Metabolic alchemy: Transformative interventions in acute kidney disease

APCN x TSN 2025

23rd Asian Pacific Congress of Nephrology

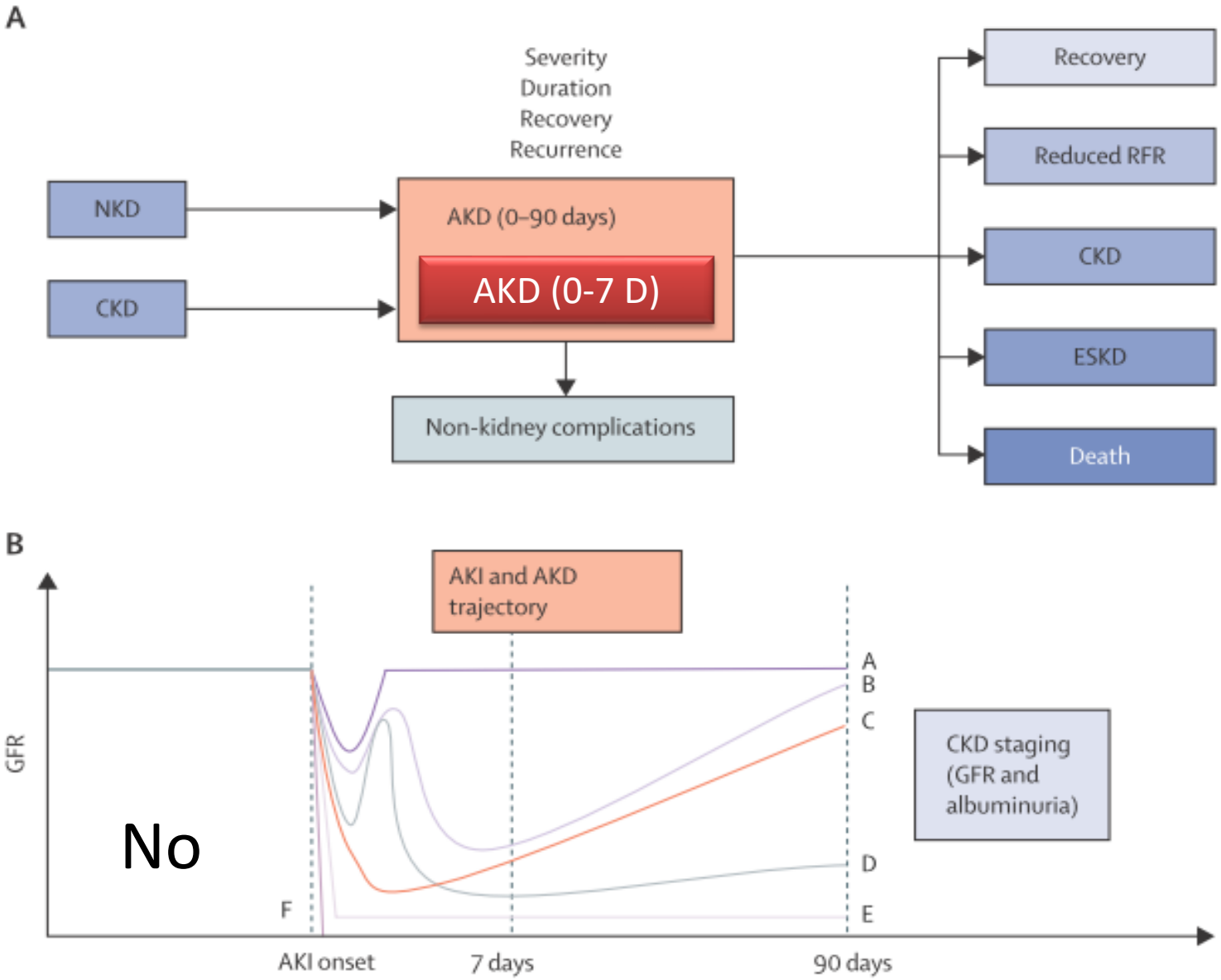
Gene, Immunology, Vast, MEtabolism at its Finest!

