Nouveautés en Insuffisance Rénale Chronique

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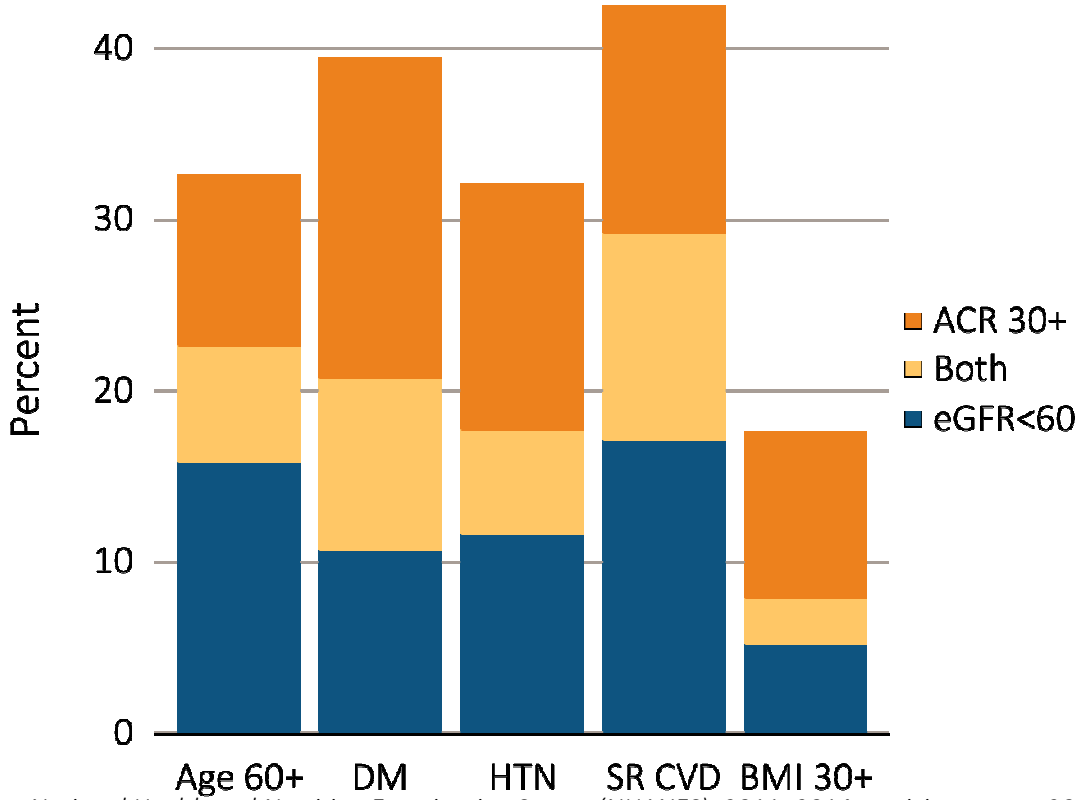
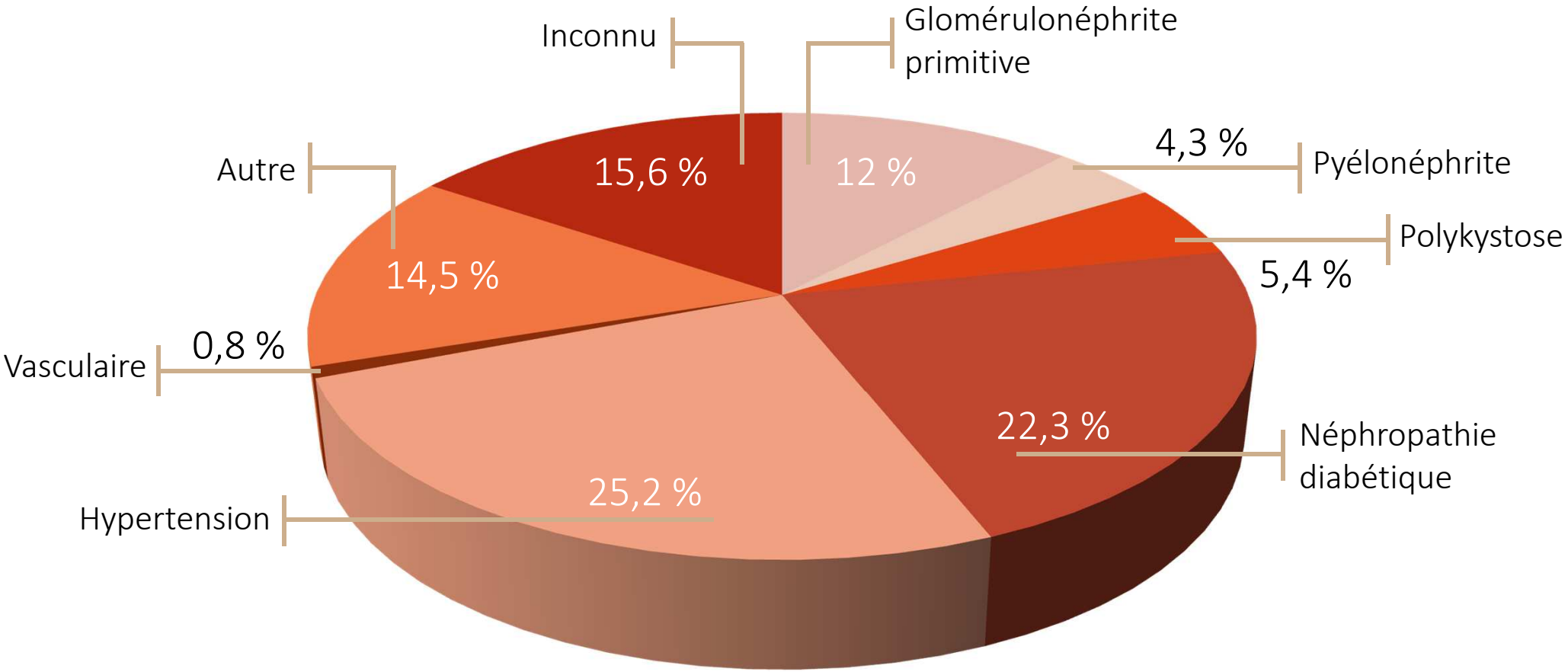
UNIVERSITÉ DE GENÈVE
HUG Hôpitaux Universitaires Genève

Figure 1.8 Distribution of markers of CKD in NHANES participants with diabetes, hypertension, self-reported cardiovascular disease, & obesity, 2011–2014



Data Source: National Health and Nutrition Examination Survey (NHANES), 2011–2014 participants age 20 & older. Single-sample estimates of eGFR & ACR; eGFR calculated using the CKD-EPI equation. Abbreviations: ACR, urine albumin/creatinine ratio; BMI, body mass index; CKD, chronic kidney disease; SR CVD, self-reported cardiovascular disease; eGFR, estimated glomerular filtration rate; HTN, hypertension.

Causes de la maladie rénale chronique



Données Inserm 2017

Qui screener?

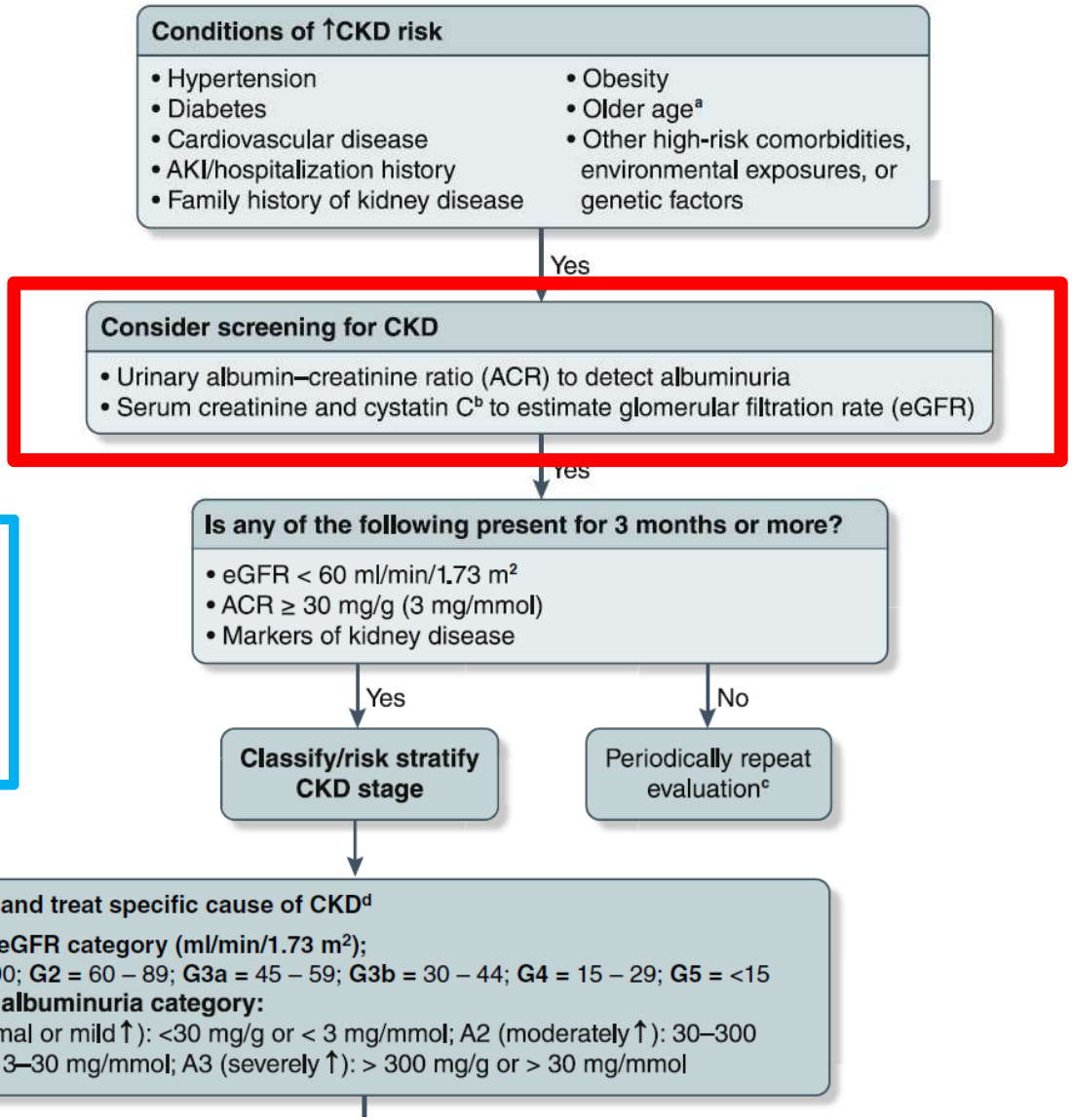
Conditions of ↑CKD risk

- Hypertension
- Diabetes
- Cardiovascular disease
- AKI/hospitalization history
- Family history of kidney disease
- Obesity
- Older age[a]
- Other high-risk comorbidities, environmental exposures, or genetic factors

Oncologic patients

Patients with immunologic disease (SLE, Sjogren, PR etc…)

Schlipak, KDIGO, Kid Int, 2021

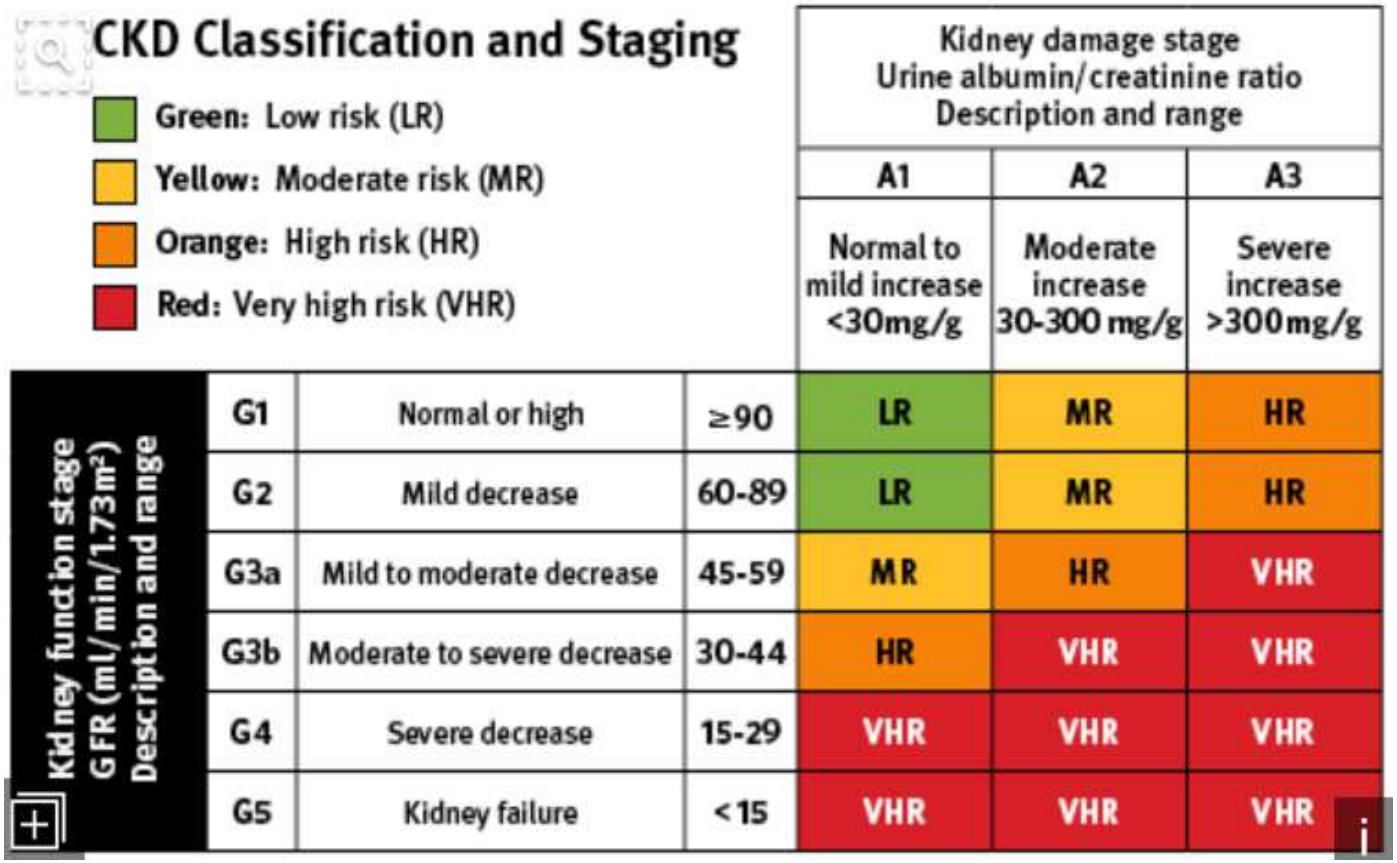


Sédiment, ultrason
Bilan immuno et viro selon

A consensus emerged that CKD screening coupled with risk stratification and treatment should be implemented immediately for high-risk persons and that this should ideally occur in primary or community care settings with tailoring to the local context.

Schlipak, KDIGO, Kid Int, 2021

Présentation clinique et classes



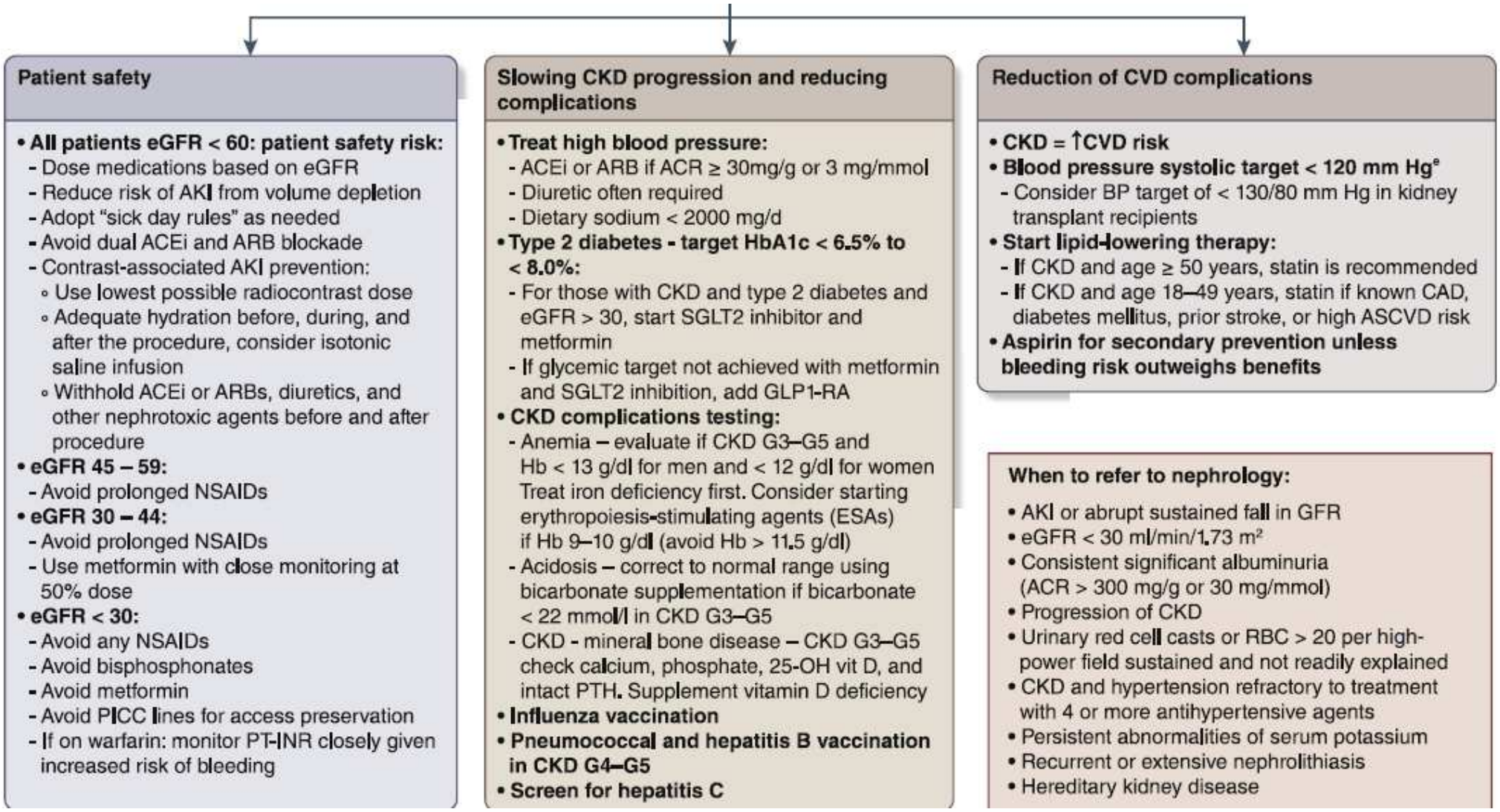
CKD Classification and Staging

- **Green:** Low risk (LR)
- **Yellow:** Moderate risk (MR)
- **Orange:** High risk (HR)
- **Red:** Very high risk (VHR)

