Kidney protection in DKD
Role of SGLT2 inhibitors

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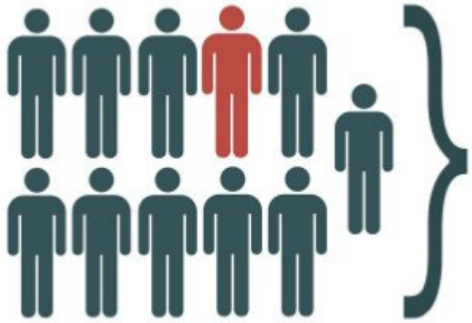
May 2024

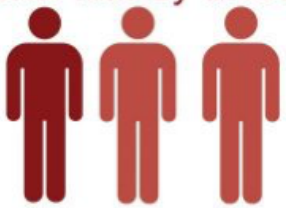
Number of diabetics will rise to 700 million by 2045

1 in 11 adults has diabetes



463 million worldwide

1 in 3
US adult diabetics have
chronic kidney disease

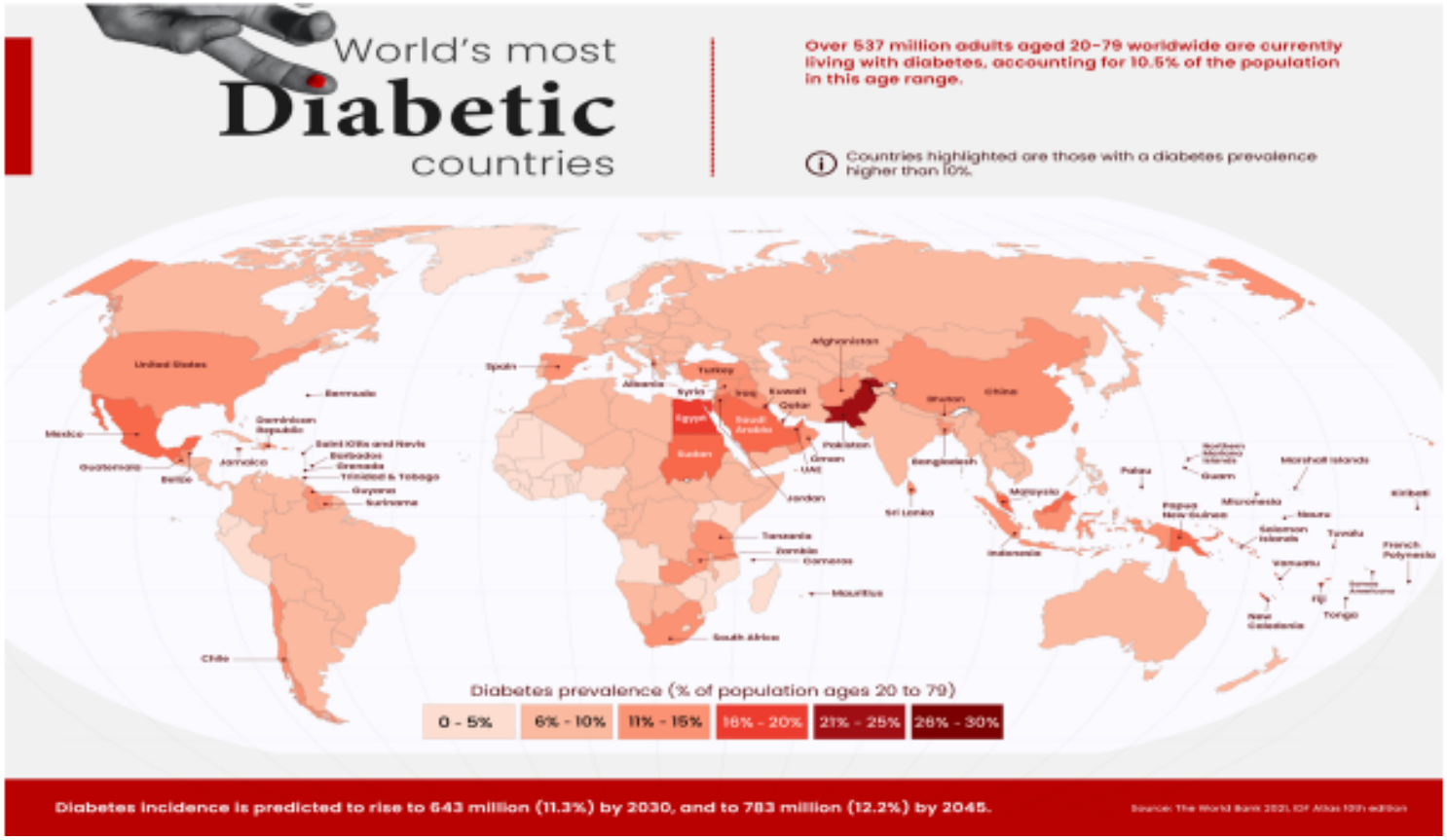


154 million

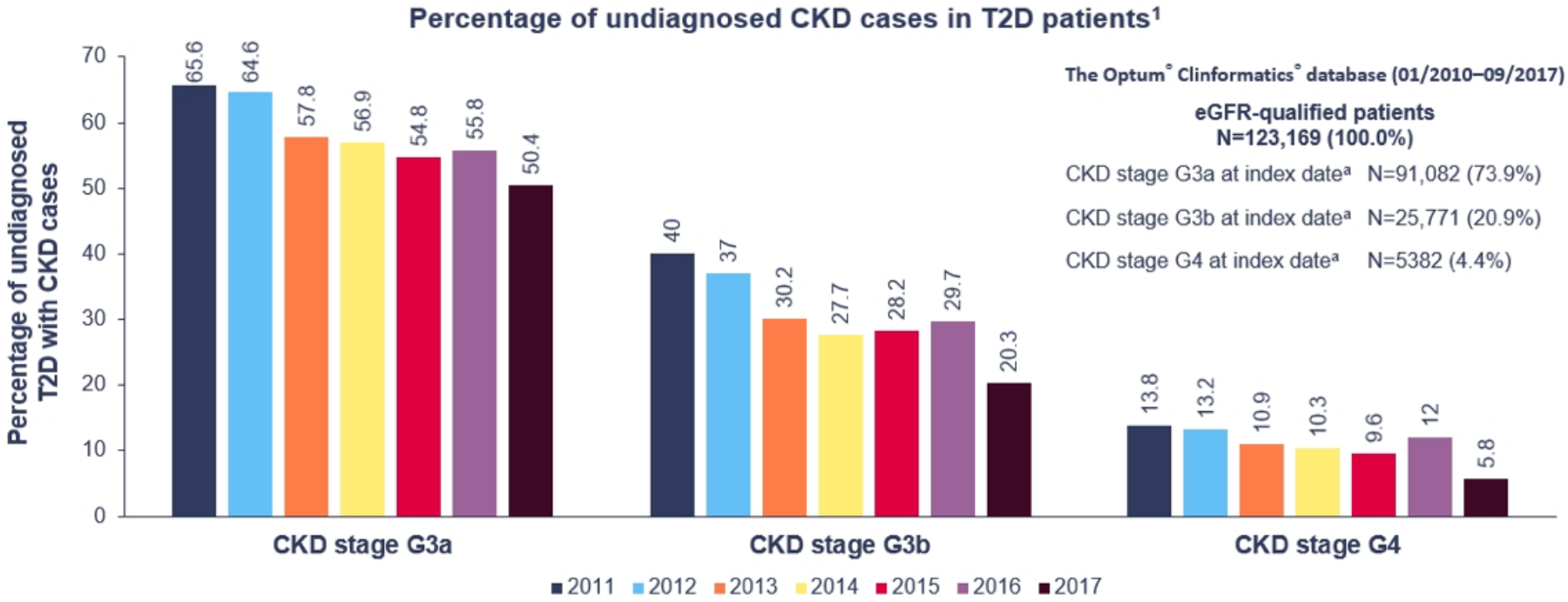
PromarkerD can predict
diabetic kidney disease
up to 4 years in advance

Kidney disease is one of the major complications of diabetes

Diabetes prevalence information based on the IDF Diabetes Atlas, 9th edition 2019

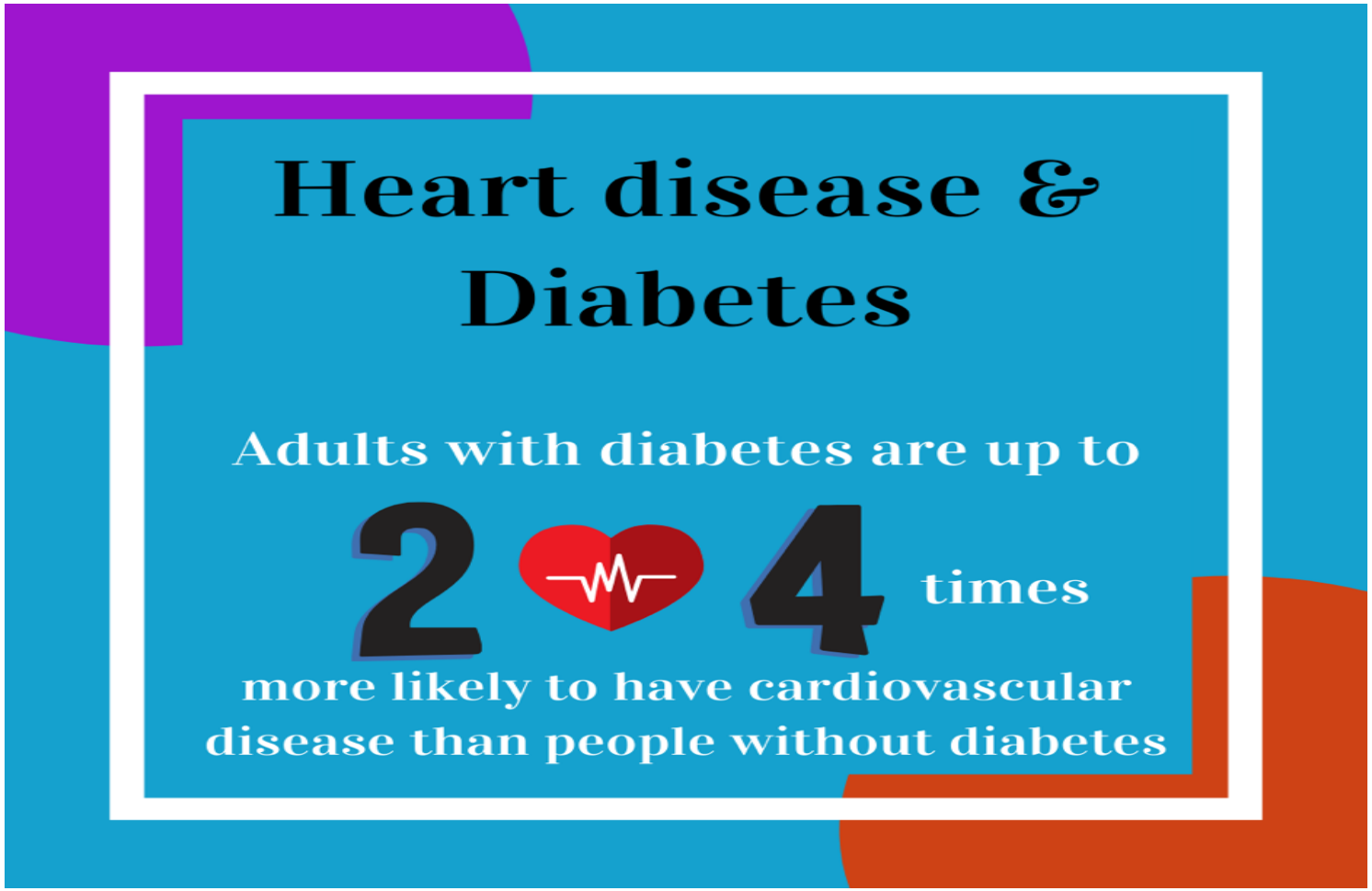

World's most
Diabetic
countries
Over 537 million adults aged 20-79 worldwide are currently living with diabetes, accounting for 10.5% of the population in this age range.
Countries highlighted are those with a diabetes prevalence higher than 10%.
Diabetes prevalence (% of population ages 20 to 79)
0 - 5%
6% - 10%
11% - 15%
16% - 20%
21% - 25%
26% - 30%
Diabetes incidence is predicted to rise to 643 million (11.3%) by 2030, and to 783 million (12.2%) by 2045.

The prevalence of undiagnosed CKD in type 2 diabetes has been decreasing, but is still over 50% in patients with CKD stage G3a



In the UK, only 39.5% of patients with microalbuminuria had a code for microalbuminuria on their record[2]

[a]The index date for CKD stage was the first serum creatinine measurement leading to an eGFR <60 mL/min/1.73 m^2
eGFR, estimated glomerular filtration rate
1. Bakris GF, et al. Presented at the National Kidney Foundation 2019 Spring Clinical Meetings; May 8th–12th, 2019; Boston, MA, USA; Poster 308; 2. Willis A, et al. *Diabetes Care* 2020. doi:10.2337/dc19-2243 [Epub ahead of print]


Heart disease &
Diabetes
Adults with diabetes are up to
2
4
times
more likely to have cardiovascular
disease than people without diabetes

DIABETES & HEART DISEASE RISK

CardioSmart
American College of Cardiology

DIABETES increases risk of HEART DISEASE:

2X MORE IN MEN

4X MORE IN WOMEN

DIABETES affects about **1 OUT OF 10 PEOPLE** in U.S.

HEART DISEASE is the **LEADING CAUSE** of death among adults with **DIABETES**

WHY are they LINKED?

