



Nephrologie et Médecine générale
Abord de la première ligne
et quelques nouveaux espoirs

Dr Guillen A MA .

www.nephrologue.be

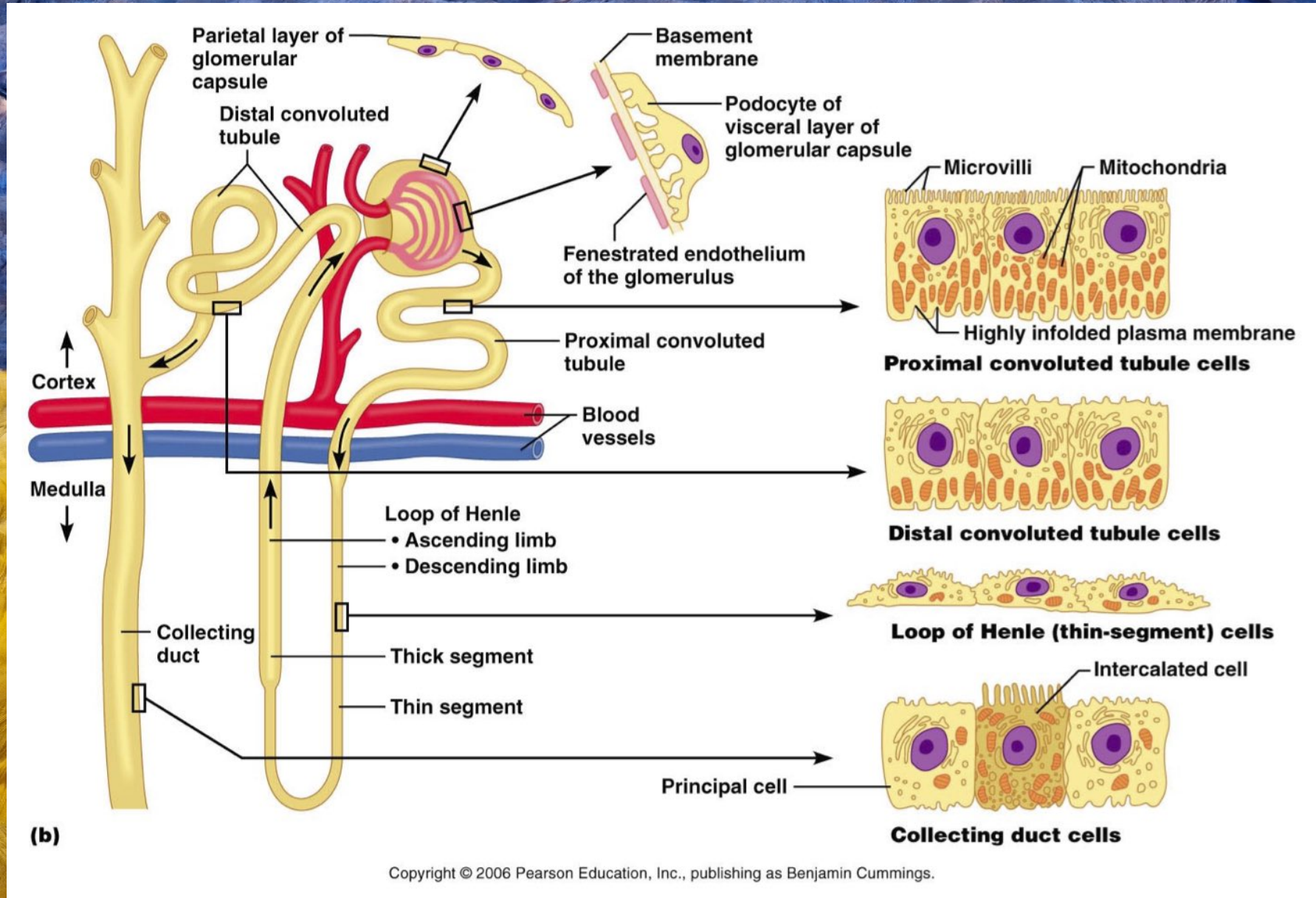
Bruxelles : Ixelles – Woluwe SP

19 avril 2023

Présentation

- Physiologie
- Définition / Epidémiolo.
- Nephroprotection
- Rappel généraux
- SGLT2I : nouvel espoir
- Autres nouveautés ciblées
- Question
- Conseil

RAPPEL PHYSIOPATHOLOGIQUE



QUELS EXAMENS DEMANDER ?



- OEDEME
- HTA
- FATIGUE
- ANEMIE
- CRAMPE
- F.RISQUE

QUELS EXAMENS DEMANDER ?

Néphrologue.be

ACCUEIL CONSULTATION **DOCUMENTS UTILES** LIENS CONFÉRENCES NEWS CONTACT DR GUILLEN M

Vous trouverez ci dessous les documents utiles pour la gestion ambulatoire des patients néphrologiques:

Consultation:

- Demande d'avis:

 [demande avis nephro.pdf](#)

- Instruction pour le prélèvement des urines de 24h:

 [urine de 24h instruction.pdf](#)

- Instruction pour le prélèvement urine orthostatique:

 [Test orthostatique.pdf](#)

- Conseil généraux pour le patient afin de préparer sa consultation de néphrologie :

 [pour la consultation.pdf](#)

- Check Liste Prise en Charge de première ligne de l'Insuffisance rénale chronique:

 [irc bilan.pdf](#)

Dépistage

Dépister la MRC dans les populations à risque

Un certain nombre de personnes ont une probabilité importante d'avoir une atteinte rénale et doivent donc être l'objet d'un dépistage systématique. Le dépistage doit porter sur les 2 indicateurs que sont le DFG estimé et le ratio albuminurie/créatininurie afin d'identifier les stades précoces de la MRC.

Facteurs de risque

- *Diabète*
- *Hypertension*
- *Obésité > 30 kg/m²*
- *Maladie cardiovasculaire*
- *Personnes âgées > 60 ans*
- *Antécédents familiaux d'insuffisance rénale chronique*
- *Uropathies obstructives*
- *Maladies de système*
- *Médicaments néphrotoxiques*
- *Bas poids de naissance (<2,5 kg)*
- *Épisodes d'insuffisance rénale aiguë*

Maladie rénale chronique

CURRENT CHRONIC KIDNEY DISEASE (CKD) NOMENCLATURE USED BY KDIGO

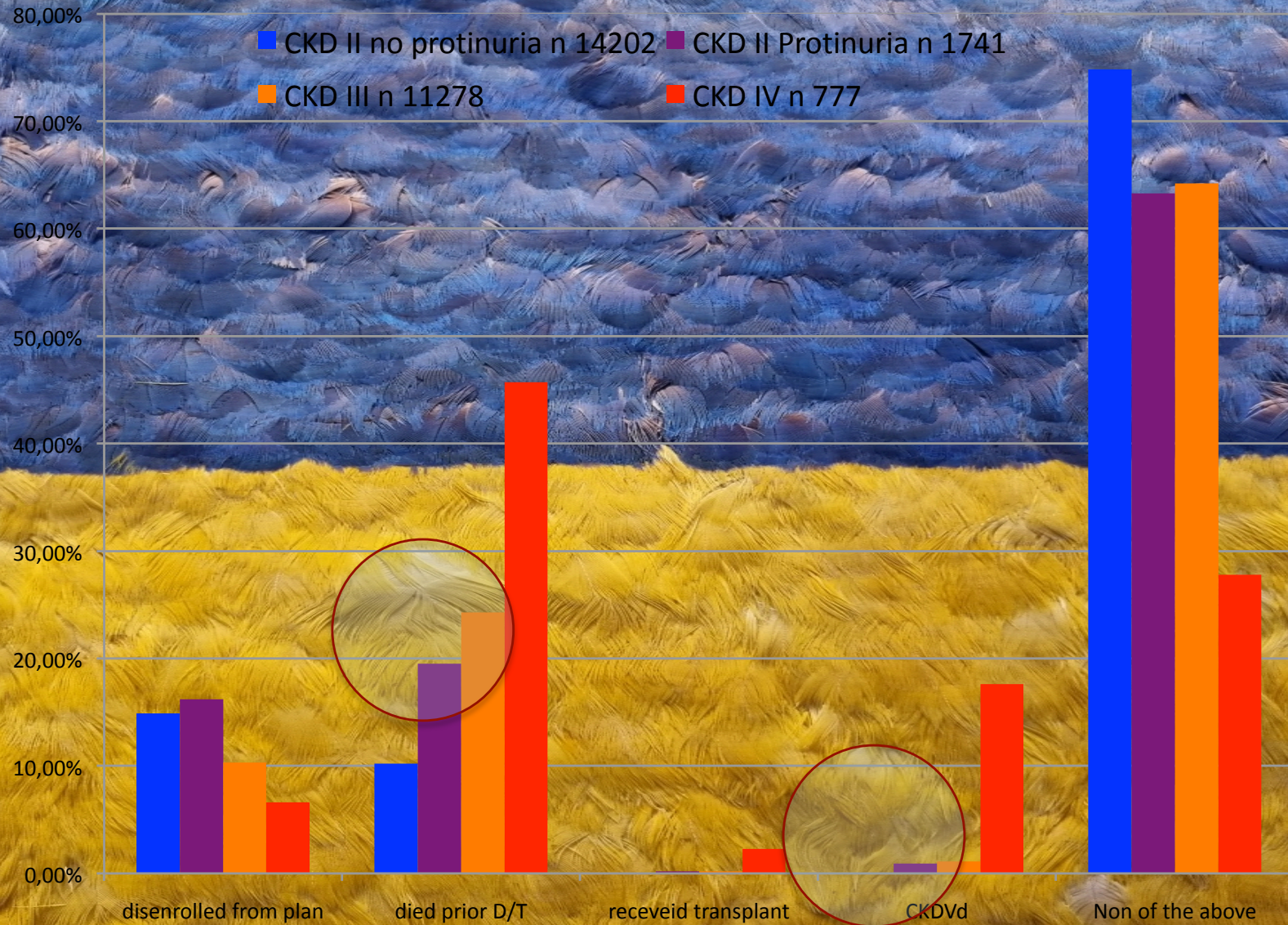
CKD is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. CKD is classified based on Cause, GFR category (G1–G5), and Albuminuria category (A1–A3), abbreviated as CGA.

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

				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
GFR categories (ml/min/1.73 m ²) Description and range	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. GFR, glomerular filtration rate.

Effets de la protéinurie



Douglas et al. Longitudinal Folow up and outcomes among a Population with KD in a Large Managed Care Organization. Arch Inter Med 2004 ; 164 : 659-663

Maladie rénale chronique

DIAGNOSTIC

- Constitutionnelle
- Fonctionnelle non-eGFR

**CURRENT CHRONIC KIDNEY DISEASE (CKD) NOMENCLATURE
USED BY KDIGO**

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Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012			Persistent albuminuria categories		
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			A1	A2	A3
			Normal to mildly increased < 30 mg/g < 3 mg/mmol	Moderately increased 30–300 mg/g 3–30 mg/mmol	Severely increased > 300 mg/g > 30 mg/mmol
GFR categories (ml/min/1.73 m ²) Description and range	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. GFR, glomerular filtration rate.

Mortalité

Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization.

Alan Go et al. N Engl J Med 2004;351:1296-305.

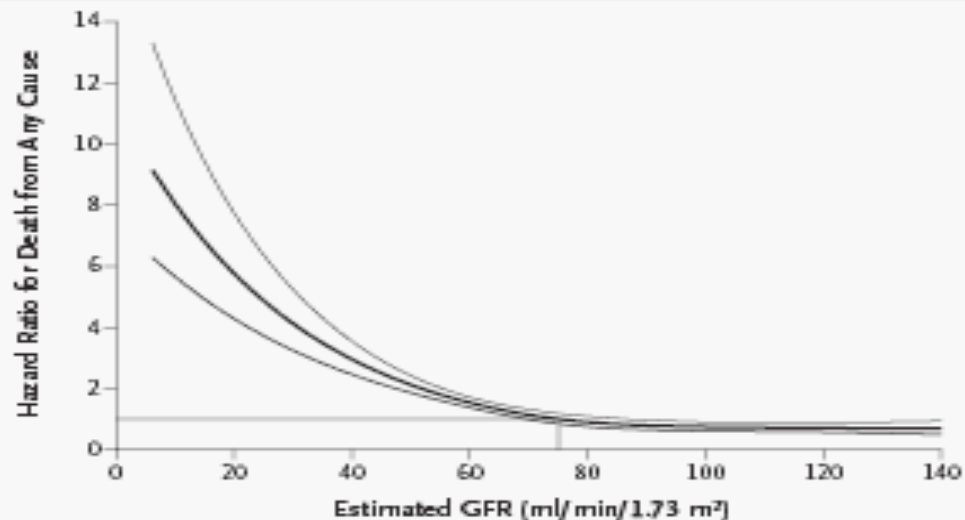


Figure 4. Unadjusted Hazard Ratio for Death from Any Cause, According to the Estimated GFR at Baseline.

The estimated hazard ratio (middle curve) is shown with the 95 percent confidence limits (upper and lower curves).

Table 2. Adjusted Hazard Ratio for Death from Any Cause, Cardiovascular Events, and Hospitalization among 1,120,295 Ambulatory Adults, According to the Estimated GFR.*

Estimated GFR	Death from Any Cause	Any Cardiovascular Event	Any Hospitalization
	adjusted hazard ratio (95 percent confidence interval)		
≥60 ml/min/1.73 m ² †	1.00	1.00	1.00
45–59 ml/min/1.73 m ²	1.2 (1.1–1.2)	1.4 (1.4–1.5)	1.1 (1.1–1.1)
30–44 ml/min/1.73 m ²	1.8 (1.7–1.9)	2.0 (1.9–2.1)	1.5 (1.5–1.5)
15–29 ml/min/1.73 m ²	3.2 (3.1–3.4)	2.8 (2.6–2.9)	2.1 (2.0–2.2)
<15 ml/min/1.73 m ²	5.9 (5.4–6.5)	3.4 (3.1–3.8)	3.1 (3.0–3.3)

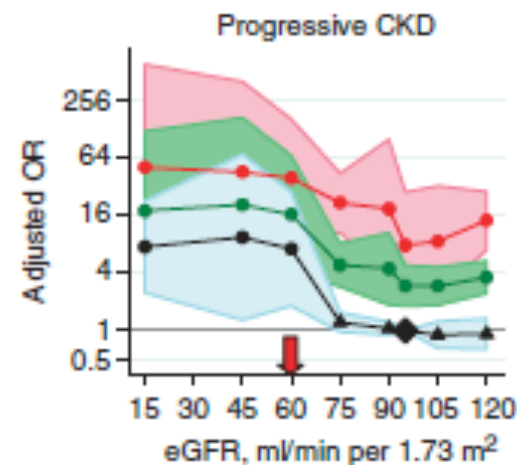
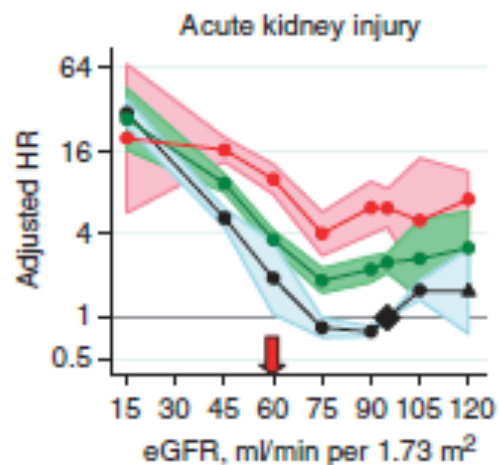
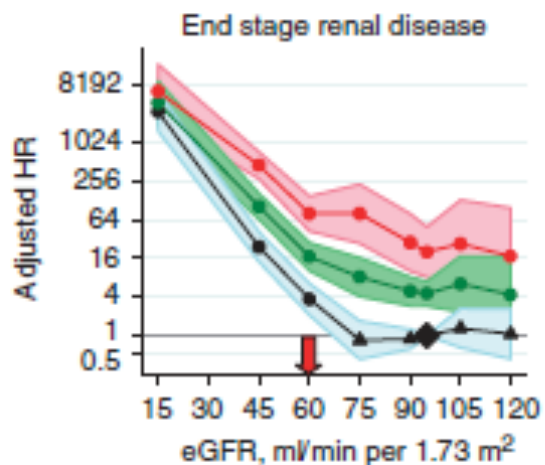
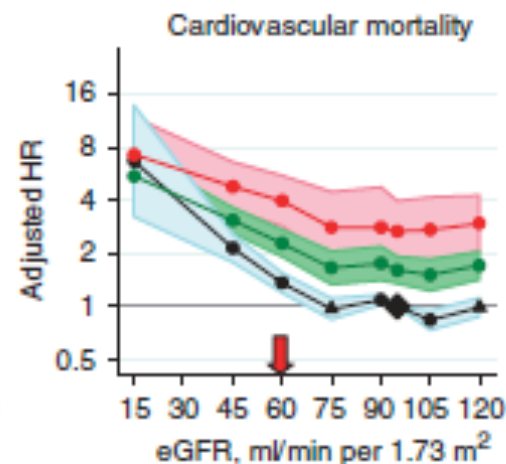
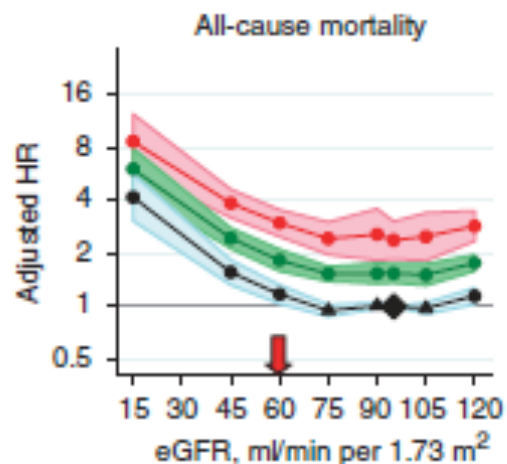
* The analyses were adjusted for age, sex, income, education, use or nonuse of dialysis, and the presence or absence of prior coronary heart disease, prior chronic heart failure, prior ischemic stroke or transient ischemic attack, prior peripheral arterial disease, diabetes mellitus, hypertension, dyslipidemia, cancer, a serum albumin level of 3.5 g per deciliter or less, dementia, cirrhosis or chronic liver disease, chronic lung disease, documented proteinuria, and prior hospitalizations.

† This group served as the reference group.