Kidney function stage GFR (ml/min/1.73m²) Description and range				Kidney damage stage Urine albumin/creatinine ratio Description and range		
				A1	A2	A3
				Normal to mild increase <30mg/g	Moderate increase 30-300 mg/g	Severe increase >300mg/g
	G1	Normal or high	≥90	LR	MR	HR
	G2	Mild decrease	60-89	LR	MR	HR
	G3a	Mild to moderate decrease	45-59	MR	HR	VHR
	G3b	Moderate to severe decrease	30-44	HR	VHR	VHR
	G4	Severe decrease	15-29	VHR	VHR	VHR
	G5	Kidney failure	<15	VHR	VHR	VHR

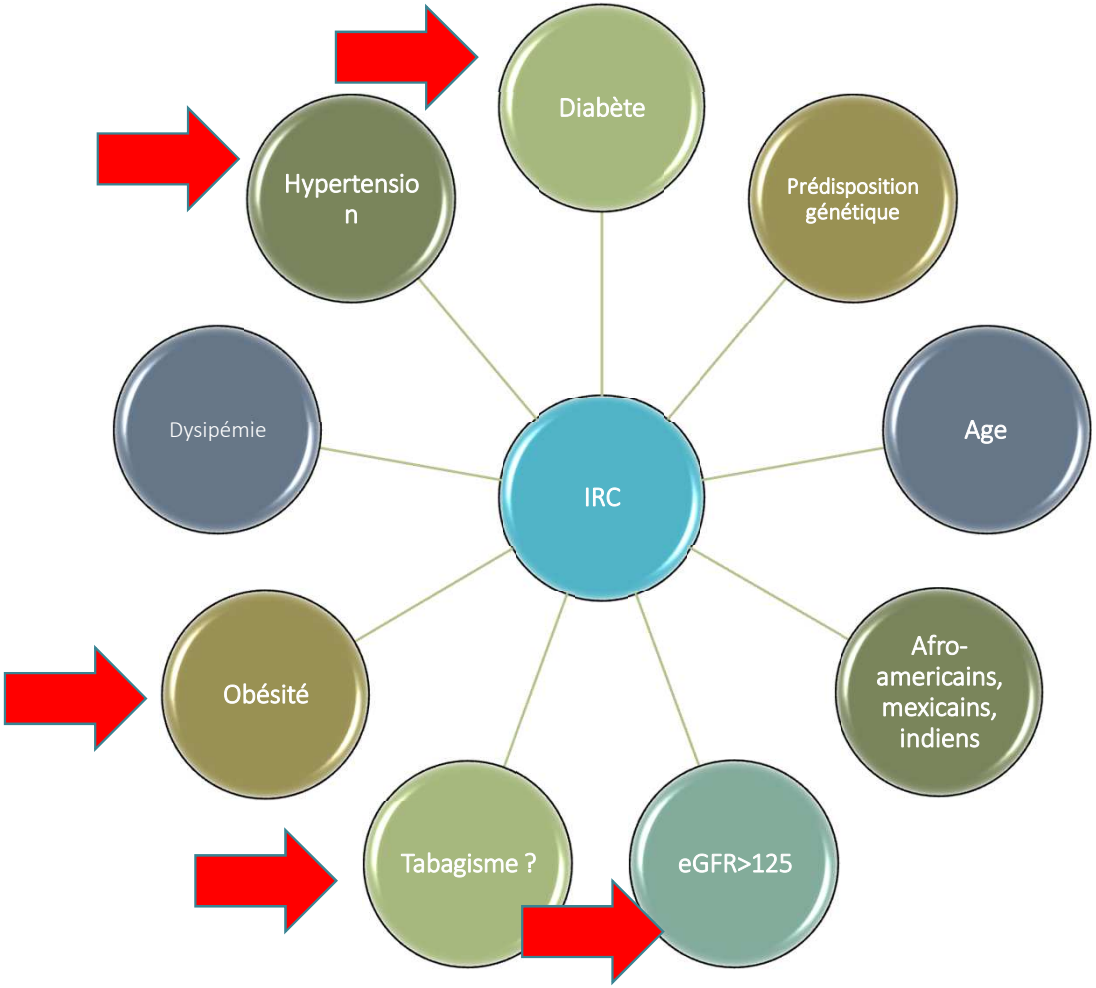
Créatinine et eGFR (evt Cystatine)

Albumine / créat urinaire

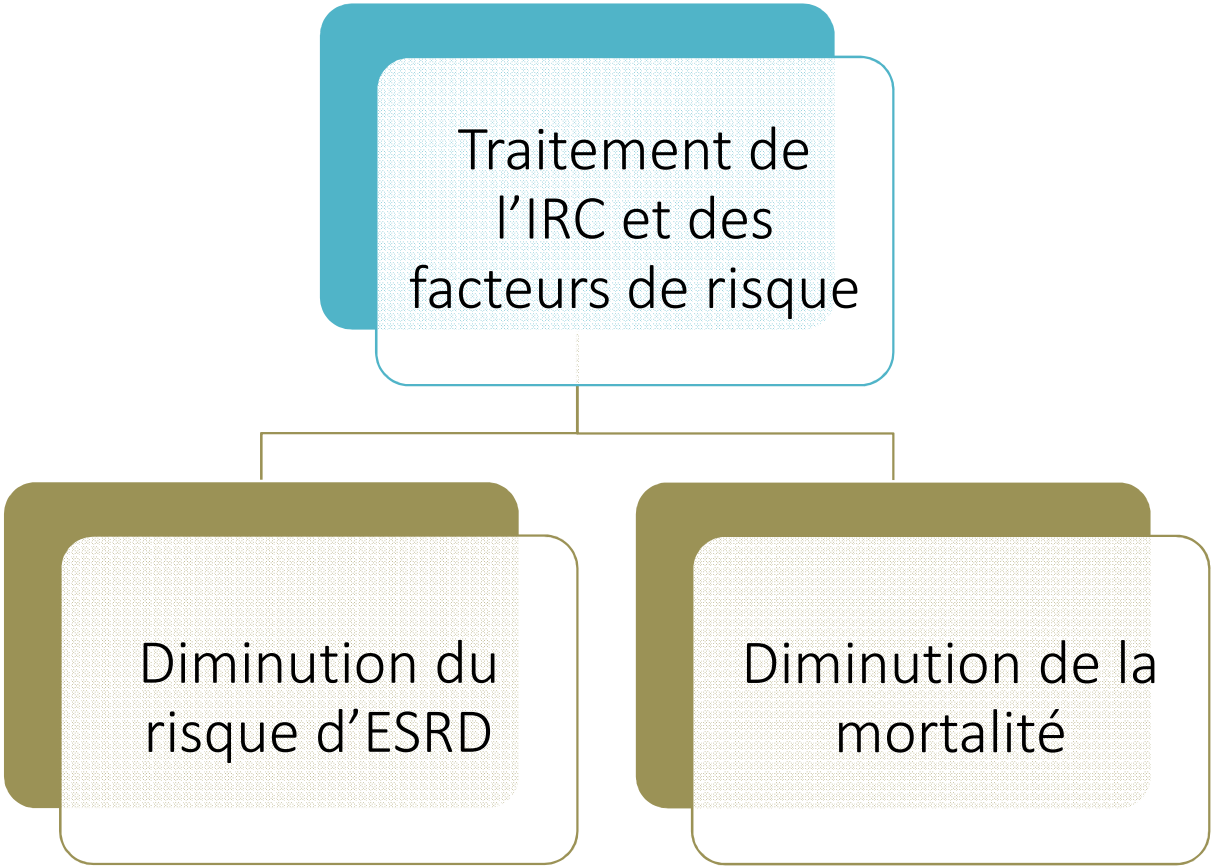


Schlipak, KDIGO, Kid Int, 2021

Facteurs de risque

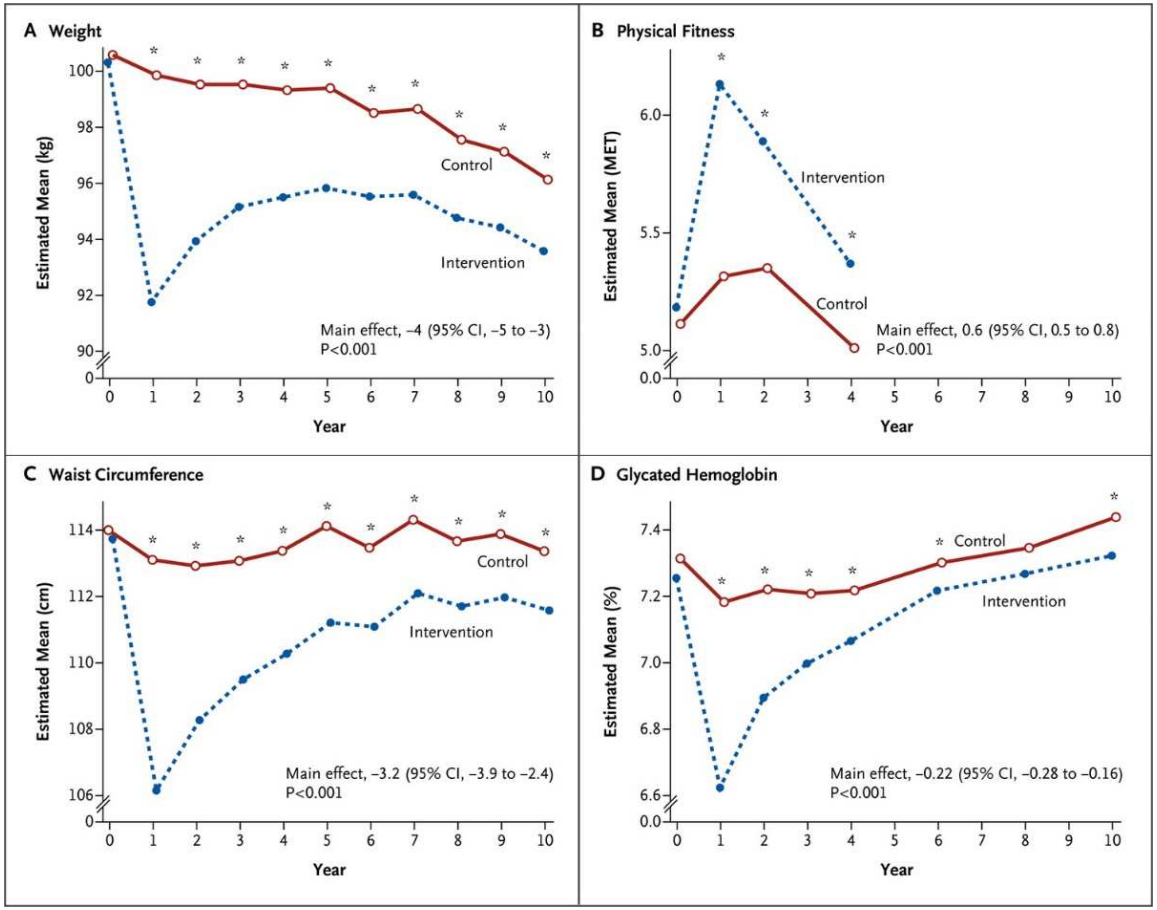


Deux objectifs



Prise en charge générale

The Look AHEAD Study: A Description of the Lifestyle Intervention and the Evidence Supporting It



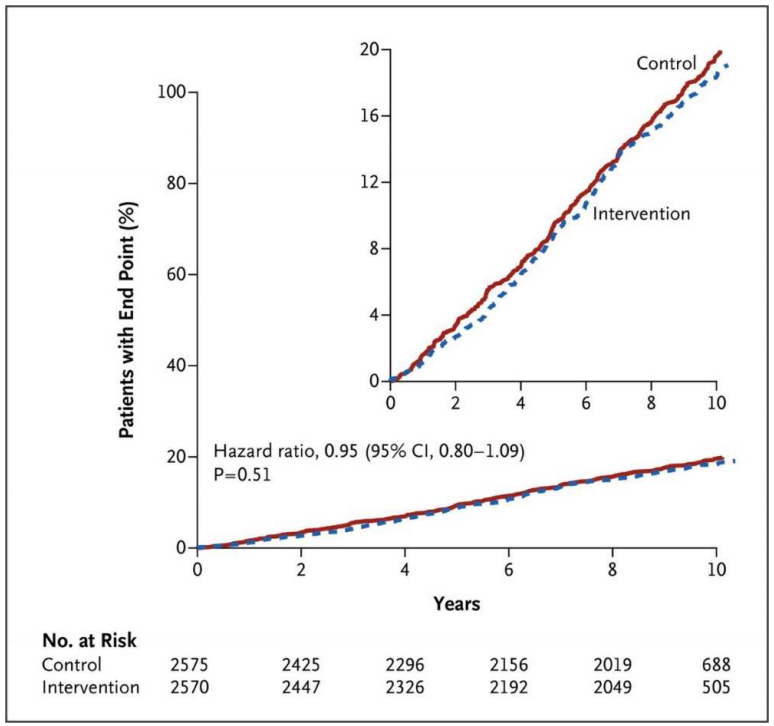
5145 patients 45-76 ans randomisés D2 et surpoids

Un bras éducation, un bras intensif augmentation activité physique (>175min/semaine) et perte de poids 7% (very low calorie diet)

Suivi de 10 ans

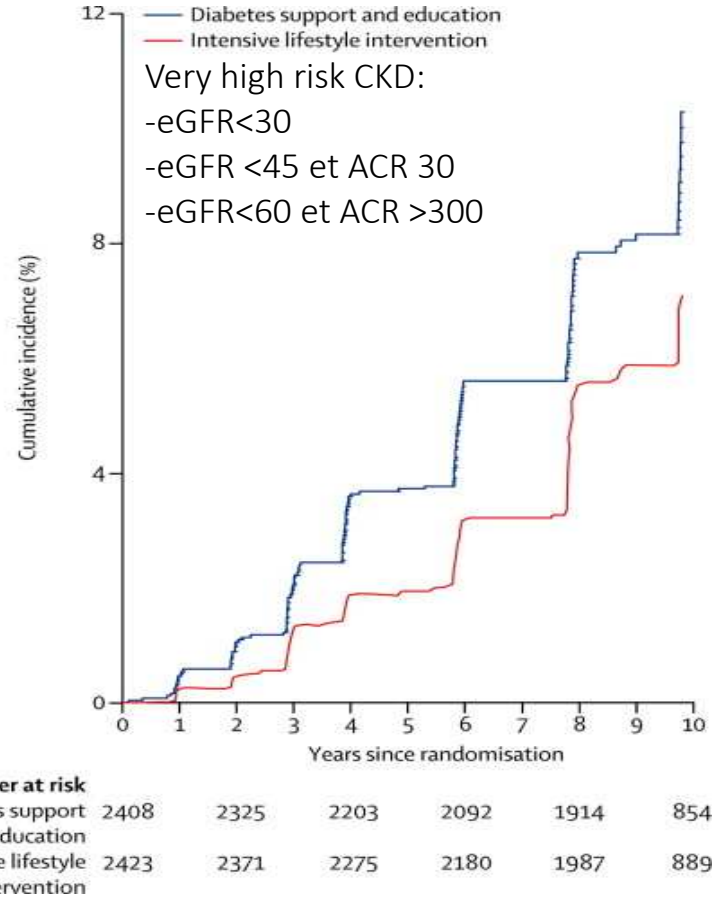
NEJM, 2013

Mortalité et événements CV



Effet albuminurie et fonction rénale

Néphropathie diabétique



NEJM, 2013

Lancet diabetes endocrinology 2014

Arrêt du tabac

Table 4 HRs of death associated with potential risk factors, overall and stratified by eGFR category

	Non-death	Death		eGFR category			
	n = 41,368	n = 16,578	Overall	15–29 mL/min	30–44 mL/min	45–59 mL/min	≥60 mL/min
	Number (%)	Number (%)	HR[a] (95% CI)	HR[b] (95% CI)	HR[b] (95% CI)	HR[b] (95% CI)	HR[b] (95% CI)
Smoking status							
Non–smoker	21,930 (53.0)	8245 (49.7)	1 (–)	1 (–)	1 (–)	1 (–)	1 (–)
Current	6819 (16.5)	3309 (20.0)	1.50 (1.44–1.57)	1.09 (0.84–1.40)	1.33 (1.18–1.50)	1.60 (1.48–1.74)	1.54 (1.46–1.63)
Former	10,815 (26.1)	4196 (25.3)	1.07 (1.03–1.12)	1.04 (0.86–1.25)	1.00 (0.91–1.11)	1.09 (1.02–1.17)	1.08 (1.03–1.14)
Unknown	1804 (4.4)	828 (5.0)	0.95 (0.88–1.02)	1.06 (0.78–1.45)	0.88 (0.73–1.06)	1.00 (0.86–1.15)	0.91 (0.82–1.01)

Basé essentiellement sur des études observationnelle
Tabagisme associé à une augmentation du risque CV en IRC et possiblement à une progression plus rapide de la néphropathie

CeaSoriano et al, 2015

Aspects nutritionnels: restriction protéique

Table 2. Recommended Dietary and Nutrient Intake in Adults, According to the CKD Stage.*

Dietary Constituent	Normal Kidney Function with Increased CKD Risk	Mild-to-Moderate CKD†	Advanced CKD†	Transition to Dialysis†	Ongoing Dialysis or Any Stage with Existing or Imminent PEW
Protein (g/kg/day)	<1.0; increase proportion of plant-based proteins	<1.0 (consider 0.6–0.8 if eGFR <45 ml/min/1.73 m^2 or rapid progression)	0.6–0.8, including 50% HBV protein, or <0.6 with addition of EAA or KA	0.6–0.8 on nondialysis days and >1.0 on dialysis days	1.2–1.4; may require >1.5 if hypercatabolic state develops

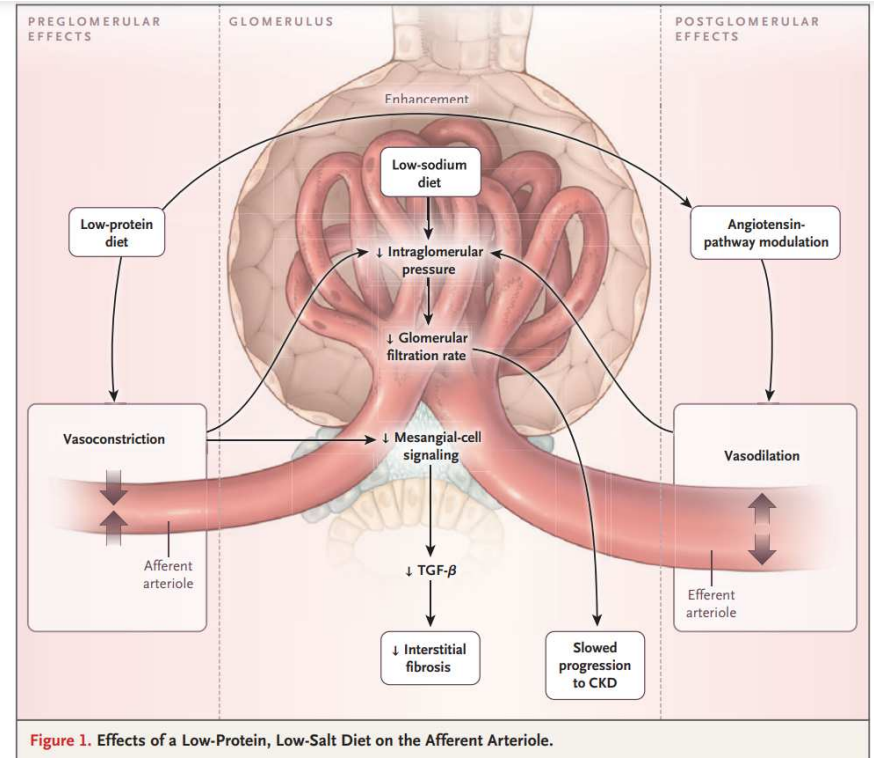


Figure 1. Effects of a Low-Protein, Low-Salt Diet on the Afferent Arteriole.