HIGH BLOOD SUGAR can damage blood vessels and cause:

- **Heart Attack**
- **Stroke**
- **Peripheral Artery Disease**

People with diabetes also may have **OTHER HEART RISK FACTORS:**

- **High Blood Pressure**
- **High Cholesterol**
- **Lack of Activity**
- **Obesity / Being Overweight**

WHAT YOU CAN DO TO PROTECT YOUR HEART

Follow **ABCs OF DIABETES** by lowering:

- **A1C** (test that measures blood sugar)
- **B**lood pressure
- **C**holesterol

QUIT SMOKING

TAKE MEDICINE if prescribed

BE ACTIVE for 30 min., 5x a week

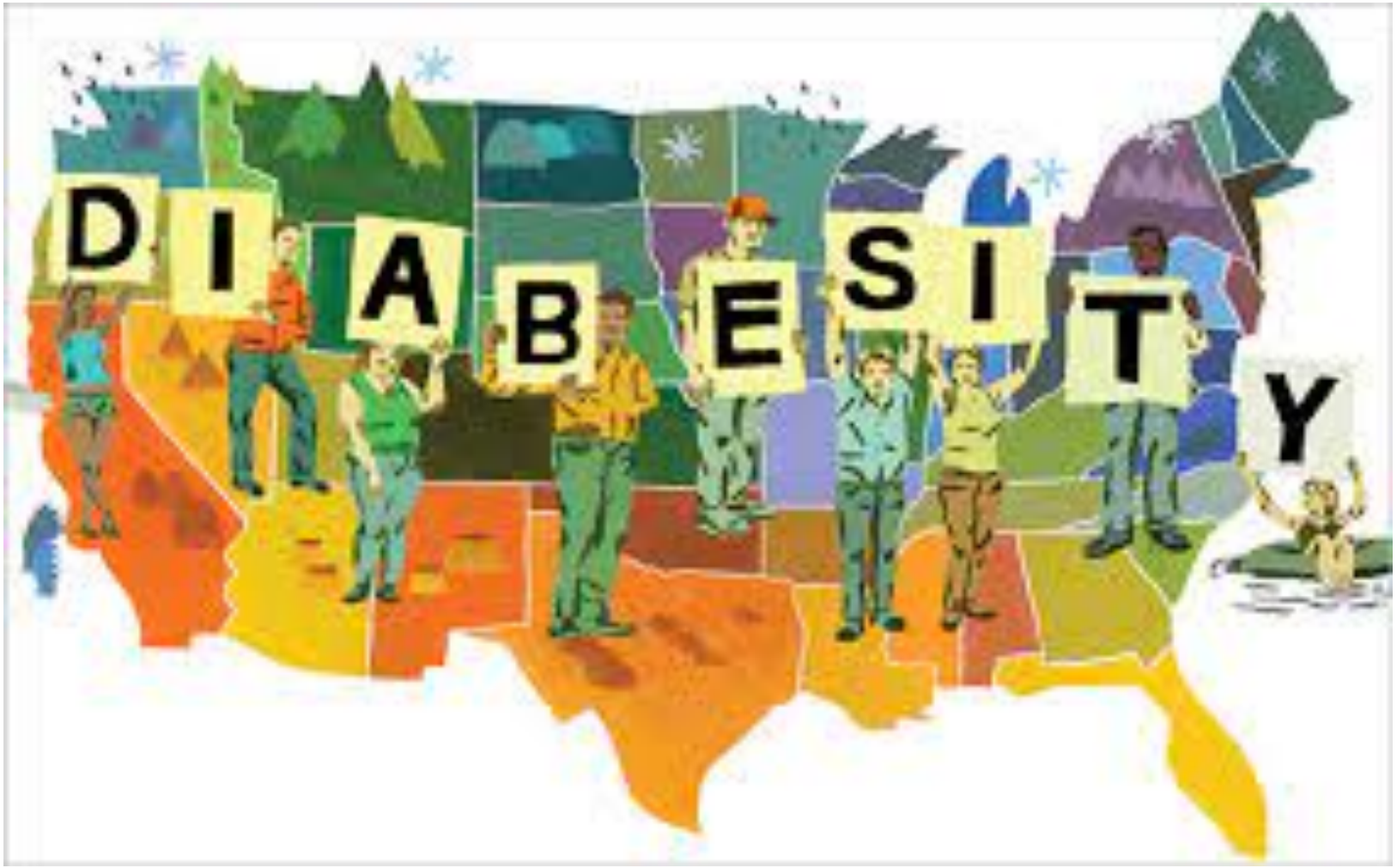
EAT more **VEGETABLES & FRUITS**

Information provided for educational purposes only. Please consult your health care provider about your specific health needs.

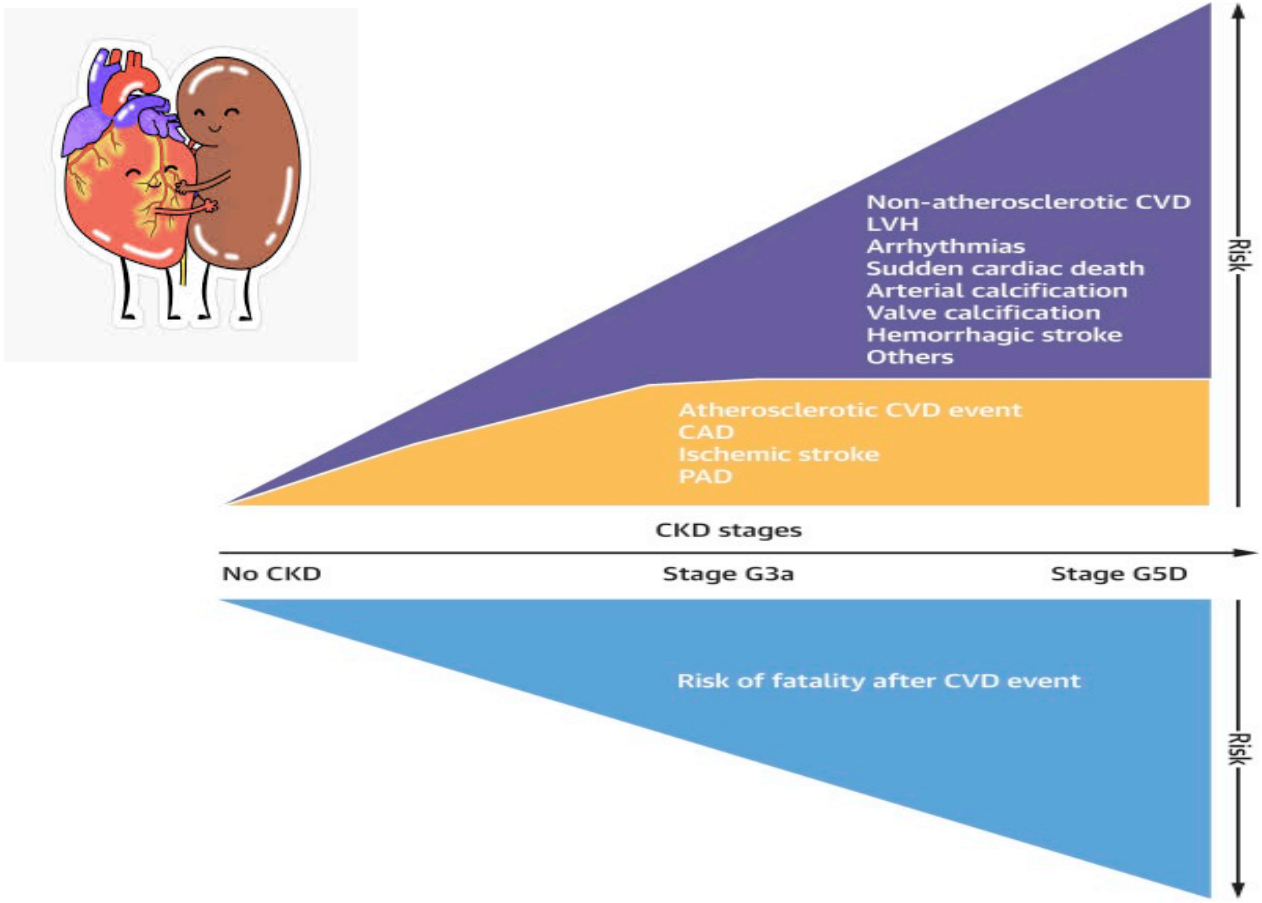
Go to *CardioSmart.org/DiabetesandHeartDisease* to learn more about diabetes and tips to protect your heart.

@CardioSmart facebook.com/CardioSmart

If you would like to download or order additional posters on various topics, visit CardioSmart.org/Posters.
CardioSmart is supported in part by Boehringer Ingelheim Pharmaceuticals Inc. and Eli Lilly and Company.

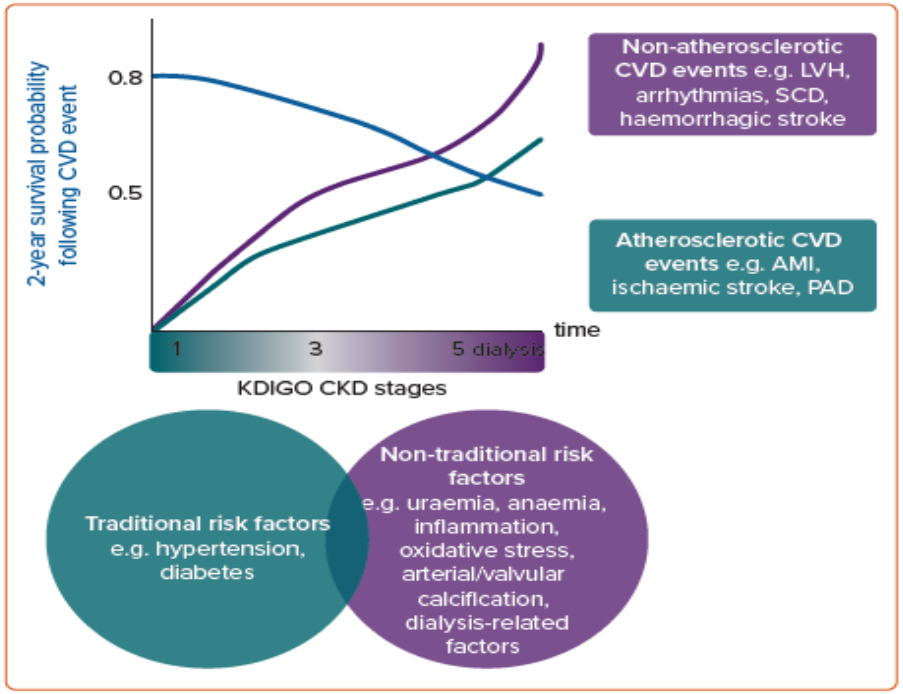

DIABESITY

CENTRAL ILLUSTRATION: Changes in Cardiovascular Disease Risk During Chronic Kidney Disease Progression

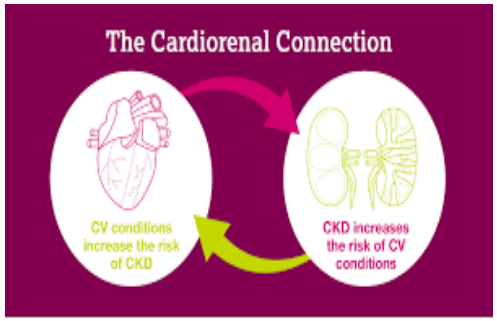


Sarnak, M.J. et al. J Am Coll Cardiol. 2019;74(14):1823–38.

Figure 1: Changing Cardiovascular Disease Risk in Progressing Chronic Kidney Disease

