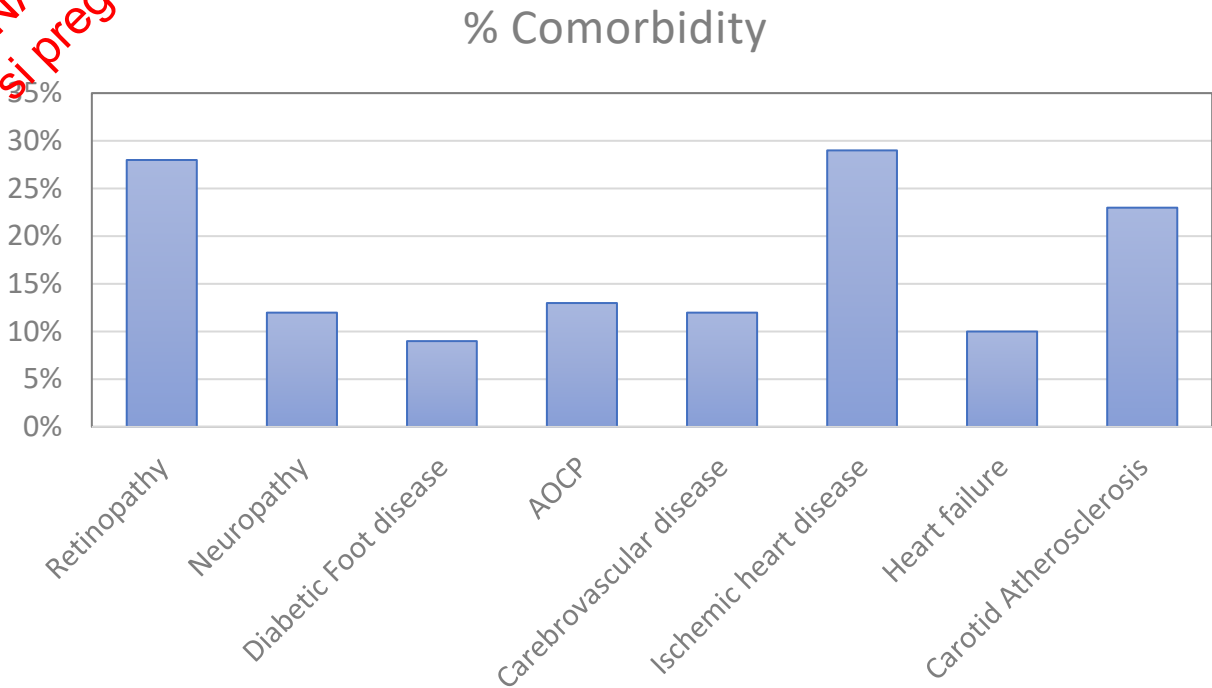
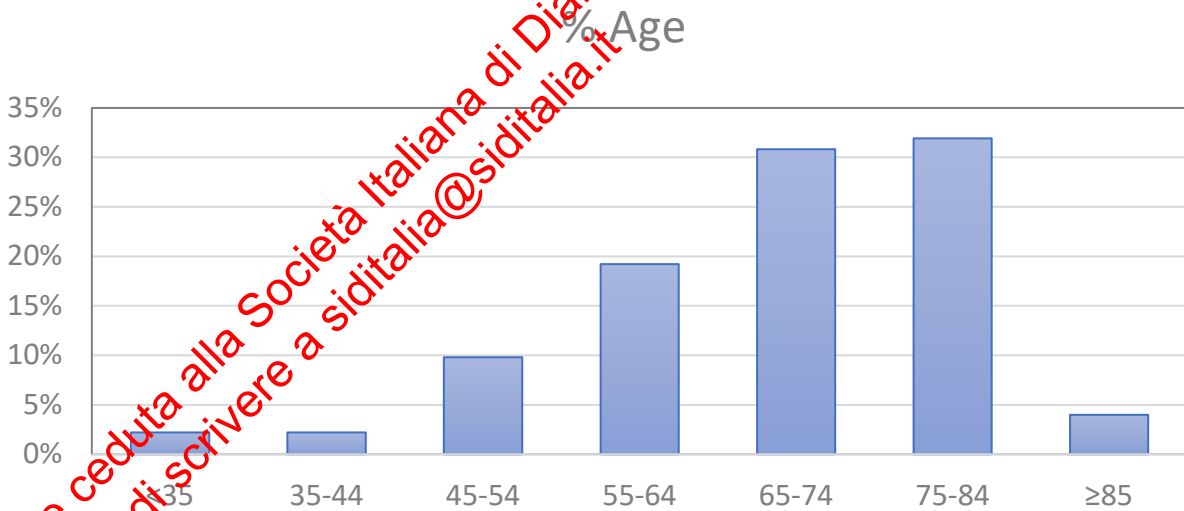


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CARATTERISTICHE BASELINE

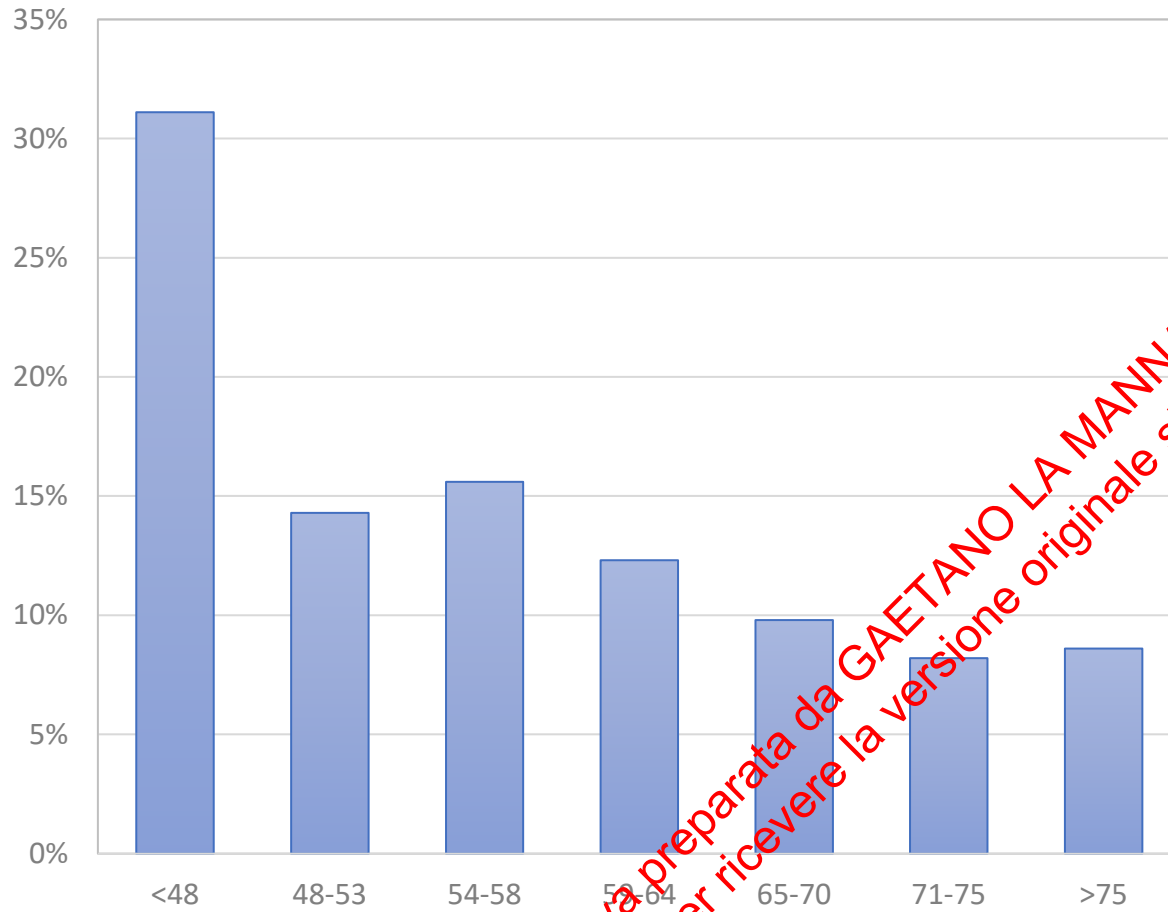
Variables	Mean SD or median [IQR] or frequency (%)
Age, years	68 ± 12
Male sex, %	75.8
Years of Diabetes, year	17 ± 10
BMI, kg/m2	84.3 ± 15.4
Waist circumference, cm	106 ± 11
Fasting blood glucose, mg/dl	148 ± 51
Hba1c (mmol/mol)	57 ± 13
Total Cholesterol, mg/dL	168 ± 45
LDL Cholesterol, mg/dL	97 ± 15
HDL Cholesterol, mg/dL	47 ± 15
Trygliceridies, mg/dL	169 ± 94

Ribichini et al, in press.

