Cardiorenal Syndrome for the PCP

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OHSU NEPHROLOGY AND HYPERTENSION

Disclosures

none

8:00 Visit

65M, DC'd 2 days ago

5 day admission for CHF exacerbation

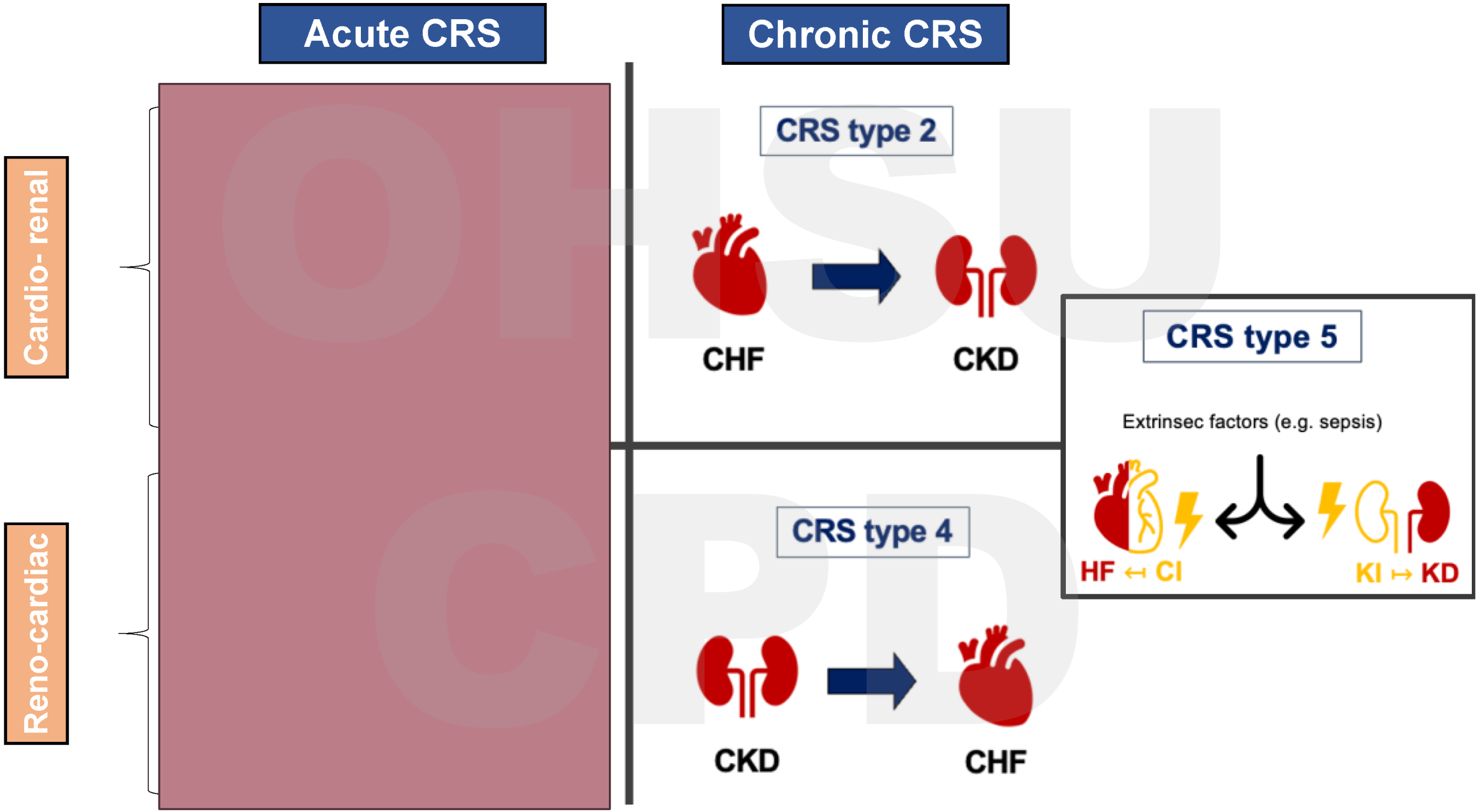
2nd admission this year

Echo: EF 30-->55% this year

Cr: 1.6, GFR 40

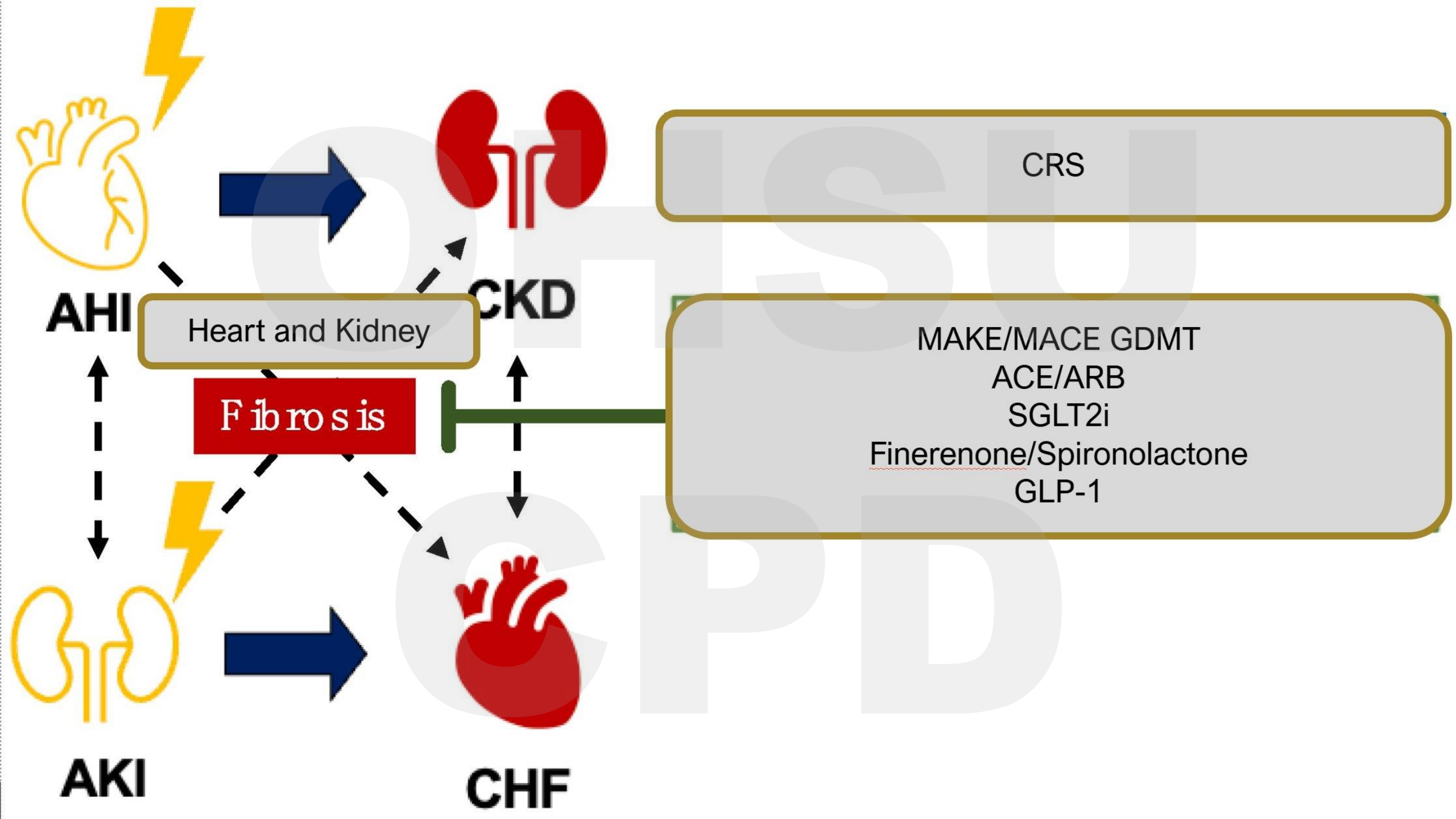
Coreg 6.25 BID
Lasix 40 BID
Losartan 25 BID
Empagliflozin 10 mg

What's the plan?
What's our long term goal?


Acute CRS
Chronic CRS
Cardio- renal
Reno-cardiac
CRS type 2
CHF
CKD
CRS type 5
Extrinsec factors (e.g. sepsis)
HF ↤ CI
KI ↦ KD
CRS type 4
CKD
CHF

Who are Cardio-Renal Patients

45F a1cs 12s for years	60M w/ metabolic syndrome	35 w/ sarcoidosis
Diabetic Kidney Disease	LHC: 3v dz EF 30%	CMRI shows cardiac infiltrate
5 g proteinuria, declining GFR	Declining GFR, lots of AKIs	Declining GFR, lots of AKIs
New HFrEF; Normal Coronaries NI cMRI	No significant proteinuria	Likely has Interstitial nephritis from sarcoidosis
Reno-Cardiac disease Type 4	Cardio-Renal disease Type 2	Cardio-Renal disease type 5 Not today's goal


CRS
AHI
CKD
Heart and Kidney
Fibrosis
MAKE/MACE GDMT
ACE/ARB
SGLT2i
Finerenone/Spironolactone
GLP-1
AKI
CHF

Treatment goal for CRS

eGFR

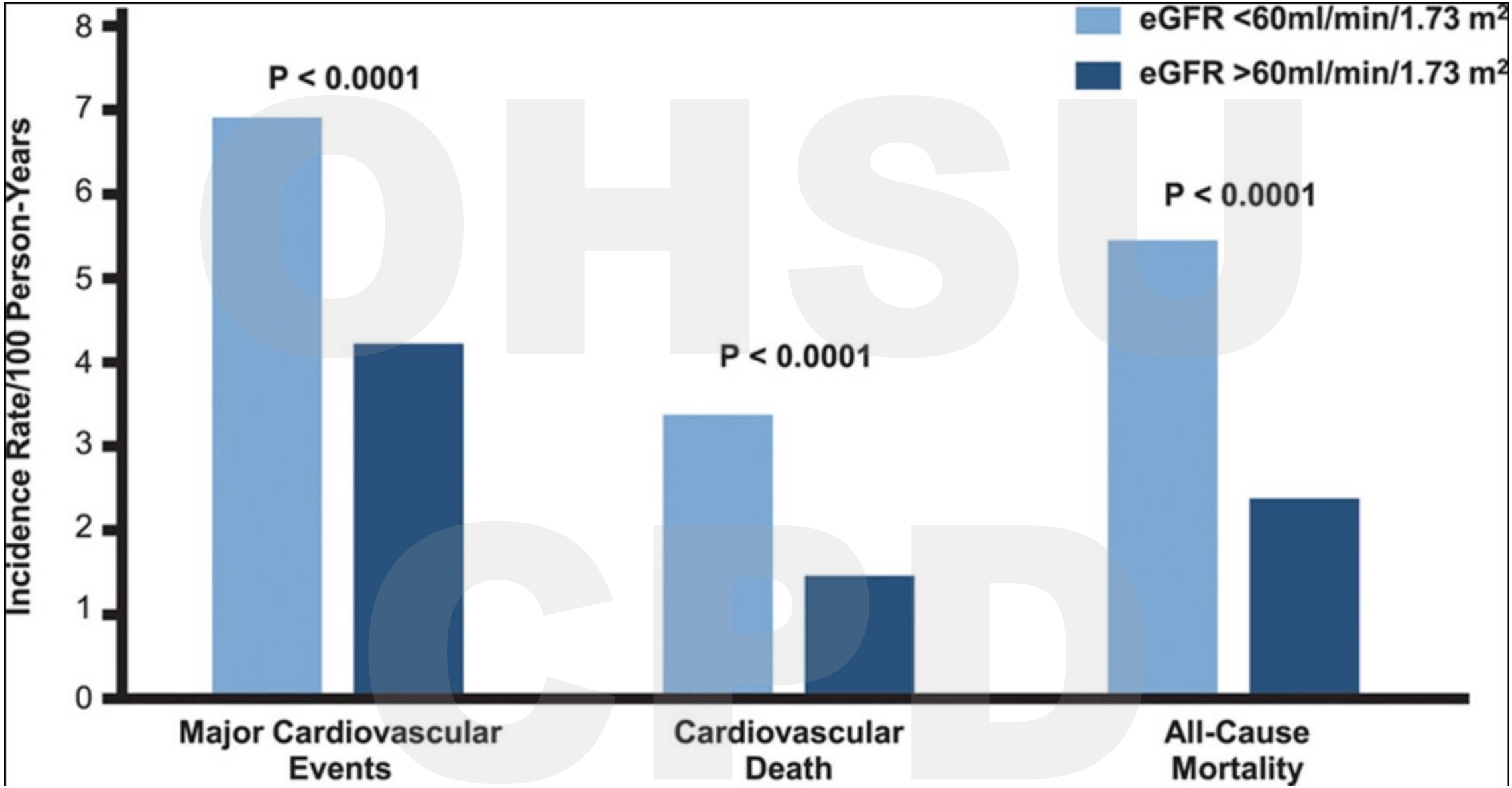
120
100
80
60
40
20
0

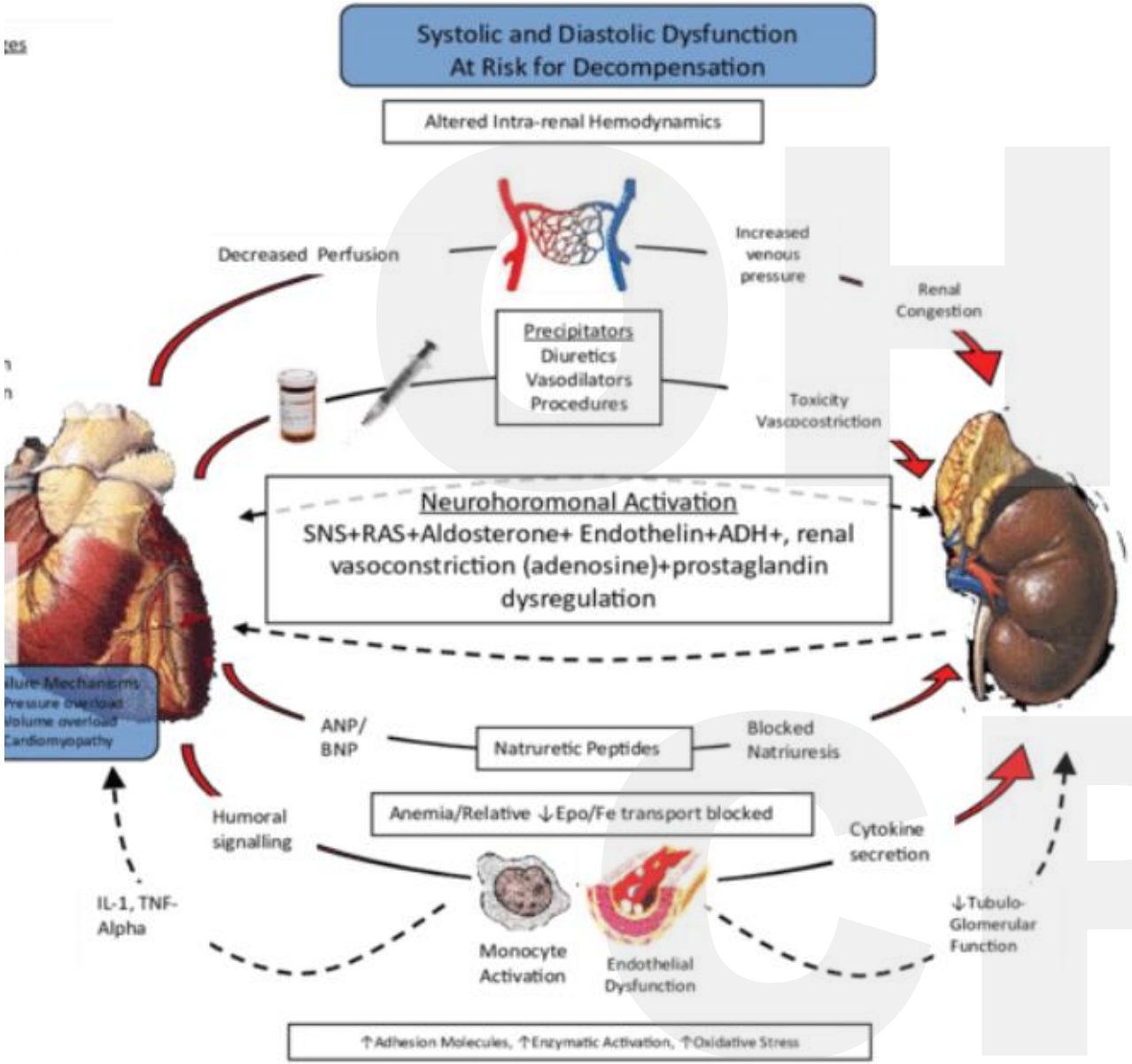
2 4 6 8 10 12 14 16 18 20 22 24 26 28 30