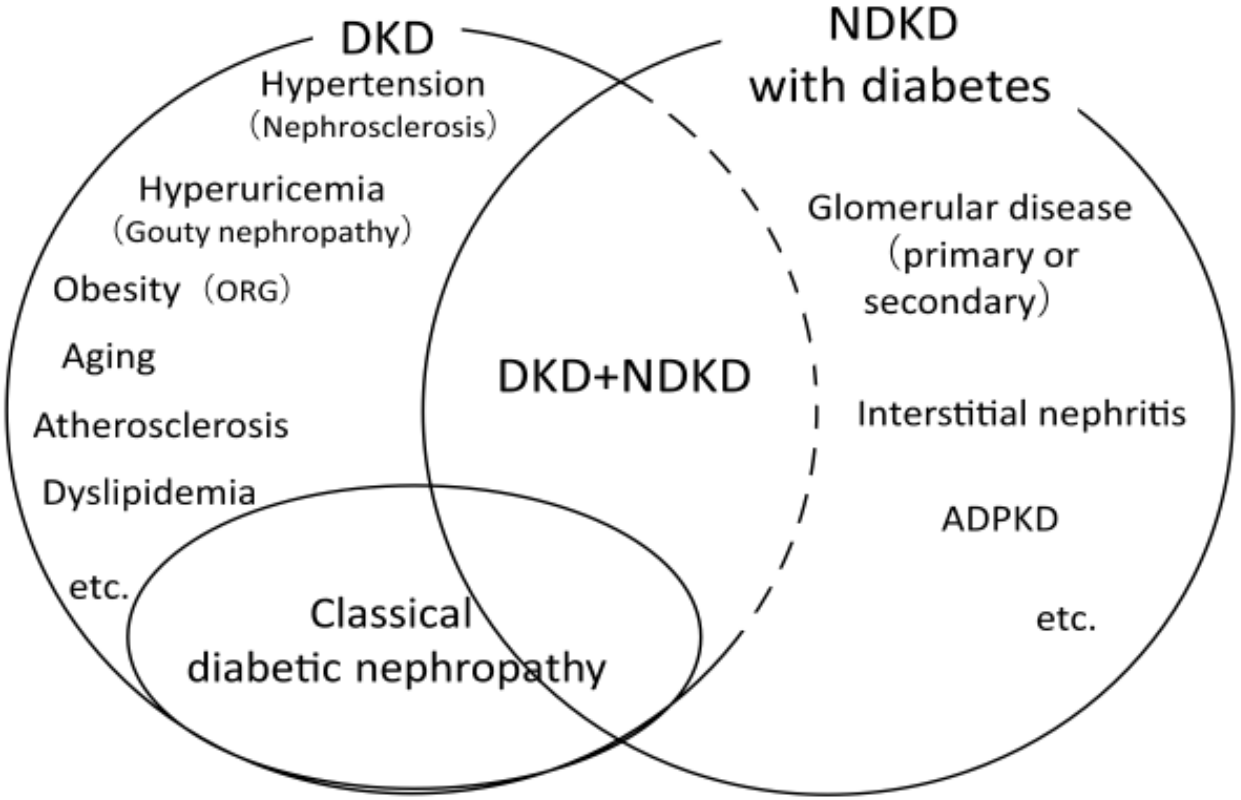


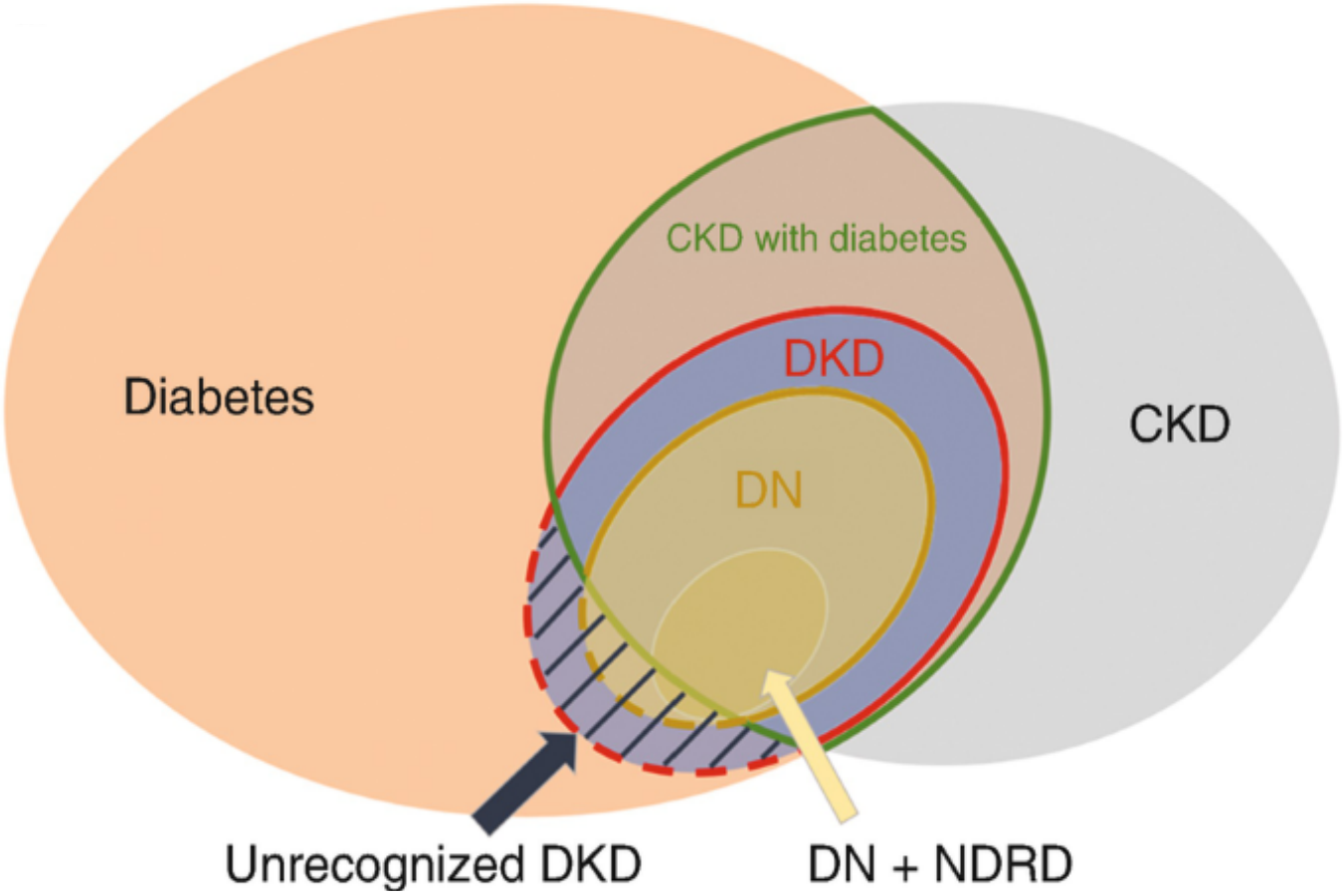
As CKD progresses, the risk of CVD events rises. Mortality following cardiovascular events also increases. Non-atherosclerotic causes contribute more than atherosclerotic causes as CKD progresses. This is reflected in the respective contribution of traditional and non-traditional risk factors in early and late-stage disease. Time is also an important factor – the longer time spent in each stage of CKD before commencing dialysis will result in longer exposure to the risk factors and greater accumulated damage and risk.[13–15] AMI = acute MI; CKD = chronic kidney disease; CVD = cardiovascular disease; KDIGO = Kidney Disease: Improving Global Outcomes Group; LVH = left ventricular hypertrophy; PAD = peripheral arterial disease; SCD = sudden cardiac death.



Globally, nearly 10% of the population has chronic kidney disease (CKD), defined as a glomerular filtration rate less than 60 mL/min/1.73 m2 and/or a urinary albumin to creatinine ratio greater than 30 mg/g (3 mg/mmol).

Persons with CKD have a substantially high risk of cardiovascular disease. Indeed, most persons with CKD are far more likely to develop a cardiovascular event than to progress to end-stage kidney disease!!!


DKD
Hypertension
（Nephrosclerosis）
Hyperuricemia
（Gouty nephropathy）
Obesity （ORG）
Aging
Atherosclerosis
Dyslipidemia
etc.
NDKD
with diabetes
Glomerular disease
（primary or
secondary）
DKD+NDKD
Interstitial nephritis
ADPKD
etc.
Classical
diabetic nephropathy


Diabetes
CKD with diabetes
DKD
DN
CKD
Unrecognized DKD
DN + NDRD

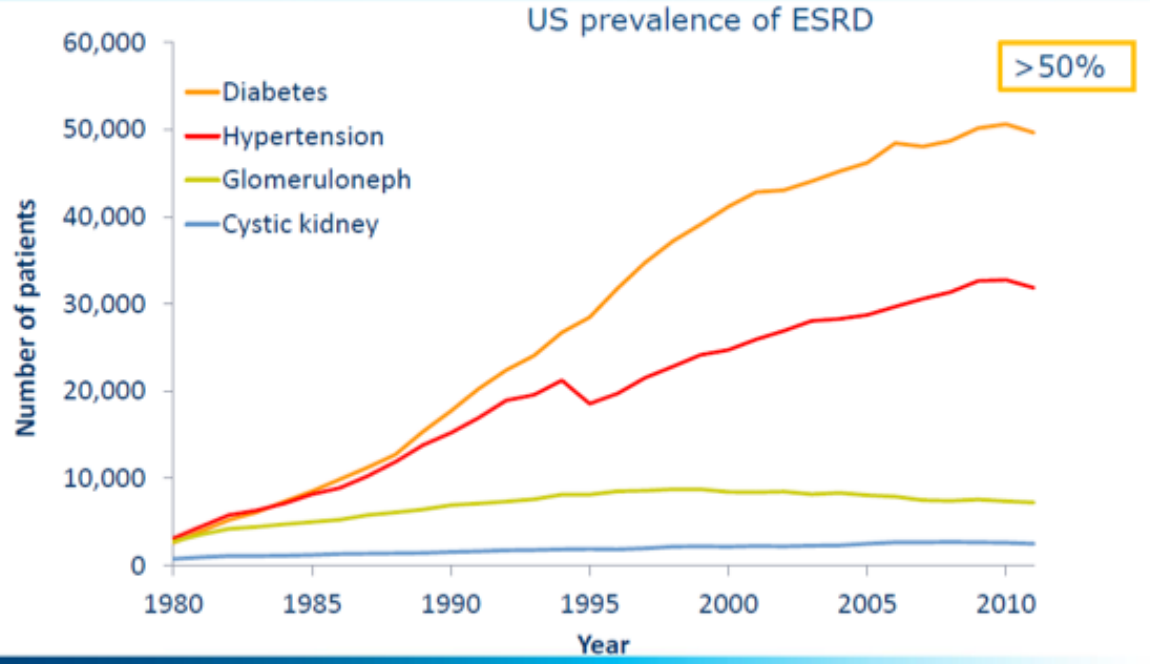
DKD, DN, and CKD with diabetes

- **"Diabetic kidney disease (DKD)"** is a **concept** that widely recognizes the pathophysiological change induced by diabetes as the onset and progressive factor of **renal injury and renal function decline**, **regardless of the level of albuminuria**.

DKD may contain multiple renal pathologies, including **nephrosclerosis** due to **hypertension**, renal changes associated with **atherosclerosis**, **obesity**-related **glomerulopathy** and **gouty nephropathy.**

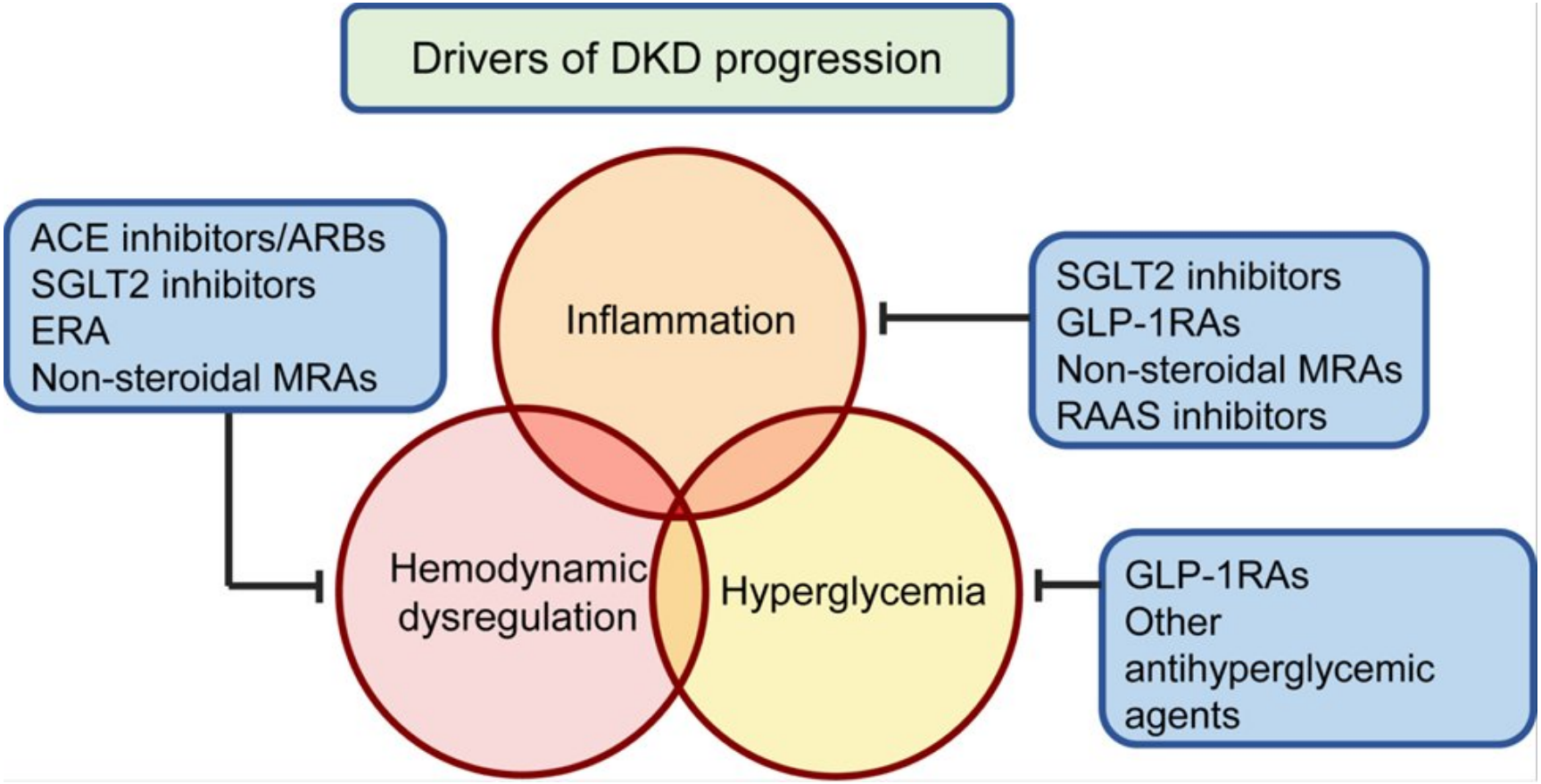
DKD needs *multi-factorial ttt against metabolic disorders* (primarily diabetes)

Diabetes is the leading cause of end-stage renal disease



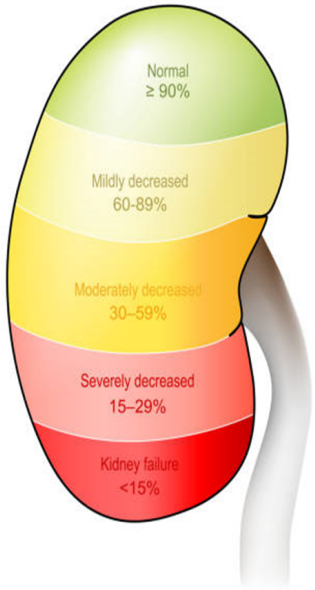
United States Renal Data System. Annual data report. 2013
www.usrds.org/atlas.htm

CREDENCE


Drivers of DKD progression
ACE inhibitors/ARBs
SGLT2 inhibitors
ERA
Non-steroidal MRAs
Inflammation
SGLT2 inhibitors
GLP-1RAs
Non-steroidal MRAs
RAAS inhibitors
Hemodynamic dysregulation
Hyperglycemia
GLP-1RAs
Other antihyperglycemic agents

		Albuminuria (ACR)			Total
CKD-stage	$eGFR_{CKD-EPI}$ (ml/min/1.73m²)	A1 (< 30 mg/g)	A2 (30 – 300 mg/g)	A3 (> 300 mg/g)	
G1	≥ 90	79 15.2%	9 1.7%	2 0.4%	90 17.3%
G2	60 – 89	257 49.4%	36 6.9%	10 1.9%	303 58.3%
G3a	45 – 59	76 14.6%	17 3.3%	3 0.6%	96 18.5%
G3b	30 – 44	15 2.9%	5 1.0%	2 0.4%	22 4.2%
G4	15 – 29	3 0.6%	2 0.4%	3 0.6%	8 1.5%
G5	< 15	0	0	1 0.2%	1 0.2%
total		430	69	21	520