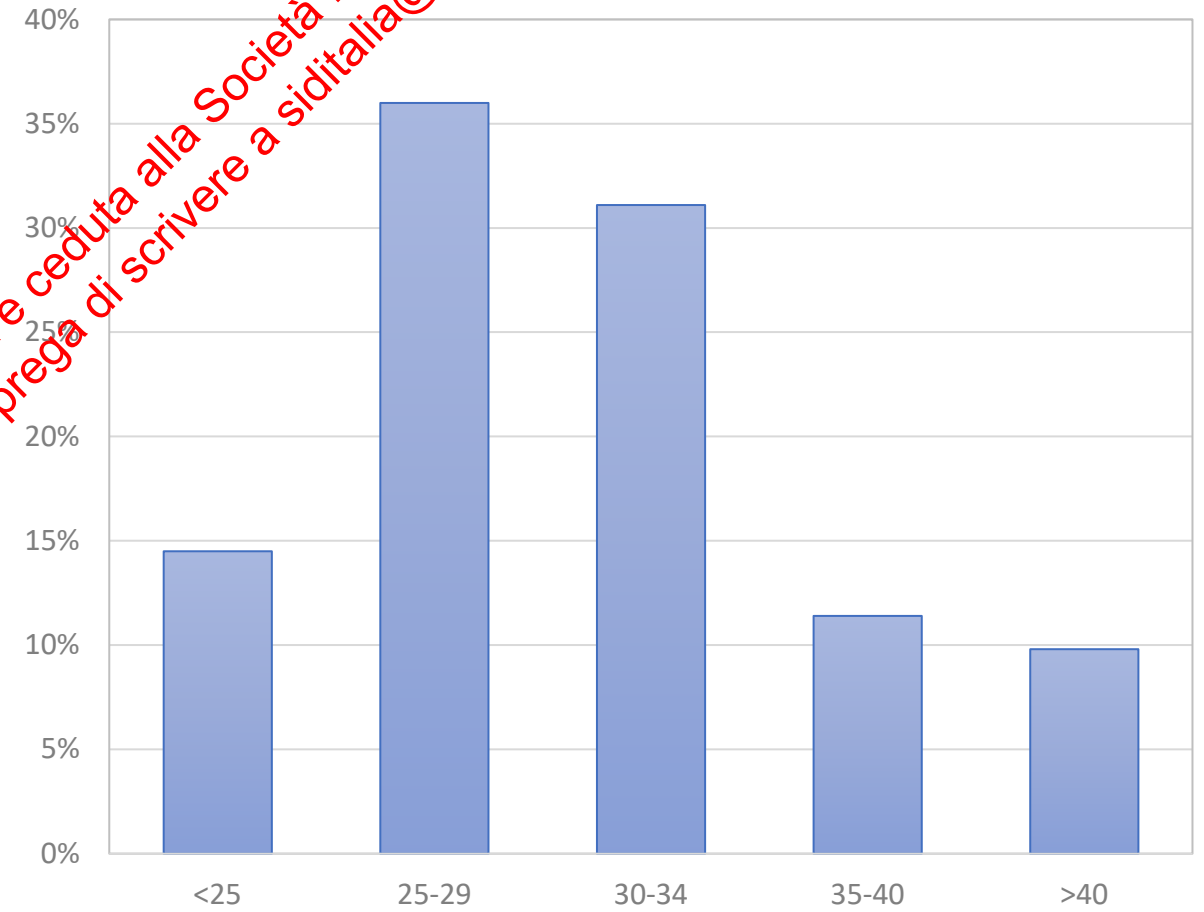


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Hba1c categories

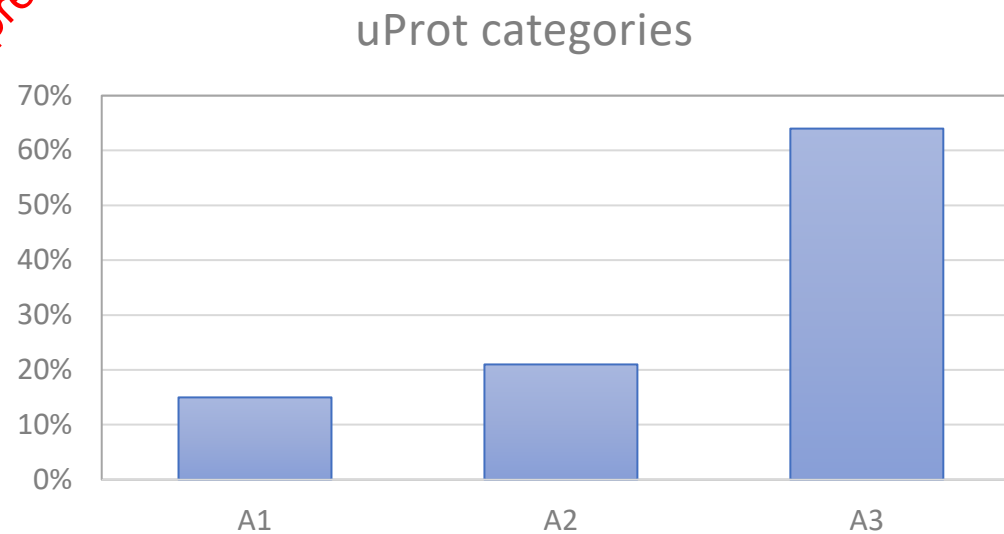
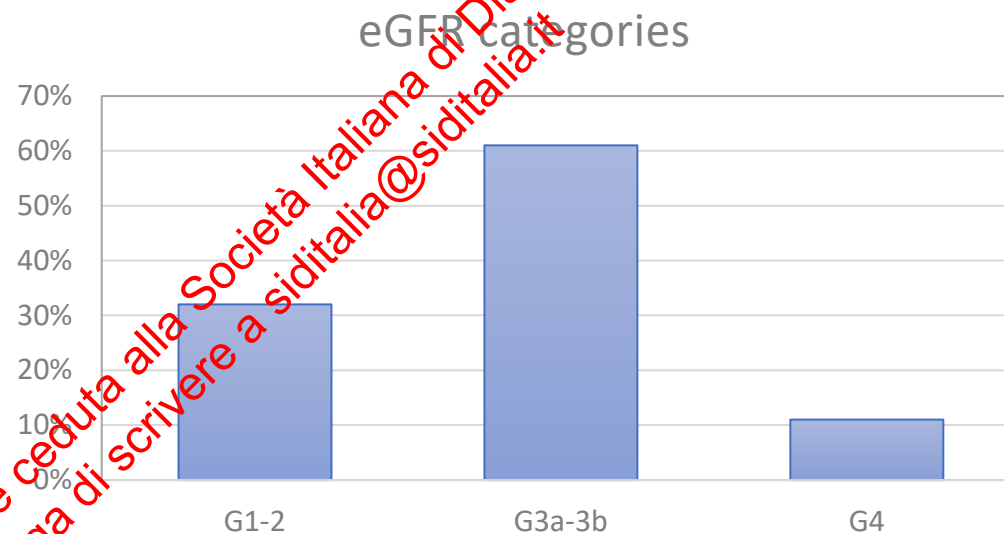