吳允升 Vin-Cent Wu

Taipei, Taiwan, on behalf of NSARF

No conflicts of interests to be disclosed

AKI, AKD to CKD



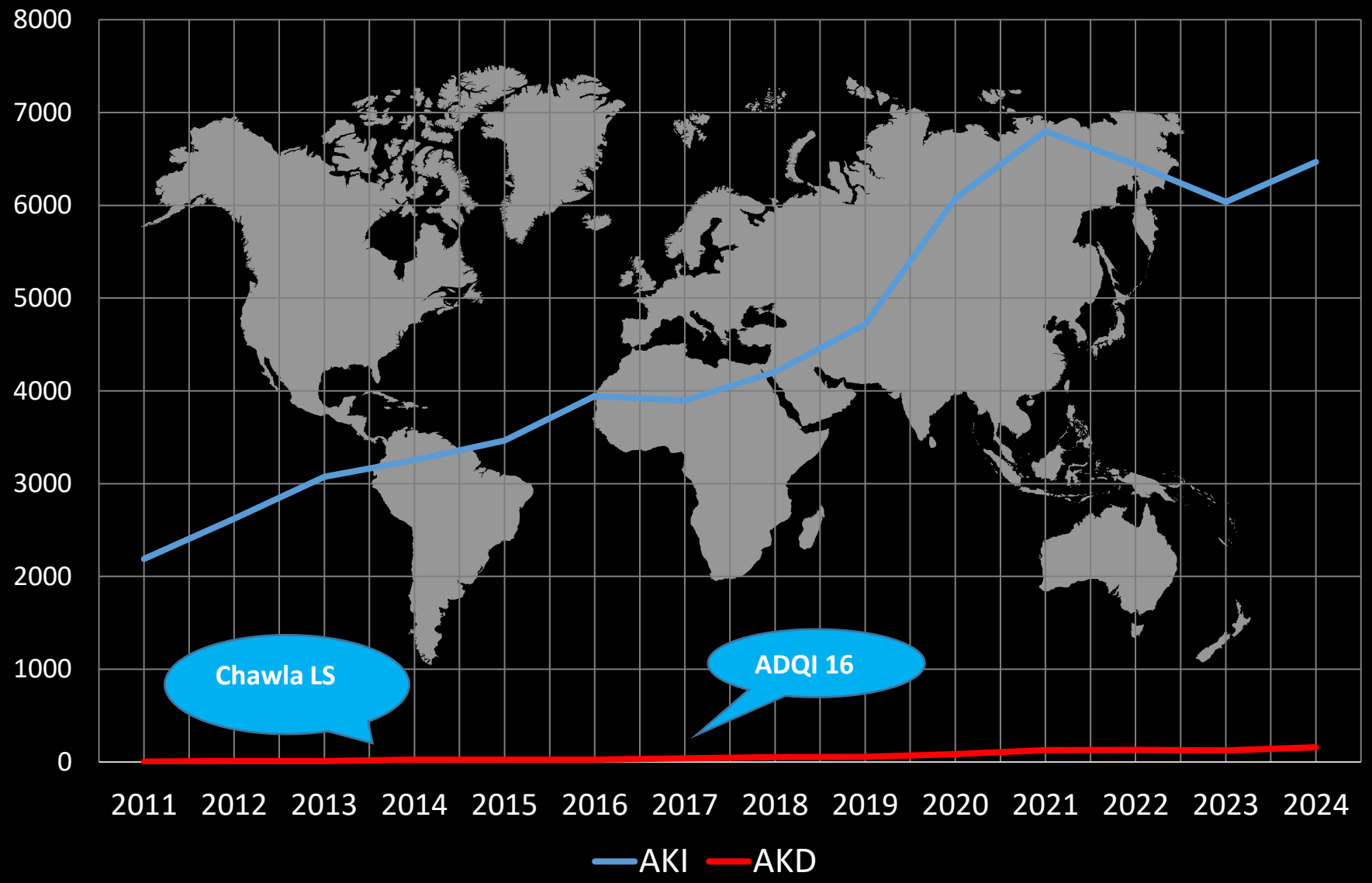
Lancet 2025; 405: 241–56

Why do we rephrase a comprehensive AKD care?