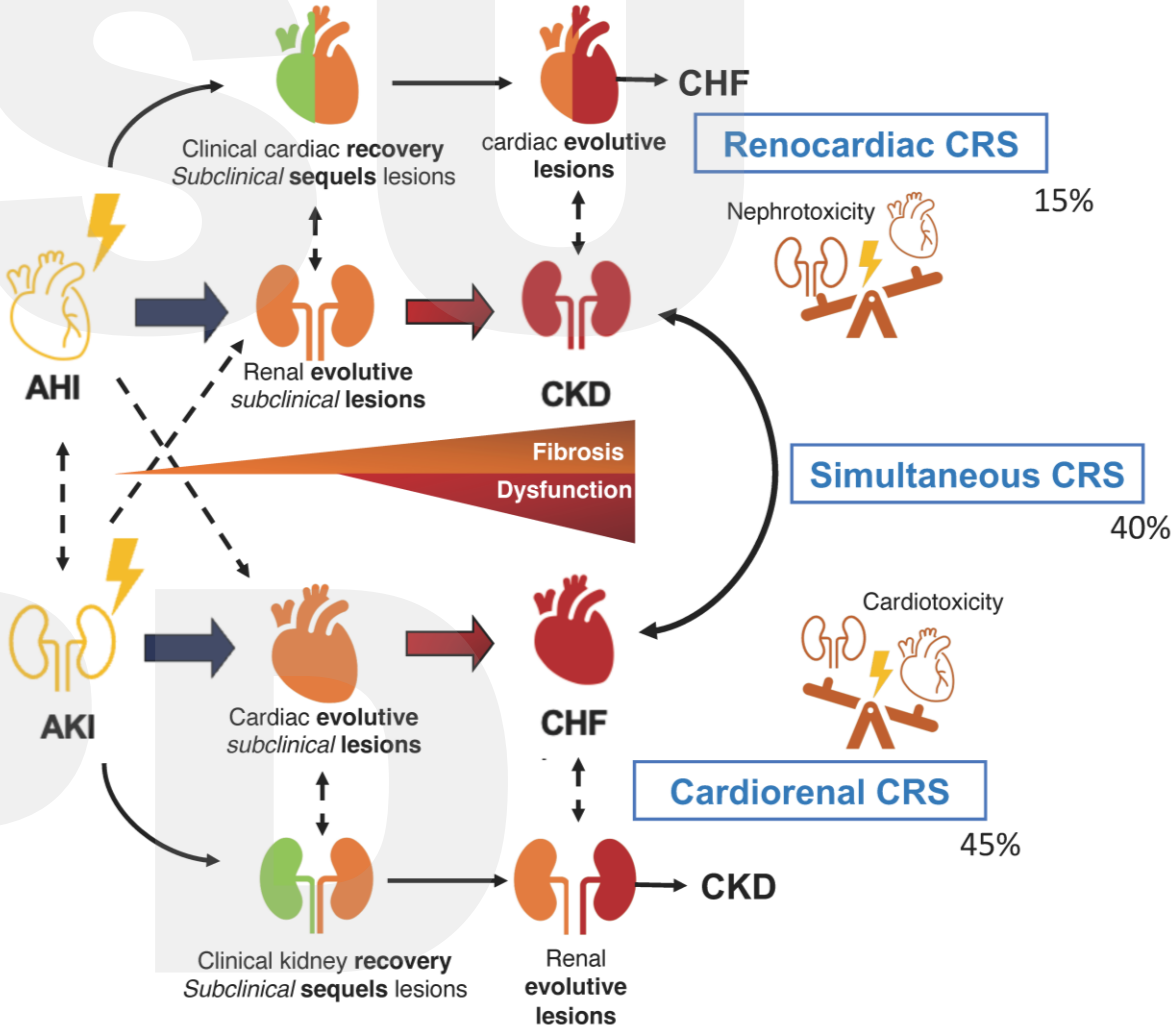
Months

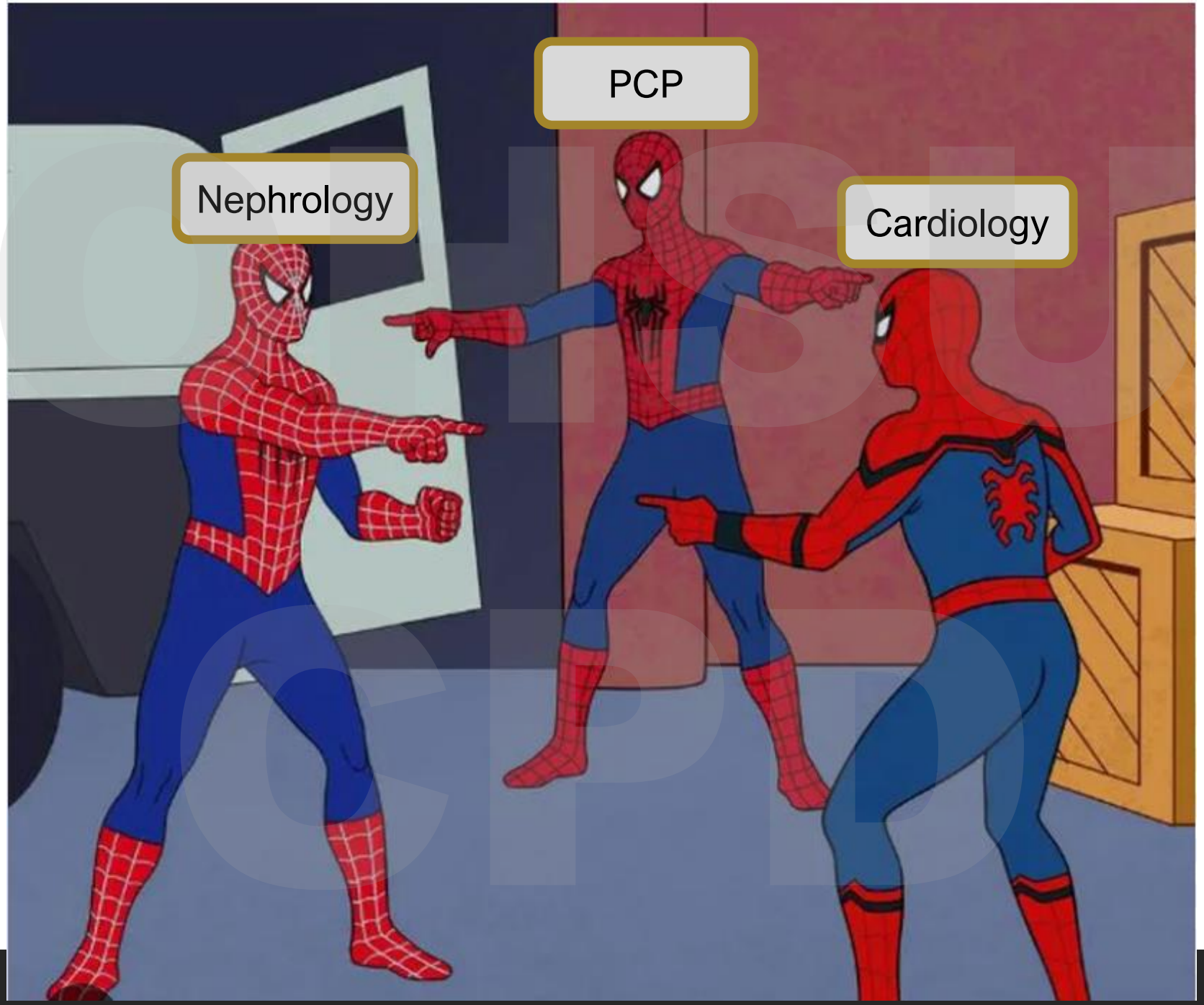
Trend w/ GDMT/Euvolemia

Trend untreated


eGFR <60ml/min/1.73 m²
eGFR >60ml/min/1.73 m²
Incidence Rate/100 Person-Years
0
1
2
3
4
5
6
7
8
P < 0.0001
P < 0.0001
P < 0.0001
Major Cardiovascular Events
Cardiovascular Death
All-Cause Mortality


Systolic and Diastolic Dysfunction
At Risk for Decompensation
Altered Intra-renal Hemodynamics
Decreased Perfusion
Increased venous pressure
Renal Congestion
Precipitators
Diuretics
Vasodilators
Procedures
Toxicity
Vasoconstriction
Neurohoromonal Activation
SNS+RAS+Aldosterone+ Endothelin+ADH+, renal vasoconstriction (adenosine)+prostaglandin dysregulation
ANP/ BNP
Natruretic Peptides
Blocked Natriuresis
Anemia/Relative ↓Epo/Fe transport blocked
Humoral signalling
Cytokine secretion
IL-1, TNF-Alpha
Monocyte Activation
Endothelial Dysfunction
↓Tubulo-Glomerular Function
↑Adhesion Molecules, ↑Enzymatic Activation, ↑Oxidative Stress


CHF
Clinical cardiac recovery
Subclinical sequels lesions
cardiac evolutive lesions
Renocardiac CRS
15%
Nephrotoxicity
AHI
Renal evolutive subclinical lesions
CKD
Fibrosis
Dysfunction
Simultaneous CRS
40%
Cardiotoxicity
AKI
Cardiac evolutive subclinical lesions
CHF
Cardiorenal CRS
45%
CKD
Clinical kidney recovery
Subclinical sequels lesions
Renal evolutive lesions


PCP
Nephrology
Cardiology


PCP
Nephrology
Cardiology
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Spending our Creatinine Cash

Achieve Euvolemia/Normotension

Maximize GDMT

Goal: Slow eGFR Decline

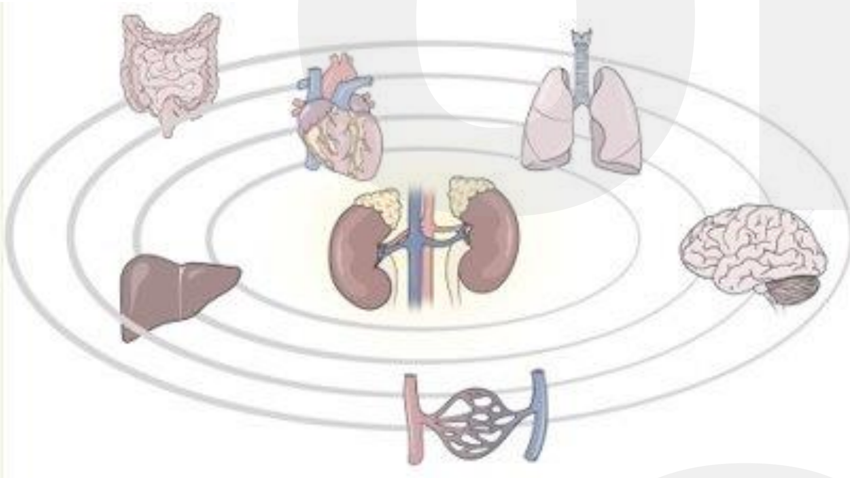
Goal: Stop MAKE/MACE events

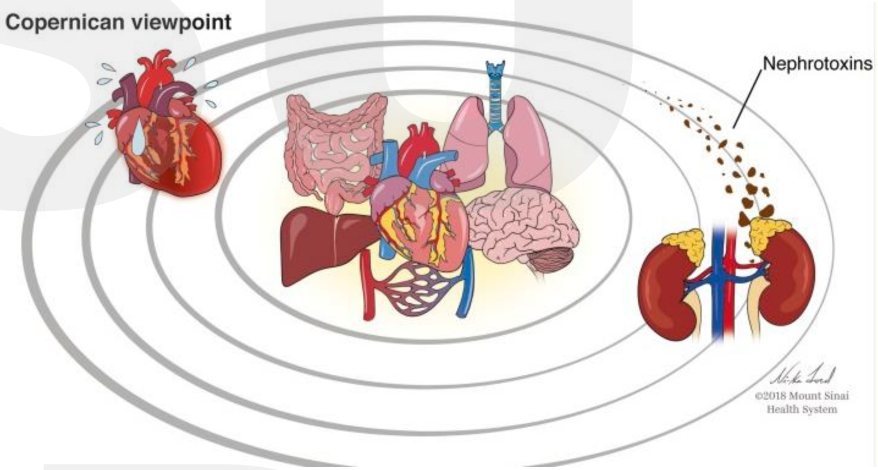
Clinical Pearls

- Hyperkalemia
- Euvolemia tips
- Proteinuria trending
- Acceptable Cr bumps
- SGLT-2 prescribing

Old

New





~~Minimize Cr bumps~~

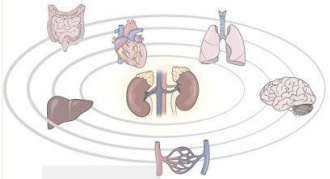
Minimize MAKE/MACE

Focus on Cr trend

Spend our Cr Cash

Spending our Creatinine Cash

CHF+Hypervolemia



Chronic RAAS Activation

Na/H2O retention

Falsely low sCr

Heart/Kidney Fibrosis

Vessel fibrosis/HTN

Normal Heart Pressures

Minimal RAS activation

GDMT/Euvolemia

Pseudo-AKI
Permissive Hyper-Creatininemia

Histologically Happy Kidneys

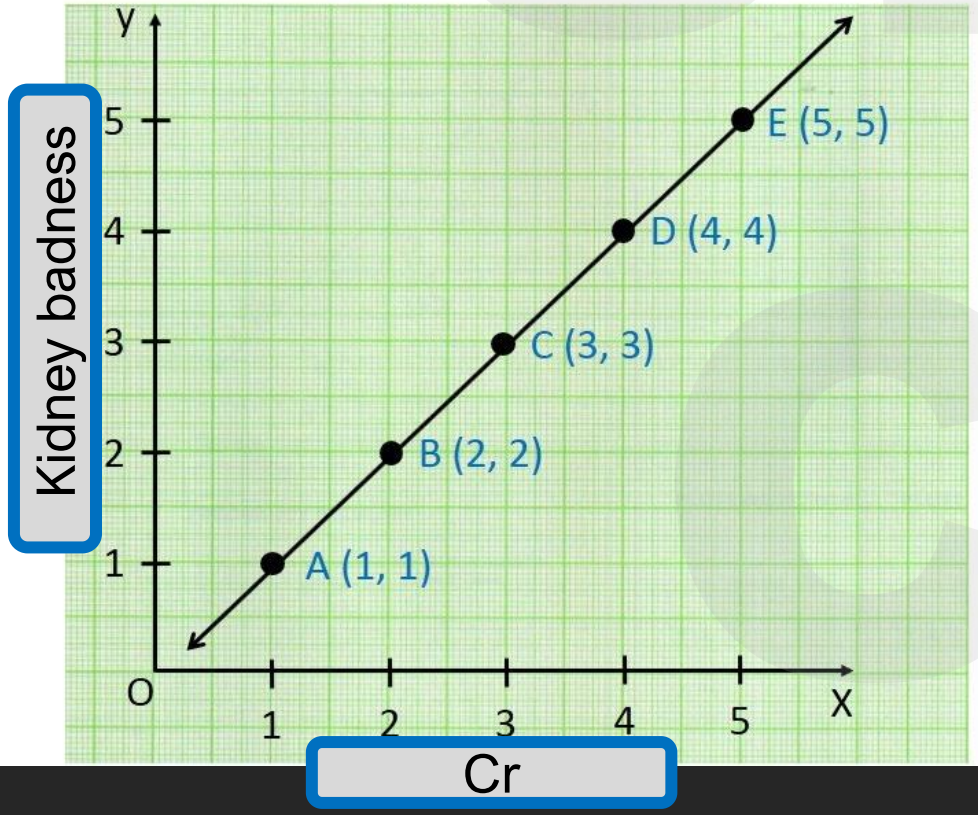
Decrease MAKE/MACE

Its OK to not be OK; Spending Cr as Cash

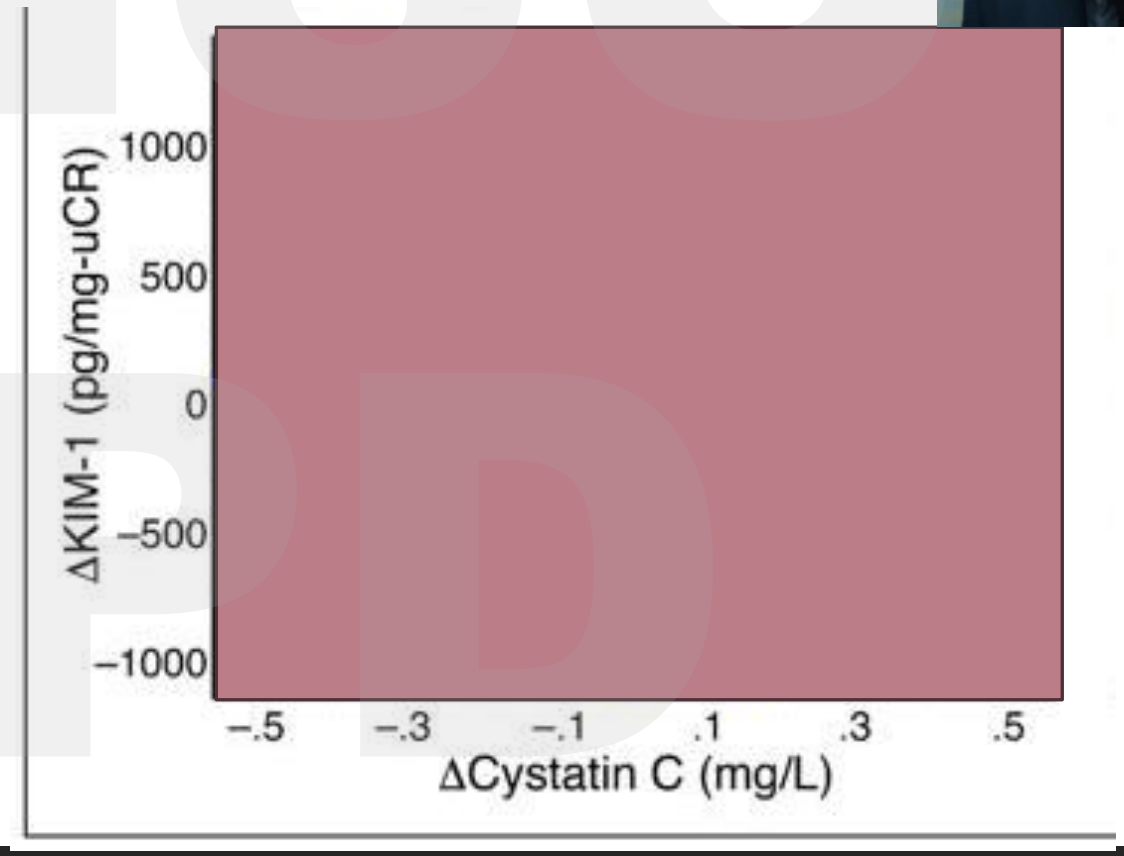
- Prove Cr ≠ Outcomes
- Spending Cr on GDMT
- Spending Cr on Euvolemia

