L'Insufficienza Renale non è un problema solo nefr

Gennaro Cice

Cardiologist Consultant IRCCS San Raffaele Roma
Cardiologist Consultant Fresenius Medical Care, Bad Homburg,Dh

PLACE 2026
Roma, 25-27 giugno 2026

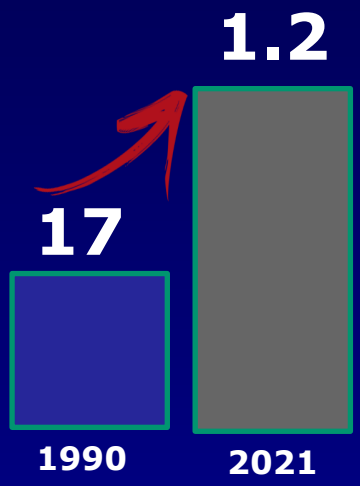
Renal Failure isn't a nephrologist problem!!

G. Cice

EPIDEMIOLOGY AND BURDEN OF CKD

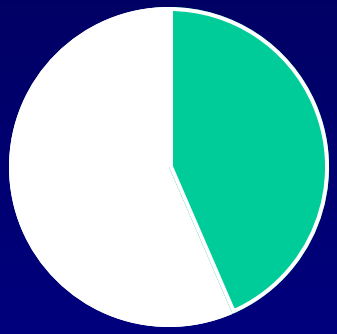
ESTIMATED PREVALENCE OF CKD GLOBALLY 9%

CKD RANK (GLOBAL DEATHS)



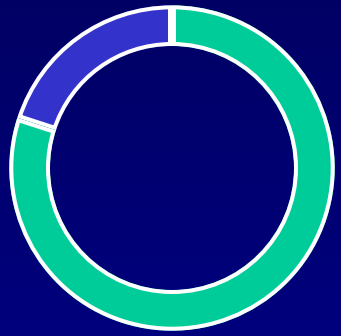
LEADING CAUSE OF CKD

43,5%DIABETES



UNDIAGNOSED CKD

80-90%

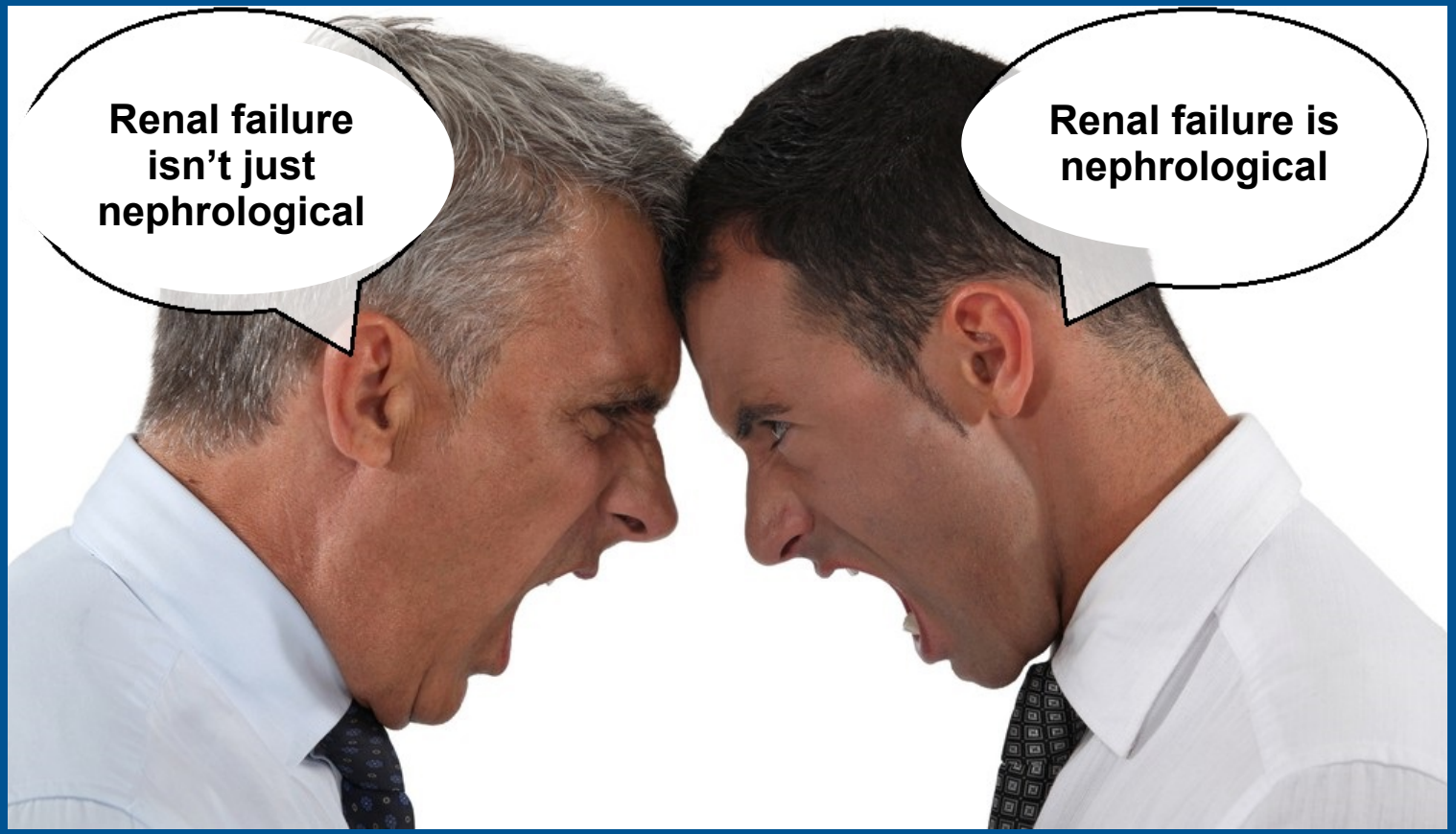


MORTALITY 1,600 million/YEAR
45.8 million disability-CKD

K-DIGO, IMPROVING GLOBAL OUTCOMES, KIDNEY INT., 2024

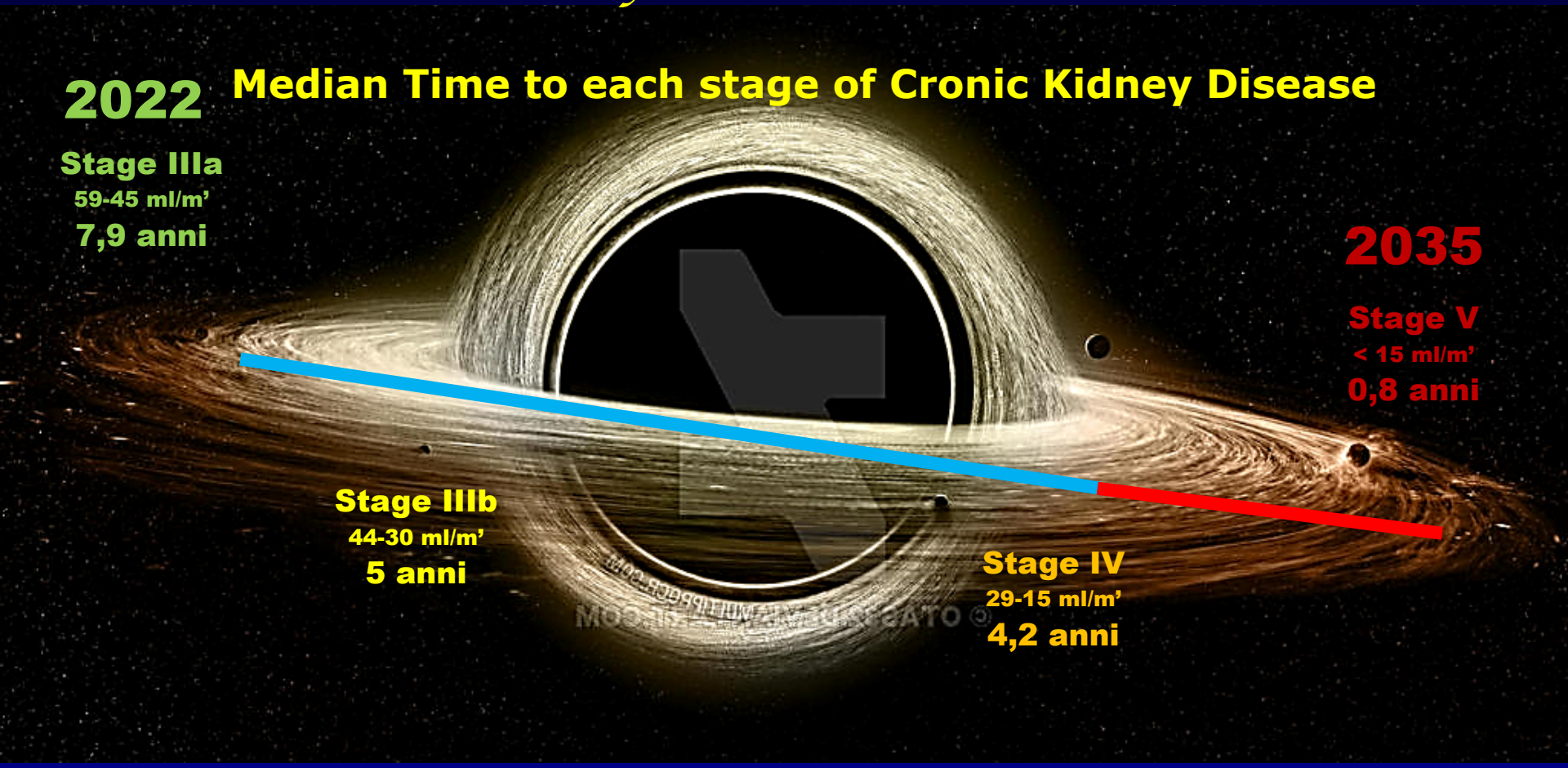
The Cardiologist chats amiably with the Nephrologist:

renal failure isn't just a nephrologist's problem !!



