PRIMO CONVEGNO REGIONALE CALABRIA 2023

LA NEFROLOGIA DEL FUTURO ED IL NURSING NEFROLOGICO UN LEGAME ESSENZIALE PER UNA MEDICINA DI QUALITÀ:

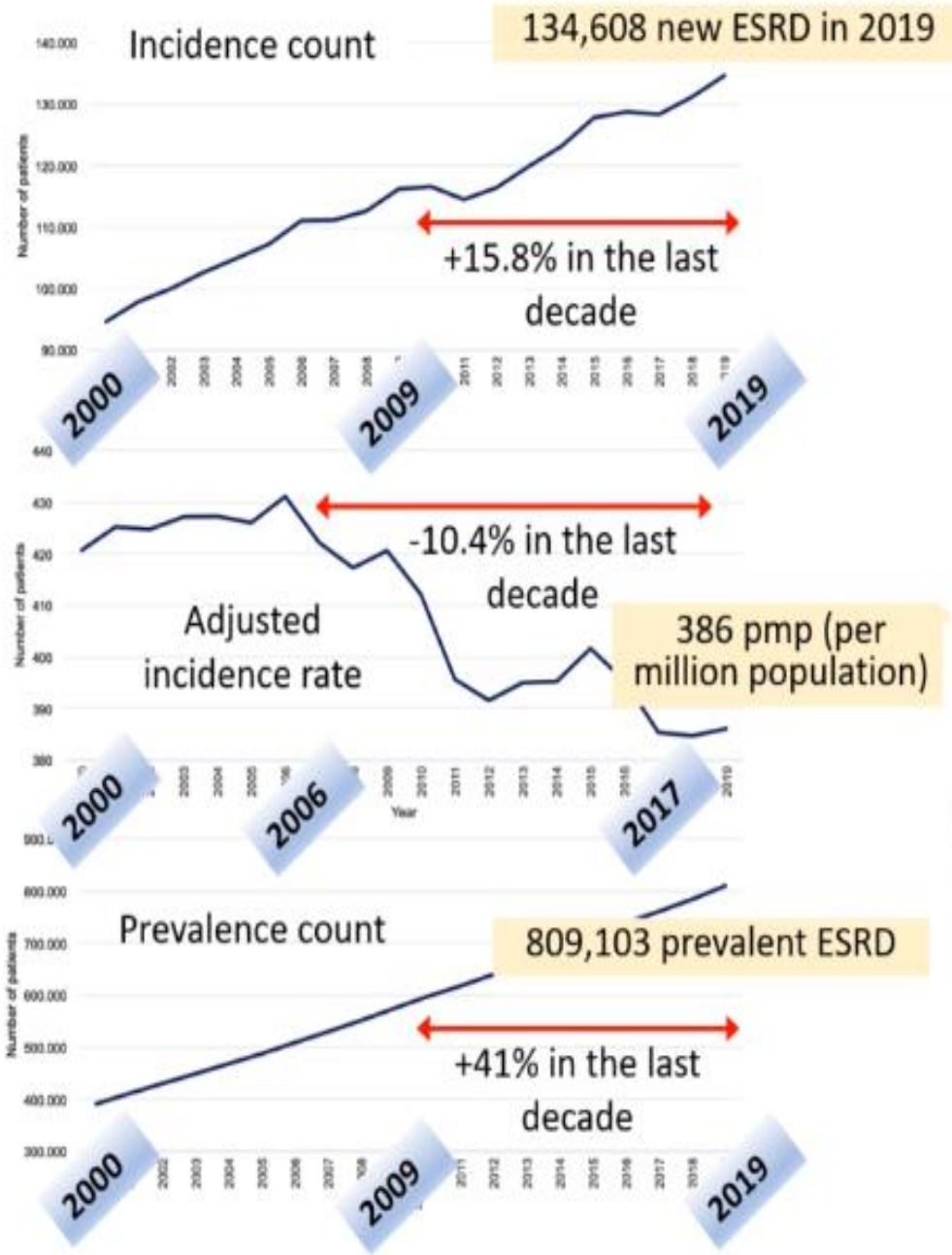
LE NUOVE FRONTIERE DELLA TERAPIA ANTIDIABETICA E PER LA PROGRESSIONE DELLA MALATTIA RENALE CRONICA

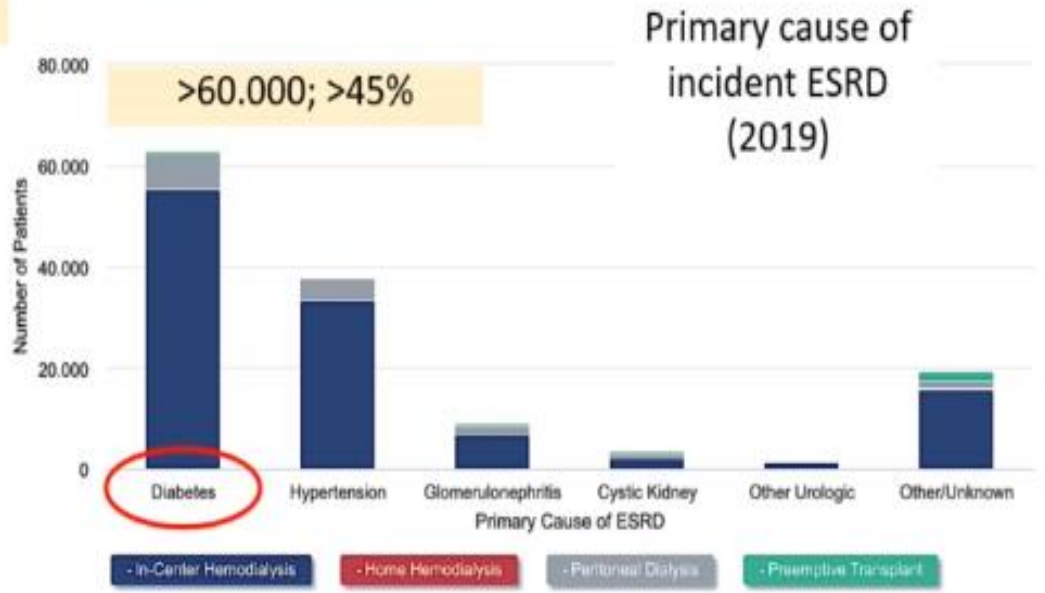
08 OTTOBRE 2023
Hotel San Francesco - Rende (CS)

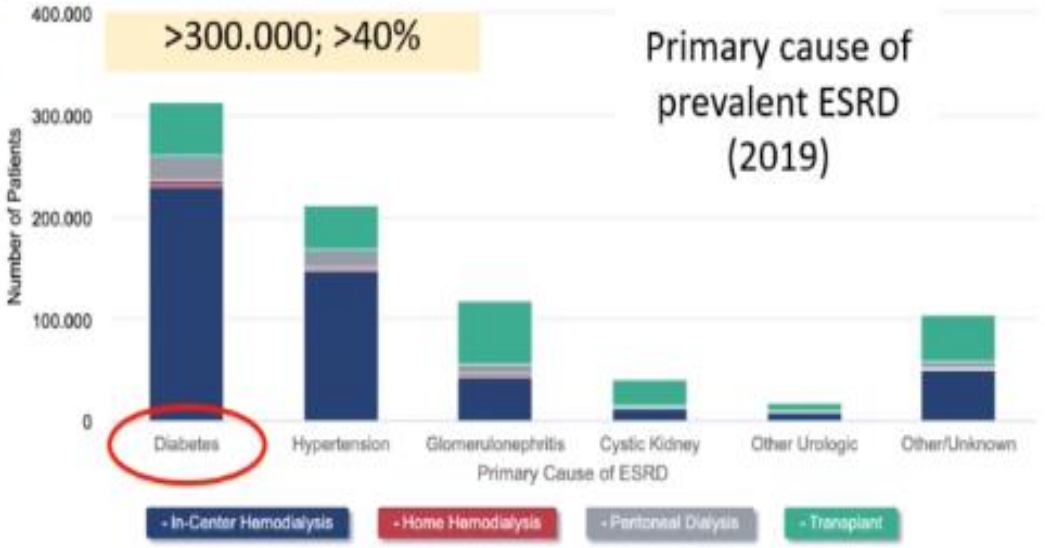
ResponsabilIi Scientifici
Giuseppe Ferraro - Francesco Barci

Dott.ssa Fiorella Iorio
Dirigente Medico
Nefrologia-Dialisi Abilitata al Trapianto
AO Annunziata di Cosenza

USRDS – 2021 ADR – ESRD (2019)







USRDS – 2021 ADR, AJKD 79 (suppl. 1): S178-S575, 2022.

Epidemiology of CKD: an update 2022

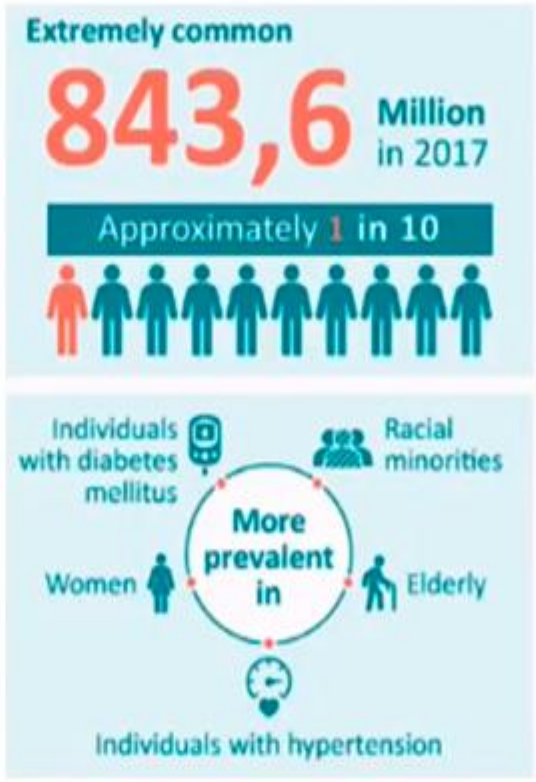
CKD …

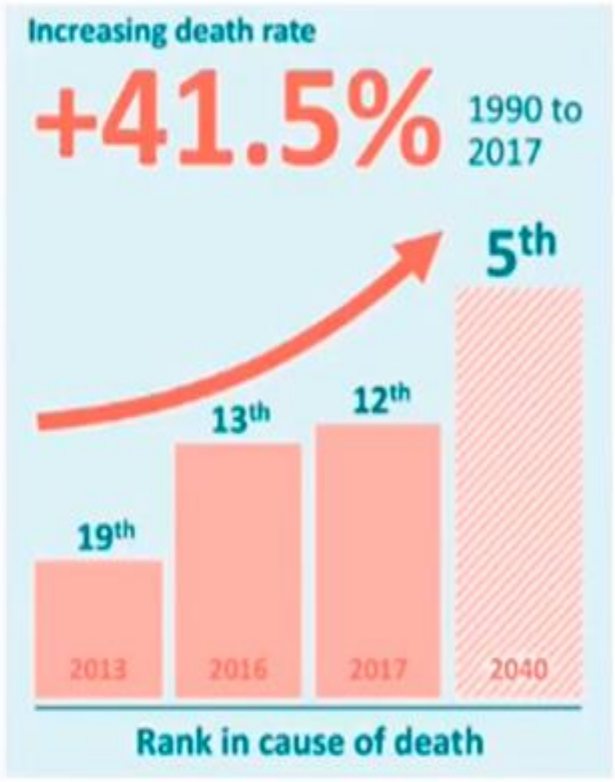
… è una condizione progressiva che interessa **>10% della popolazione generale nel mondo**, pari a >800 milioni di individui nel 2017

… **è più prevalente** negli individui adulti, femmine, e **nelle persone con diabete mellito** e ipertensione

… è emersa quale **una delle principali cause di mortalità nel mondo** (globalmente, nel 2017, 1.2 milioni (95% UI 1.1-1.3) di persone sono morte per CKD)

… è una di un piccolo numero di **malattie non trasmissibili** che ha dimostrato **un aumento nel rischio di morte (+41.5%)** nel corso delle ultime due decadi