BMI categories

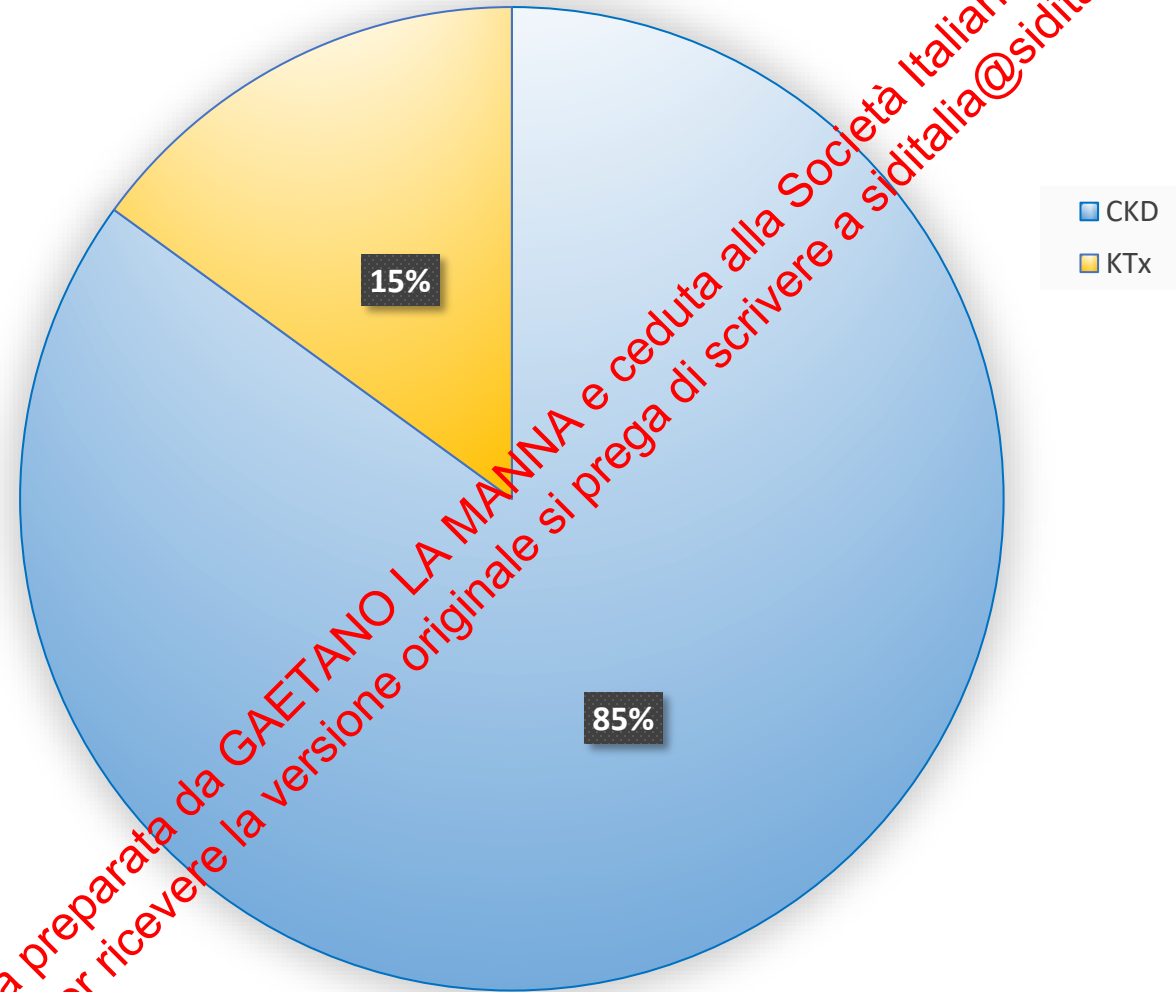


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Variables	Mean SD or median [IQR] or frequency (%)
sCreat, mg/dL	1.5 ± 0.8
eGFR, ml/min	51 ± 23
uProt, mg/24h	675 [224-1740]
Years of CKD, years	5 ± 5
PAS, mmHg	132 ± 21
PAD, mmHg	76 ± 11