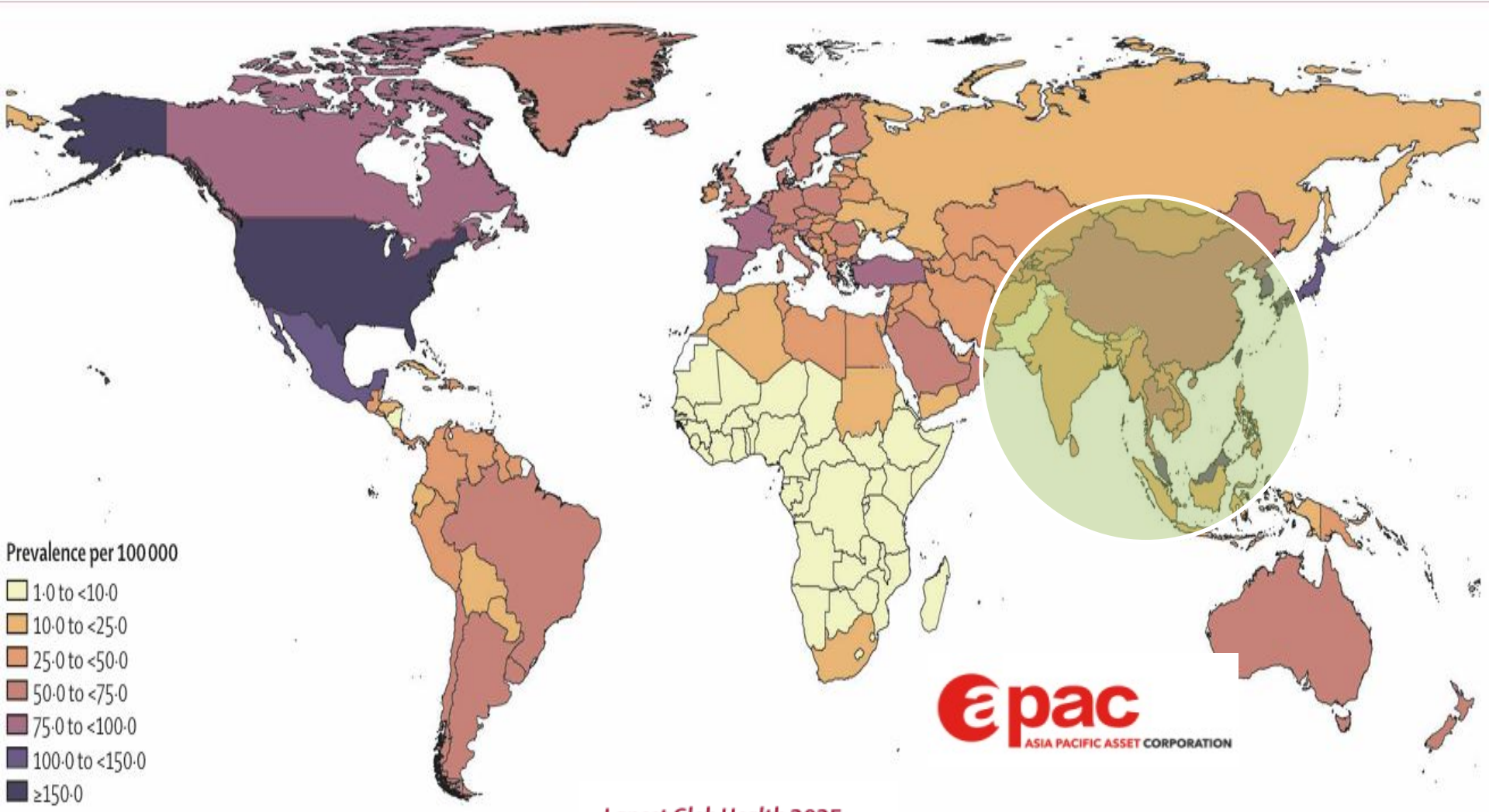
TRB

TWICE
I'm gonna be a star

AKI and AKD study from Pubmed



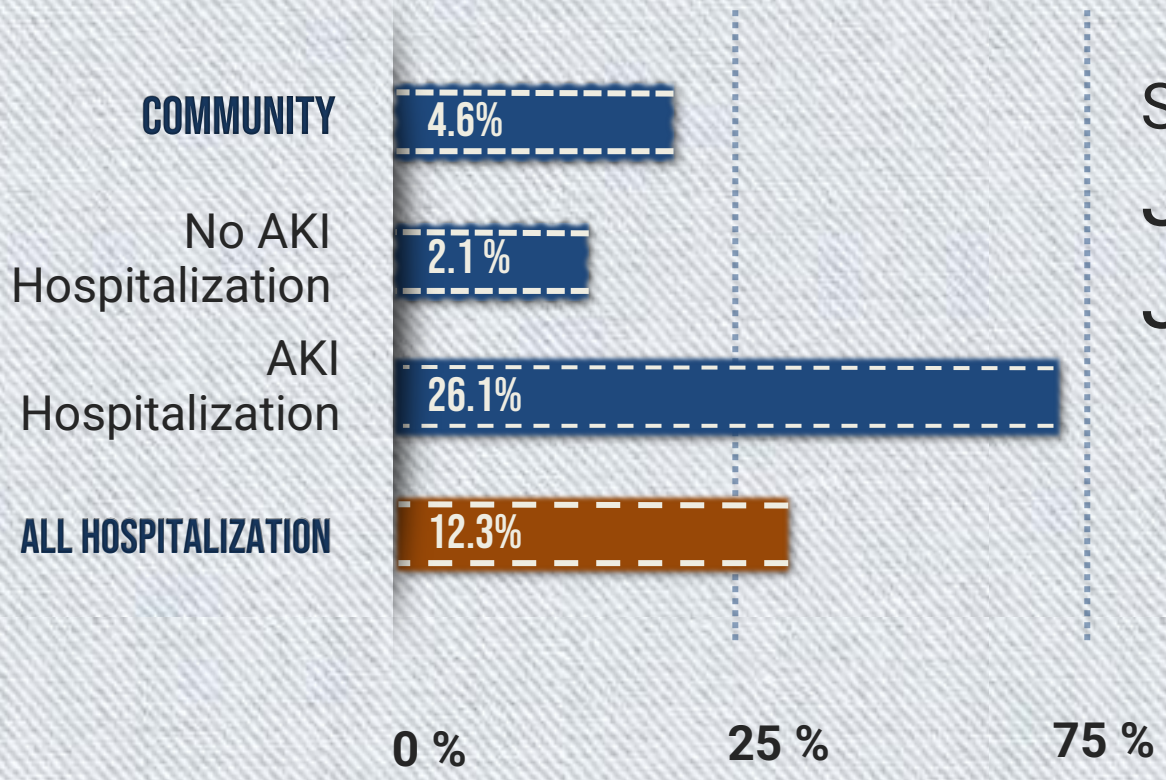
Global age-standardised prevalence of RRT