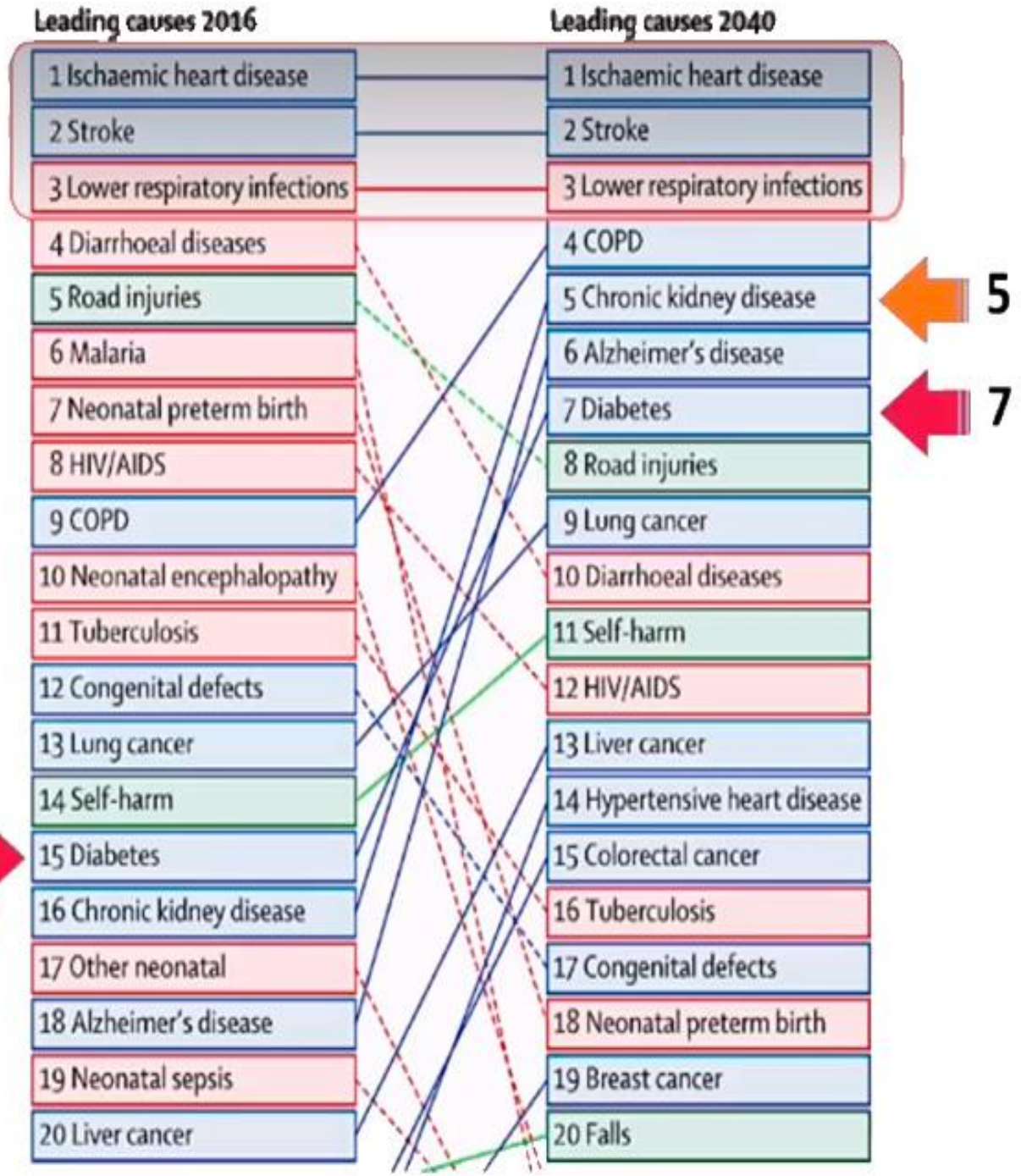


Kovesdy CP. Kidney International Supplements 2022; 12: 7–11
GBD Chronic Kidney Disease Collaboration. Lancet 2020; 395: 709–33

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

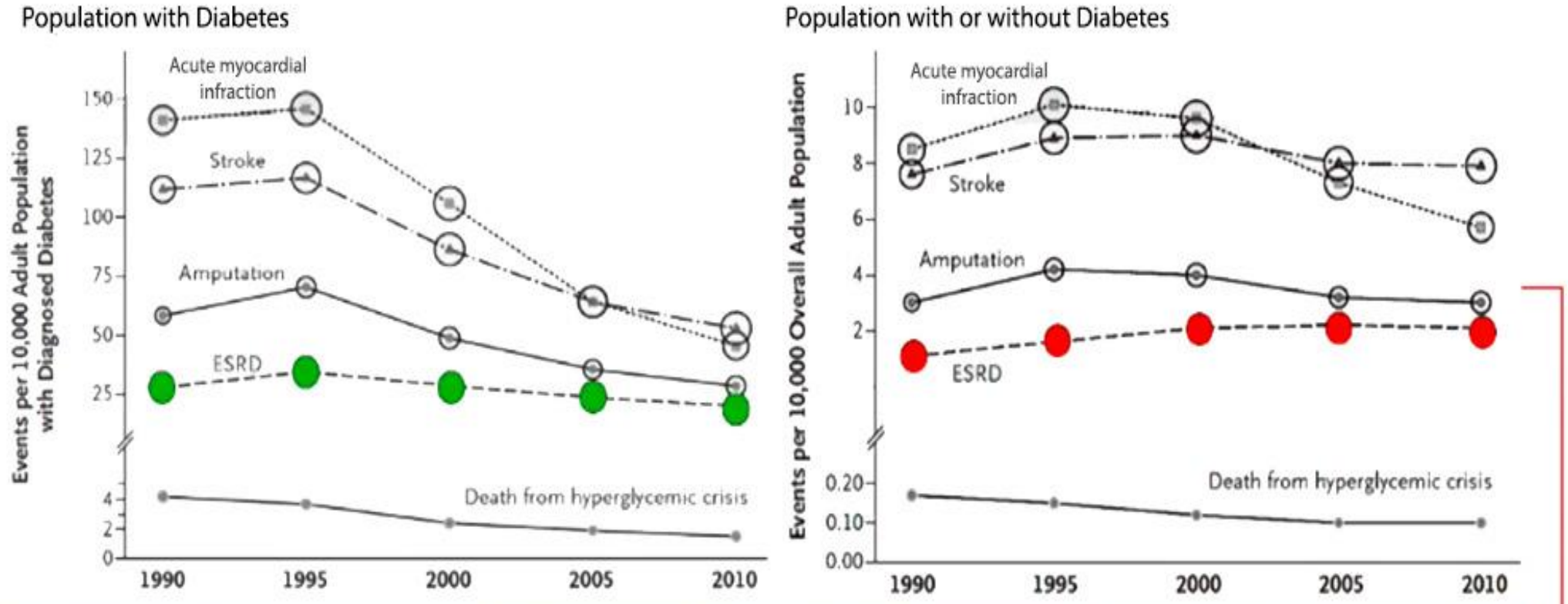
Leading 20 causes of years of life lost (YLLs) globally in 2016 and 2040

Red = communicable, maternal, neonatal, and nutritional disease
Blue = non communicable causes
Green = injuries



Foreman KJ et al., Lancet 2018; 392: 2052-90

Changes in Diabetes-Related Complications in the United States, 1990-2010



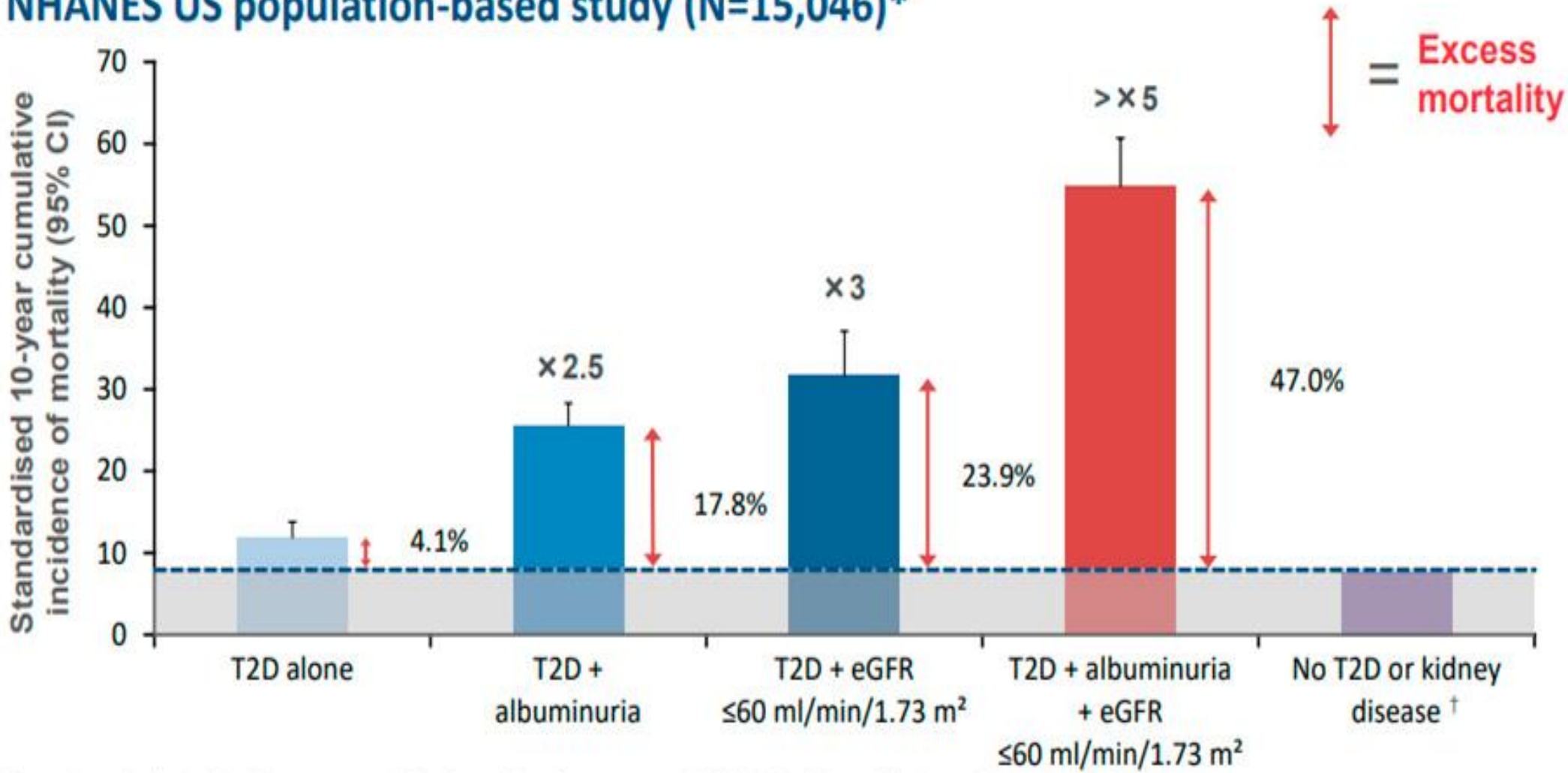
Within population ..	AMI	Stroke	Amputation	ESRD	Death from hyperglycemic crisis
.. with diabetes	-68%	-53%	-51%	-28%	-64%
.. with or without diabetes	-32%	+3.4%	-0.5%	+91%*	-42%

* From 1.1 to 2.1 cases per 10,000 population

Gregg EW, et al., 1990-2010. N Engl J Med. 2014; 370: 1514-23.

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)

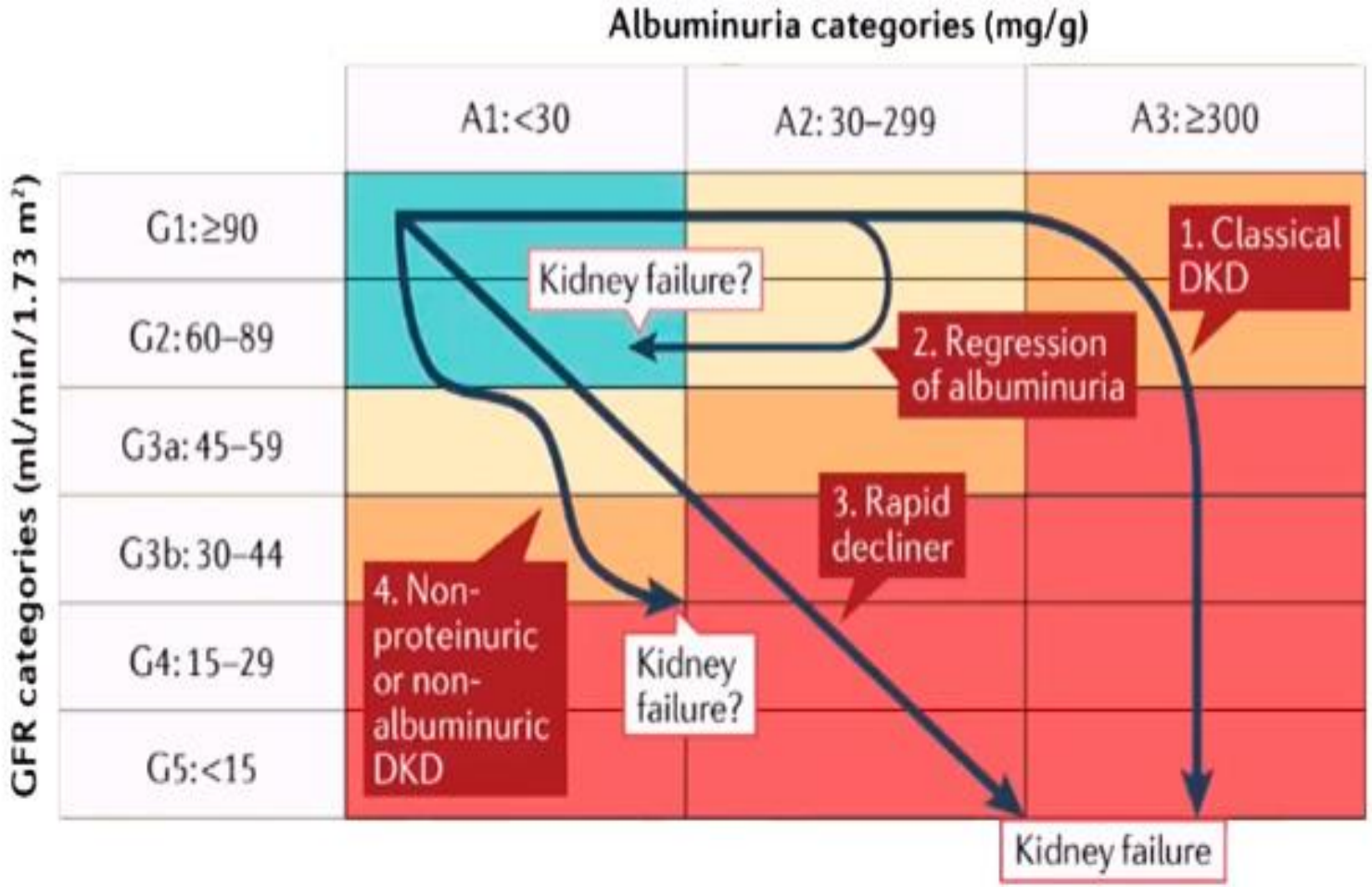
*Adults aged ≥20 years with diabetes mellitus participating in National Health and Nutrition Examination Surveys from 1988 to 2014; †Kidney disease defined as albuminuria, impaired glomerular filtration or both. DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; T2D, type 2 diabetes. Afkarian M *et al. J Am Soc Nephrol* 2013;24:302

DKD phenotypes

- Diabetic kidney disease (DKD) is traditionally characterized by hyperfiltration, persistent high albuminuria and a subsequent decline in the glomerular filtration rate (GFR); this trajectory is widely recognized as the classical phenotype of DKD (1).