- We estimated the longitudinal glomerular filtration rate (GFR) among 1,120,295 adults within a large, integrated system of health care delivery in whom serum creatinine had been measured between 1996 and 2000 and who had not undergone dialysis or kidney transplantation

The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report

Summary of relative risks from continuous meta-analysis

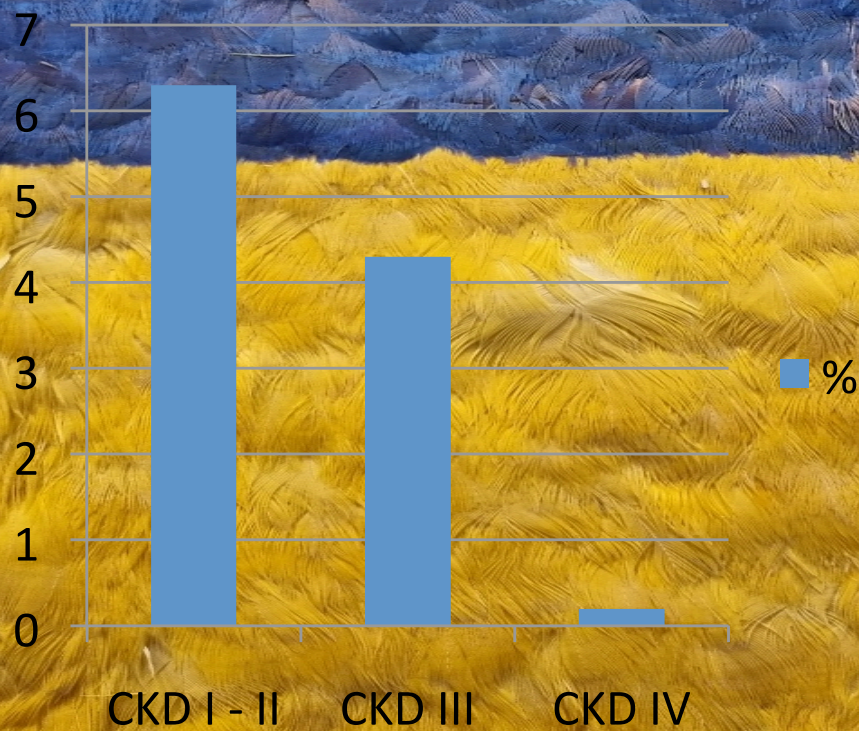


CKD USA us Europa

CJASN 2008 616 623

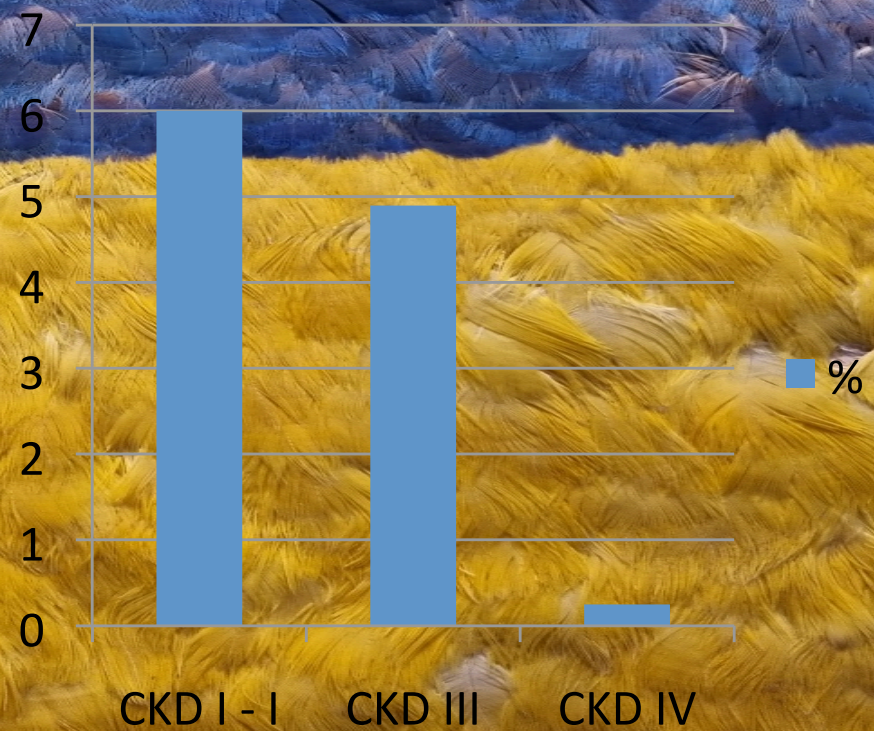
USA (NAHES)

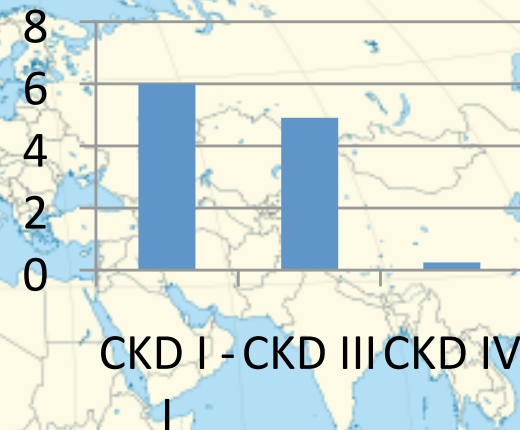
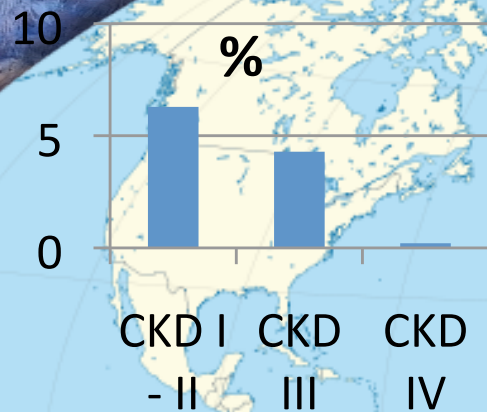
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Europe (HUNT, PREVEND, EPIRCE)

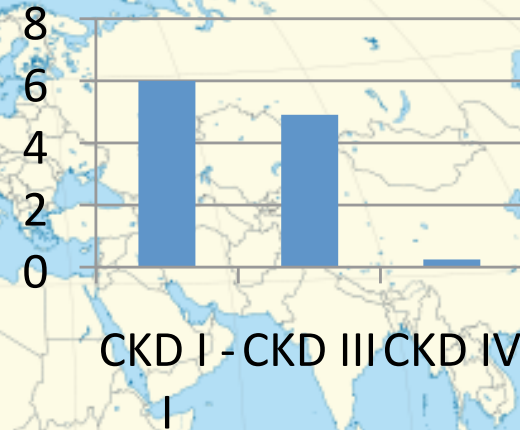
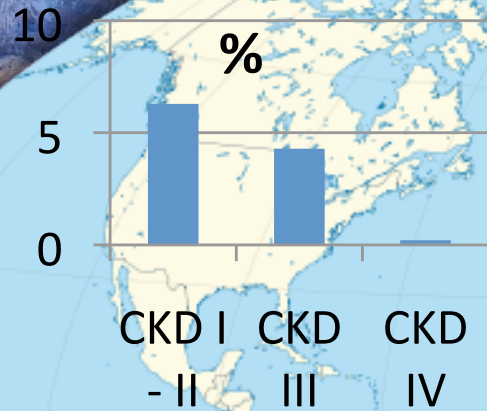
%





- Semblables pays industrialisés
- 10% CKD.
- ! 55 – 85 ! > 65 ans : 15 % ?
- majoration cout mortalité morbidité

Cout



- Hospitalisation pour CVD → 10 000 euros
- Cout traitement HTA/ANEMIE/CVD → 100 - 1000 euros
- Cout Dialyse → 50 000 euros
- Cout maladie oncologique et infectiologie → >50 000 euros

Maladie rénale chronique

Peut on la ralentir ?

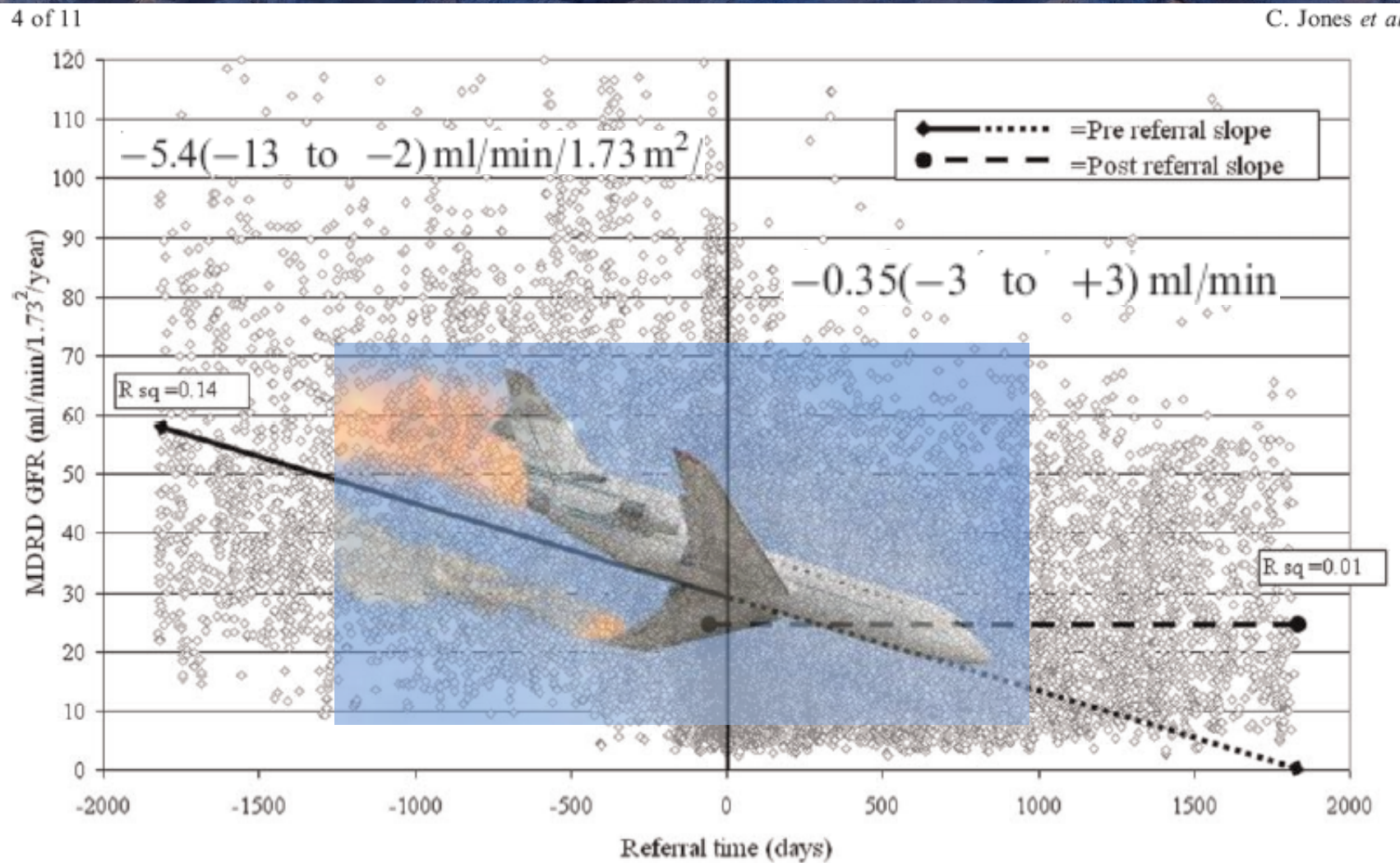


Fig. 1. Decline in MDRD GFR in the 5 years prior to and following nephrology referral with regression lines of summary pre- and post-referral GFR slopes (each point is a single GFR measure).

Quelques bases dans la gestion de la MRC

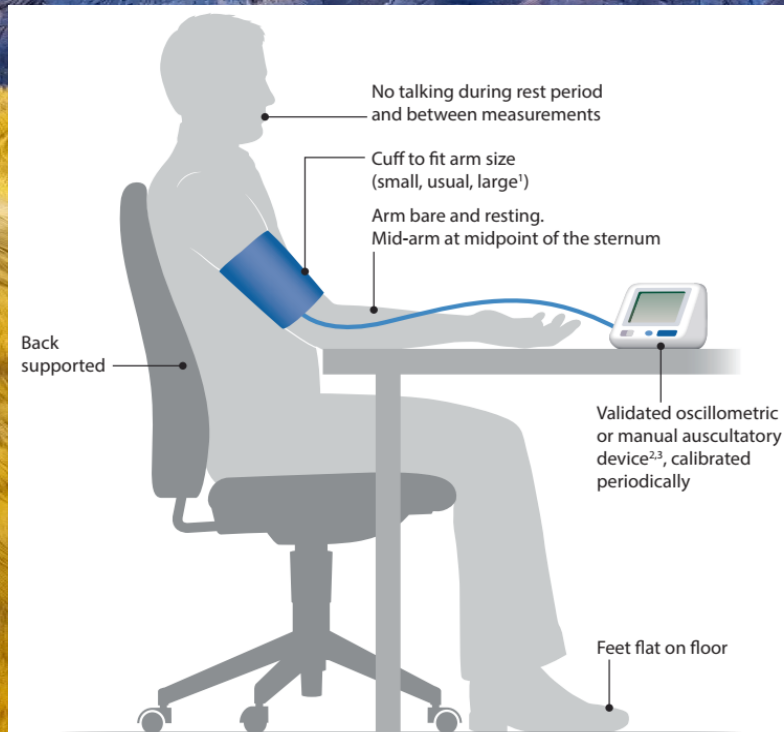


HYPERTENSION

Global Science. Local Change.

KDIGO is *the* global nonprofit organization developing and implementing evidence-based clinical practice guidelines in kidney disease.

[GO TO ALL GUIDELINES](#)



- Quiet room (no talking by patient or observer)
- No smoking, caffeine, or exercise for ≥ 30 min before measurement
- Empty bladder
- Note the time of most recent BP medication taken before measurements
- Relax for > 5 min
- At first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings
- Separate repeated measurements by 1–2 minutes
- Use an average of ≥ 2 readings obtained on ≥ 2 occasions
- Provide patients with the SBP/DBP readings verbally and in writing

¹Use the correct cuff size, such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used

²See validated electronic devices lists at www.stridebp.org

³For auscultatory readings, either the stethoscope diaphragm or bell may be used. Use a palpated radial pulse obliteration pressure to estimate SBP, then inflate the cuff 20–30 mm Hg above this level for auscultatory determination of BP level. Deflate the cuff pressure 2 mm Hg per second, and listen for Korotkoff sounds

RATIONALE FOR TARGET SBP <120 MM HG IN CKD

- For most patients with CKD, a cardiovascular event is a more likely outcome than ESKD.¹
- SPRINT confirmed cardiovascular and survival benefits in non-diabetic CKD.²
- ACCORD showed marked reduction in stroke in diabetes, but only included 401 patients with eGFR <60 ml/min/1.73m²; nonetheless, benefits of SBP <120 mm Hg in the standard glycemia arm similar to those seen in SPRINT.^{3,4}
- Meta-analyses demonstrate reduction of CV risk proportional to BP lowering, though some show lower proportional risk reduction in the presence of CKD and of DM.^{5,6,7}

BLOOD PRESSURE MANAGEMENT IN PATIENTS WITH CKD, WITH OR WITHOUT DIABETES, NOT RECEIVING DIALYSIS

Recommendation 3.1.1: We suggest that adults with high BP and CKD be treated with a target systolic blood pressure (SBP) of <120 mm Hg, using standardized office BP measurement (2B).

This recommendation is weak according to GRADE because there is less certainty that the benefits outweigh the harms in the following scenarios:

- CKD G4 and G5
- Diabetes
- Individuals with SBP 120-129 mm Hg
- Patients with very low baseline diastolic BP, particularly in the presence of coronary artery disease
- Specific etiology of CKD
- Severely increased proteinuria
- Older age
- Younger age
- Very frail
- “White coat” hypertension

Individualization is KEYⁿ

BICARBONATE 22

- DYSPNEE
- APETIT
- AMYOTROPHIE
- SHIFT POTASSIQUE
- SHIFT CALCEMIQUE
- CARDIOPATHIE
- OSTEOPOROSE
- INSULINO
- RESISTANCE

BICARBONATE

Effect of sodium bicarbonate on systolic blood pressure in chronic kidney disease: A systematic review and meta-analysis

CJASN
Clinical Journal of the American Society of Nephrology



**Systematic review
and meta-analysis**



2110
Participants



38 ml/min
eGFR



60 years
Mean age



136 mm Hg
mean systolic BP



27 weeks
Median follow-up



22 mmol/l
Serum bicarbonate

Outcomes



Random effects
meta-analysis suggests
that sodium bicarbonate
does not influence SBP



No increase in the use
of antihypertensive
medications



No increase in the use
of diuretics



14
Randomized
controlled trials

Study Arms



Intervention arm
Sodium bicarbonate



Control arm
Placebo or no intervention

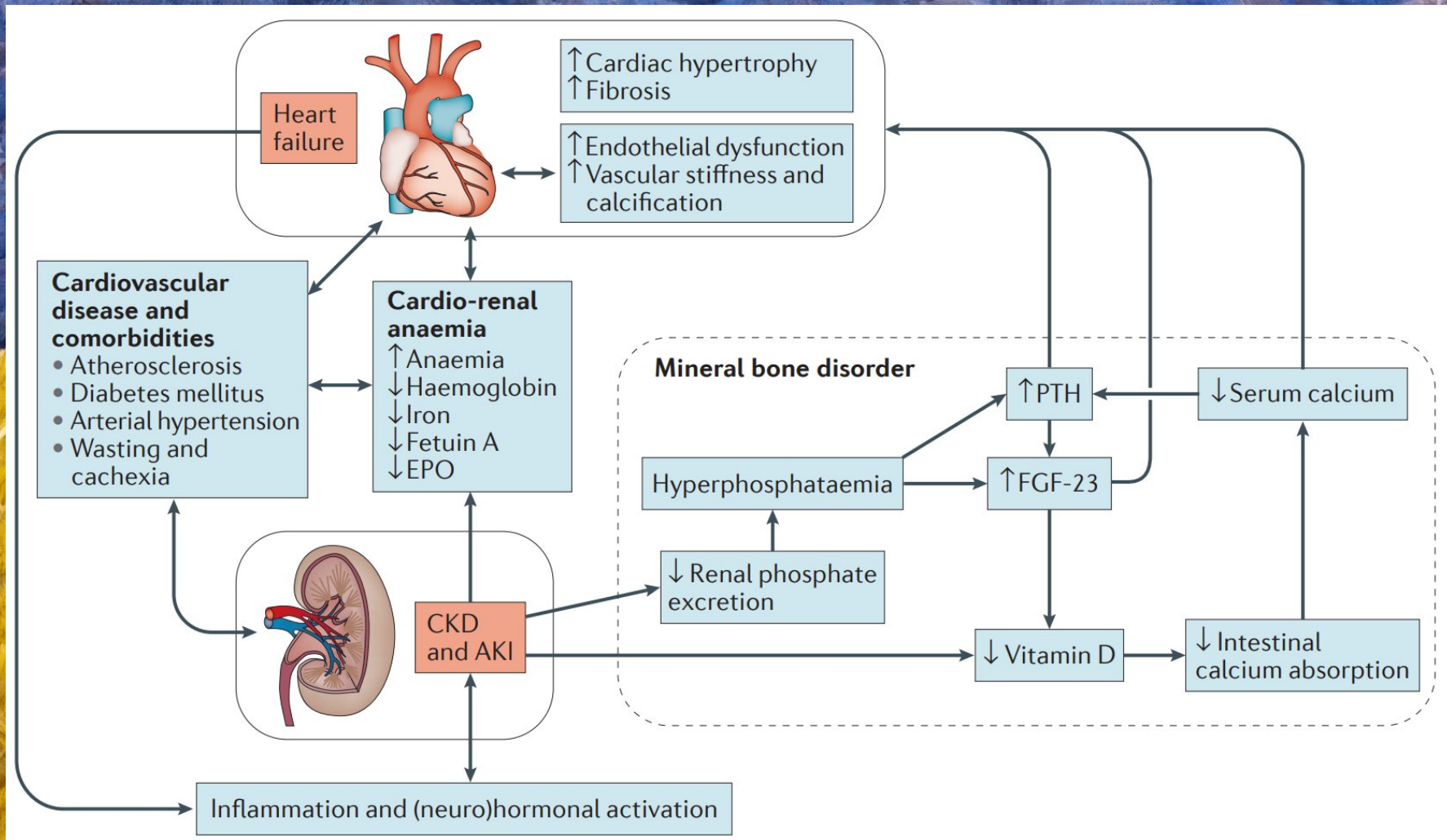


CKD
Stages 1-5
non-dialysis patients

Conclusions: Results suggest, with moderate certainty, that sodium bicarbonate supplementation does not adversely affect systolic BP in CKD or negatively influence antihypertensive medication requirements.