Prove Cr ≠ Outcomes

Expectation

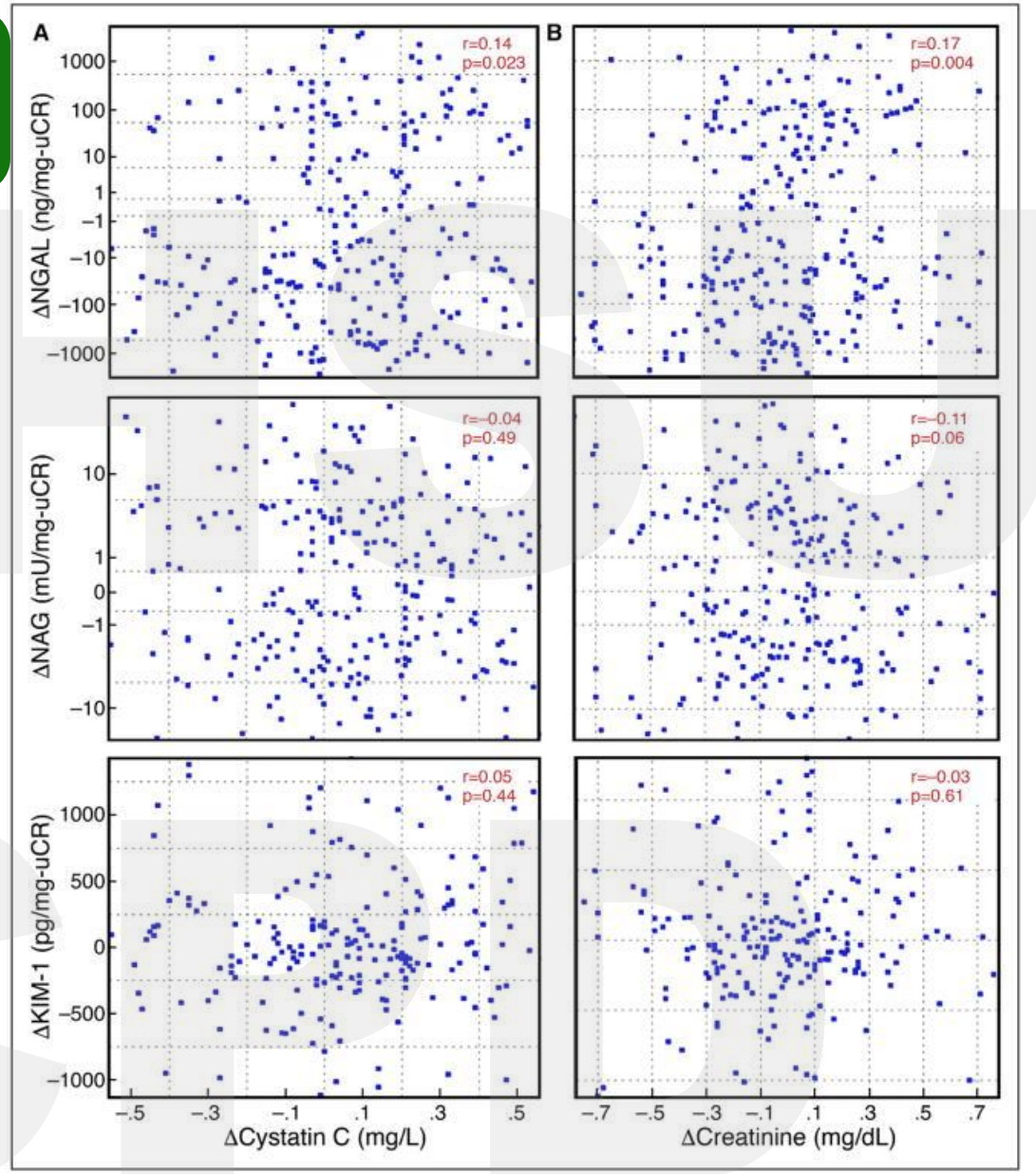


Reality



Prove Cr ≠ Outcomes

This is CHF+CKD, not other renal dz



NGAL, NAG, KIM-1: well validated biomarkers of tubular injury

Grain of salt

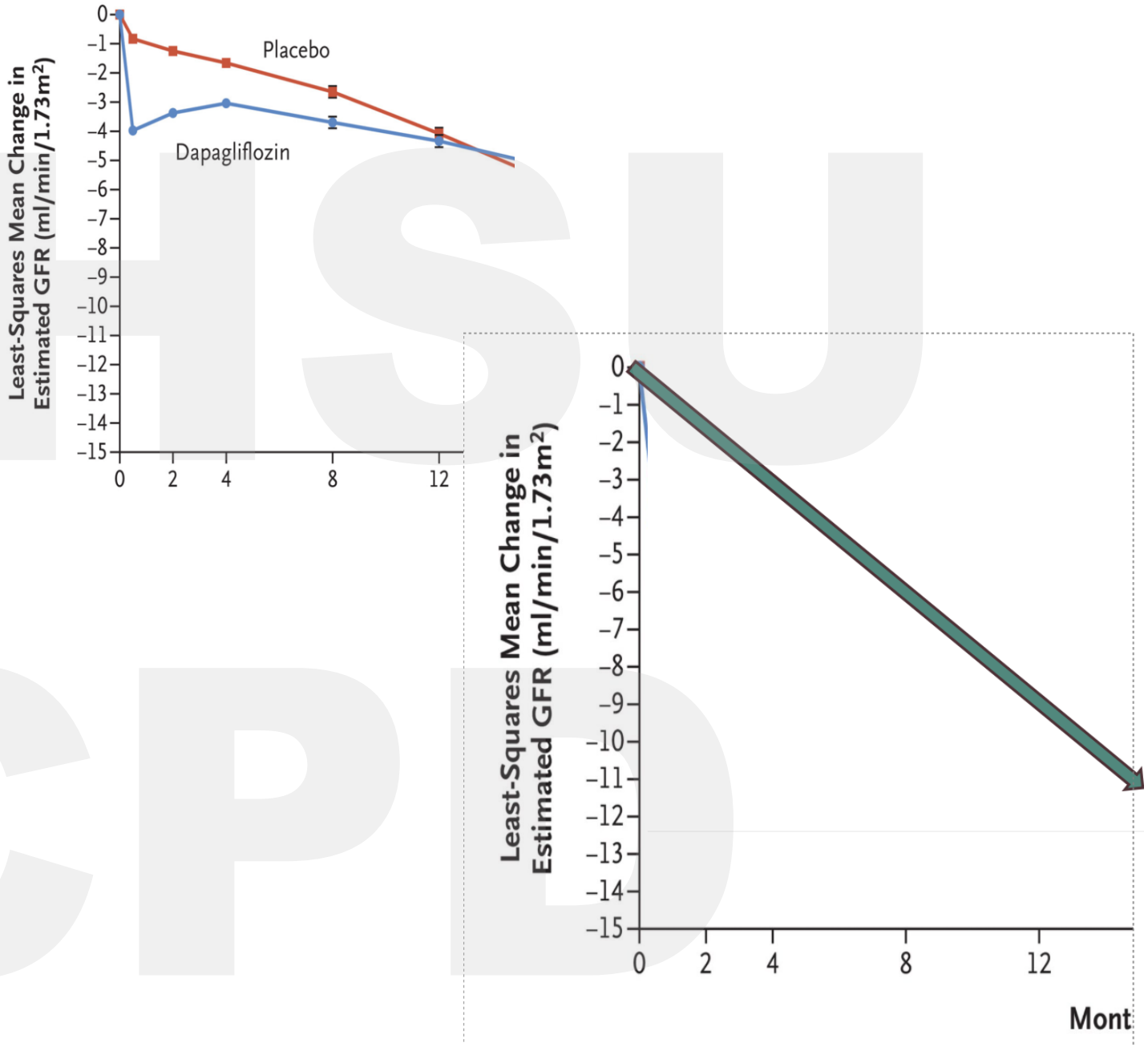
Do not ignore sCr completely.

Emphasis on trend

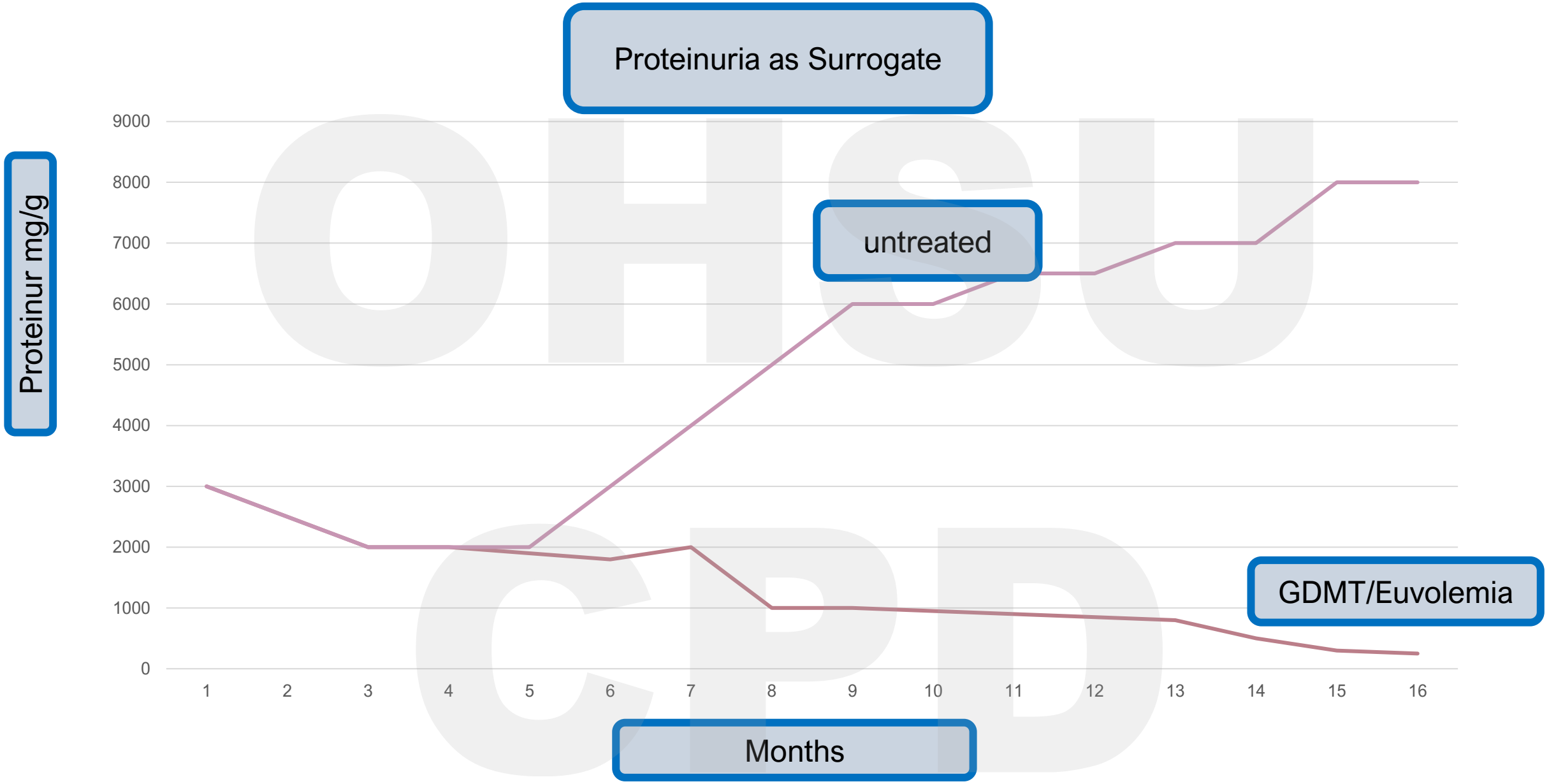
Potassium, phosphorous, calcium, PTH

Response to diuresis

Non cardio-kidney disease?

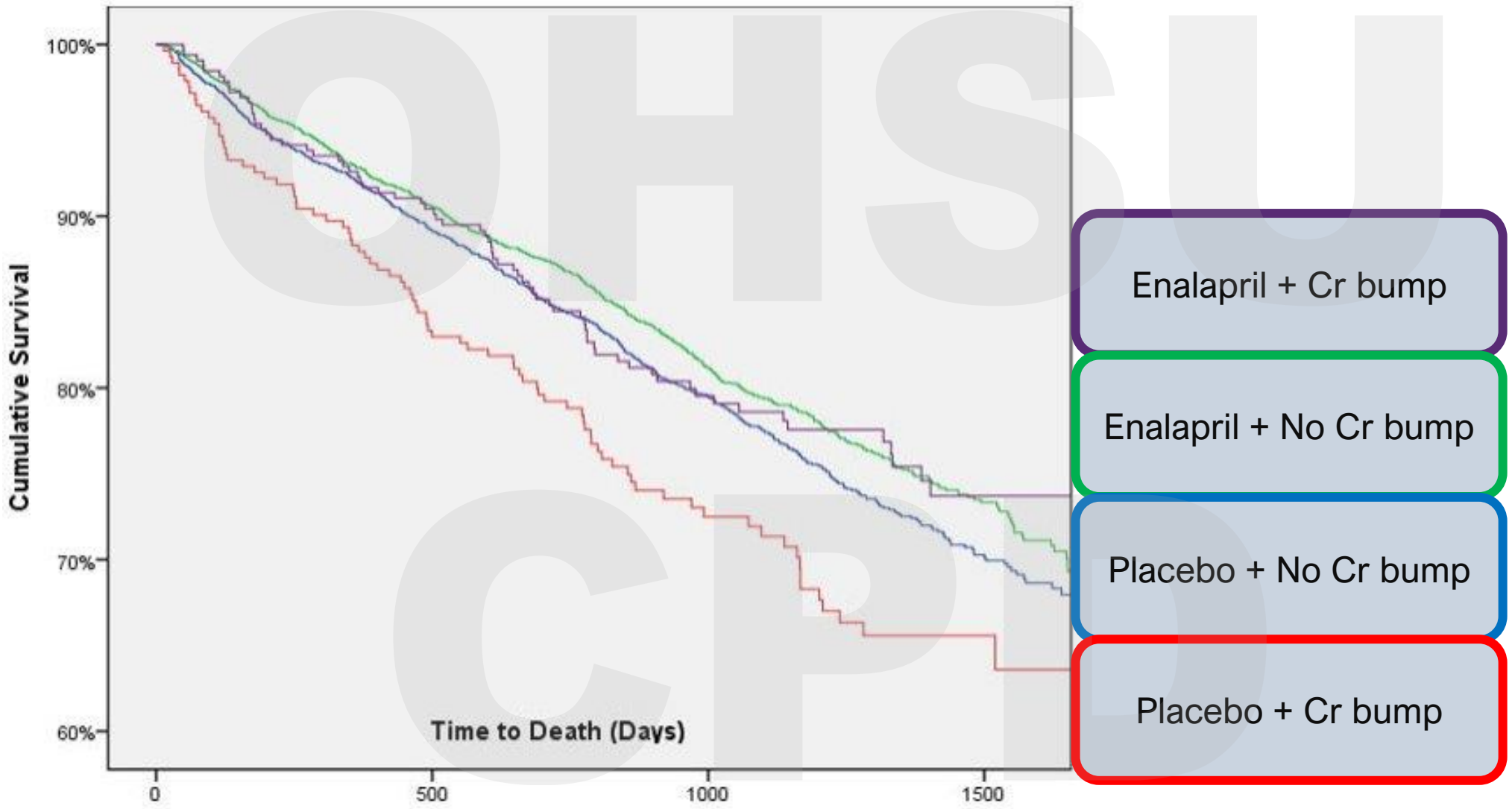


CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (ml/min/1.73 m²) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat 3	Treat 3
	G4	Severely decreased	15–29	Treat* 3	Treat* 3	Treat 4+
	G5	Kidney failure	<15	Treat 4+	Treat 4+	Treat 4+


Proteinuria as Surrogate
Proteinur mg/g
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
untreated
GDMT/Euvolemia
Months

Spending the Cash of Creatinine on ACE/ARB

Spending the Cash of Creatinine → Buy GDMT: ACEi/ARB



Enalapril + Cr bump

Enalapril + No Cr bump

Placebo + No Cr bump

Placebo + Cr bump

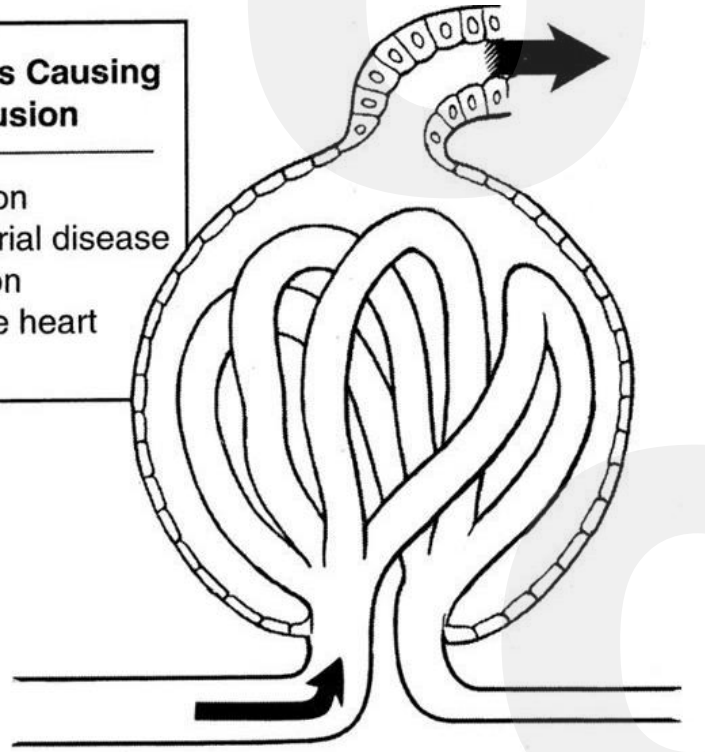
Effect of chronic RAAS

Chronic RAAS Activation

Hyperfiltration=proteinuria

Conditions Causing Hypoperfusion

- Hypotension
- Renal arterial disease
- Dehydration
- Congestive heart failure



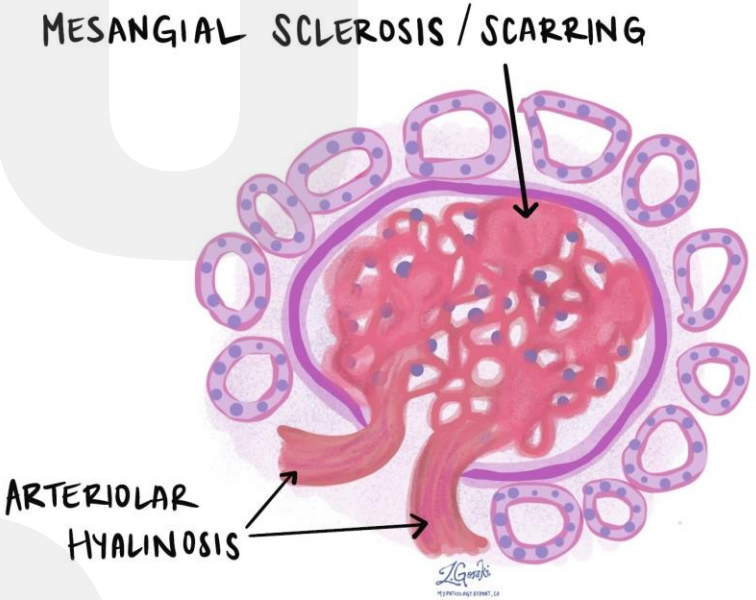
Afferent Arteriole (Decreased flow)

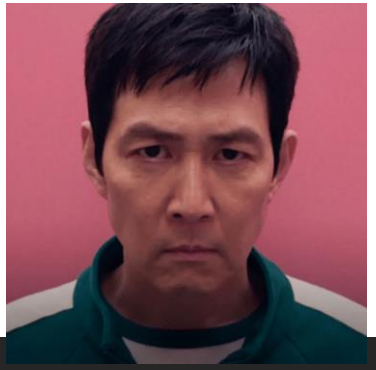
Efferent Arteriole (Constricted)