G. Cice

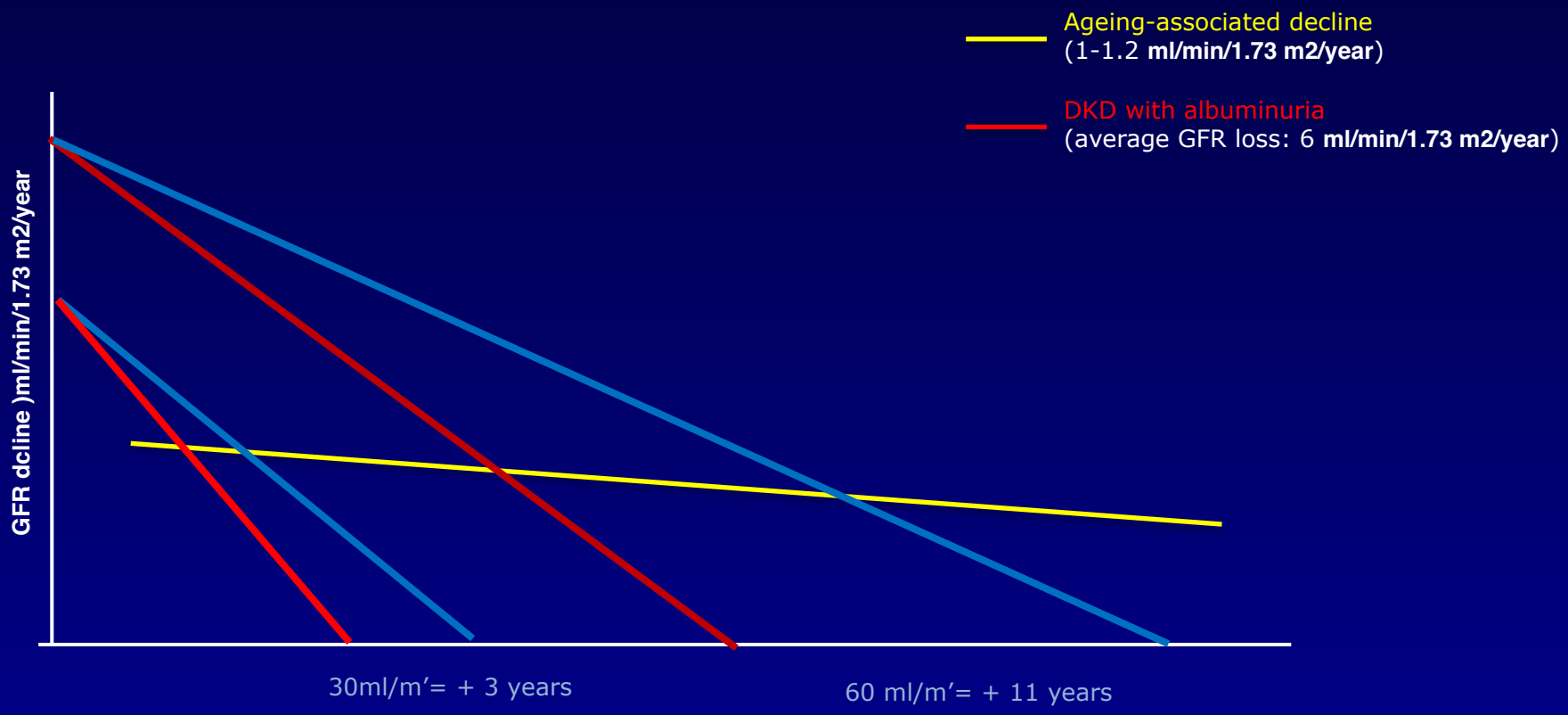
Renal Failure isn't just a nephrologist's problem



G. Cice modified from Go As et al. Ciculation 2019, 119: 1363-9

CHANGES IN eGFR SLOPE OVER TIME BY TIME OF INTERVENTION

Early identification of CKD has the potential to reverse, delay or prevent progression of disease



adapted from Gohda T, Int j Mol Sci, 2022 - K-DIGO, IMPROVING GLOBAL OUTCOMES, Kidney International, 2024

Renal Failure isn't just a nephrologist problem:

things to know about CKD

1) How to evaluate renal function ?
2) Who are uremic patients ?
3) Cardiovascular risk and CKD!!
4) How to slow down the filtrate's fall ??
5) What to do, what to use !!
6) Renal mechanism of action

Take home message !!

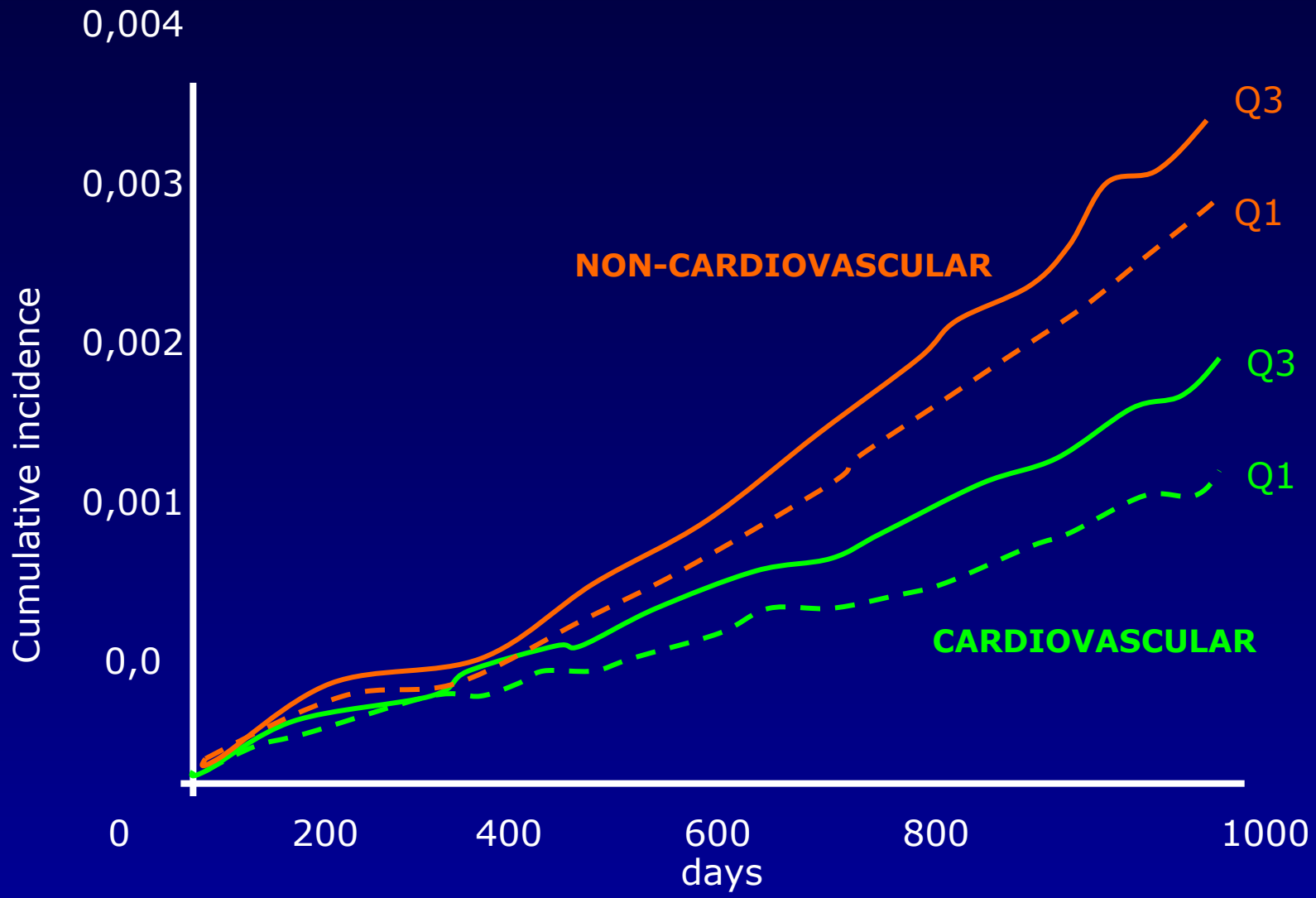
CHONIC KIDNEY DISESE

on the necessity and the limits of classifiction:
Just as orthodoxy requires critique!!

STAGE	DESCIPTION	eGFR (ml/min/1.73 m2)	
1	KIDNEY DAMAGE WITH NORMAL FUNCTION	>90	Urinary markers AlbU/ ProtU
2	KIDNEY DAMAGE WITH MILD DECREASE OF FUNCTION	60-89	
3	MODERATE DECREASE OF FUNCTION	30-59	
4	SEVERE DECREASE OF FUNCTION	15-29	
5	END STAGE RENAL DISEASE	<15 or dialysis	

G. Cice

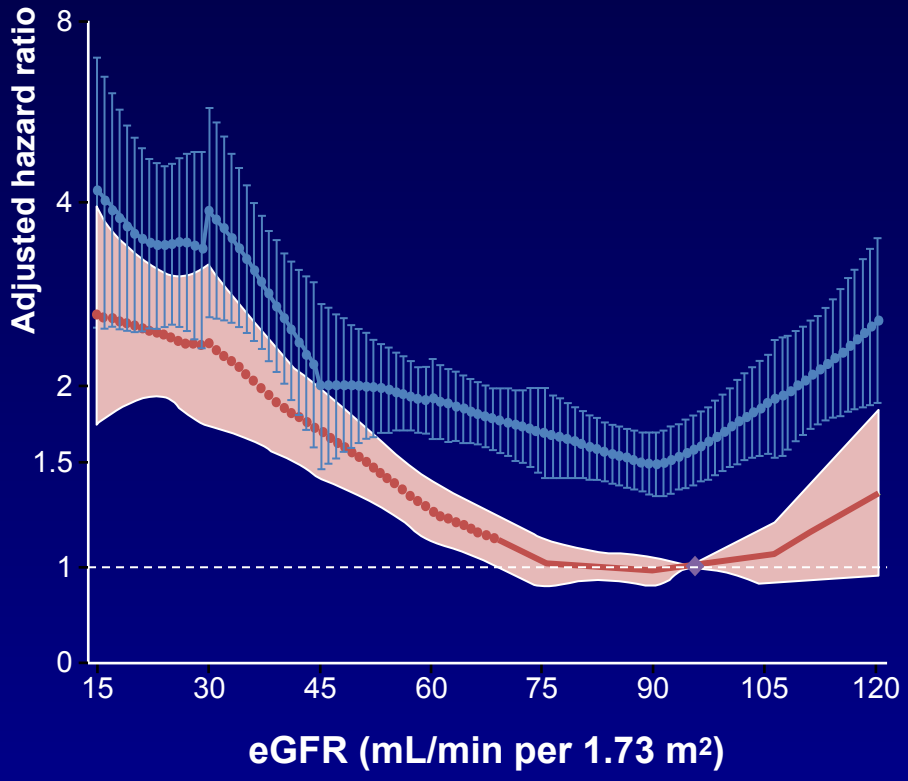
micro Albuminuria
eAER: 30-300 mg/die or UACR: 30-300 mg/g
predicts CV and non CV death
in the normal population



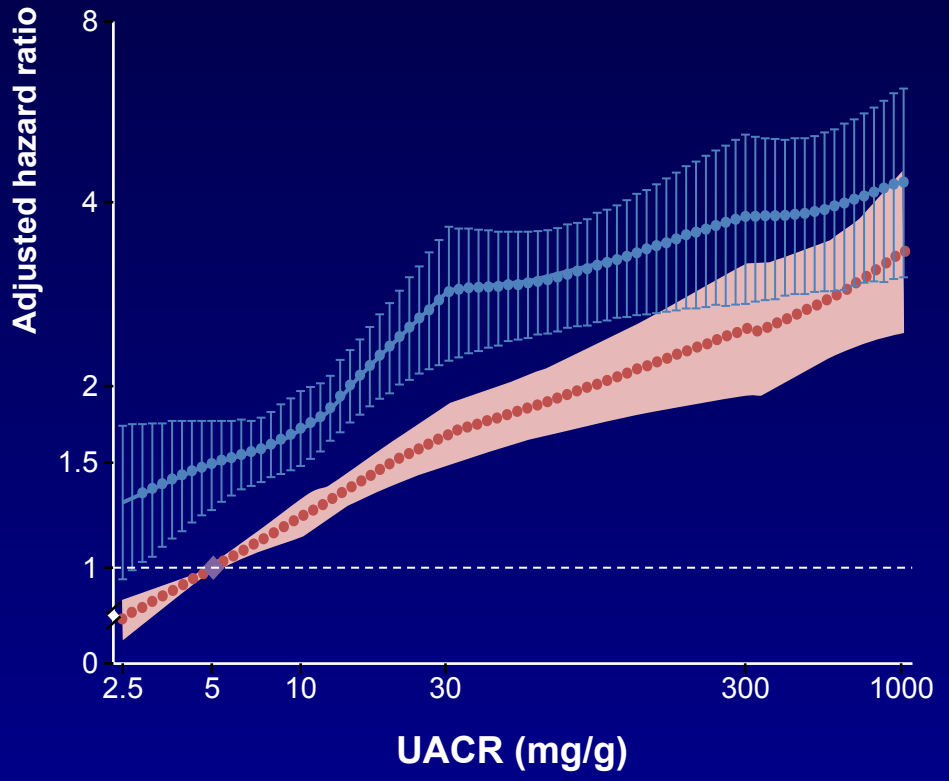
Kidney Disease Improving Global Outcames 2024