Chronic kidney disease

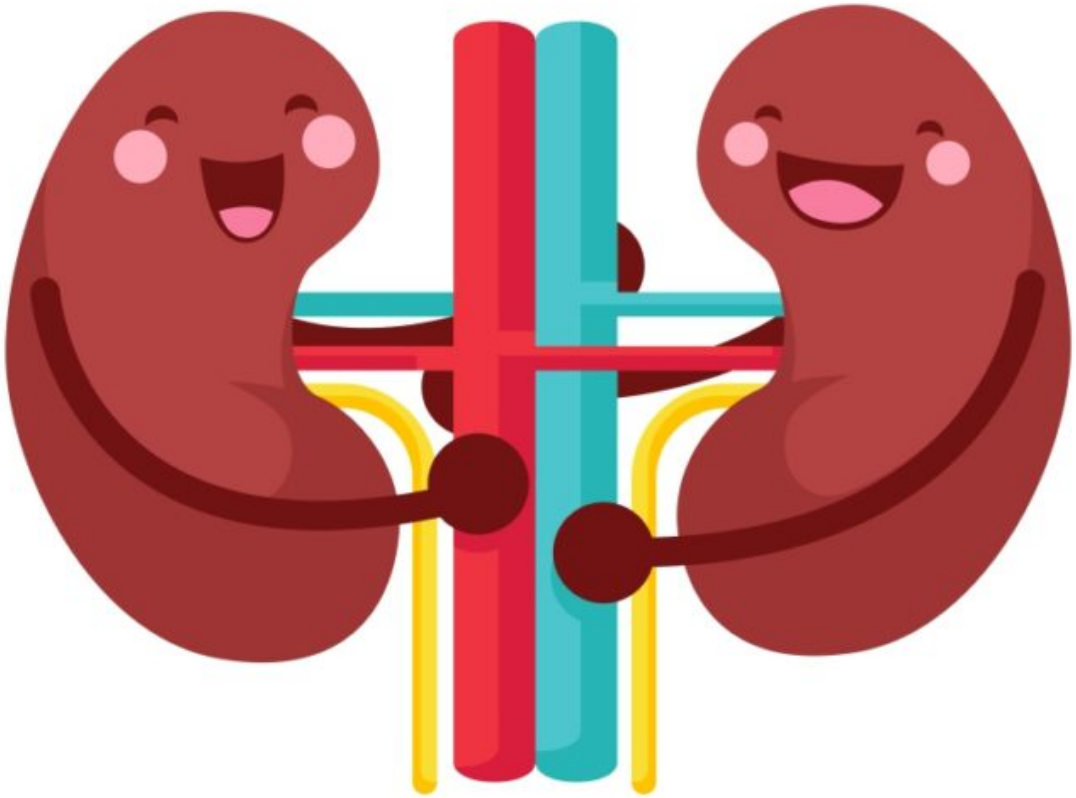


Prognosis of CKD and by eGFR and Albuminuria Categories: KDIGO 2012

eGFR categories (mL/min/1.73m²) Description and range				Persistent albuminuria categories Urine ACR (mg/mmol) Description and range		
				A1	**A2**	**A3**
				Normal	Microalbuminuria	Macroalbuminuria
				male < 2.5 female < 3.5	male 2.5 – 25 female 3.5 – 35	male > 25 female > 35
	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			

low risk if no other markers of kidney disease, no CKD) Moderately increased risk high risk very high risk

Protect
your Kidneys from Diabetes

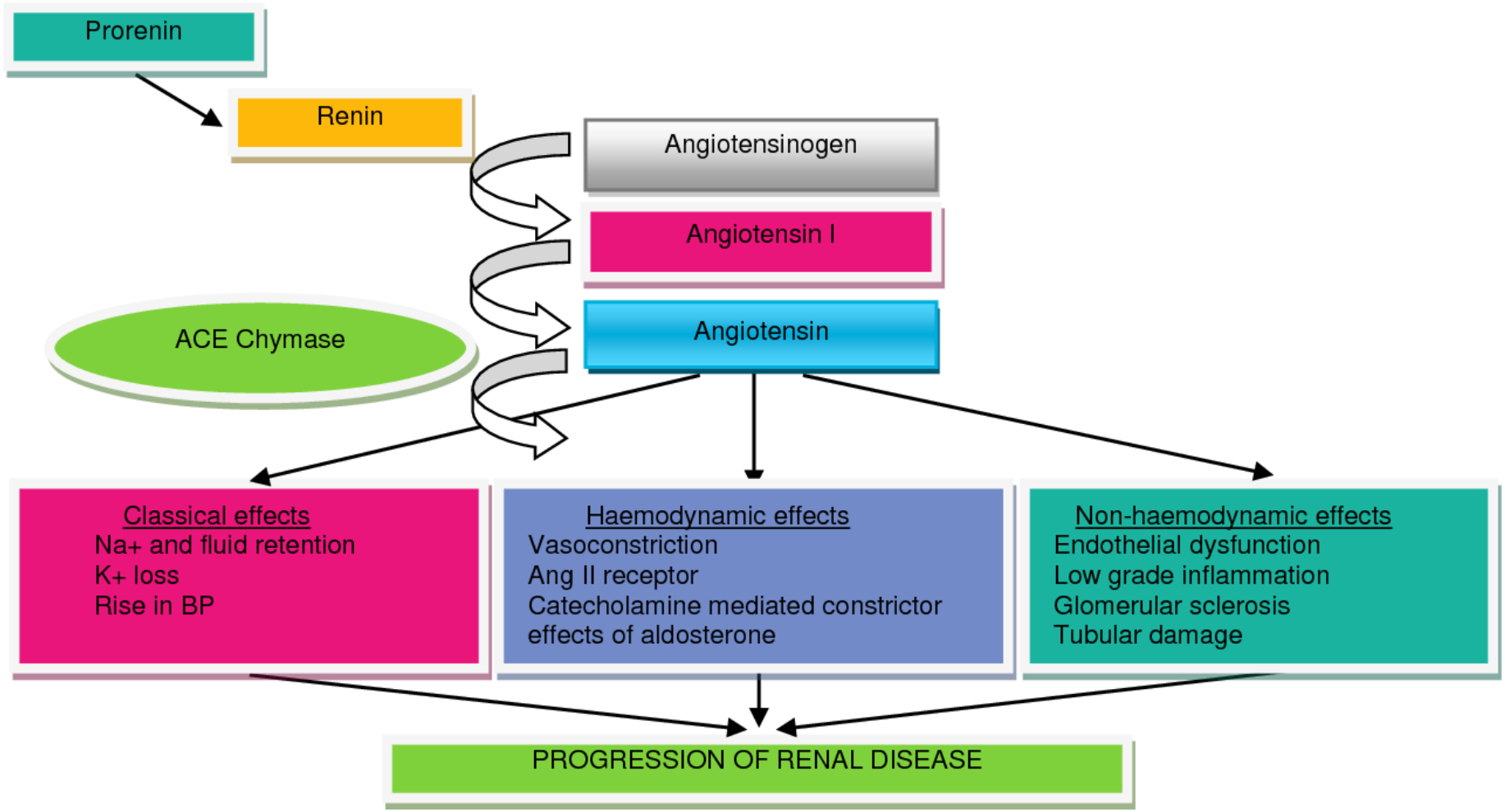


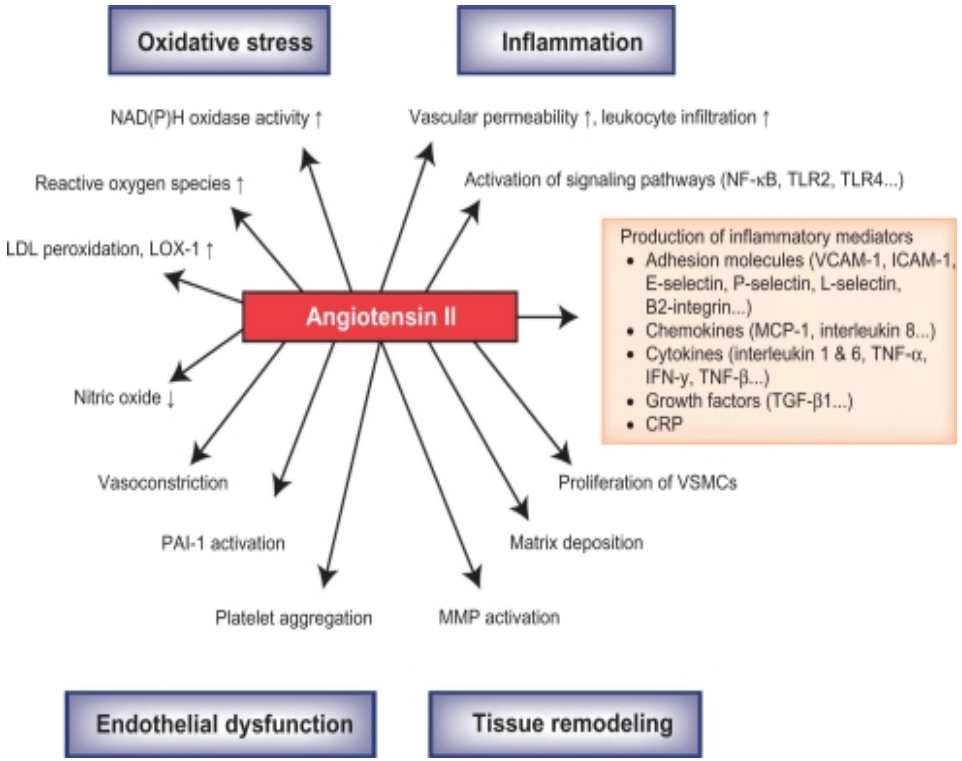
A 68 years old man with long lasting diabetes was referred
because of **decreasing eGFR**.
He is taking Atorvastatin, Metformin, Gliclazide, sitagliptin and valsartan 320mg.
BP= 130/80 BMI= 32
HbA1C= 8 LDL= 60 Na=139 K=5.2
Serum CR=2.4 **eGFR= 38CC/min eGFR=45CC/min (last year)** Urine Alb/Urine Cr= 800mg/g
CKD stage: **G3b, A3**

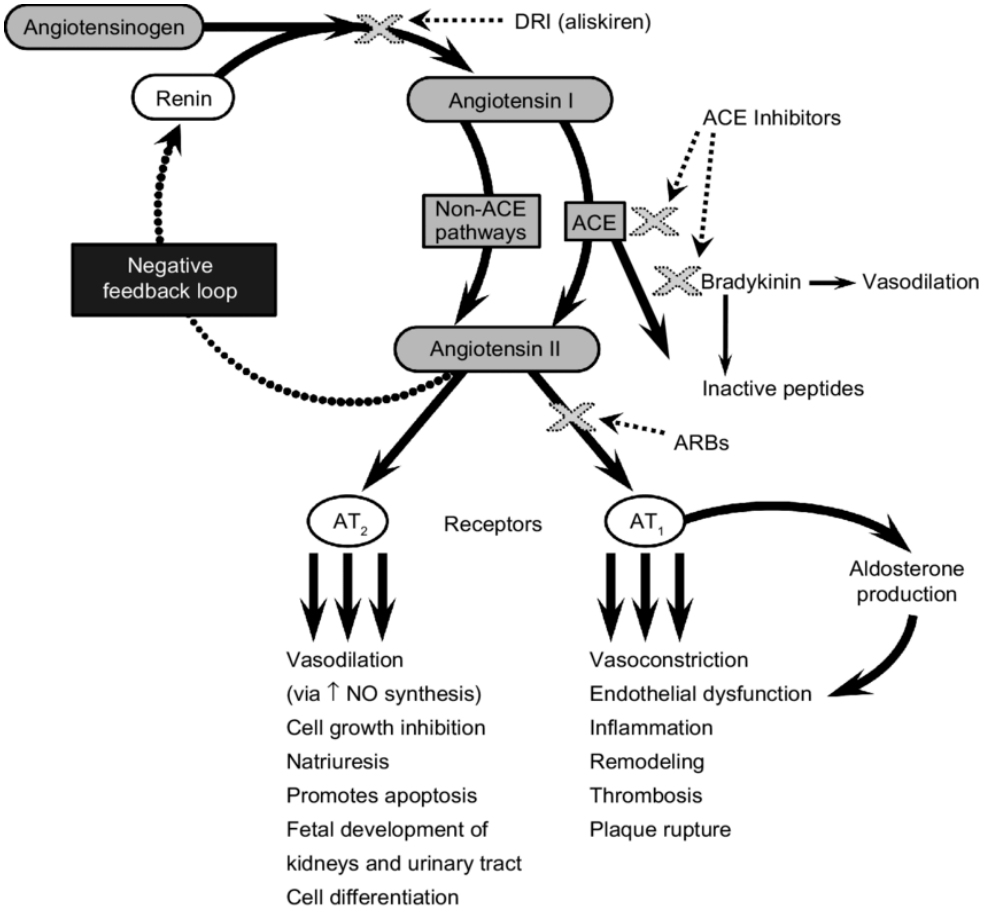
What do you recommend?
Add MRB?
Add SGLT2i ?

Does SGLT2i improve kidney outcome at this stage?