- However, trajectories of kidney function (changes of GFR and albuminuria over time) may differ from this classical phenotype.

- Three alternative, non-classical phenotypes of DKD have also been described, characterized by:
  - regression of albuminuria (2)
  - rapid GFR decline (3)
  - absence of proteinuria or albuminuria (4).



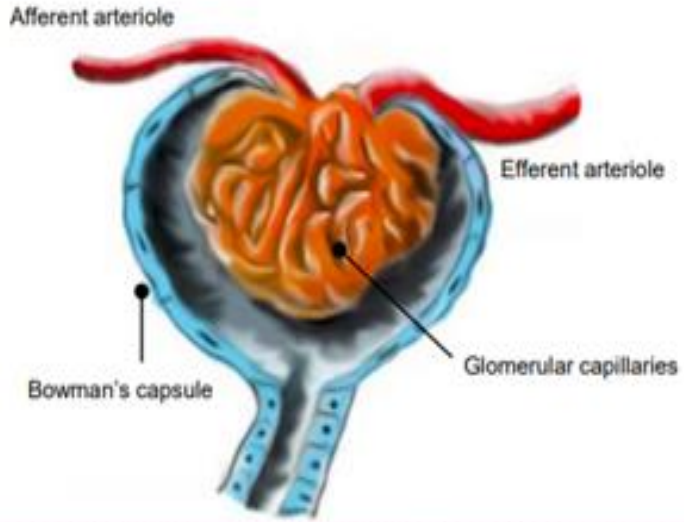
Oshima M, et al. Nat Rev Nephrol. 2021; 17: 740-750.

SGLT2 inhibition and RAAS blockade both reduce glomerular hyperfiltration by complementary mechanisms[1-3]

SGLT2 inhibitors

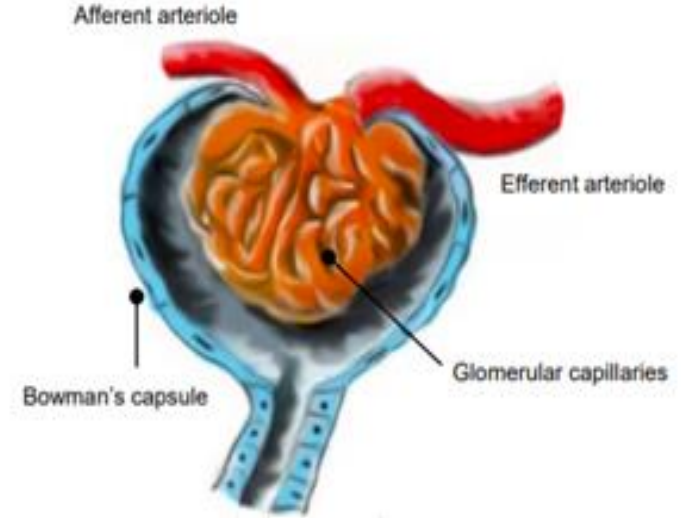
Afferent constriction[1-3]

Due to increased Na+ delivery to the macula densa[1-3]



RAAS blockade

Efferent vasodilation[1]



CLINICAL IMPLICATIONS

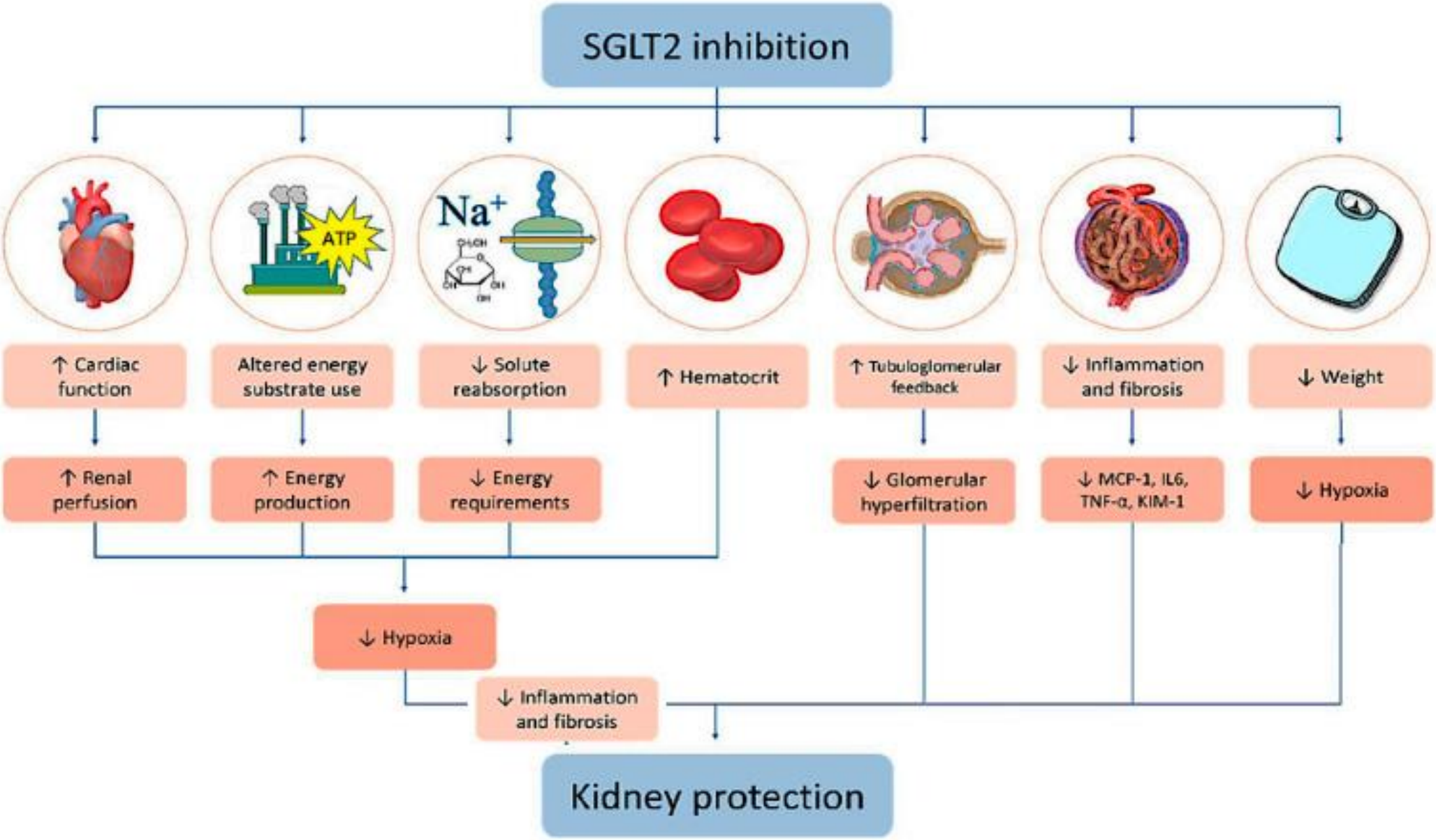
- Decreased glomerular pressure[1,3]
- Reduction in albuminuria[1,2]

- Decreased glomerular pressure[1,3]
- Reduction in albuminuria[4]

SGLT2, sodium-glucose cotransporter 2; Na, sodium; RAAS, renin-angiotensin-aldosterone system.

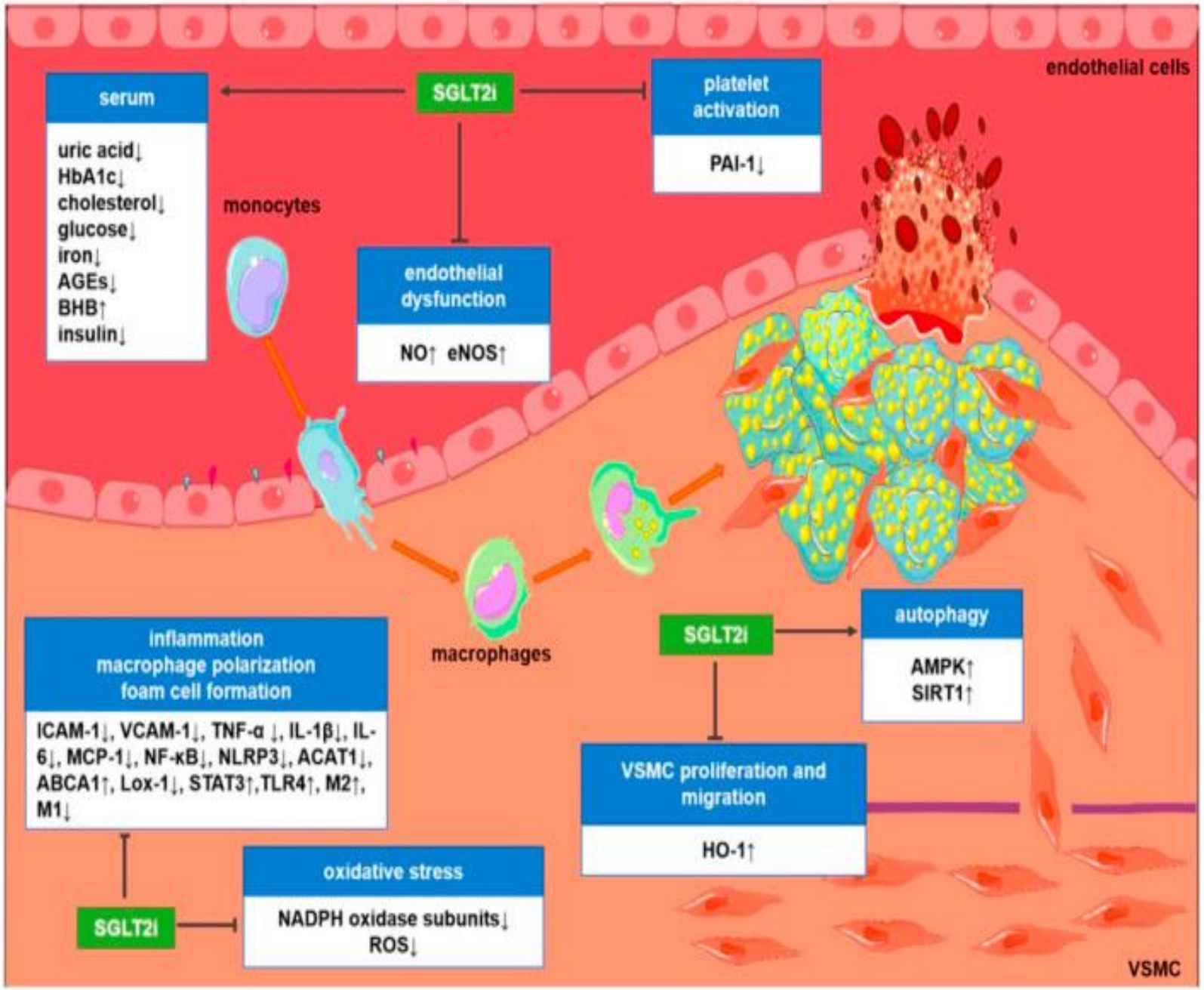
1. Van Bommel EJ, et al. *Clin J Am Soc Nephrol*. 2017;12(4):700-710. 2. Seidu S, et al. *Prim Care Diabetes*. 2018;12(3):265-283. 3. Cherney DZ, et. al. *Circulation*. 2014 Feb 4;129(5):587-97. 4. Heerspink HJ, et al. *Diabetes Care*. 2011;34 Suppl 2:S325-9. 5. Adapted from: Shiraishi M, et al. *FASEB J*. 2003;17(15):2284-6.

Potential mechanisms for kidney protection with SGLT2 inhibitors



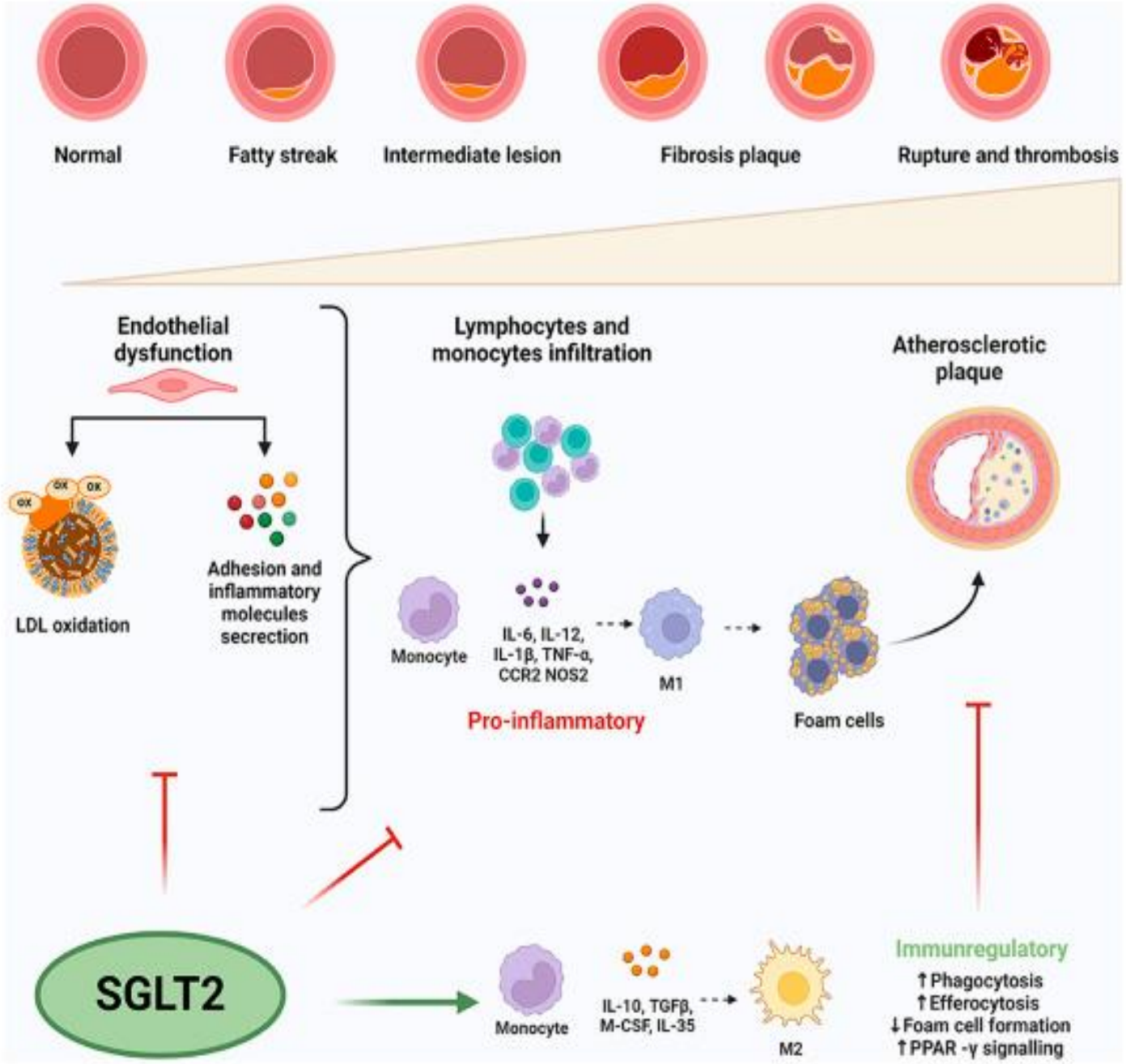
Liu H et al., Current Diabetes Reports 22: 317–332, 2022

Among others, potential anti-inflammatory mechanisms for vascular (and kidney) protection with SGLT2 inhibitors



Liu H et al., Theranostics 11: 4502-4515, 2021

Sodium-glucose co-transport 2 inhibitors' effects on inflammation in atherosclerosis.