Beverley Beynon-Cobb, Panayiotis Louca, Ewout J. Hoorn, et al. *Effect of Sodium Bicarbonate on Systolic Blood Pressure in CKD*. CJASN doi: 10.2215/CJN.000000000000119. Visual Abstract by Momen Abbasi, MD

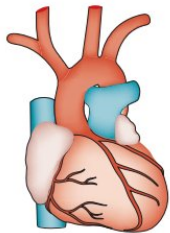
SYNDROME CARDIO RENAL



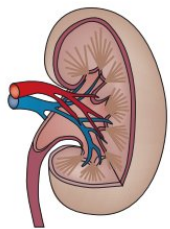
Sd CR classification

Type 1: acute cardio-renal syndrome

Acute HF leading to AKI

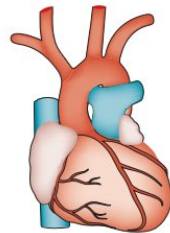


Altered cardiac and/or renal haemodynamics might be of particular importance

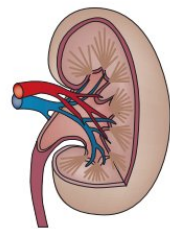


Type 2: chronic cardio-renal syndrome

Chronic HF leading to progressive and permanent CKD

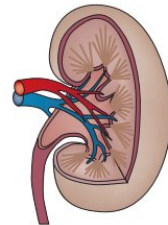


Accelerated renal cell apoptosis and replacement fibrosis might be of particular importance

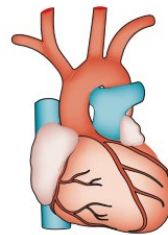


Type 3: acute reno-cardiac syndrome

AKI causing acute HF

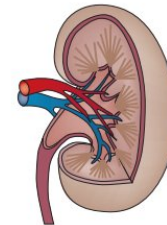


Salt and water imbalance, uraemia-induced effects and neuro-hormonal dysregulation might be key in this setting

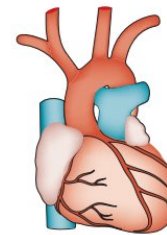


Type 4: chronic reno-cardiac syndrome

CKD leading to chronic HF and CKD progression



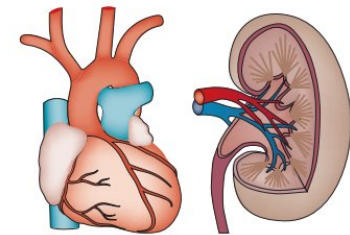
CKD-induced myopathy might be of particular importance in this setting



Type 5: secondary cardio-renal syndrome

Systemic insult (e.g. in severe sepsis and/or septic shock)

Microcirculatory dysfunction, altered innate and adaptive immune responses and cytokine release, and other effects result in simultaneous organ injury



Le probleme de la volémie & diurétique

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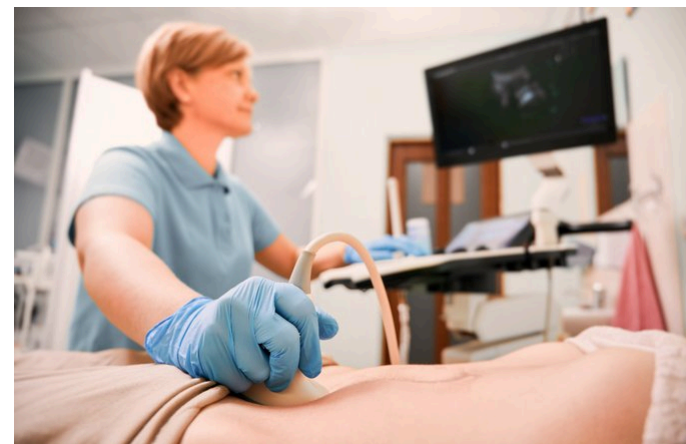
Magazine

Puzzles & Games

Video

COULD ULTRASOUND REPLACE THE STETHOSCOPE?

Miniaturization, experimentation, and A.I. have unlocked revolutionary potential in an old technology.



By Clifford Marks January 20, 2023

L'important c'est l'effet

- D de l'ANSE :

- Crampe
- Potassium
- Calcium out

- Thiazide :

- Sodium
- Perte d'effet
- Calcium in

- INHIBITEUR MR :
spironolactone

- Hypotenseur
- Effet pleiotropique
- Potassium
- Acidose

Oxygène

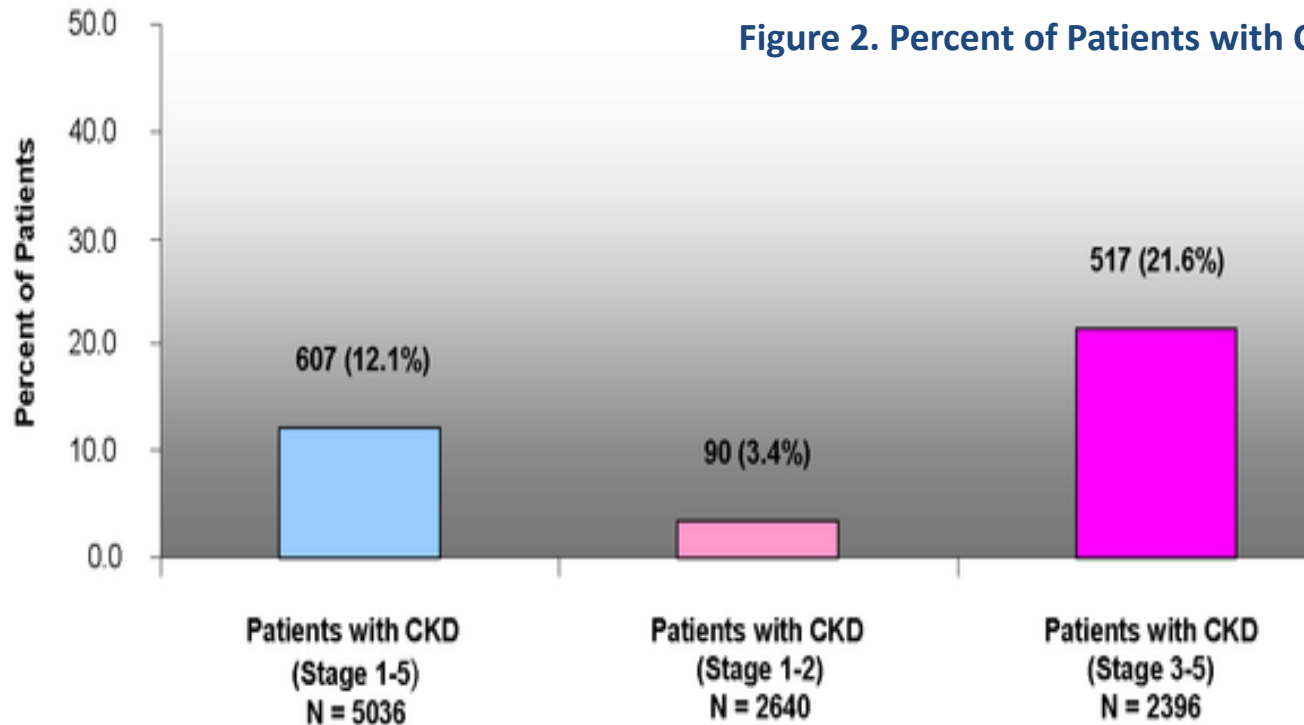
- CIBLE Hémoglobine :
- 11 gramme

- CIBLE Martiale
- Ferritine > 100

- EPO
- Fer Oral
- Fer IV
- Autres support
- HIFinhibiteur

Le dépistage est il bien réalisé ?

Figure 2. Percent of Patients with CI



Szczech LA, Stewart RC, Su HL, DeLoskey RJ, Astor BC, et al. (2014) Primary Care Detection of Chronic Kidney Disease in Adults with Type-2 Diabetes: The ADD-CKD Study (Awareness, Detection and Drug Therapy in Type 2 Diabetes and Chronic Kidney Disease). PLOS ONE 9(11): e110535. <https://doi.org/10.1371/journal.pone.0110535>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0110535>

POTENTIAL IMPLICATIONS

Potential implications of the 2021 KDIGO blood pressure guideline for adults with chronic kidney disease in the United States

2021 KDIGO Guideline

What's new for adults with CKD and high BP?



Recommends treatment to SBP <120 mmHg using standardized office BP measurement



Recommends ACEi/ARBs for adults with albuminuria and high BP (SBP ≥120 mmHg)

Current Study Goals

Determine potential implications of 2021 KDIGO guideline compared to:

2012 KDIGO guideline
2017 ACC/AHA guideline

Data Source

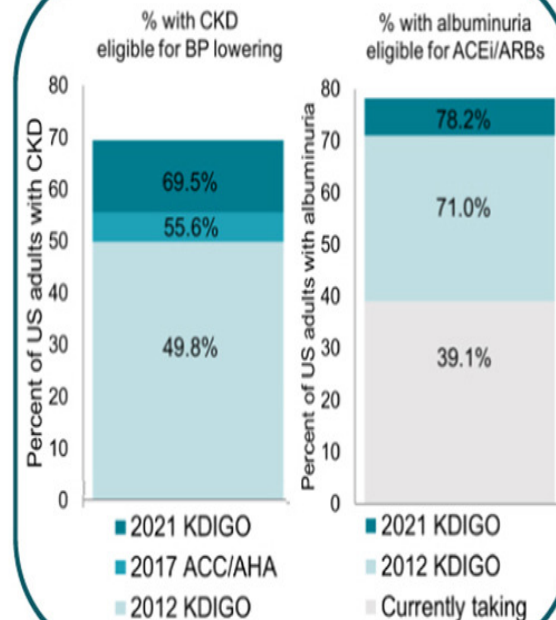


National Health and Nutrition Examination Survey 2015-2018

N=9,419 adults aged ≥20 years with CKD

BP based on mean of up to 3 standardized measurements

Results

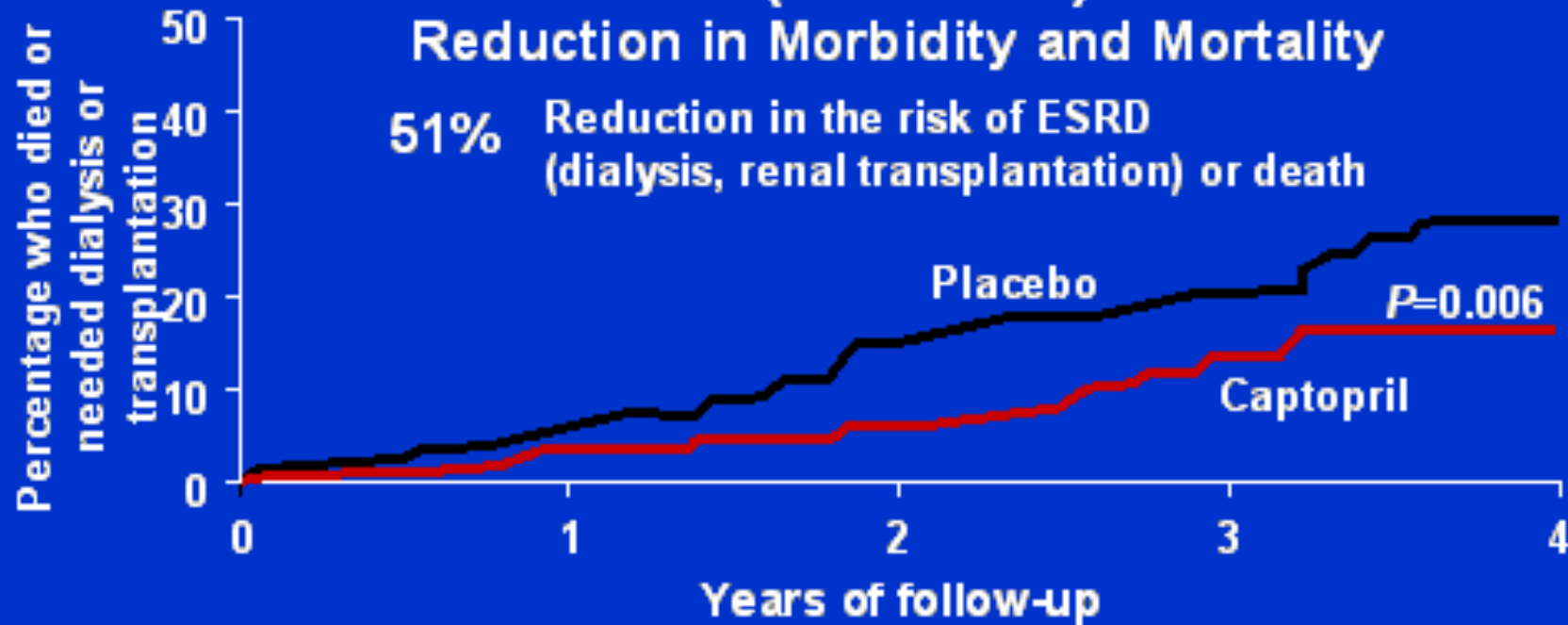


CONCLUSION:

Based on the 2021 KDIGO guideline, 69.5% of US adults with CKD are eligible for BP lowering. Among those with albuminuria, 78.2% are eligible but only 39.1% take ACEi/ARBs.

Effect of ACE Inhibition on Diabetic Kidney Disease

- 48% reduction in the risk of doubling of serum creatinine ($P=0.007$)



Lewis et al. N Engl J Med. 1993;329:1456.

Expansion of Cortical Interstitium Is Limited by Converting Enzyme Inhibition in Type 2 Diabetic patients with Glomerulosclerosis

DANIEL J. CORDONNIER,* NICOLE PINEL,§ CLAIRE BARRO,CLAIRE MAYNARD,* PHILIPPE ZAOUÏ,* SERGE HALIMI,*BRUNO HURAUULT DE LIGNY,† YVES REZNIC,† DOMINIQUE SIMON,‡RUDOLF W. BILOUS,§ FOR THE DIABIOPSIES GROUP^a
 J Am Soc Nephrol 10: 1253–1263, 1999

Table 4. Longitudinal renal function*

Group	Mean BP (mmHg)		Creatinine Clearance (ml/min)		Proteinuria ^b (mg/24 h)		Urine Na (mmol/24 h)	
	M0	M24	M0	M24	M0	M24	M0	M24
Placebo (n = 10)	109 ± 12	108 ± 10	119 ± 54	102 ± 53	547 (191,1567)	881 (239,3242)	145 ± 75	120 ± 68
Perindopril (n = 9)	101 ± 12	96 ± 11	124 ± 23	109 ± 31	668 (226,1369)	436 (187,1016)	202 ± 136	171 ± 88

* Results are given as mean ± SD. M, month.

^b P < 0.05 versus respective baseline values between groups. Results are expressed as geometric mean and antilog of the 95% confidence interval of the mean.

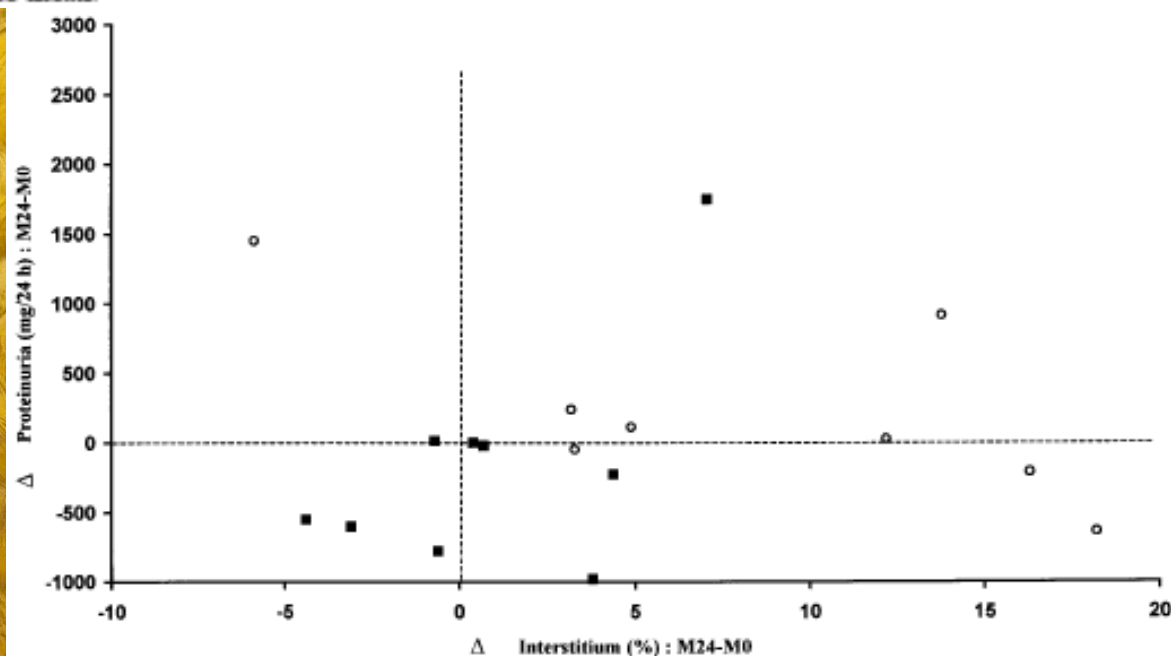
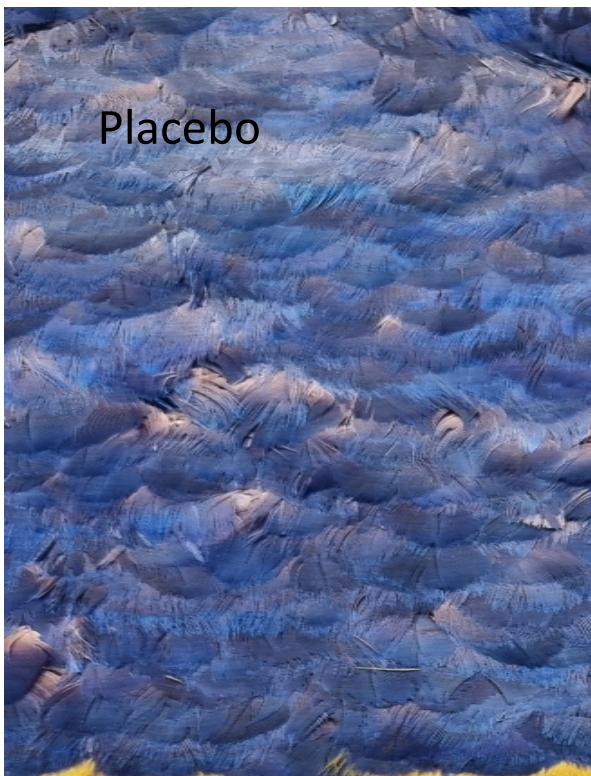
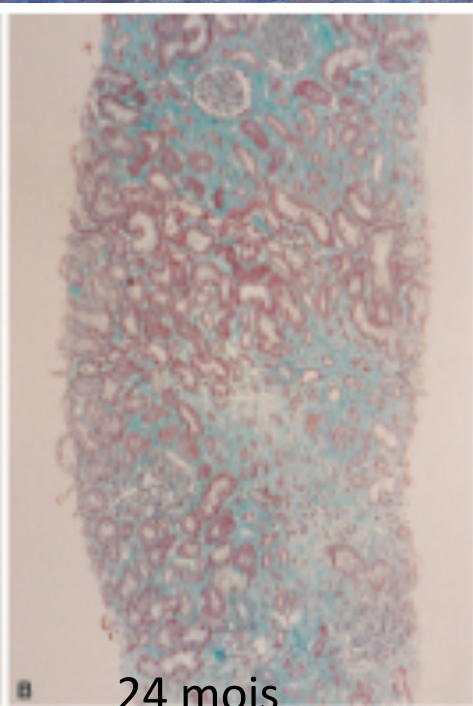


Figure 3. Individual changes at 24 mo from baseline in mean cortical interstitium fractional volume (x-axis) and in proteinuria (y-axis) for Perindopril (■) and placebo (○) groups.