Kalanthar Zadeh and Fouque NEJM 2018

What's the story with treating metabolic acidosis in CKD? A systematic review.

CJASN
Clinical Journal of American Society of Nephrology

Clinical trials on the treatment of metabolic acidosis

14 Trials

1394 subjects

Treatment of metabolic acidosis resulted in:

Change in HCO_3

HCO_3 increase

3.3 mmol/L
95% CI 2.4, 4.3

Moderate certainty

GFR decline

-3.3 ml/min
95% CI -4.4, -2.1

Low certainty

ESKD

RR 0.3
95% CI 0.2, 0.6

Very-low certainty

HTN

RR 1.4
95% CI 1.1, 1.8

Conclusions Oral alkali or a reduction in dietary acid intake may slow the rate of kidney function decline and potentially reduce the risk of end-stage kidney disease in patients with CKD and metabolic acidosis.

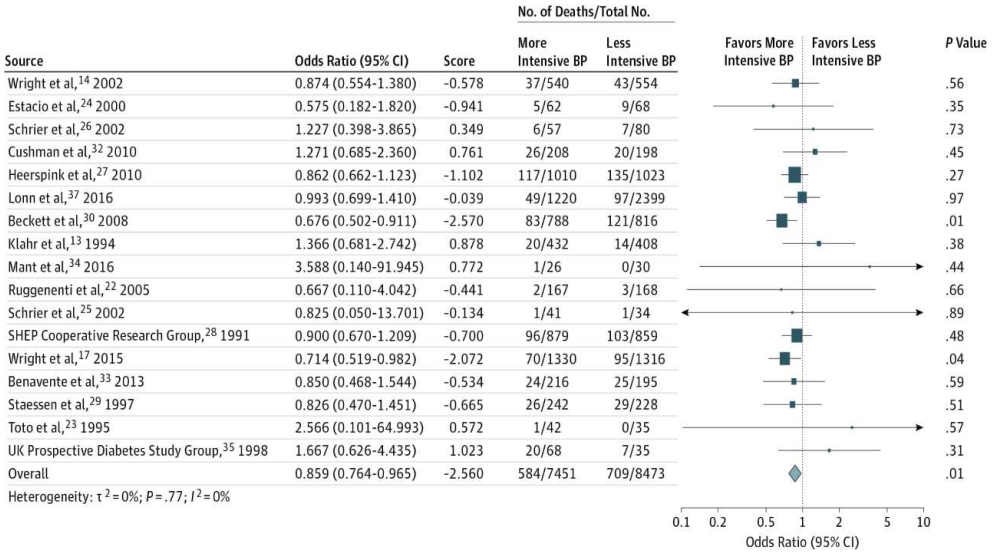
Sankar Navaneethan, Jun Shao, Jerry Buysse, and David Bushinsky.
Effects of Treatment of Metabolic Acidosis in CKD: A Systematic Review and Meta-Analysis. CJASN doi: 10.2215/CJN.13091118. Visual Abstract by Joel Topf, MD, FACP

Que 4 études et effet peut être du à l'alimentation

The JAMA Network

From: **Association Between More Intensive vs Less Intensive Blood Pressure Lowering and Risk of Mortality in Chronic Kidney Disease Stages 3 to 5A Systematic Review and Meta-analysis**

JAMA Intern Med. 2017;177(10):1498-1505. doi:10.1001/jamainternmed.2017.4377



Source	Odds Ratio (95% CI)	Score	No. of Deaths/Total No. More Intensive BP	No. of Deaths/Total No. Less Intensive BP	P Value
Wright et al,[14] 2002	0.874 (0.554-1.380)	-0.578	37/540	43/554	.56
Estacio et al,[24] 2000	0.575 (0.182-1.820)	-0.941	5/62	9/68	.35
Schrier et al,[26] 2002	1.227 (0.398-3.865)	0.349	6/57	7/80	.73
Cushman et al,[32] 2010	1.271 (0.685-2.360)	0.761	26/208	20/198	.45
Heerspink et al,[27] 2010	0.862 (0.662-1.123)	-1.102	117/1010	135/1023	.27
Lonn et al,[37] 2016	0.993 (0.699-1.410)	-0.039	49/1220	97/2399	.97
Beckett et al,[30] 2008	0.676 (0.502-0.911)	-2.570	83/788	121/816	.01
Klahr et al,[13] 1994	1.366 (0.681-2.742)	0.878	20/432	14/408	.38
Mant et al,[34] 2016	3.588 (0.140-91.945)	0.772	1/26	0/30	.44
Ruggenenti et al,[22] 2005	0.667 (0.110-4.042)	-0.441	2/167	3/168	.66
Schrier et al,[25] 2002	0.825 (0.050-13.701)	-0.134	1/41	1/34	.89
SHEP Cooperative Research Group,[28] 1991	0.900 (0.670-1.209)	-0.700	96/879	103/859	.48
Wright et al,[17] 2015	0.714 (0.519-0.982)	-2.072	70/1330	95/1316	.04
Benavente et al,[33] 2013	0.850 (0.468-1.544)	-0.534	24/216	25/195	.59
Staessen et al,[29] 1997	0.826 (0.470-1.451)	-0.665	26/242	29/228	.51
Toto et al,[23] 1995	2.566 (0.101-64.993)	0.572	1/42	0/35	.57
UK Prospective Diabetes Study Group,[35] 1998	1.667 (0.626-4.435)	1.023	20/68	7/35	.31
Overall	0.859 (0.764-0.965)	-2.560	584/7451	709/8473	.01

Heterogeneity: $\tau^2 = 0\%$; $P = .77$; $I^2 = 0\%$

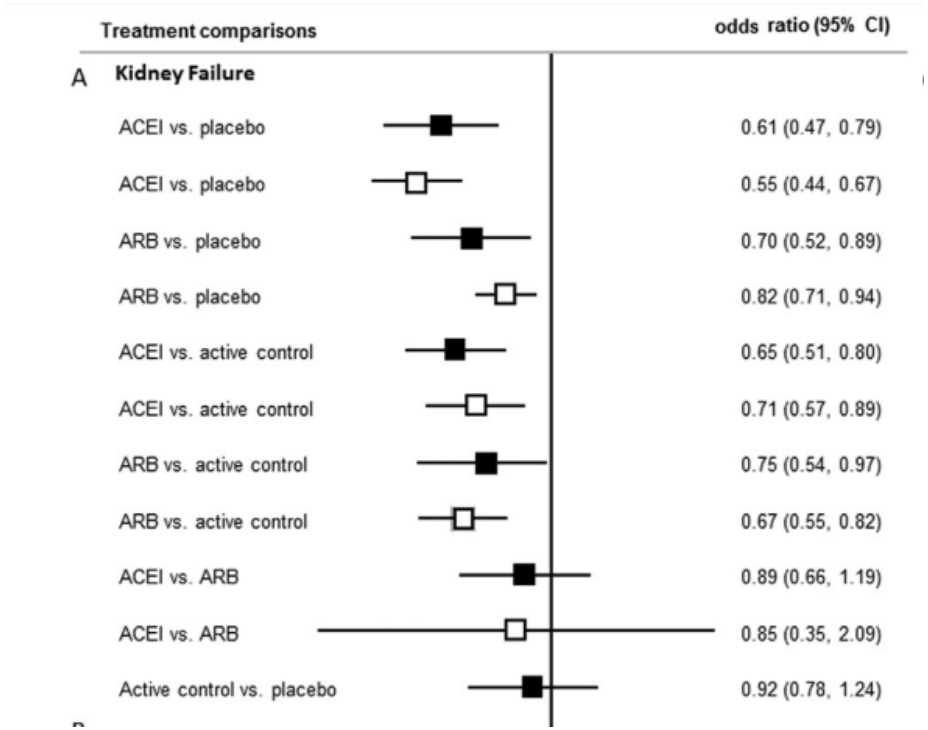
TAS moy atteintes 132 versus 140 mmHg

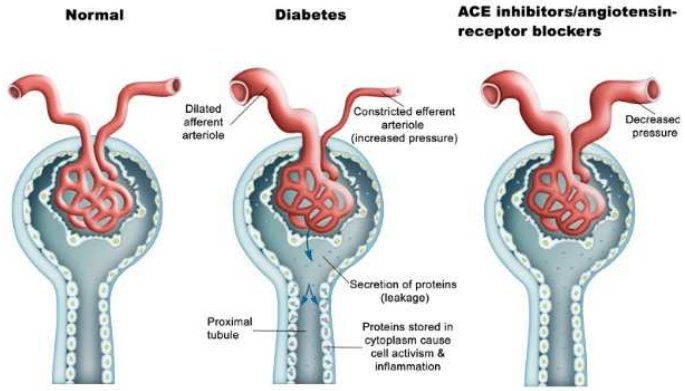
Figure Legend:

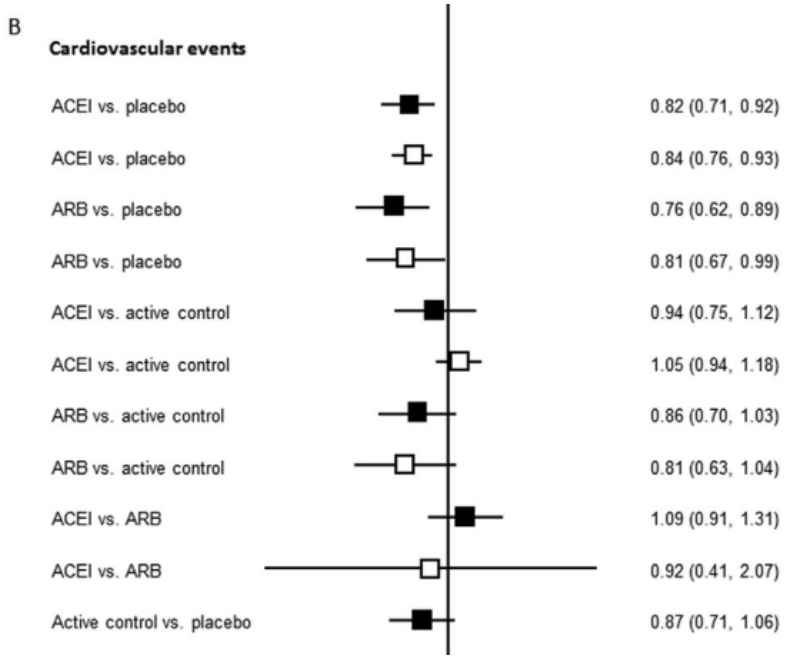
Effect of Intensive Blood Pressure (BP) Lowering on Risk of Mortality in Hypertensive Trial Participants With Chronic Kidney DiseaseIn the 18 included trials, there were 584 deaths among 7451 participants in the more intensive BP arm and 709 deaths among 8473 participants in the less intensive BP arm during the trial phase. The trial by Howard et al had no mortality outcomes in both BP arms (more intensive vs less intensive) and was dropped from the analysis.

Pharmacologie: blocage du RAA

Meta-analyse en réseau de 119 études randomisées



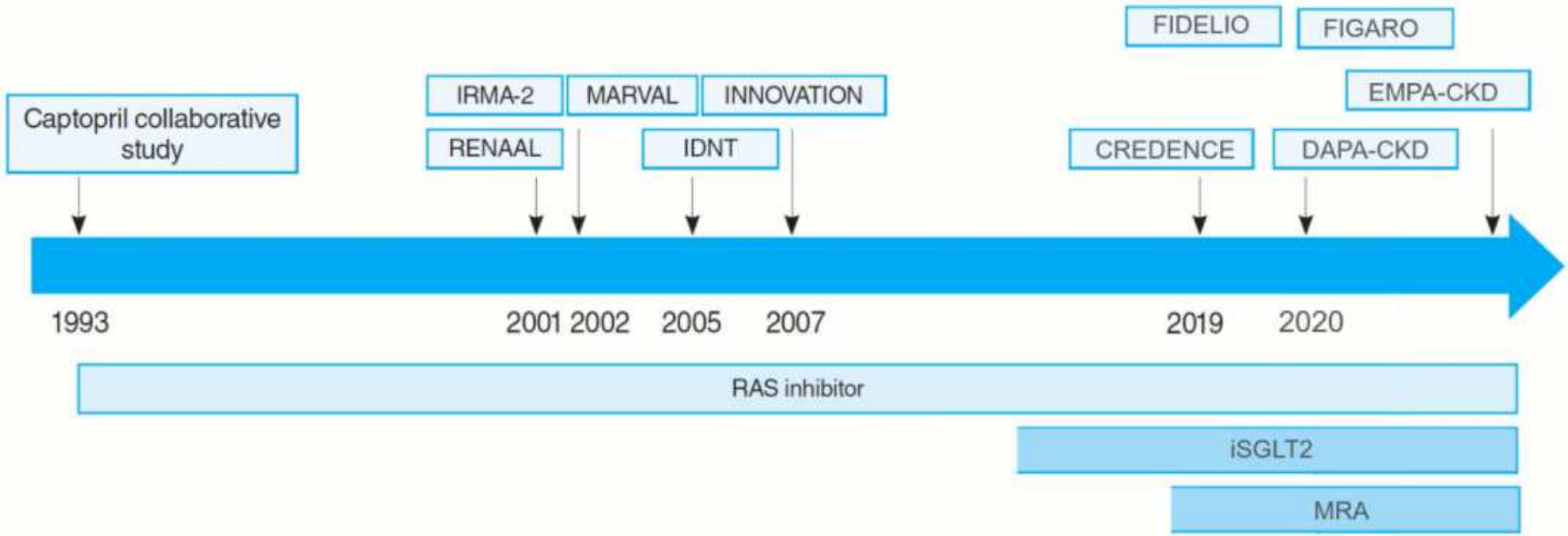




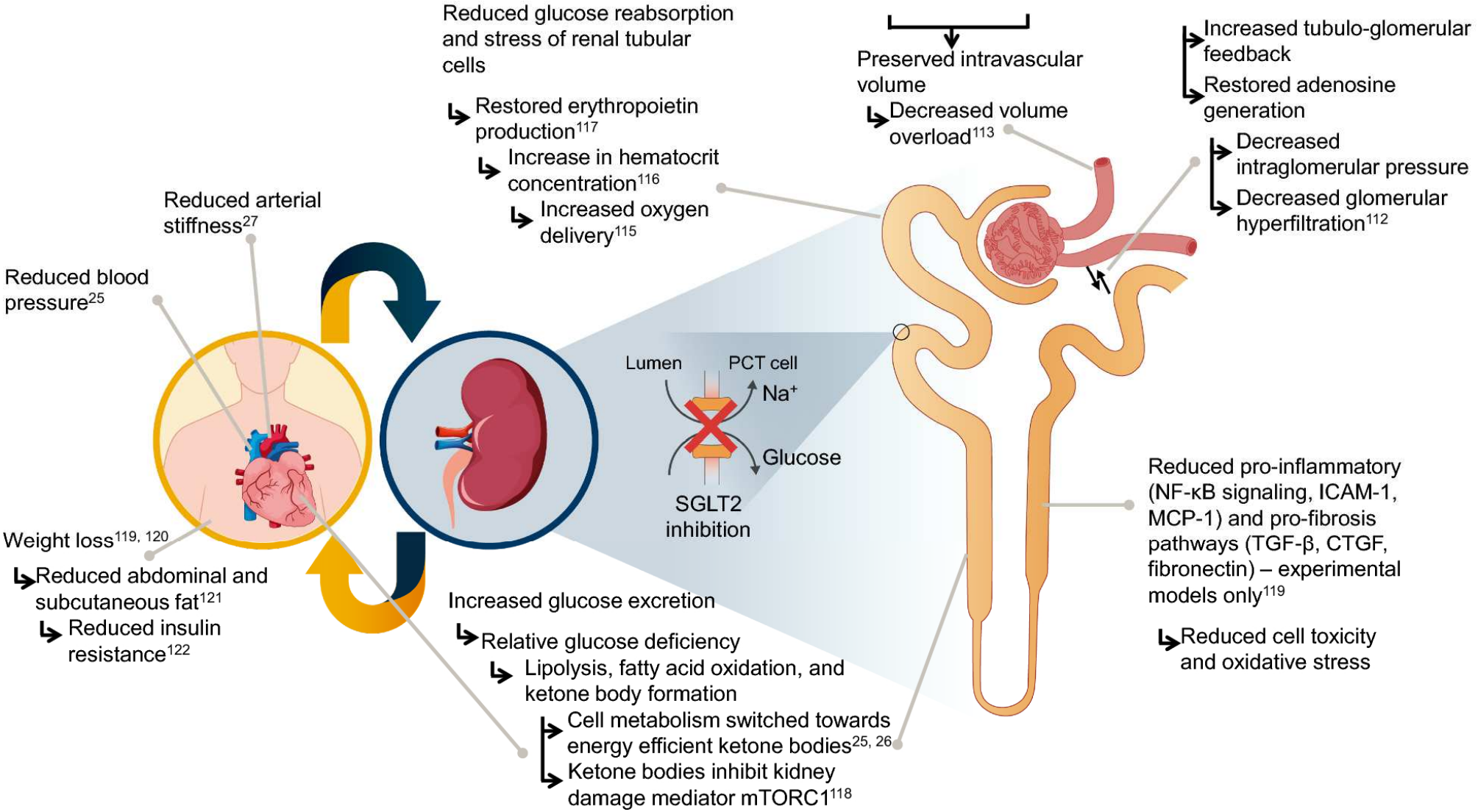
Xinfang Xie et al, AJKD 2016

Peut on faire plus que le blocage du RAA par les IEC/Sartans dans TOUTES IRC?