Lancet Glob Health 2025;
13: e1378–95

THE PREVALENCE OF AKD

1,031,234 PATIENTS (21 STUDIES)

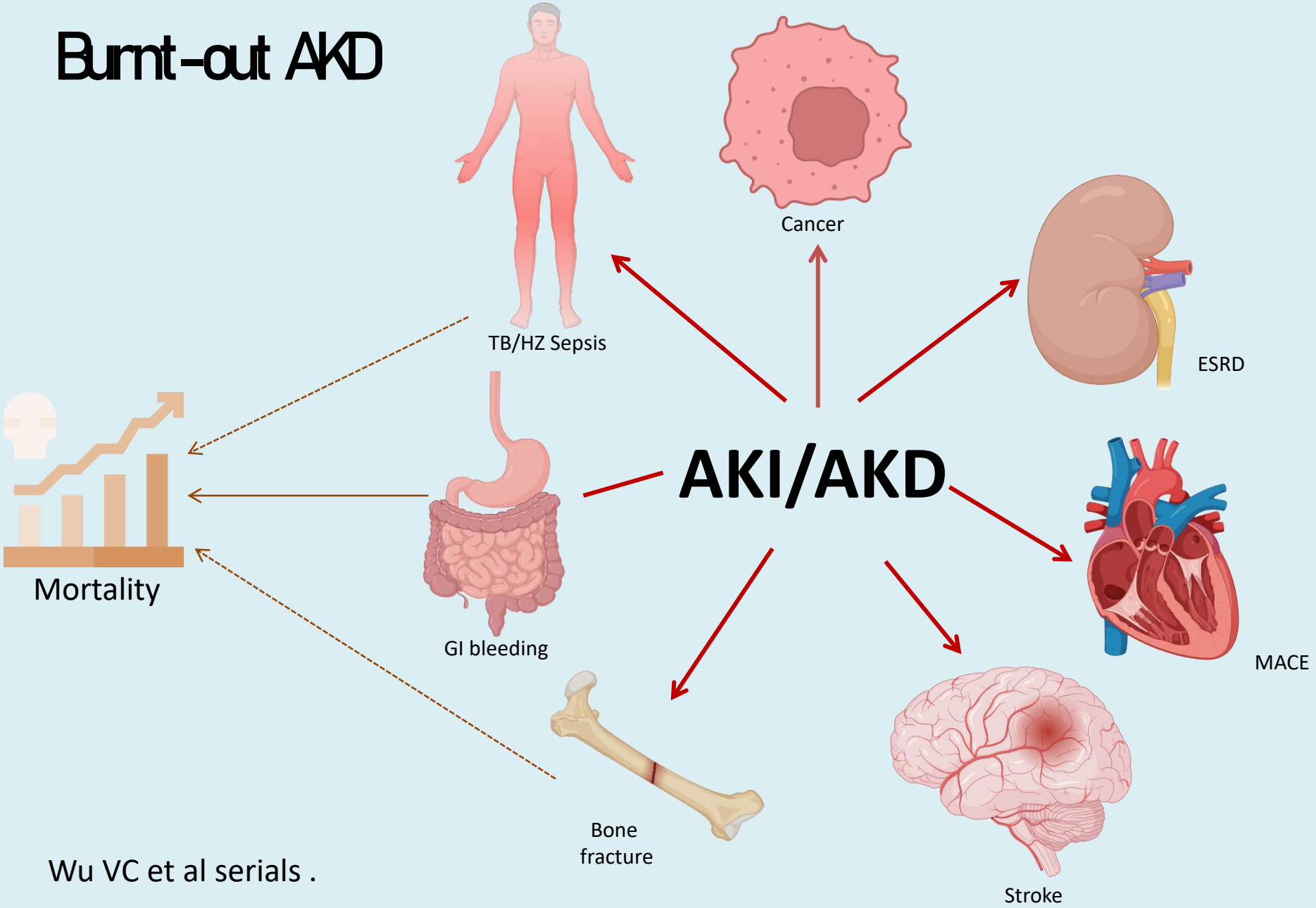


Systematic review

January 2000-January 2022

2022 Wu VC et al. eClinMedicine

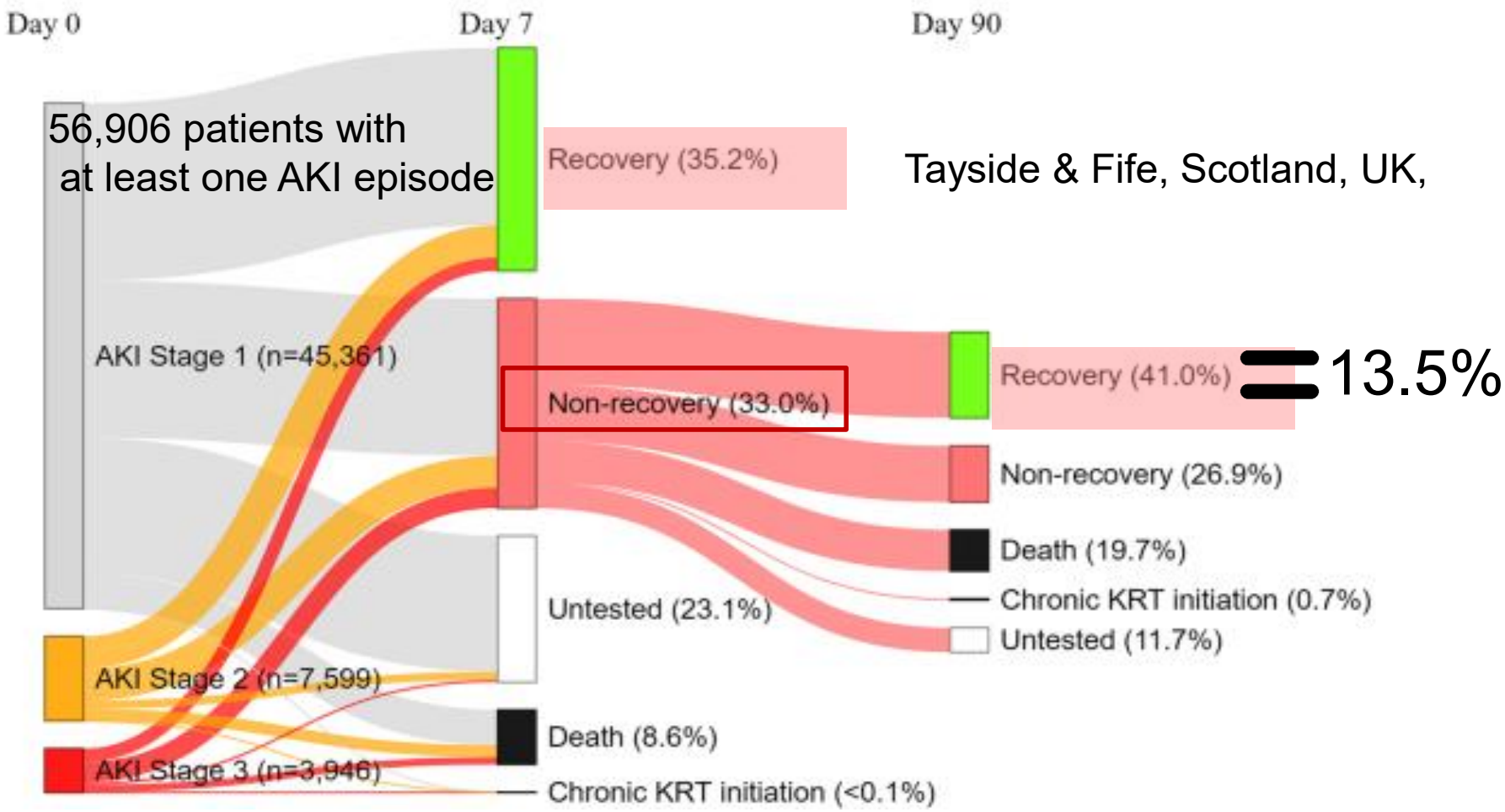
Burnt-out AKD



Wu VC et al serials .

SCIENTIFIC REPORTS JASN Journal of the American Heart Association OPEN ACCESS PLoS one BioMed Research International CRITICAL CARE JBMR Cancer Research Clinical Oncology CJASN

High incidence of Late recovery



Wang *et al. BMC Medicine* (2022) 20:229

Management of patients with dialysis-requiring AKI

Low (<10%) recovery phenotype, guideline

Re dialysis

Consideration for early (30 d) transition to ESRD diagnosis with appropriate shift in management

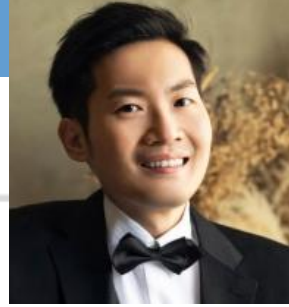
Patients with 3 or more of the following:

1. Advanced baseline CKD (eGFR <15 or eGFR <30 with A3 albuminuria)
2. Older age (>75 yr)
3. Significant comorbidities (decompensated liver or heart failure)
4. Prolonged duration of dialysis dependence (>90 d)