Placebo



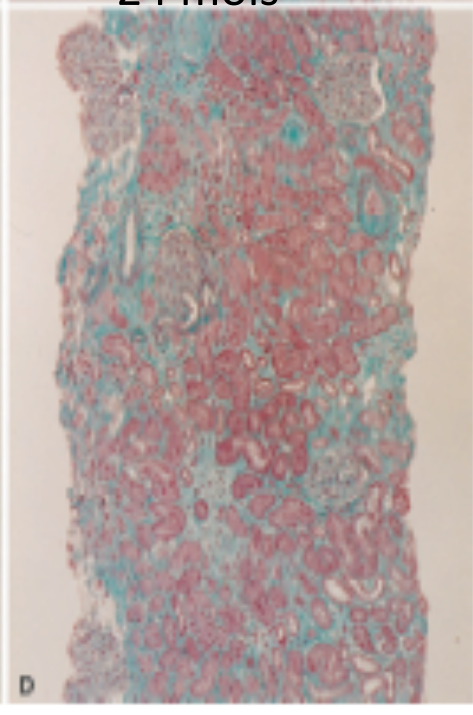
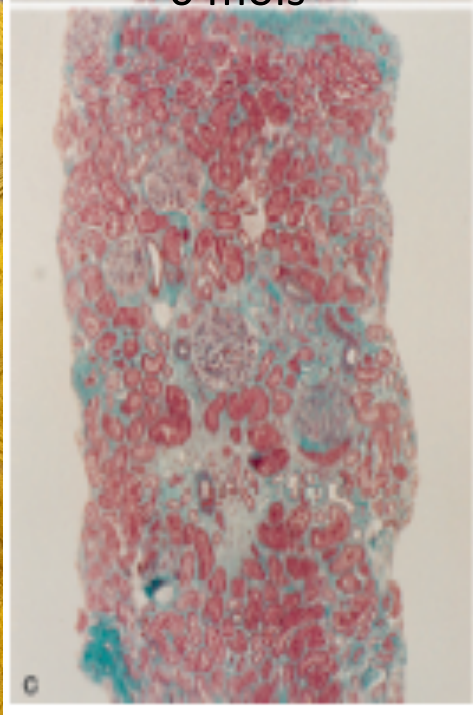
0 mois



24 mois



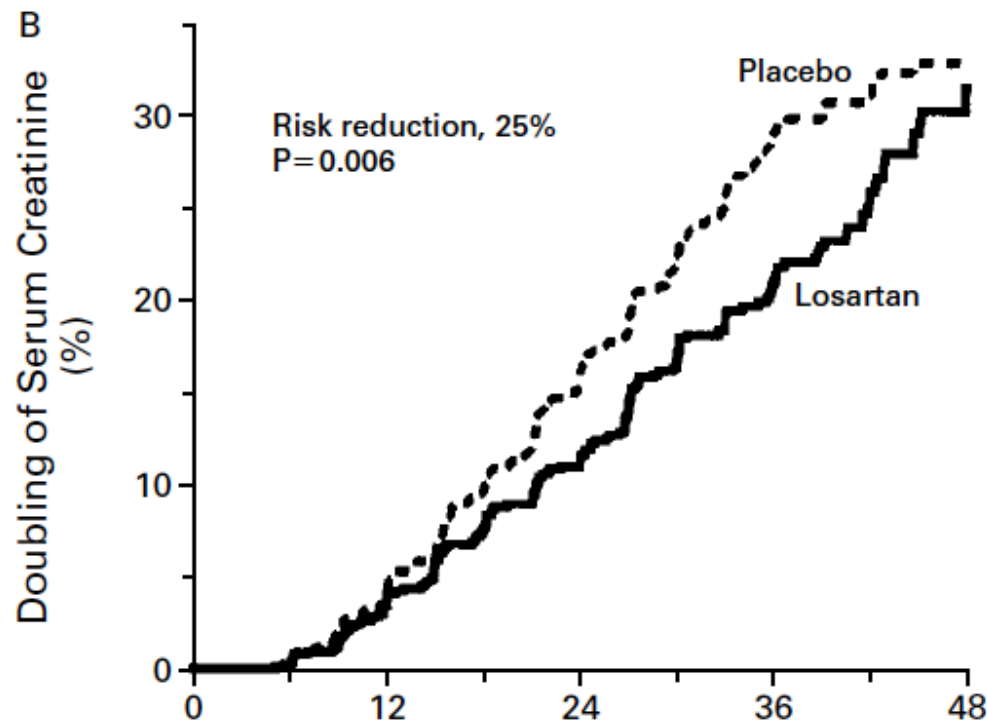
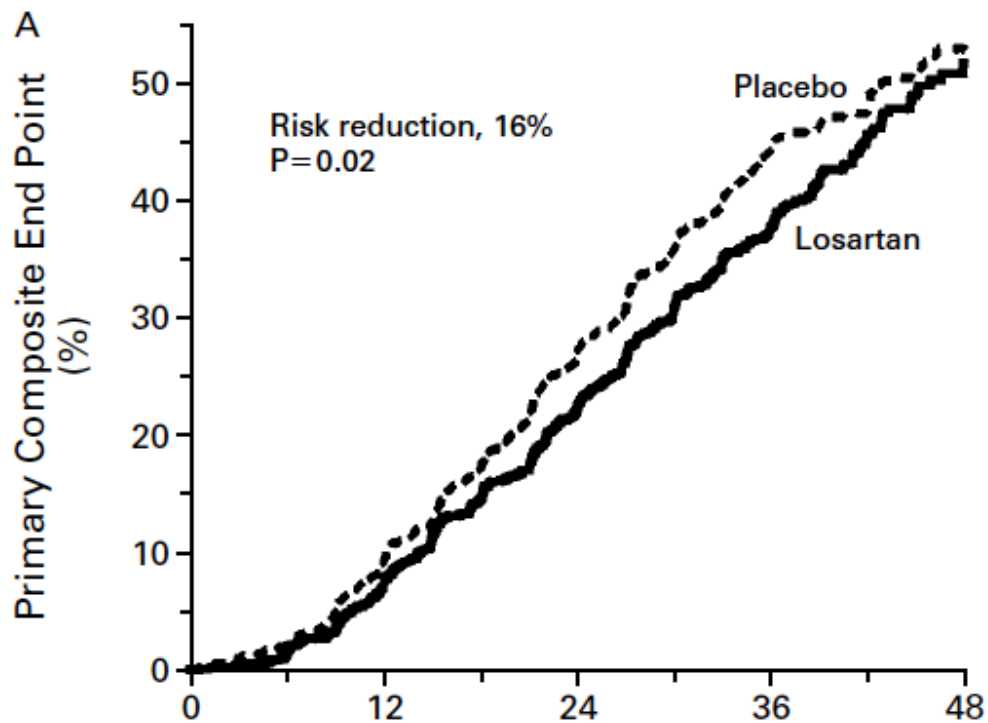
Perindopril

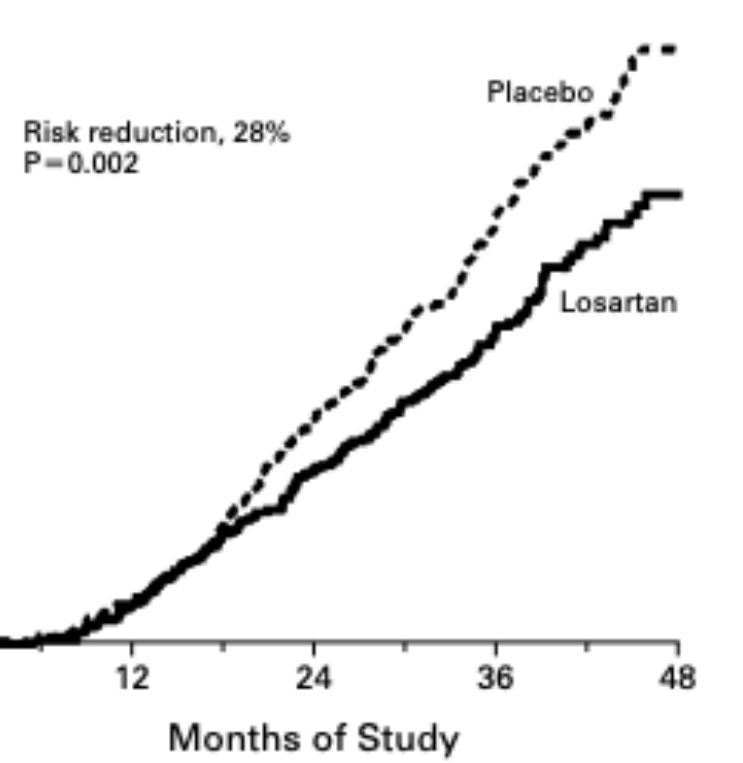
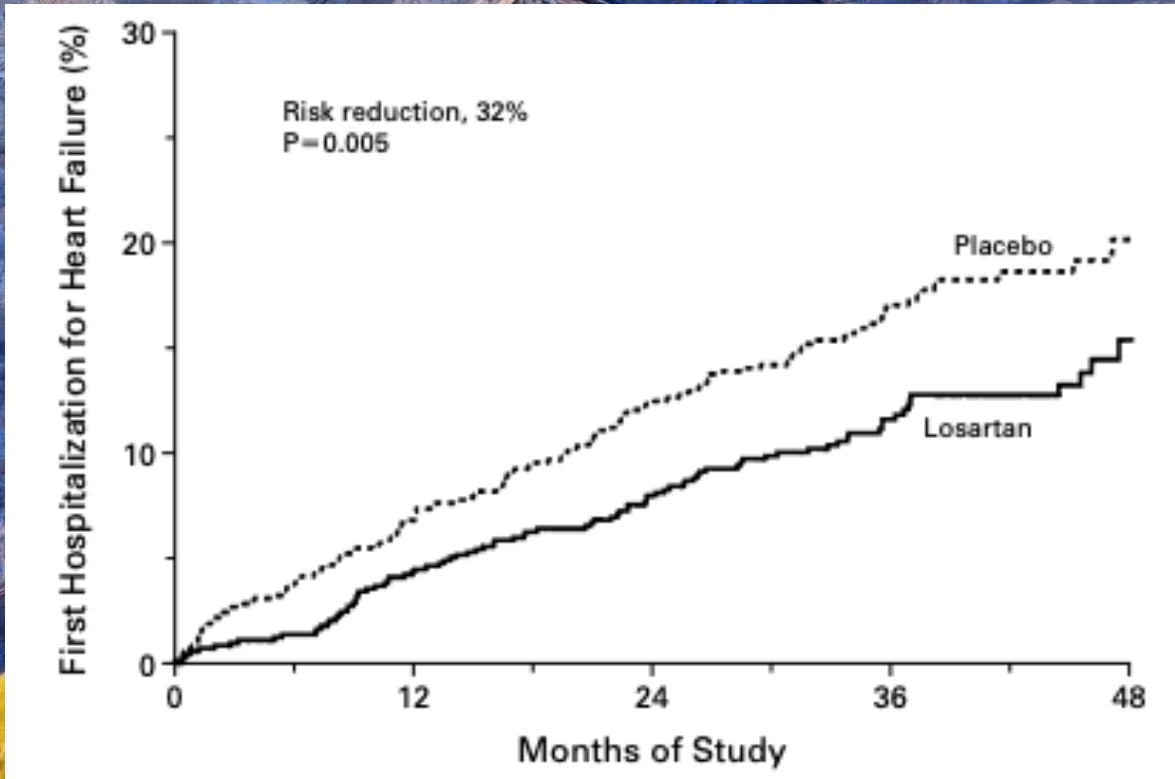


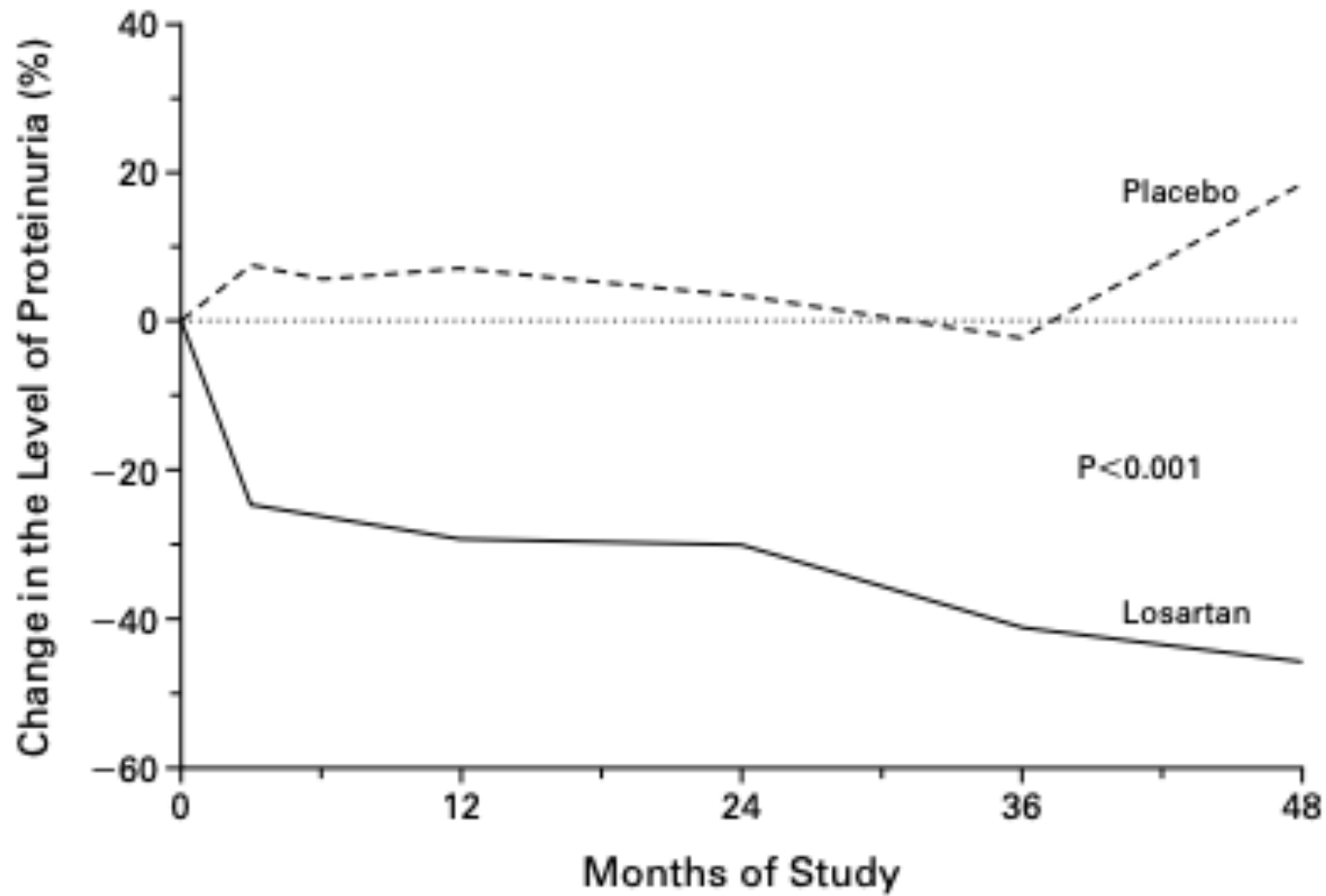
EFFECTS OF LOSARTAN ON RENAL AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH TYPE 2 DIABETES AND NEPHROPATHY

BARRY M. BRENNER, M.D., MARK E. COOPER, M.D., PH.D., DICK DE ZEEUW, M.D., PH.D., WILLIAM F. KEANE, M.D.,
WILLIAM E. MITCH, M.D., HANS-HENRIK PARVING, M.D., GIUSEPPE REMUZZI, M.D., STEVEN M. SNAPINN, PH.D.,
ZHONXIN ZHANG, PH.D., AND SHAHNAZ SHAHINFAR, M.D., FOR THE RENAAL STUDY INVESTIGATORS*

N Engl J Med, Vol. 345, No. 12 · September 20, 2001 · www.nejm.org · 861







NO. AT RISK

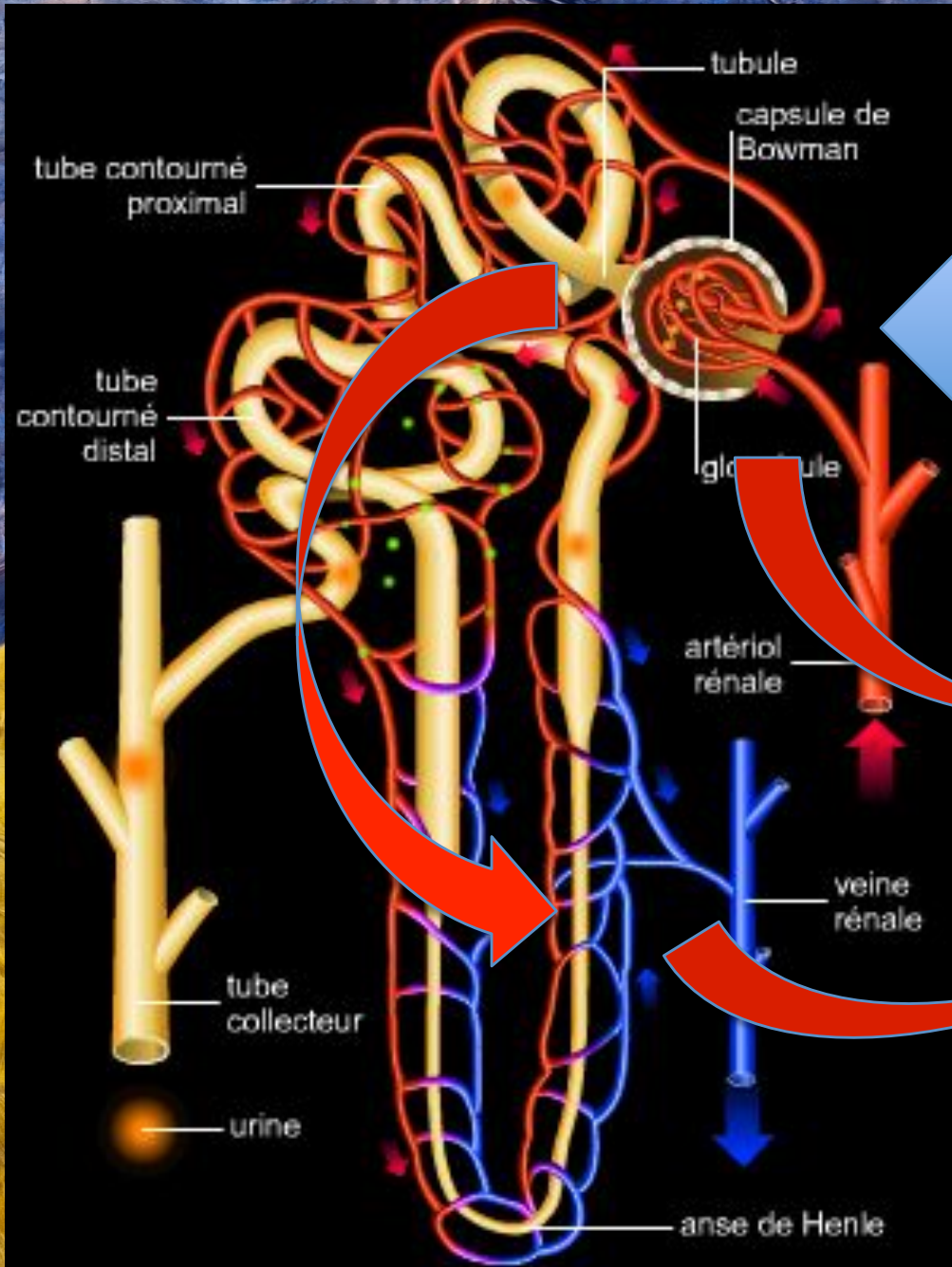
Placebo	762	632	529	390	130
Losartan	751	661	558	438	167

Figure 3. Median Changes from Base Line in the Level of Proteinuria.

Proteinuria was measured as the urinary albumin-to-creatinine ratio in a first morning specimen. The mean follow-up time was 3.4 years.



Plus de 25 ans d'observation ...



Lésion glomérulaire

Detailed description: A large blue arrow points from the right towards the glomerulus in the diagram, indicating the site of glomerular injury.

TOXINE
UREMIQUE
Maladie
chronique
Cardiovasculaire
Immun osseux

Detailed description: A blue starburst shape contains text listing associated conditions: TOXINE UREMIQUE, Maladie chronique, Cardiovasculaire, and Immun osseux. Red arrows point from this starburst towards the tubules in the diagram.