IMPACT OF eGFR AND ALBUMINURIA ON CV MORTALITY IN PATIENTS WITH CKD

CV mortality according to eGFR in participants with and without diabetes



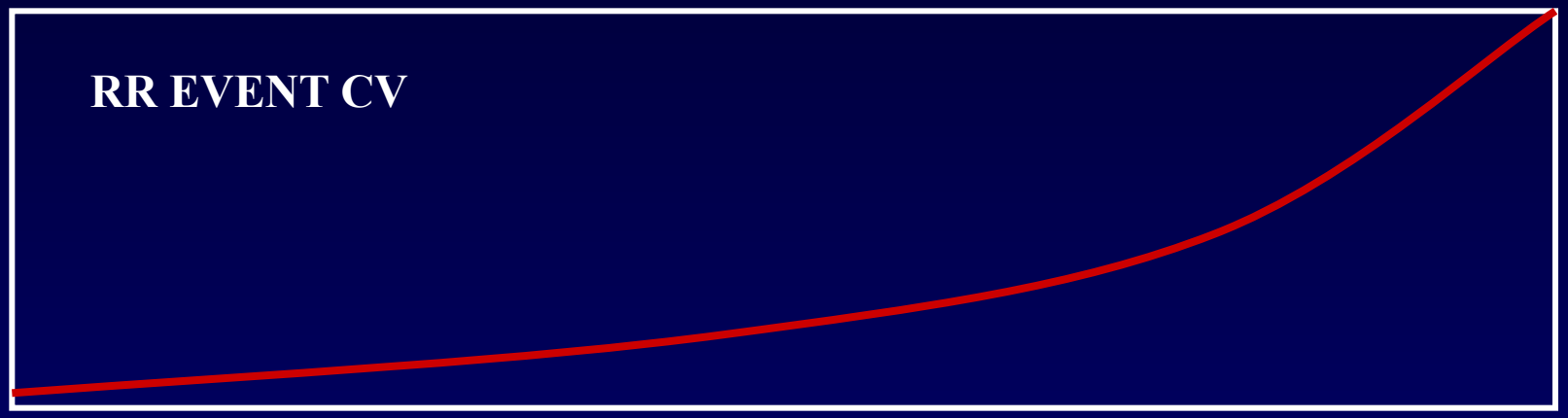
CV mortality according to UACR in participants with and without diabetes

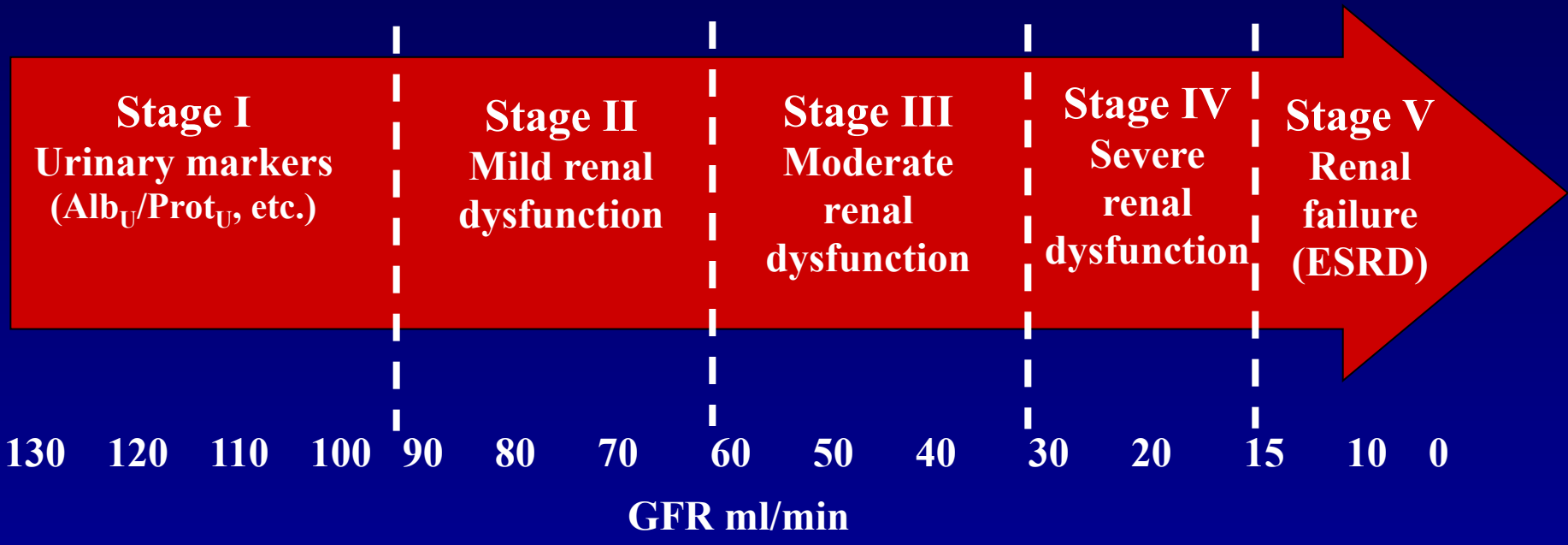


Diabetes Non-diabetes

Fox CS, et al. Lancet 2012;380:1662–1674

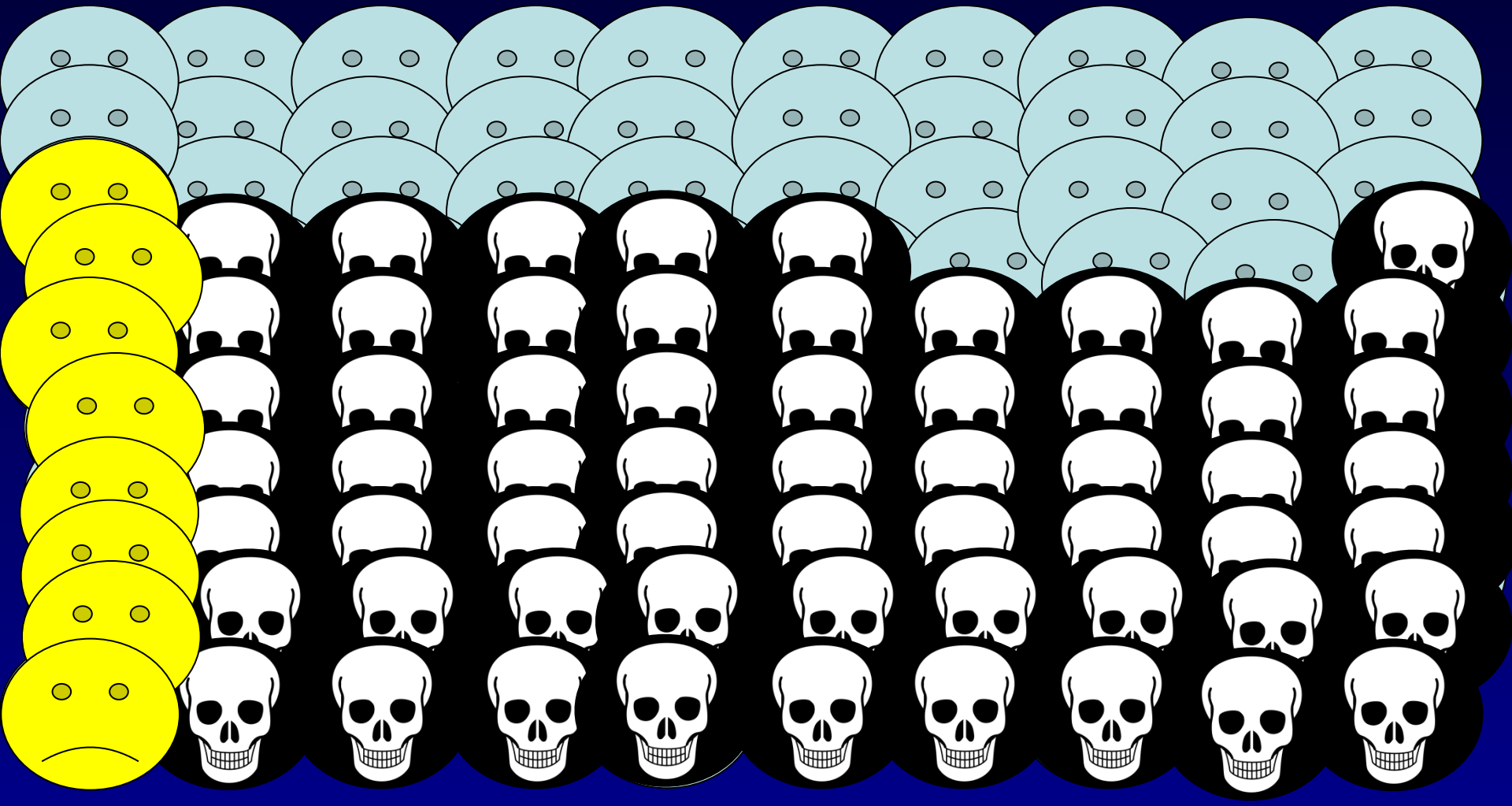
CKD AND CARDIOVASCULAR RISK





Foley RN, Am J Kidney Dis, 1998

CKD: TO RRT OR TO DEATH

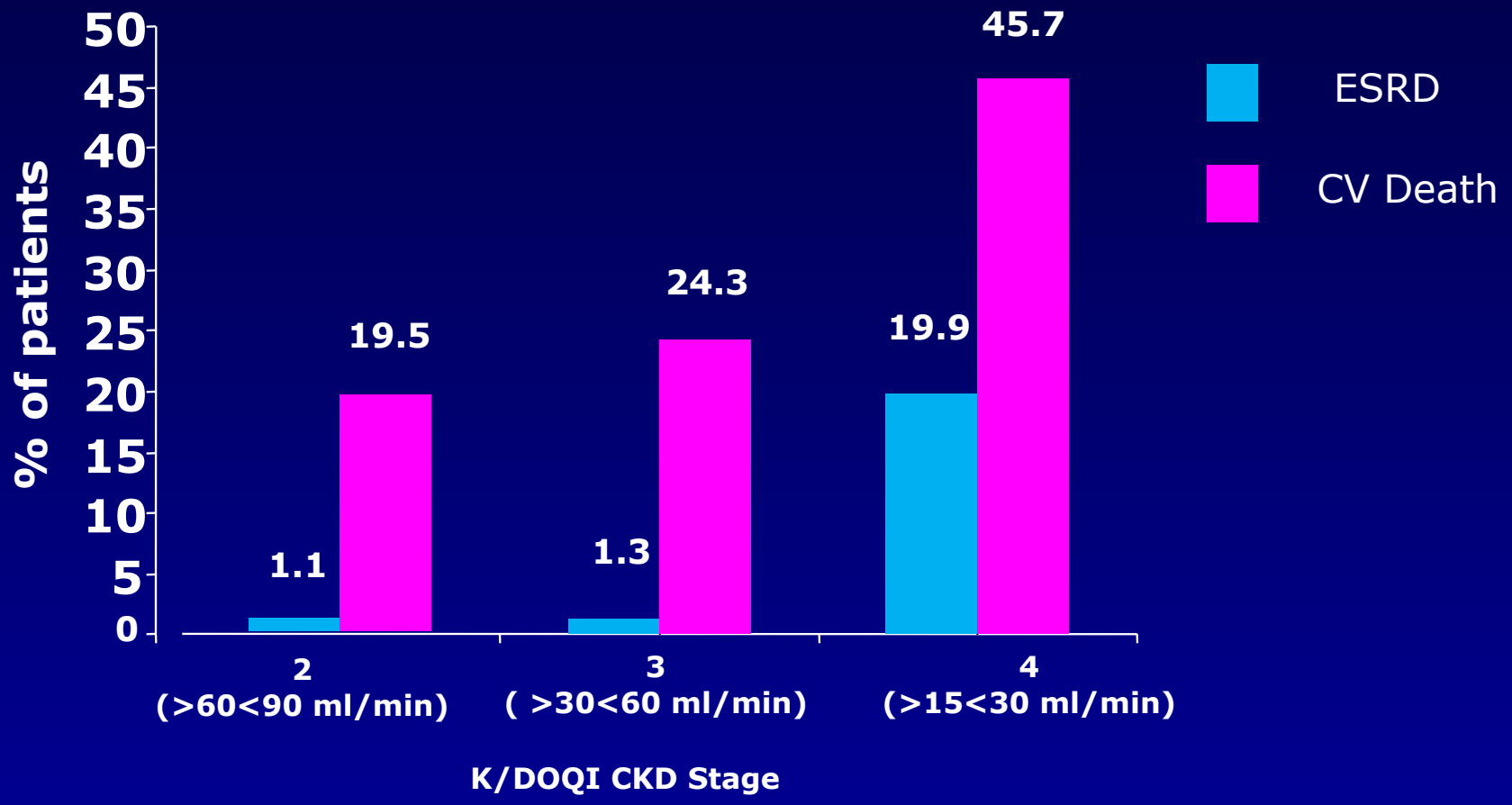


Tuesday morning 10 years later: 8 patients need RRT,

65 patients have died from CV deaths, 27 have ongoing CKD

CARDIOVASCULAR DEATH OCCOURS BEFORE OF ESRD

27.998 CKD patients. FU 66 months



Keith DS et al, Arch Intern Med 2004

Renal Failure isn't just a nephrologist's problem?