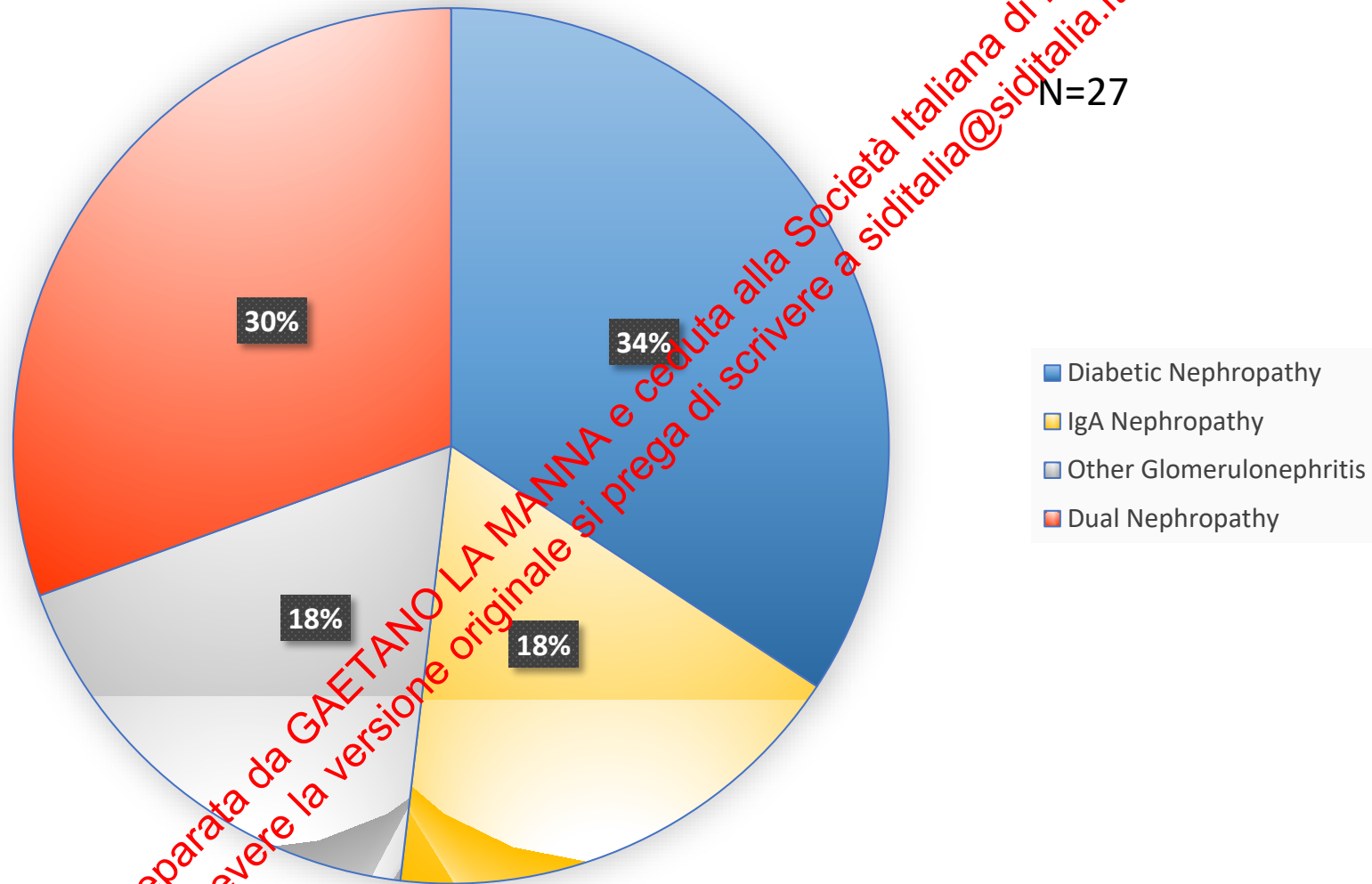


CKD/KTx



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KIDNEY BIOPSIES



Dual Nephropathy: Diabetic Nephropathy + other glomerular disease

The Modern Spectrum of Renal Biopsy Findings in Patients with Diabetes

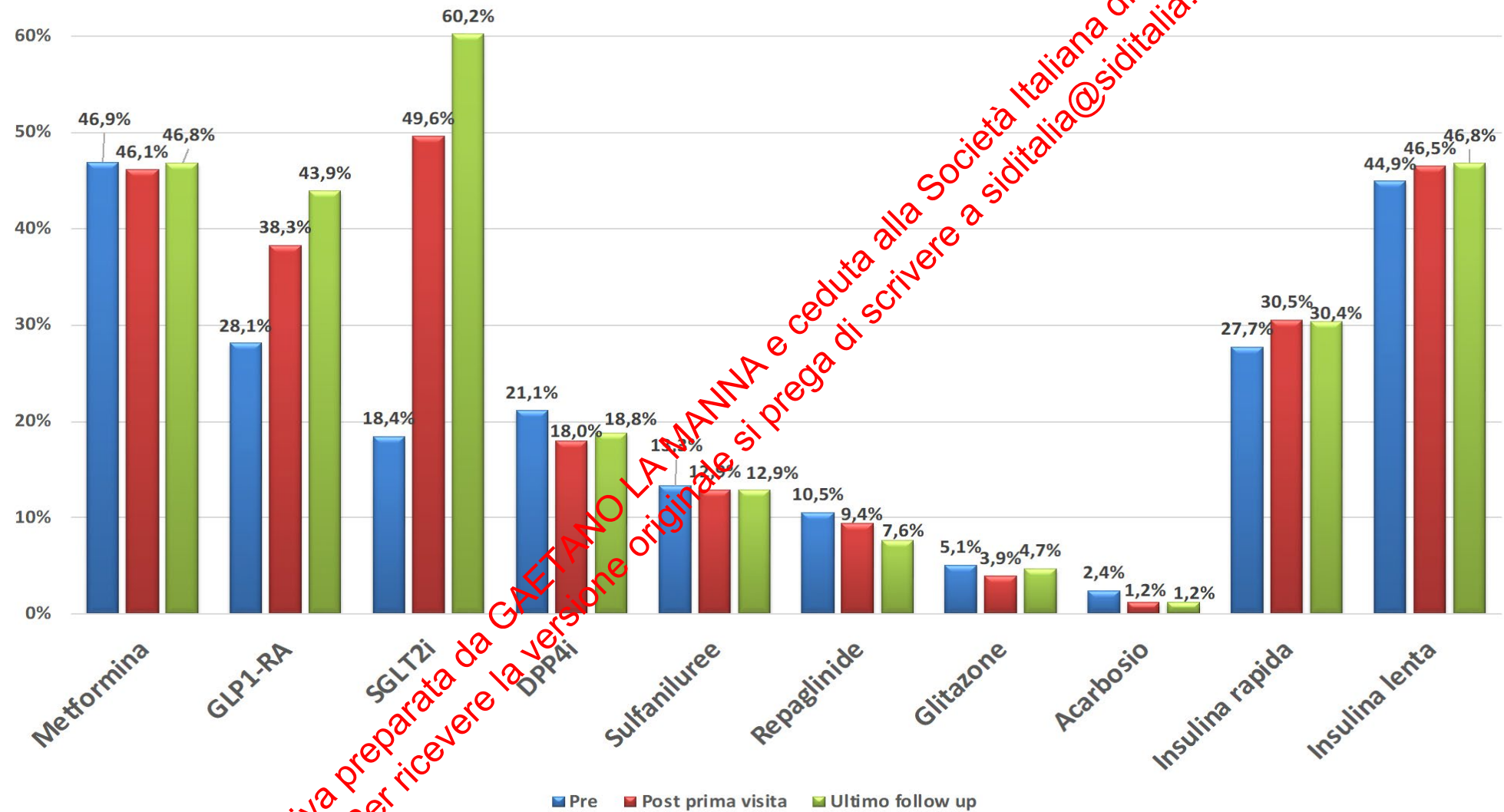
Shree G. Sharma,* Andrew S. Bomback,[†] Jai Radhakrishnan,[‡] Leal C. Herlitz,[‡] Michael B. Stokes,[‡] Glen S. Markowitz,[‡] and Vivette D. D'Agati[‡]

Types of NDRD (n)	NDRD Alone (n=220)	DN Plus NDRD (n=164)	P Value ^a
Acute tubular necrosis (109)	38 (17.3)	71 (43.3)	<0.001
FSGS (69)	48 (21.8)	21 (12.8)	0.02
Primary FSGS (6)	6 (2.7)	0 (0.0)	0.03
Secondary FSGS (63) ^b			
HTN related	19 (8.6)	20 (6.1)	0.35
HTN plus obesity related	16 (7.3)	10 (6.1)	0.65
Obesity related	4 (1.8)	1 (0.6)	0.30
Other ^c	3 (1.4)	0 (0.0)	0.13
Hypertensive nephrosclerosis (70) ^b	39 (17.7)	31 (18.9)	0.77
IgA nephropathy (35)	23 (10.5)	12 (7.3)	0.29
Membranous GN (23)	18 (8.2)	5 (3.0)	0.04
Pauci-immune crescentic GN (19)	15 (6.8)	4 (2.4)	0.05
Acute interstitial nephritis (18)	11 (5.0)	7 (4.3)	0.73
Amyloidosis (10)	7 (4.5)	0 (0)	0.01
Myeloma cast nephropathy (10)	8 (3.6)	2 (1.2)	0.14
Acute postinfectious GN (6)	3 (1.4)	3 (1.8)	0.72
Atheroembolic disease (5)	4 (0.9)	3 (1.8)	0.43
Others (10)	5 (2.3)	5 (3.0)	0.64

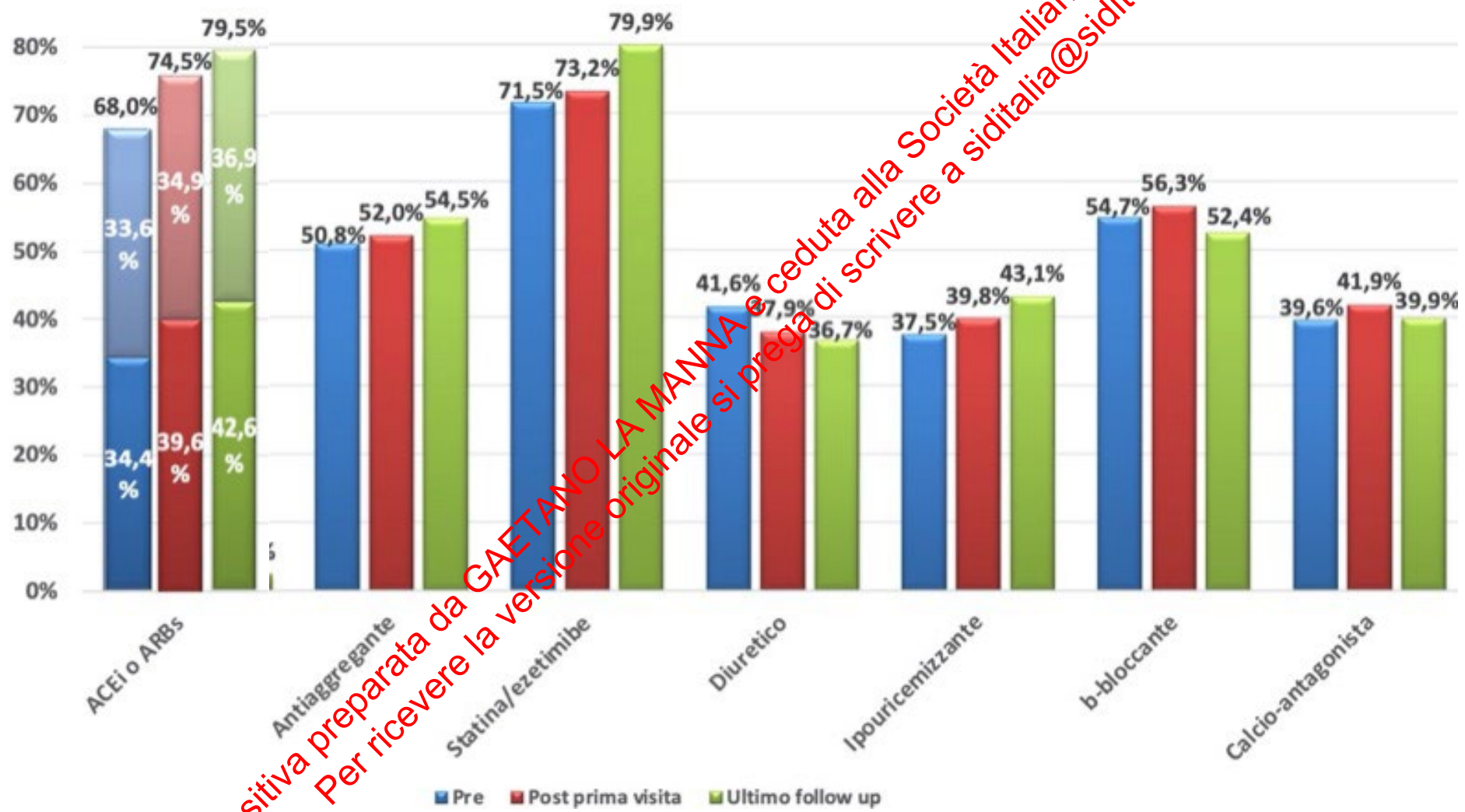
Among 620 patients with diabetes whose renal biopsy samples were analysed:

- 33% had diabetic nephropathy alone, 27% had diabetic nephropathy plus a superimposed nondiabetic renal disease, and 36% had nondiabetic renal disease alone.
- FSGS accounted for 22% of the cases of nondiabetic renal disease and 13% of the cases of diabetic nephropathy plus nondiabetic renal disease.