Essais cliniques



Adapté de Yamazaki et al. Diabetes Metab J 2021;45:11-26



Giorgino et al. Cardiovasc Diabetol (2020

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

DAPACKD

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

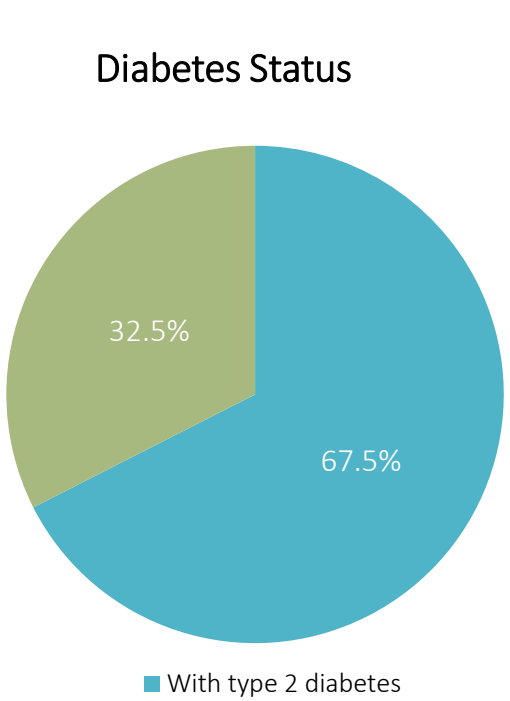
- Composite of sustained ≥50% eGFR decline, ESKD, or renal death
- Composite of CV death or hHF
- All-cause mortality

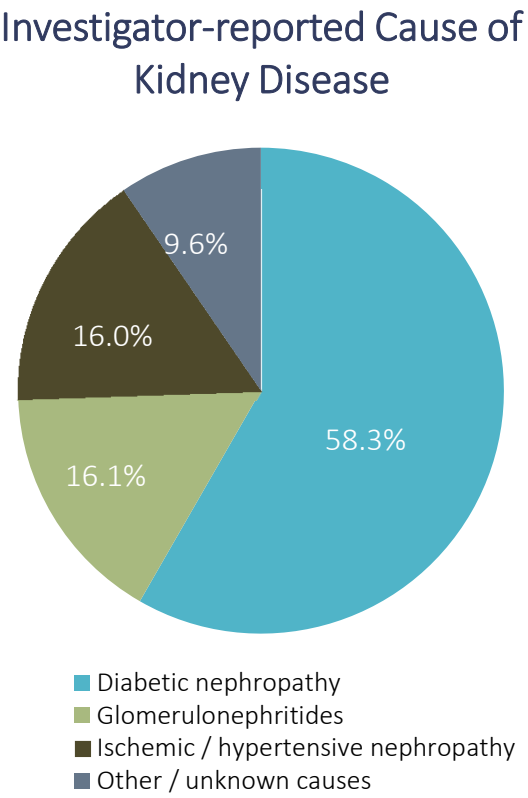
[a]ESKD defined as the need for maintenance dialysis (peritoneal or hemodialysis) for more than 28 days, renal transplantation or sustained eGFR <15mL/min/1.73m² for at least 28 days.

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 et al. *N Engl J Med*. 2020; 383:1436-1446.

Diabetes Status and Investigator-reported Cause of Kidney Disease at Baseline

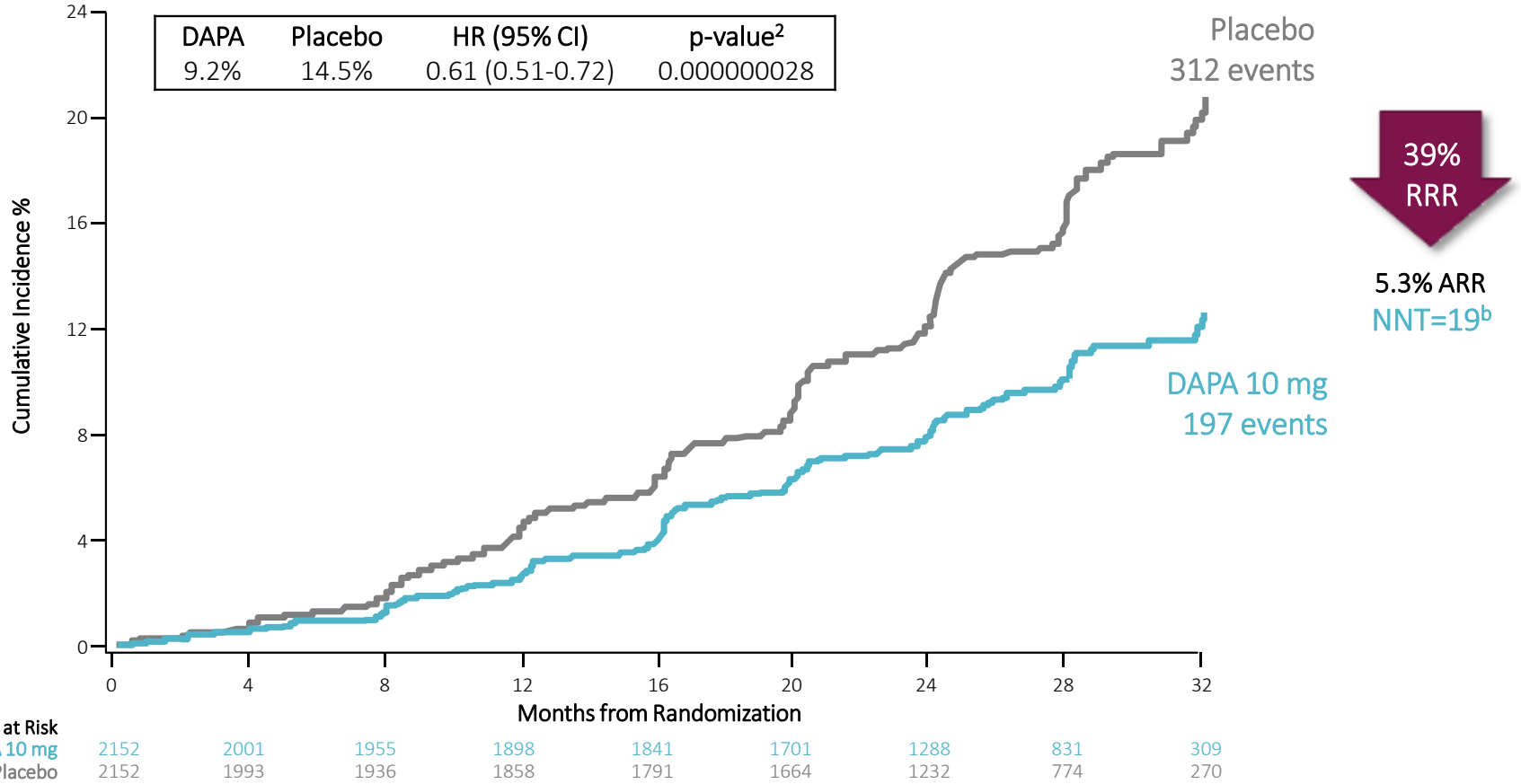




CKD Etiologies

Wheeler DC et al. *Nephrol Dial Transplant*. 2020;35:1700–1711.

Endpoint composite primaire:
Sustained ≥50% eGFR Decline, ESKD, Renal or CV Death[a,1]



[a]ESKD defined as the need for maintenance dialysis (peritoneal or hemodialysis) for at least 28 days and renal transplantation or sustained eGFR <15mL/min/1.73m^2 for at least 28 days. Renal death was defined as death due to ESKD when dialysis treatment was deliberately withheld for any reason.[3]; [b]95% CI, 15 to 27.

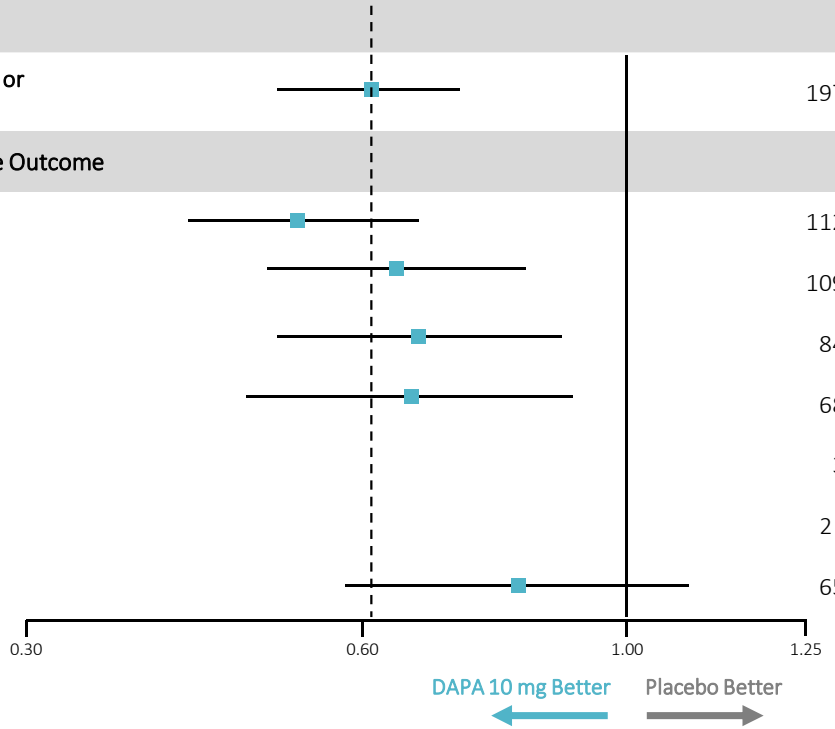
ARR = absolute risk reduction; CV = cardiovascular; DAPA = dapagliflozin; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; HR = hazard ratio; ; NNT = number needed to treat; RRR = relative risk reduction.

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.

Primary Composite Outcome: All Components Contributed to the Observed Treatment Effect[1]

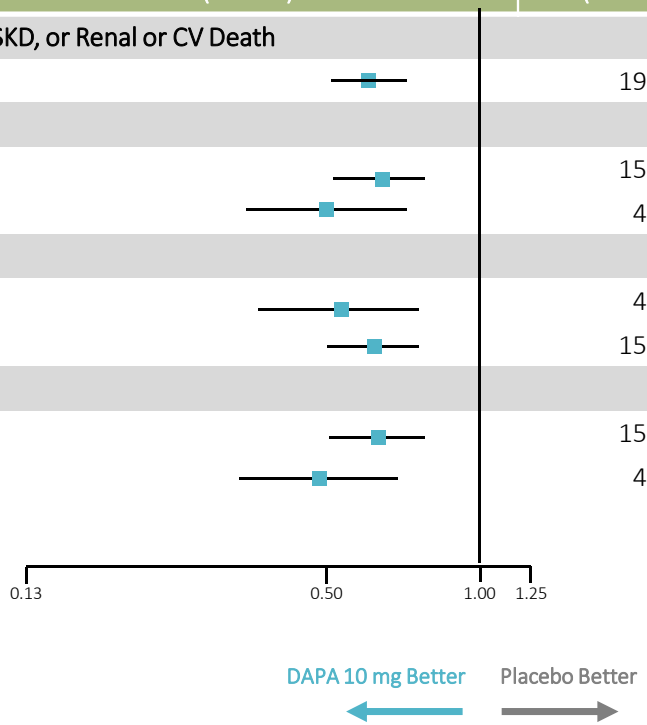
	Number of Events (%)				
	DAPA 10 mg (n=2152)	Placebo (n=2152)	HR	95% CI	p-value[2]
Primary Composite Outcome					
Composite of ≥50% eGFR Decline, ESKD, or Renal or CV Death	197 (9.2)	312 (14.5)	0.61	(0.51, 0.72)	0.000000028
Components of the Primary Composite Outcome					
≥50% eGFR Decline	112 (5.2)	201 (9.3)	0.53	(0.42, 0.67)	<0.0001
ESKD	109 (5.1)	161 (7.5)	0.64	(0.50, 0.82)	0.0004
eGFR <15mL/min/1.73m^2	84 (3.9)	120 (5.6)	0.67	(0.51, 0.88)	0.0045
Chronic Dialysis[a]	68 (3.2)	99 (4.6)	0.66	(0.48, 0.90)	0.0080
Transplantation[a]	3 (0.1)	8 (0.4)	NC		
Renal Death	2 (<0.1)	6 (0.3)	NC		
CV Death	65 (3.0)	80 (3.7)	0.81	(0.58, 1.12)	0.2029



[a]There were 69 endpoint events for dapagliflozin and 100 endpoint events for placebo for the combined chronic dialysis and renal transplantation endpoint (HR 0.66; 95% CI 0.49, 0.90).
CV = cardiovascular; DAPA = dapagliflozin; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; HR = hazard ratio; NC = not calculable.
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.

Primary Composite Outcome: Treatment Benefit Consistent Across Prespecified Subgroups[1]

	Number of Events				
HR (95% CI)	DAPA 10 mg (n=2152)	Placebo (n=2152)	HR	95% CI	p-value Interaction[2]
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)	



Profil sur en IRC non diabétique, pas acidocétose
Infections mycotiques possibles

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.

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.

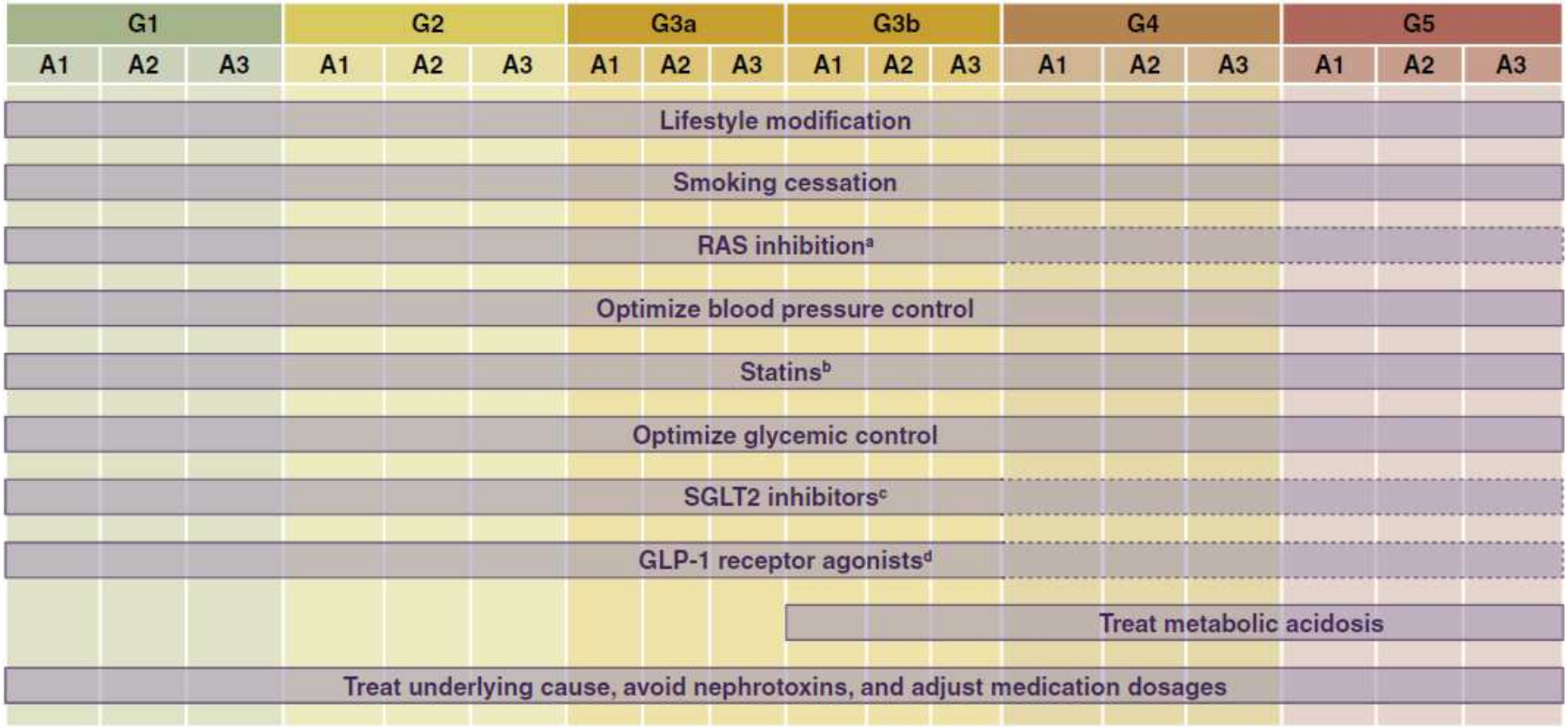


Figure 3 | Interventions to slow chronic kidney disease (CKD) progression and/or reduce cardiovascular risk. [a]Unclear if and when to

Schlipak, KDIGO, Kid Int, 2021

Néphropathie diabétique

Contrôle glycémique

2.2 Glycemic targets

Recommendation 2.2.1: We recommend an individualized HbA1c target ranging from <6.5% to <8.0% in patients with diabetes and CKD not treated with dialysis (Figure 9) *(1C)*.