Scisciola L et al., Front Cardiovasc Med, 2022

FINO AL 2019 LE EVIDENZE SUGGERIVANO UN BENEFICIO DELLE GLIFOZINE SULLA PROGRESSIONE DELLA CKD MA NON AVEVAMO TRIAL AD HOC

Table. Baseline Characteristics From Included Cardiovascular and Kidney Outcomes Trials With SGLT2 Inhibitors[a]

Characteristic	No. (%)[b] EMPA-REG outcome[19] (n = 7020)	CANVAS program[20] (n = 10 142)	DECLARE-TIMI 58[21] (n = 17 160)	CREDENCE[22] (n = 4401)	VERTIS CV[16] (n = 8246)
SGLT2 inhibitor	Empagliflozin	Canagliflozin	Dapagliflozin	Canagliflozin	Ertugliflozin
Duration of follow-up, median, y	3.1	2.4	4.2	2.6	3.0
Patient characteristics					
Men	5016 (71.5)	6509 (64.2)	10 738 (62.6)	2907 (66.1)	5769 (70.0)
Women	2004 (28.5)	3633 (35.8)	6422 (37.4)	1494 (33.9)	2477 (30.0)
Age, mean (SD), y	63.1 (8.6)	63.3 (8.3)	63.9 (6.8)	63.0 (9.2)	64.4 (8.1)
Race/ethnicity					
White	5081 (72.4)	7944 (78.3)	13 653 (79.6)	2931 (66.6)	7240 (87.8)
Asian	1517 (21.6)	1284 (12.7)	2303 (13.4)	877 (19.9)	498 (6.0)
Black or African American	357 (5.1)	336 (3.3)	603 (3.5)	224 (5.1)	235 (2.8)
Other/missing	65 (0.9)	578 (5.7)	601 (3.5)	369 (8.4)	273 (3.3)
Diabetes characteristics					
HbA_{1c}, mean (SD), %	8.1 (0.8)	8.2 (0.9)	8.3 (1.2)	8.3 (1.3)	8.2 (1.0)
Diabetes duration, mean (SD), y	57 > 10[c]	13.5 (7.8)	11.8 (7.8)	15.8 (8.6)	13.0 (8.3)
Cardiovascular characteristics					
Established cardiovascular disease	7020 (100)	6656 (65.6)	6974 (40.6)	2220 (50.4)	8246 (100)
History of heart failure	706 (10.1)	1461 (14.4)	1724 (10.0)	652 (14.8)	1958 (23.7)
Renal characteristics					
Reduced kidney function[d]	1819 (25.9)	2039 (20.1)	1265 (7.4)	2631 (59.8)	1807 (21.9)
Urine ACR ≥300 mg/g	769 (11.0)	760 (7.6)	1169 (6.8)	3874 (88.0)	755 (9.2)
Cardiovascular medications					
ACEI or ARB blockade	5666 (80.7)	8116 (80.0)	13 950 (81.3)	4395 (99.9)	6686 (81.1)
β-Blocker	4554 (64.9)	5421 (53.5)	9030 (52.6)	1770 (40.2)	5692 (69.0)
Statin/ezetimibe	5403 (77.0)	7599 (74.9)	12 868 (75.0)	3036 (69.0)	6790 (82.3)
Antihyperglycemic medications					
Insulin	3387 (48.2)	5095 (50.2)	7013 (40.9)	2884 (65.5)	3900 (47.3)
Metformin	5193 (74.0)	7825 (77.2)	14 068 (82.0)	2545 (57.8)	6292 (76.3)
Sulfonylurea	3006 (42.8)	4361 (43.0)	7322 (42.7)	1268 (28.8)	3390 (41.1)
DPP-4 inhibitor	796 (11.3)	1261 (12.4)	2888 (16.8)	751 (17.1)	911 (11.0)
GLP-1 receptor agonist	196 (2.8)	407 (4.0)	750 (4.4)	183 (4.2)	278 (3.4)

DAPA-CKD:
Dapagliflozin in Patients With Chronic Kidney Disease[1,2]

Objective To assess whether treatment with dapagliflozin, compared with placebo, reduced the risk of renal and CV events in patients with CKD with or without T2D, and who were receiving standard of care including a maximum tolerated dose of an ACEi or ARB

Key Inclusion Criteria
- ≥18 years of age
- eGFR ≥25 to ≤75 mL/min/1.73m²
- UACR ≥200 to ≤5000 mg/g
- Stable max tolerated dose of ACEi/ARB for ≥4 weeks
- With and without T2D

Key Exclusion Criteria
- T1D
- Polycystic kidney disease, lupus nephritis, ANCA-associated vasculitis
- Immunosuppressive therapy ≤6 months prior to enrollment

1:1 Double-blind

- Dapagliflozin 10 mg + standard of care
- Placebo + standard of care

4304 Randomized
Median follow-up 2.4 years

End Points

Primary Outcome
Composite of sustained ≥50% eGFR decline, ESKD[a], renal or CV death

Secondary Outcomes
- Composite of sustained ≥50% eGFR decline, ESKD, or renal death
- Composite of CV death or hHF
- All-cause mortality

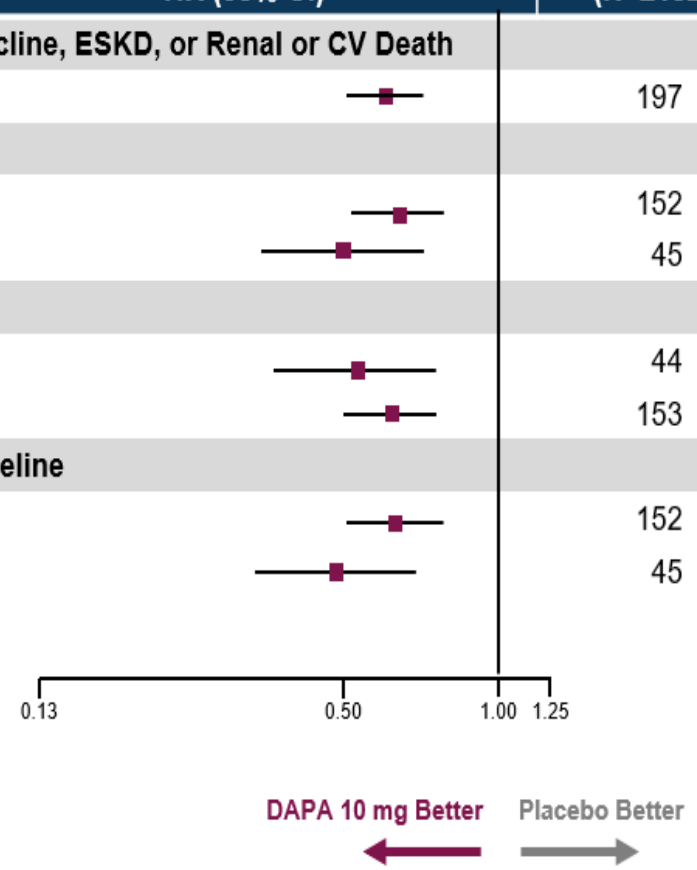
[a]ESKD defined as the need for maintenance dialysis (peritoneal or hemodialysis) for at least 28 days and renal transplantation or sustained eGFR <15mL/min/1.73m² for at least 28 days.

ACEi = angiotensin-converting enzyme inhibitor; ANCA = anti-neutrophil cytoplasmic antibody; ARB = angiotensin-receptor blocker; CKD = chronic kidney disease; CV = cardiovascular; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; hHF = hospitalization for heart failure; T1D = type 1 diabetes; T2D = type 2 diabetes; UACR = urinary albumin-to-creatinine ratio.

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

Primary Composite Outcome: Treatment Benefit Consistent Across Prespecified Subgroups

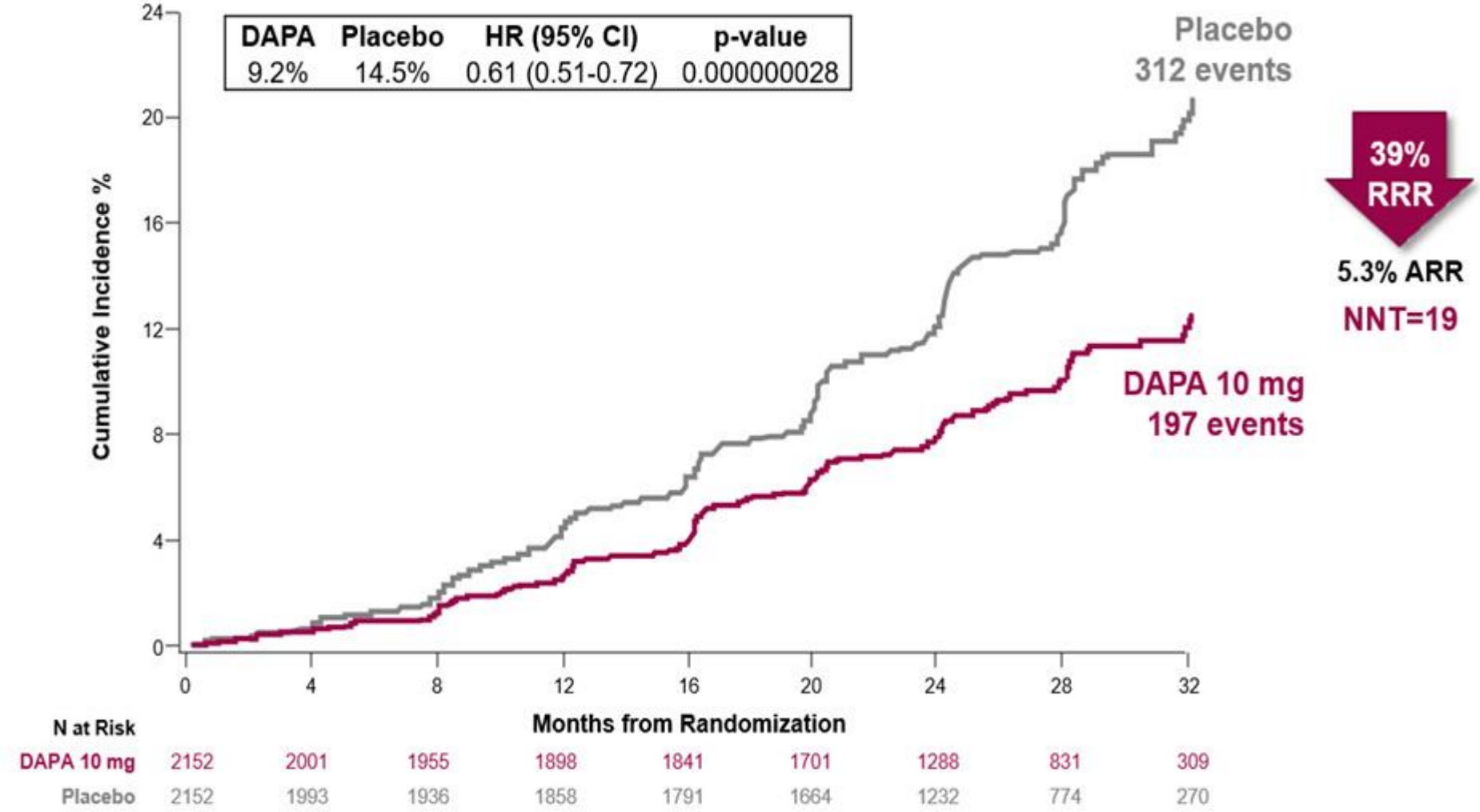
	Number of Events				
HR (95% CI)	DAPA 10 mg (N=2152)	Placebo (N=2152)	HR	95% CI	p-value Interaction
Composite of ≥50% eGFR Decline, ESKD, or Renal or CV Death					
All Patients	197	312	0.61	(0.51, 0.72)	
T2D at Baseline					0.24
Yes	152	229	0.64	(0.52, 0.79)	
No	45	83	0.50	(0.35, 0.72)	
UACR (mg/g) at Baseline					0.52
≤1000	44	84	0.54	(0.37, 0.77)	
>1000	153	228	0.62	(0.50, 0.76)	
eGFR (mL/min/1.73m^2) at Baseline					0.22
<45	152	217	0.63	(0.51, 0.78)	
≥45	45	95	0.49	(0.34, 0.69)	



CV = cardiovascular; DAPA = dapagliflozin; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; HR = hazard ratio; T2D = type 2 diabetes; UACR = urinary albumin-to-creatinine ratio.