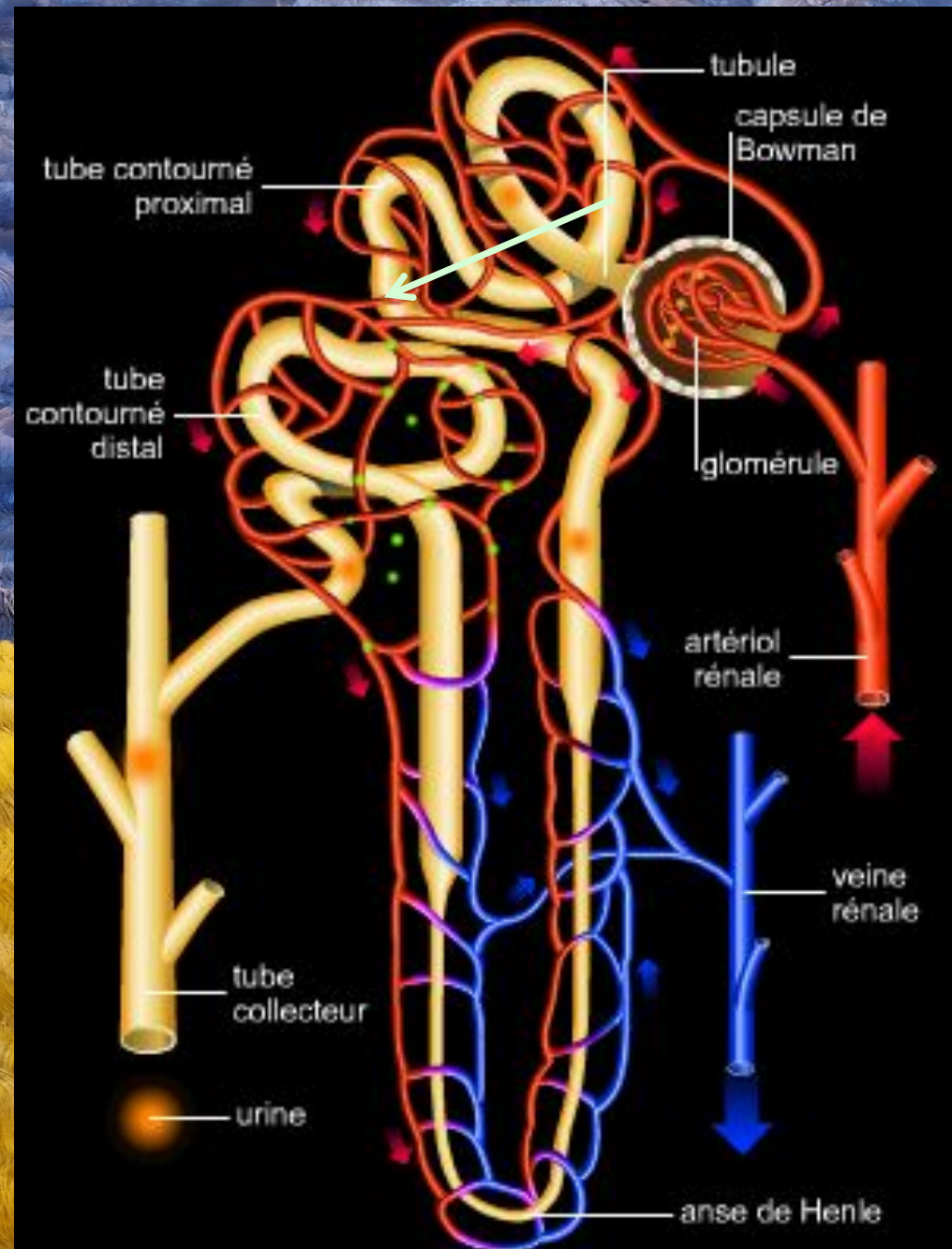


Mme Muriel	Mme Verlaine	Mr José
49 ans	30 ans	59 ans
Biopsie : IgA	GENE: Apol (2x) + Alport (1x)	Biopsie: HSF. Gene: NR
IEC full dose TA < 120/60 mmHG Orthostatisme	IEC dose complete, TA 128/60 Orthostatisme	IEC Perindo:10 mg 120/70
E GFR 69.	E GFR 65	eGFR 57
Protéinurie 1,9 g/24h	Protéinurie: 2,3 g/24h	Protéinurie:2,9 g/24H
purpura et microhématurie fluctuante	Père greffé	



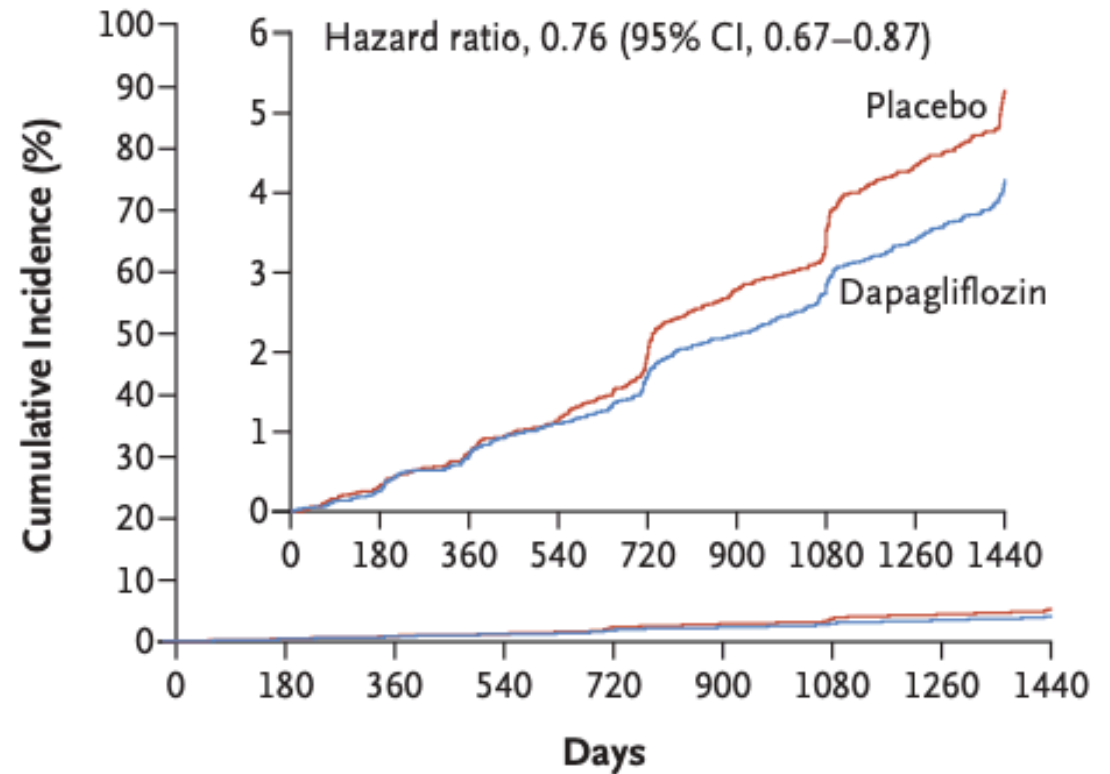
SGLT2 et REIN

- (1) inhibition absorption Glu/Na
- (2) Na stimule M/D
- (3) Vasoconstriction a aff , vasodilatation a eff
- (4) Diminution pression intraglomérulaire



TRIAL Cardiovasculaire safety T2D => Renal Safety

C Renal Composite



No. at Risk

Placebo	8578	8508	8422	8326	8200	8056	7932	7409	5389
Dapagliflozin	8582	8533	8436	8347	8248	8136	8009	7534	5472

Renal trial



Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy

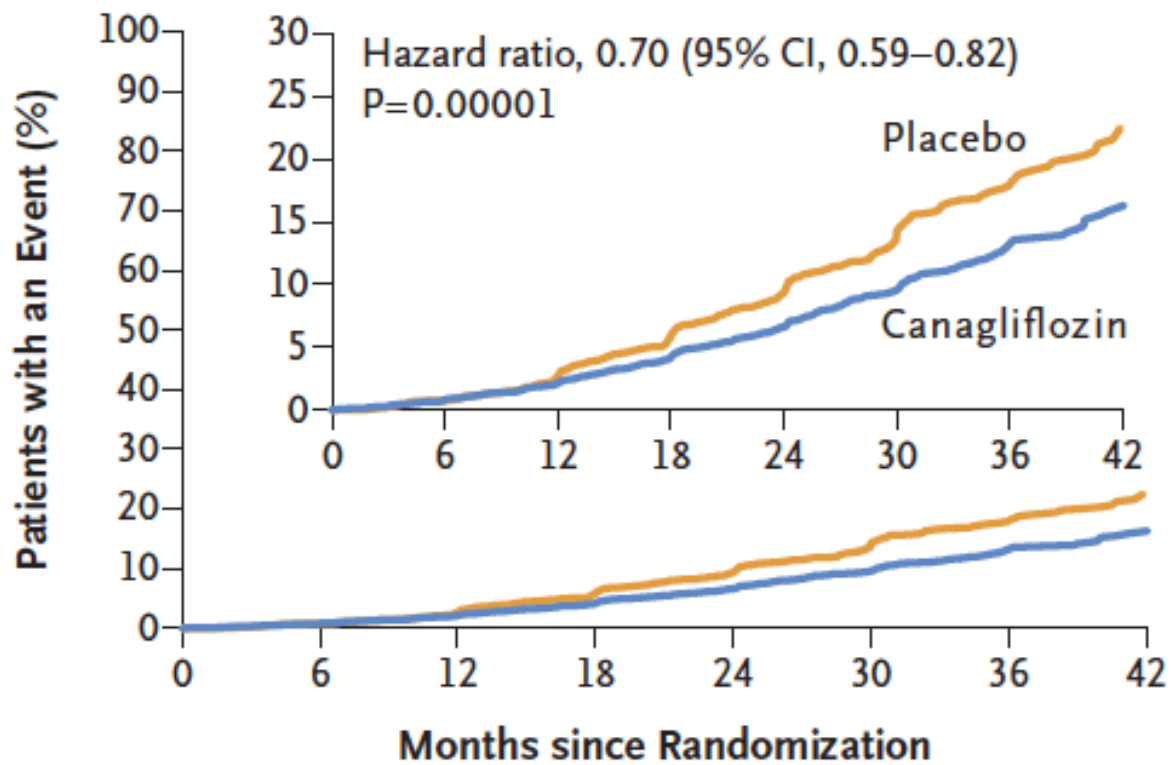
Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Canagliflozin (N=2202)	Placebo (N=2199)	All Patients (N=4401)
Age — yr	62.9±9.2	63.2±9.2	63.0±9.2
Female sex — no. (%)	762 (34.6)	732 (33.3)	1494 (33.9)
Race or ethnic group — no. (%)†			
White	1487 (67.5)	1444 (65.7)	2931 (66.6)
Black	112 (5.1)	112 (5.1)	224 (5.1)
Asian	425 (19.3)	452 (20.6)	877 (19.9)
Other	178 (8.1)	191 (8.7)	369 (8.4)
Current smoker — no. (%)	341 (15.5)	298 (13.6)	639 (14.5)
Hypertension — no. (%)	2131 (96.8)	2129 (96.8)	4260 (96.8)
Heart failure — no. (%)	329 (14.9)	323 (14.7)	652 (14.8)
Duration of diabetes — yr	15.5±8.7	16.0±8.6	15.8±8.6
Cardiovascular disease — no. (%)	1113 (50.5)	1107 (50.3)	2220 (50.4)
Amputation — no. (%)	119 (5.4)	115 (5.2)	234 (5.3)
Body-mass index‡	31.4±6.2	31.3±6.2	31.3±6.2
Blood pressure — mm Hg			
Systolic	139.8±15.6	140.2±15.6	140.0±15.6
Diastolic	78.2±9.4	78.4±9.4	78.3±9.4
Glycated hemoglobin — %	8.3±1.3	8.3±1.3	8.3±1.3
Estimated GFR — ml/min/1.73 m ² §	56.3±18.2	56.0±18.3	56.2±18.2
Median urinary albumin-to-creatinine ratio (IQR)¶	923 (459–1794)	931 (473–1868)	927 (463–1833)

SAFE

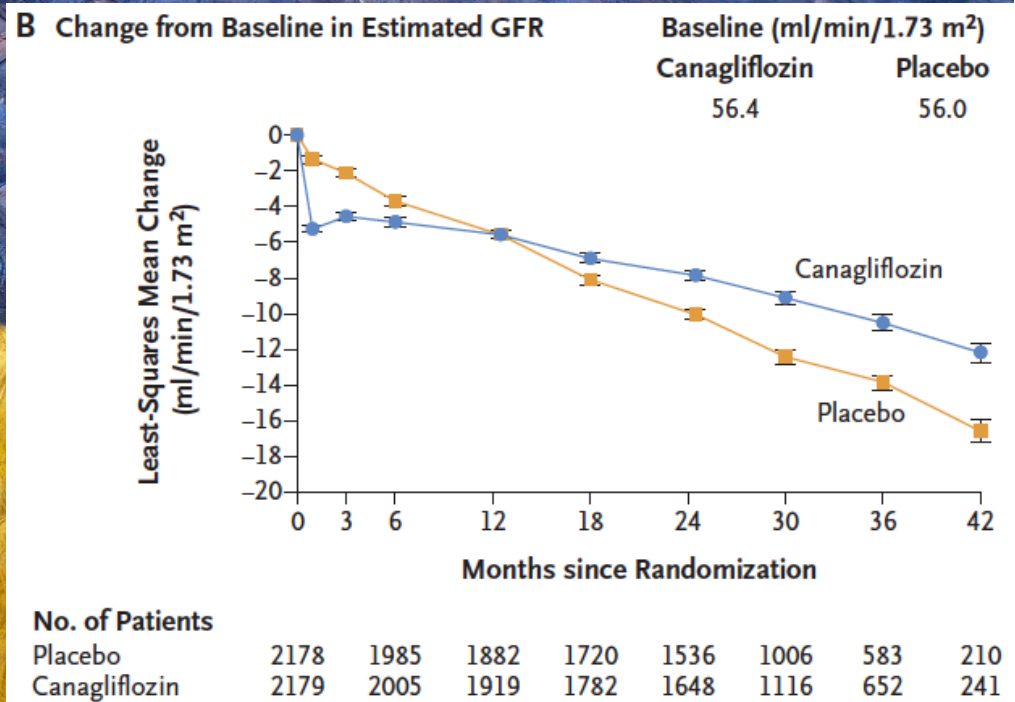
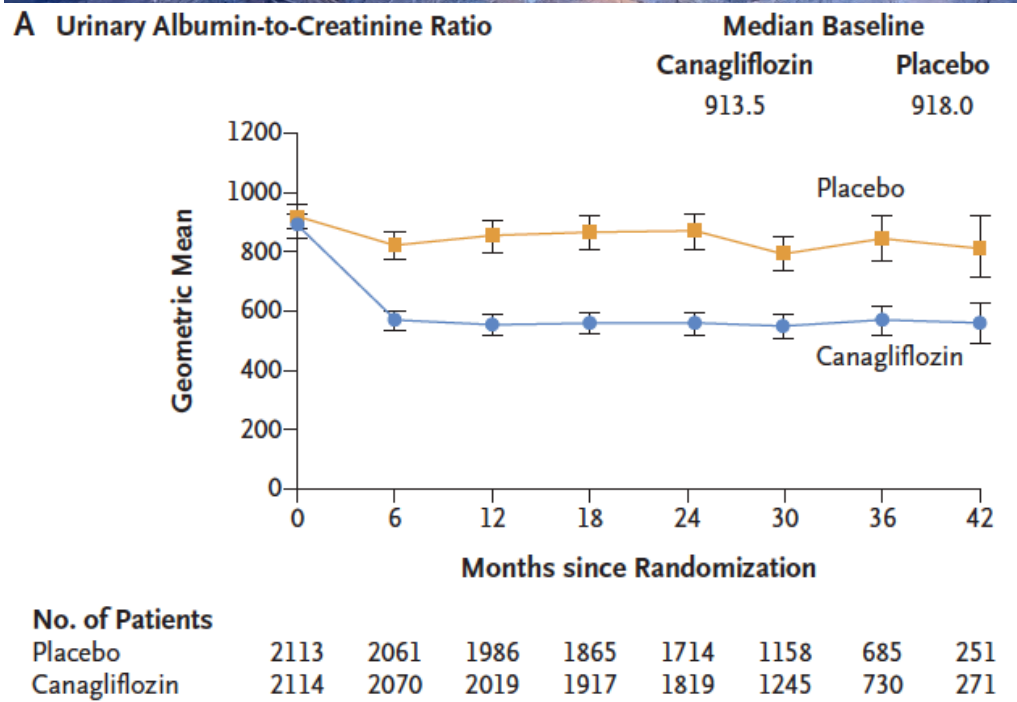
Safety†							NA
Any adverse event	1784/2200	1860/2197	351.4	379.3	0.87 (0.82–0.93)		NA
Any serious adverse event	737/2200	806/2197	145.2	164.4	0.87 (0.79–0.97)		NA
Serious adverse event related to trial drug	62/2200	42/2197	12.2	8.6	1.45 (0.98–2.14)		NA
Amputation	70/2200	63/2197	12.3	11.2	1.11 (0.79–1.56)		NA
Fracture	67/2200	68/2197	11.8	12.1	0.98 (0.70–1.37)		NA
Cancer							
Renal-cell carcinoma	1/2200	5/2197	0.2	0.9	NA		NA
Breast cancer§	8/761	3/731	4.1	1.6	2.59 (0.69–9.76)		NA
Bladder cancer	10/2200	9/2197	1.7	1.6	1.10 (0.45–2.72)		NA
<hr/>							
Acute pancreatitis	5/2200	2/2197	1.0	0.4	NA		NA
Hyperkalemia¶	151/2200	181/2197	29.7	36.9	0.80 (0.65–1.00)		NA
Acute kidney injury	86/2200	98/2197	16.9	20.0	0.85 (0.64–1.13)		NA
Diabetic ketoacidosis	11/2200	1/2197	2.2	0.2	10.80 (1.39–83.65)		NA

A Primary Composite Outcome



No. at Risk

Placebo	2199	2178	2132	2047	1725	1129	621	170
Canagliflozin	2202	2181	2145	2081	1786	1211	646	196



The NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

Dapagliflozin in Patients with Chronic Kidney Disease

Hiddo J.L. Heerspink, Ph.D., Bergur V. Stefánsson, M.D.,
Ricardo Correa-Rotter, M.D., Glenn M. Chertow, M.D., Tom Greene, Ph.D.,
Fan-Fan Hou, M.D., Johannes F.E. Mann, M.D., John J.V. McMurray, M.D.,
Magnus Lindberg, M.Sc., Peter Rossing, M.D., C. David Sjöström, M.D.,
Roberto D. Toto, M.D., Anna-Maria Langkilde, M.D., and David C. Wheeler, M.D.,
for the DAPA-CKD Trial Committees and Investigators*

DAPA CKD

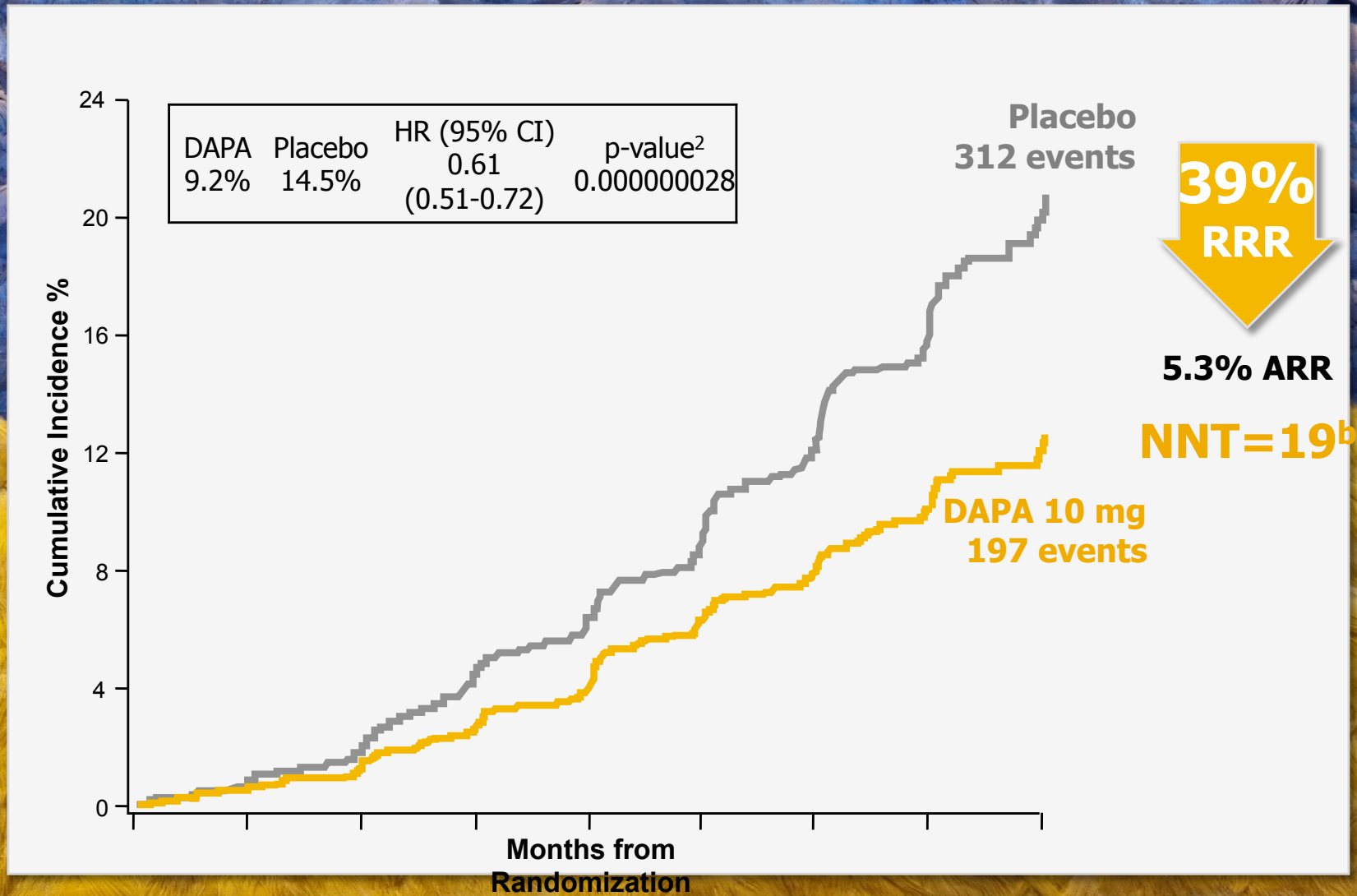
Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