G. Cice

EFFECTIVE APPROACHES TO CKD PATIENTS
(until the end of 2020)

Slow the progression toward ESRD by controlling the underlyng renal disease and factor contributing to decline of renal function such hypertension, dyslipidemia,diabetes

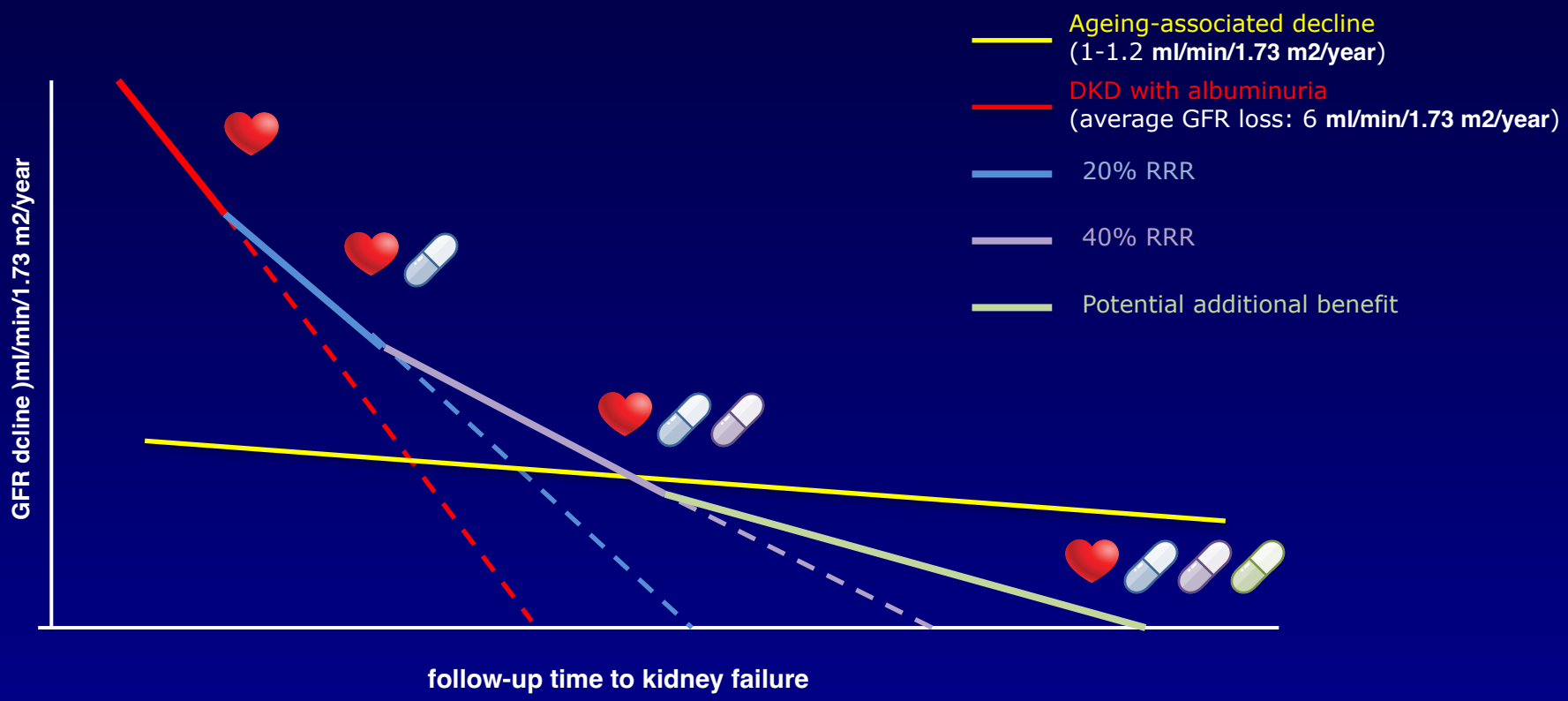
Dicreased sodium intake may enhance the Renoprotective effect of RAASI

Glicemic Control in preventing the developpement microvascular complication

Other strategies include correcting chronic metabolic acidosis, following low protein diets, avoiding potential nephrotoxin such as nonsteroidal anti-inflammatories and Io-contrast, checking the calcium phosphorus balance,lower uric acid

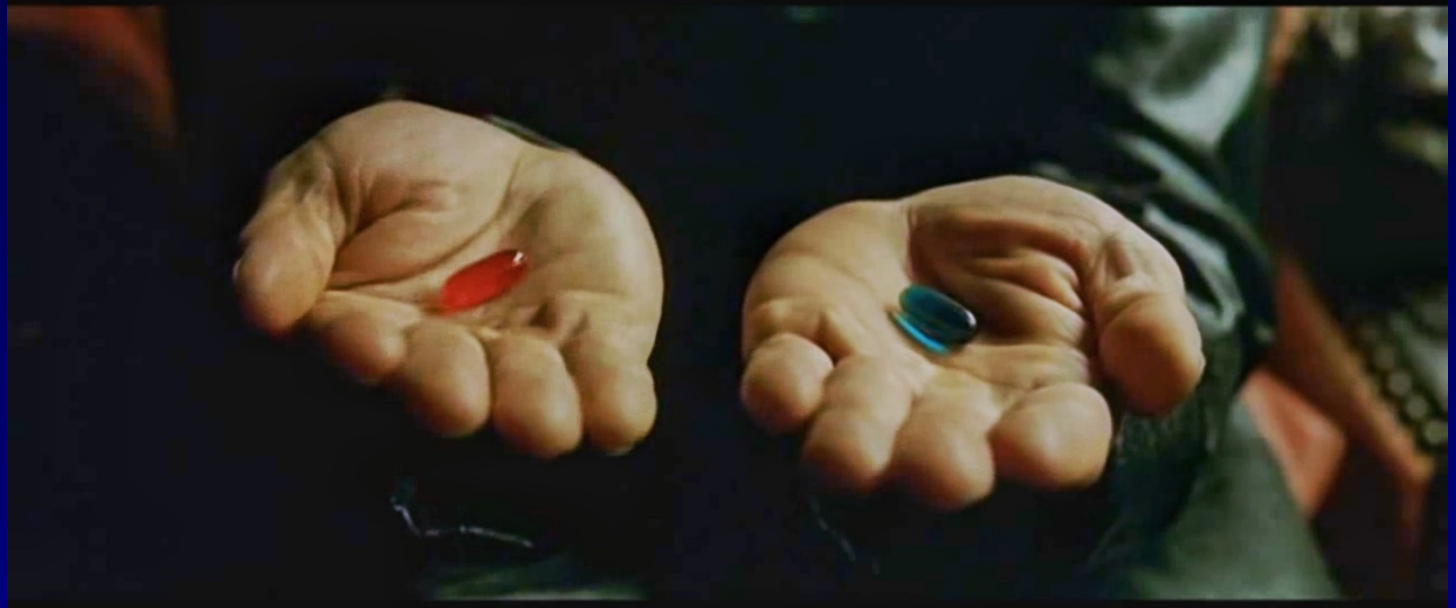
KDIGO –G. L.- Kidney Int. 2020
hen T N.K. Found. AJKD 2021
Appel L. N Engl.J. Med 2010
Hirsh JS Kidney Int: 2020
Wang L. Am. J. Neprol. 2020
Saran R US Renal Data S. 2019

EXPANDING THE THERAPY OPTIONS FOR CHRONIC KIDNEY DISEASE



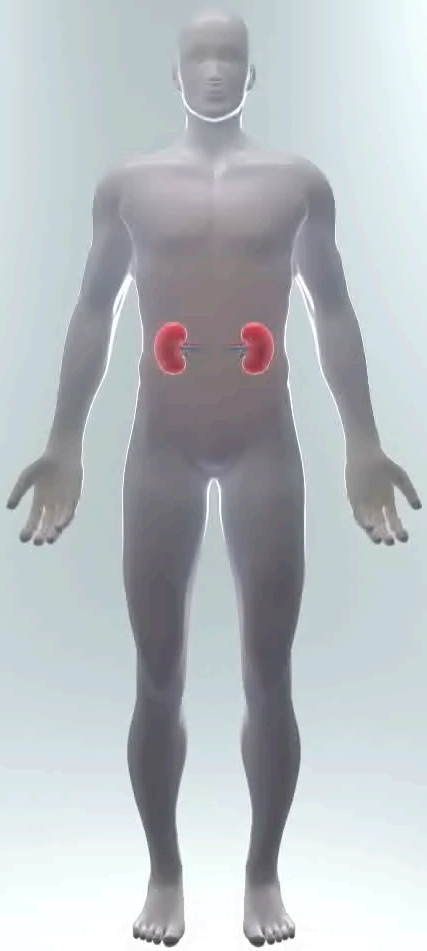
K-DIGO, IMPROVING GLOBAL OUTCOMES, 2024

Why do SGLT2i slow down the GFR decline and others antidiabetic don't?