Dapagliflozin 10 mg was started. 2 weeks later, GFR decreased to 32 CC/min.
What is your suggestion now?
Dapagliflozin was continued.
6 months later, GFR was 40 CC/min and A/C ratio was 500m/gr


Prorenin
Renin
Angiotensinogen
Angiotensin I
ACE Chymase
Angiotensin
Classical effects
Na+ and fluid retention
K+ loss
Rise in BP
Haemodynamic effects
Vasoconstriction
Ang II receptor
Catecholamine mediated constrictor effects of aldosterone
Non-haemodynamic effects
Endothelial dysfunction
Low grade inflammation
Glomerular sclerosis
Tubular damage
PROGRESSION OF RENAL DISEASE


Oxidative stress
Inflammation
NAD(P)H oxidase activity ↑
Vascular permeability ↑, leukocyte infiltration ↑
Reactive oxygen species ↑
Activation of signaling pathways (NF-κB, TLR2, TLR4...)
LDL peroxidation, LOX-1 ↑
Angiotensin II
Production of inflammatory mediators
Adhesion molecules (VCAM-1, ICAM-1, E-selectin, P-selectin, L-selectin, B2-integrin...)
Chemokines (MCP-1, interleukin 8...)
Cytokines (interleukin 1 & 6, TNF-α, IFN-γ, TNF-β...)
Growth factors (TGF-β1...)
CRP
Nitric oxide ↓
Vasoconstriction
Proliferation of VSMCs
PAI-1 activation
Matrix deposition
Platelet aggregation
MMP activation
Endothelial dysfunction
Tissue remodeling


Angiotensinogen
DRI (aliskiren)
Renin
Angiotensin I
ACE Inhibitors
Non-ACE pathways
ACE
Negative feedback loop
Bradykinin
Vasodilation
Angiotensin II
Inactive peptides
ARBs
AT2
Receptors
AT1
Aldosterone production
Vasodilation
(via ↑ NO synthesis)
Cell growth inhibition
Natriuresis
Promotes apoptosis
Fetal development of kidneys and urinary tract
Cell differentiation
Vasoconstriction
Endothelial dysfunction
Inflammation
Remodeling
Thrombosis
Plaque rupture

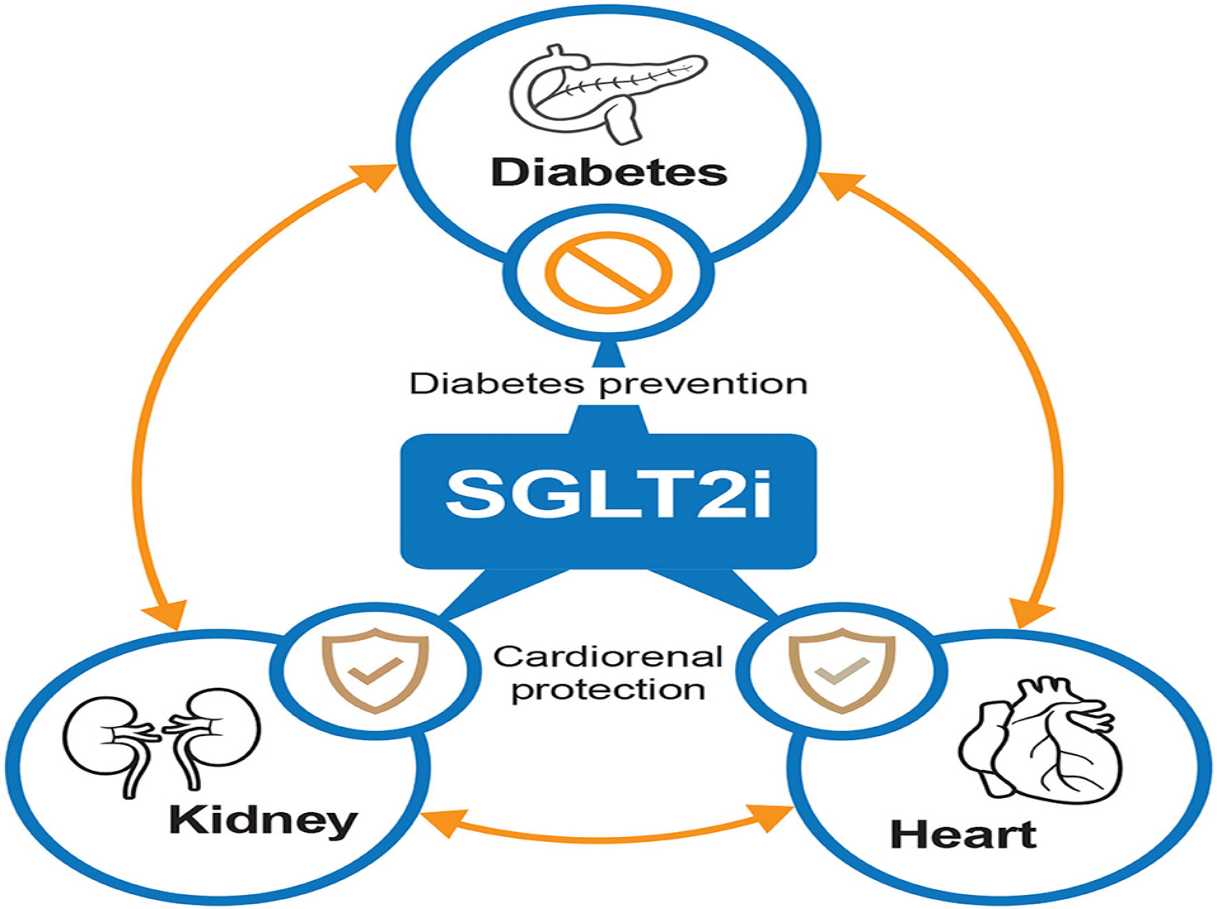
The progression of kidney disease has decreased with advances in blood pressure (BP) control and renin-angiotensin- aldosterone system (RAAS) blockade

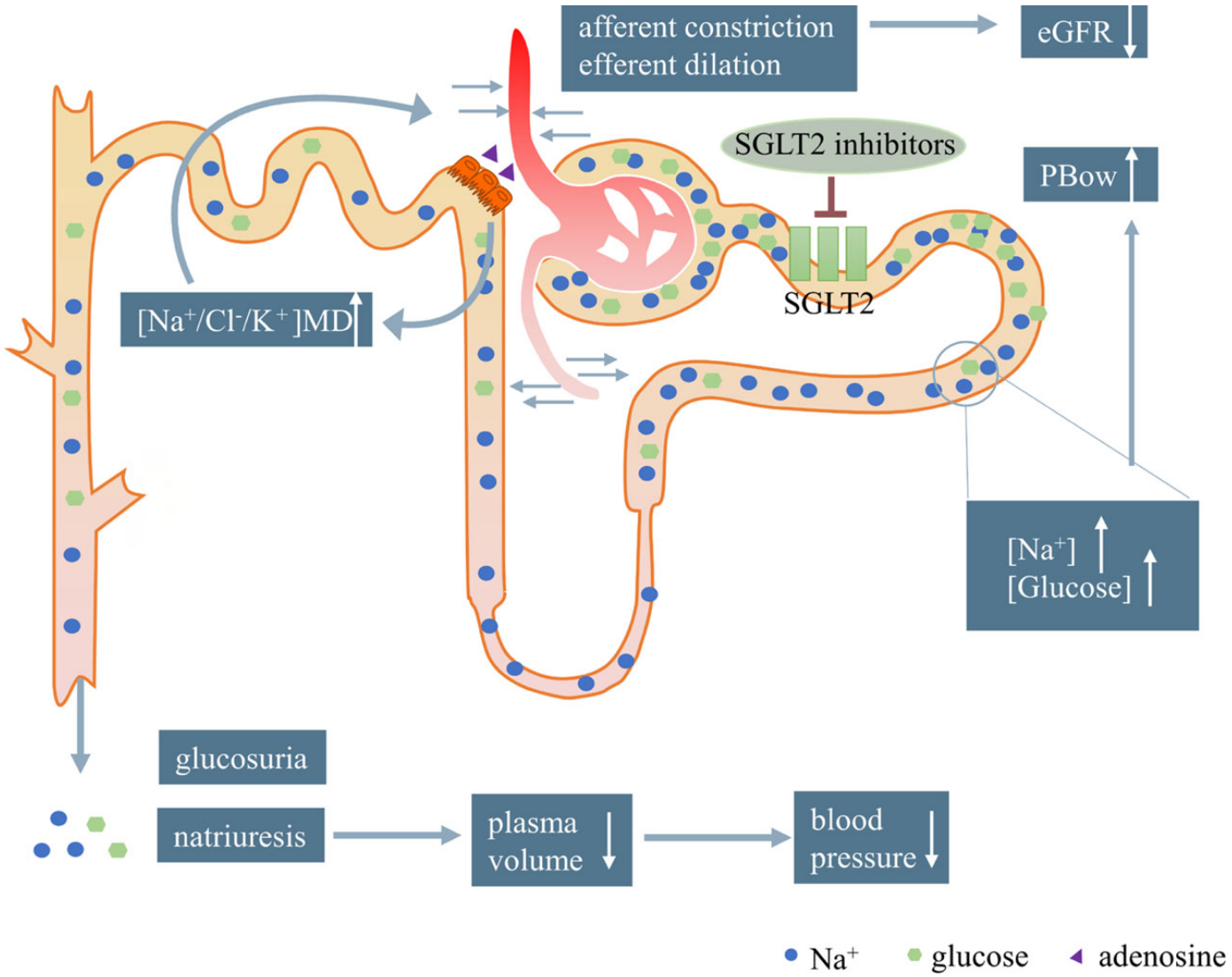
But, It is not enough

Reno-protective efficacy of RAAS blockers remains unsatisfactory in patients with DKD

(They decrease CKD progression by 20-30%)


2015
BREAKING NEWS


Diabetes
Diabetes prevention
SGLT2i
Cardiorenal protection
Kidney
Heart


afferent constriction
efferent dilation
eGFR
SGLT2 inhibitors
PBow
SGLT2
[Na+/Cl-/K+]MD
[Na+]
[Glucose]
glucosuria
natriuresis
plasma volume
blood pressure
Na+
glucose
adenosine