Heerspink HJL. Presented at: ESC Congress – The Digital Experience; August 29 - September 1, 2020.

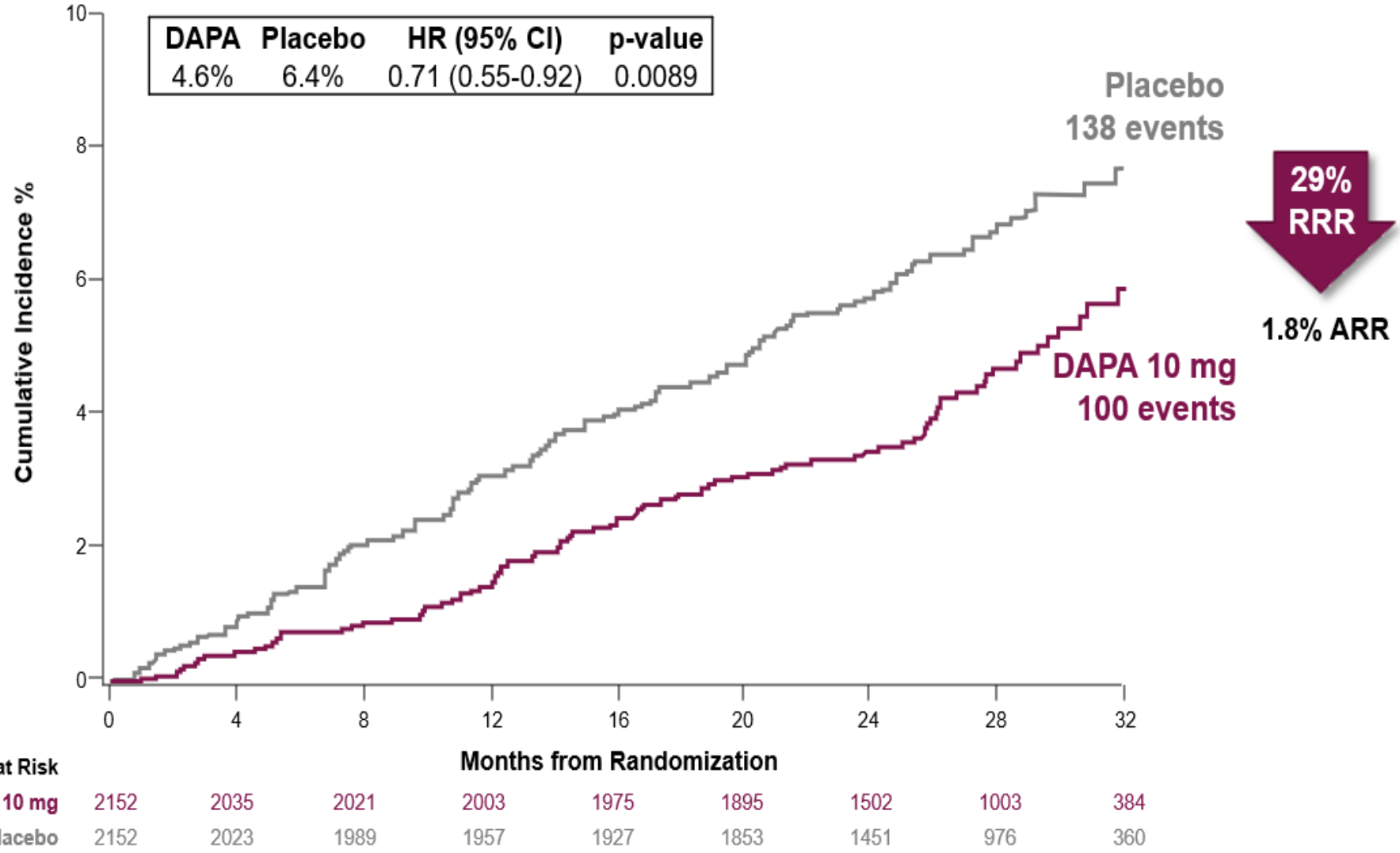
Primary Composite Outcome: Sustained ≥50% eGFR Decline, ESKD, Renal or CV Death[a]



[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/1.73m² for at least 28 days. Renal death was defined as death due to ESKD when dialysis treatment was deliberately withheld for any reason.[2] ARR = absolute risk reduction; 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.

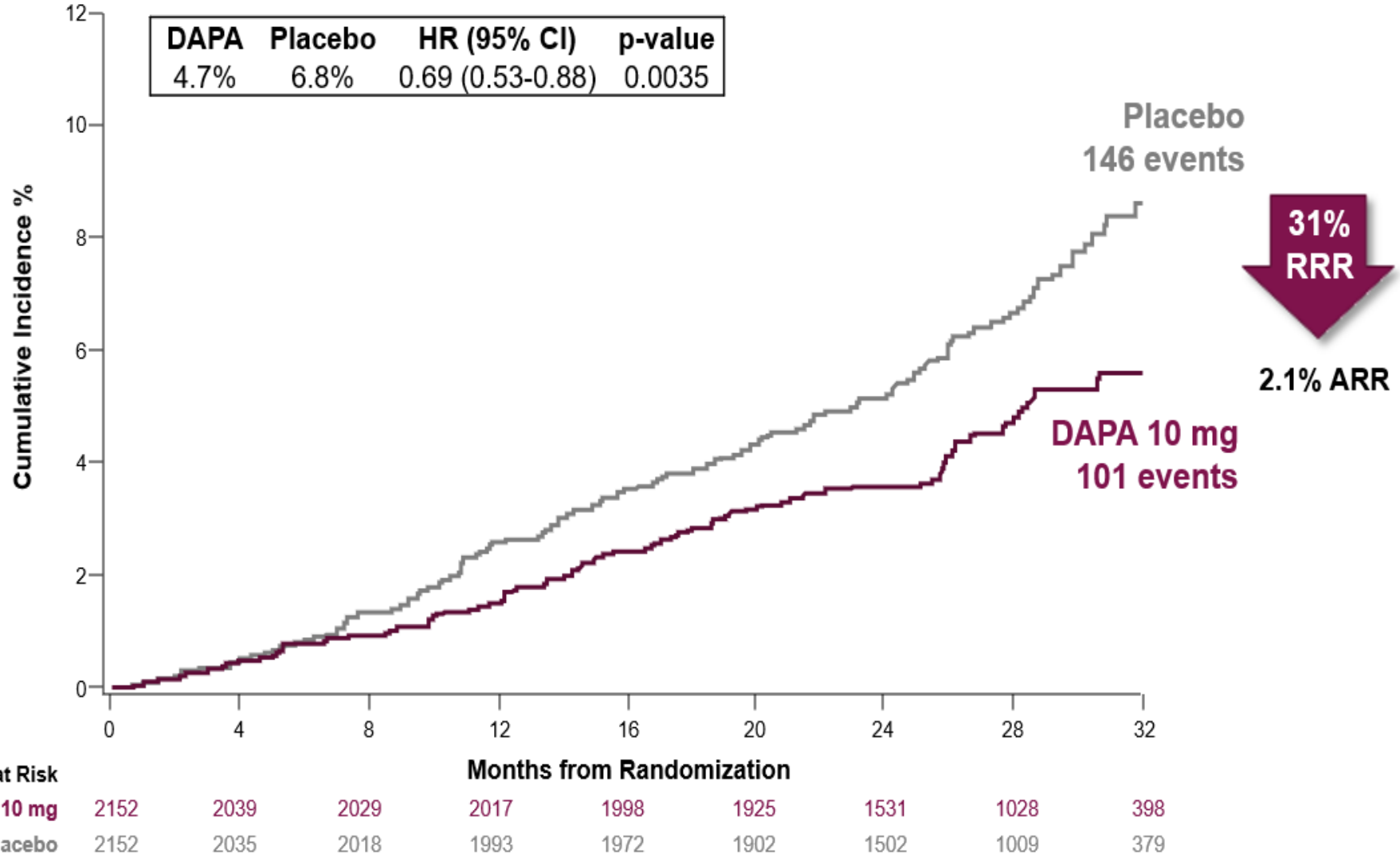
Secondary Composite Outcome: CV Death or Hospitalization for Heart Failure



ARR = absolute risk reduction; CV = cardiovascular; DAPA = dapagliflozin; HR = hazard ratio; RRR = relative risk reduction.

Heerspink HJL. Presented at: ESC Congress – The Digital Experience; August 29 - September 1, 2020.

Secondary Outcome: All-cause Mortality

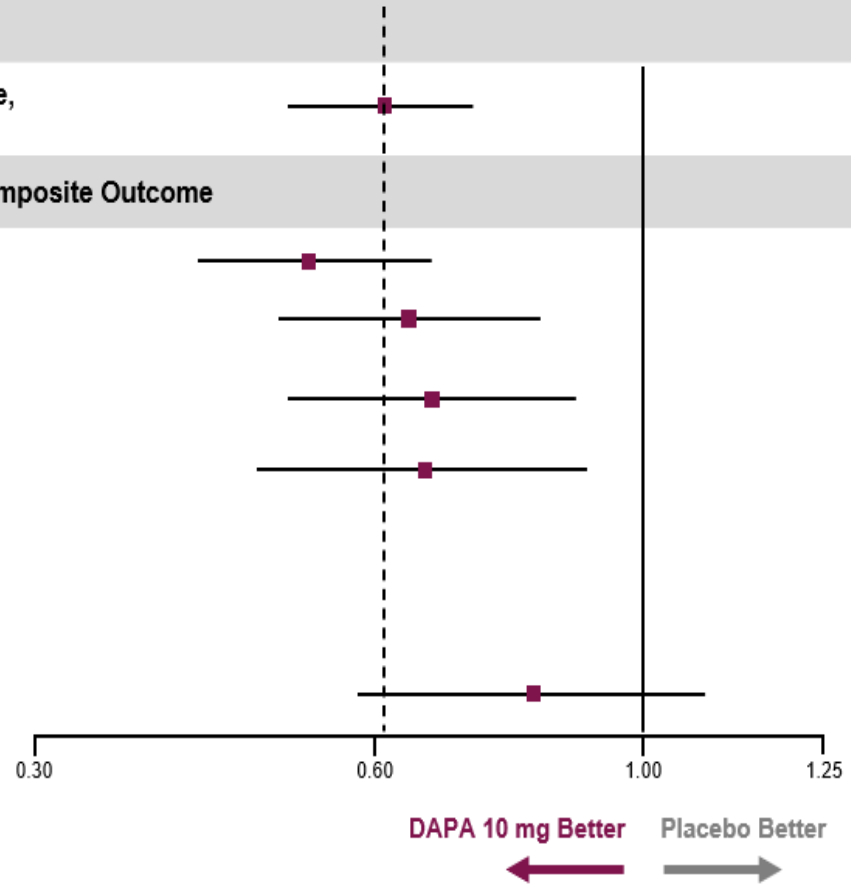


ARR = absolute risk reduction; DAPA = dapagliflozin; HR = hazard ratio; RRR = relative risk reduction.

Heerspink HJL. Presented at: ESC Congress – The Digital Experience; August 29 - September 1, 2020.

Primary Composite Outcome: All Components Contributed to the Observed Treatment Effect

	Number of Events				
	DAPA 10 mg (N=2152)	Placebo (N=2152)	HR	95% CI	p-value
Primary Composite Outcome					
Composite of ≥50% eGFR Decline, ESKD, or Renal or CV Death	197	312	0.61	(0.51, 0.72)	0.000000028
Components of the Primary Composite Outcome					
≥50% eGFR Decline	112	201	0.53	(0.42, 0.67)	<0.0001
ESKD	109	161	0.64	(0.50, 0.82)	0.0004
eGFR <15mL/min/1.73m^2	84	120	0.67	(0.51, 0.88)	0.0045
Chronic Dialysis	68	99	0.66	(0.48, 0.90)	0.0080
Transplantation	3	8	NC		
Renal Death	2	6	NC		
CV Death	65	80	0.81	(0.58, 1.12)	0.2029



CV = cardiovascular; DAPA = dapagliflozin; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; HR = hazard ratio; NC = not calculable

Heerspink HJL. Presented at: ESC Congress – The Digital Experience; August 29 - September 1, 2020.