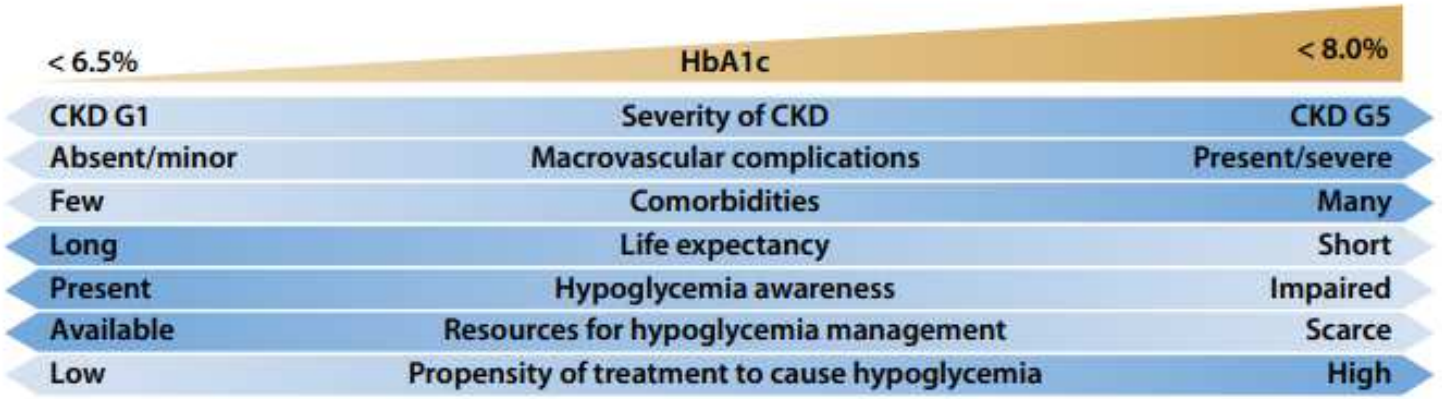
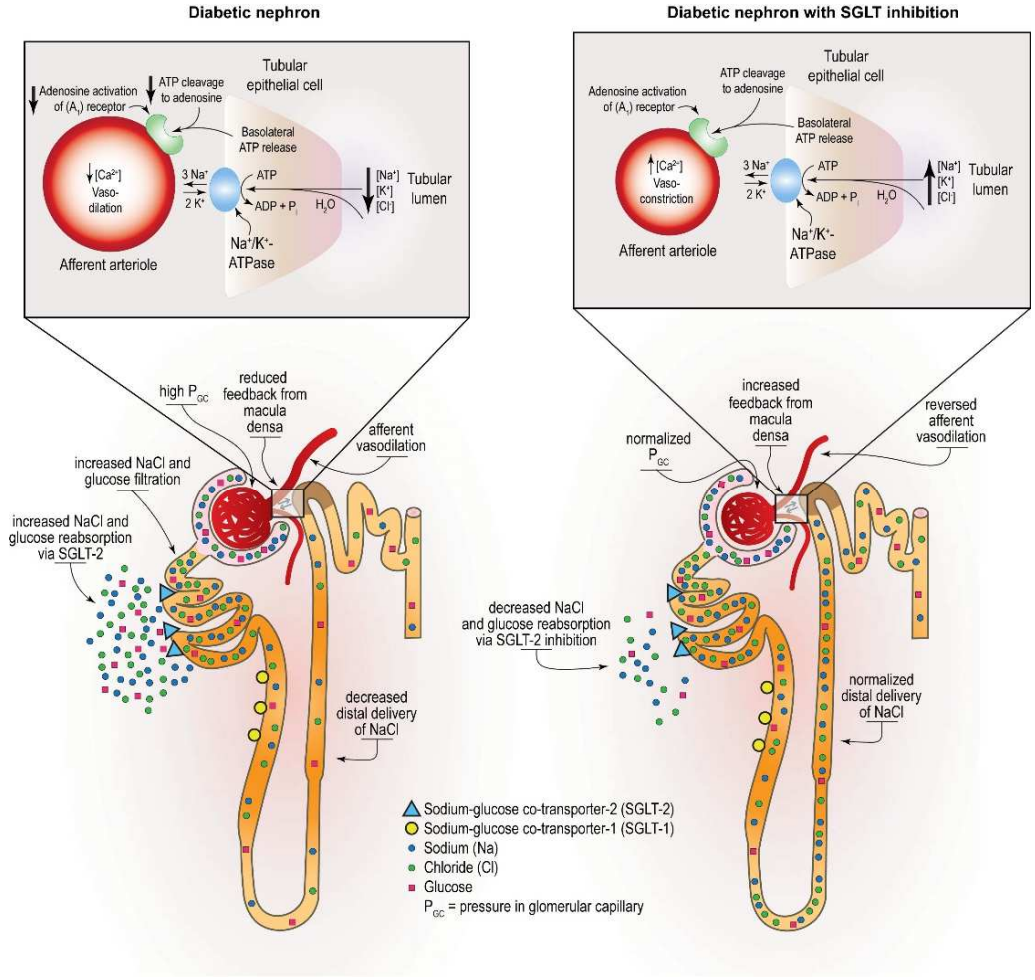


Figure 9 | Factors guiding decisions on individual HbA1c targets. CKD, chronic kidney disease; G1, estimated glomerular filtration rate (eGFR) ≥90 ml/min per 1.73 m^2; G5, eGFR <15 ml/min per 1.73 m^2; HbA1c, glycated hemoglobin.

Attention en hypoglycémie en IRC: privilégier des ttt sans risque hypoglycémie si possible

Inhibition de SGLT-2



Tuttle et al. AJKD 2020

Meta-analyse ND: endpoints rénaux

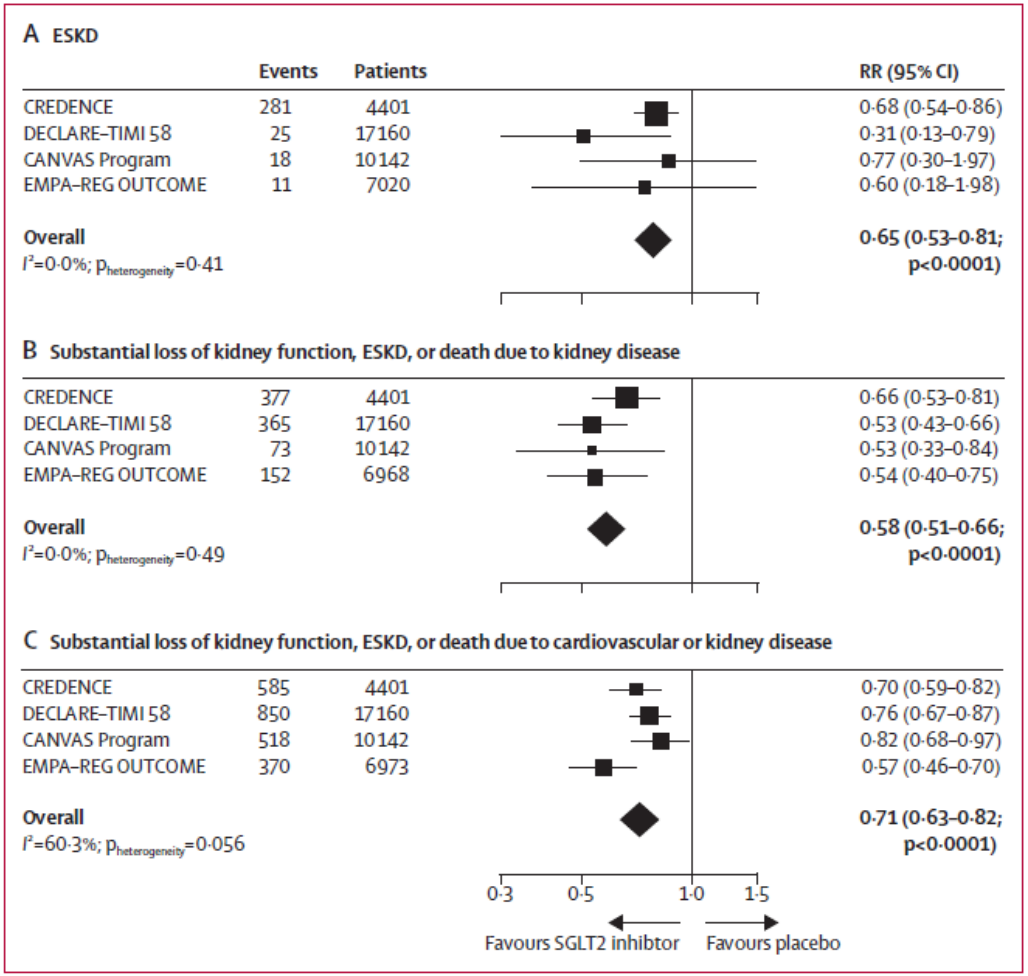


Figure 2: **Effect of SGLT2 inhibitors on ESKD (A), substantial loss of kidney function, ESKD, or death due to kidney disease (B), and substantial loss of kidney function, ESKD, or death due to cardiovascular or kidney disease (C)**

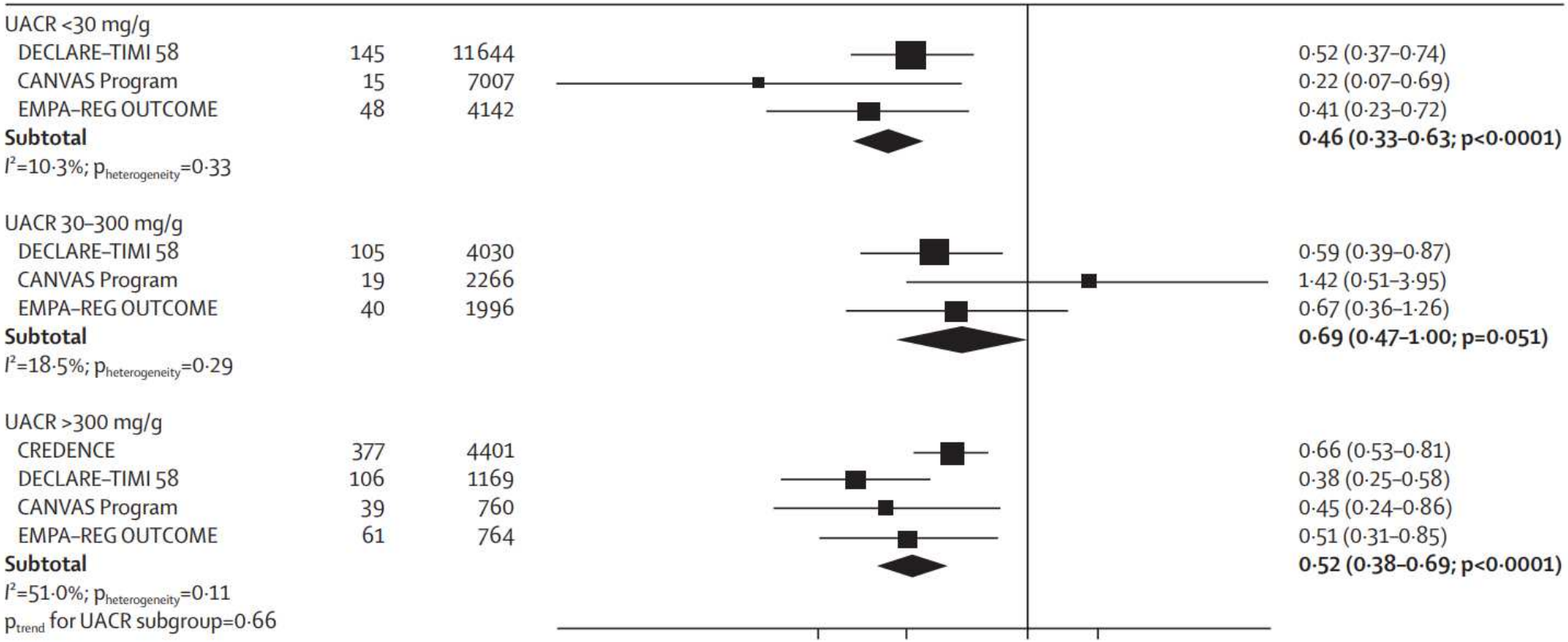
Effet indépendant du degré de dysfonction rénale ET du degré d'albuminurie (pas comme les IEC)

Diminution du risque d'IRA (pas comme les IEC)

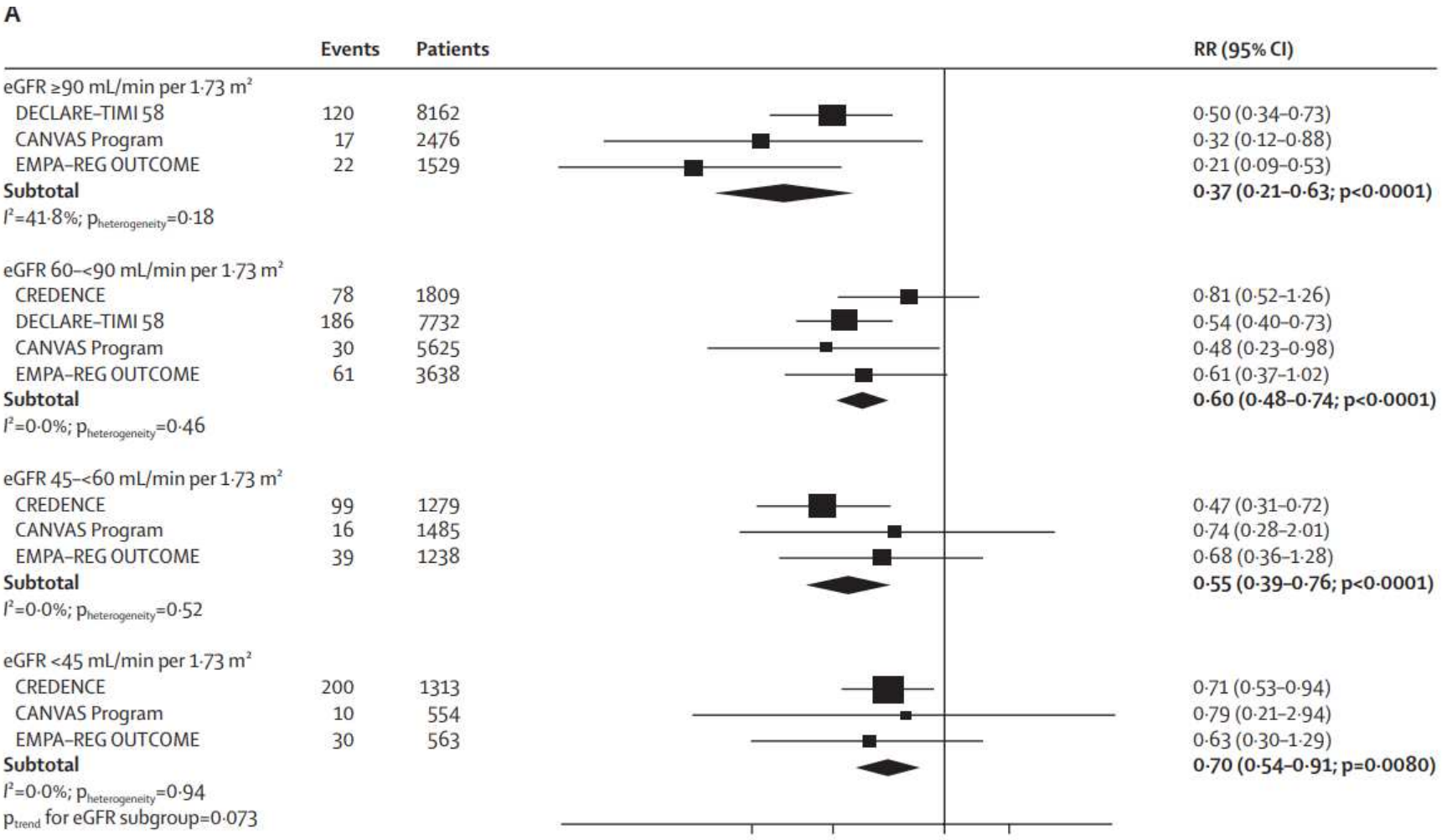
Attention a l'acidocétose euglycémique, aux infections fongiques

Neuen, Lancet 2019

B



Neuen, Lancet 2019



Neuen, Lancet 2019

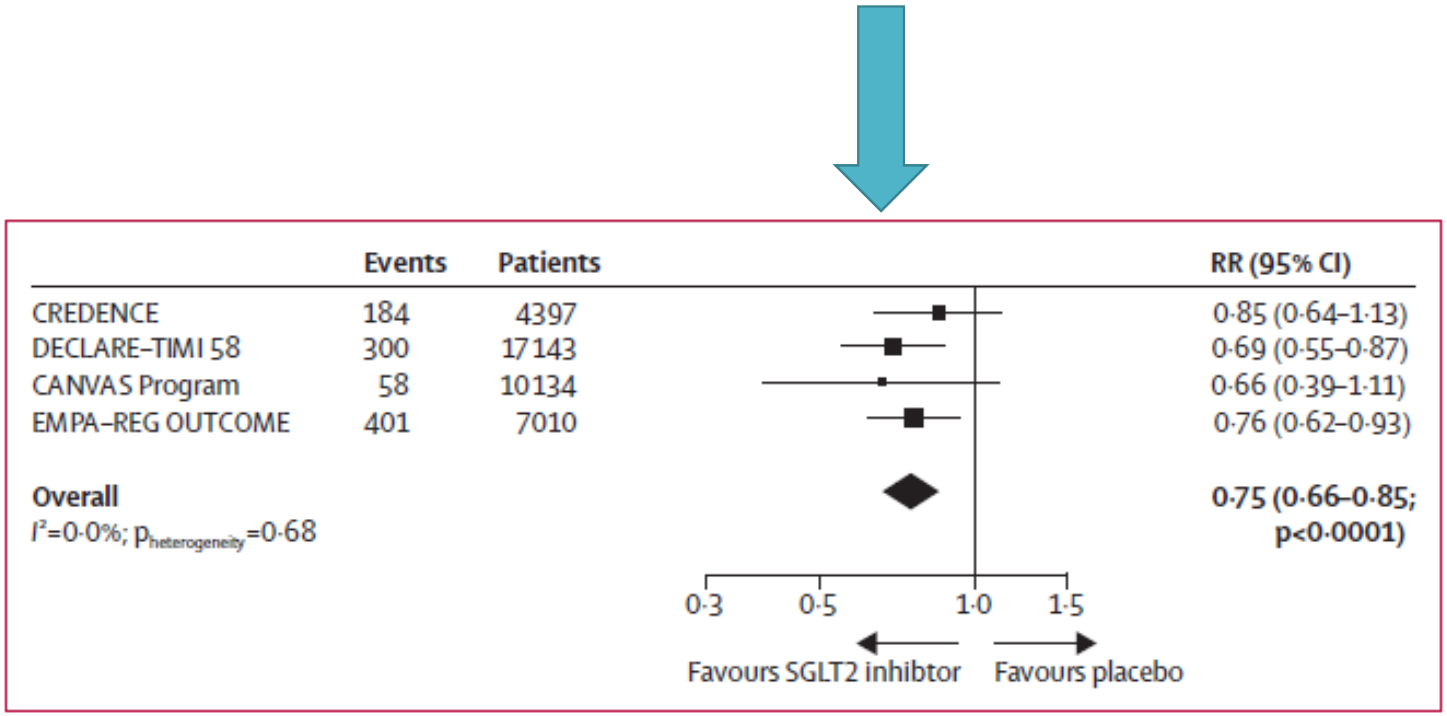


***Figure 3*: Effect of SGLT2 inhibitors on acute kidney injury**

Weights were from random-effects meta-analysis. SGLT2=sodium-glucose co-transporter-2. RR=relative risk.

Neuen, Lancet 2019

Chapter 4: Antihyperglycemic therapies in patients with type 2 diabetes (T2D) and CKD

Practice Point 4.1: Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with metformin and a sodium–glucose cotransporter-2 inhibitor (SGLT2i), and additional drug therapy as needed for glycemic control (Figure 18).

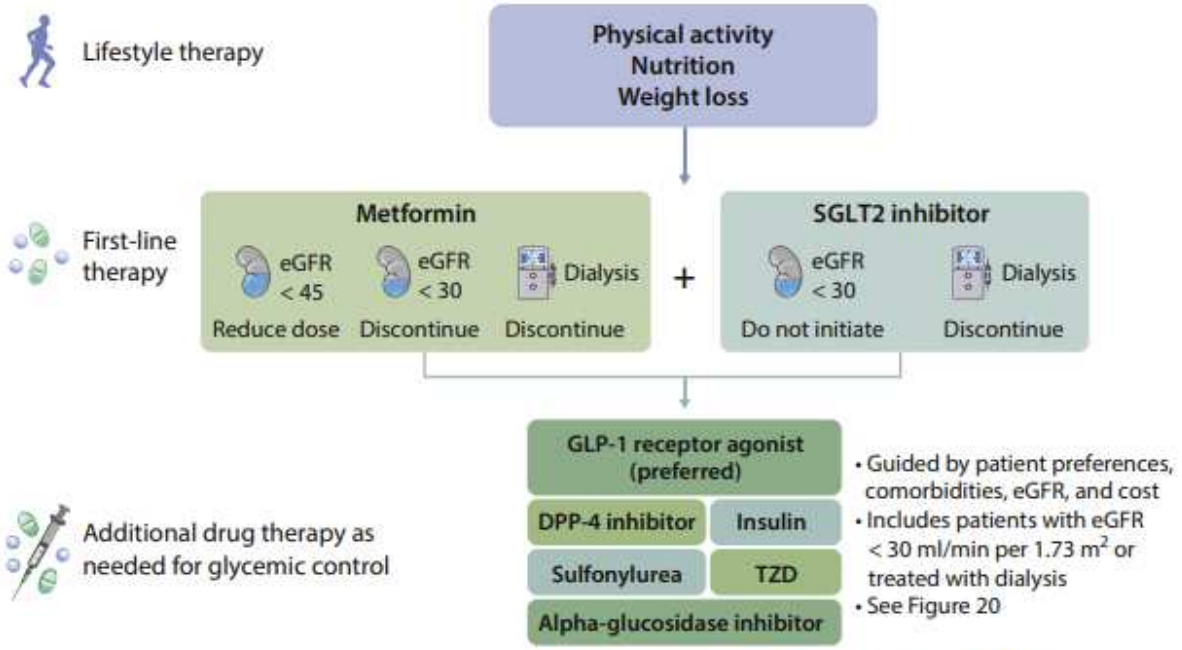


Figure 18 | Treatment algorithm for selecting antihyperglycemic drugs for patients with T2D and CKD. Kidney icon indicates estimated glomerular filtration rate (eGFR; ml/min per 1.73 m^2); dialysis machine icon indicates dialysis. CKD, chronic kidney disease; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium–glucose cotransporter-2; T2D, type 2 diabetes; TZD, thiazolidinedione.