More glomerular Flow

More GFR

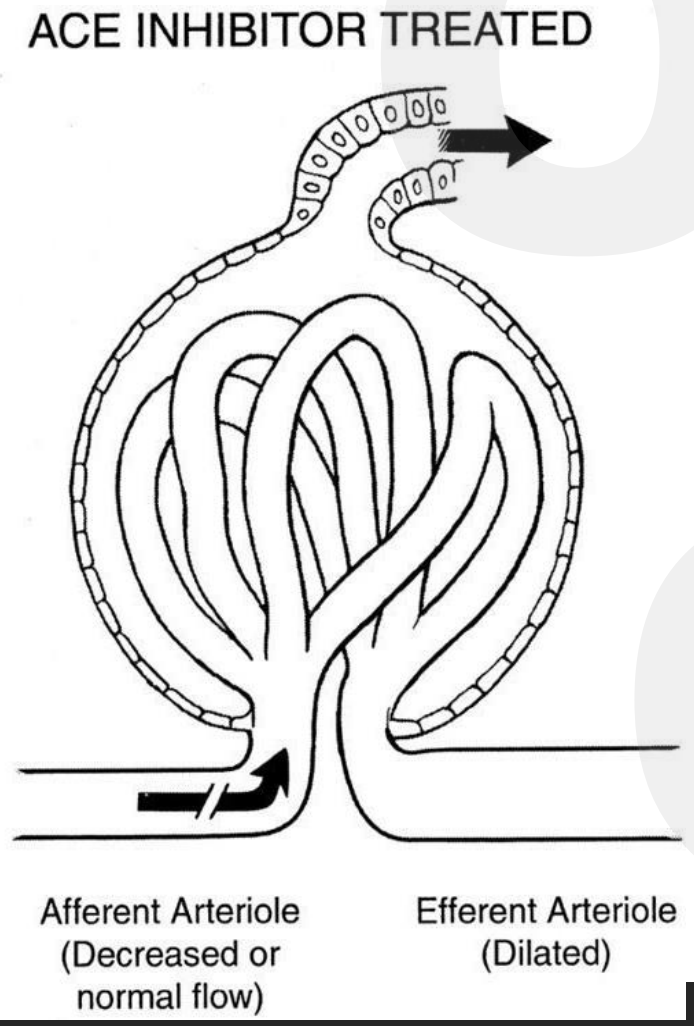
Lower sCr





Why does ACE/ARB raise sCr

Less proteinuria

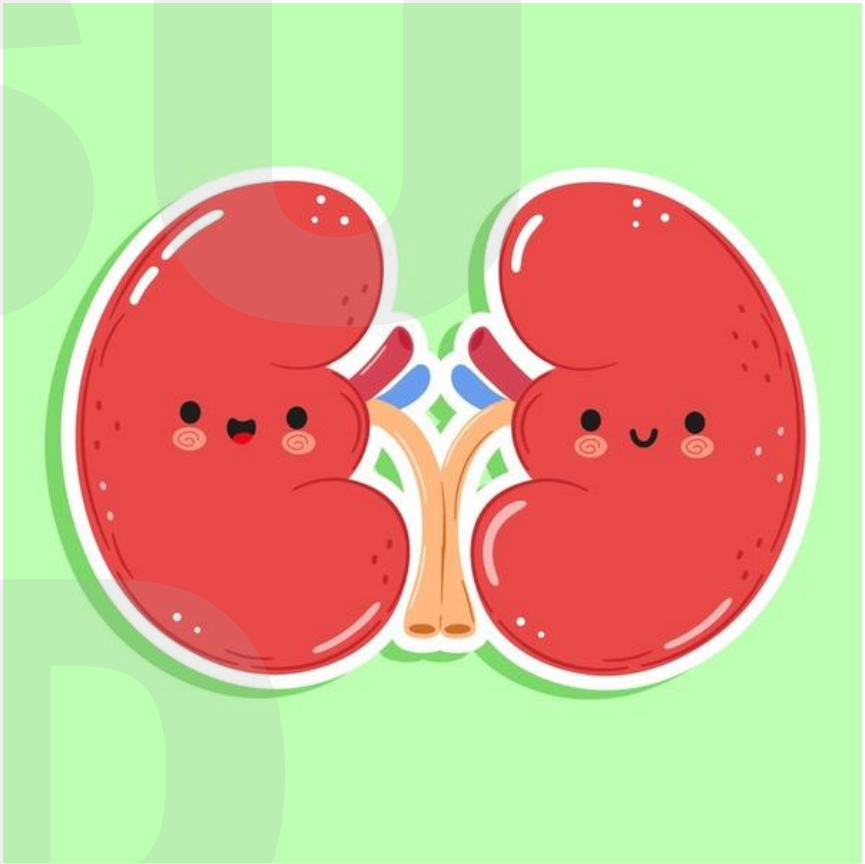


Less glomerular Flow

Less GFR

higher sCr

Higher serum K



8:00 Visit

65M, DC'd 2 days ago

5 day admission for CHF exacerbation

2nd admission this year

Echo: EF 30-->55% this year

Cr: 1.6, GFR 40

Carvedilol 6.25 BID
Torsemide 20 BID

Start GDMT: Losartan 25 qd

8:00 Visit

	1st visit	1 week later
Cr	1.6	1.9
K	4.3	5.2

It's OK to have some K

-Comfort w/ STABLE K <5.4ish

-Considering renal artery duplex early

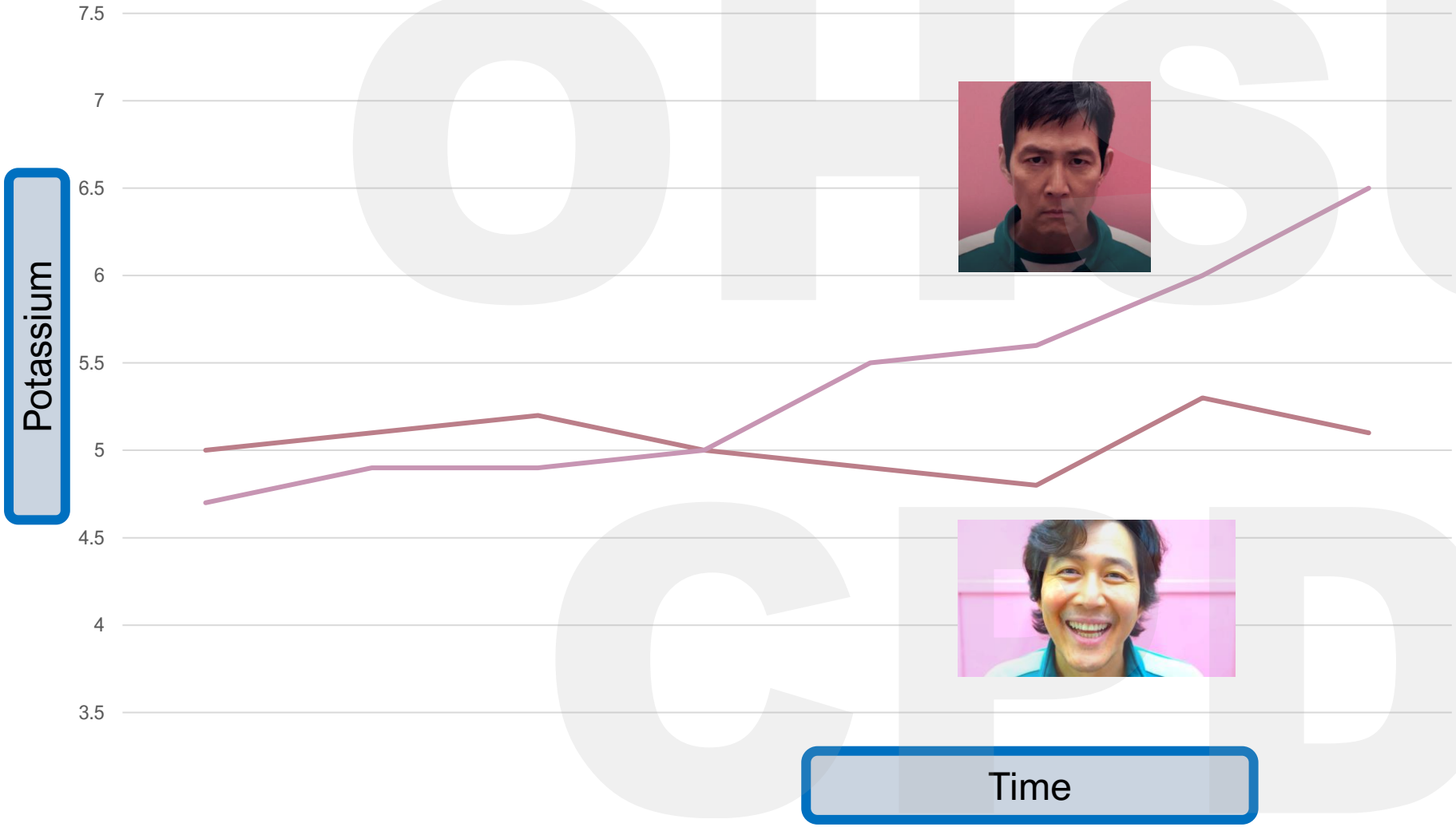
-Avoiding STRICT K diets

-Thiazides/Loops?

-Lokelma/Patiromer

-Alleviating constipation

It's ok to have some K



GFR down

less K in urine

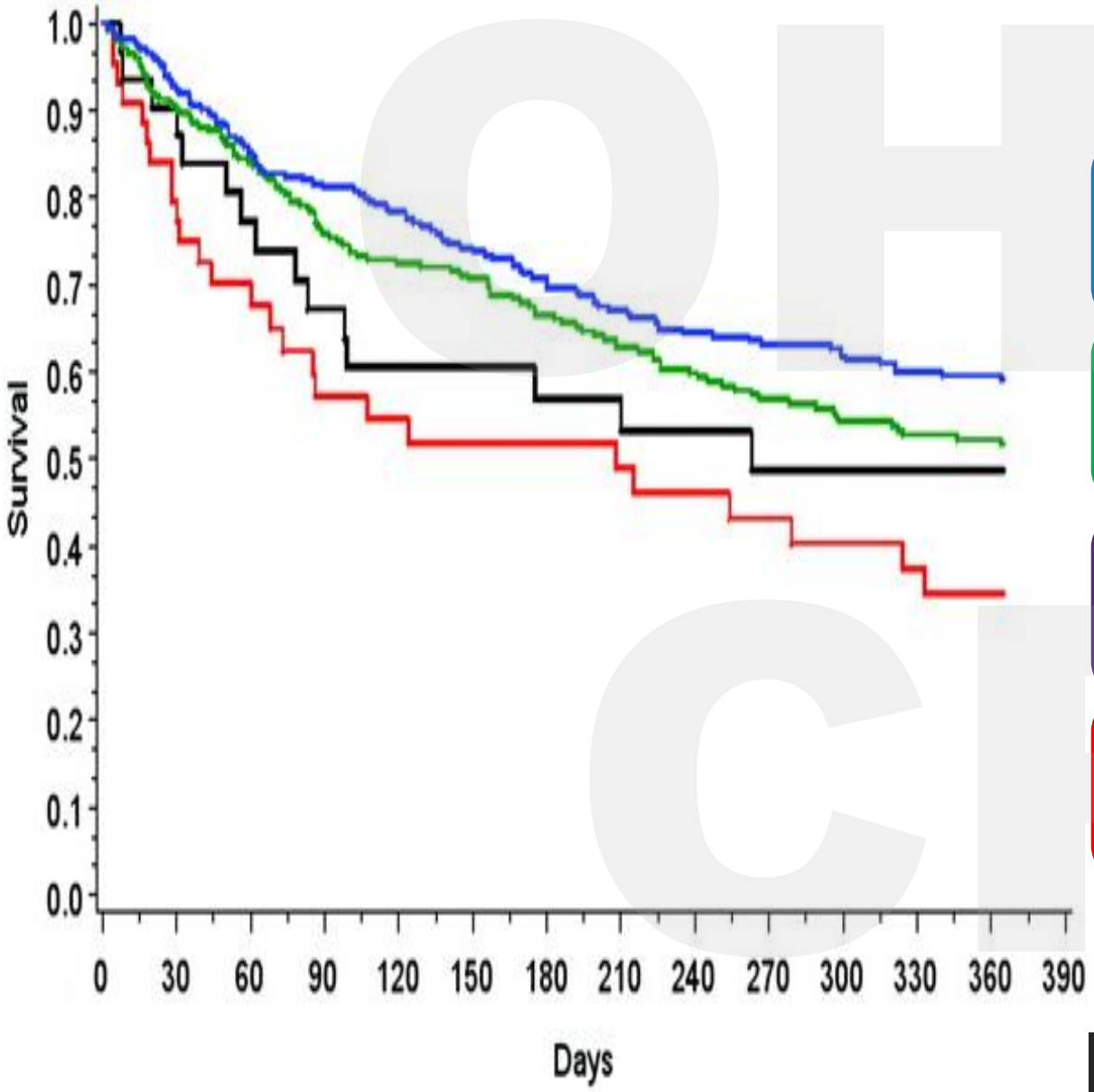
Normokalemia

More K in stool

Small intestine secretes more K

Spending our Creatinine Cash on Euvolemia

Spending the Cash of Creatinine → Buy Euvolemia



- Euvolemia + Cr Bump
- Euvolemia + No Cr bump
- Hypervol + No Cr bump
- Hypervol + Cr bump

Spending the Cash of Creatinine → Buy euvolemia

THE INFLUENCE OF VENOUS PRESSURE ON THE ISOLATED MAMMALIAN KIDNEY.

By F. R. WINTON.
Beit Memorial Fellow.

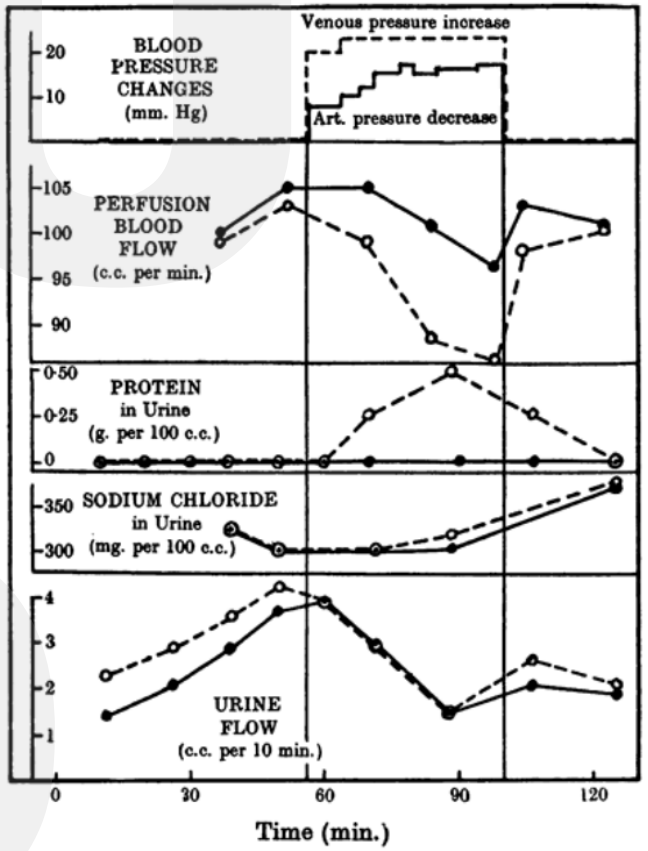
(*From the Department of Pharmacology, University College, London.*)

Renal vein clamping → Worse renal perfusion

Renal artery clamping

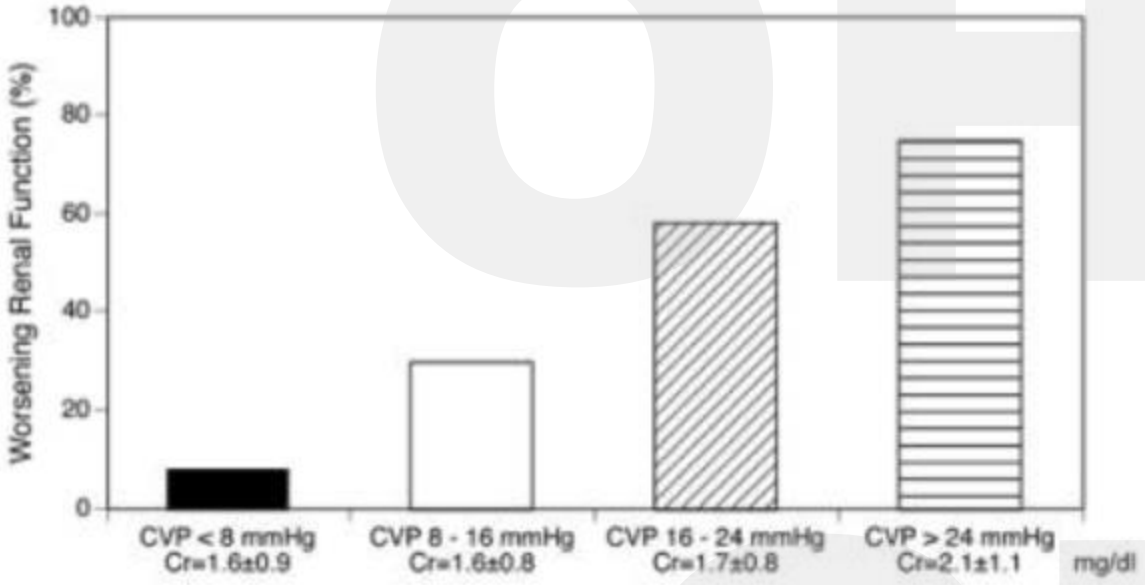
More proteinuria

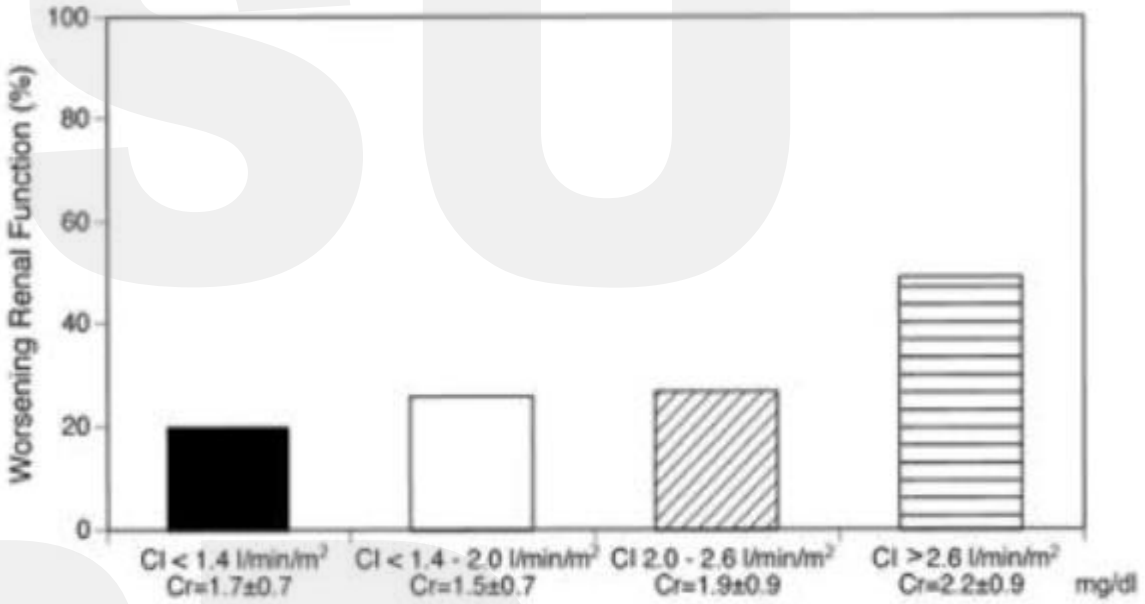
Worse Cr



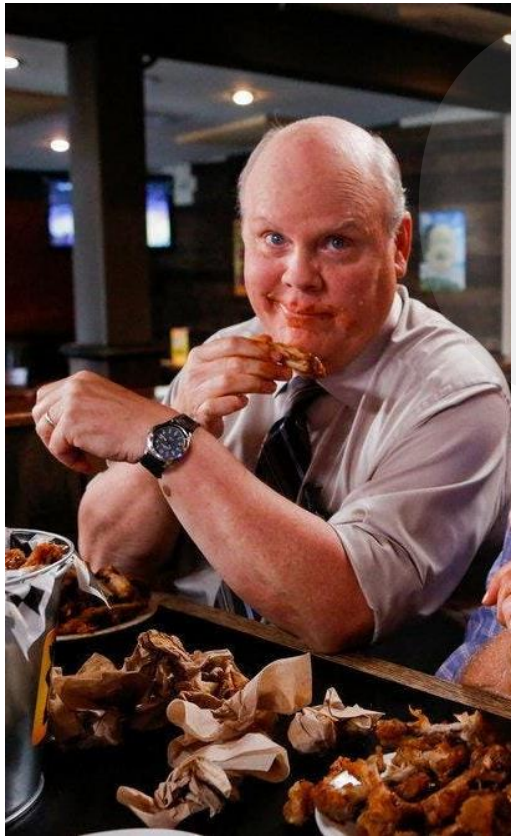
Spending the Cash of Creatinine

Buy euvolemia





8:45 Visit



67M, DC'd 3 days ago

10 day admission for CHF exacerbation

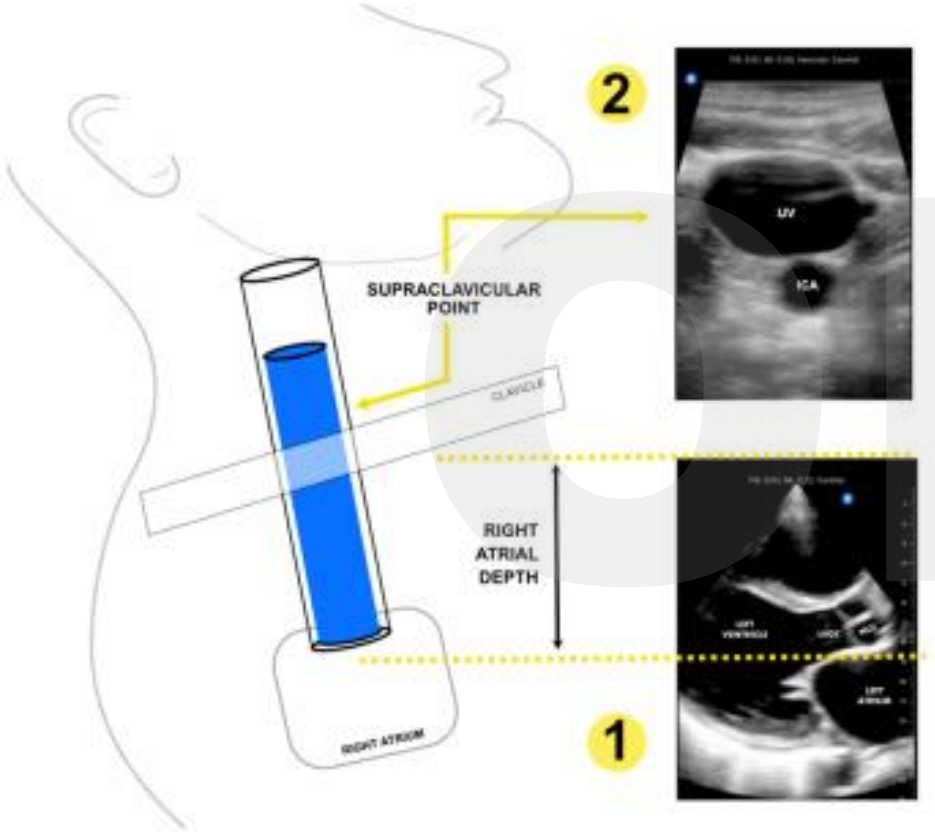
Cr peaked near DC, trended down

Echo: Elevated RVSP, dilated IVC

Cr: 1.3, GFR 66

JVD hard to find
Lower extremity edema
Big belly
No crackles
155/85

What can we use to determine euvolemia?