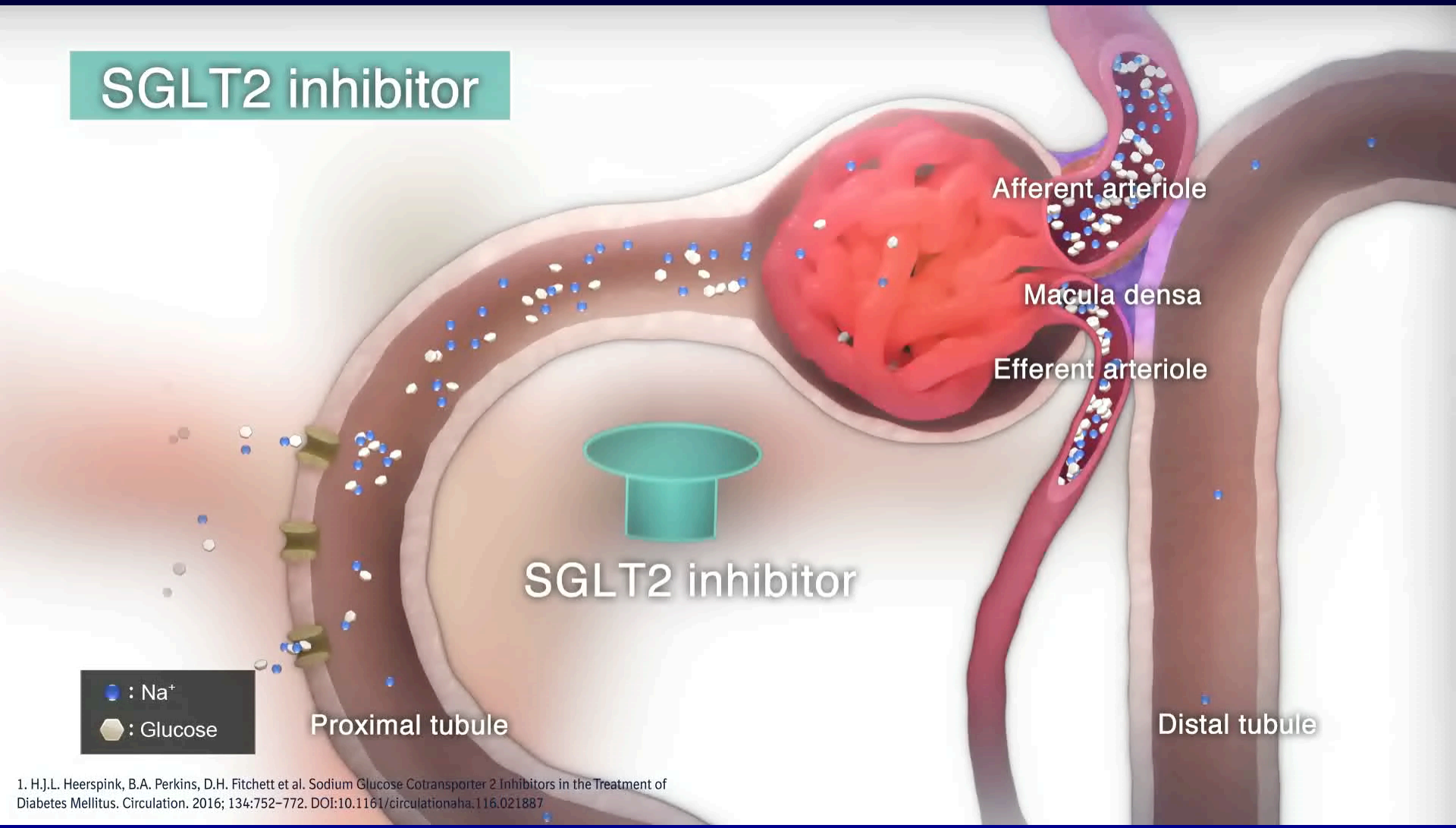
Regulatory mechanisms of glomerular blood flow!


3FX



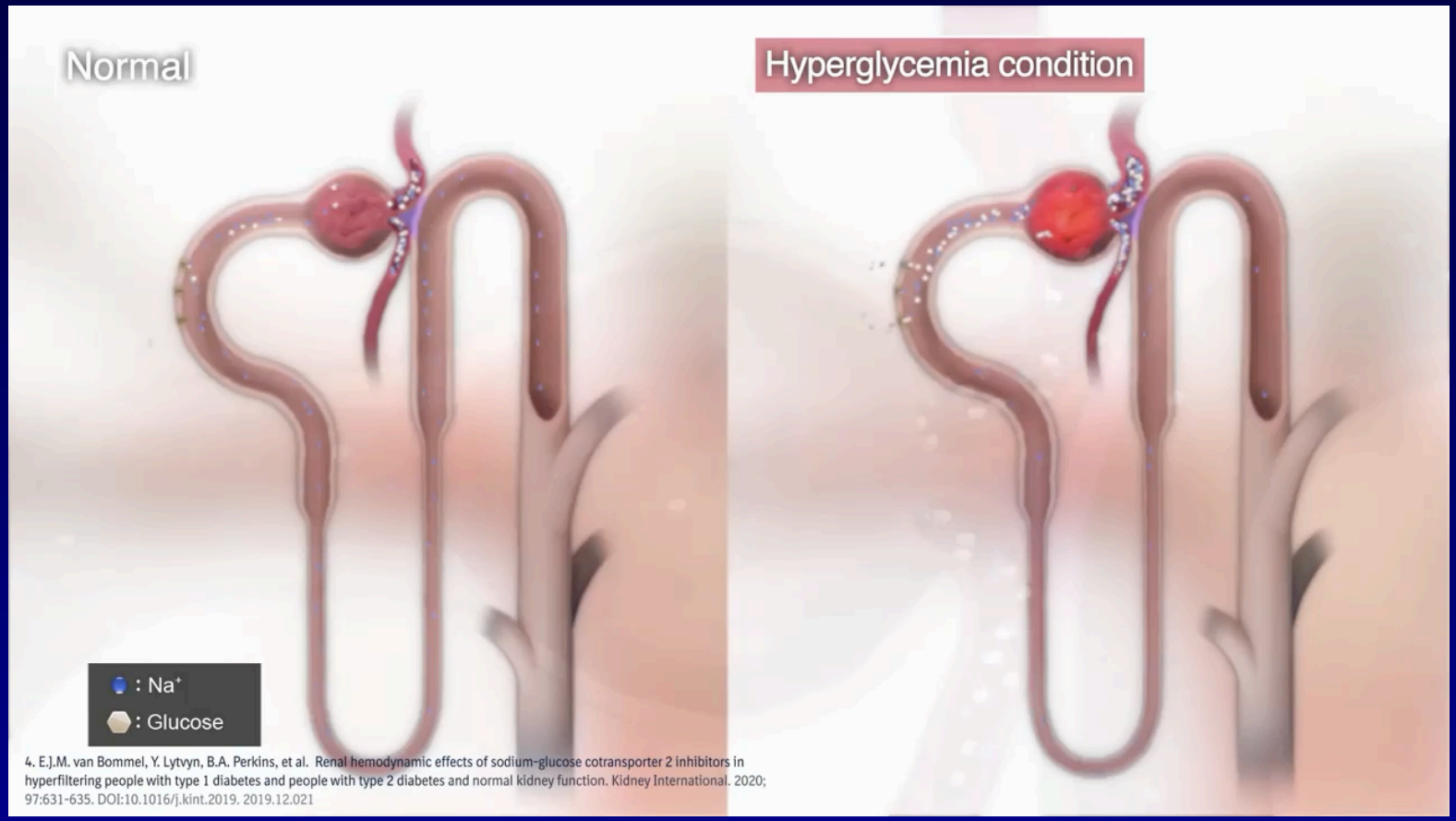
1. H.J.L. Heerspink, B.A. Perkins, D.H. Fitchett et al. Sodium Glucose Cotransporter 2 Inhibitors in the Treatment of Diabetes Mellitus. Circulation. 2016; 134:752–772. DOI:10.1161/circulationaha.116.021887

SGLT2 inhibitor



1. H.J.L. Heerspink, B.A. Perkins, D.H. Fitchett et al. Sodium Glucose Cotransporter 2 Inhibitors in the Treatment of Diabetes Mellitus. Circulation. 2016; 134:752–772. DOI:10.1161/circulationaha.116.021887

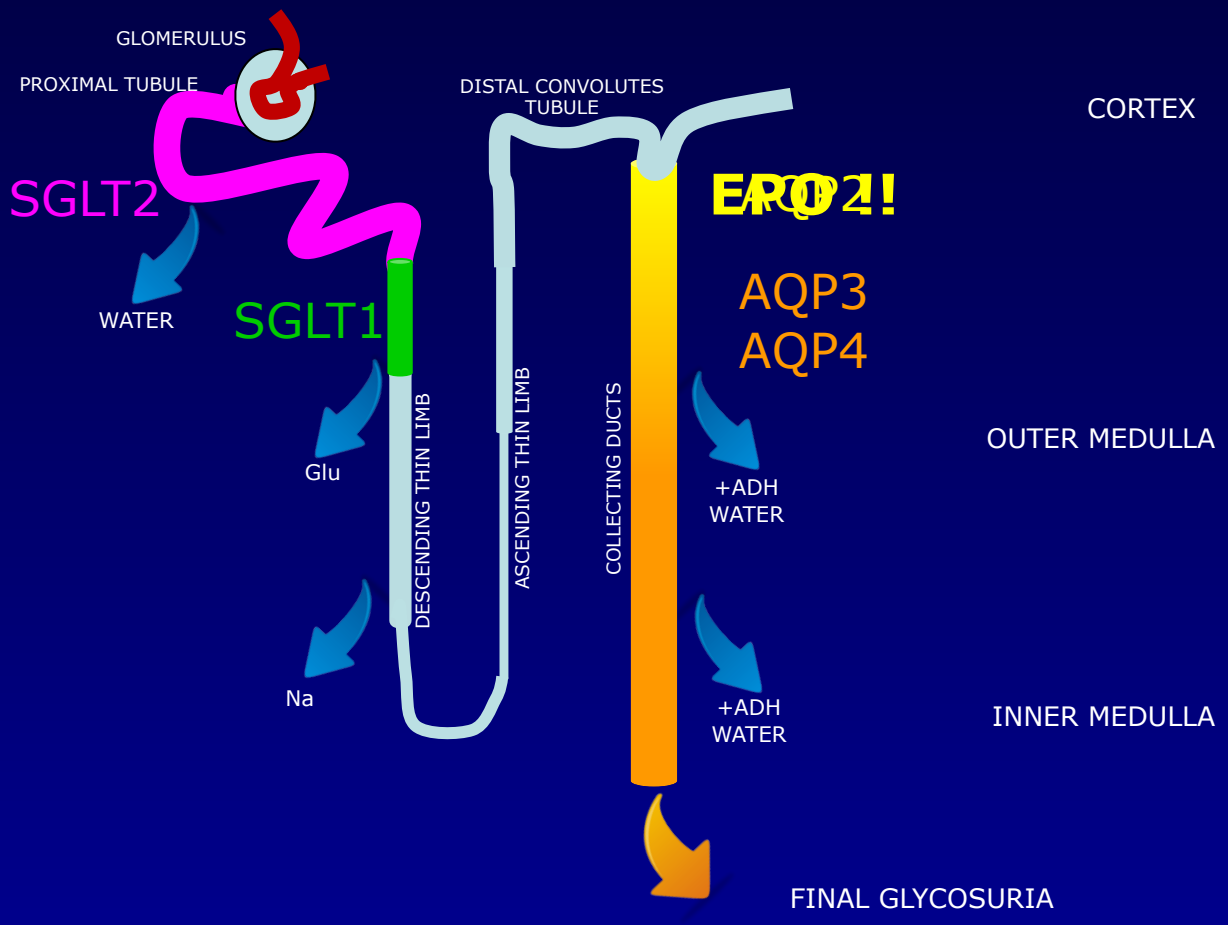
SGLT2-i and acute eGFR decrease…then it works !



4. E.J.M. van Bommel, Y. Lytvyn, B.A. Perkins, et al. Renal hemodynamic effects of sodium-glucose cotransporter 2 inhibitors in hyperfiltering people with type 1 diabetes and people with type 2 diabetes and normal kidney function. Kidney International. 2020; 97:631-635. DOI:10.1016/j.kint.2019. 2019.12.021

G. Cice

SGLT-2 inhibitor: DOPING ??