MODIFICHE TERAPEUTICHE - ANTIDIABETICI



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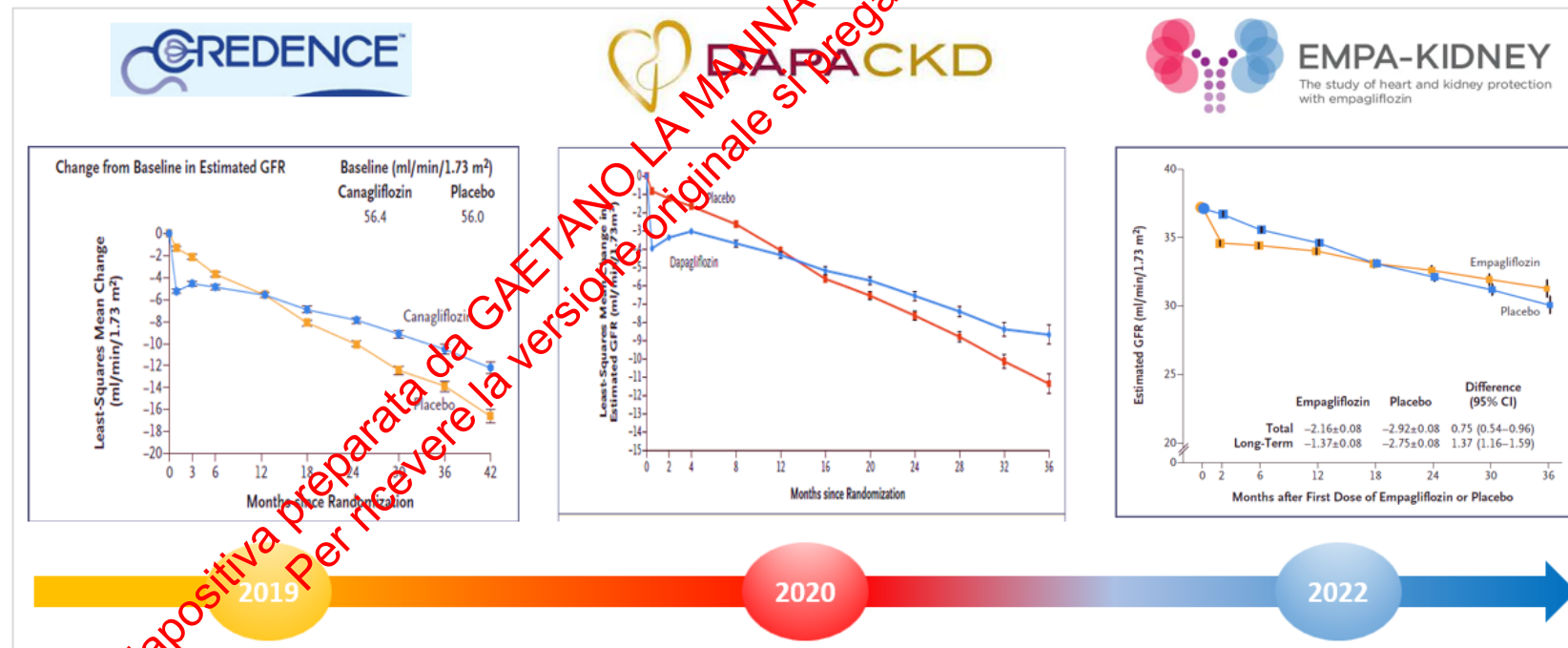
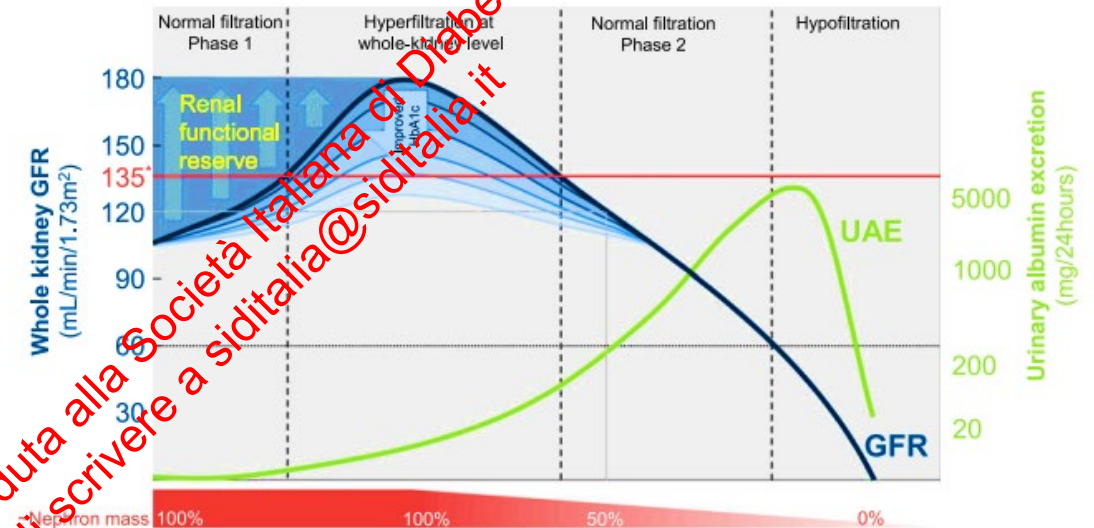
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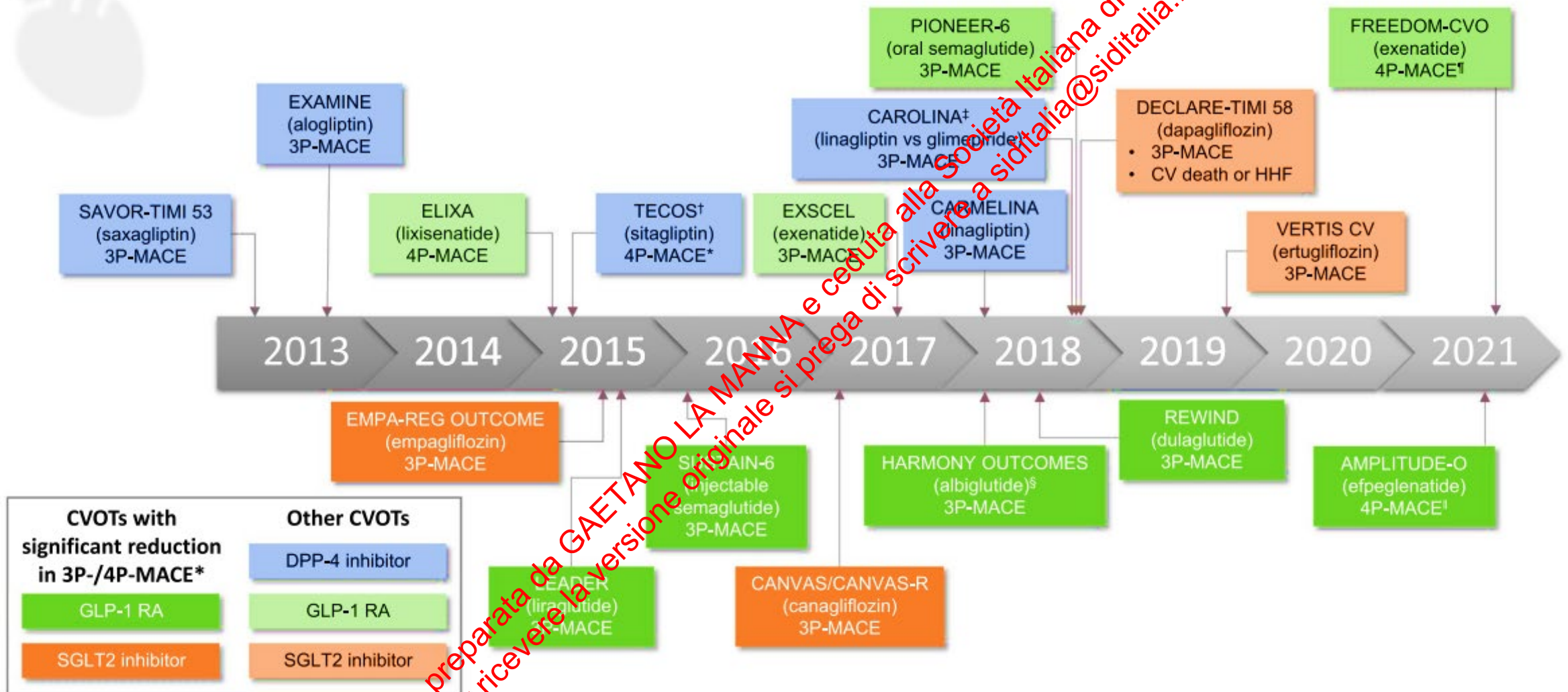
Variables	n. of patients	First visit	Last follow-up visit	p
		mean ± SD or median ± [IQR] or frequency (%)	mean ± SD or median ± [IQR] or frequency (%)	
Body weight (kg)	155	84,3 ± 15,4	82,4 ± 14,6	<0,001
BMI (Kg/m ²)	155	29,8 ± 5,1	29,1 ± 4,7	<0,001
Waist circumference (cm)	53	106 ± 11	104 ± 11	0,004
men	39	106 ± 12	103 ± 11	0,006
women	11	105 ± 11	104 ± 12	0,594
Systolic Blood Pressure (mmHg)	97	132 ± 21	132 ± 18	0,749
Diastolic Blood Pressure (mmHg)	97	76 ± 11	75 ± 9	0,195
Fasting blood glucose (mg/dL)	150	152 ± 52	143 ± 49	0,103
HbA1c (mmol/mol)	156	57 ± 13	56 ± 13	0,104
Total Cholesterol (mg/dL)	144	173 ± 49	163 ± 50	0,003
HDL-cholesterol (mg/dL)	139	47 ± 16	46 ± 11	0,413
LDL-cholesterol (mg/dL)	139	100 ± 38	92 ± 38	0,009
Trygliceridies (mg/dL)	143	178 ± 101	168 ± 100	0,168
Uric Acid (mg/dL)	84	6,4 ± 1,7	5,9 ± 1,4	0,021
Serum Creatinine (mg/dL)	169	1,5 ± 0,5	1,6 ± 0,7	0,029
eGFR (mg/ml/1.73 m ²) - Overall	169	51 ± 21	49 ± 22	0,008
eGFR stages G1-G2	40	85,1 ± 17,2	77,5 ± 20,4	<0,001
eGFR stages G3a-G3b	115	44,5 ± 7,1	42 ± 11,8	0,616
eGFR stages G4-G5	13	22,2 ± 5,4	23,3 ± 9	0,660
Albuminuria (mg/L)	86	143 [28-437]	114 [28-320]	0,024
Proteinuria (mg/24-h) - Overall	94	1930 [293-3084]	755 [335-2342]	0,014
first quartile (34-224 mg/24h)	18	107 [85-199]	155 [116-278]	0,019
second quartile (225-660 mg/24h)	24	365 [270-485]	488 [254-793]	0,012
third quartile (675-1680 mg/24h)	27	1120 [900-1400]	760 [460-1100]	0,105
fourth quartile (1800 - 22060 mg/24h)	15	4158 [3039-6143]	3150 [1620-5495]	<0,001
Total haemoglobin (mg/dL)	138	13,2 ± 1,9	13,4 ± 2,2	0,092
Natriemia (mmol/L)	118	140 ± 3	140 ± 4	0,919
Serum potassium (mmol/L)	118	4,7 ± 0,5	4,6 ± 0,5	0,039