LE LINEE GUIDA KDIGO 2020 RACCOMANDANO L'UTILIZZO DEGLI SGLT2-I IN TUTTI I PAZIENTI CON MALATTIA RENALE CRONICA INDIPENDENTEMENTE DALLA PRESENZA O MENO DI ALBUMINURIA, INDIPENDENTEMENTE DAL FENOTIPO POICHÉ HANNO MOSTRATO DI ESSERE IN GRADO DI RALLENTARE LA PROGRESSIONE DEL DANNO RENALE

PARADOSSALMENTE L'UTILIZZO DI QUESTI FARMACI È STATO FINO AD UN ANNO FA CIRCA FA LIMITATO NEI PAZIENTI CON FILTRATO GLOMERULARE MOLTO BASSO

- Da pochi giorni Empagliflozin è prescrivibile ma non ancora rimborsabile anche nei pazienti con e-GFR fino a 20 ml/min indipendentemente dall'indicazione SC

- Dapagliflozin può essere iniziato e continuato fino a valori di e-GFR ≥ 25 ml/min

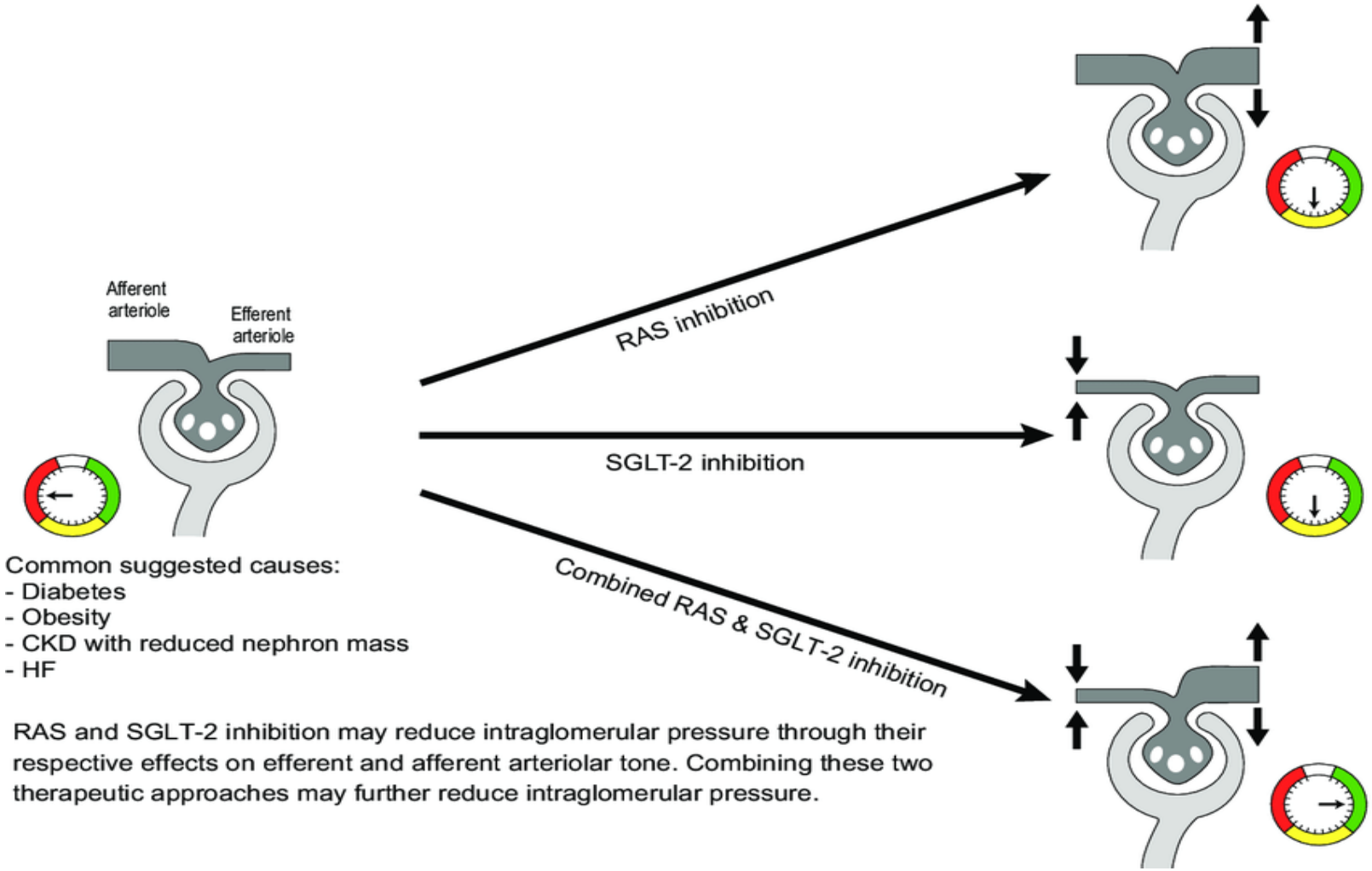
2023...

IL MEDICINALE DAPAGLIFLOZIN È CLASSIFICATO AI FIN DELLA RIMBORSABILITÀ ALLE CONDIZIONI QUI SOTTOINDICATE

Nuova Indicazioni Rimborsata
Dapagliflozin è indicato negli adulti per il trattamento della Malattia Renale Cronica

La prescrizione del medicinale è soggetta a diagnosi e piano terapeutico web based

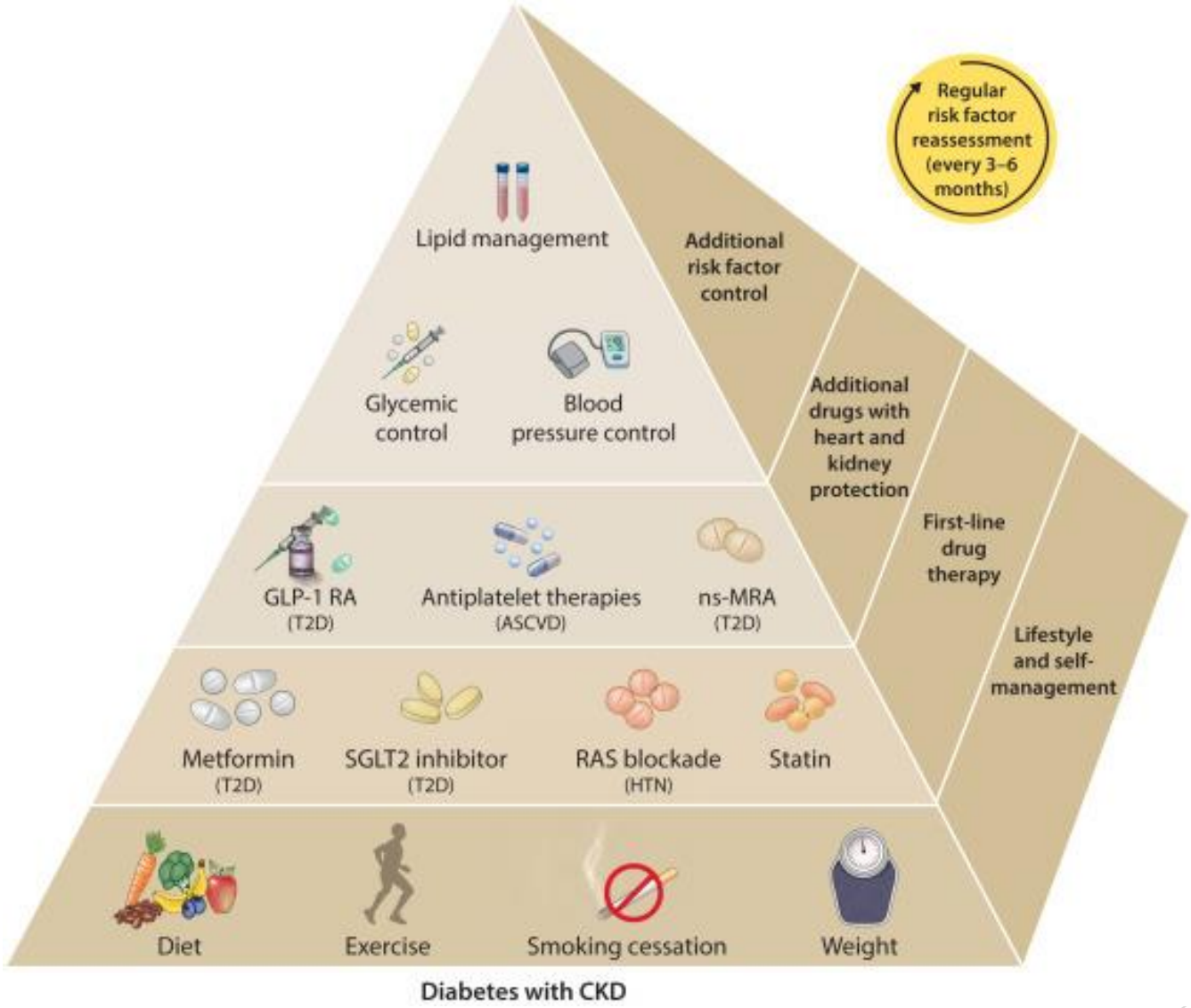
SGLT2 ? UNA NUOVA RISORSA A FUNZIONE RENALE RIDOTTA



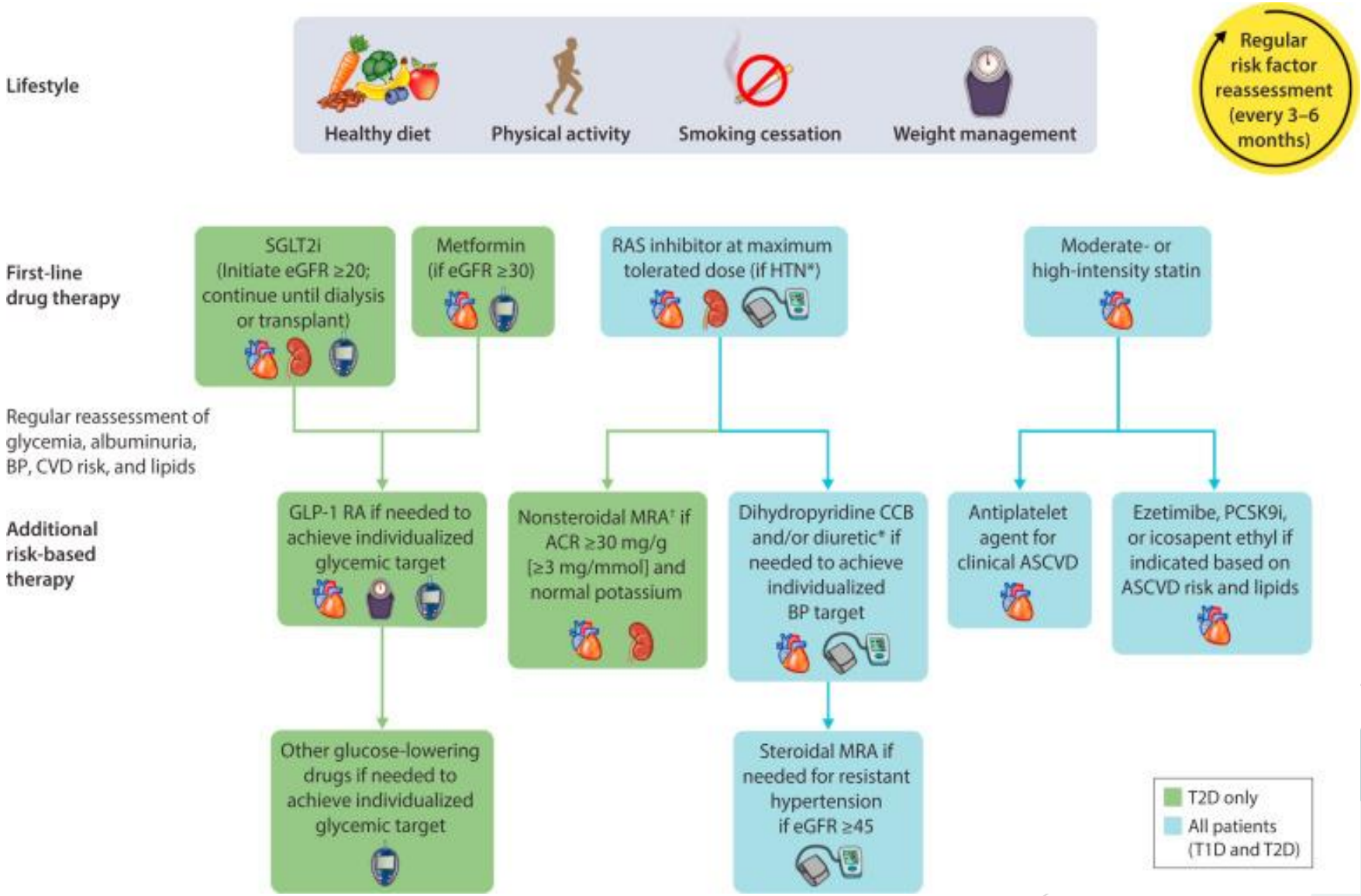
Common suggested causes:
- Diabetes
- Obesity
- CKD with reduced nephron mass
- HF

RAS and SGLT-2 inhibition may reduce intraglomerular pressure through their respective effects on efferent and afferent arteriolar tone. Combining these two therapeutic approaches may further reduce intraglomerular pressure.

KDIGO 2022 – LINEE GUIDA NEFROPATIA DIABETICA



CONSENSUS ADA E KDIGO 2022 – NEFROPATIA DIABETICA



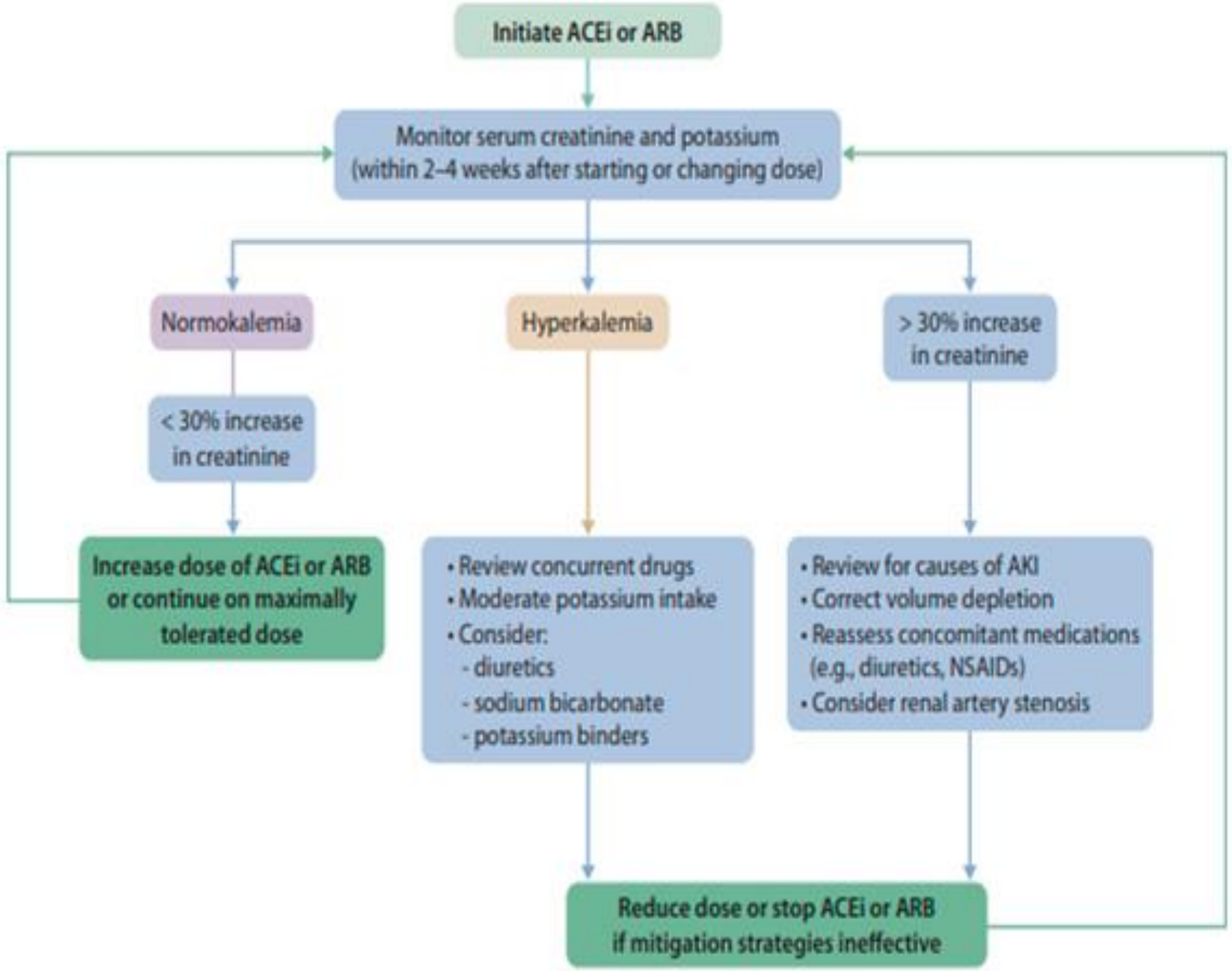


Figure 4| Monitoring of serum creatinine and potassium during angiotensin-converting enzyme inhibitor (ACEi) or angiotensin II receptor blocker (ARB) treatment—dose adjustment and monitoring of side effects. AKI, acute kidney injury; NSAID, nonsteroidal anti-inflammatory drug.