Characteristic	Dapagliflozin (N=2152)	Placebo (N=2152)
Age — yr	61.8±12.1	61.9±12.1
Female sex — no. (%)	709 (32.9)	716 (33.3)
Race — no. (%)†		
White	1124 (52.2)	1166 (54.2)
Black	104 (4.8)	87 (4.0)
Asian	749 (34.8)	718 (33.4)
Other	175 (8.1)	181 (8.4)
Weight — kg	81.5±20.1	82.0±20.9
Body-mass index‡	29.4±6.0	29.6±6.3
Current smoker — no. (%)	283 (13.2)	301 (14.0)
Blood pressure — mm Hg		
Systolic	136.7±17.5	137.4±17.3
Diastolic	77.5±10.7	77.5±10.3
Estimated GFR		
Mean — ml/min/1.73 m ²	43.2±12.3	43.0±12.4
Distribution — no. (%)		
≥60 ml/min/1.73 m ²	234 (10.9)	220 (10.2)
45 to <60 ml/min/1.73 m ²	646 (30.0)	682 (31.7)
30 to <45 ml/min/1.73 m ²	979 (45.5)	919 (42.7)
<30 ml/min/1.73 m ²	293 (13.6)	331 (15.4)

Table 1. Demographic and Clinical Characteristics of the Participants at Baseline.*

Characteristic	Dapagliflozin (N=2152)	Placebo (N=2152)
Age — yr	61.8±12.1	61.9±12.1
Female sex — no. (%)	709 (32.9)	716 (33.3)
Race — no. (%) [†]		
White	1124 (52.2)	1166 (54.2)
Black	104 (4.8)	87 (4.0)
Asian	749 (34.8)	718 (33.4)
Other	175 (8.1)	181 (8.4)
Weight — kg	81.5±20.1	82.0±20.9
Hemoglobin — g/liter	128.6±18.1	127.9±18.0
Serum potassium — mEq/liter	4.6±0.5	4.6±0.6
Urinary albumin-to-creatinine ratio [‡]		
Median (interquartile range)	965 (472–1903)	934 (482–1868)
>1000 — no. (%)	1048 (48.7)	1031 (47.9)
Type 2 diabetes — no. (%)	1455 (67.6)	1451 (67.4)
Cardiovascular disease — no. (%) [¶]	813 (37.8)	797 (37.0)
Heart failure — no. (%)	235 (10.9)	233 (10.8)
Previous medication — no. (%)		
ACE inhibitor	673 (31.3)	681 (31.6)
ARB	1444 (67.1)	1426 (66.3)
Diuretic	928 (43.1)	954 (44.3)
Statin	1395 (64.8)	1399 (65.0)

Dapagliflozin significantly slowed progression of kidney disease and reduced the risk of adverse outcomes (sustained $\geq 50\%$ egfr decline, ESKD, renal or CV death)^{a,1}



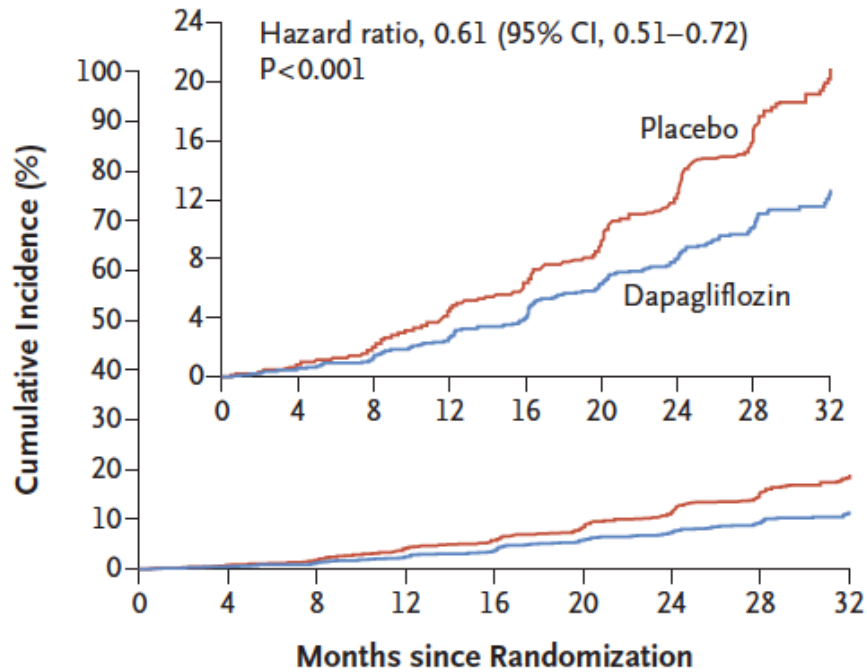
aESKD defined as the need for maintenance dialysis (peritoneal or hemodialysis) for at least 28 days and renal transplantation or sustained eGFR <15mL/min/1.73m² for at least 28 days. Renal death was defined as death due to ESKD when dialysis treatment was deliberately withheld for any reason.³; ^b95% CI, 15 to 27.

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 et al. N Engl J Med. 2020; 383:1436-1446; 2. Heerspink HJL. Presented at: ESC Congress – The Digital Experience; August 29 – September 1, 2020; 3. Heerspink HJL et al. Nephrol Dial Transplant. 2020;35:274–282.

DAPA CKD

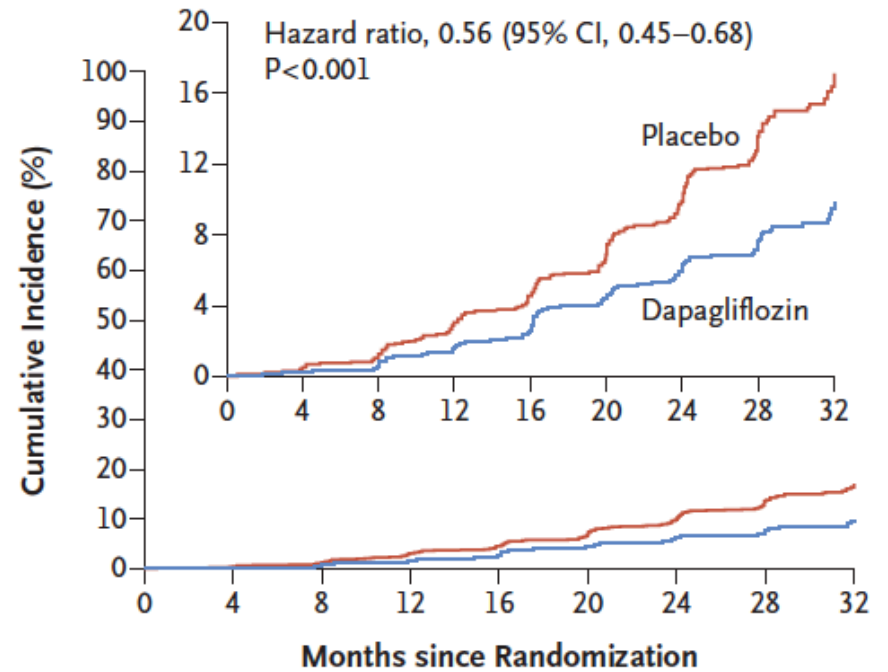
A Primary Composite Outcome



No. at Risk

Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

B Renal-Specific Composite Outcome

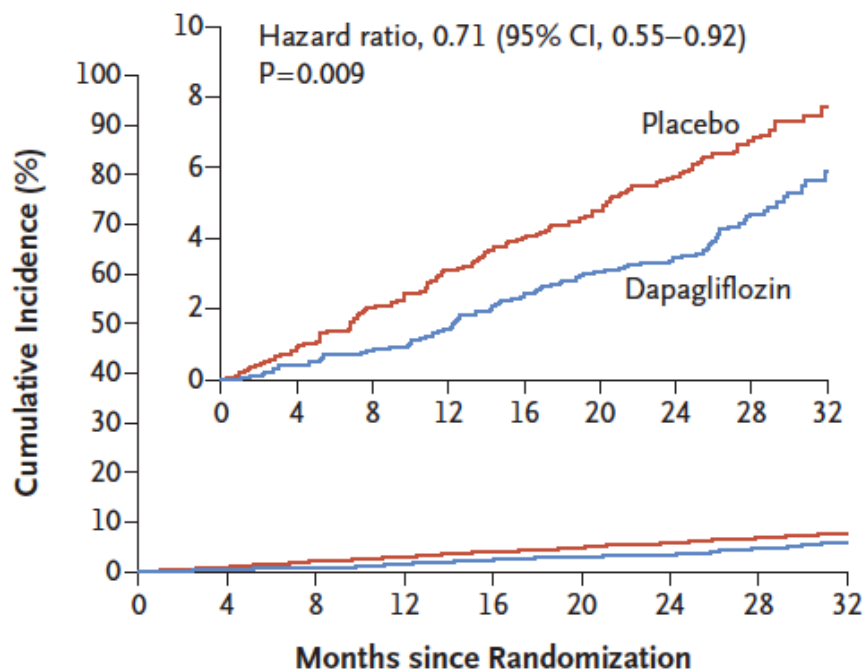


No. at Risk

Placebo	2152	1993	1936	1858	1791	1664	1232	774	270
Dapagliflozin	2152	2001	1955	1898	1841	1701	1288	831	309

DAPA CKD

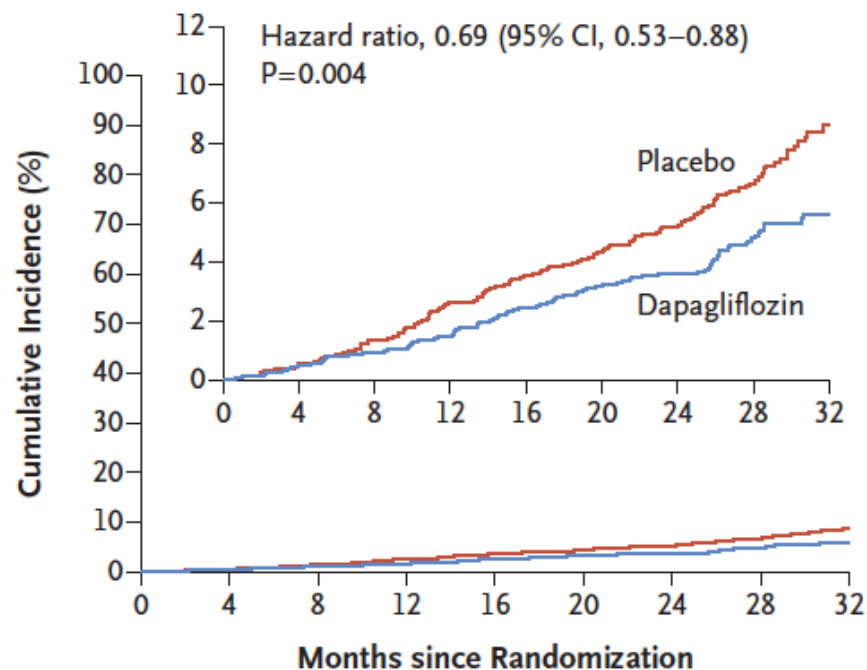
C Composite of Death from Cardiovascular Causes or Hospitalization for Heart Failure



No. at Risk

Placebo	2152	2023	1989	1957	1927	1853	1451	976	360
Dapagliflozin	2152	2035	2021	2003	1975	1895	1502	1003	384

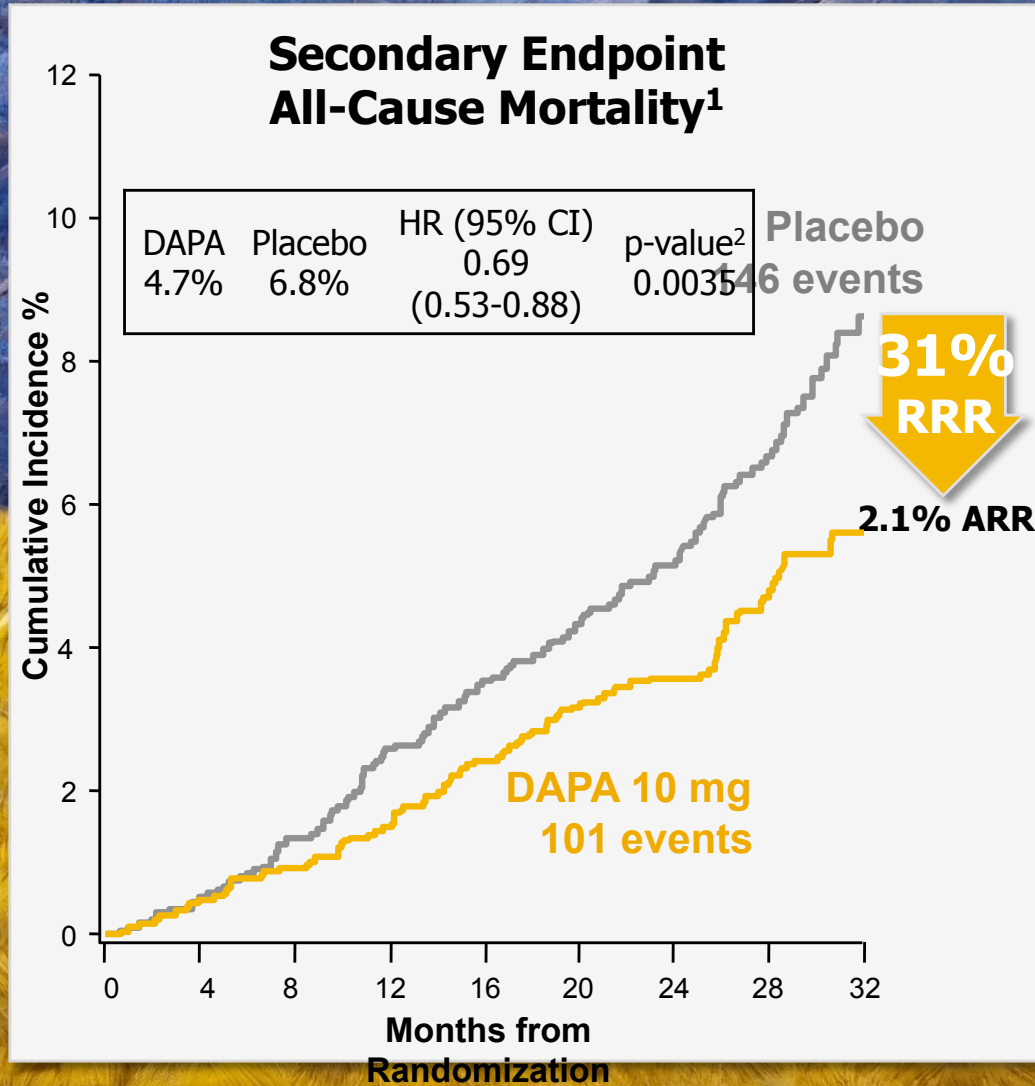
D Death from Any Cause



No. at Risk

Placebo	2152	2035	2018	1993	1972	1902	1502	1009	379
Dapagliflozin	2152	2039	2029	2017	1998	1925	1531	1028	398

Dapagliflozin demonstrated a significant marked reduction in death from any cause.^{1,2*}



All-cause mortality by causes of death and by dialysis initiation³

	DAPA n/N (%)	Placebo n/N (%)	Total n/N (%)
Overall mortality	101/2152 (4.7)	146/2152 (6.8)	247/4304 (5.7)
CV death	41/2152 (1.9)	50/2152 (2.3)	91/4304 (2.1)
Non-CV death	36/2152 (1.7)	66/2152 (3.1)	102/4304 (2.4)
Undetermined	24/2152 (1.1)	30/2152 (1.4)	54/4304 (1.3)
Overall mortality by dialysis initiation			
Without chronic dialysis	89/2084 (4.3)	121/2053 (5.9)	210/4137 (5.1)
With chronic dialysis	12/68 (17.6)	25/99 (25.3)	37/167 (22.2)

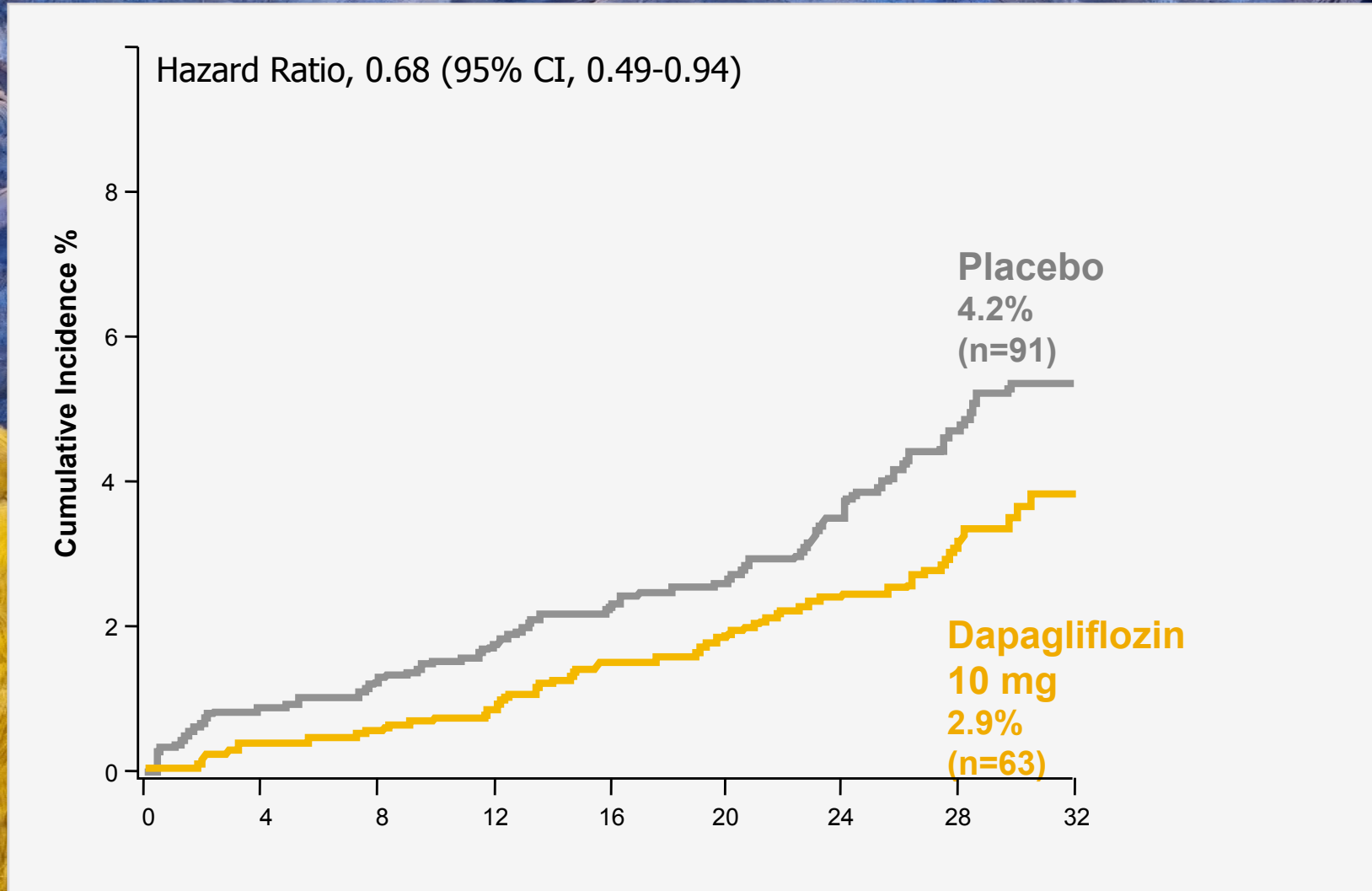
ARR = absolute risk reduction; CV = cardiovascular; DAPA = dapagliflozin; RRR = relative risk reduction

The DAPA-CKD trial was stopped early due to efficacy benefit. Because of the unplanned early stop, this secondary endpoint is considered nominal.