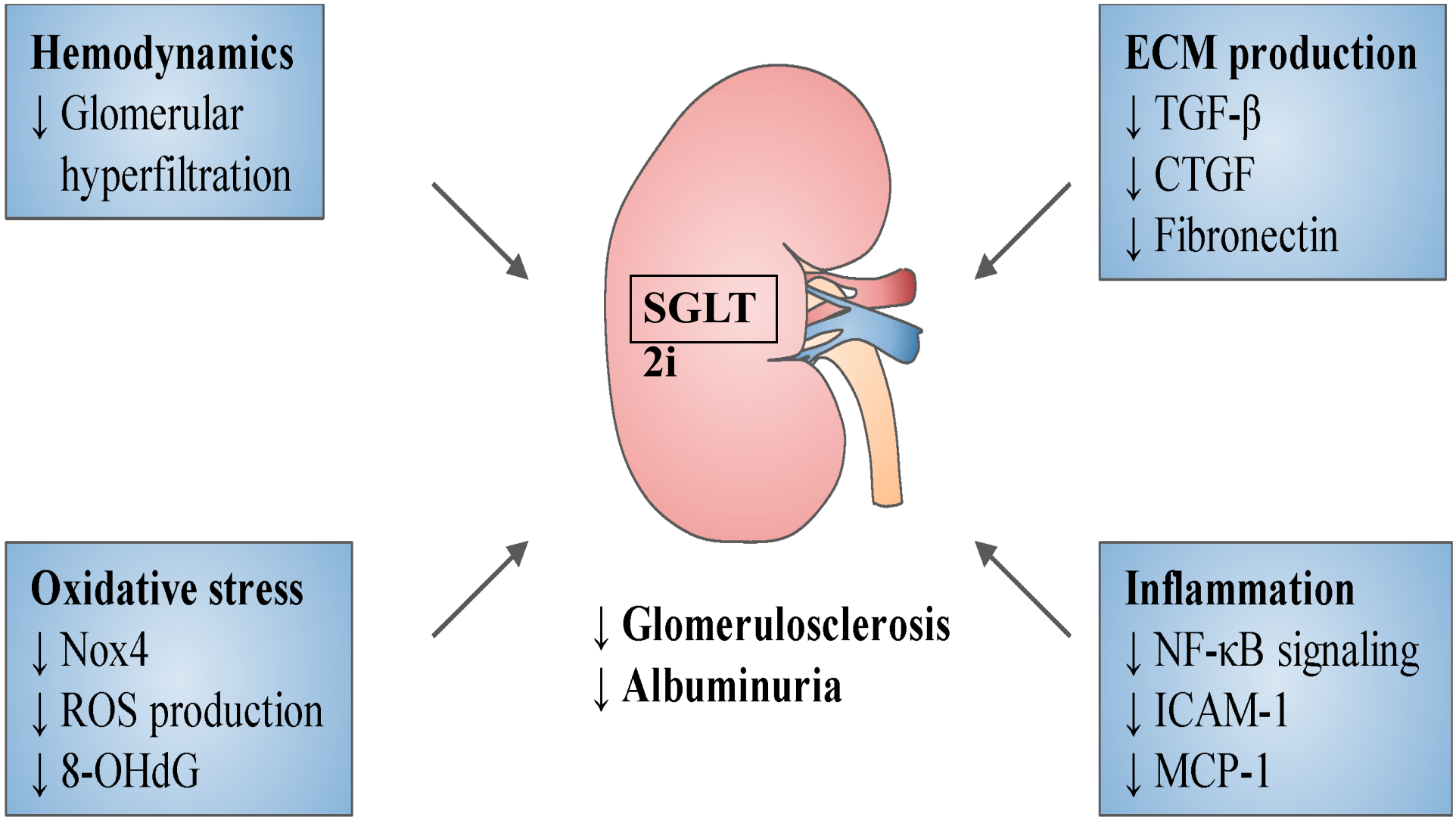
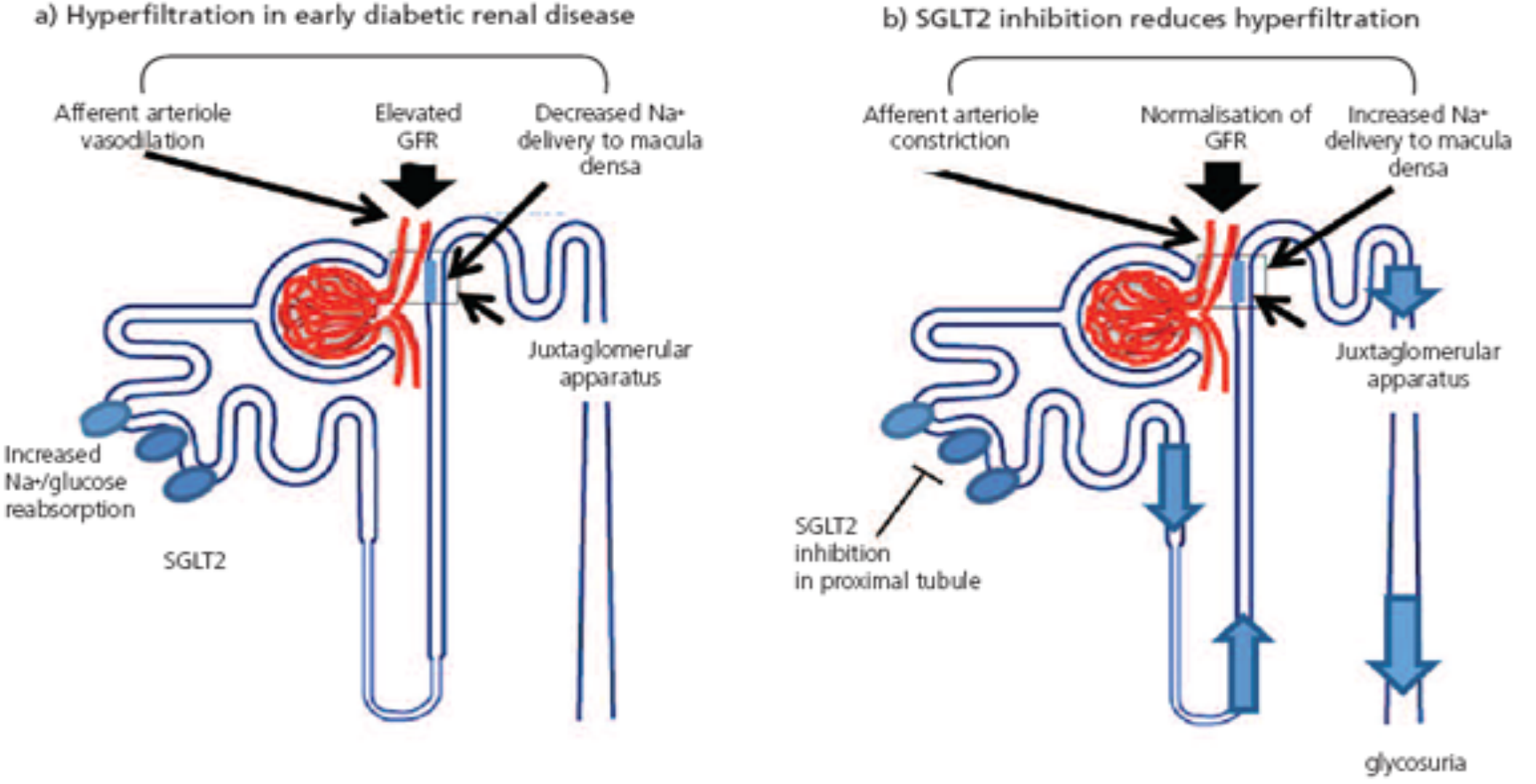
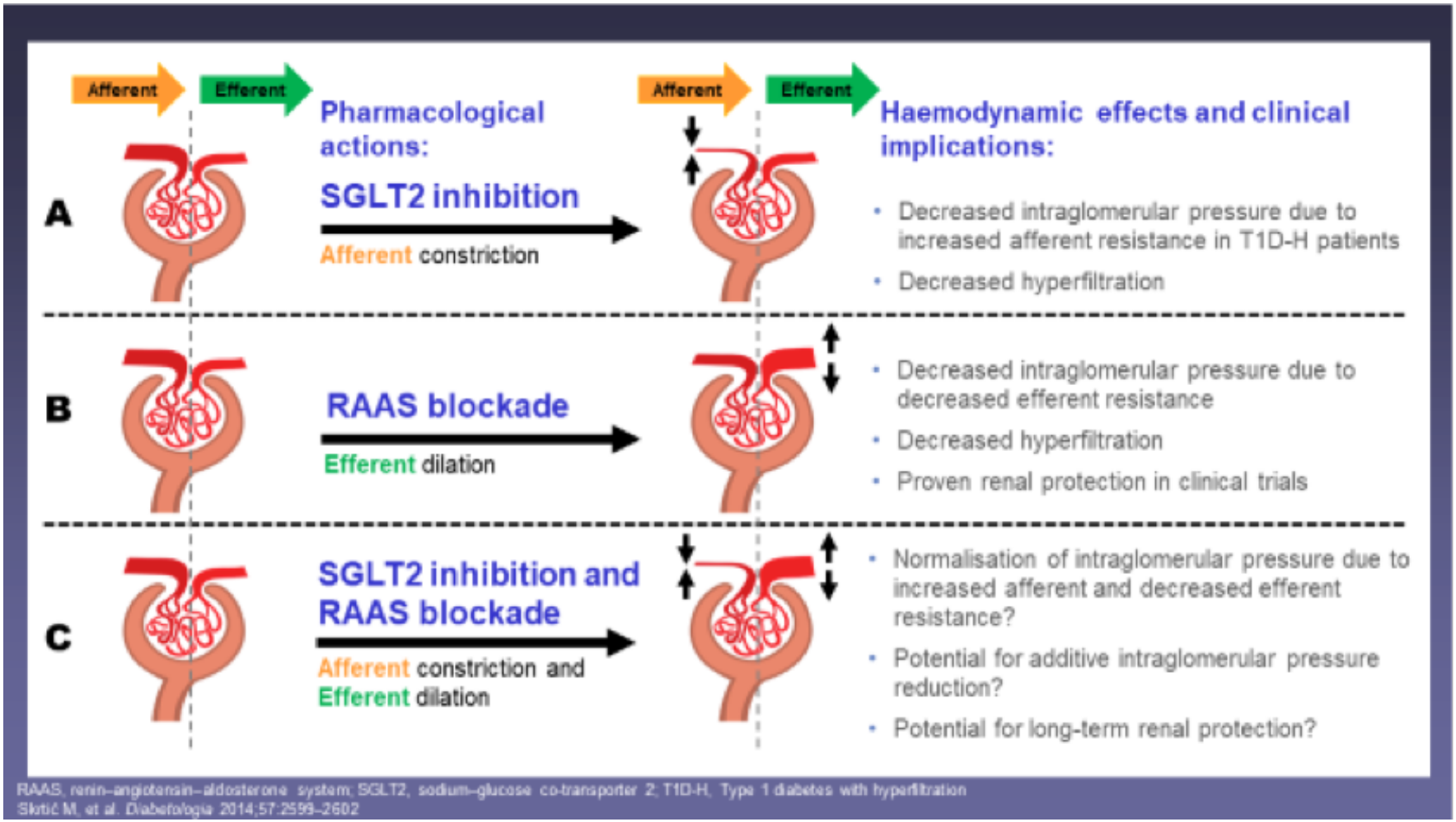

Hemodynamics
↓ Glomerular hyperfiltration
ECM production
↓ TGF-β
↓ CTGF
↓ Fibronectin
SGLT 2i
Oxidative stress
↓ Nox4
↓ ROS production
↓ 8-OHdG
↓ Glomerulosclerosis
↓ Albuminuria
Inflammation
↓ NF-κB signaling
↓ ICAM-1
↓ MCP-1

Figure 3. Arteriolar tone, Na^+/glucose reabsorption and tubuloglomerular feedback (TGF) in early diabetic renal disease (a) and effects of SGLT2 inhibition (b)





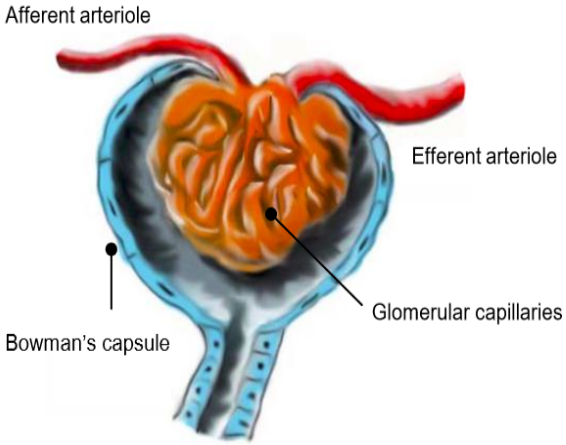
RAAS, renin–angiotensin–aldosterone system; SGLT2, sodium–glucose co-transporter 2; T1D-H, Type 1 diabetes with hyperfiltration
Skrtić M, et al. *Diabetologia* 2014;57:2599–2602

SGLT2 inhibition and RAAS blockade both reduce glomerular pressure by complimentary mechanisms