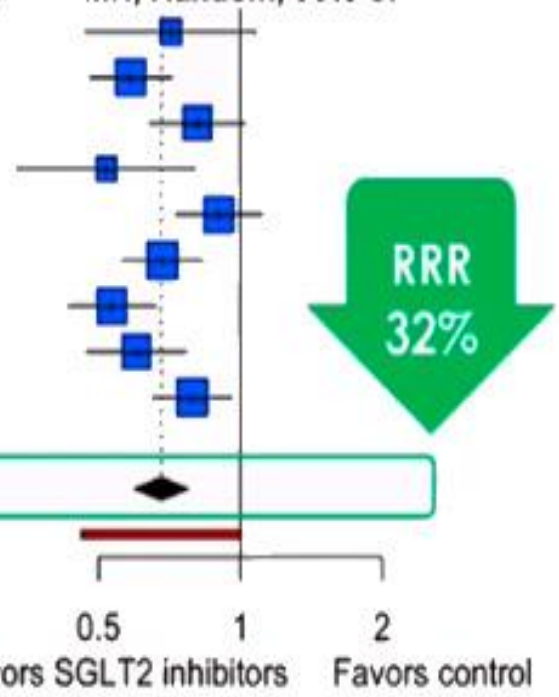
SGLT2 inhibitors and cardiovascular and renal outcomes: a meta-analysis and trial sequential analysis

Renal outcomes

Study	SGLT2 inhibitors Events	Total	Control Events	Total	Weight	Risk Ratio MH, Random, 95% CI
Bhatt / SCORED 2020	37	5292	52	5292	6.3%	0.71 [0.47; 1.08]
Heerspink / DAPA-CKD 2020	142	2152	243	2152	13.1%	0.58 [0.48; 0.71]
Cannon / VERTIS CV 2020	175	5499	108	2747	11.7%	0.81 [0.64; 1.02]
Packer / EMPEROR-Reduced 2020	30	1863	58	1867	6.0%	0.52 [0.34; 0.80]
McMurray / DAPA-HF 2019	153	2373	170	2371	12.6%	0.90 [0.73; 1.11]
Perkovic / CREDENCE 2019	153	2202	224	2199	13.2%	0.68 [0.56; 0.83]
Wiviott / DECLARE–TIMI 58 2019	127	8582	238	8578	12.5%	0.53 [0.43; 0.66]
Neal / CANVAS 2017	113	5795	141	4347	11.3%	0.60 [0.47; 0.77]
Zinman / EMPA-REG OUTCOME 2015	246	4687	155	2333	13.3%	0.79 [0.65; 0.96]
Total (95% CI)		**38445**		**31886**	**100.0%**	**0.68 [0.60; 0.77]**
Prediction interval						**[0.46; 1.00]**

Heterogeneity: $Tau^2 = 0.0229$; $Chi^2 = 20.86$, df = 8 ($P < 0.01$); $I^2 = 62\%$

Test for overall effect: $Z = -5.87$ ($P < 0.01$)



9 trials were included (70,331patients)

Renal outcome was different among trials

Barbarawi M, Heart Fail Rev 2022

Association of SGLT2 inhibitors with cardiovascular, kidney, and safety outcomes among patients with DKD: a meta-analysis

A total of 26,106 participants with DKD from 8 large-scale trials were included

Outcome	No. studies	No. events	Sample size	HR (95% CI)
MACE	6	2271	21,913	0.83 (0.75–0.93)
Kidney composite	5	1197	21,195	0.66 (0.58–0.75)
HHF	6	1219	22,346	0.62 (0.55–0.71)
Cardiovascular death	5	953	20,539	0.84 (0.74–0.96)
Fatal and nonfatal MI	5	498*	20,108	0.78 (0.67–0.92)
Fatal and nonfatal stroke	5	332*	20,108	0.76 (0.59–0.97)
All-cause mortality	5	1451	21,406	0.86 (0.77–0.96)

RRR 34%

EMPA-REG OUTCOME, CANVAS, DECLARE-TIMI 58, CREDENCE, DAPA-CKD, VERTIS-CV, SCORED, SOLOIST-WHF

Kidney composite outcomes = worsening kidney function, end-stage kidney disease, or death from renal or cardiovascular causes

Kaze AD, Cardiovasc Diabetol 2022

Association of SGLT2 inhibitors with cardiovascular, kidney, and safety outcomes among patients with DKD: a meta-analysis

Outcome	No. studies	No. events	Sample size	HR (95% CI)
Overall (eGFR < 60 mL/min/1.73m^2)				
MACE	6	2102	20,106	0.82 (0.74–0.91)
Kidney composite	4	530	16,480	0.65 (0.55–0.78)
HHF	6	1125	20,106	0.61 (0.54–0.70)
eGFR < 45 mL/min/1.73m^{2**}				
MACE	3	347	2437	0.75 (0.60–0.93)
Kidney composite	2	225	1867	0.70 (0.54–0.92)
HHF	3	166	2437	0.60 (0.44–0.82)

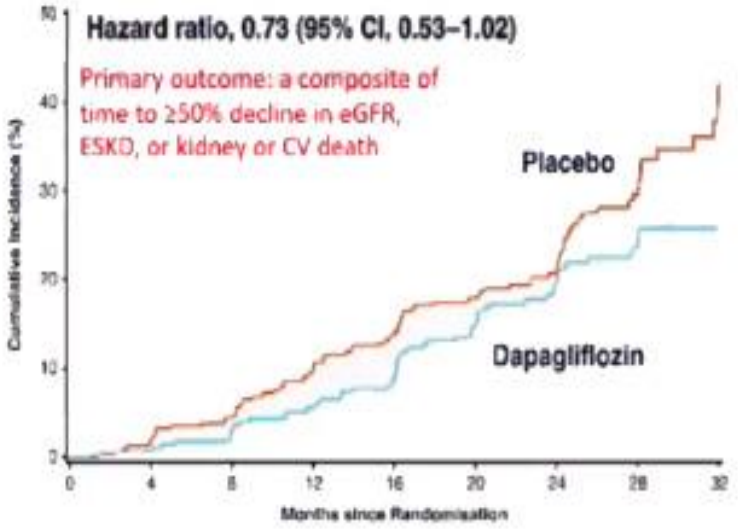
RRR 35%

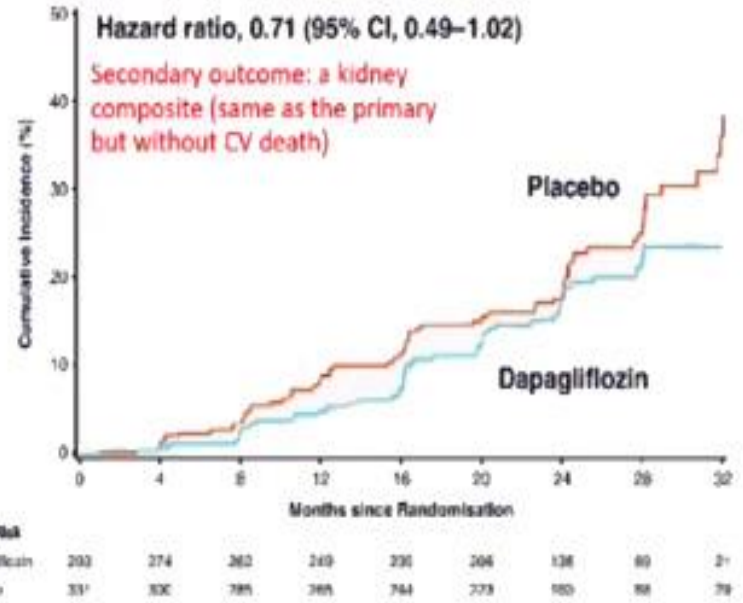
RRR 30%

Kidney composite outcomes = worsening kidney function, end-stage kidney disease, or death from renal or cardiovascular causes

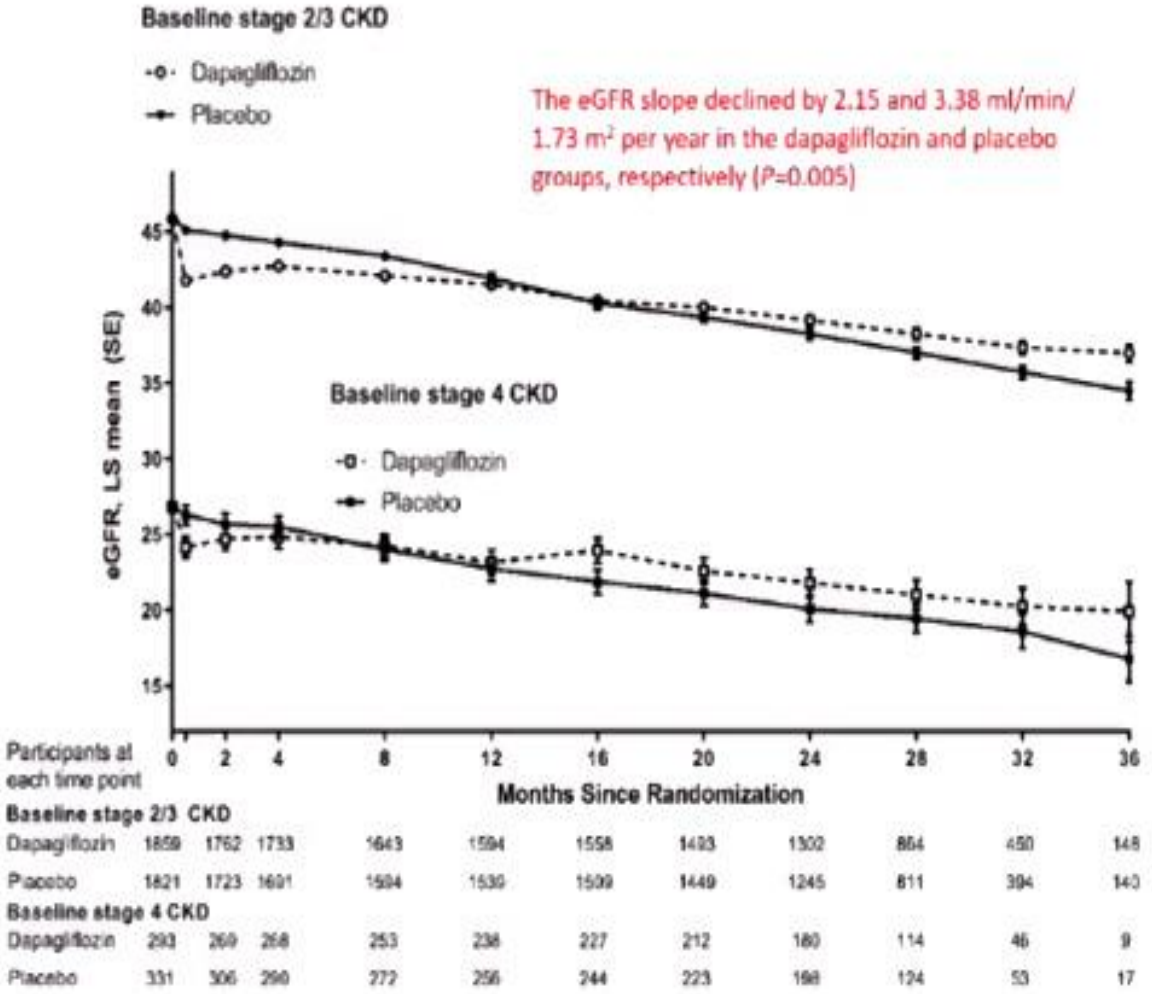
Kaze AD, Cardiovasc Diabetol 2022

Effects of dapagliflozin in stage 4 CKD (DAPA-CKD)