Mean follow-up: 24 months

Factors associated with Delta eGFR

Predictors	Multivariate		
	Beta	95% CI	p-Value
eGFR at baseline	-0,168	-0,254, -0,081	<0,001
Proteinuria 24-h at baseline	-0,001	-0,001, 0.000	0,015





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KIDNEY SPECIFIC TRIALS – SGLT2i

CREDENCE

Double-blind, Placebo-controlled,
Multicenter RCT (N = 4.401)

Inclusion criteria

T2 DM
eGFR 30-90 ml/min and UACR 300-5000 mg/g

Canagliflozin vs Placebo

2019

Median follow-up 2.6 y

Outcome: ESKD, doubling of sCr or death
from renal causes

HR 0.66 (CI 0.53 to 0.81)

N Engl J Med 2019; 380:2295-306

DAPA-CKD

Double-blind, Placebo-controlled,
Multicenter RCT (N = 4.304)

Inclusion criteria

With and without T2 DM
eGFR 25-75 ml/min and UACR 200-5000 mg/g

Dapagliflozin vs Placebo

2020

Median follow-up 2.4 y

Outcome: ESKD, sustained 50% eGFR decline
or death from renal causes

HR 0.56 (CI 0.45 to 0.88)

N Engl J Med 2020; 383:1436-1446

EMPA-KIDNEY

Double-blind, Placebo-controlled,
Multicenter parallel group RCT (N = 6.609)

Inclusion criteria

With and without T2 DM
eGFR 20-45 ml/min or
eGFR 45-90 ml/min and UACR 200-5000 mg/g

Empagliflozin vs Placebo

2022

Median follow-up 2.0 y

Outcome: Progression of kidney disease or
death from CV causes

HR 0.72 (CI 0.64 to 0.82)

N Engl J Med 2023; 388:117-127

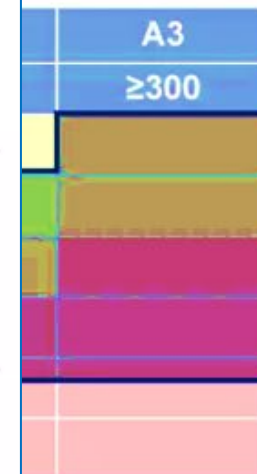
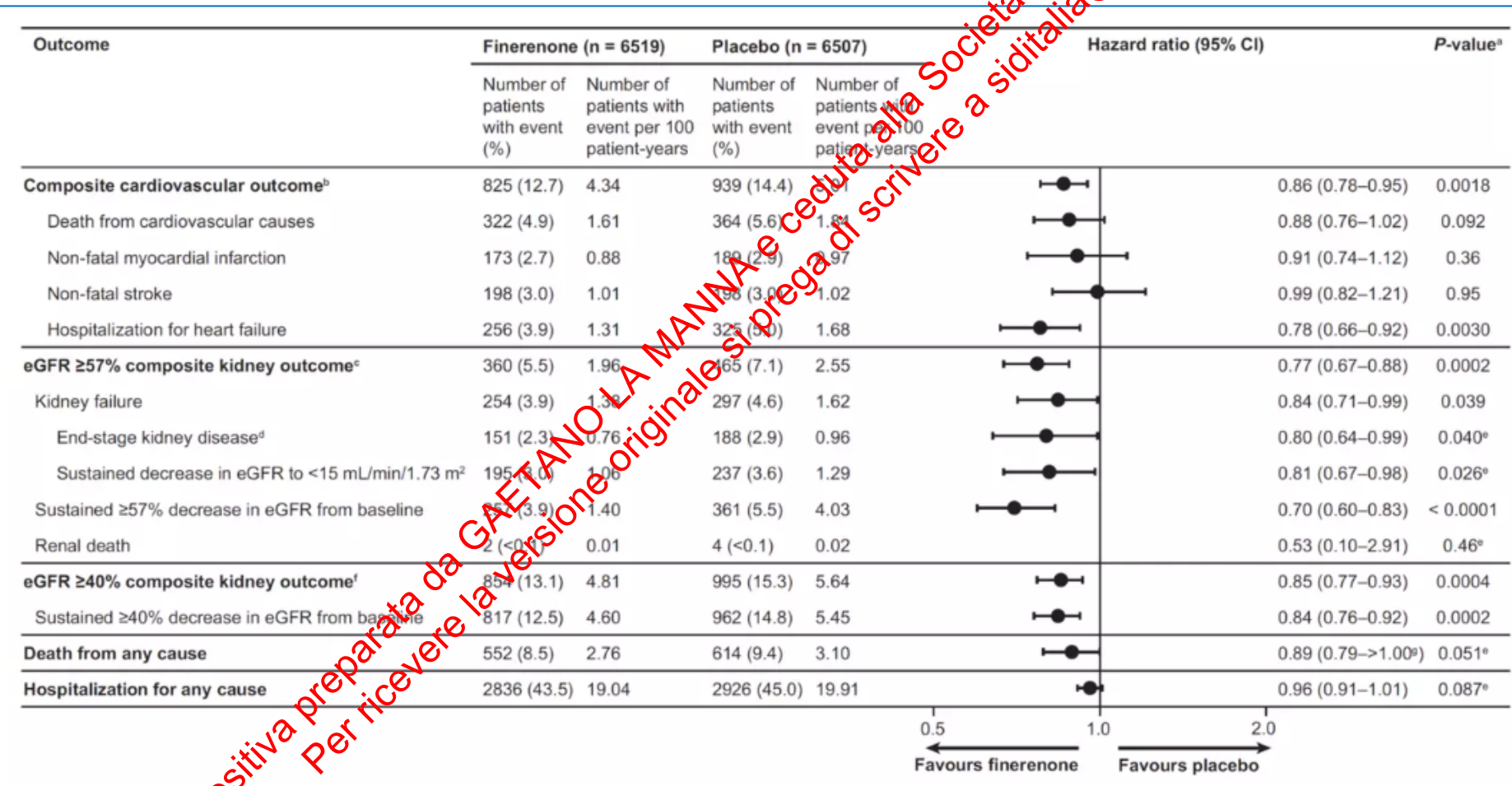
Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis