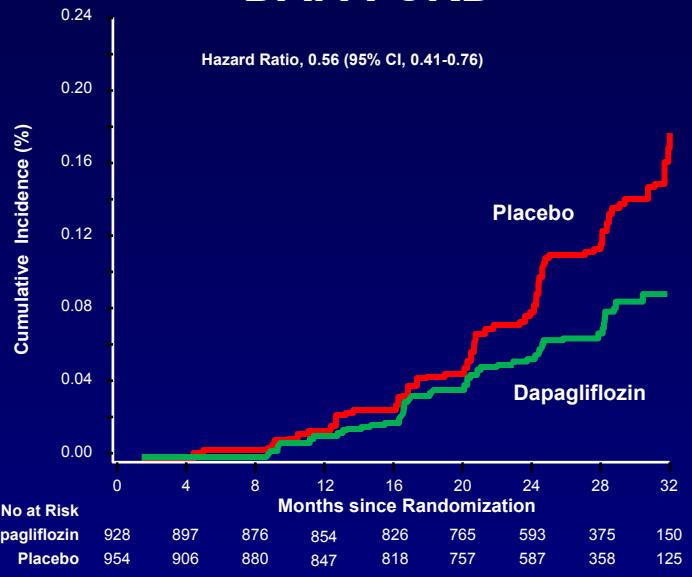


G. Cice

RENAL COMPOSITE OUTCOME

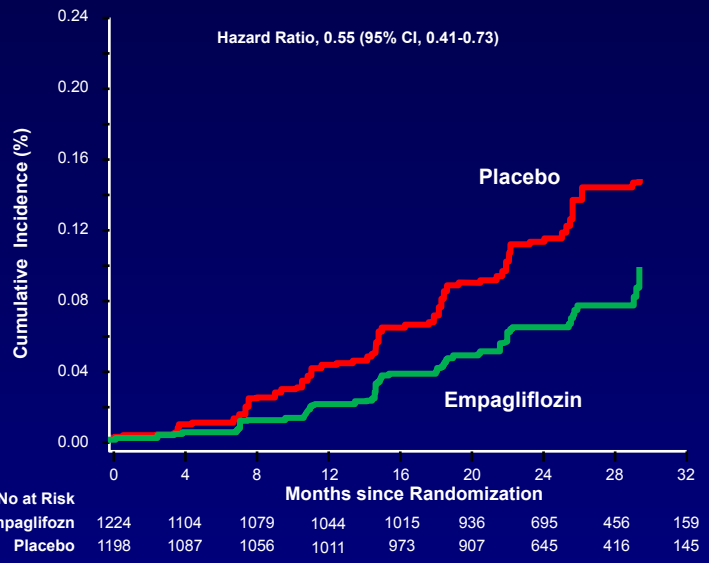
KIDNEY DISEASE PROGRESSION or CV DEATH

DAPA-CKD



No at Risk									
Dapagliflozin	928	897	876	854	826	765	593	375	150
Placebo	954	906	880	847	818	757	587	358	125

EMPA-KIDNEY



No at Risk									
Empaglifozn	1224	1104	1079	1044	1015	936	695	456	159
Placebo	1198	1087	1056	1011	973	907	645	416	145

p-interaction=0.95

[a]Sustained ≥50% eGFR decline, ESKD, or renal death;

eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease.

1. Heerspiink HJL, Stefansson BV, Correa Rotter R, et al. Dapaglifozin in patients with Chronic Kidney Disease. N Engl J Med; 2020:. 8; 383(15): 1436-1446
2. Herrington WG, Staplin N, Wanner c, et al. . Empaglifozin in patients with Chronic Kidney Disease. N Engl J Med. 2023; 388: 117-127.

What to do to slow GFR decline:

CKD is a predominantly cardiologic and internal medicine syndrome due to the cardiac mortality it cause

Slowing the decline of CKD means reducing the incidence of new cardiovascular events

Test:

Serum creatinine for kidney function : eGFR

Albuminuria for kidney damage : UACR

Glycemic Control : HbA1c < 7-6,5% for all ??

Dyslipidemic Control: C-LDC target <100 mg/dl ??

Blood Pressure Control : 130/80 mmhg…for everyone ?

Cornerstone for albuminuria : ACEi/Arb/Aliskiren and SGLT2i !!!

Standard of cure :


Thanks for your attention!
The Speaker's suits are tailor-made
and his exclusive property!

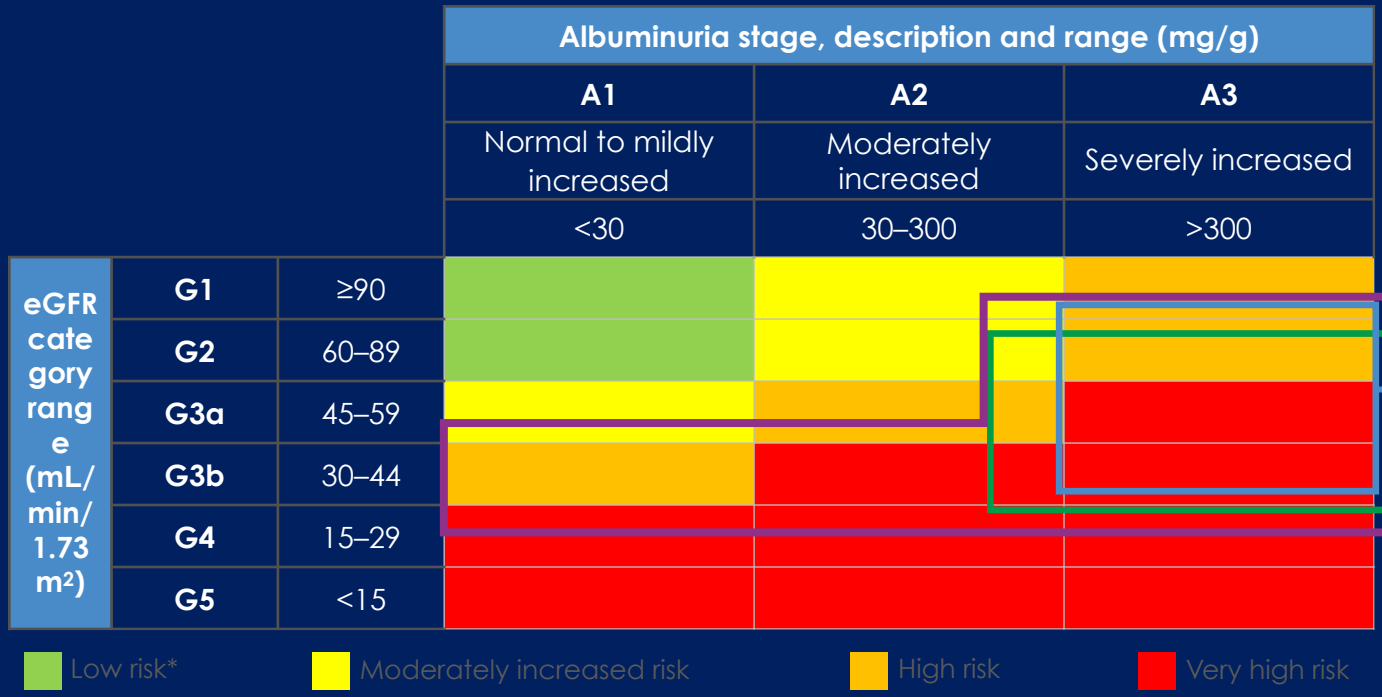
SELECT OUCOMES FROM THE DAPA-CKD AND EMPA KIDNEY TRIALS

OUTCOME		DAPA-CKD N=4304	EMPA-KIDNEY N=6609
PRIMARY ENDPOINT			
DAPA-CKD Composite of≥50% sustained eGFR decline, ESKD (dialisys/ transplantation/ sustained eGFR decline<15), renal or CV death	**EMPA-Kidney** Composite of 40% sustained eGFR decline, ESKD (dialisys/ transplantation/ sustained eGFR decline<10), renal or CV death	✓ 39% RRR NNT=19	✓ 28%RRR NNT=27
KEY SECONDARY ENDPOINTS			
ALL-CAUSE DEATH		✓ 31% RRR	✗ 13%RRR
COMPOSITE OF CV DEATH OR hHF		✓ 29% RRR	✗ 16%RRR

G. Cice

EMPA-KIDNEY enrolled a CKD population with a broad range of eGFR, with and without albuminuria[1]

Prognosis of CKD by eGFR and albuminuria categories[2]



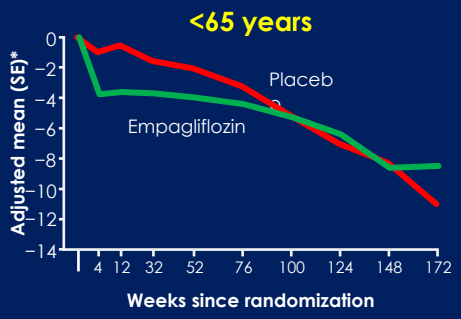
EMPA-KIDNEY population[1]
Patients with or without diabetes and eGFR ≥45 to <90 mL/min/1.73m² **and** UACR ≥200 mg/g
or
eGFR ≥20 to <45 mL/min/1.73m²

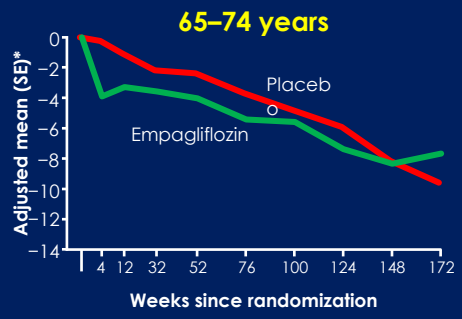
CREDENCE population[3]
Patients with T2D and CKD and eGFR ≥30 to <90 mL/min/1.73m² **and** UACR >300 mg/g

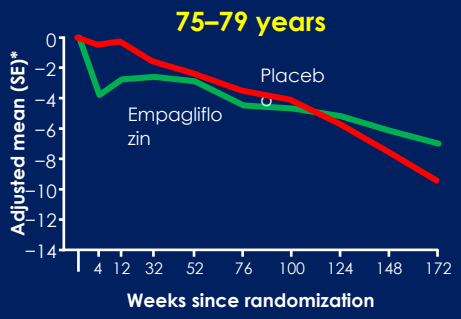
DAPA-CKD population[4]
Patients with or without T2D and eGFR ≥25 to ≤75 mL/min/1.73m² **and** UACR ≥200 mg/g

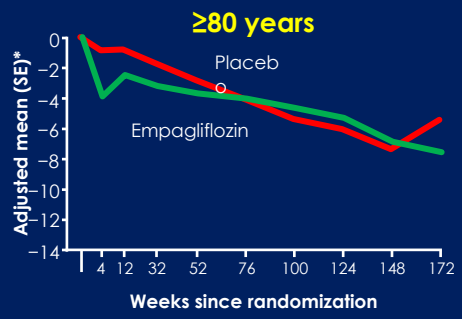
G. Cice

EMPEROR-PRESERVED: EFFECT OF EMPAGLIFLOZIN ON THE MEAN CHANGE IN EGFR FROM BASELINE BY AGE









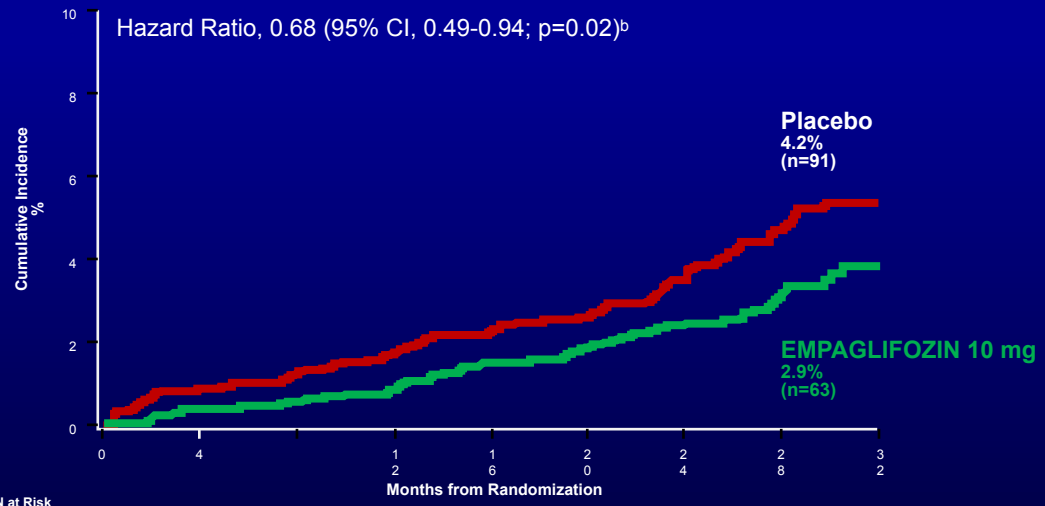
INTERACTION *P*-VALUE AT WEEK 52:
P=0.10

*The eGFR adjusted mean differences (mL/1.73m²/year)
eGFR, estimated glomerular filtration rate; SE, standard error.