624 participants with stage 4 CKD

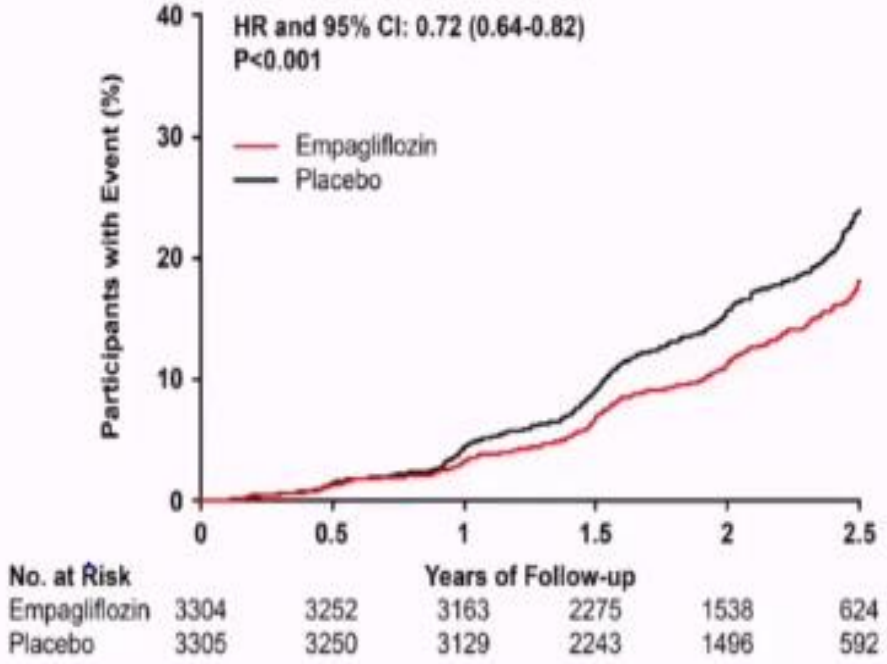


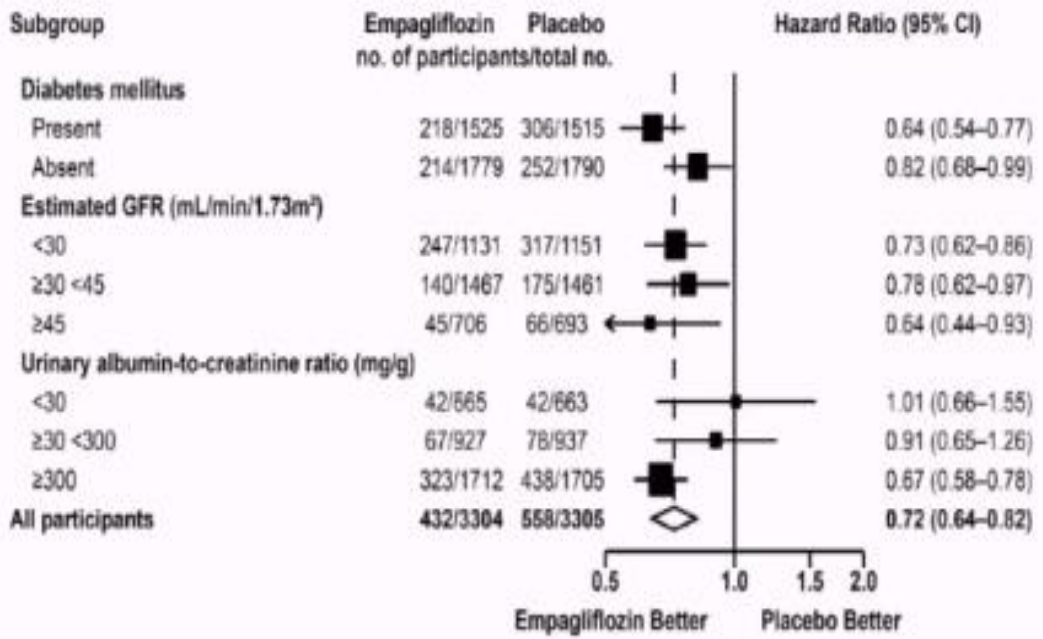
Chertow GM, J Am Soc Nephrol 2021

Empagliflozin in patients with CKD
The EMPA-KIDNEY Collaborative Group

6609 patients underwent randomization; median FU 2.0 years

The primary outcome was a composite of progression of kidney disease (defined as ESKD, a sustained decrease in eGFR to <10 ml/min/1.73 m², a sustained decrease in eGFR of ≥40% from baseline, or death from renal causes) or death from cardiovascular causes

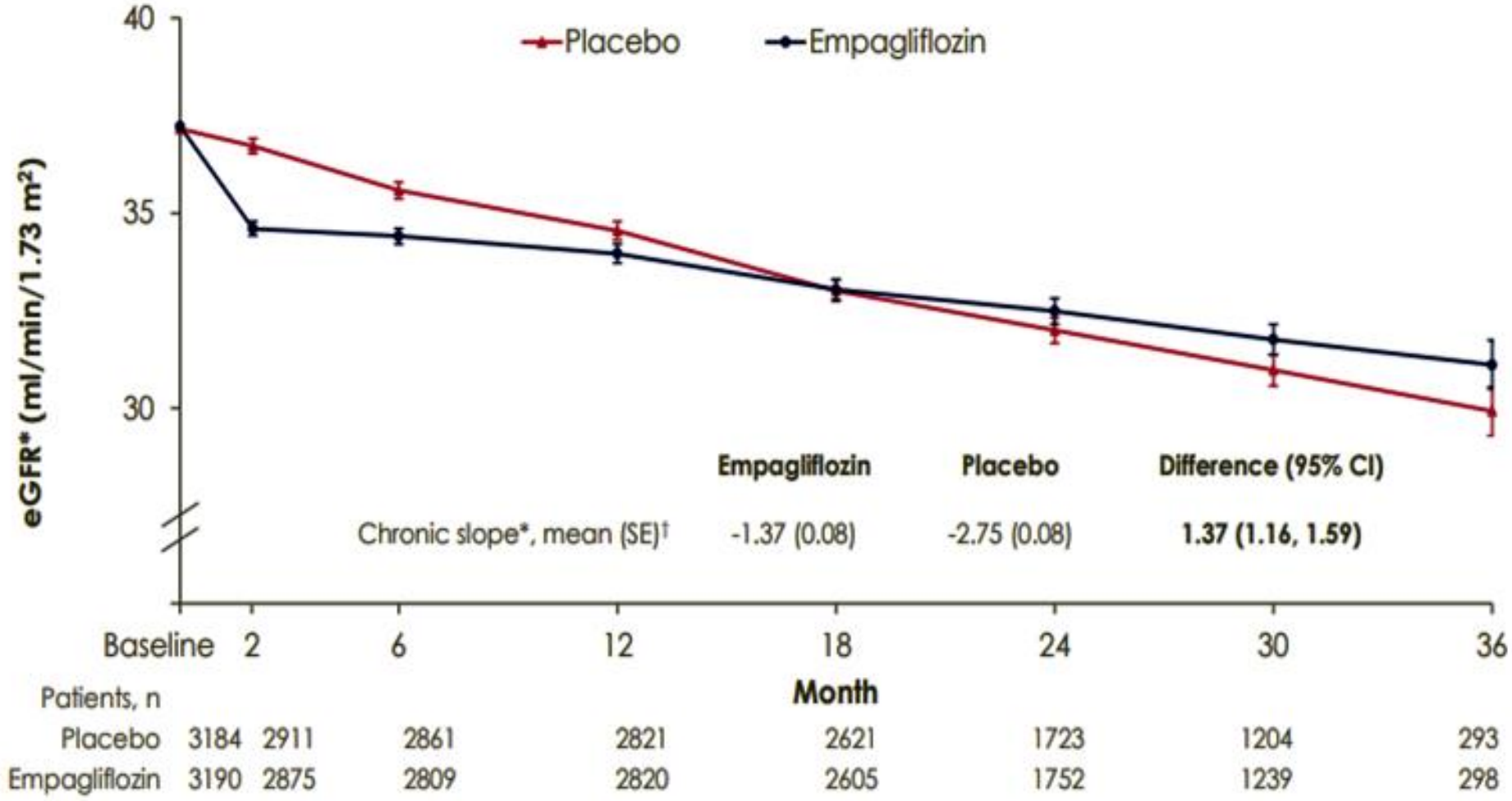




42 fewer primary outcomes per 1000 patients treated for 2 years

The EMPA-KIDNEY Collaborative Group, N Engl J Med 2023

Prespecified tertiary outcome: Annual rate of change in eGFR



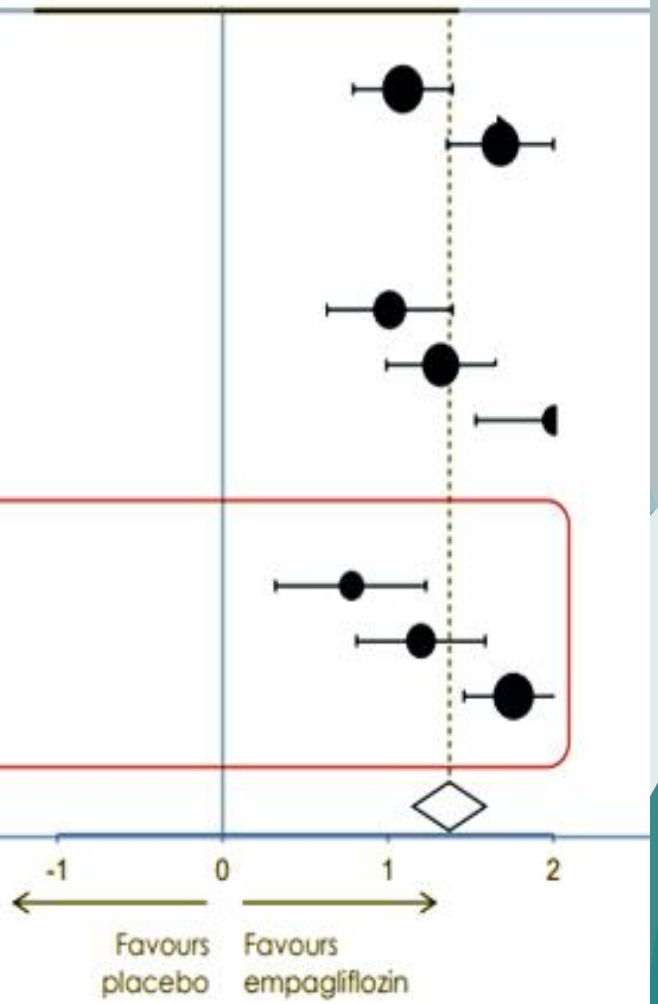
* Referred to as long-term slope in figure 3. Prespecified tertiary outcome included the mean annual rates of change in eGFR in ml/min/1.73 m² per year from baseline to the final follow-up visit (chronic slope, referred to as "Long-term") by treatment allocation were estimated using shared parameter models. For the plot, linear mixed model repeated measures analyses were used to estimate mean eGFR by treatment allocation at each scheduled follow-up visit (prespecified exploratory assessment). *MMRM results over time (adjusted mean, 95% CI); model includes age, sex, diabetes status, UACR, region, treatment by visit interaction, baseline value by visit interaction; †Mean annual rates of change in eGFR from 2 months to the final follow-up visit (chronic slope, referred to as"Long term") by treatment allocation were estimated using shared parameter models.

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; MMRM, mixed model for repeated measures; UACR, urine albumin-to-creatinine ratio.

The EMPA-KIDNEY Collaborative Group. N Engl J Med 2022; DOI: 10.1056/NEJMoa2204233

Annual rate of change in eGFR by key subgroups – Chronic slope

Subgroup	Empagliflozin	Placebo	Absolute difference (95% CI)
	Annual rate of change in eGFR, ml/min/1.73m², mean (SE)		
Diabetes			
No	-1.66 (0.11)	-2.75 (0.11)	1.09 (0.79, 1.39)
Yes	-1.05 (0.12)	-2.73 (0.12)	1.68 (1.36, 2.00)
eGFR, ml/min/1.73m²			
<30	-1.84 (0.14)	-2.85 (0.14)	1.01 (0.63, 1.39)
≥30 to <45	-1.18 (0.12)	-2.50 (0.12)	1.32 (0.99, 1.65)
≥45	-1.58 (0.17)	-3.60 (0.17)	2.01 (1.53, 2.49)
UACR, mg/g			
A1 (<30) normal to mildly increased	-0.11 (0.17)	-0.89 (0.16)	0.78 (0.32, 1.23)
A2 (≥30 to ≤300) moderately increased	-0.49 (0.14)	-1.69 (0.14)	1.20 (0.81, 1.59)
A3 (>300) severely increased	-2.35 (0.11)	-4.11 (0.11)	1.76 (1.46, 2.05)
All participants	**-1.37 (0.08)**	**-2.75 (0.08)**	**1.37 (1.16, 1.59)**



Mean annual rates of change in eGFR from 2 months to the final follow-up visit ('chronic slopes') by treatment allocation were estimated using shared parameter models

eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio.

The EMPA-KIDNEY Collaborative Group. *N Engl J Med* 2022; DOI: 10.1056/NEJMoa2204233

TAKE HOME MESSAGE

Le Gliflozine sono farmaci

- **da utilizzare SEMPRE se non controindicati**
- **add-on alla terapia standard (RAASi) che va ottimizzata e possibilmente non sospesa**
- **non sono gravati dall'effetto di Iperkaliemia**
- **nel pz nefropatico sono sicuri ed efficaci in prevenzione primaria e secondaria**
- **potrebbero essere addirittura i farmaci di prima scelta nel fenotipo non albuminurico ma con declino della funzione renale (Riduzione dello slope e-GFR)**

I BENEFICI DIMOSTRATI A LIVELLO CARDIO RENALE NON HANNO PRECEDENTI NELLA STORIA DELLA MEDICINA NEFRO-CARDIOVASCOLARE!

NON UTILIZZARLI NEL PAZIENTE NEFROPATICO SIGNIFICHEREBBE DAVVERO TOGLIERE AL PAZIENTE UN ARMA «VINCENTE»

LA NOSTRA ESPERIENZA CON DAPAGLIFLOZIN

- 116 Pz (♀ 45 / ♂ 71)
- Età media 74 anni
- e-GFR medio 45 ml/min

- Da gennaio 2022 – Aprile 2023
- e-GFR medio 44 ml/min, sovrapponibile alla perdita fisiologica
- Non aumento dei casi di IVU