Rajiv Agarwal^{1*}, Gerasimos Filippatos^{2*}, Bertram Pitt³, Stefan D. Anker⁴, Peter Rossing^{5,6}, Amer Joseph⁷, Peter Kolkhof⁸, Christina Nowack⁹, Martin Gebel¹⁰, Luis M. Ruilope^{11,12,13}, and George L. Bakris¹⁴; on behalf of the FIDELIO-DKD and FIGARO-DKD investigators[†]

Albuminuria category
(mg albumin/g creatinine)

GFR categories
(mL/min/1.73 m²)

G1
G2
G3a
G3b
G4
G5



^a e: fatal MI, non-fatal MI, non-fatal stroke, hospitalization for HF
^b come: failure, ^a sustained decrease in eGFR from baseline,

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3160 patients

- T2D, $HbA_{1c} \leq 10\%$
- $eGFR \leq 75$ to $\geq 50^*$ and $UACR > 300$ to < 5000 mg/g OR $eGFR < 50$ to $\geq 25^*$ and $UACR > 100$ to < 5000 mg/g
- RAAS blocker

Semaglutide s.c. 1 mg O/W

Placebo +

Novo Ends Semaglutide Kidney Study Early Due to Strong Efficacy Signals

Published: Oct 11, 2023

- $eGFR < 15$ mL/min/1.73 m²
- renal replacement therapy (dialysis or kidney transplant)
- CV death
- All-cause death

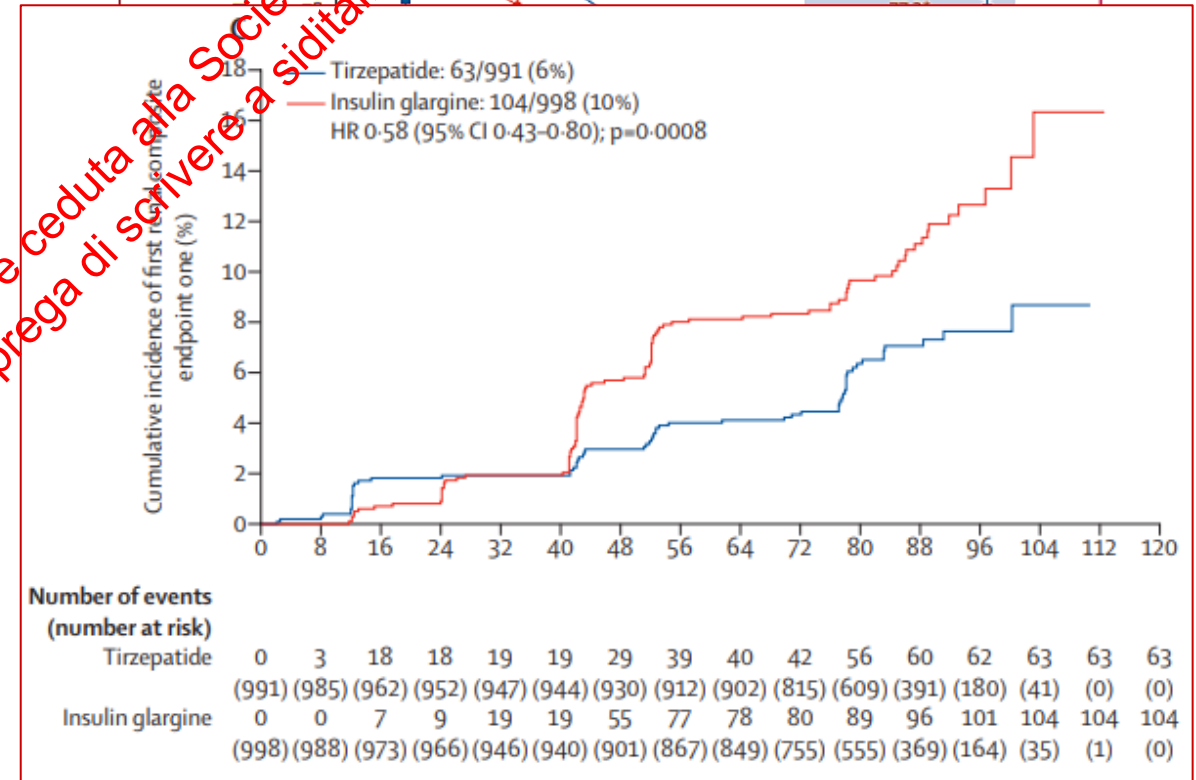
5 weeks

Follow up

Effects of tirzepatide versus insulin glargine on kidney outcomes in type 2 diabetes in the SURPASS-4 trial: post-hoc analysis of an open-label, randomised, phase 3 trial

Hiddo J L Heerspink, Naveed Sattar, Imre Pavo, Axel Haupt, Kevin L Duffin, Zhengyu Yang, Russell J Wiese, Katherine R Tuttle, David Z I Cherney

- Post-Hoc analysis of the SURPASS-4 trial (2002 patients were randomly assigned to tirzepatide and to insulin glargine)
- The **kidney composite outcome** was time to first occurrence of eGFR decline of at least 40% from baseline, end-stage kidney disease, death owing to kidney failure, or new-onset macroalbuminuria
- Overall, during the 104 weeks follow-up, the **mean eGFR slope** was -1.4 mL/min per year in the Tirzepatide group and -3.6 mL/min per year in the insulin group (between-group difference 2.2 mL/min)
- Tirzepatide stabilised UACR over time compared with insulin glargine, resulting in a gradual increase over time in the UACR difference between the two treatment groups.



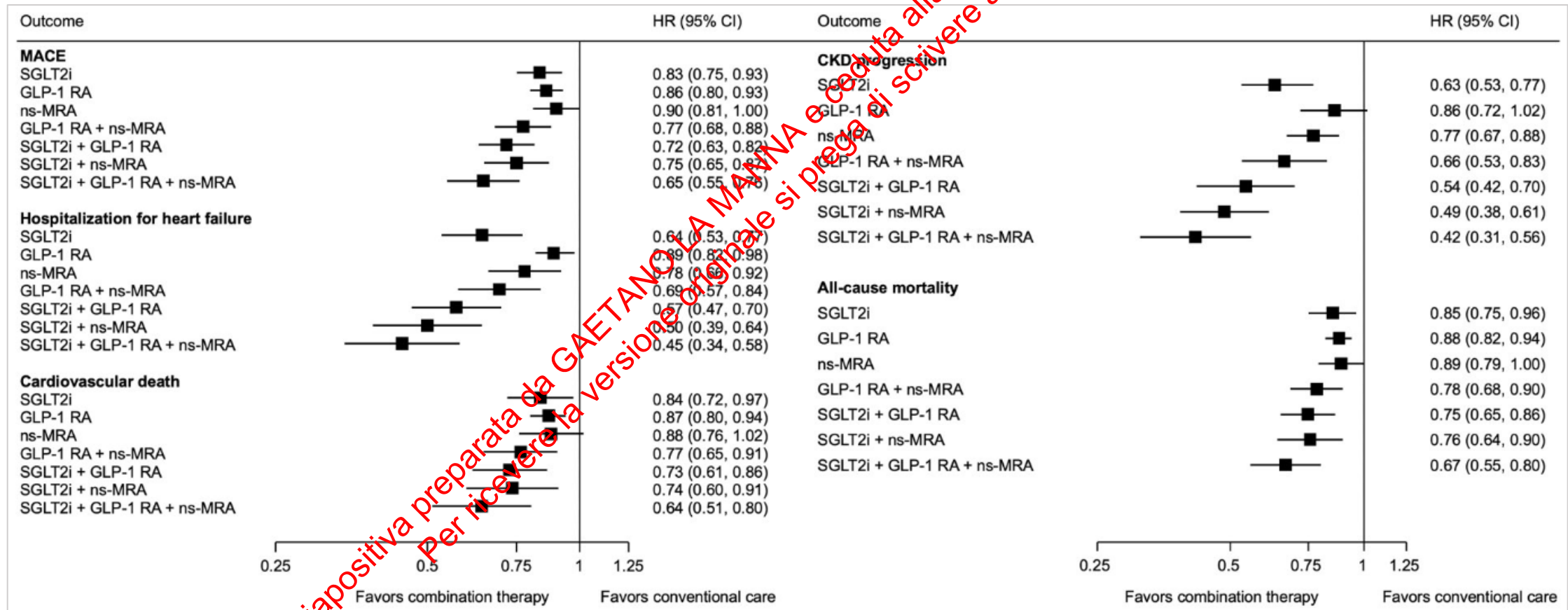
Number of events (number at risk)	0	3	18	18	19	19	29	39	40	42	56	60	62	63	63	63
Tirzepatide	(991)	(985)	(962)	(952)	(947)	(944)	(930)	(912)	(902)	(815)	(609)	(391)	(180)	(41)	(0)	(0)
Insulin glargine	(998)	(988)	(973)	(966)	(946)	(940)	(901)	(867)	(849)	(755)	(555)	(369)	(164)	(35)	(1)	(0)