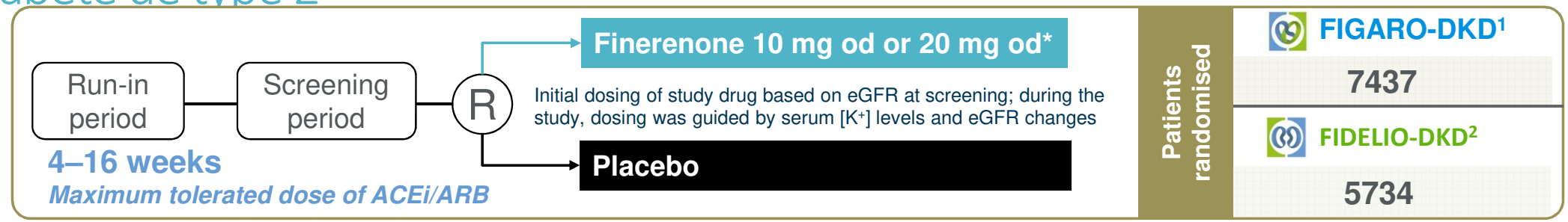
KDIGO 2020

SGLT2 i et IRC

- Introduction de canagliflozin 100 mg jusque clairance de 30ml/min/1.71
- Introduction de dapagliflozin 10 mg jusque 25 ml/min/1.73 m2
- Etude sur empa kidney positive, jusque sortie jusque 45 ml/min/.173 m2
- On n’arrête pas les médicaments jusque la dialyse

CREDENCE, DAPA-CKD, EMPA CKD en cours

FIGARO-DKD and FIDELIO-DKD ont investigué l'effet de la finerenone sur les issues cardiaques et rénales chez plus de 13000 patients avec une IRC et un diabète de type 2



	FIGARO-DKD[1]	FIDELIO-DKD[2]
Primary endpoint	**Composite endpoint:** Time to CV death, non-fatal MI, non-fatal stroke, or hospitalisation for HF	**Composite endpoint:** Time to kidney failure,# sustained ≥40% eGFR decline, or renal death
Key secondary endpoint	Same as primary endpoint in **FIDELIO-DKD**	Same as primary endpoint in **FIGARO-DKD**

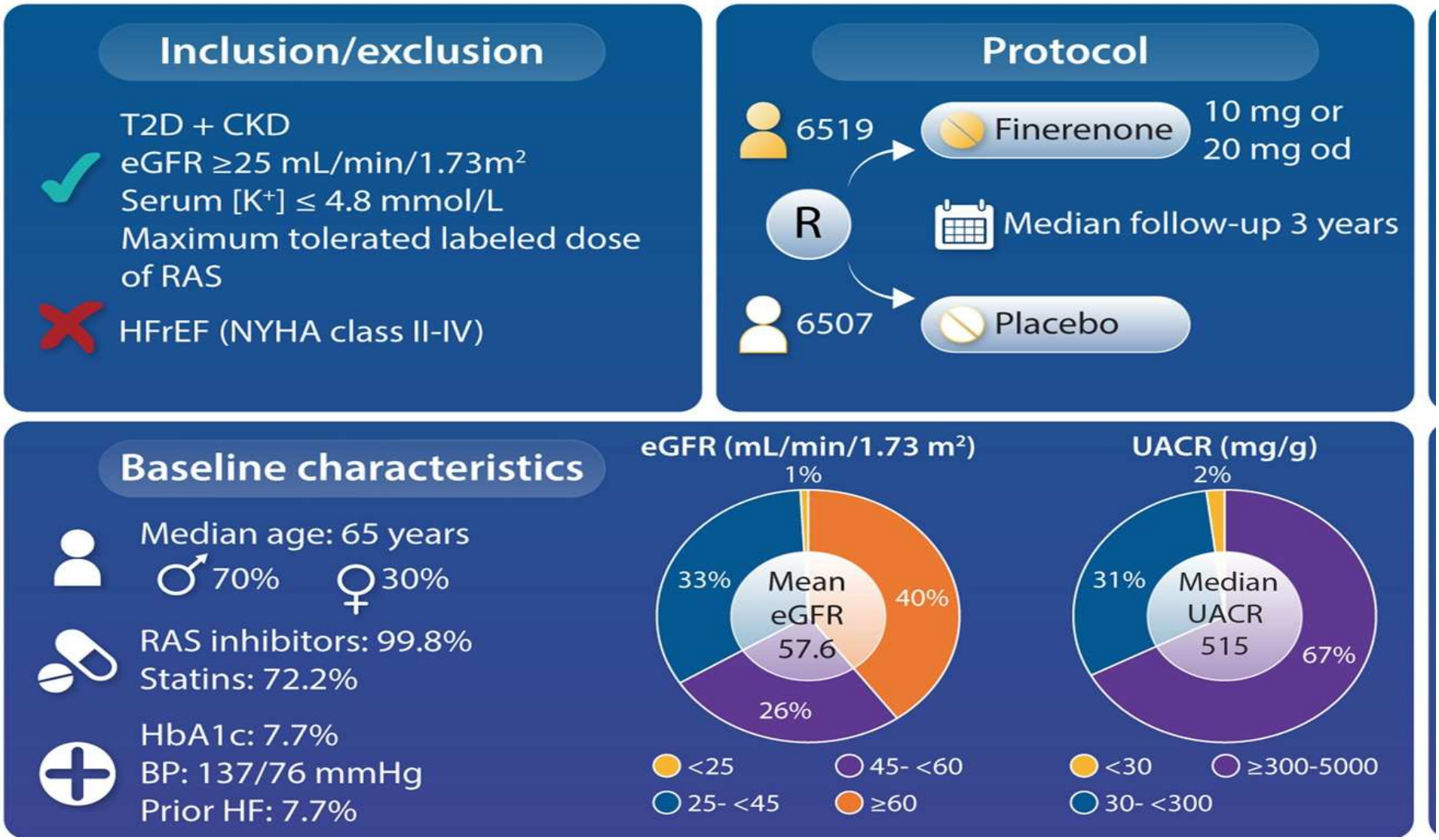
FIDELITY[3]
Pooled analysis

Key outcomes

CV composite:
Time to CV death, non-fatal MI, non-fatal stroke, or hospitalisation for HF

57% kidney composite:
Time to kidney failure,# sustained ≥57% eGFR decline, or renal death

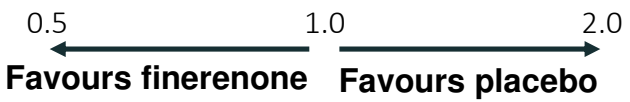
1. Pitt B et al. N Engl J Med 20212. Bakris GB, et al. N Engl J Med 2020 3. Agarwal R et al. Eur Heart J 2021



Agarwal R et al. Eur Heart J 2021;

La Finerenone diminue significativement l'incidence de chaque composant de l'endpoint composite rénale, y compris l'IRT (mais pas la mort rénale)

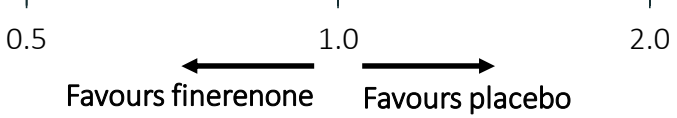
Outcome	Finerenone (n=6519) n (%)	Placebo (n=6507) n (%)	HR (95% CI)	*p*-value
eGFR 57% composite kidney outcome	360 (5.5)	465 (7.1)	0.77 (0.67–0.88)	0.0002
Kidney failure	254 (3.9)	297 (4.6)	0.84 (0.71–0.99)	0.039
ESKD[#]	151 (2.3)	188 (2.9)	0.80 (0.64–0.99)	0.040[‡]
eGFR <15 ml/min/1.73 m^2[¶]	195 (3.0)	237 (3.6)	0.81 (0.67–0.98)	0.026[‡]
≥57% decrease in eGFR from baseline[¶]	257 (3.9)	361 (5.5)	0.70 (0.60–0.83)	<0.0001
Renal death	2 (<0.1)	4 (<0.1)	0.53 (0.10–2.91)	–



≥57% decrease in eGFR is equivalent to doubling of serum creatinine

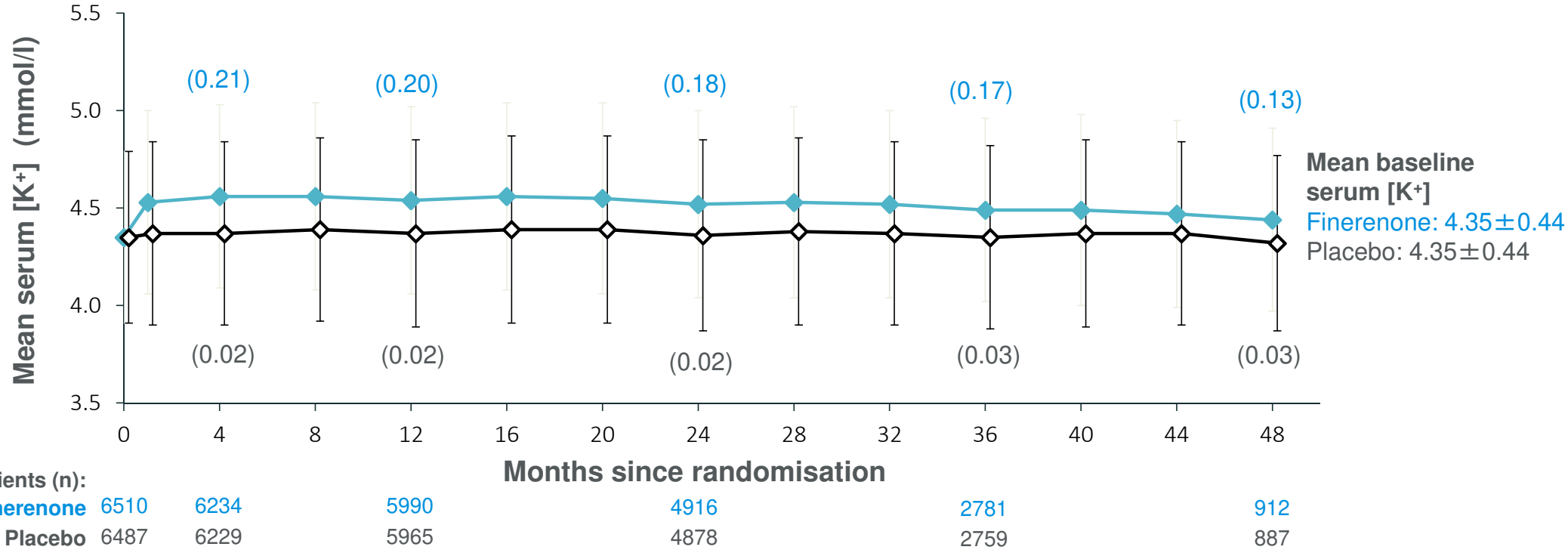
L'effet renal mixte de la finérenone selon les sous populations

	Finerenone	Placebo	Hazard ratio (95% CI)	*p*-value for interaction
	n/N (n per 100 PY)			
Overall	360/6519 (1.96)	465/6507 (2.55)	0.77 (0.67–0.88)	
Baseline eGFR (ml/min/1.73 m^2)*				
25–<45	188/2117 (3.42)	225/2115 (4.14)	0.83 (0.68–1.01)	0.6244
45–<60	62/1717 (1.31)	87/1717 (1.83)	0.72 (0.52–1.00)	
≥60	90/2603 (1.14)	130/2592 (1.66)	0.70 (0.53–0.92)	
Baseline UACR (mg/g)#				
30–<300	38/2076 (0.57)	40/2023 (0.62)	0.94 (0.60–1.47)	0.6673
≥300	321/4321 (2.85)	424/4371 (3.71)	0.75 (0.65–0.87)	



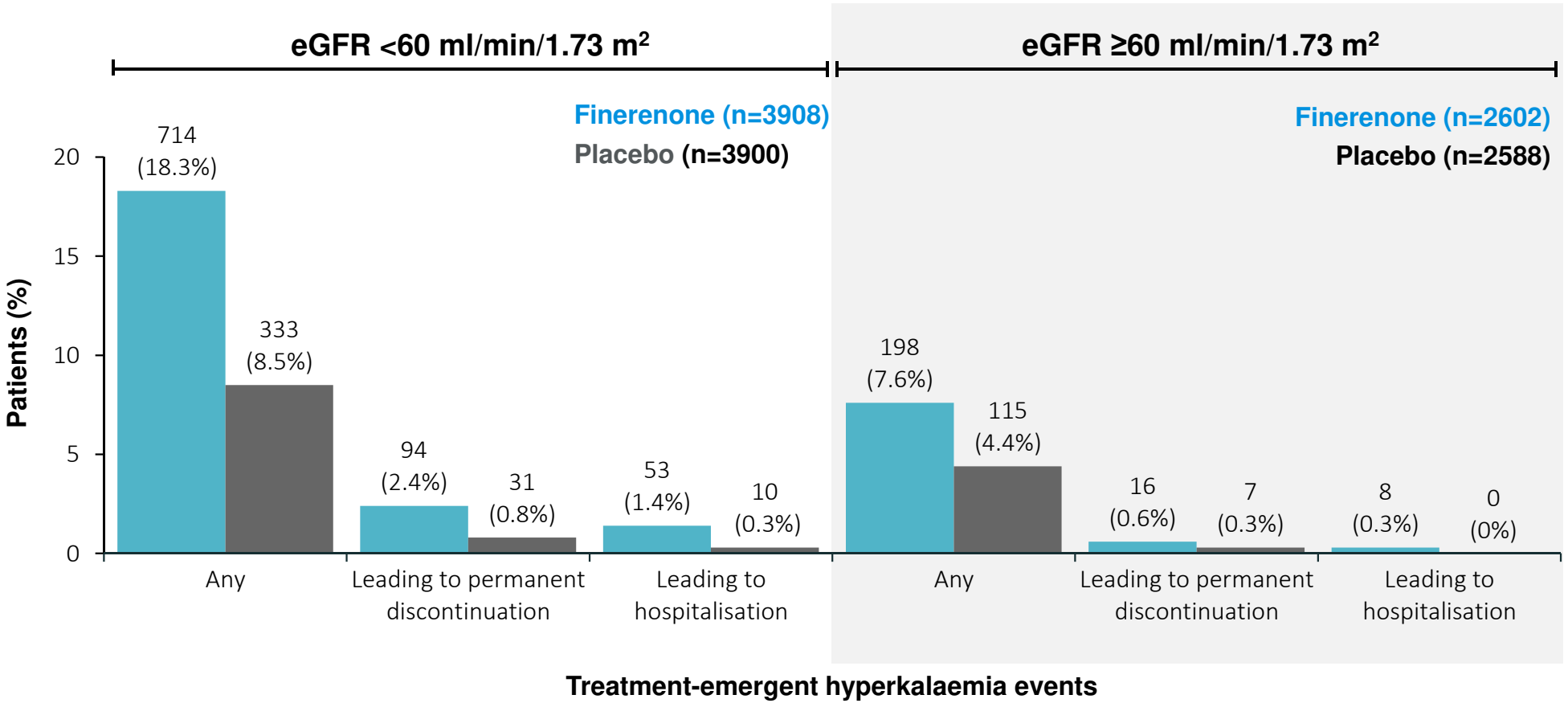
Hyperkaliémie

Différence maximal de [K⁺] sérique entres les groups de 0.19 mmol/l à 4 mois



Patients (n):						
Finerenone	6510	6234	5990	4916	2781	912
Placebo	6487	6229	5965	4878	2759	887

Risque d’hyperkaliémie



BAKRIS G, *ET AL. ASN* 2021; POSTER PO2531; JASN 2022

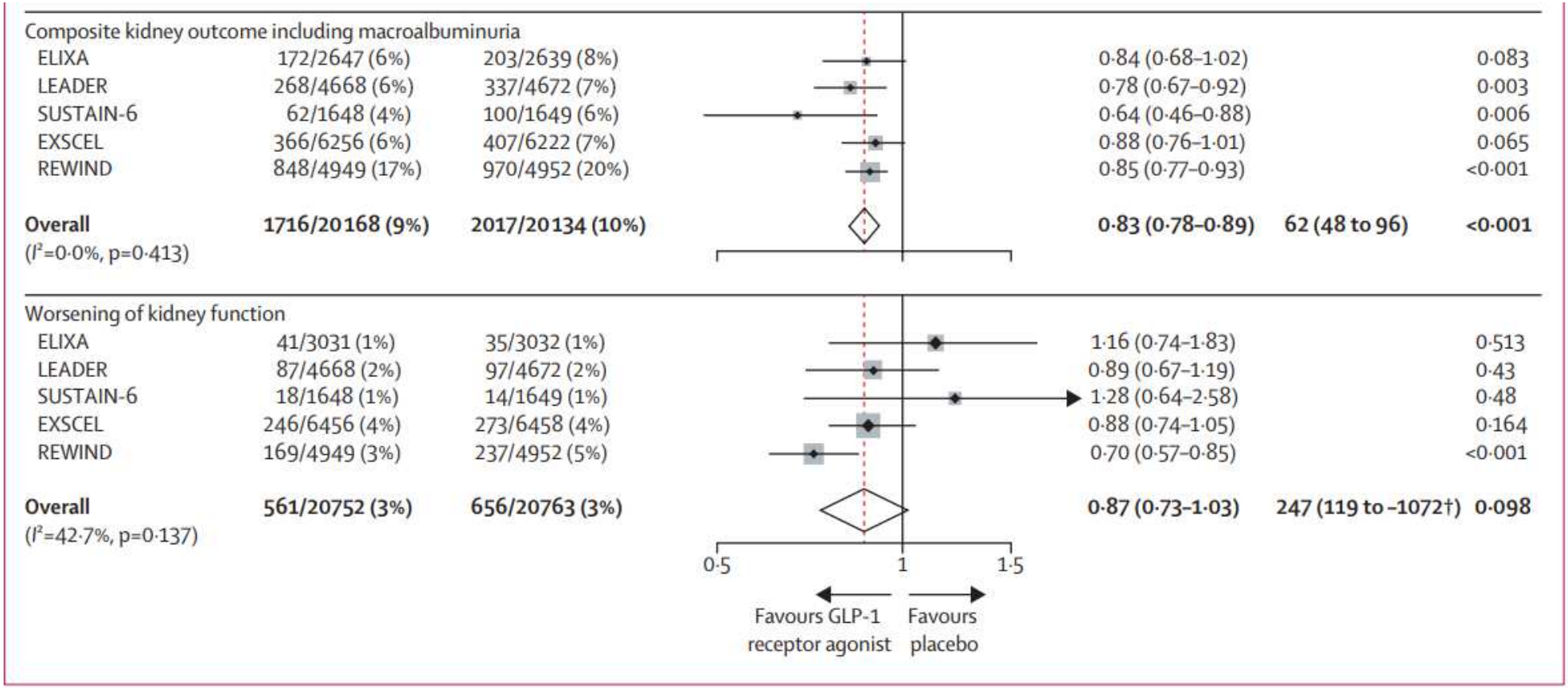


Figure 4: **All-cause mortality, hospital admission for heart failure, and kidney outcomes**

Krisetnesn, Lancet endoc, 2019

Perte de poids
Pas hypoglycémie
Utilisé à Clairances basses

Chapter 4: Antihyperglycemic therapies in patients with type 2 diabetes (T2D) and CKD

Practice Point 4.1: Glycemic management for patients with T2D and CKD should include lifestyle therapy, first-line treatment with metformin and a sodium–glucose cotransporter-2 inhibitor (SGLT2i), and additional drug therapy as needed for glycemic control (Figure 18).