JASN 36: 926–939, May, 2025

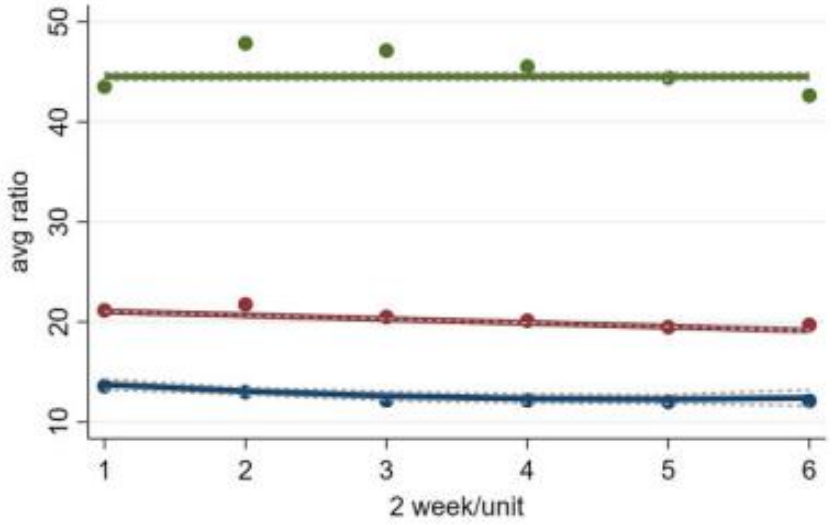
Clinical Kidney Journal, 2025, vol. 18, no. 6, sfaf175

https:/doi.org/10.1093/ckj/sfaf175
Advance Access Publication Date: 29 May 2025
Original Article



ORIGINAL ARTICLE

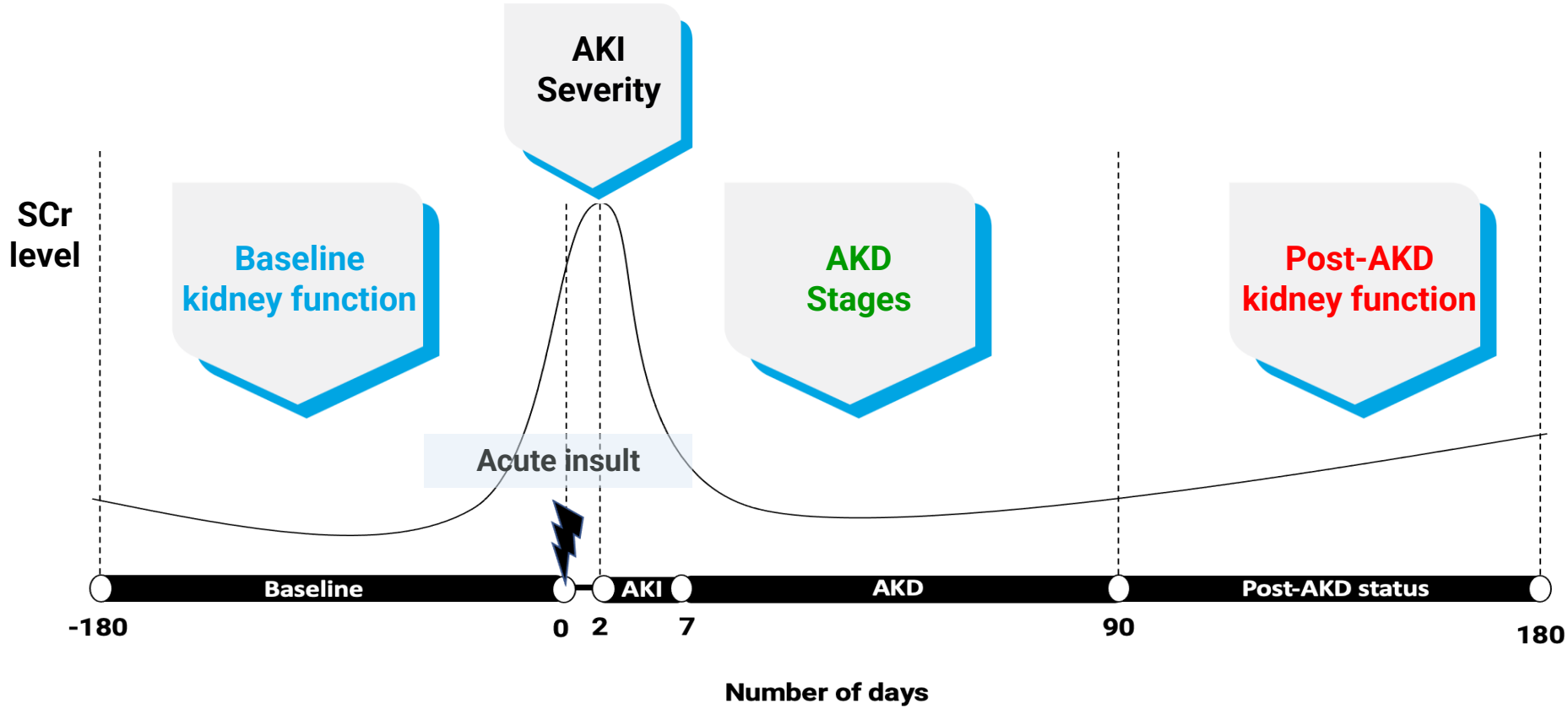
Trajectories of urea–to–creatinine ratio and risk of clinical outcomes in survivors of acute kidney disease: a population-based study