SGLT2 inhibitors

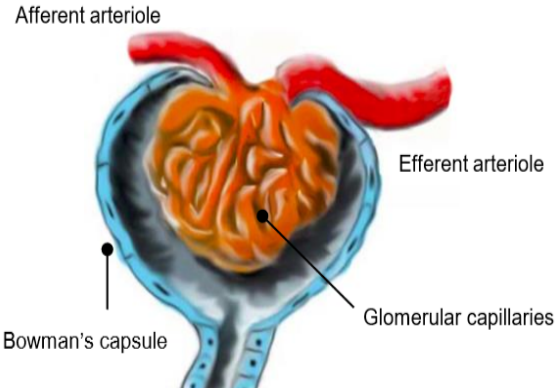
Afferent vasoconstriction

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



RAAS blockade

Efferent vasodilation

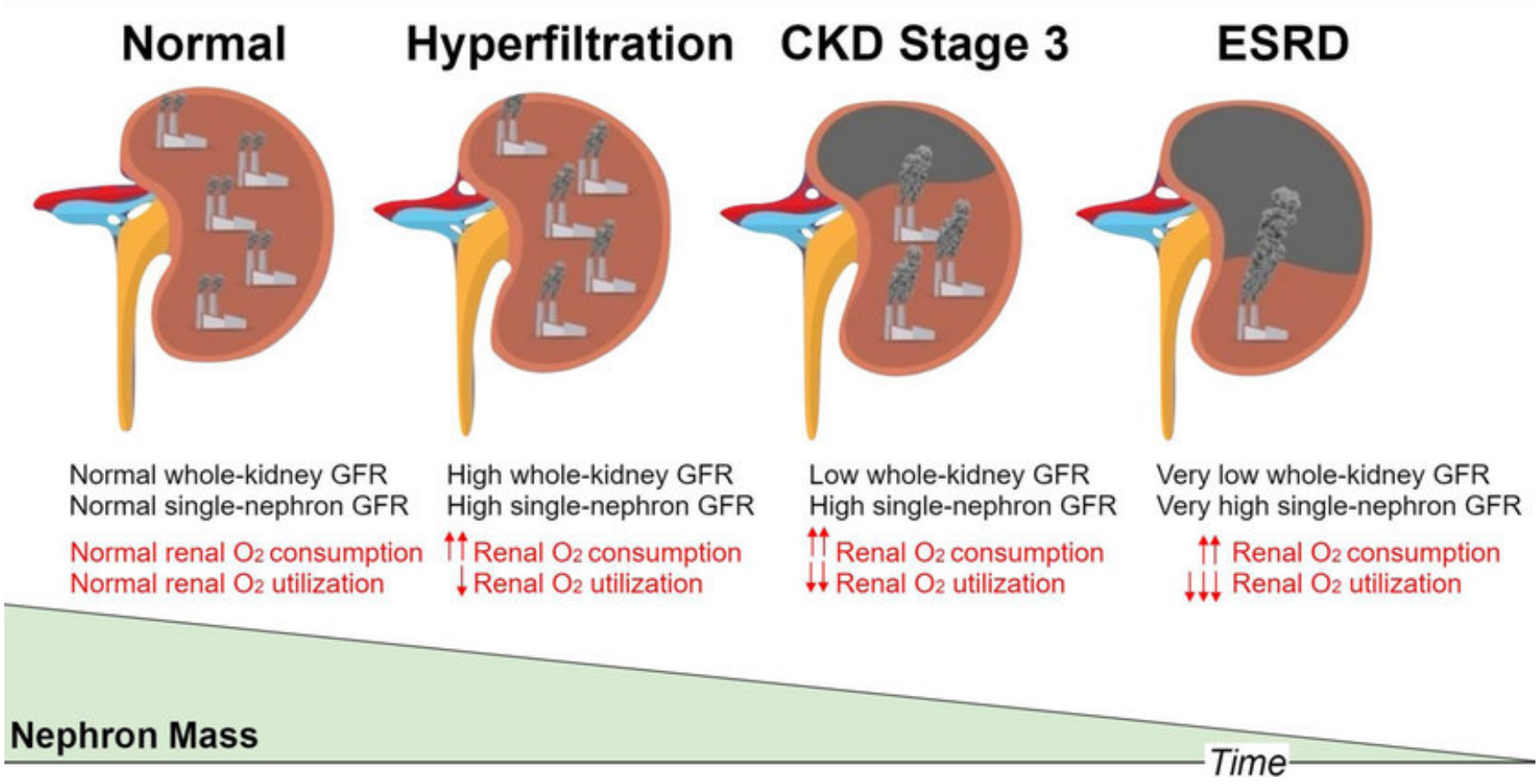


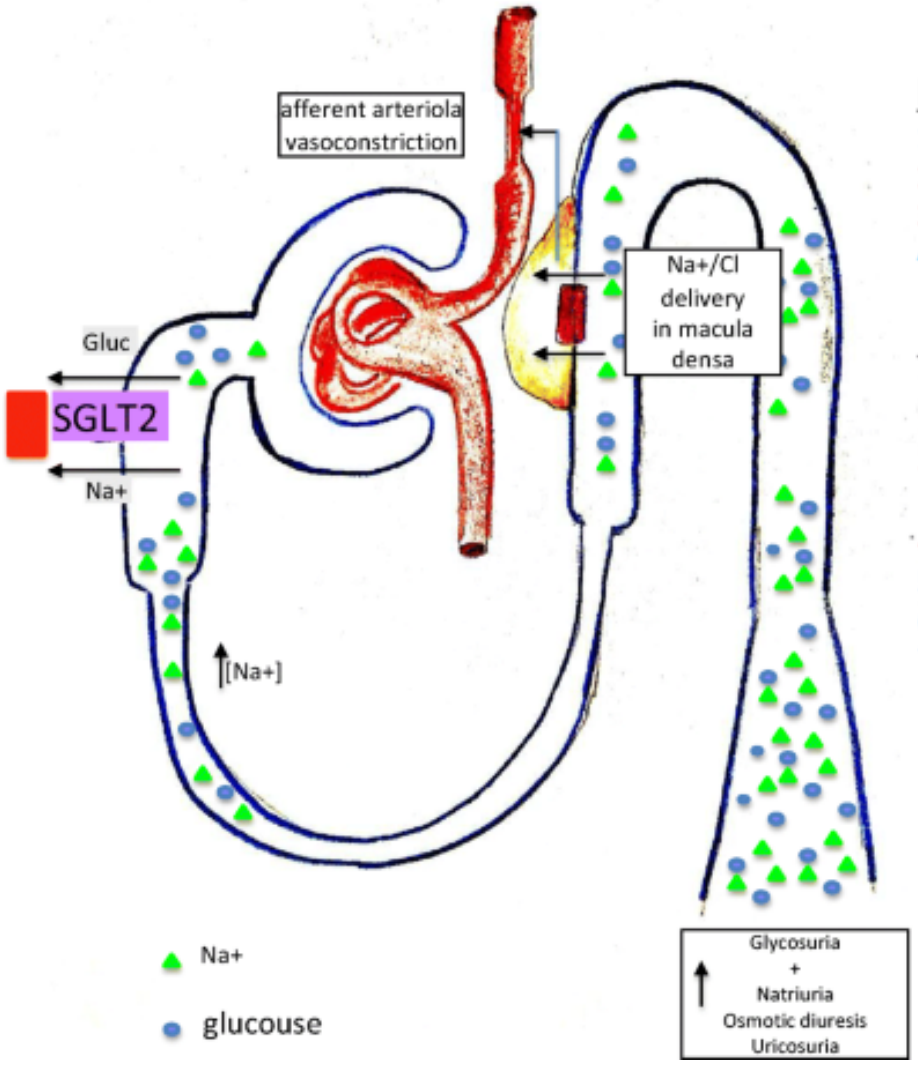
CLINICAL IMPLICATIONS

- Decreased glomerular pressure
- Reduction in albuminuria

- Decreased glomerular pressure
- Reduction in albuminuria

Hyper-filtration & CKD





Direct Renal Effects

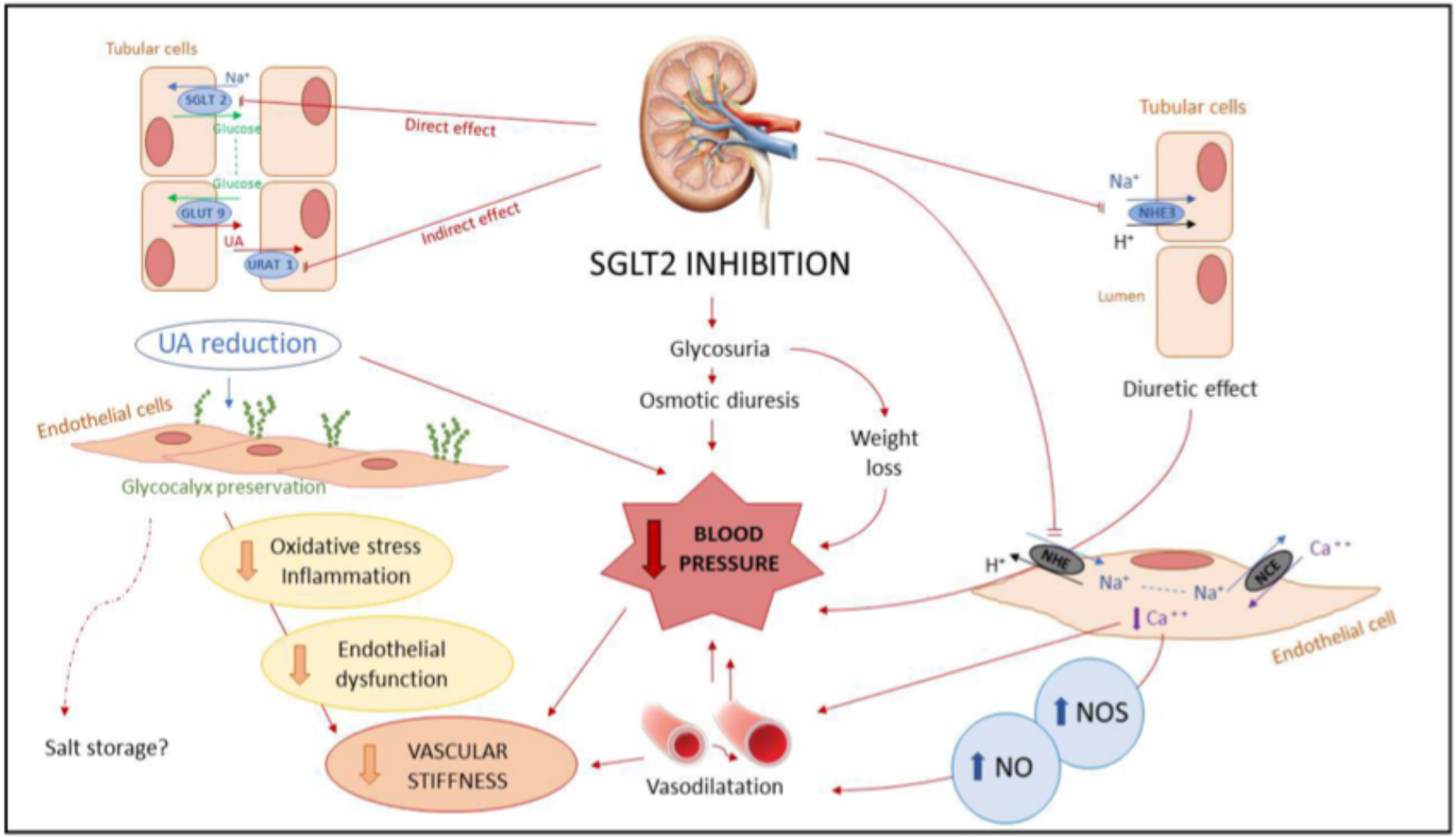
1. Osmotic diuresis—> intestitial pressure
2. Reduction of oxigen consumption
3. Reduction of oxidative stress and inflammation
4. Reduction of intragolmerular ipertension

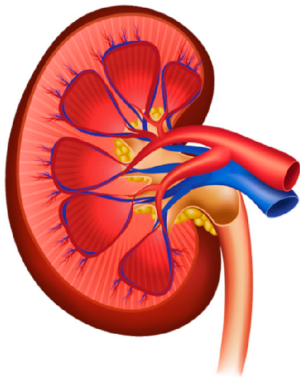
Indirect Renal Effects

1. Reduction of blood pressure
2. Reduction of body fat and body weight
3. Reduction of oxidative stress and inflammation
4. Uricosuria
5. Reduction of plasma volume
6. Activation of AT2 type 2
7. Sympathetic system modulation

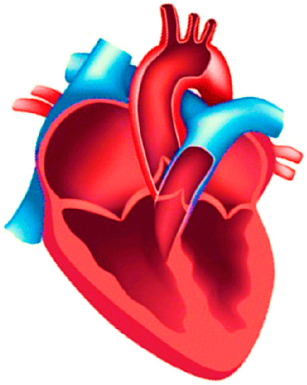
Mostly due to glycosuria

Mostly due to natriuresis


Tubular cells
Na+
SGLT 2
Glucose
Glucose
GLUT 9
UA
URAT 1
Direct effect
Indirect effect
SGLT2 INHIBITION
Tubular cells
Na+
NHE3
H+
Lumen
Diuretic effect
UA reduction
Endothelial cells
Glycocalyx preservation
Glycosuria
Osmotic diuresis
Weight loss
BLOOD PRESSURE
Oxidative stress Inflammation
Endothelial dysfunction
VASCULAR STIFFNESS
Salt storage?
Vasodilatation
H+
NHE
Na+
Na+
NCE
Ca++
Ca++
Endothelial cell
NOS
NO



SGLT2 inhibitors and cardiorenal protection



KIDNEY		HEART	
increase	Diuresis, natriuresis and glycosuria	Preload and afterload	decrease
decrease	Hyperfiltration	Myocardial contractility	increase
increase	Glomerular afferent arteriole vasoconstriction and efferent arteriole vasodilatation	Endothelial inflammation and oxidative stress	decrease
decrease	Tubular energy consumption, apoptosis, oxidative stress, tubulointerstitial inflammation and fibrosis	FFA oxydation, ketogenesis, mitocondrial function, cardiomyocytes energy efficiency	increase
increase	HIF-2α, erythropoiesis and renal oxygenation	Arrhythmias, myocardial hypertrophy, HF progression	decrease
↓ CHRONIC KIDNEY DISEASE PROGRESSION		CARDIAC AND CORONARY ENDOTHELIAL FUNCTION ↑	

KDIGO provided recommendations on SGLT2 inhibitors and nonsteroidal MRAs in patients with diabetes and CKD

Update: KDIGO recommends SGLT2 inhibitors for patients with type 2 diabetes, CKD, and eGFR ≥20 mL/min/1.73 m² (Grade 1A§)

Key evidence|| for SGLT2 inhibitors vs. placebo

- All-cause mortality: 8.0% vs. 9.0%; HR, 0.88 (95% CI, 0.82 to 0.95) (17 RCTs, *n* = 31 523)
- CV mortality: 6.3% vs. 7.0%; HR, 0.90 (CI, 0.83 to 0.98) (12 RCTs, *n* = 46 442)
- 3-point MACE: 12% vs. 13%; HR, 0.88 (CI, 0.82 to 0.95) (10 RCTs, *n* = 40 866)
- Composite kidney outcome: 6.3% vs. 10%; HR, 0.60 (CI, 0.52 to 0.70) (8 RCTs, *n* = 34 788)
- Amputation: 3.5% vs. 2.9%; HR, 1.22 (CI, 0.97 to 1.53) (7 RCTs, *n* = 27 954)

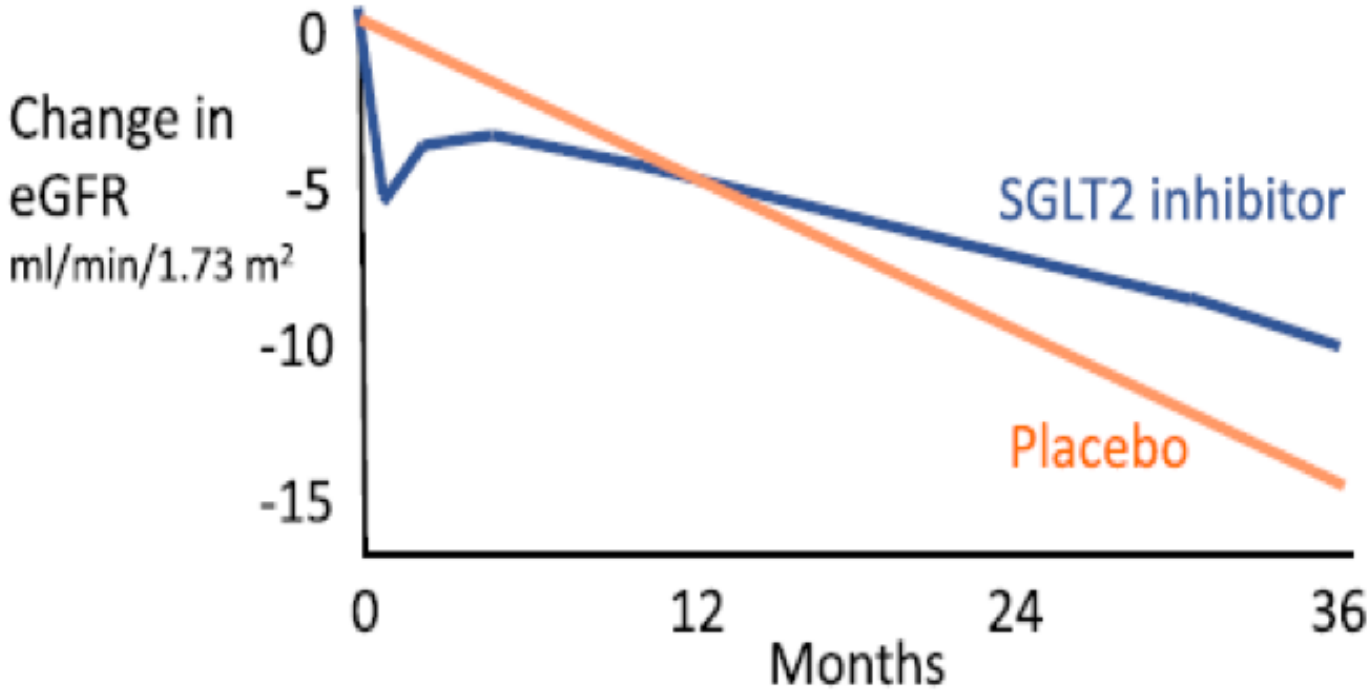
Start MRA if K< 5
Synergistic effects of nsMRA and SGLT2i