Böhm M *et al. J Am Coll Cardiol.* 2022;80:1.

CUMULATIVE INCIDENCE OF AKI

[a]Pre-specified exploratory endpoint. Defined as doubling of serum creatinine



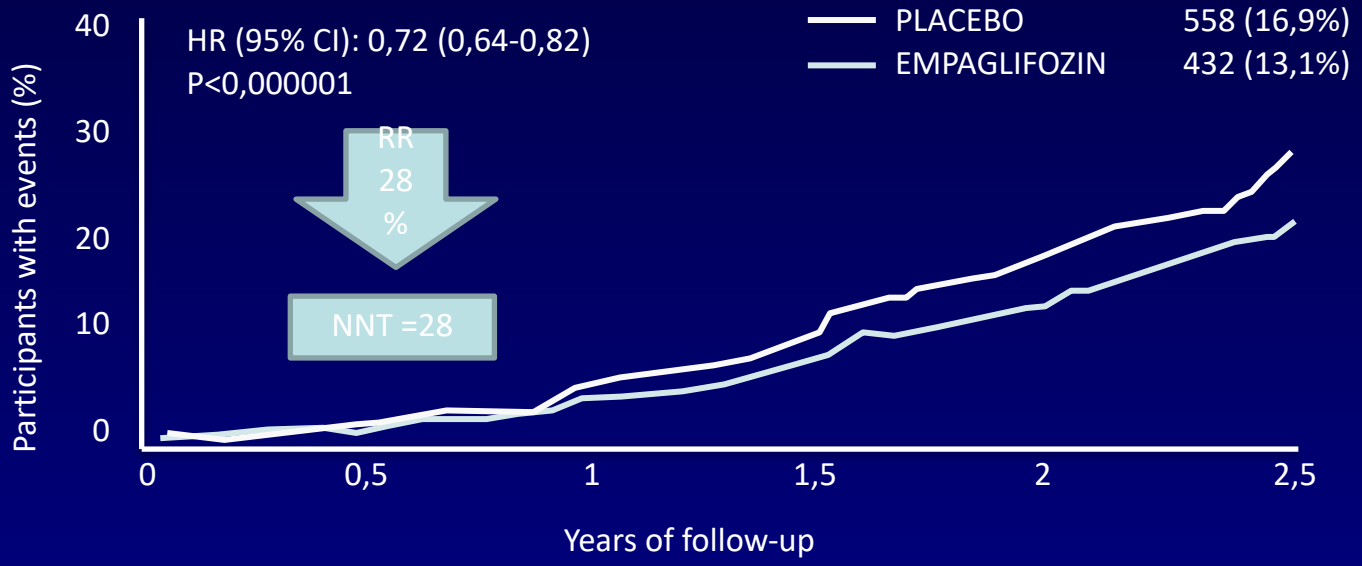
[b]Subdistribution HR, 0.69; 95% CI, 0.50 to 0.95; p=0.02 using the Fine-Gray model which accounted for the competing risk of death.
AKI = acute kidney injury; CI = confidence interval.

EMP-KIDNEY COLLBORTIVE GROUP, New Eng J Med 2022l

G. Cice

EMPA-KIDNEY

PRIMARY COMPOSITE OUTCOME: KIDNEY DISEASE PROGRESSION OR CV DEATH



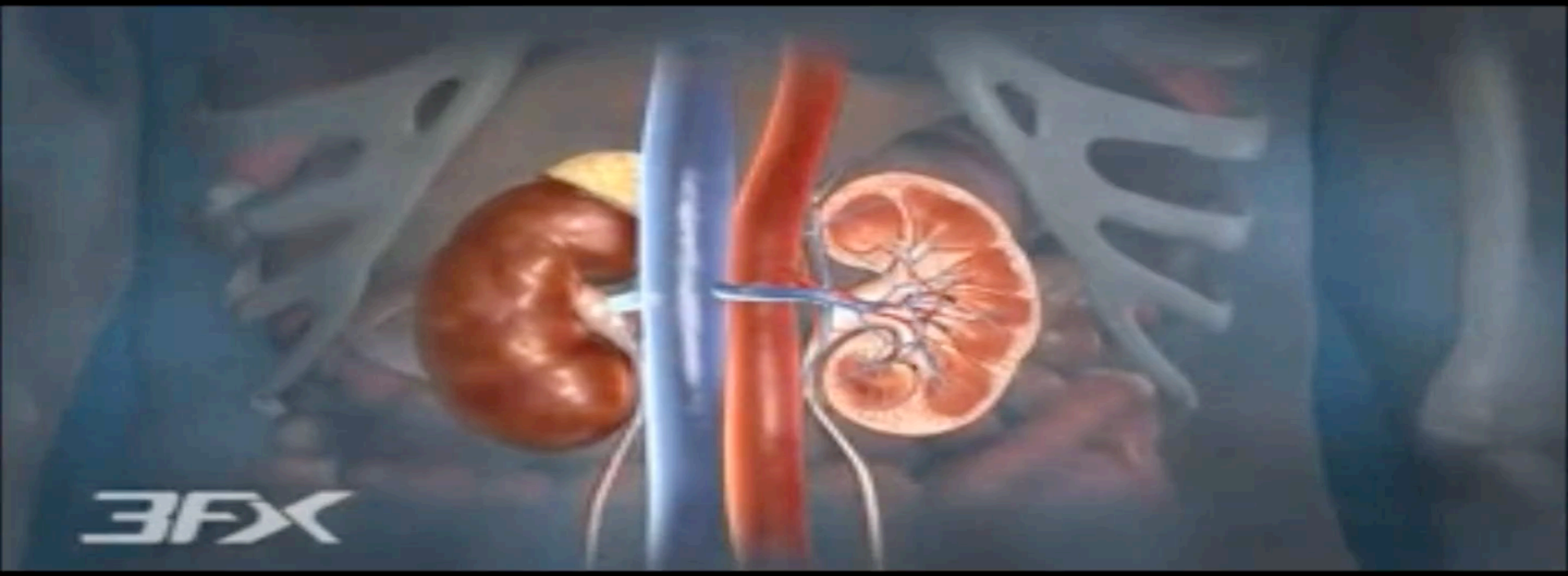
STUDY POPULATION

PLACEBO	3305
EMPAGLIFOZIN	3304

LARGEST TRIAL EVER WITH RENAL ENDPOINT

G. Cice

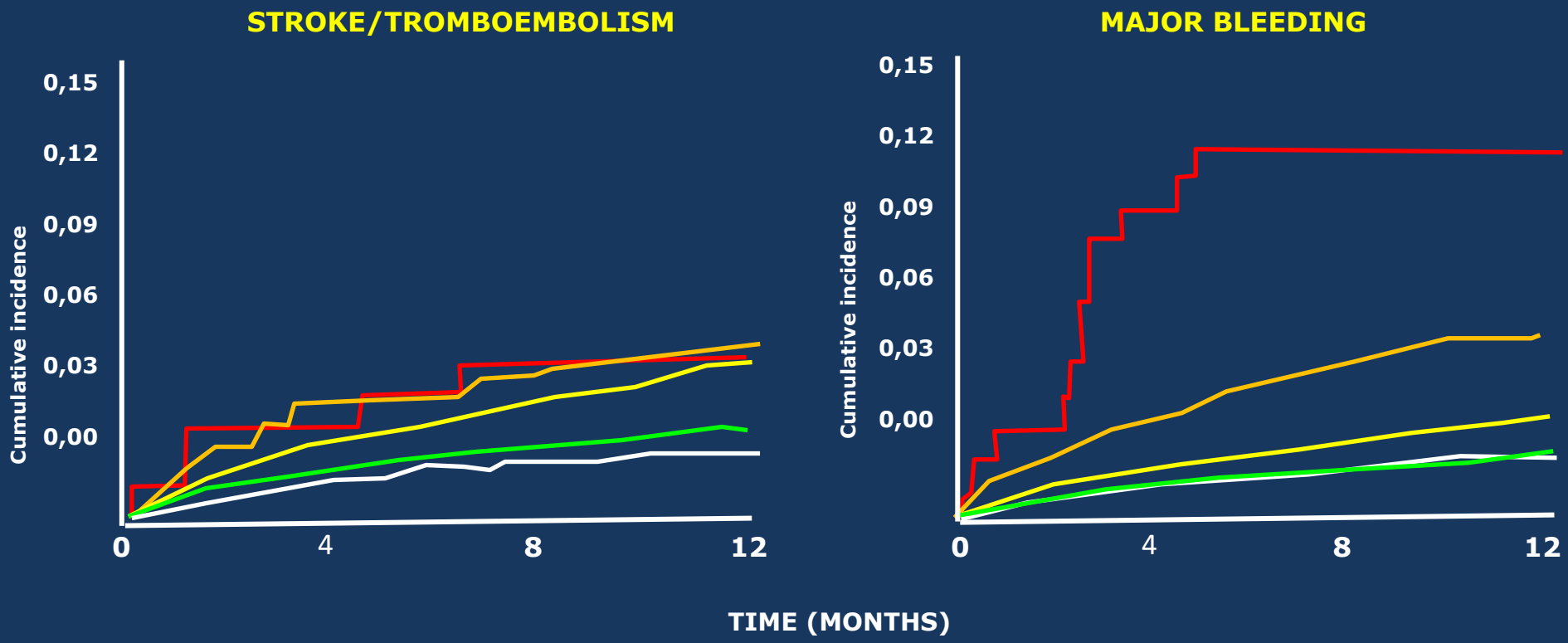
RENAL FAILURE EVALUATION



The Inulin (or Iotalamato, PAI) Clearance !!
Creatinine ? Inverse exponential relationship with GFR !!
Creatinine-Based Approximation of GFR !!??
Cockroft-Gault formula
MDRD formula
CKD-EPI formula