1. Heerspink HJL et al. N Engl J Med. 2020; 383:1436-1446; 2. Heerspink HJL. Presented at: ESC Congress – The Digital Experience; August 29 – September 1, 2020;

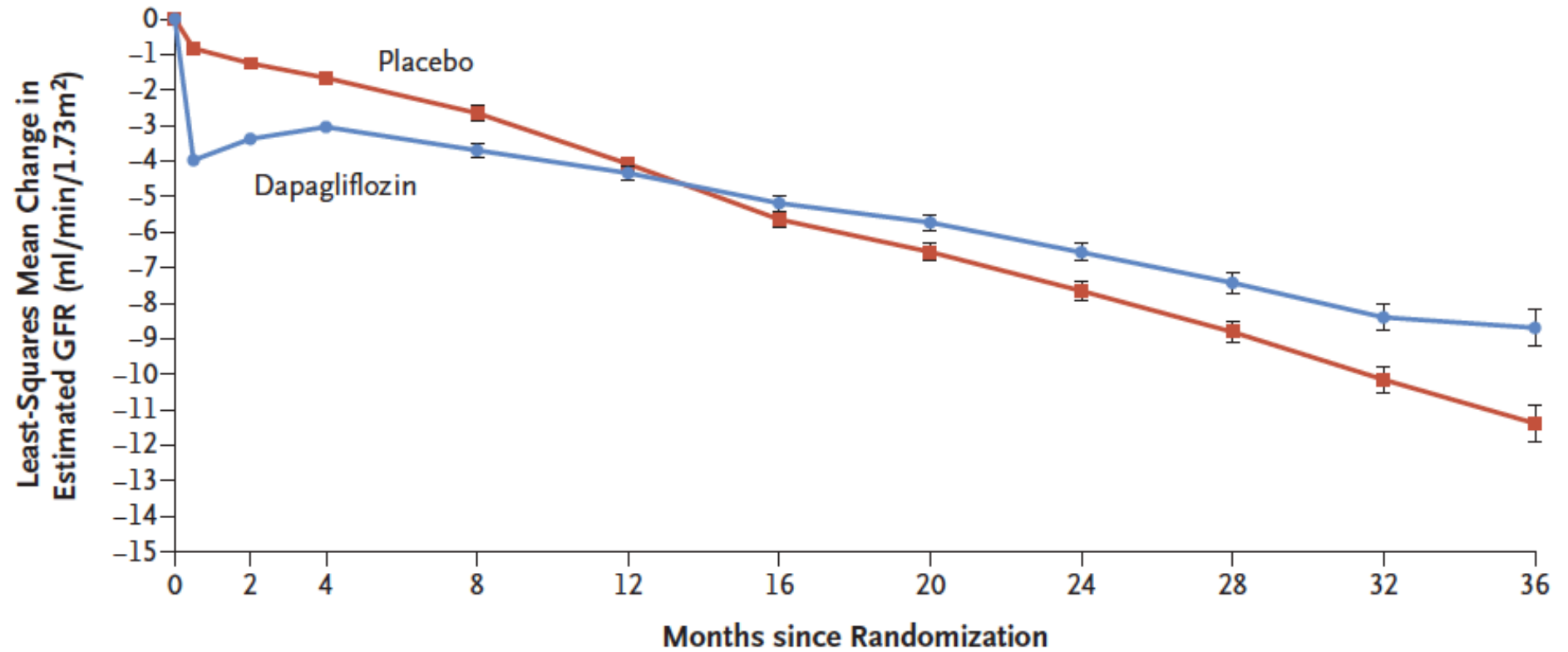
3. Heerspink HJL et al. Eur Heart J. 2021;42:1216-1227.

In a prespecified analysis, dapagliflozin reduced the risk of AKI versus placebo



AKI = acute kidney injury; CI = confidence interval
Heerspink HJL et al. Presented at: ERA-EDTA Congress; June 5-8, 2021; Virtual.

DAPA CKD

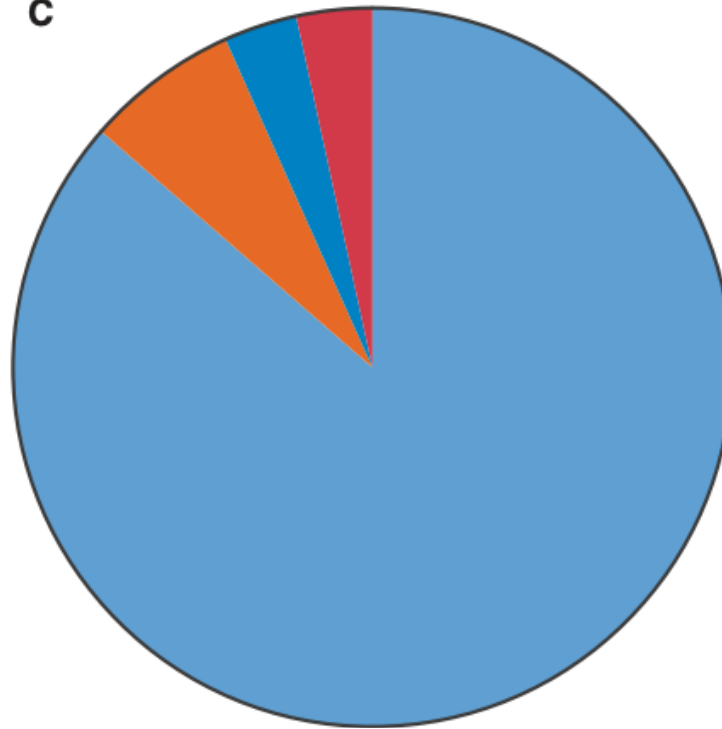


No. of Participants

Placebo	2152	2029	1981	1866	1795	1753	1672	1443	935	447	157
Dapagliflozin	2152	2031	2001	1896	1832	1785	1705	1482	978	496	157

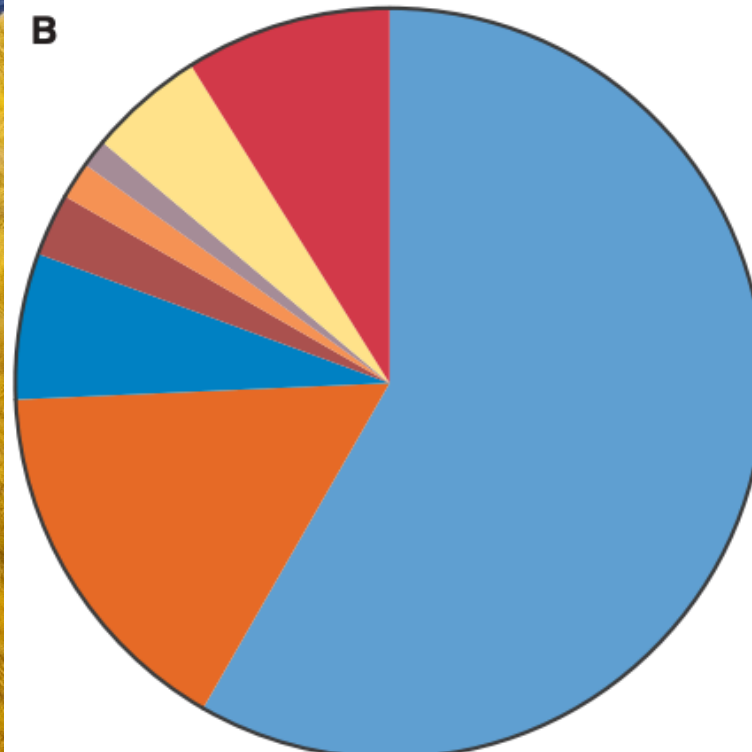
DAPA CKD ETIOLOGIE

C



- 86.4% Diabetic Nephropathy
- 6.9% Ischaemic/Hypertensive Nephropathy
- 3.3% Glomerulonephritis
- 3.4% Other

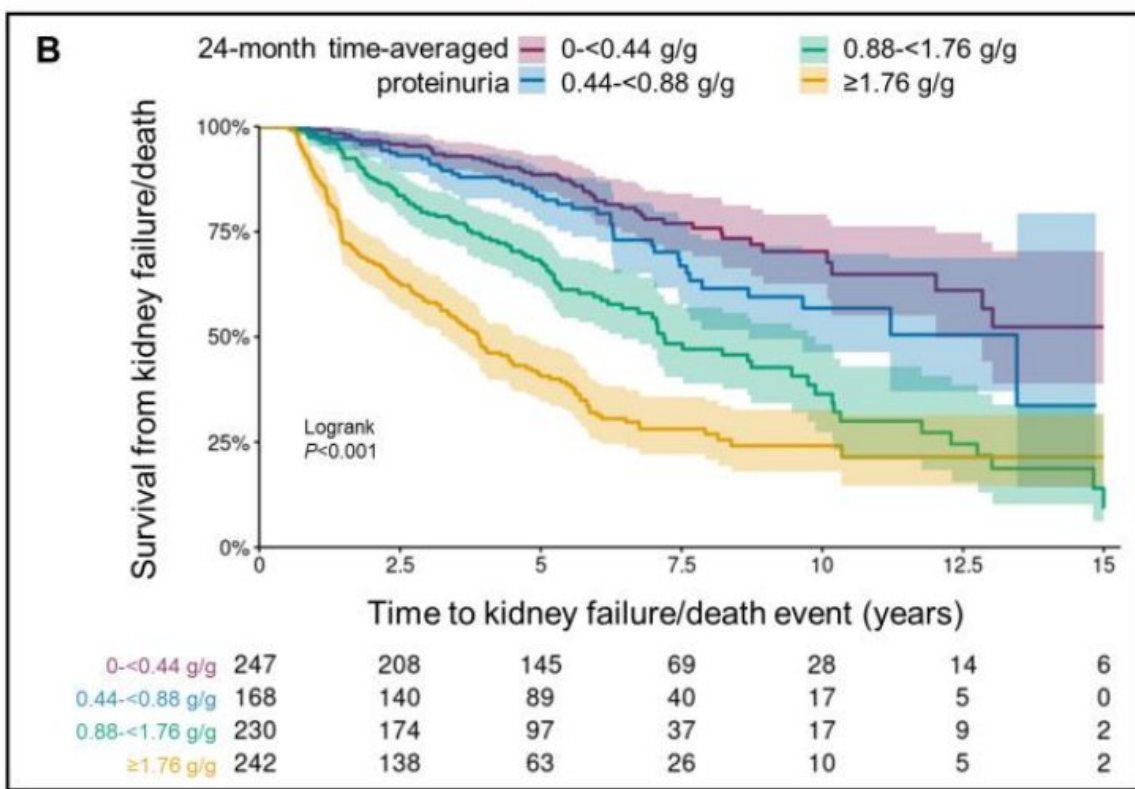
B



- 58.3% Diabetic Nephropathy
- 16.0% Ischaemic/Hypertensive Nephropathy
- 6.3% IgA Nephropathy
- 2.7% Focal Segmental Glomerulosclerosis
- 1.6% Chronic Pyelonephritis
- 1.2% Chronic Interstitial Nephritis
- 5.0% Unknown Cause
- 8.9% Other

MALADIE BERGER – IgA Nephropathie

- Dépôt d'IgA
- Microhématurie
- HTA



- La protéinurie est de très mauvais pronostic

DAPA CKD IgA

A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy.

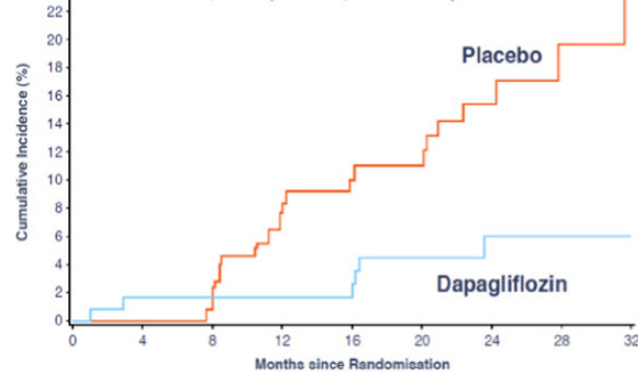
DAPA-CKD population:

- eGFR 25-75 mL/min/1.73m²
- UACR 200-5000 mg/g
- Receiving a stable, maximally tolerable ACEi/ARB dose
- With and without type 2 diabetes

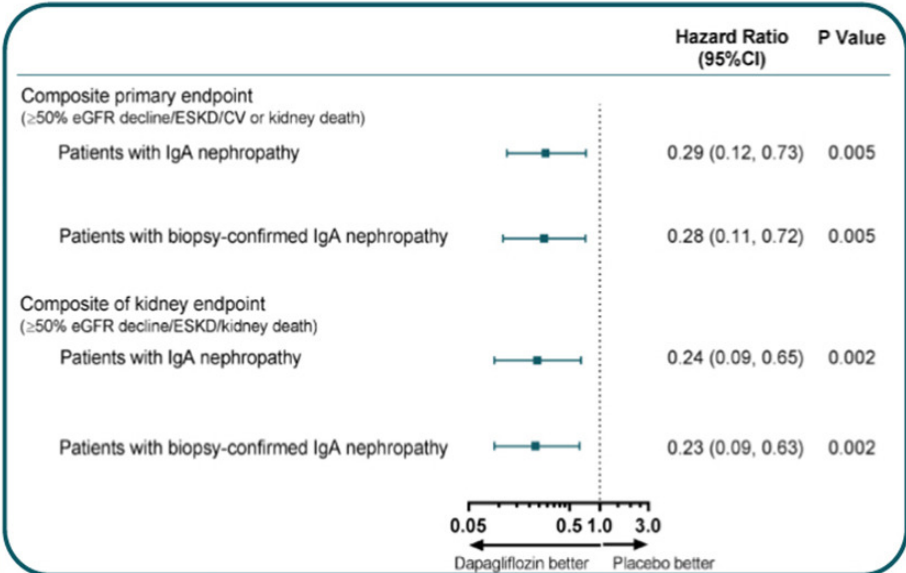


Composite primary endpoint in patients with IgA nephropathy (n=270)

Hazard ratio, 0.29 (95% CI, 0.12–0.73)



IgA, immunoglobulin A; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockers; CKD, chronic kidney disease; ESKD, end-stage kidney disease



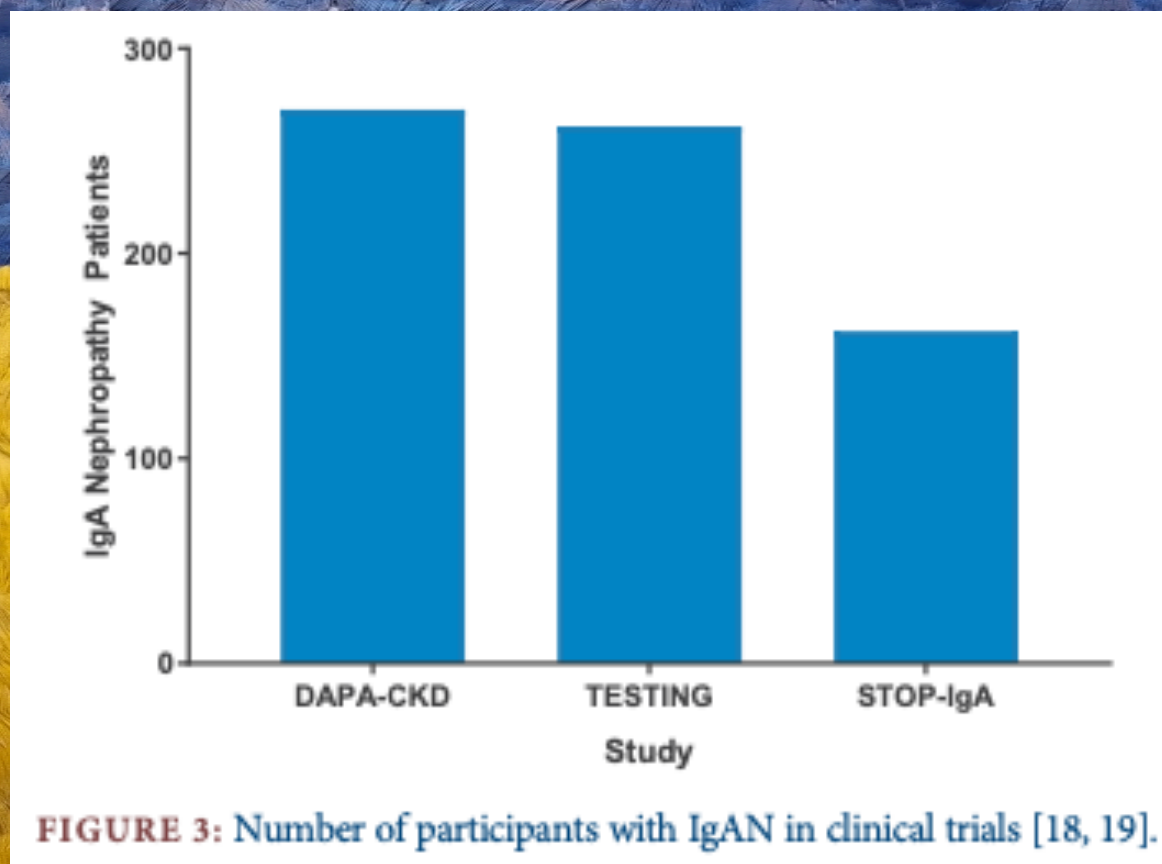
CONCLUSION:

In patients with IgA nephropathy, when added to ACEi/ARB therapy, dapagliflozin significantly and substantially reduced the risk of CKD progression

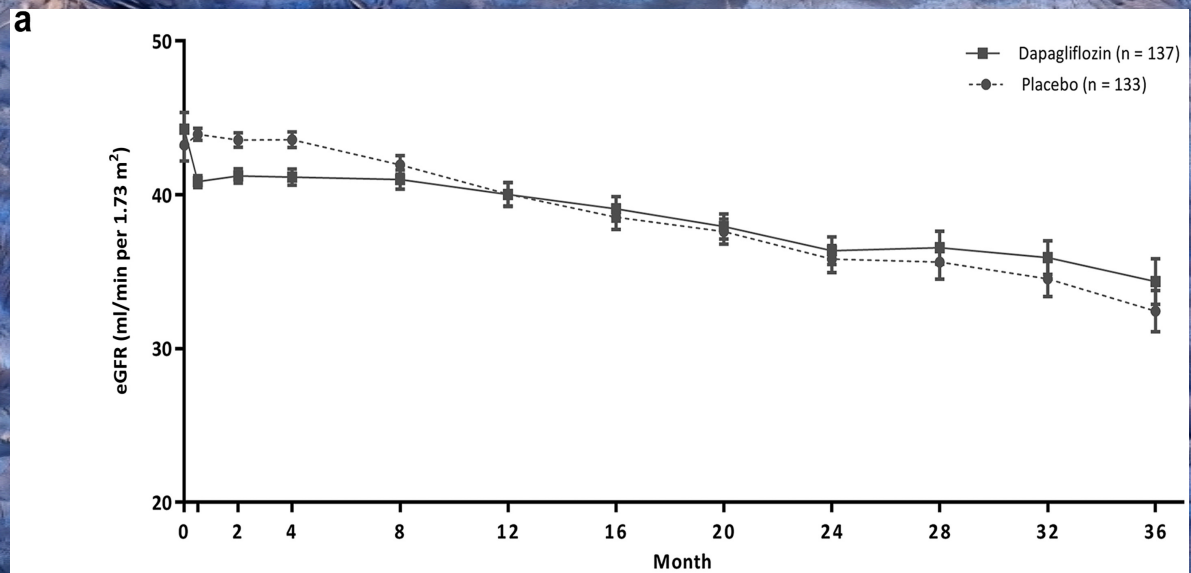
DAPA CKD IgA

A pre-specified analysis of the DAPA-CKD trial demonstrates the effects of dapagliflozin on major adverse kidney events in patients with IgA nephropathy