9717 AKD survivors were enrolled with a mean follow-up of 1.3 ± 0.9 years.

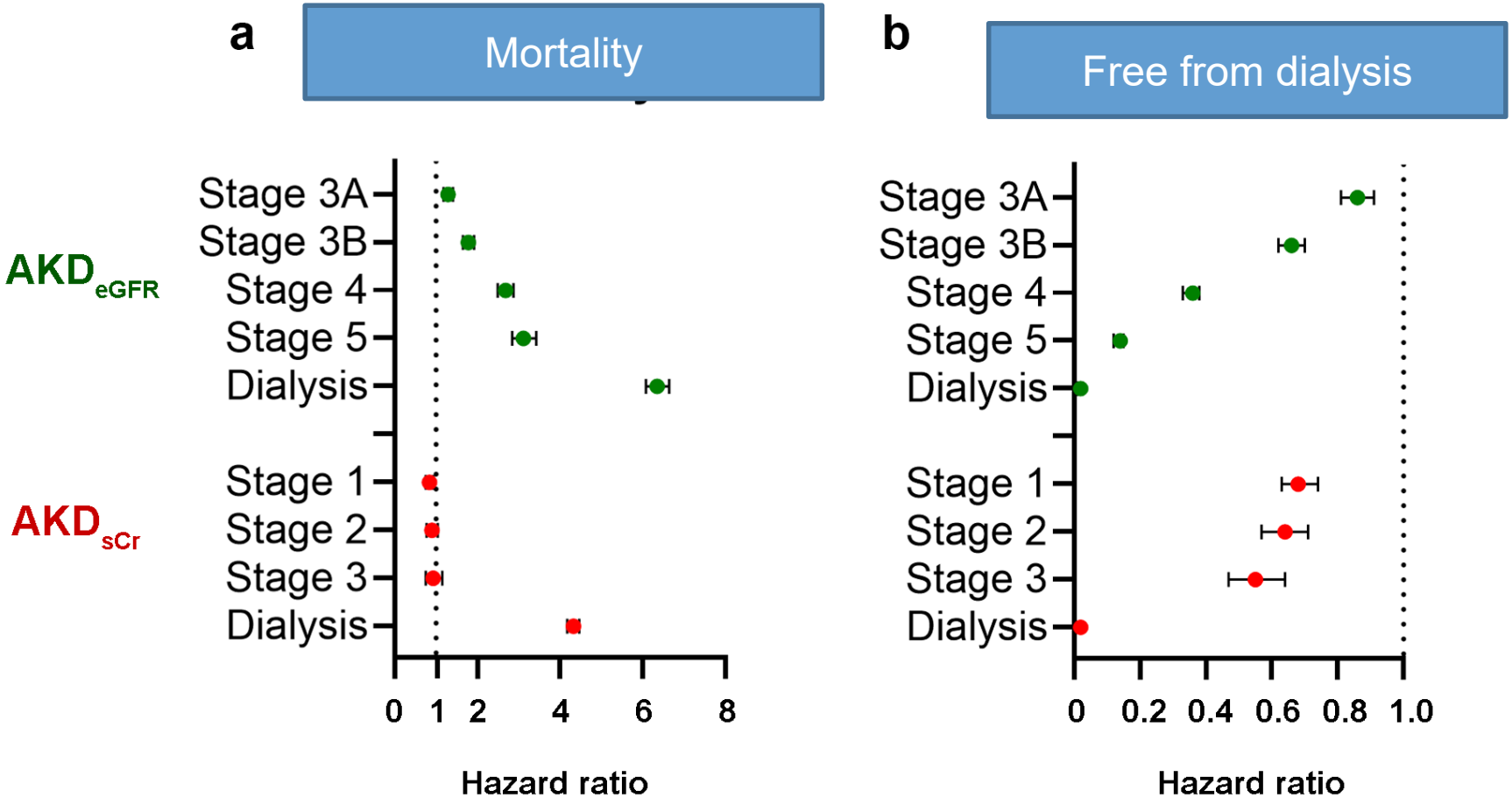
Pan, Wu et al, Clinical Kidney Journal, 2025, vol. 18, no. 6, sfaf175

Which renal function status plays a key role in assessing prognosis after dialysis-requiring AKI?



2024 Pan , Wu et al, JAMA NETW

AKD stages and long-term Mortality / sustained renal recovery



40,849 hospitalized patients, recovery AKI-D

2025, Pan , **Kidney Medicine**

At what time points does renal function status play a key role in assessing adverse outcomes in patients with AKI-D?