European Kidney Function Consortium Equation

ATRIAL FIBRILLATION: RENAL FUNCTION AND THE RISK OF STROKE/TROMBOEMBOLISM AND BLEEDING

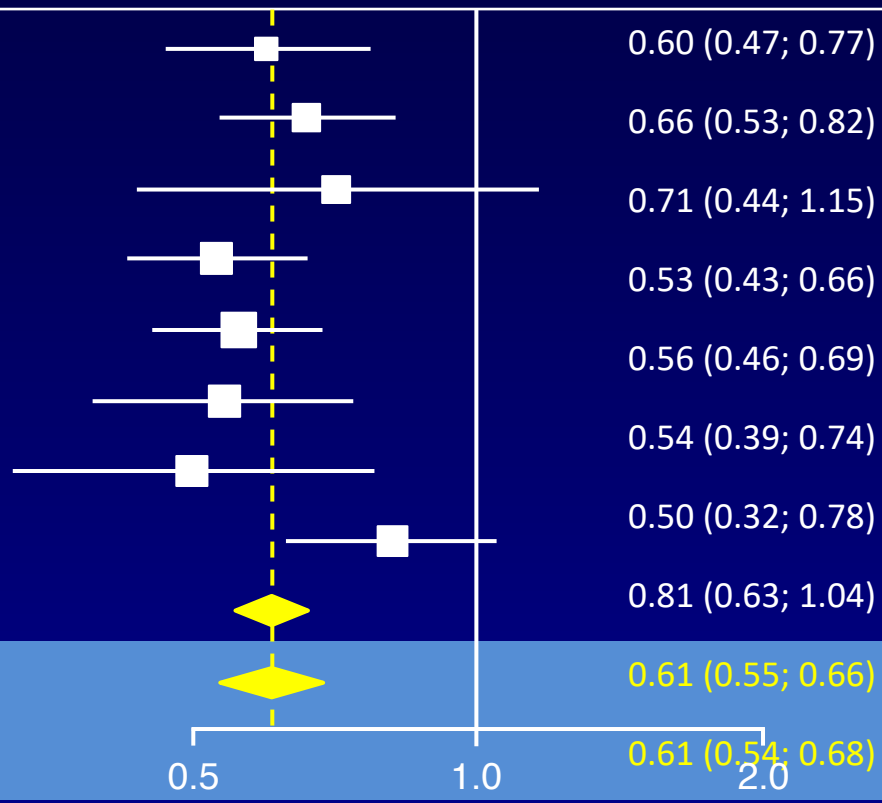


AN Bonde, Stroke. 2016;47:2707-2713

SODIUM–GLUCOSE COTRANSPORTER-2 INHIBITORS

EVIDENCE: KIDNEY OUTCOMES WITH SGLT-2i

Study	Trial	SGLT-2i (N)	Placebo (N)	HR (95% CI)
CANVAS Program	CVOT	5790	4344	0.60 (0.47; 0.77)
CREDENCE	CKD	2200	2197	0.66 (0.53; 0.82)
DAPA-HF	CHF	2373	2371	0.71 (0.44; 1.15)
DECLARE-TIMI-58	CVOT	8574	8569	0.53 (0.43; 0.66)
DAPA-CKD	CKD	2152	2152	0.56 (0.46; 0.69)
EMPA-REG	CVOT	4687	2333	0.54 (0.39; 0.74)
EMPEROR-REDUCED	CHF	1863	1867	0.50 (0.32; 0.78)
VERTIS-CV	CVOT	5493	2745	0.81 (0.63; 1.04)
Fixed effect model				0.61 (0.55; 0.66)
Random effects model				0.61 (0.54; 0.68)



Heterogeneity I^2 = 26%, τ^2 = 0.0076, p = 0.22

* composite kidney outcomes differed in composition from trial to trail (doubling of serum creatinine or >40% drop in the eGFR, ESKD, or need for RRT

CI, confidence interval; CHF, chronic heart failure; CKD, chronic kidney disease; CVOT, cardiovascular outcomes trial; HR, hazard ratio;

Schmidt, Argyropoulos and Singh (2021); doi:10.34067/KID.0000622021

Ideal disclosures

G. Cice

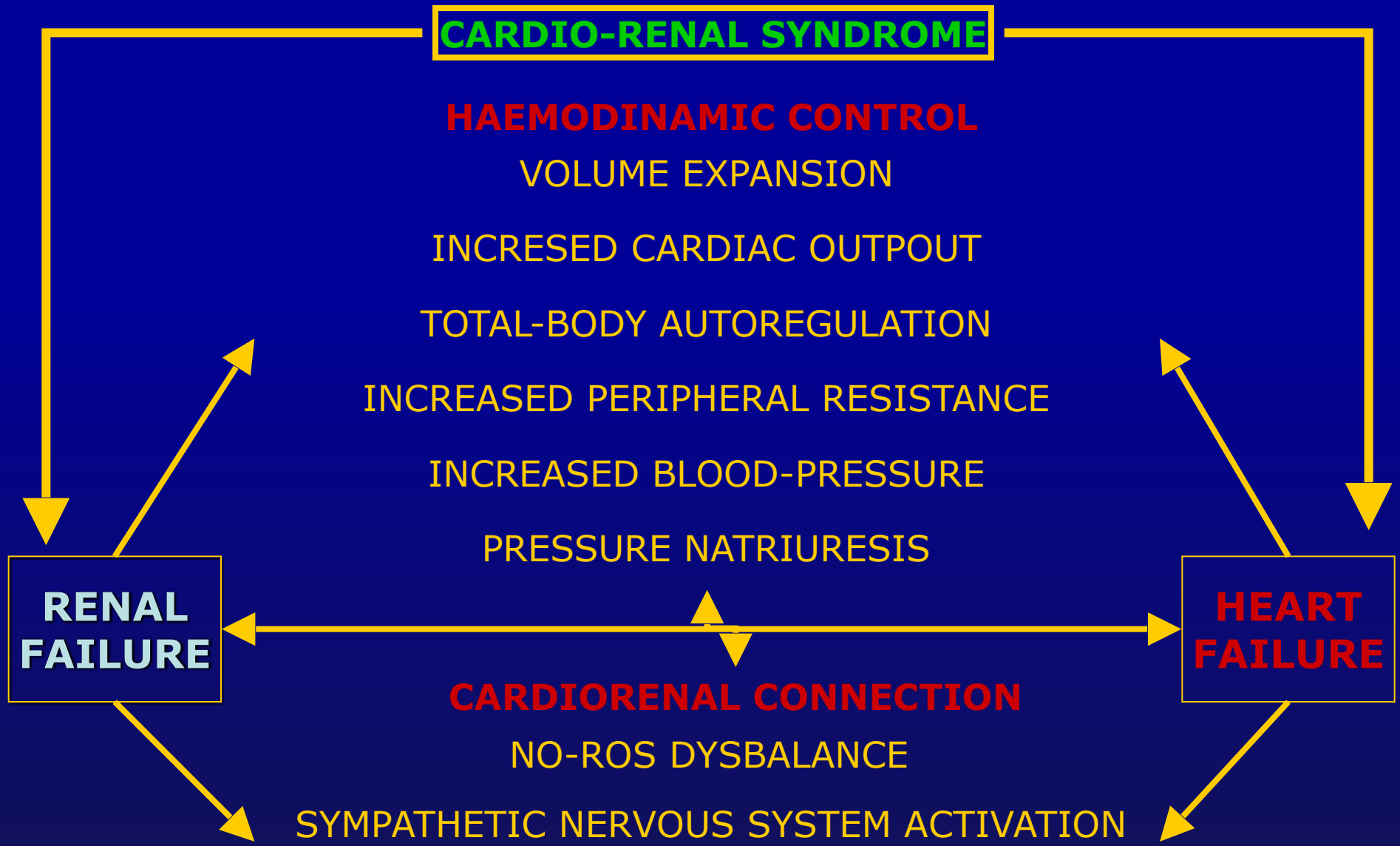
END-STAGE RENAL FAILURE:JUST THE TIP OF THE ICEBERG

49.000 patients with ESDR

42.000 HD / 30.000 TX

The kidney is a determining factor in cardiovascular health!

G. Cice



Bongartz LG, Eur Heart J 2005

Cardio Renal Syndrome

- CRS is categorized into five subtypes based on the primary organ affected (heart or kidney) and whether the dysfunction is acute or chronic.

  - **Type 1 (Acute Cardiorenal):** Acute heart failure leading to acute kidney injury (AKI).

  - **Type 2 (Chronic Cardiorenal):** Chronic heart failure leading to chronic kidney disease (CKD).

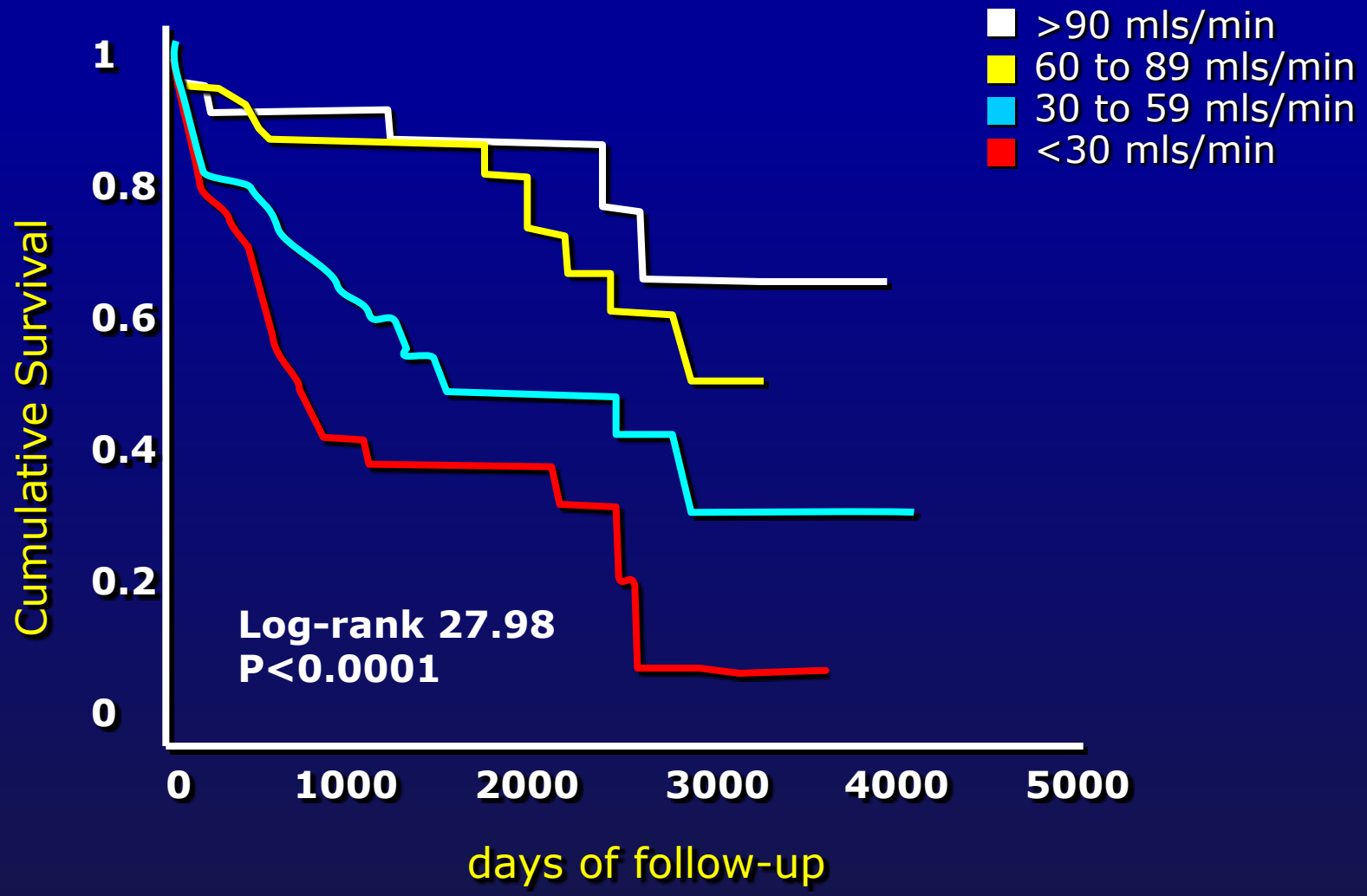
  - **Type 3 (Acute Renocardiac):** AKI leading to acute heart failure.

  - **Type 4 (Chronic Renocardiac):** CKD leading to heart issues, like ventricular hypertrophy or diastolic dysfunction.

  - **Type 5 (Secondary Cardiorenal):** Simultaneous acute or chronic dysfunction of both heart and kidneys due to systemic conditions like sepsis.

Ronco Cl et all. Jacc. 2008

SURVIVAL RATES IN CV PATIENTS STRATIFIED BY CREATININE CLEARANCE



KDIGO-Kidney Disease Improving Global Outcames // https: 2004.

HEART & KIDNEY

HUSBAND & WIFE

August 2016
ACC/AHA/ESC Joint Scientific Session