One and Done

1 MEASURE RIGHT ATRIAL DEPTH

In parasternal long axis view, measure depth of where non-coronary cusp attaches to posterior wall of left ventricular outflow tract. This approximates the Right Atrial Depth (RAD) in centimeters

2 SUPRACLAVICULAR POINT

With patient at 45°, gently rest probe just above clavicle in transverse view

JVD PRESENT

Internal jugular vein is distended with minimal or absent pulsations with inspiration

FIND WINE BOTTLE SIGN

Slide probe up neck to find meniscus where vein completely collapses (wine bottle sign, WBS). Measure the vertical distance to WBS in centimeters

RAP* = RAD + vertical distance to WBS

JVD ABSENT

Internal jugular vein is collapsed or partially engorged but collapses with each breath

LOWER TO 30°

DOES VEIN ENGORGE

YES

RAP* = RAD x 0.75

NO

LOWER TO 0°

VEIN ENGORGE?

YES

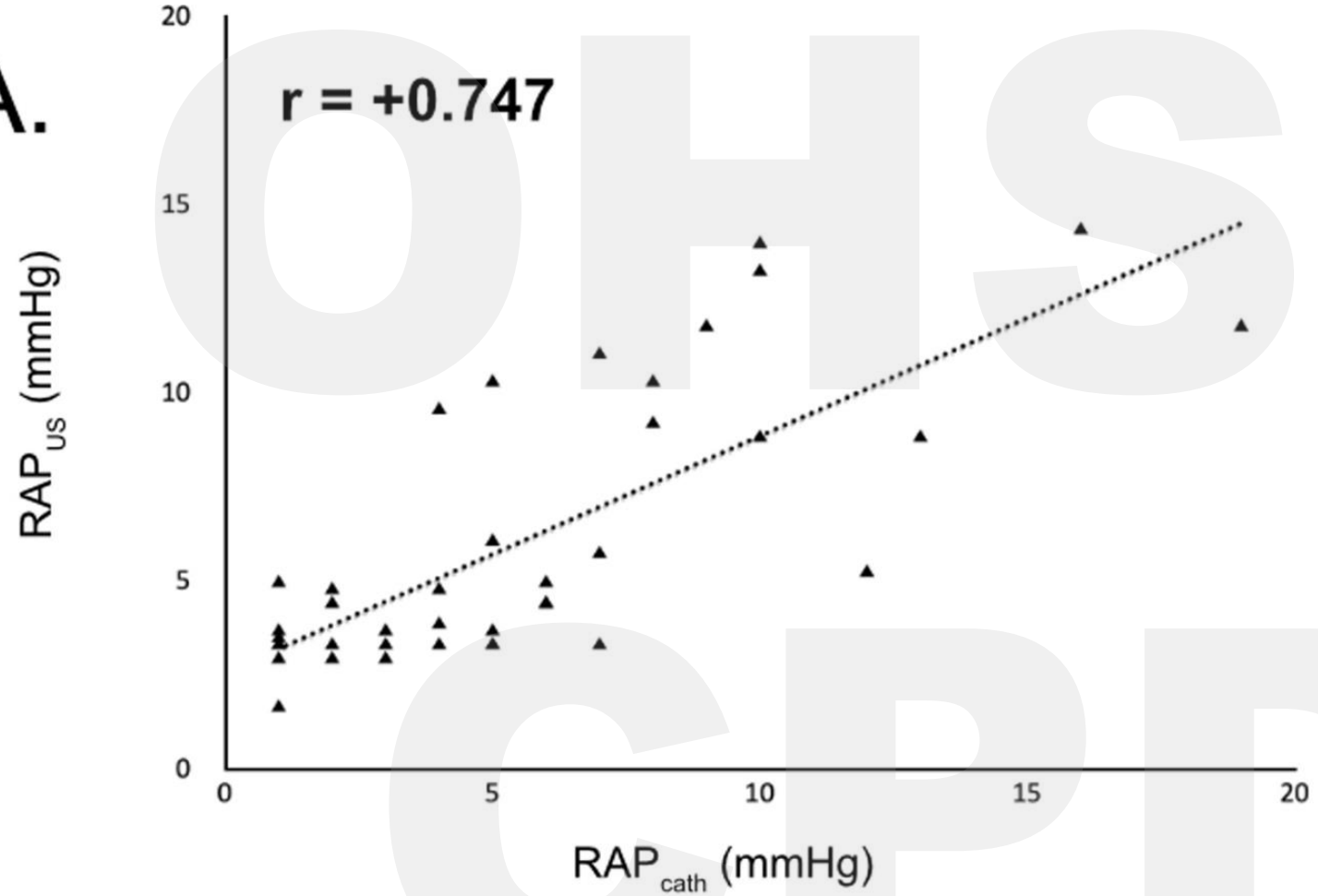
RAP* = RAD x 0.5

NO

RAP* = RAD x 0.25

* Convert cm H2O to mmHg by multiplying by 0.74

A.



Grain of salt

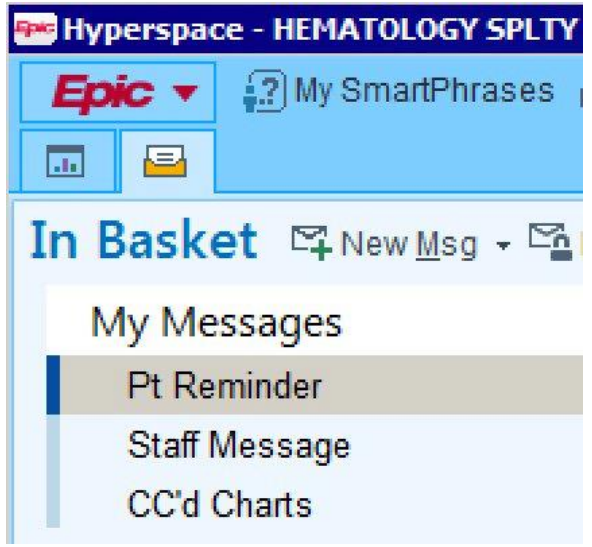
Euvolemia is hard!

Avoid Orthostasis

EDW is tricky, muscle/fat

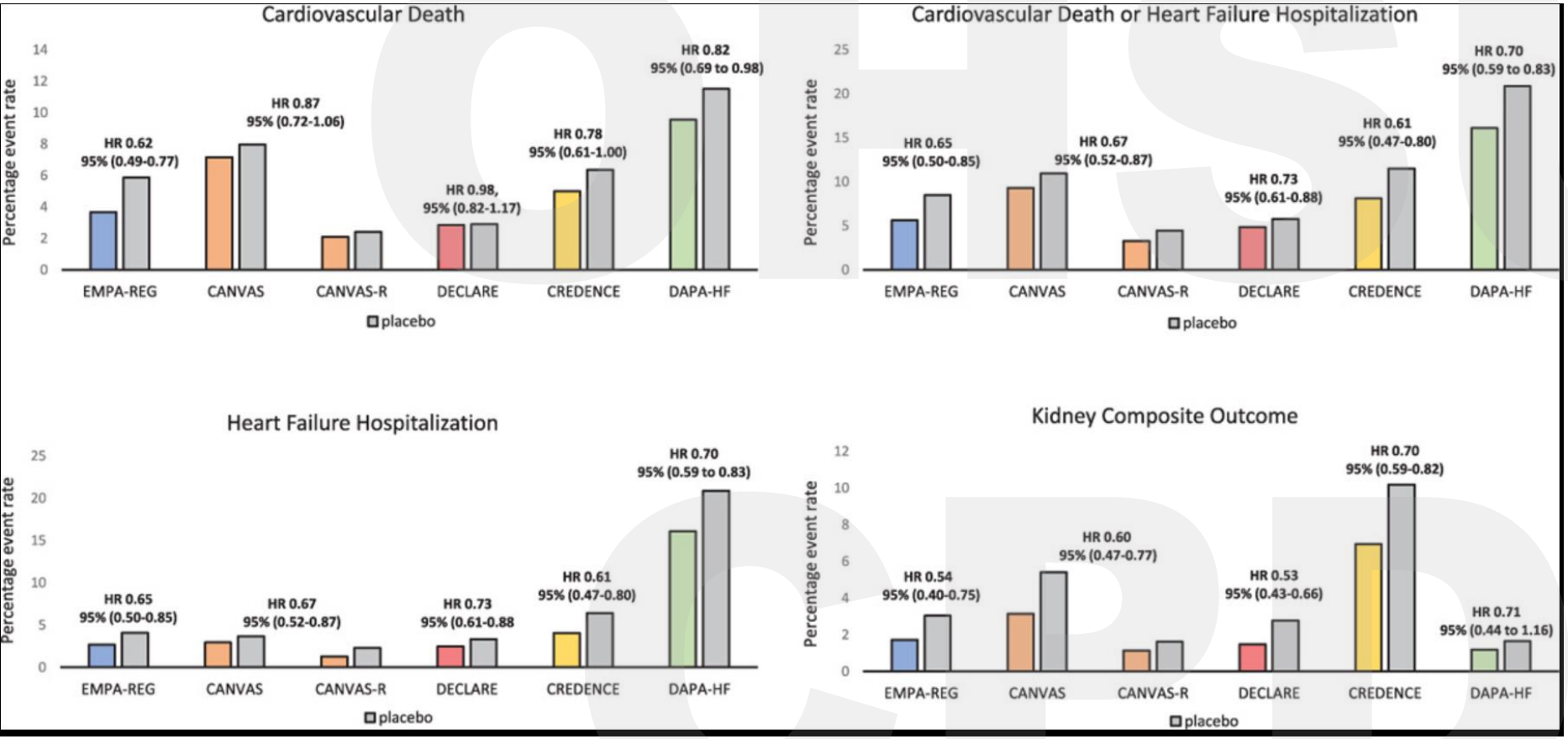
Diminishing returns...

Call us!



Spending Cr Cash on SGLT-2

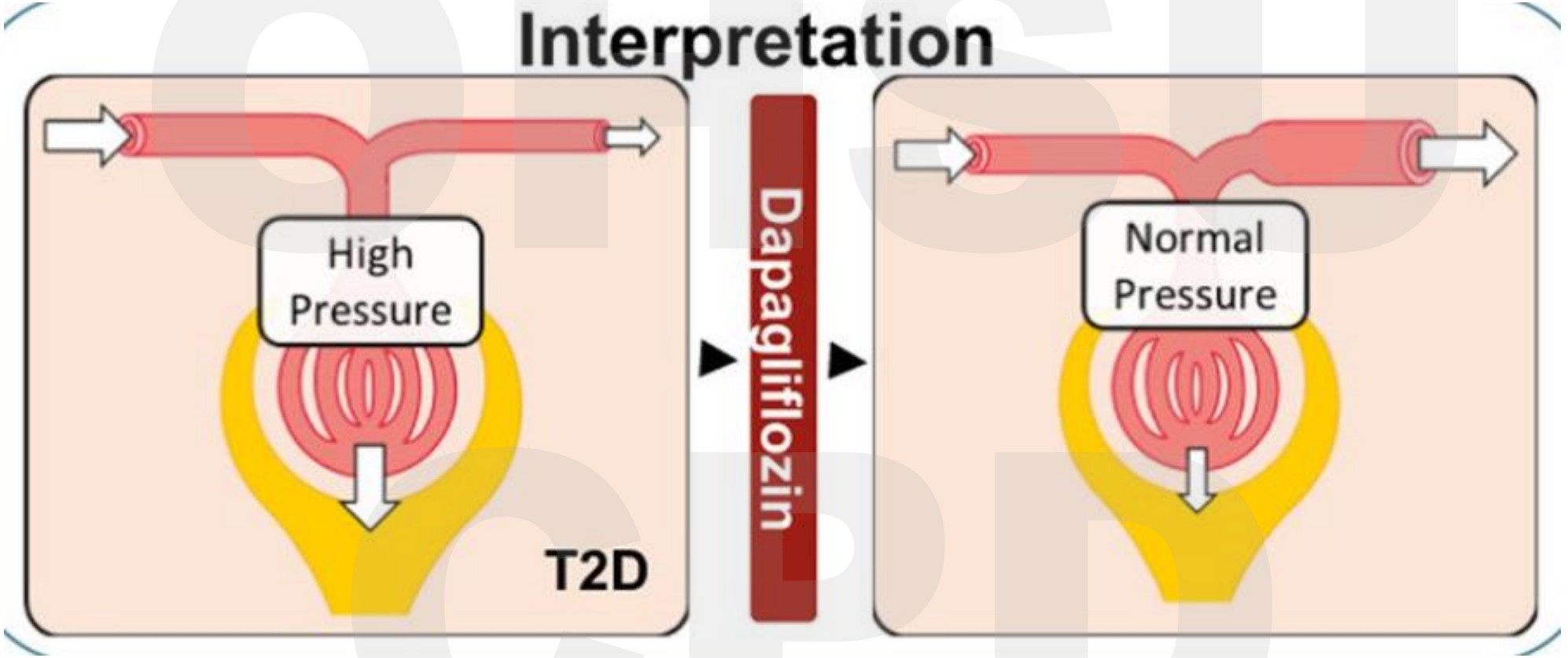
Spending the Cash of Creatinine → Buy GDMT: SGLT-2



Starting even at eGFR<20

ESRD?

Spending the Cash of Creatinine → Buy GDMT: SGLT-2



TGF effects? Or?

9:00 Visit

67F, DM, CHF, CKD

A1cs around 9

Cr 1.3, GFR 50s

HFrecEF 50%, sp PCI x1 3 years ago

Proteinuria 4 g-->1.5g

Carvedilol 25 bid
Losartan 100 qd
Spironolactone 50 mg qd

135/65
No pitting edema
JVD 8cm

Target proteinuria+start GDMT
Empagliflozin

	1st visit	1 week later
SCr	1.3	1.5
K	4.3	4.4

A1cs around 9

135/65

Euvolemic

CAD=PAD=?

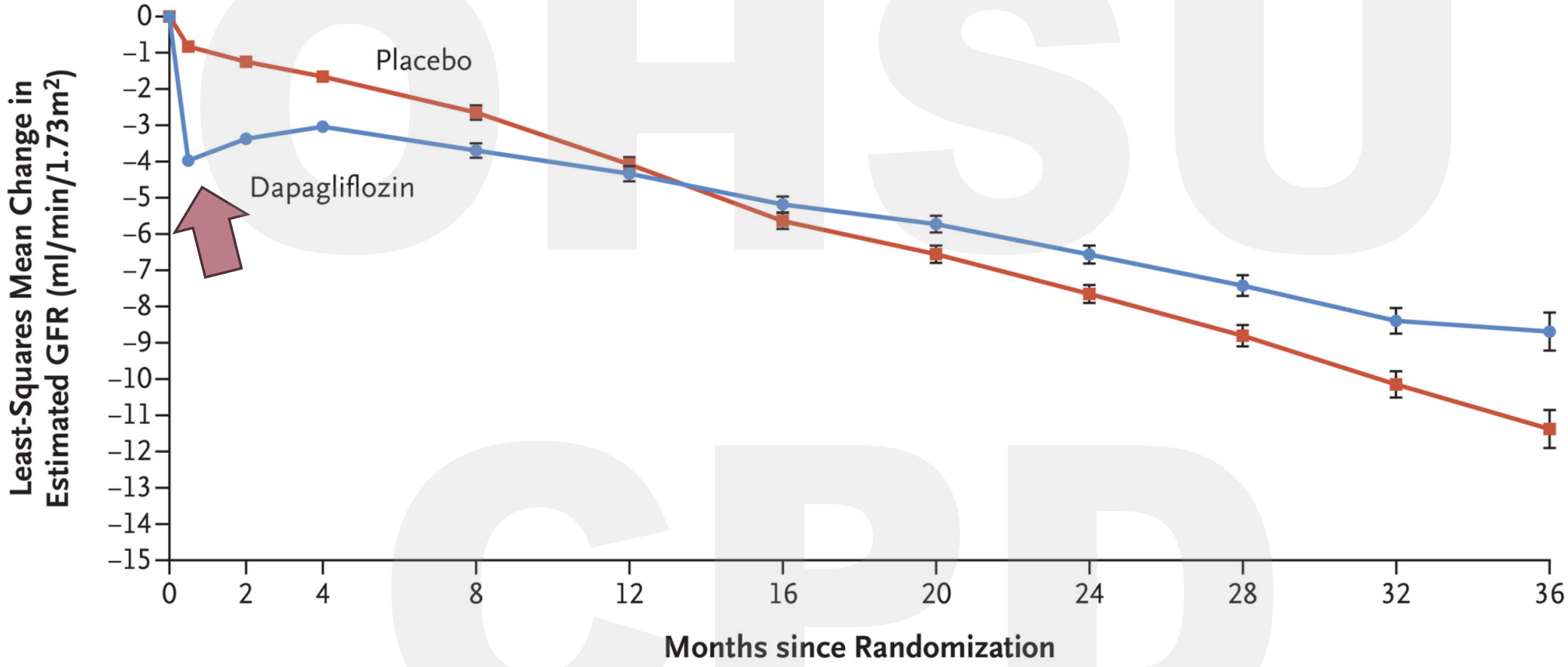
DKA Risk?