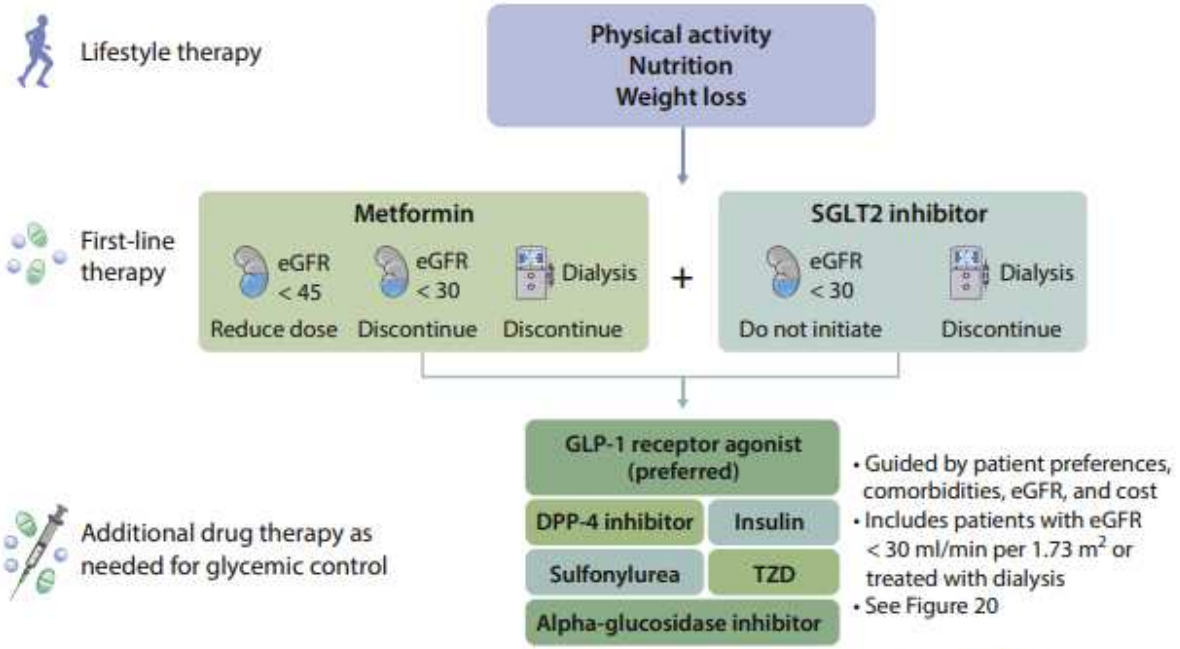


Figure 18 | Treatment algorithm for selecting antihyperglycemic drugs for patients with T2D and CKD. Kidney icon indicates estimated glomerular filtration rate (eGFR; ml/min per 1.73 m^2); dialysis machine icon indicates dialysis. CKD, chronic kidney disease; DPP-4, dipeptidyl peptidase-4; GLP-1, glucagon-like peptide-1; SGLT2, sodium–glucose cotransporter-2; T2D, type 2 diabetes; TZD, thiazolidinedione.

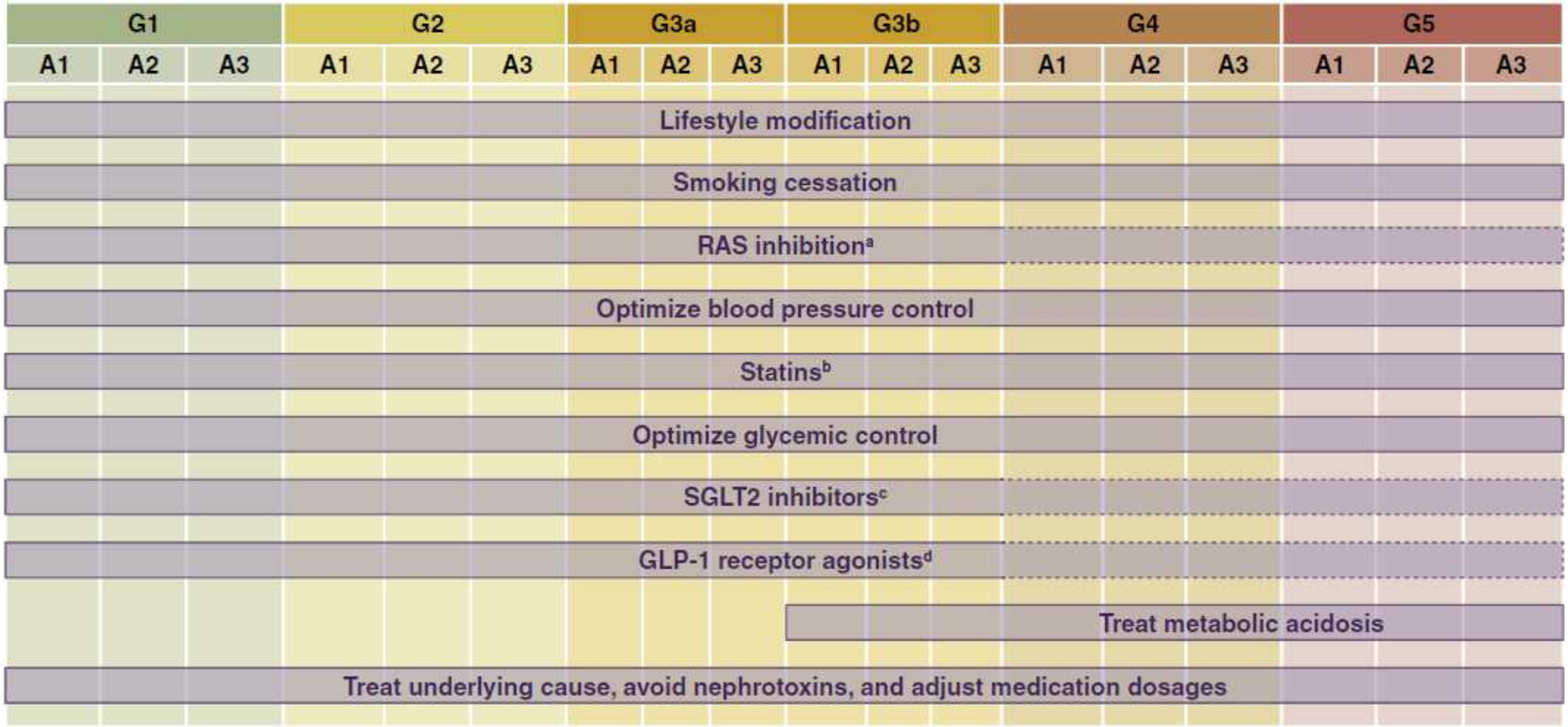


Figure 3 | Interventions to slow chronic kidney disease (CKD) progression and/or reduce cardiovascular risk. [a]Unclear if and when to

Finrenone

Schlipak, KDIGO, Kid Int, 2021

Recommandations pour le dépistage et l'identification de l'insuffisance rénale chronique (IRC)

pour les médecins généralistes

Société suisse de néphrologie

1 L'IRC en Suisse

- En raison du vieillissement de la population suisse et de la hausse des maladies qui nuisent aux reins (ex. le diabète, l'hypertension artérielle), la prévalence de l'insuffisance rénale chronique (IRC) augmente.[1] Les données suggèrent qu'un adulte sur dix en Suisse est atteint d'IRC.[2]
- Il est important de prévenir, de détecter rapidement l'IRC et de prendre en charge de manière optimale ces patients.
- Cet objectif ne peut être atteint que dans le cadre d'un effort collaboratif impliquant les médecins généralistes et les spécialistes.

2 Définition de l'IRC

- L'IRC est définie comme «une anomalie de la structure ou de la fonction rénale, présente pendant plus de 3 mois avec des implications pour la santé».[3]
- L'IRC est classée en fonction de sa cause, du DFGe et de la categorie de l'albuminurie (Figure 1).[3]

3 Détection précoce de l'IRC

- Des traitements sont disponibles pour prévenir la progression de l'IRC, réduire ses complications (comme les maladies CV) et en conséquence, de réduire significativement la morbidité ou mortalité liée.
- Cependant, étant donné que l'IRC est souvent asymptomatique, elle est largement sous-diagnostiquée. 9 néphropathes sur 10 ignorent leur maladie.[4] Par conséquent, les personnes présentant un risque accru d'IRC devraient être dépistées.
- Les patients souffrant d'hypertension artérielle, de diabète sucré ou de maladies cardiovasculaires doivent être dépistés pour l'IRC[5] au moins une fois par an.[3,6]
- Les autres populations à risque devraient également faire l'objet d'un dépistage régulier (Figure 2).
- L'approche du dépistage consiste à la fois à déterminer le DFGe (par mesure de la créatinine, cystatine C, ou les deux) et à quantifier l'albuminurie.[3,6]

l'IRC

est classée en fonction de:

- Cause (C)
- DFGe (G)
- Albuminurie (A)

Risque faible (peut refléter une IRC si d'autres marqueurs d'insuffisance rénale sont présents; sinon pas d'IRC)
Risque modérément accru
Risque modéré à fortement accru
Risque élevé
Risque très élevé

Catégories de DFGe (ml/min/1.73m²) Description et valeur				Catégories Albuminurie Description et intervalles		
				A1	A2	A3
				Normale à modérément augmentée	Modérément augmentée	Gravement augmentée
				<30mg/g <3 mg/mmol	30-300mg/g 3-30mg/mmol	>300mg/g >30mg/mmol
G1	Normal ou hyperfiltration	≥90		1 si IRC	Traiter 1	Référer 2
G2	Diminution légère	60-89		1 si IRC	Traiter 1	Référer 2
G3a	Diminution légère à modérée	45-59		Traiter 1	Traiter 2	Référer 3
G3b	Diminution modérée à sévère	30-44		Traiter 2	Traiter 3	Référer 3
G4	Sévèrement diminué	15-29		Référer 3	Référer 3	Référer 4+
G5	Insuffisance rénale terminale	≤15		Référer 4+	Référer 4+	Référer 4+

Figure 1 - Classification et stratification des risques de l'IRC selon KDIGO. Les grilles DFGe et Albuminurie montrent le risque de progression, de morbidité et de mortalité par couleur, du risque le plus bas au risque le plus élevé (vert, jaune, orange, rouge, rouge foncé). Les chiffres figurant dans les boîtes [illegible] fois par année).

Conditions présentant un risque accru d'IRC

- Hypertension artérielle
- Diabète
- Maladies cardiovasculaires
- Antécédents d'insuffisance rénale aiguë
- Antécédents familiaux d'une maladie rénale
- Maladies systémiques prédisposantes à l'IRC (ex. VIH, LED, vascularite)
- Traitement avec des médicaments néphrotoxiques
- Obésité
- Âge avancé

↓ oui

Dépistage de l'IRC

- Rapport albumine et créatinine urinaire (ACR) pour détecter l'albuminurie*

et

- Créatinine sérique ou cystatine C pour estimer le taux de filtration glomérulaire (DFGe)

* Pour déterminer l'ACR, l'albumine et la créatinine doivent être mesurées à partir d'une urine ponctuelle au moins une fois par an. Le rapport albumine sur créatinine fournit l'ACR. Les unités sont données en fonction de celles utilisées par chaque laboratoire. L'ACR en mg/g correspond approximativement à l'excrétion quotidienne d'albumine en mg. Si l'ACR est donné en mg/mmol, il doit être multiplié par un facteur 10 pour arriver à l'excrétion journalière d'albumine.

L'un des éléments suivants est présent pendant ≥ 3 mois?

- DFGe <60ml/min/1.73m²

ou

- ACR ≥30mg/g (3mg/mmol)*

↓ oui → Diagnostic de l'IRC confirmé
Classification IRC/ Stratification du risque selon la figure 1

↓ non → Répétition périodique de l'évaluation si le statut de risque persiste

↓ Prise en charge de l'IRC ou référer le patient au néphrologue

Interventions thérapeutiques

- Arrêt du tabagisme, pratique d'une activité physique régulière et alimentation saine
- Perte de poids si l'IMC >25kg/m²
- Éviter les médicaments néphrotoxiques
- Adapter le médicament à la fonction rénale
- Optimiser la pression artérielle et le contrôle lipidique
- Envisager l'inhibition du système RAA si l'ACR >30mg/g (3mg/mmol) et pas de contre-indication
- Initiation d'un iSGLT2 approuvé pour l'utilisation dans l'IRC si le DFGe ≥25ml/min et si aucune contre-indication
- Patients IRC et DT2
  - Optimiser le contrôle glycémique pour les patients diabétiques de type 2
  - Envisager l'iSGLT-2 si aucune contre-indication
  - Envisager le GLP-1RA (si l'iSGLT2 et/ou la metformine ne sont pas tolérés)
  - Considérer la Finérénone quand approuvée pour cette indication et si pas de contre-indication

Référer au néphrologue si

- IRA ou chute brutale et persistante du DFGe
- IRC d'origine inconnue
- DFGe <30ml/min/1.73m²
- ACR systématiquement >300mg/g (30mg/mmol)
- Progression de l'IRC/détérioration du DFGe
- Microhématurie glomérulaire
- IRC + hypertension résistante
- Anomalies persistantes du potassium sérique
- Maladie rénale héréditaire
- Néphrolithiase récurrente ou étendue

Figure 2 - Algorithme suggéré pour dépister, stratifier et gérer les personnes à risque ou atteintes d'IRC et quand se référer à un néphrologue (IRA: insuffisance rénale aiguë, iSGLT2: inhibiteur du co-transporteur sodium-glucose type 2, GLP1-RA: agonistes des récepteurs du peptide 1 semblable au glucagon, IRC: insuffisance rénale chronique, système RAA rénine-angiotensine-aldostérone, rapport ACR: rapport albumine créatinine urinaire, DFGe: débit estimé de filtration glomérulaire, VIH: virus de l'immunodéficience humaine, LED: lupus érythémateux disséminé).[3,5,6]

Auteurs: Harold Seeger, Sophie de Seigneux, Pietro Cippà, pour la Société suisse de néphrologie.

Références: 1. Xie Y, et al., Kidney Int. 2018;94(3):567-81. 2. Ogna VF, et al., Swiss Med Wkly. 2016;146:w14313. 3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. Kidney Int 2013;3 (Suppl):1-150. 4. GBD Chronic Kidney Disease Collaboration. Lancet.2020;395(10225):709-733. 5. Shlipak MG, et al., for Conference Participants, Kidney International (2020), doi: https://doi.org/10.1016/j.kint.2020.10.012. 6. SGED: GDMD Kriterien für ein „gutes" Disease Management Diabetes in der Grundversorgung, https://www.agedassed.ch/fileadmin/user_upload/6_Diabetologie/64_Ressourcen_Hausarzt/Diabetes_Kriterien_2017_SGED_def.pdf.
7. American Diabetes Association. Diabetes Care, 2021 Jan;44: 10.2337/dc21-S005. 8. Delanaye P, et al. IASN 30: 1785-1805, 2019.

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Schweiz. Gesellschaft für Nephrologie, Postfach 567, 3076 Worb, www.swissnephrology.ch

SGN-SSN
Schweizerische Gesellschaft für Nephrologie
Société Suisse de Néphrologie
Società Svizzera di Nefrologia
Swiss Society of Nephrology

Conclusion

- L'IRC est fréquente et coûteuse
- Cette pathologie nécessite un dépistage systématique des populations à risque
- Sa Prise en charge est globale
- Traitement néphroprotecteurs
  - IEC-Sartan
  - Inhibiteurs SGLT2 (gliflozines) en IRC diabétique ET NON diabétique
  - Analogues GLP-1 en cas de DT2
  - Pas de double blocage RAA actuellement (=pas de combinaison IEC et sartans)
  - Finrenone en cas de DT2 si pas d'hyperkaliémie
- Informer les patients

Au cabinet		< 140/90 mmHg
Auto-mesure		< 135/85 mmHg
MAPA	**jour + nuit**	< 125/80 mmHg
	jour	< 135/85 mmHg
	nuit	< 120/70 mmHg

Table 23 Office blood pressure treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke[a]/TIA	
18 - 65 years	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	**Target to <140 to 130** *if tolerated*	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	70–79
65 - 79 years[b]	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	70–79
≥80 years[b]	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	70–79
Office DBP treatment target range (mmHg)	70–79	70–79	70–79	70–79	70–79	

CAD = coronary artery disease; CKD = chronic kidney disease (includes diabetic and non-diabetic CKD); DBP = diastolic blood pressure; SBP = systolic blood pressure; TIA = transient ischaemic attack.

[a]Refers to patients with previous stroke and does not refer to blood pressure targets immediately after acute stroke.

[b]Treatment decisions and blood pressure targets may need to be modified in older patients who are frail and independent.