	0	42	52	78	88	104	Baseline	Last measurement on treatment	Safety follow-up
Number at risk									
Tirzepatide	870	838	833	567	279	102	816	816	816
Insulin glargine	897	847	859	577	279	90	809	809	809

Estimated Lifetime Cardiovascular, Kidney and Mortality Benefits of Combination Treatment With SGLT2 Inhibitors, GLP-1 Receptor Agonists, and Non-steroidal MRA Compared With Conventional Care in Patients With Type 2 Diabetes and Albuminuria

Brendon L. Neuen , Hiddo J.L. Heerspink, Priya Vart, Brian L. Claggett, Robert A. Fletcher, Clare Arnott, Juliana de Oliveira Costa, Michael O. Falster, Sallie-Anne Pearson, Kenneth W. Mahaffey, Bruce Neal, Rajiv Agarwal, George Bakris, Vlado Perkovic, Scott D. Solomon and Muthiah Vaduganathan

Data from 2 SGLT2i trials (CANVAS and CREDENCE), 2 non-steroidal MRA trials (FIDALIO-DKD and FIGARO-DKD) and 8 GLP-1 RA trials to estimate the relative effects of combination therapy versus conventional care on cardiovascular, kidney and mortality outcomes



M. F., ♂, 73 y

Anamnesi remota:

- Ipertensione arteriosa
- Ex abitudine tabagica
- Dislipidemia
- Diabete Mellito di tipo II dal 2010
- Obesità I grado
- BPCO
- HFpEF (STEMI nel 1998 trattato con trombolisi)
- Malattia renale cronica dal 2012

10/2020 Biopsia Renale: Nefropatia Diabetica

Conclusioni diagnostiche

L'analisi ha documentato un quadro di glomerulonefrite mesangiale da inquadrare nel contesto della sindrome metabolica-malattia diabetica. L'esame ultrastrutturale dimostra la presenza di membrane basali di spessore aumentato (412 nm) con espansione del mesangio e assenza di depositi elettrondensi.

4 classes proposed by the Renal Pathology Society in 2010:

- Class I - GBM thickening,
- **Class II - Mesangial expansion,**
- Class III - Nodular sclerosis,
- Class IV - Advanced diabetic glomerulosclerosis.

02/2021 - I visita Nefro-Diabetologia:

Esami:

sCreat 1.42 mg/dL, eGFR 49 ml/min, uProt 3486 mg/die

Hba1c 65 mg/dL, Col.tot 215 mg/dL, LDL 134 mg/dL, HDL 55 mg/dL, Trigliceridi 306 mg/Dl

Terapia:

Irbesartan 300 mg,

Exenatide 5 mcg x 2,

Bisoprololo 1,25 mg x 2,

Simvastatina/Ezetimibe 20/10 mg,

Cardioasa 100 mg,

Allopurinolo 300 mg ½ cp

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CASO CLINICO

+ Dapagliflozin 10 mg

+ Canrenone 50 mg

Simva/Eze
20/10 mg

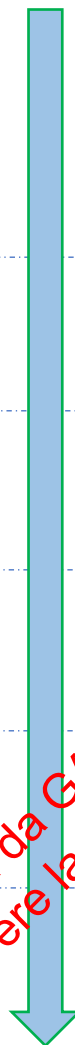


Atorva/Eze
40/10 mg

Exenatide
10 mcg

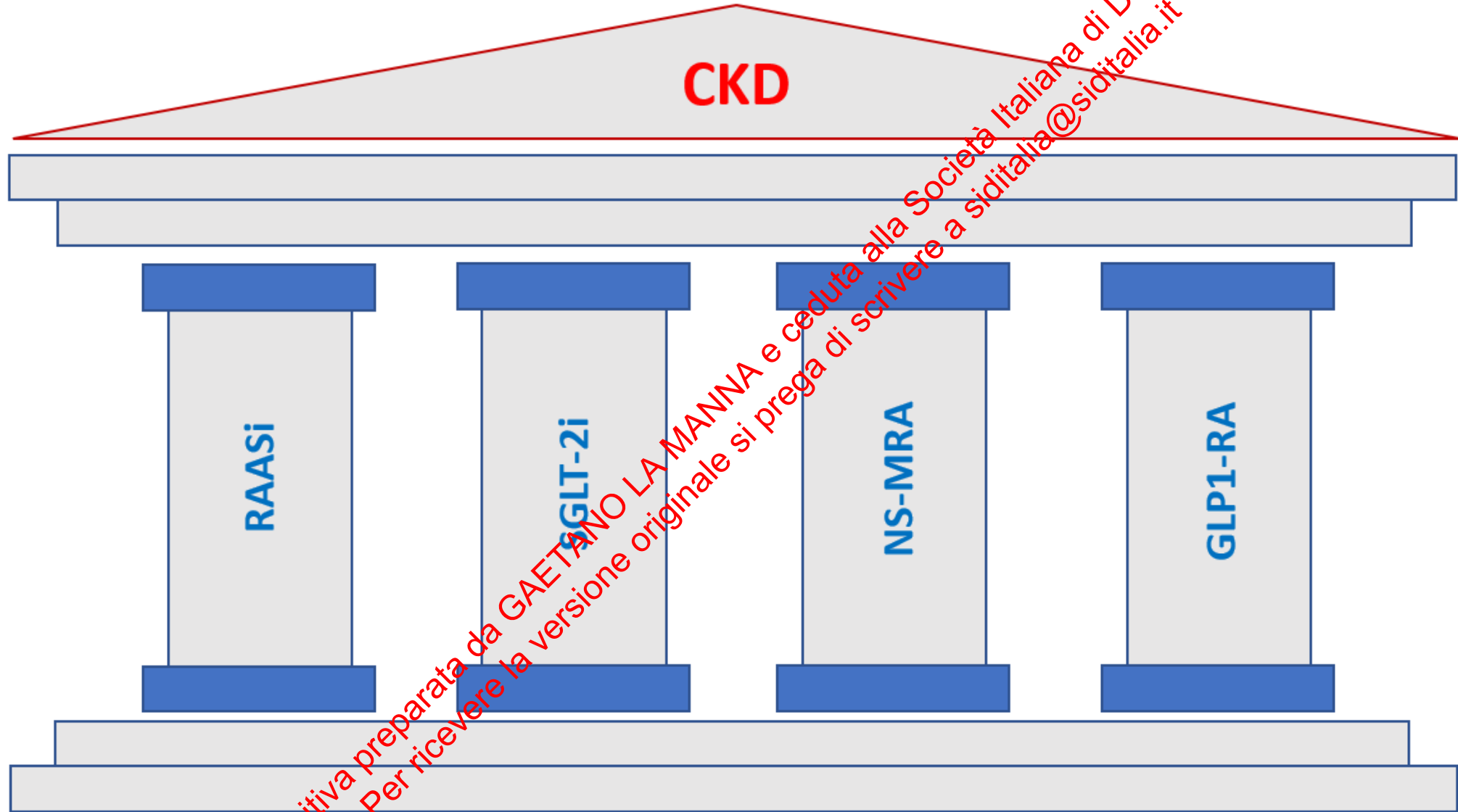


Semaglutide
1 mg



	sCreat mg/dL	eGFR mL/min	U _{Prot} mg/die	Hba1c mmol/ mol	LDL mg/dL	HDL mg/dL	Tg mg/dL
02/2021	1.42	49	3486	65	164	45	215
03/2022	1.44	48	2300	58	134	58	302
10/2022	1.64	41	900	55	122	54	395
03/2023	1.64	40	580	60	104	54	250
10/2023	1.69	39	370	53	104	58	220

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