BP changes?

Hypovolemic AKI? Falls? Fx?

Amputations?

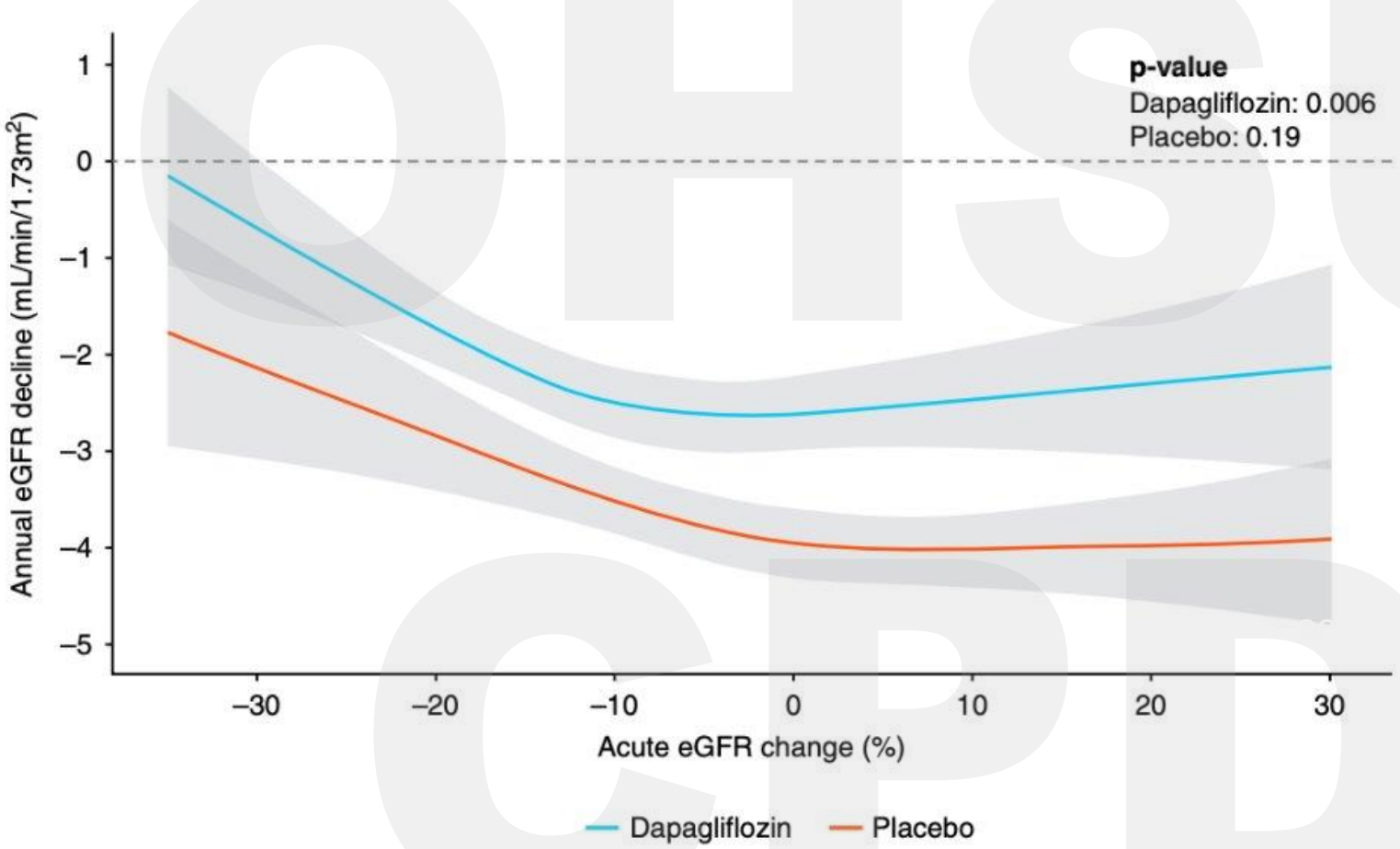
Spending the Cash of Creatinine → Buy GDMT: SGLT-2



Spending the Cash of Creatinine

Buy GDMT: SGLT-2

C



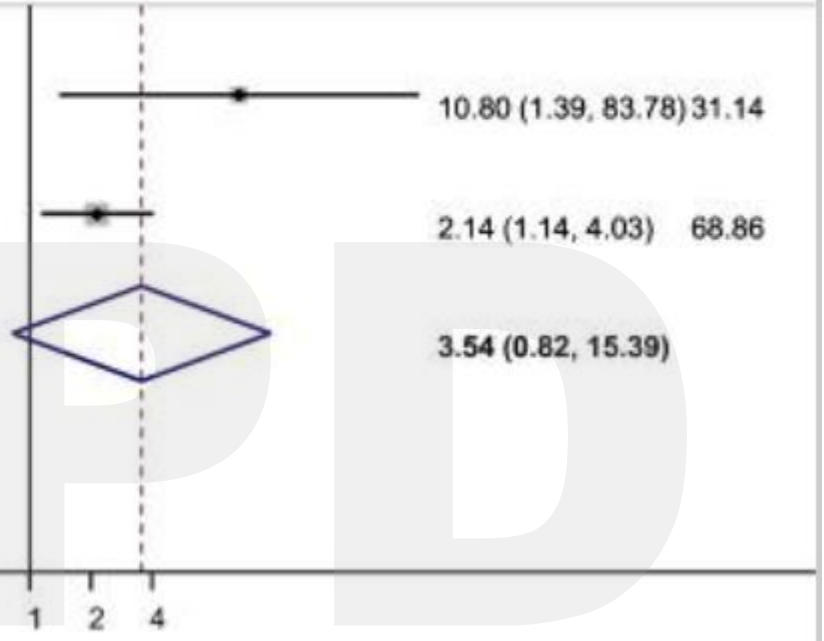
DKA Risk?	Euglycemic DKA is real, relates to a1c > flozin use
BP changes?	BPs tend to go down, but not dangerously
Hypovolemic AKI? Falls? Fx?	No signal for this, look for other causes
Amputations?	Probably not real
UTI?	Not seen in RCTs; simple UTI vs Hx Pyelo?
Fungal infections	Risk is real, relates to BMI: talk about hygiene, weight loss

Spending the Cash of Creatinine → Buy GDMT: SGLT-2

RCTs

D Diabetic Ketoacidosis

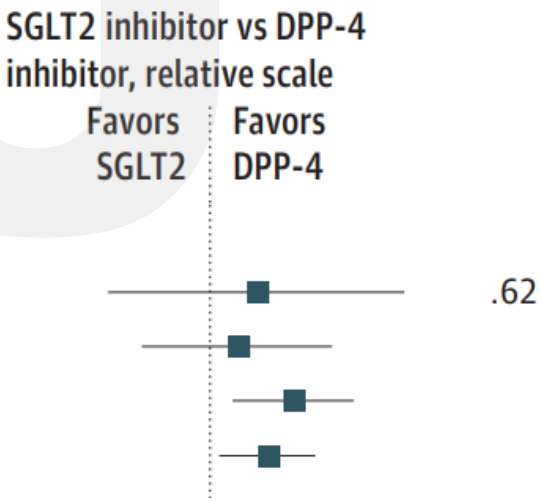
Study	SGLT2 inhibitor No Cases/ No at Risk	SGLT2 inhibitor Rate/1000 Person-years	Placebo No Cases/ No at Risk	Placebo Rate/1000 Person-years	Relative risk (95% CI)	Weight, %
CREDENCE	11/2200	2.2	1/2197	0.2	10.80 (1.39, 83.78)	31.14
SCORED	30/5291	NR	14/5286	NR	2.14 (1.14, 4.03)	68.86
Overall (I-squared = 54.3%, p = 0.139)					**3.54 (0.82, 15.39)**	



Spending the Cash of Creatinine → Buy GDMT: SGLT-2

Large retrospective insurance cohort

	SGLT2 inhibitor events, No. (IR/1000 PY)	DPP-4 inhibitor events, No. (IR/1000 PY)	RD/1000 PY (95% CI)	HR (95% CI)
Diabetic ketoacidosis				
Subgroup HbA_{1c} <7.5% (n = 24 052)	6 (0.72)	4 (0.49)	0.23 (-0.52 to 0.98)	1.49 (0.42 to 5.26)
Subgroup HbA_{1c} 7.5%-9% (n = 32 290)	13 (1.16)	10 (0.9)	0.25 (-0.59 to 1.10)	1.27 (0.65 to 2.89)
Subgroup HbA_{1c} >9% (n = 30 932)	47 (4.81)	22 (2.43)	2.38 (0.67 to 4.09)	2.06 (1.62 to 3.42)
Overall population (n = 87 274)	66 (2.25)	36 (1.27)	0.45 (-0.09 to 0.98)	1.73 (1.06 to 2.43)



I consider a1c before starting

Glp-1?

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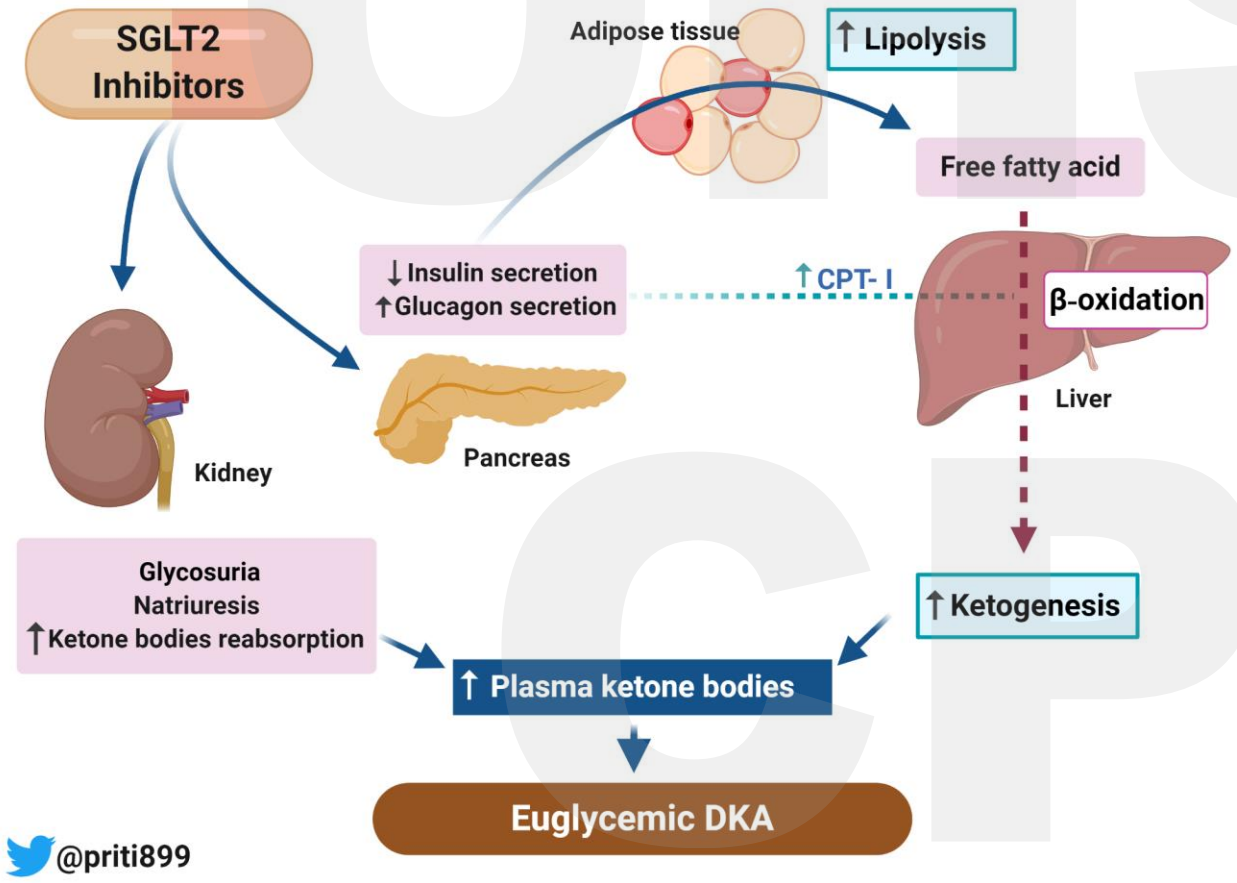
Spending the Cash of Creatinine → Buy GDMT: SGLT-2

Risk is real, relates to a1c



@priti899

Spending the Cash of Creatinine → Buy GDMT: SGLT-2

RCTs

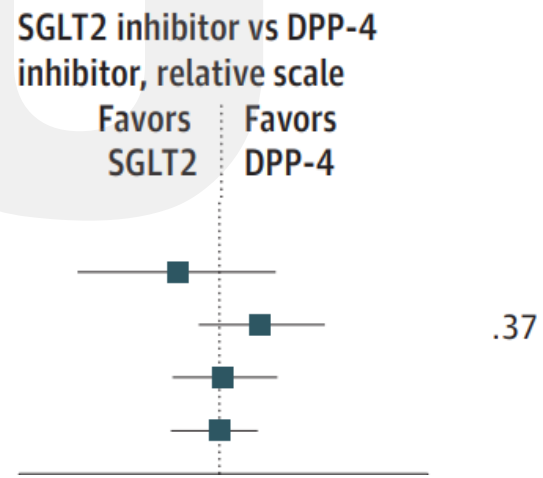
E Amputation

Study	SGLT2 inhibitor No Cases/ No at Risk	SGLT2 inhibitor Rate/1000 Person-years	Placebo No Cases/ No at Risk	Placebo Rate/1000 Person-years	Relative risk (95% CI)	Weight, %
CANVAS Program (eGFR <45)	NR	9.4	NR	9.1	0.87 (0.30, 2.52)	9.58
CANVAS Program (eGFR 45-60)	NR	10	NR	3.4	3.22 (1.40, 7.40)	14.39
CREDENCE	70/2200	12.3	63/2197	11.2	1.11 (0.79, 1.56)	42.28
EMPAREG-OUTCOME(eGFR <45)	NR	11.4	NR	11.7	0.97 (0.07, 12.66)	1.86
EMPAREG-OUTCOME(eGFR 45-60)	NR	10	NR	11	0.91 (0.06, 13.44)	1.69
SCORED	32/5291	NR	33/5286	NR	0.97 (0.60, 1.57)	30.19
Overall (I-squared = 25.4%, p = 0.244)					**1.21 (0.85, 1.72)**	

Spending the Cash of Creatinine → Buy GDMT: SGLT-2

Large retrospective insurance cohort

	SGLT2 inhibitor events, No. (IR/1000 PY)	DPP-4 inhibitor events, No. (IR/1000 PY)	RD/1000 PY (95% CI)	HR (95% CI)
Lower-limb amputation				
Subgroup HbA_{1c} <7.5% (n = 24 052)	9 (1.08)	13 (1.59)	-0.51 (-1.62 to 0.60)	0.69 (0.29 to 1.61)
Subgroup HbA_{1c} 7.5%-9% (n = 32 290)	32 (2.85)	22 (1.99)	0.86 (-0.43 to 2.15)	1.44 (0.84 to 2.48)
Subgroup HbA_{1c} >9% (n = 30 932)	37 (3.78)	33 (3.62)	0.16 (-1.57 to 1.90)	1.05 (0.66 to 1.68)
Overall population (n = 87 274)	78 (2.56)	68 (2.46)	0.09 (-0.67 to 0.85)	1.02 (0.66 to 1.38)



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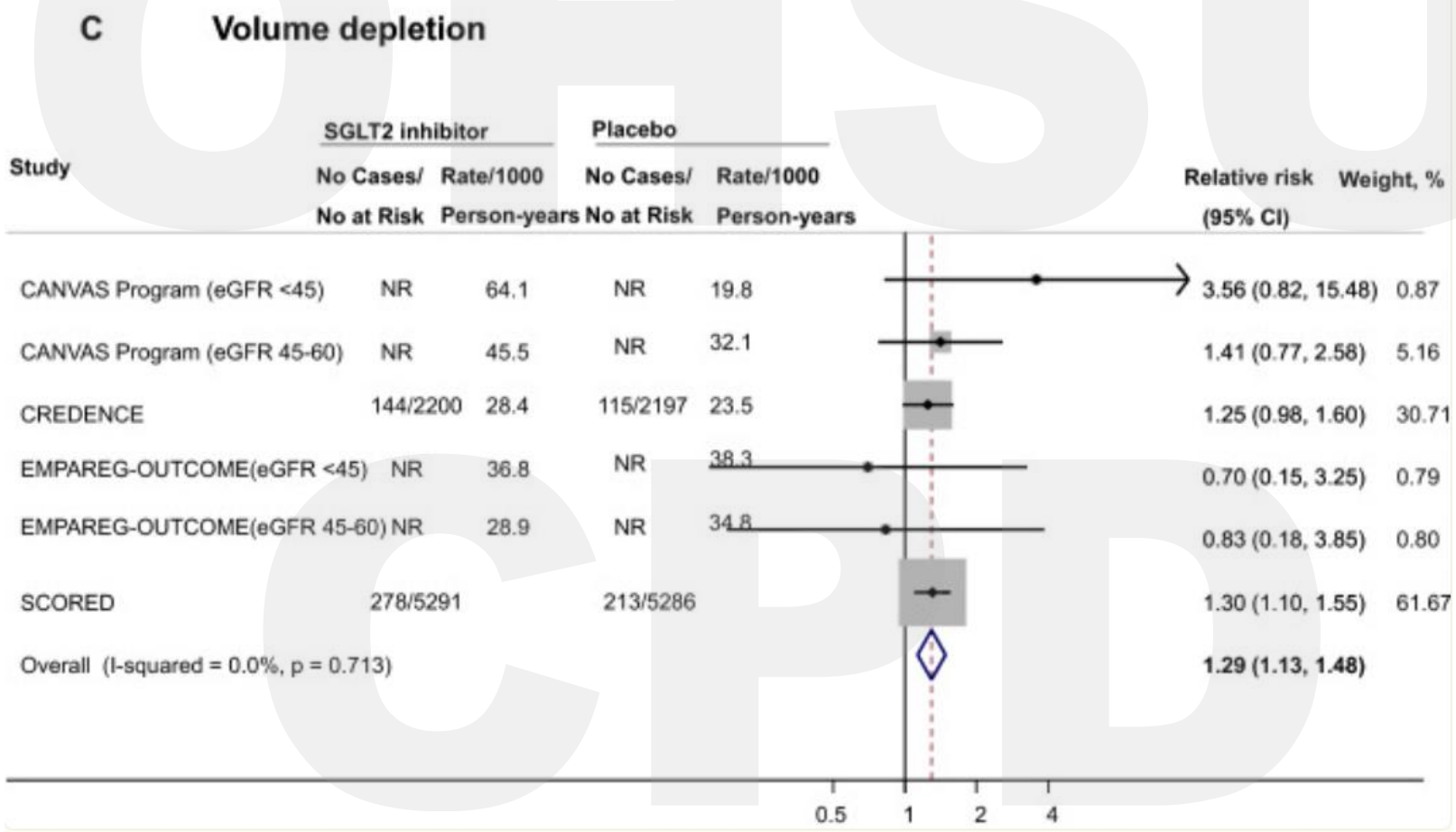
Spending the Cash of Creatinine → Buy GDMT: SGLT-2