2018 ESC/ESH Guidelines for themanagement of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH)European Heart Journal (2018) 00, 1–98

Poster: PO2531 Year: 2021 - Finerenone and Kidney Outcomes in Patients with CKD and T2D: Results from FIDELITY

Finerenone and kidney outcomes in patients with CKD and T2D: Results from FIDELITY

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RATIONALE AND OBJECTIVE

- FIDELITY is a **prespecified pooled analysis** evaluating patient-level efficacy and safety data from the phase III FIDELIO-DKD (NCT02540993) and FIGARO-DKD (NCT02545049) trials
- Here, we report kidney outcomes with finerenone across a spectrum of patients with CKD and T2D

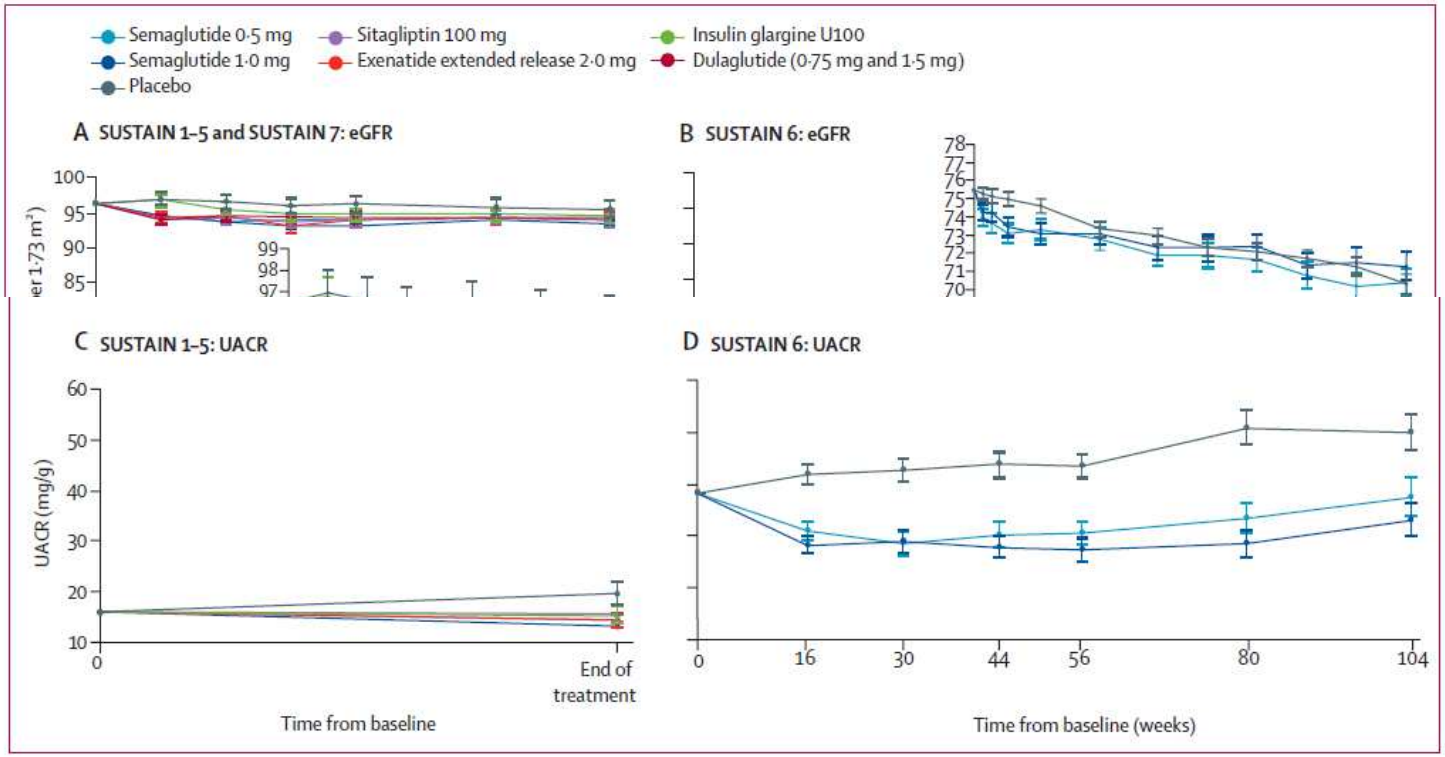
KEY FINDINGS

- Results of FIDELITY suggest that finerenone significantly **reduces progression of CKD by 23%** as well as the risk of **end-stage kidney disease by 20%**
- Moreover, finerenone slows CKD progression **across the spectrum of CKD severity**

Effects of once-weekly subcutaneous semaglutide on kidney function and safety in patients with type 2 diabetes: a post-hoc analysis of the SUSTAIN 1–7 randomised controlled trials

Johannes F E Mann, Thomas Hansen, Thomas Idorn, Lawrence A Leiter, Steven P Marso, Peter Rossing, Jochen Seufert, Sayeh Tadayon, Tina Vilsbøll

Avantage majeur: perte de poids et ok a clairances basses (moins de 25)



Mann et al. Lancet 2020

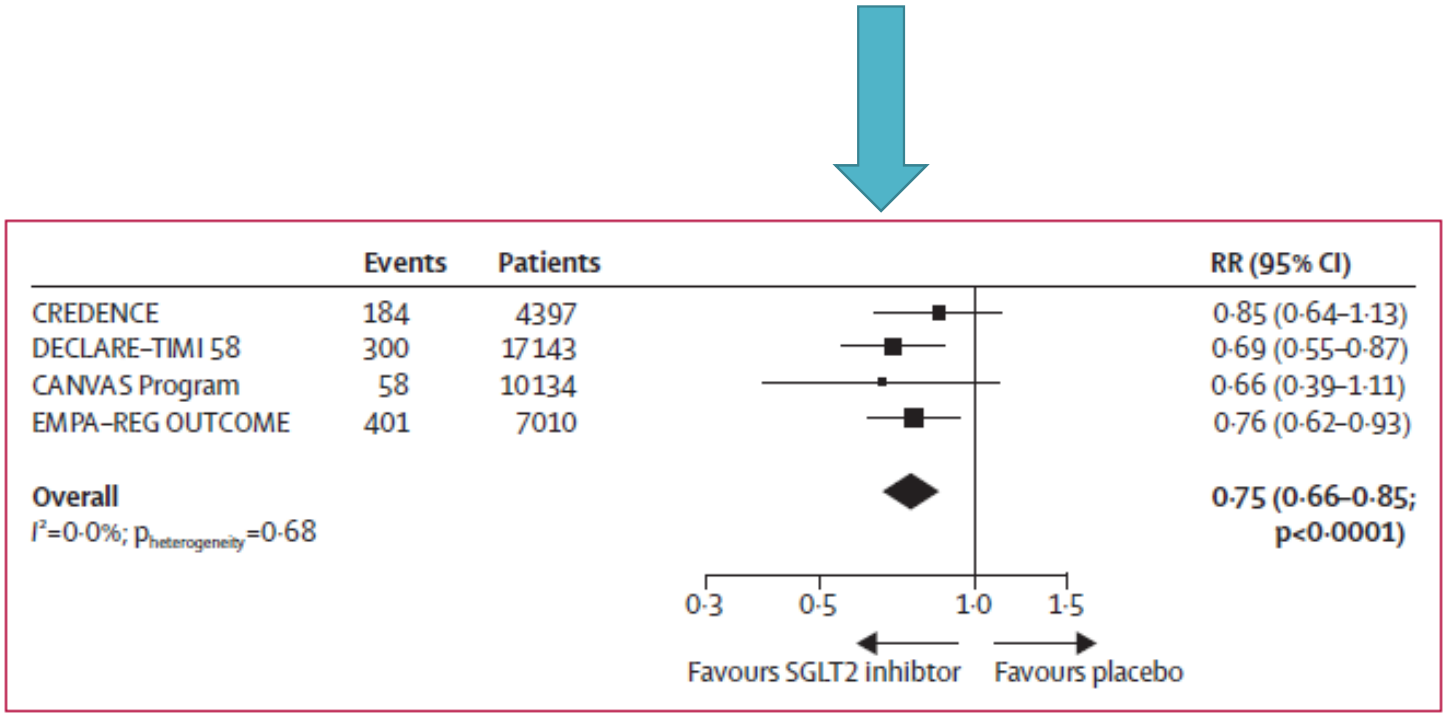
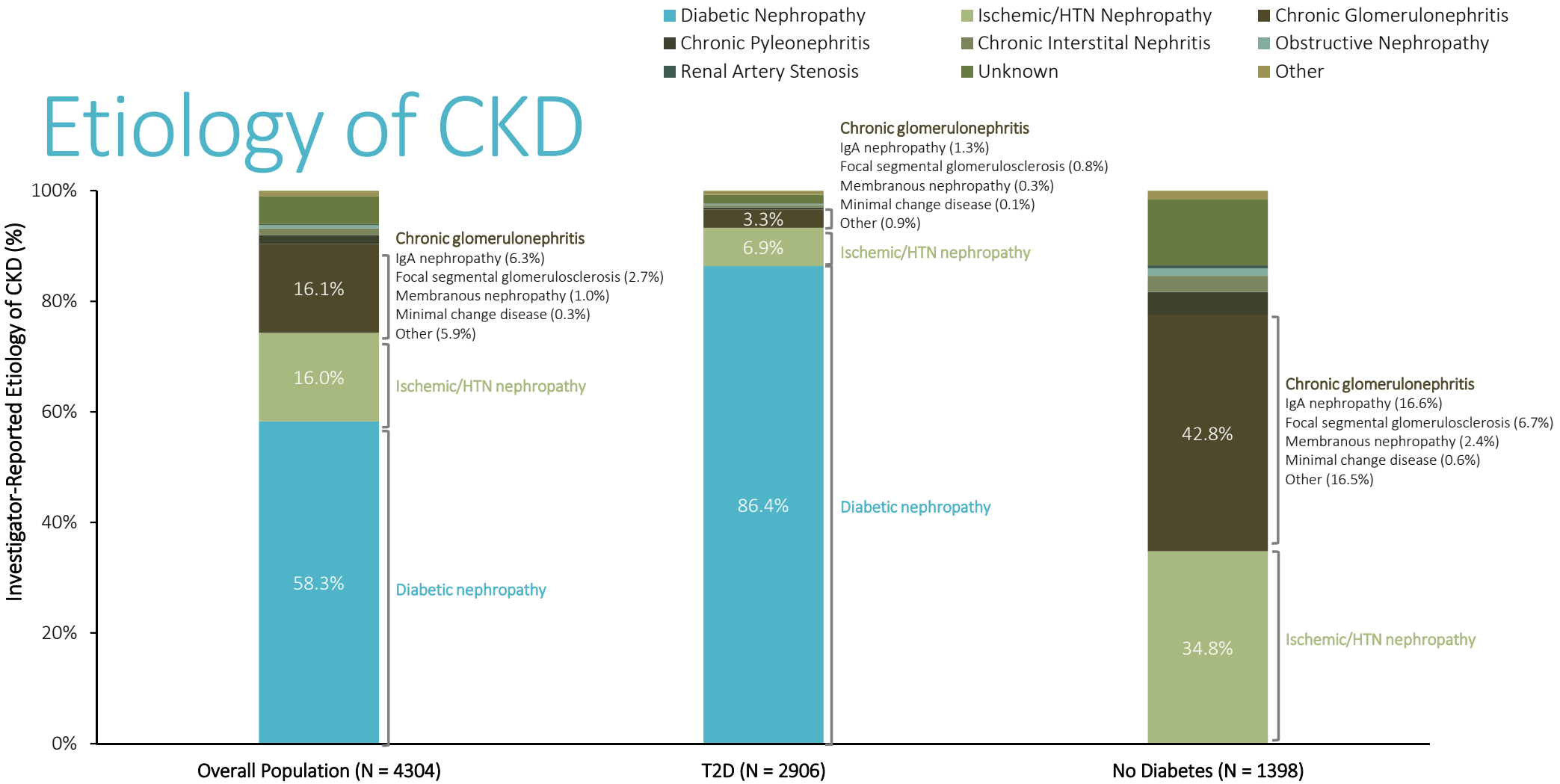


***Figure 3*: Effect of SGLT2 inhibitors on acute kidney injury**

Weights were from random-effects meta-analysis. SGLT2=sodium-glucose co-transporter-2. RR=relative risk.

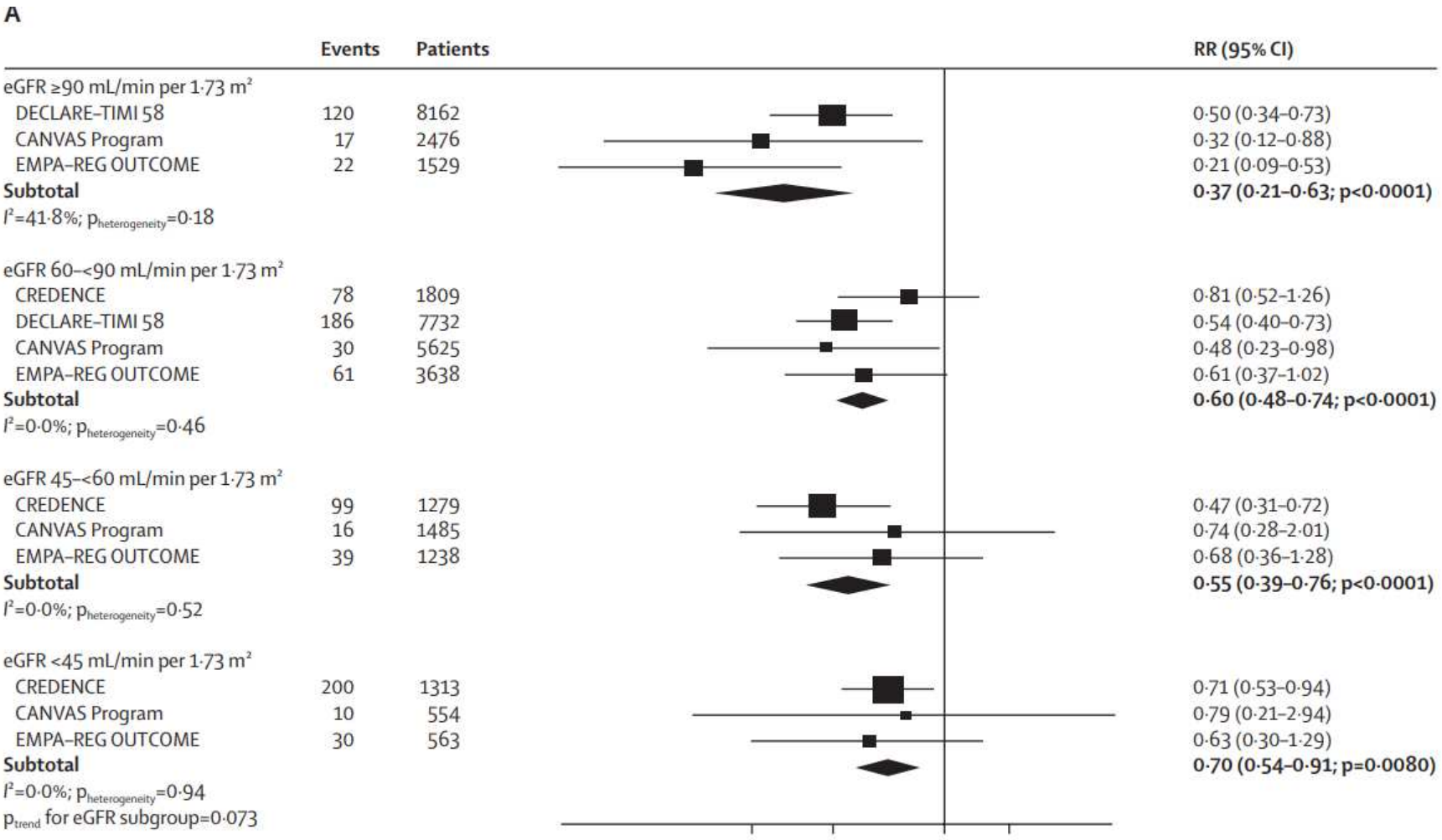
Neuen, Lancet 2019

Etiology of CKD



HTN = hypertensive; IgA = immunoglobulin A; T2D = type 2 diabetes.

Wheeler DC et al. *Nephrol Dial Transplant*. 2020;35:1700–1711.



Neuen, Lancet 2019

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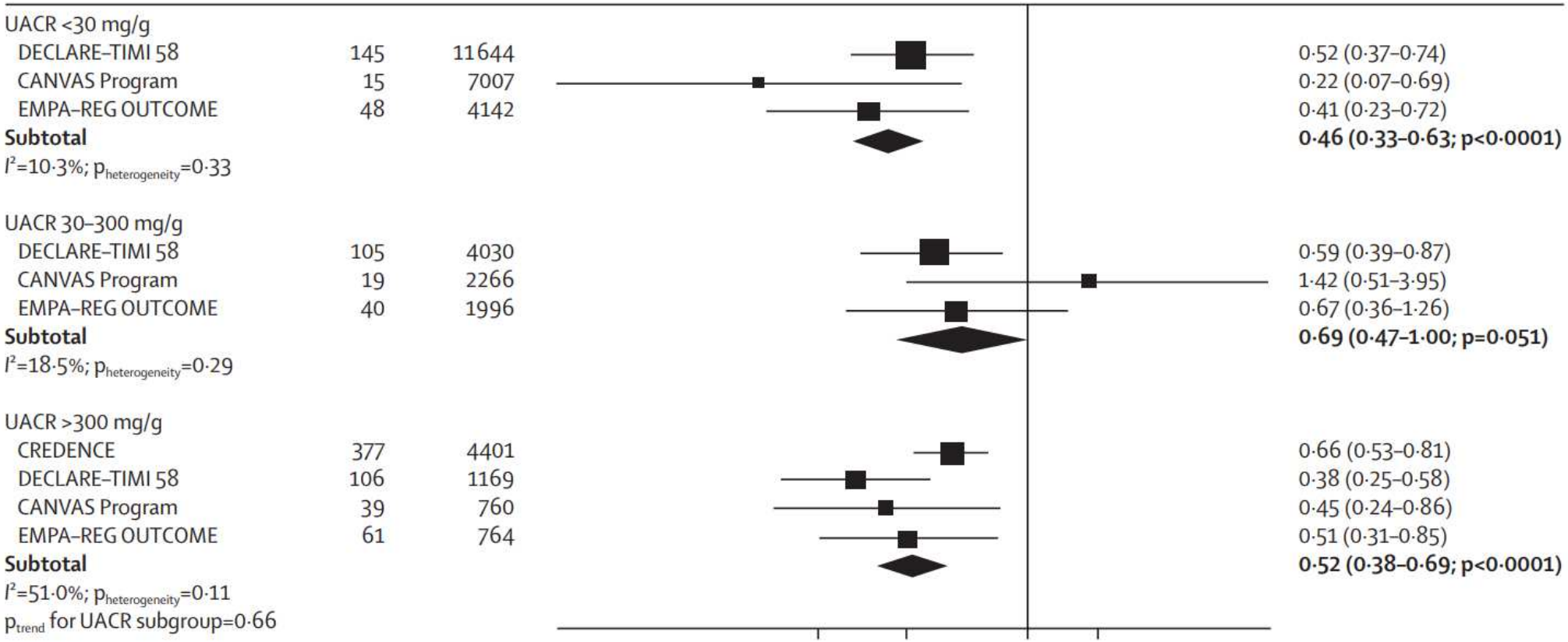

Neuen, Lancet 2019