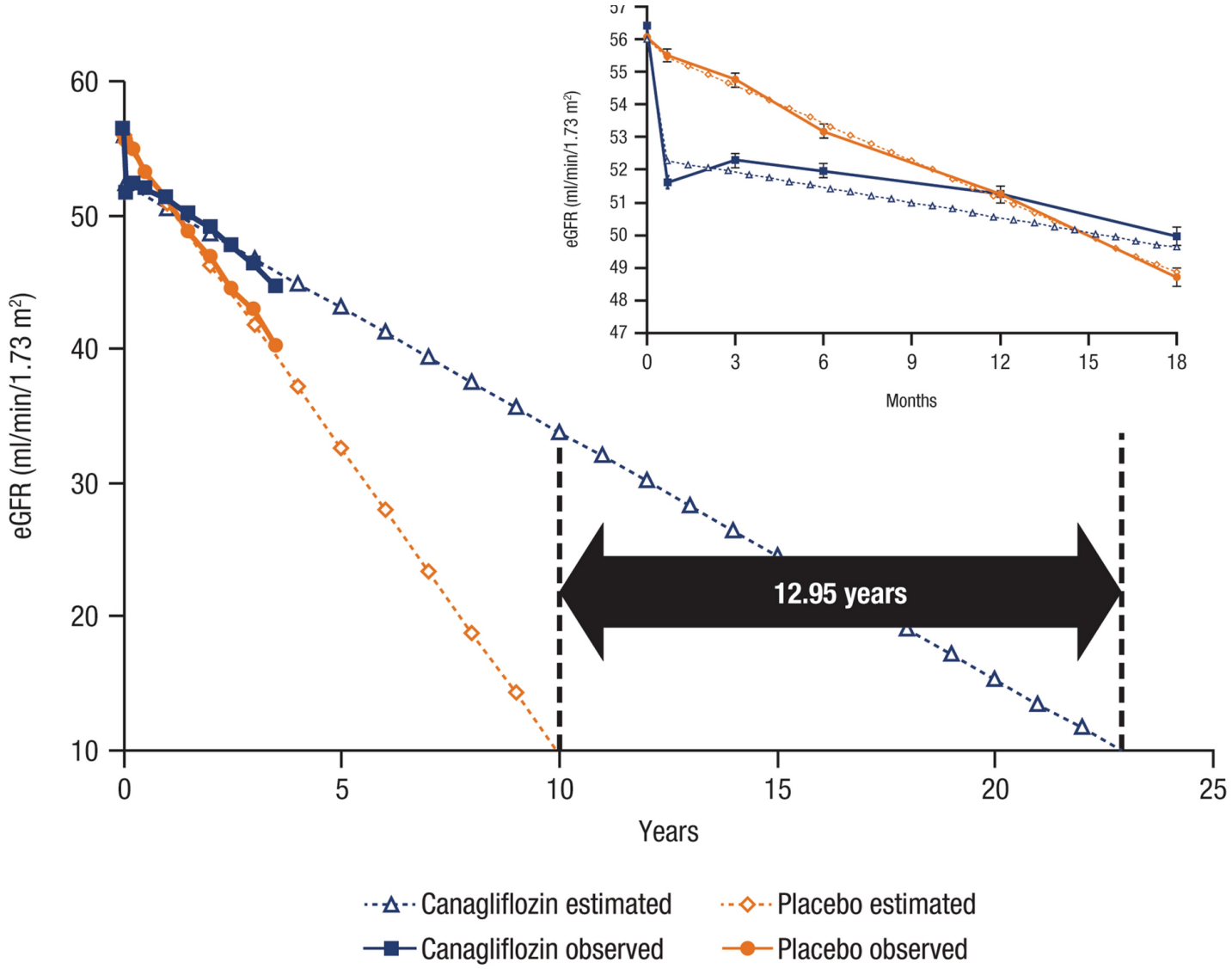
A 68 years old man with long lasting diabetes was referred
because of **decreasing eGFR**.
He is taking Atorvastatin, Metformin, Gliclazide, sitagliptin and valsartan 320mg.
BP= 130/80 BMI= 32
HbA1C= 8 LDL= 60 Na=139 K=5.2
Serum CR=2.4 **eGFR= 38CC/min eGFR=45CC/min (last year)** Urine Alb/Urine Cr= 800mg/g
CKD stage: **G3b, A3**

What do you recommend?
Add MRB?
Add SGLT2i ?

Does **SGLT2i** improve kidney outcome at this stage?

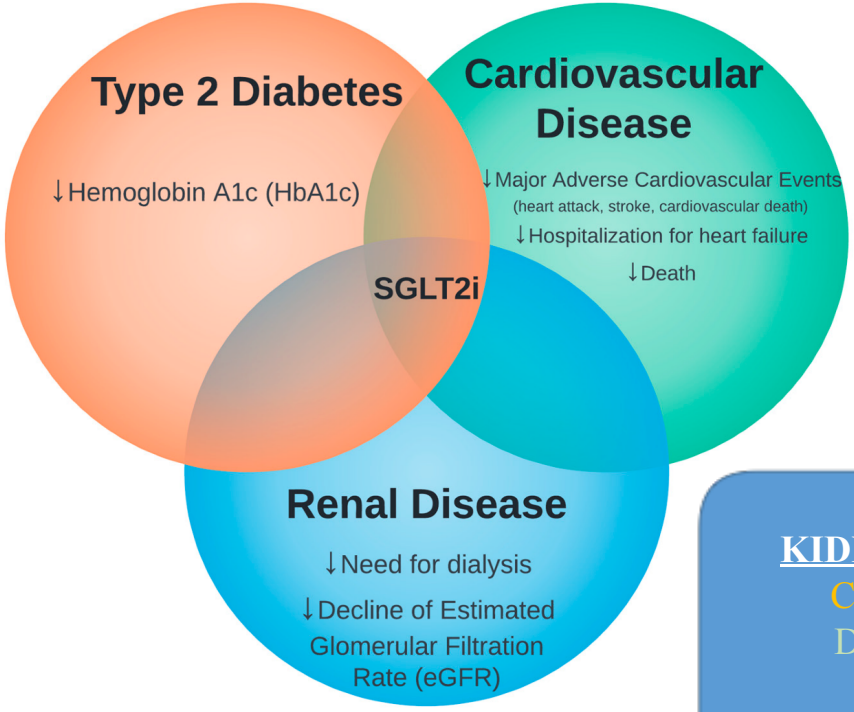
Dapagliflozin 10 mg was started. 2 weeks later, GFR decreased to 32 CC/min.
What is your suggestion now?
Dapagliflozin was continued.
6 months later, GFR was 40 CC/min and A/C ratio was 500m/gr.


Change in
eGFR
ml/min/1.73 m²
0
-5
-10
-15
SGLT2 inhibitor
Placebo
0
12
24
36
Months


eGFR (ml/min/1.73 m²)
60
50
40
30
20
10
0
5
10
15
20
25
Years
12.95 years
eGFR (ml/min/1.73 m²)
56
55
54
53
52
51
50
49
48
47
0
3
6
9
12
15
18
Months
Canagliflozin estimated
Placebo estimated
Canagliflozin observed
Placebo observed

3 types of SGLT2i trials

CVO TRIALS
EMPA-REG
CANVAS
DECLARE
VERTIS-CV



HF TRIALS
DAPA-HF
DELIVER
SOLOIST-WHF
EMPEROR- Reduced
EMPEROR-Preserved

Empa
Dapa
Cana
Ertu
Sota

KIDNEY TRIALS
CREDENCE
DAPA-CKD
SCORED
EMPA-KIDNEY

SGLT2 Inhibitors and Renal Outcomes : A comparison of RCTs

Infographic by-: Priti Meena, M.D @Priti899

CREDENCE

Double-blind, Placebo-controlled,
Multicentric RCT
(N=4401)

Inclusion:
Type 2 DM
eGFR: ≥30-90
and UACR: >300-≤5000 mg/g

Canagliflozin VS placebo

2019

Median follow-up: 2.62 yrs

Renal-specific composite of ESKD, 2* S. Cr or death from renal causes:
HR 0.66; (0.53 to 0.81)

CV death, MI, or stroke:
HR 0.80 (0.67 -0.95)
Hospitalization for heart failure:
HR 0.61; (0.47 to 0.80)

DAPA-CKD

Double-blind, Placebo-controlled,
Multicentric RCT
(N=4304)

Inclusion:
eGFR: ≥25-75 and
UACR: ≥200-≤5000 mg/g

With or without DM

Dapagliflozin VS placebo

2020

Median follow up : 2.4 yrs

Composite of sustained decline in eGFR of at least 50%, ESKD, or death from renal causes:
HR 0.56; (0.45 to 0.68)

Composite of death from CV causes or hospitalization for heart failure:
HR 0.71; (0.55 to 0.92)

EMPA-KIDNEY

Double-blind, Placebo-controlled,
Multicentric parallel group RCT
(N=6609)

Inclusion:
eGFR: ≥20-45 or
eGFR ≥45 to <90 with UACR ≥200 mg/g

With or without DM

Empagliflozin VS placebo

2022

Median follow-up: 2 yrs

Progression of kidney disease or death from CV causes:
HR 0.72; (0.64 to 0.82)

Rate of hospitalization from any cause:
HR 0.86; (0.78 to 0.95)

CV: cardiovascular, ESKD: End-stage kidney diseases, eGFR: estimated glomerular filtration rate in ml per minute per 1.73 m^2 HR: Hazard ratio, MI: Myocardial infarction, RCT: Randomized Controlled Trials, S.Cr: Serum creatinine, SGLT2: Sodium-glucose Cotransporter-2 (SGLT2) Inhibitors, UACR: urinary albumin-to-creatinine ratio

Does Dapagliflozin compared to placebo reduce the risk of kidney failure and CV events in CKD patients with and without T2DM?

DAPA-CKD

21 Countries
286 Centers

≥ 18 yo

eGFR ≥ 25 to ≤ 75ml/min

UACR ≥ 200 to ≤ 5000mg/g

Max tolerated dose of ACEi/ARB

With and without T2DM

Mean Age 62y, 67% ♂
eGFR 43ml/min
UACR 949mg/g
ACEi/ARB 97%
With T2DM 67.5%

MEAN FOLLOW-UP: 2.4 YEARS

10 mg
DAPAGLIFLOZIN
+STANDARD CARE
N=2152

N=4304

P
PLACEBO
+STANDARD CARE
N=2152

Sustained ≥ 50% decline in GFR, ESKD, Renal or CV Death	Sustained ≥ 50% decline in GFR, ESKD, Renal Death	CV Death or hHF	All-cause Mortality
9.2%	6.6%	4.6%	4.7%
HR 0.61 (95% CI 0.51-0.72) p<0.001 NNT=19	HR 0.56 (0.45-0.68) p<0.001	HR 0.71 (0.55-0.92) p=0.009	HR 0.69 (0.53-0.88) p=0.004
14.5%	11.3%	6.4%	6.8%

Benefit of Dapagliflozin on primary end-point was consistent in patients with and without T2DM
% of patients who discontinued the drug or who experienced SAE was similar in both groups
DKA, 2 in placebo group vs none in Dapagliflozin group
No DKA or severe hypoglycemia in patients without T2DM

CONCLUSION: Dapagliflozin compared to placebo significantly reduced the risk of kidney failure, CV death or hospitalization for HF and all-cause mortality in patients with CKD with and without T2DM. Dapagliflozin was well-tolerated, in keeping with its established safety profile.

DAPA-CKD
Heerspink et al (2020). Dapagliflozin in Patients with Chronic Kidney Disease. *New England Journal of Medicine.* September 24,2020
DOI: 10.1056/NEJMoa2024816
Visual Abstract by: Ana Naidas, MD

Empagliflozin in Patients with Chronic Kidney Disease (EMPA-KIDNEY)

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Multicenter
- 241 centers
- 8 countries

Double-blind

6,609 patients

- eGFR 20 – 45 ml/min/1.73m2
  Regardless of the level of albuminuria
- eGFR 45 – 90 ml/min/1.73m2
  UACR >200

Feb 2019 – Apr 2021

Pre-randomization phase 15wks of placebo

Empagliflozin 10mg/day

Placebo

CKD progression & death from CV causes	Hospitalizations from any cause	Hospitalization for HF or death from CV causes	Death from any cause
13.1%	24.8% per 100 patients/year	4.0%	4.5%
0.72 (0.64 – 0.82, P<0.001)	0.86 (0.78 – 0.95, P = 0.003)	0.84 (0.67 – 1.07, P = 0.15)	0.87 (0.70 – 1.08, P = 0.21)
16.9%	29.2% per 100 patients/year	4.6%	5.1%

Conclusion: among a wide range of patients with chronic kidney disease who were at risk for disease progression, empagliflozin therapy led to a lower risk of progression of kidney disease or death from cardiovascular causes than placebo.

Reference: EMPA-KIDNEY Collaborative Group. (2022). Empagliflozin in Patients with Chronic Kidney Disease. *New England Journal of Medicine.*

VA by Denisse Arellano, MD @deniise_am

Review

Can SGLT2 inhibitors solve the unmet therapeutic need in chronic kidney disease?

CKD is a global health problem with more than 850 million people affected worldwide

The number of patients receiving renal replacement therapy (dialysis or renal transplantation) is estimated to more than double from 2.618 [illegible] in 2010 to 5.439 million in 2030

The main focus of CKD treatment has become preserving renal function rather than replacing it through multifactorial therapy aimed at preventing end-stage renal kidney disease and CV events

SGLT2i provide renal and CV protection mainly

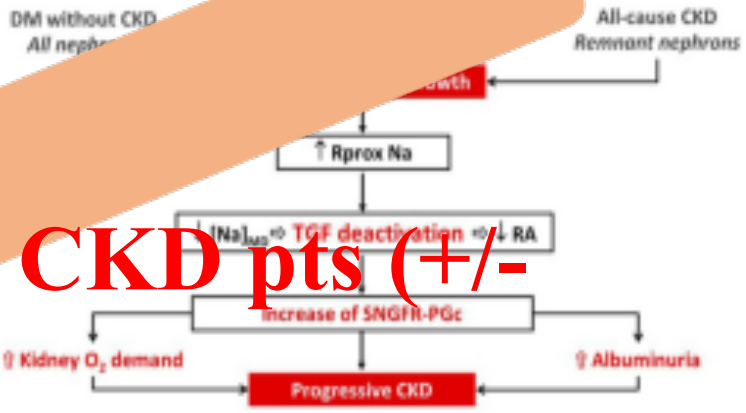
Reduce glomerular hypertension [illegible]

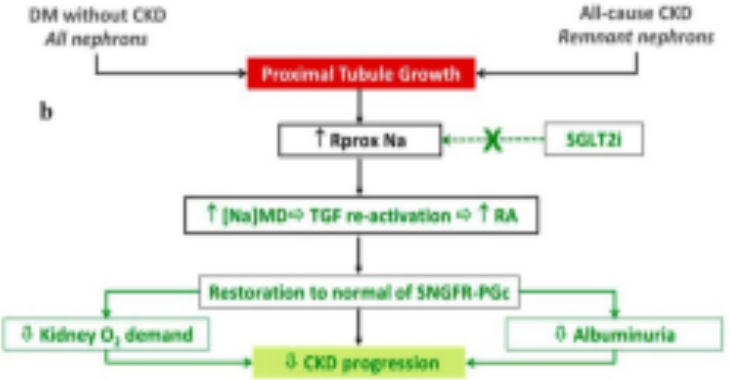
[illegible]uria, promote fatty acid oxidation and ketogenesis

De[illegible]gression of CKD

Reduced CV events

SGLT2i as std of care in CKD pts (+/- T2DM)





Conclusions

The use of SGLT2i will likely be extended to the whole CKD population as standard of therapy

SGLT2 inhibitors

Glycemic control
Hemodynamic control
Weight loss
Antioxidant
AntiInflammatory
Anti-fibrosis
Hypouricemic
RAS inhibition
Antinatriuretic