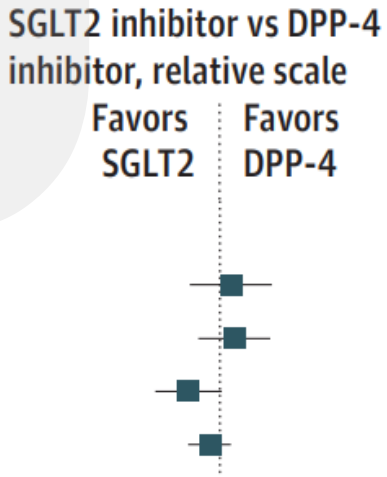
RCTs



Spending the Cash of Creatinine → Buy GDMT: SGLT-2

Large retrospective insurance cohort

	SGLT2 inhibitor events, No. (IR/1000 PY)	DPP-4 inhibitor events, No. (IR/1000 PY)	RD/1000 PY (95% CI)	HR (95% CI)
Hypovolemia				
Subgroup HbA_{1c} <7.5% (n = 24 052)	75 (9.03)	67 (8.21)	0.82 (-2.02 to 3.65)	1.10 (0.79 to 1.53)
Subgroup HbA_{1c} 7.5%-9% (n = 32 290)	101 (9.04)	89 (8.07)	0.97 (-1.46 to 3.40)	1.13 (0.85 to 1.50)
Subgroup HbA_{1c} >9% (n = 30 932)	81 (8.33)	101 (11.24)	-2.92 (-5.76 to 0.07)	0.76 (0.57 to 1.02)
Overall population (n = 87 274)	257 (8.80)	258 (9.12)	-0.23 (-1.77 to 1.32)	0.93 (0.76 to 1.09)



Think of it as a gentle diuretic

Loop diuretic resistance

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Spending the Cash of Creatinine → Buy GDMT: SGLT-2

Large retrospective insurance cohort

	SGLT2 inhibitor events, No. (IR/1000 PY)	DPP-4 inhibitor events, No. (IR/1000 PY)	RD/1000 PY (95% CI)	HR (95% CI)	SGLT2 inhibitor vs DPP-4 inhibitor, relative scale: Favors SGLT2 / Favors DPP-4
Genital infections					
Subgroup HbA_{1c} <7.5% (n = 24 052)	469 (58.22)	196 (24.27)	33.96 (27.69 to 40.23)	2.41 (2.04 to 2.85)	<.01
Subgroup HbA_{1c} 7.5%-9% (n = 32 290)	738 (68.5)	243 (22.28)	46.22 (40.54 to 51.90)	3.10 (2.68 to 3.58)	
Subgroup HbA_{1c} >9% (n = 30 932)	640 (68.04)	341 (38.38)	29.66 (23.00 to 36.32)	1.82 (1.60 to 2.08)	
Overall population (n = 87 274)	1847 (65.41)	780 (27.99)	37.53 (33.98 to 41.09)	2.17 (1.98 to 2.36)	

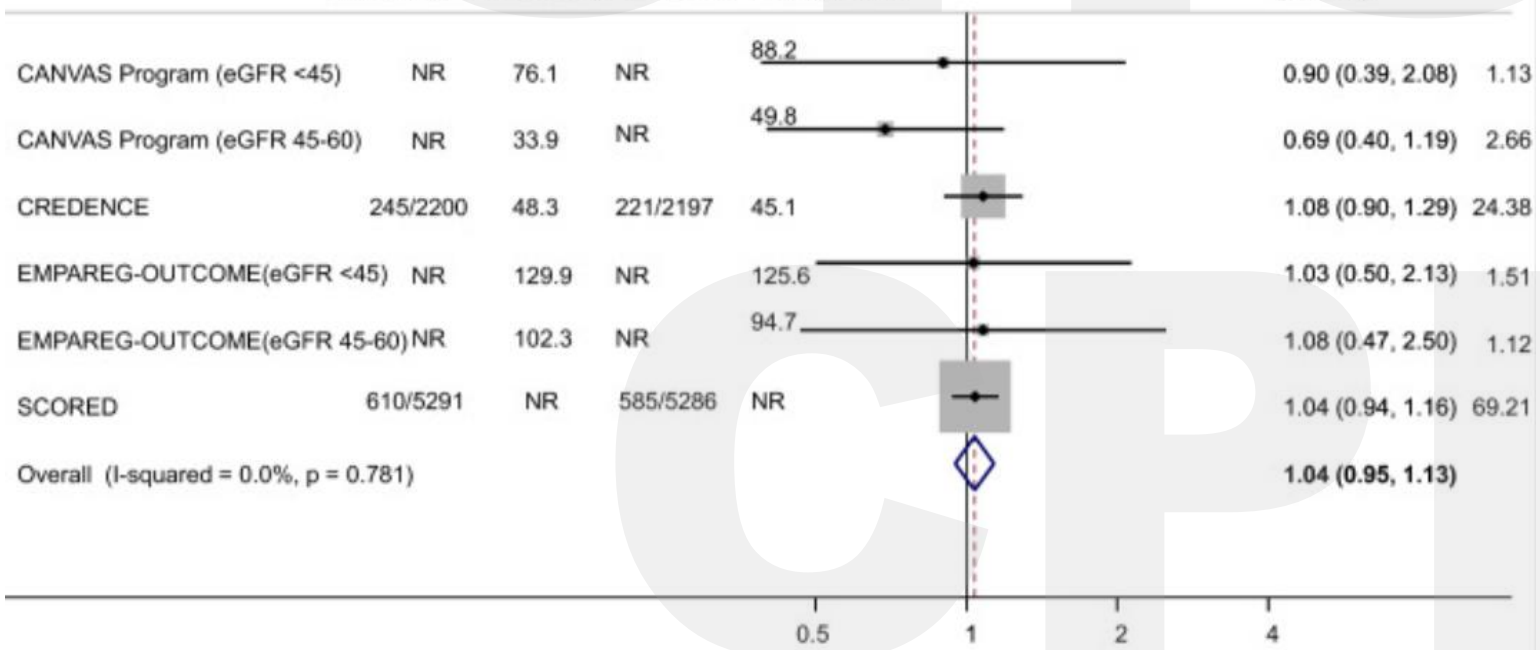
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2800884

Spending the Cash of Creatinine → Buy GDMT: SGLT-2

RCTs

G Urinary Tract Infection

Study	SGLT2 inhibitor No Cases/ No at Risk	SGLT2 inhibitor Rate/1000 Person-years	Placebo No Cases/ No at Risk	Placebo Rate/1000 Person-years	Relative risk (95% CI)	Weight, %
CANVAS Program (eGFR <45)	NR	76.1	NR	88.2	0.90 (0.39, 2.08)	1.13
CANVAS Program (eGFR 45-60)	NR	33.9	NR	49.8	0.69 (0.40, 1.19)	2.66
CREDENCE	245/2200	48.3	221/2197	45.1	1.08 (0.90, 1.29)	24.38
EMPAREG-OUTCOME(eGFR <45)	NR	129.9	NR	125.6	1.03 (0.50, 2.13)	1.51
EMPAREG-OUTCOME(eGFR 45-60)	NR	102.3	NR	94.7	1.08 (0.47, 2.50)	1.12
SCORED	610/5291	NR	585/5286	NR	1.04 (0.94, 1.16)	69.21
Overall (I-squared = 0.0%, p = 0.781)					**1.04 (0.95, 1.13)**	



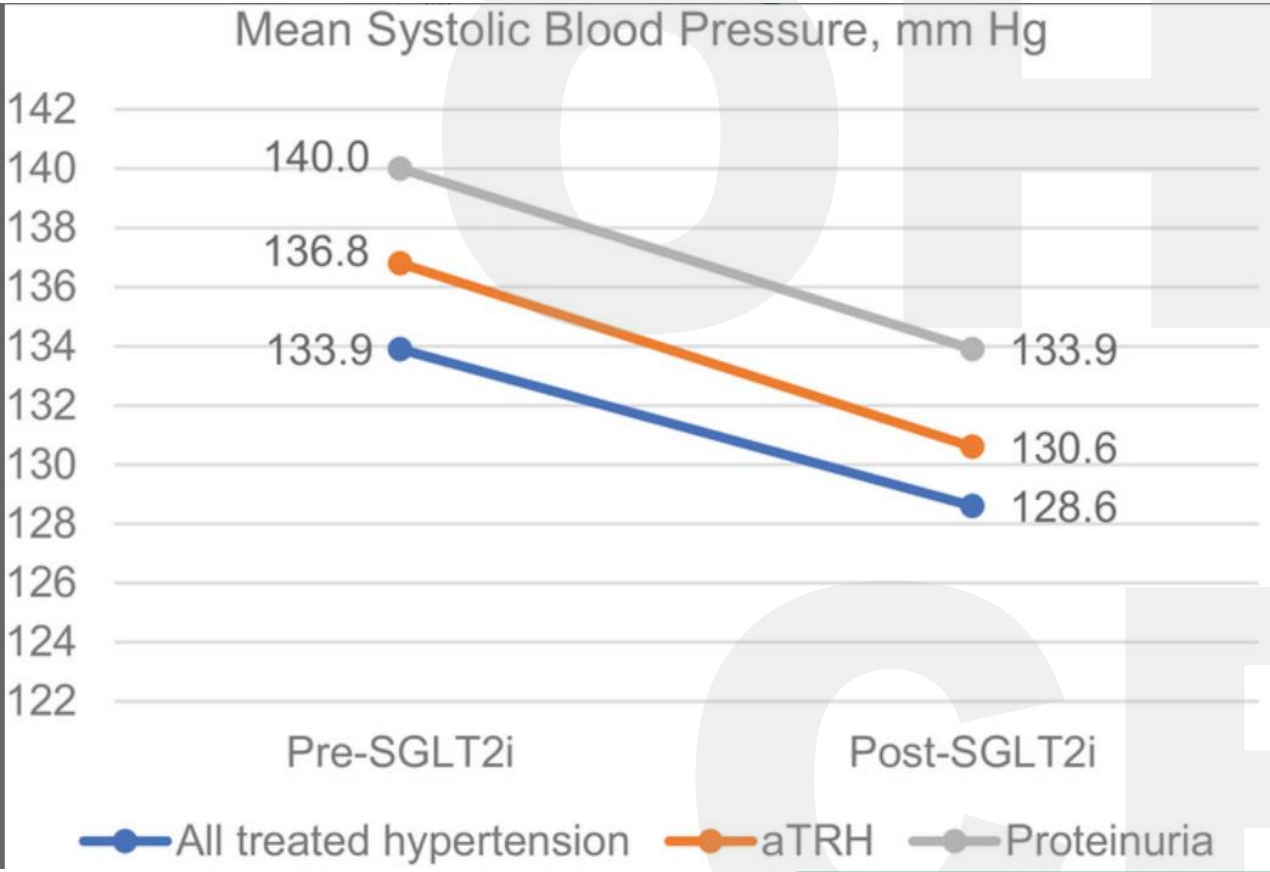
RCTs

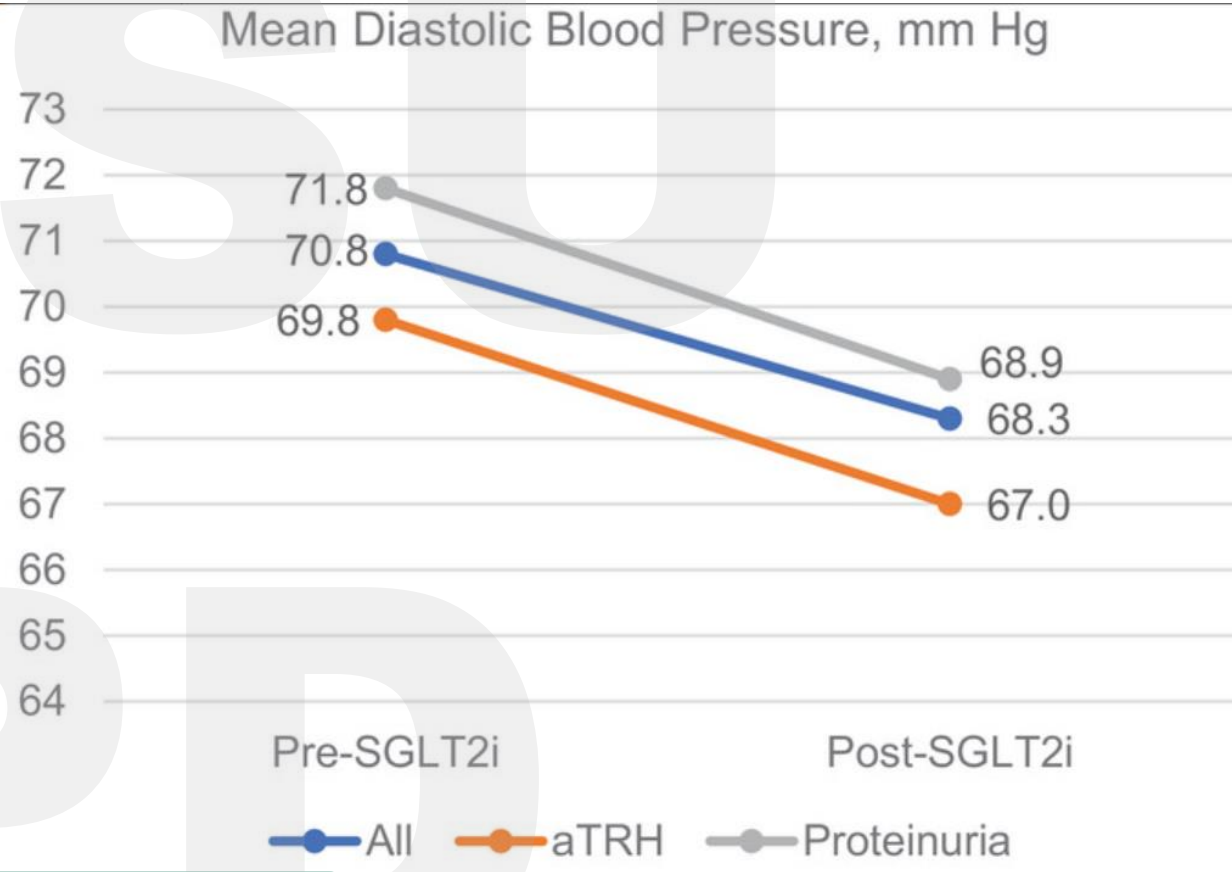
Comparison	Study (Publication Yr)	Patients (*n*)	Outcome
Meta-analysis			
SGLT2i versus active comparator	Puckrin *et al.* (2018) ([10])	22 trials: 15,966	Random-effects model risk ratio 1.08; 95% CI, 0.93 to 1.25 I^2 22; 95% CI, 0 to 54
Retrospective cohort			
SGLT2i versus GLP1-RA	Varshney *et al.* (2021) ([12])	474	Composite genitourinary infection (HR=0.78; 95% CI, 0.26 to 2.37)
SGLT2i versus DPP4i	Fisher *et al.* (2020) ([13])	416,488	Urosepsis (HR=0.58; 95% CI, 0.42 to 0.8)
SGLT2i versus DPP4i or GLP1-RA	Dave *et al.* (2019) ([11])	SGLT2i versus DPP4i: 123,752; SGLT2i versus GLP1-RA: 111,978	Severe UTI: • SGLT2i versus DPP4i: HR=0.98; 95% CI, 0.68 to 1.41 • SGLT2i versus GLP1-RA: HR=0.72; 95% CI, 0.53 to 0.99 Treated outpatient UTI: • SGLT2i versus DPP4i: HR=0.96; 95% CI, 0.89 to 1.04 • SGLT2i versus GLP1-RA: HR=0.91; 95% CI, 0.84 to 0.99

Beware BMI and A1c

Frequent UTI vs Urosepsis

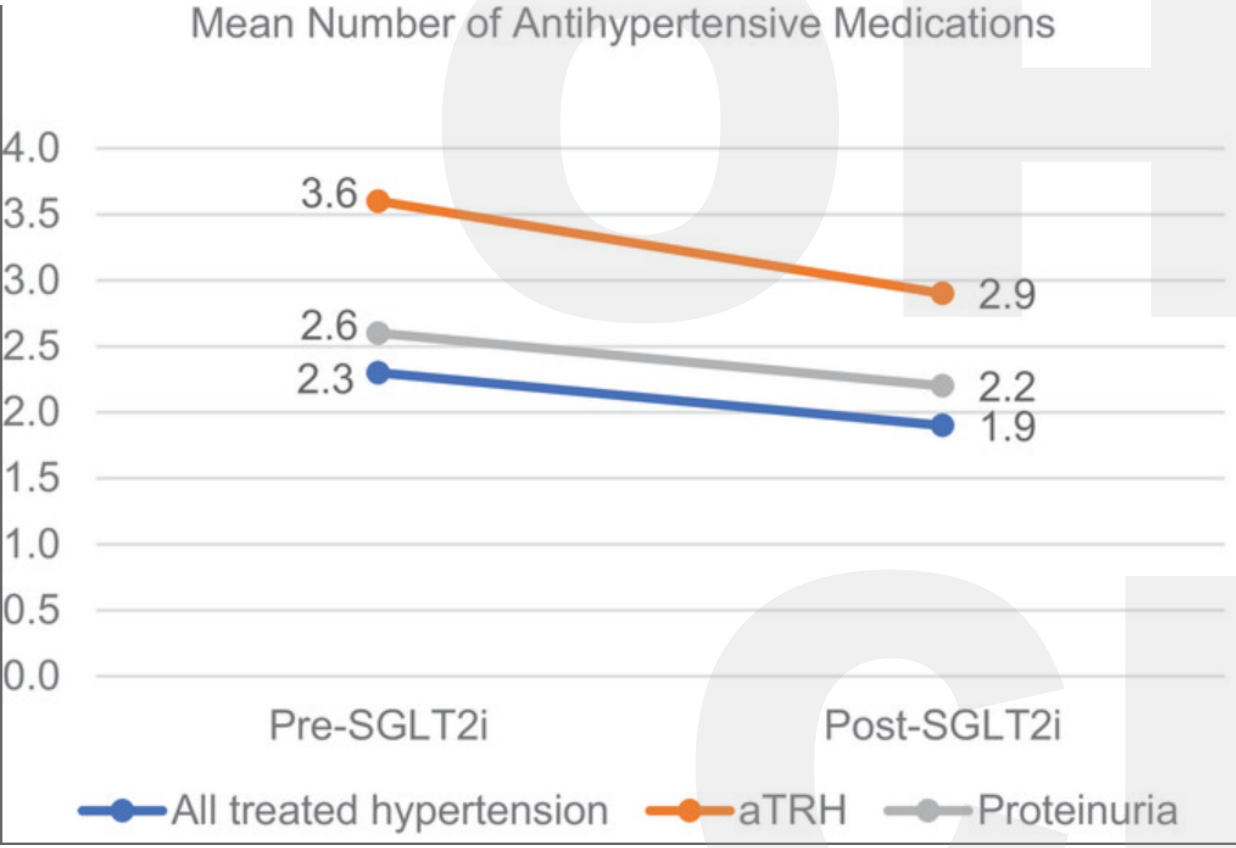
Spending the Cash of Creatinine → Buy GDMT: SGLT-2