David C. Wheeler et al. KI Avril 2021

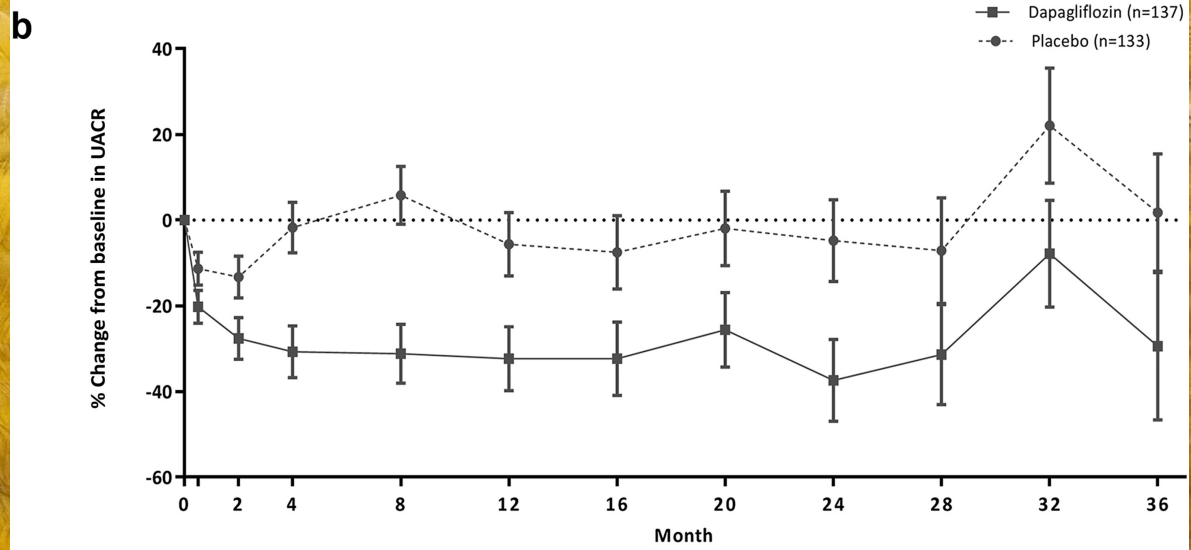


DAPA CKD IGA



Participants per time point

Dapagliflozin	137	130	121	111	95	99	98	95	77	53	34	10
Placebo	133	129	124	118	105	100	98	93	80	45	28	19



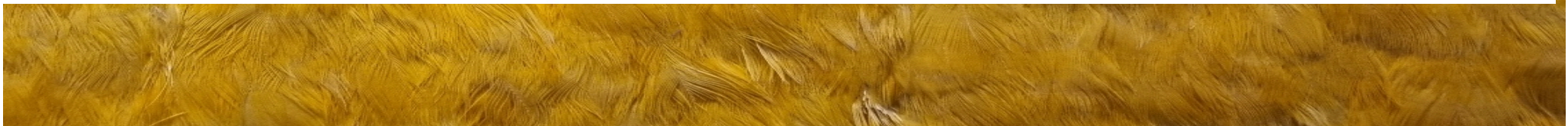
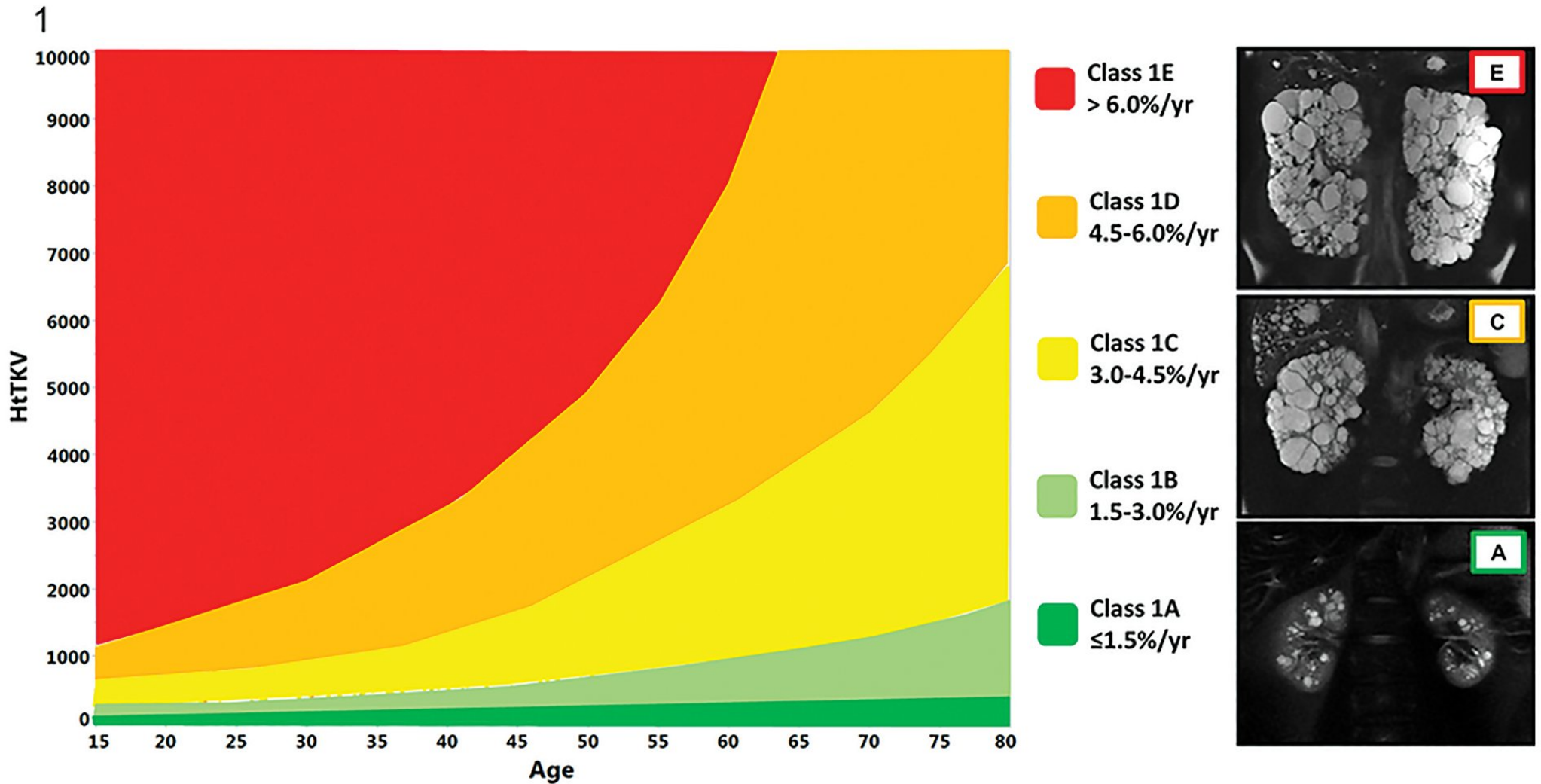
Participants per time point

Dapagliflozin	137	130	121	111	95	99	98	95	77	53	34	10
Placebo	133	129	124	118	105	100	98	93	80	45	28	19

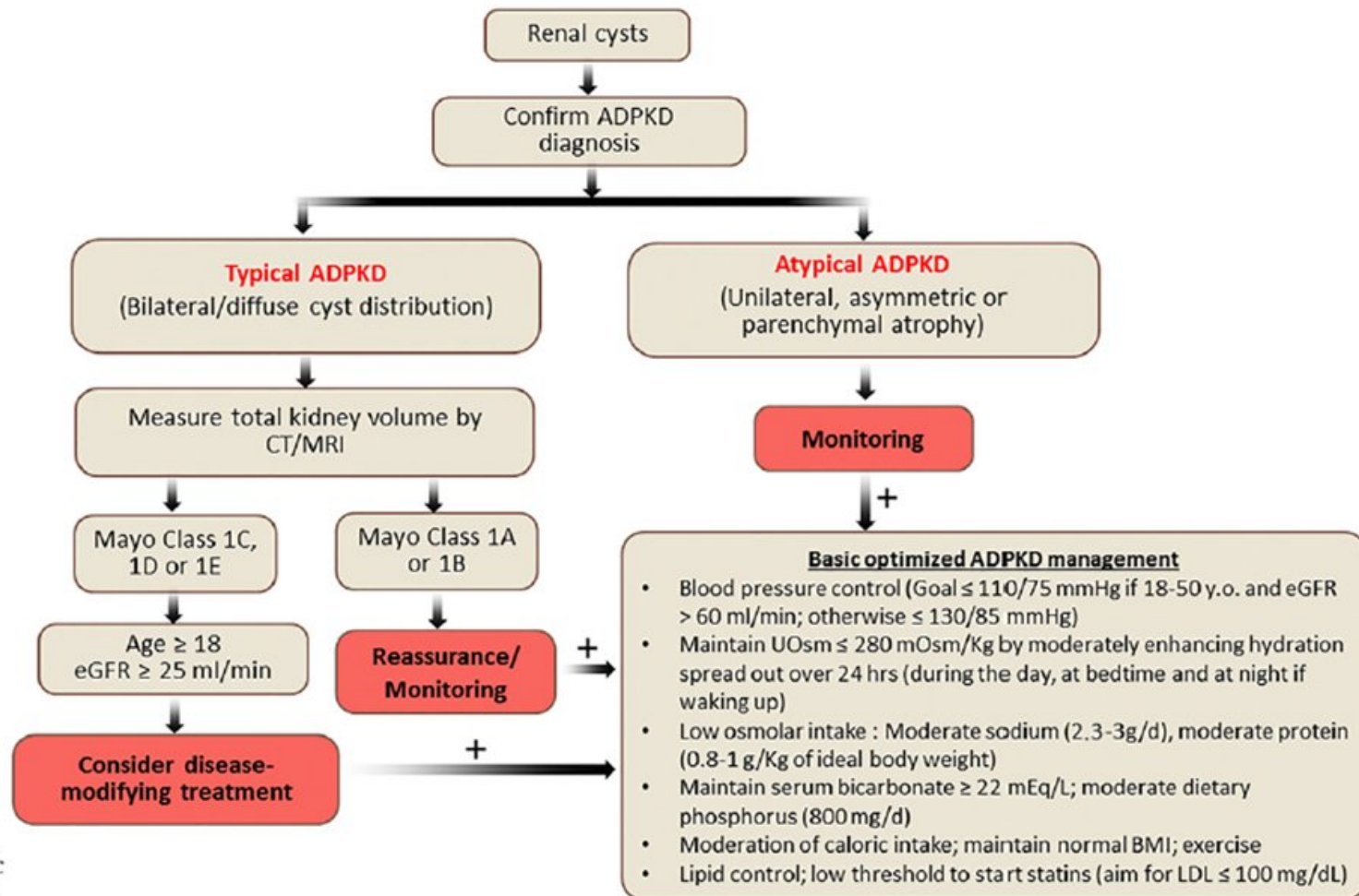
SGLT2R surveillance

- Avant : Urine avec ACR/PCR !
- Pendant:
 - Pression artérielle
 - Infection
 - Evolution eGFR (La pente doit ralentir)
- Si arrêt apparition d'une Protéinurie !

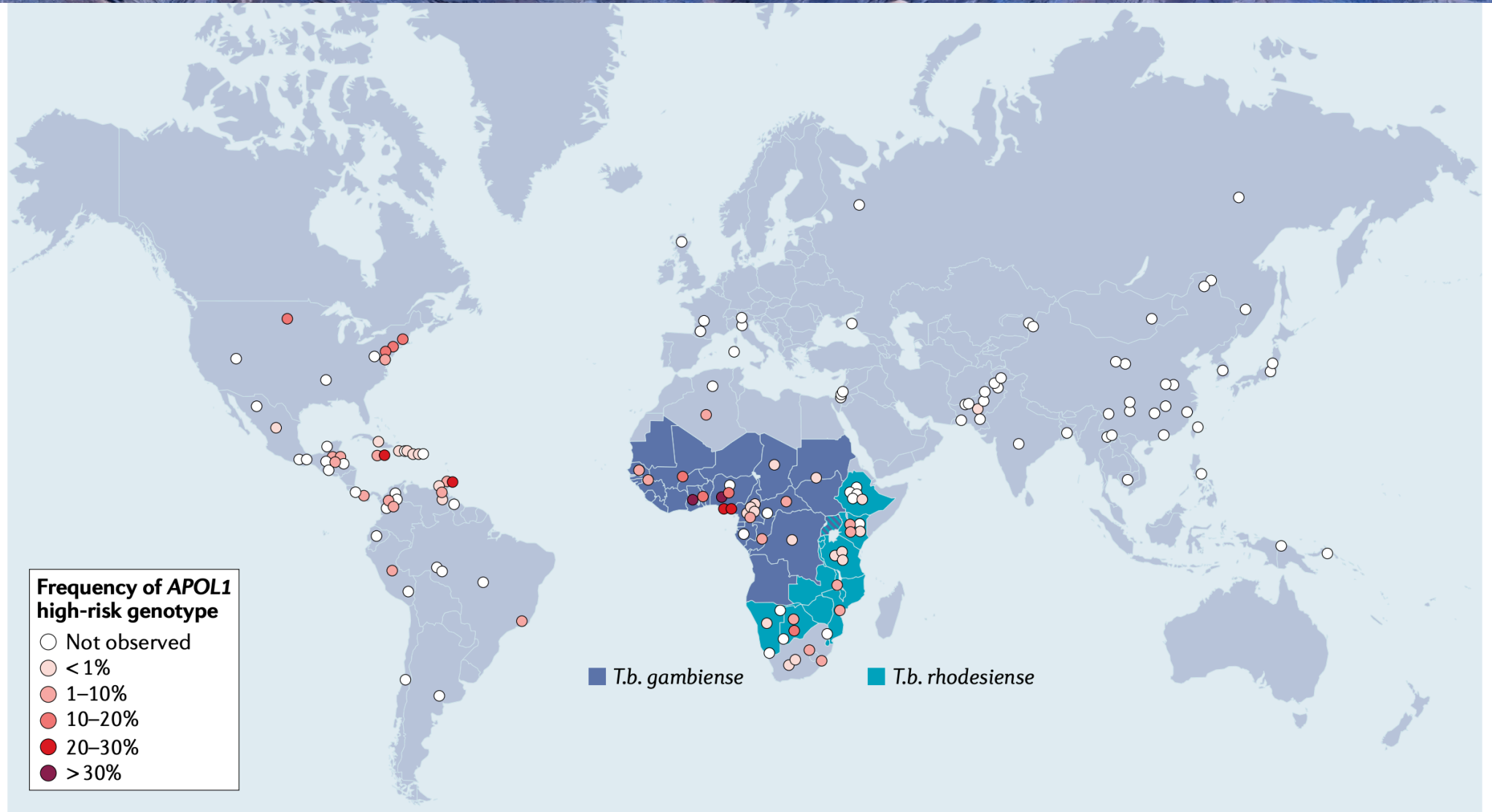
BUVEZ BEAUCOUP ... A D P K D ?



TOLVAPTAN GAIN : 10 ans ?



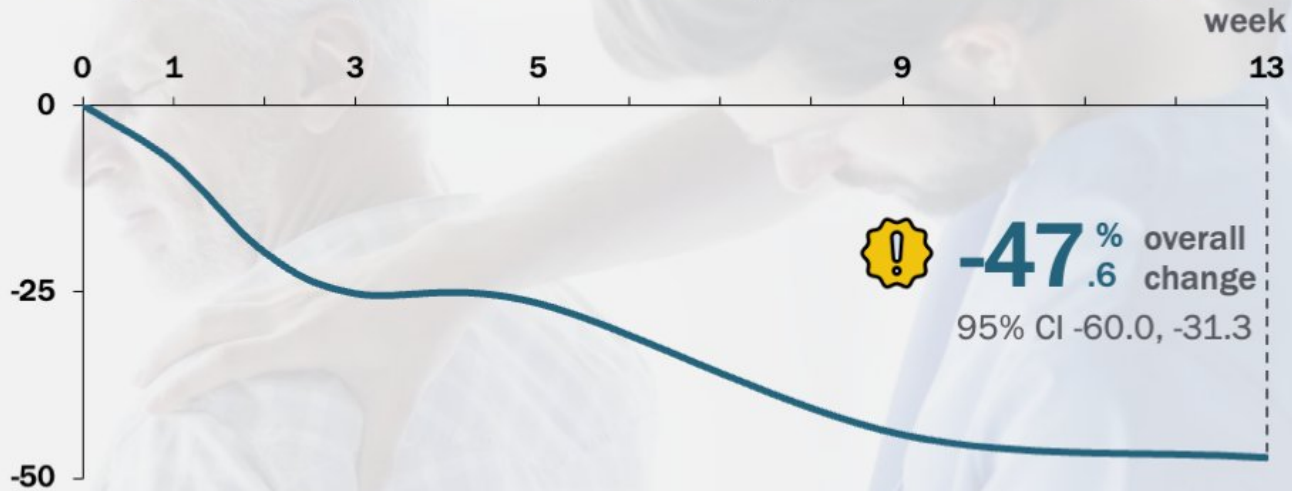
GENETIQUE : APOL1



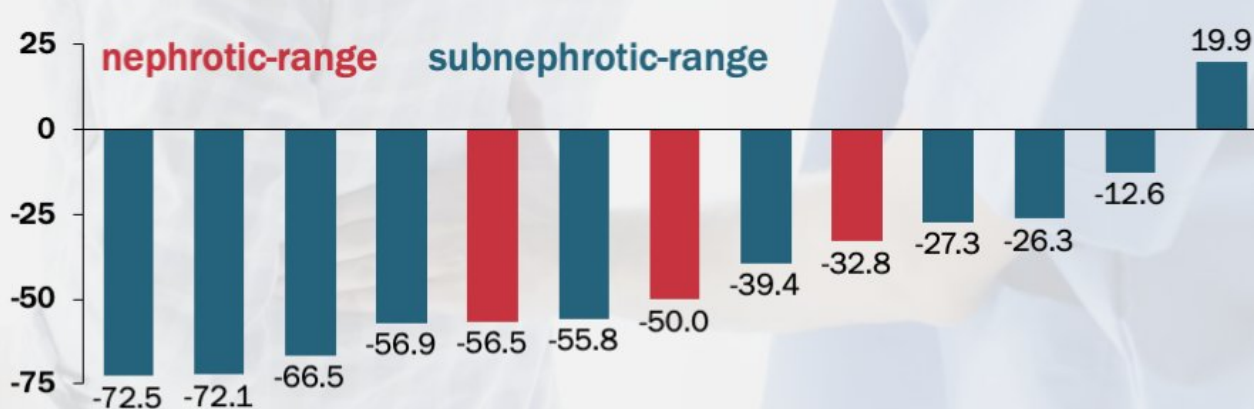


Inaxaplin reduced proteinuria in patients with two *APOL1* variants and fg-glomerulosclerosis

Change in urinary PtC ratio over time, geometric % change



Change in urinary PtC ratio in each participant at week 13



Hamdy FC et al. *N Engl J Med.* 2023

fg-glomerulosclerosis – focal segmental glomerulosclerosis, PtC – protein-to-creatinine

created by **MAG**

Remerciements

- A votre compétence dans le dépistage



À vos questions

Qu'elle soit nécessaire, ou même justifiée, ne croyez jamais que la guerre n'est pas un crime

ernest-hemingway