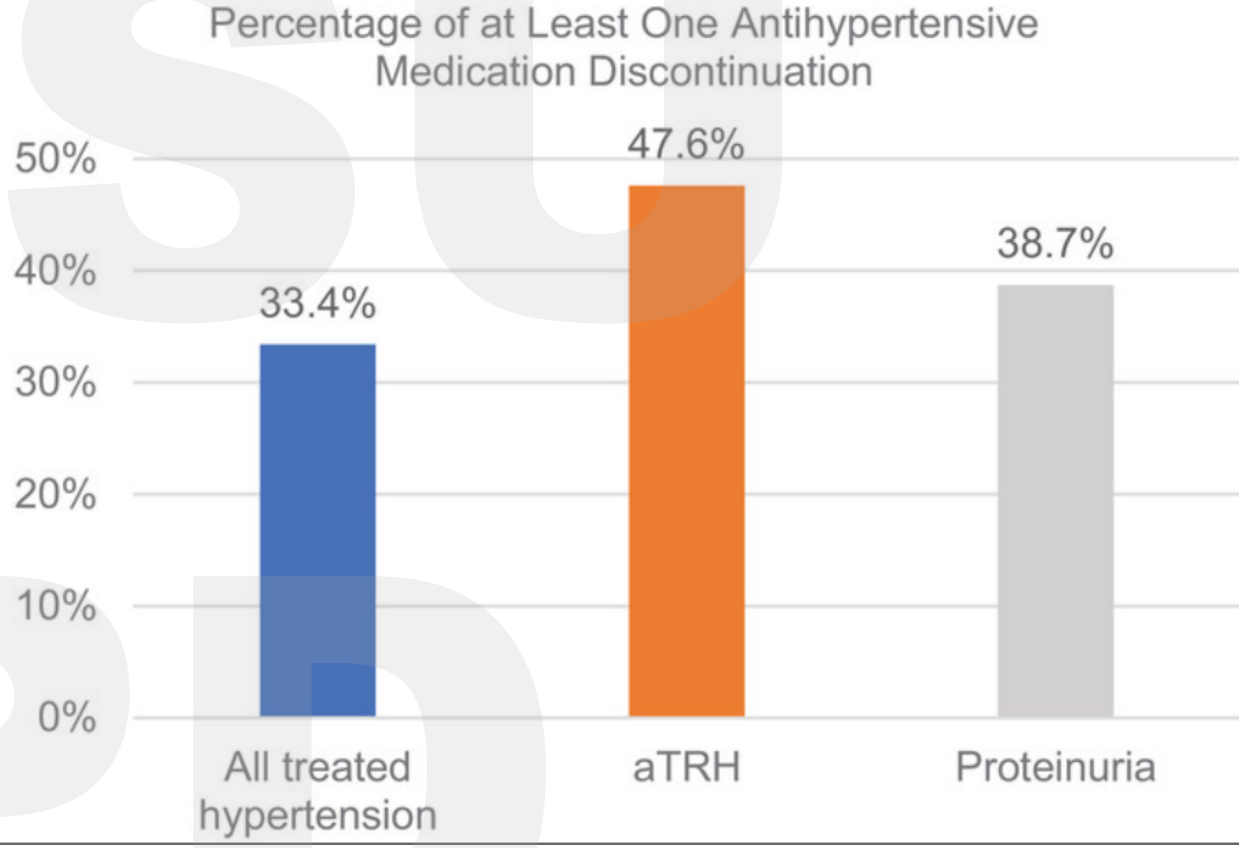




aTRH= apparent tx resistant HTN

Spending the Cash of Creatinine → Buy GDMT: SGLT-2

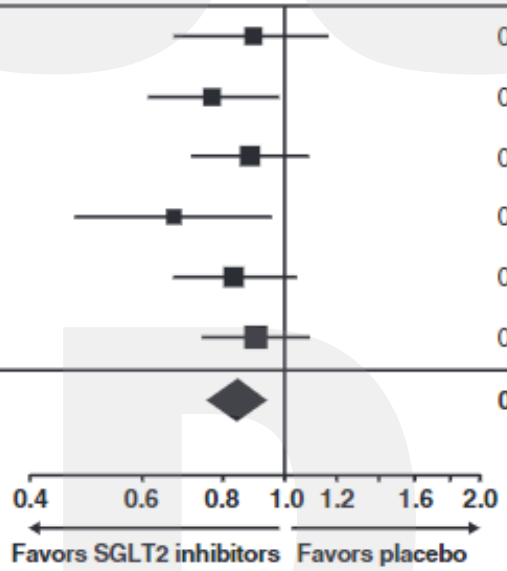




aTRH= apparent tx resistant HTN

SGLT2i either K neutral or improve hyperkalemia risk

	SGLT2 inhibitors		Placebo		
	n/N	Events per 1000 patient-years	n/N	Events per 1000 patient-years	Hazard Ratio (95% CI)
CANVAS Program	137/5795	8.2	85/4347	9.2	0.89 (0.67, 1.17)
CREDENCE	121/2202	21.6	154/2199	27.9	0.77 (0.61, 0.98)
DAPA-CKD	159/1455	56.9	179/1451	65.3	0.88 (0.71, 1.09)
DECLARE-TIMI 58	53/8582	1.6	78/8578	2.3	0.67 (0.47, 0.95)
EMPA-REG OUTCOME	216/4687	17.2	124/2333	20.5	0.83 (0.67, 1.04)
VERTIS CV	291/5493	18.7	157/2745	21.2	0.90 (0.74, 1.09)
Overall (I^2=0.0%; $P_{heterogeneity}$=0.71)					**0.84 (0.76, 0.93)** P<0.001



Circulation. 2022;145:1460–1470

DKA Risk?	Euglycemic DKA is real, relates to a1c>flozin use
BP changes?	BPs tend to go down, but not dangerously
Hypovolemic AKI? Falls? Fx?	No signal for this, look for other causes
Amputations?	Probably not real, ris
UTI?	Not seen in RCTs, simple UTI vs Hx Pyelo?
Fungal infections	Risk is real, relates to BMI: talk about hygiene, weight loss

Spending our Creatinine Cash

Achieve Euvolemia/Normotension

Maximize GDMT

Goal: Slow eGFR Decline

Goal: Stop MAKE/MACE events

Use of SGLT2i Versus DPP4i as an Add-On Therapy and the Risk of PAD-Related Surgical Events (Amputation, Stent Placement, or Vascular Surgery): A Cohort Study in Veterans With Diabetes

Background

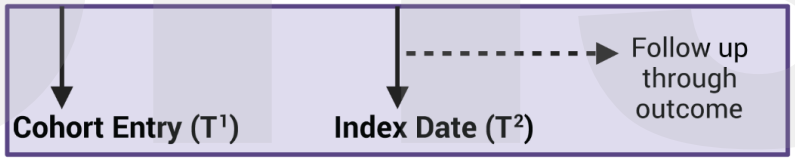
Among high risk Veterans, is the use of SGLT2i as an add-on therapy associated with an increased risk for peripheral artery disease (PAD)-related events when compared to DPP4i?

Our national cohort consisted of **U.S. Veterans with diabetes** who received care from the Veterans Health Administration between **10/01/2001 and 12/31/2021**

Retrospective Cohort Study Design

Filled a first prescription for metformin, insulin, or sulfonylurea

New prescription fill of DPP4i or SGLT2i



Measured Outcomes

- **Amputation**
- **Stent**
- **Bypass**

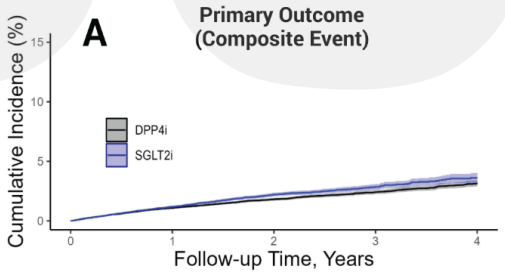
Primary Outcome:
Time to 1st surgical event *(composite)*

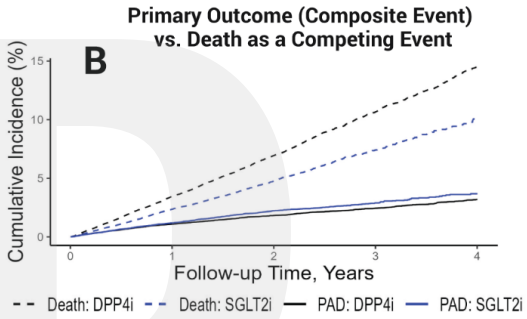
Secondary Outcome:
Time to each individual event *(separate)*

A **Cox proportional hazards model** for time-to-event analysis compared the risk of a PAD-related event between SGLT2i and DPP4i in a **propensity score-weighted cohort,** with a competing risk of death and allowing for events to occur up to 90 days or 360 days after stopping SGLT2i.

Results

Median Age: 69 years old
Median HbA_{1c} : 8.4%
Median Time with Diabetes: 10 years





DPP4i Episodes:
45% - saxagliptin
34% - alogliptin
15% - sitagliptin
6% - linagliptin

SGLT2i Episodes
94% - empagliflozin
4% - canagliflozin
2% - dapagliflozin

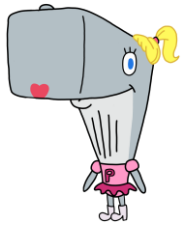
Number of Events:
874 - SGLT2i users
780 - DPP4i users

The cause-specific aHR for SGLT2i users compared to DPP4i users:
1.18 [1.08-1.29]

Summary:

The addition of SGLT2i as an add-on therapy was associated with an increased risk of amputations, stent placement, or revascularization surgeries compared to DPP4i.

DPP4i, dipeptidyl peptidase 4 inhibitor; SGLT2i, sodium-glucose cotransporter 2 inhibitor



Clinical Pearls via Case

Heart Failure and Edema Costs in Patiromer and Sodium Zirconium Cyclosilicate Users

KIDNEY360
Accessing Our World From Every Angle

Methods and Cohort

Retrospective study
2019-2021

Event rates and mean costs derived from de-identified Clinformatics Data Mart (CDM) Database

Model to estimate adjusted economic impact of potassium-binders on:
HF hospitalizations
Edema events
Prescription costs

Outcomes

HF hospitalization rate
Patiromer 25.1 versus SZC 35.8 hospitalizations
Difference of 10.7 events / 100 person-years (95% CI: 2.6-18.8)

Edema hospitalization or ED events
Patiromer 3.4 versus SZC 7.1
Difference of 3.6 events / 100 person-years (95% CI: 1.7-7.1)

Respective costs PPPY*	Patiromer	SZC
HF hospitalization & edema	$8,526	$12,622
Potassium-binder cost	$10,649	$7,981
Total	$19,175	$20,603

Mean HF hospitalization, edema events and 30-count prescription cost savings
Patiromer = $1,428 PPPY (95% CI: –$1,508 to $4,652)

*adjusted to 2021 US dollars

HF= heart failure, SZC= sodium zirconium cyclosilicate, ED= emergency department, PPPY= per person per year

Conclusions: Hospitalization and ED costs offset the difference in drug costs. Model outcomes were driven by HF hospitalization cost and least influenced by edema ED visit cost. A limitation was that the CDM data extract used for event costs may differ from the CDM extract used for event rates.

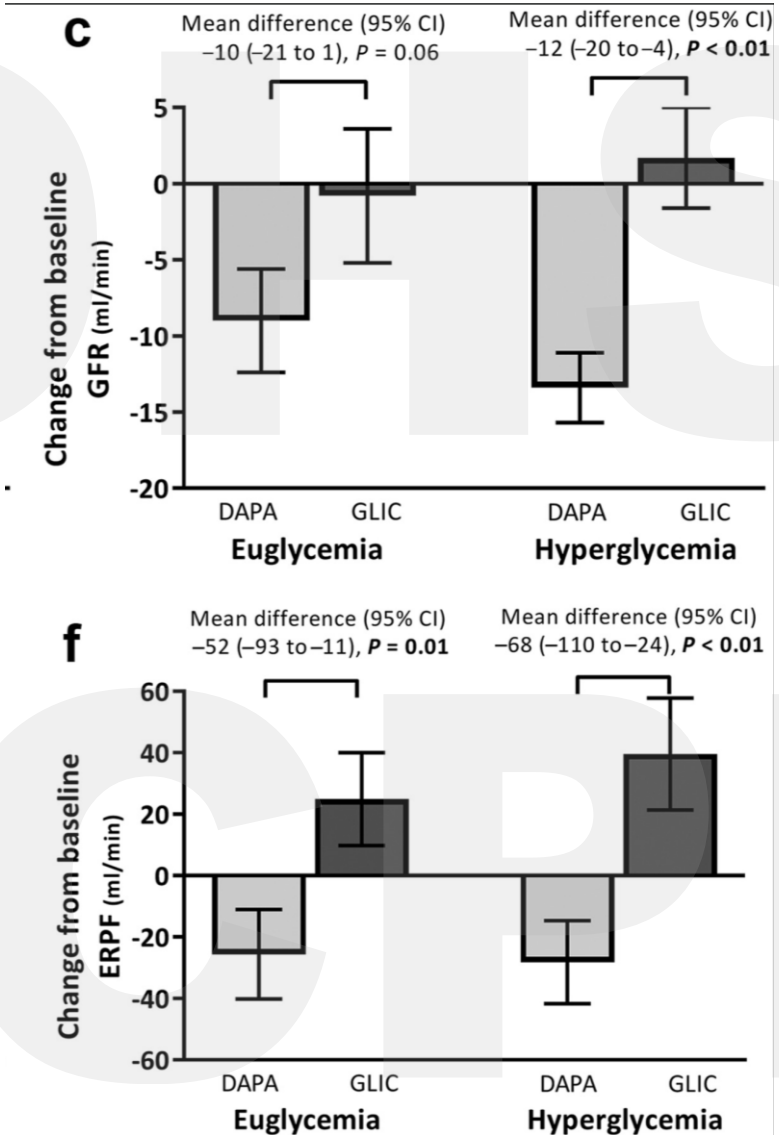
Nathan Kleinman, Jennifer Kammerer, Charuhas Thakar. ***Heart Failure and Edema Costs in Patiromer and SZC Users***. *Kidney 360*. DOI: 10.34067/KID.0000000000000483

Visual Abstract by Brian Rifkin, MD

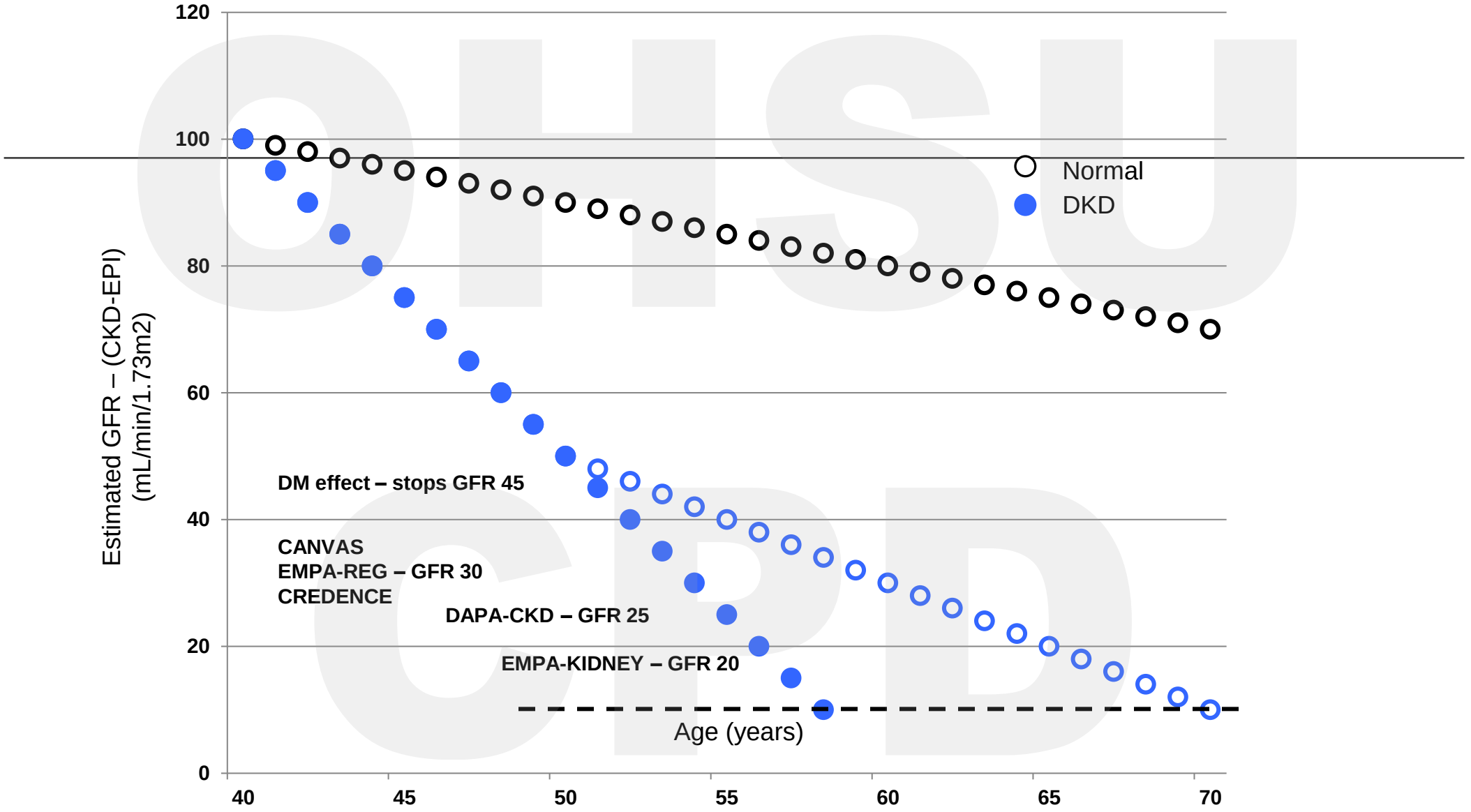
400mg Na per 5 g Lokelma(Sodium Zirconium Cyclosilicate)

Spending the Cash of Creatinine

Buy GDMT: SGLT-2



Advanced CKD – Can I still start SGLT2i?



DAPA-CKD – subgroup continuing SLGT2i when starting dialysis – RRR mortality 21%

Spending the Cash of Creatinine → Buy GDMT: ACEi/ARB

	Baseline	Follow-up	p-value	Baseline	Follow-up	p-value
CVP (mmHg)	18 ±7*	11 ±8**	< 0.001	12 ±6	8 ±5	< 0.001
PCWP (mmHg)	25 ±7′	19 ±5′	< 0.001	24 ±7	18 ±5	< 0.001
CI (l/min/m^2)	2.0±0.8†	2.7±0.7‡	< 0.001	1.8 ±0.4	2.4 ±0.5	< 0.001

GFR Down

Less K in urine

Normokalemia

Small intestine secretes more K

More K in stool