Population-based study

Dialysis-requiring AKI patients (AKI-D) survivors

Post-AKD kidney function follow up

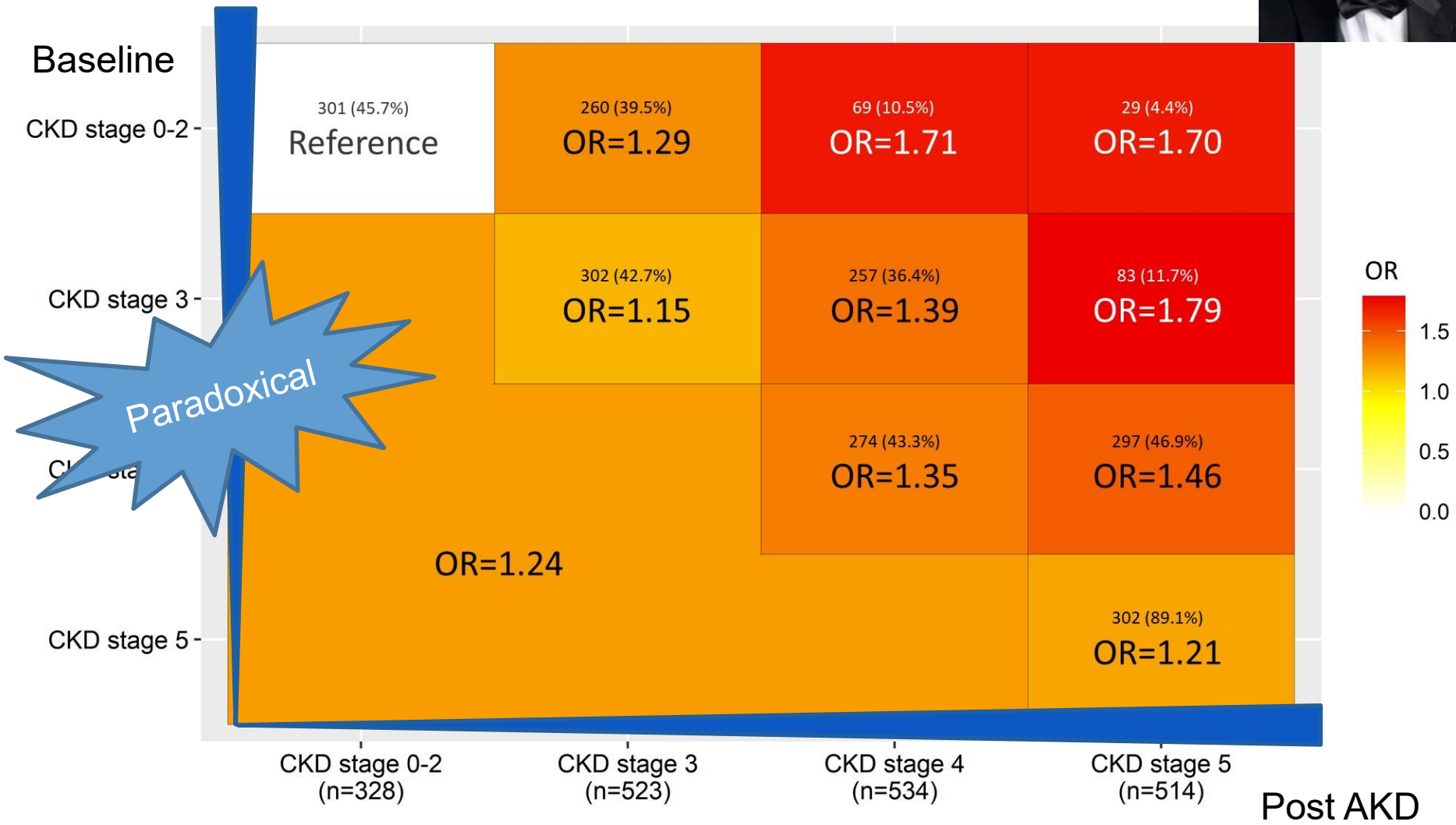
n = 6703

HR/sHR		All-cause mortality	ESKD	MACE	Readmission
Baseline CKD stage	3	0.85*	2.43***	1.36*	1.93
	4	0.73***	3.98***	1.60**	1.91
	5	0.58***	6.09***	1.40*	1.86*
AKD stage	1	1.00	1.85*	0.96	1.04
	2	0.59*	1.67	0.42	1.00
	3	1.22	1.17	0.95	1.12
Post-AKD CKD stage	3	1.18*	19.33**	1.49**	1.06
	4	1.55***	90.54***	1.52*	1.23**
	5	1.51***	326.49***	1.96***	1.64***

Conclusions: Baseline together with post-AKD kidney function could predict long-term prognosis of AKI-D survivors. Further coordination of care to reduce post-AKD-CKD severity was warrant.

2024 Pan, Wu et al.JAMA Netw Open

Risk of Mortality or Major Adverse Cardiac Event



Patients who could survival to AKD

2024 Pan, Wu et al.JAMA Netw Open

AKD ratio and clinical outcomes

NSARF
NTUH Surgery Intensive Care Unit Acute Renal Failure Group

N= 51,529 incident AKI-D

N= 7,564 weaned from AKI-D and survival more than 90 days

7564

from Jan, 2015 to Dec, 2018

1.2±0.9 years Follow-up

Scre ratio and clinical outcomes

AKD stages

0	97.3%
1	1.4%
2	1.2%
3	0.3%

AKD Ratio

Dip	44.2%
1-1.8	46.7%
≧1.8	9.1%

Hazard Ratio

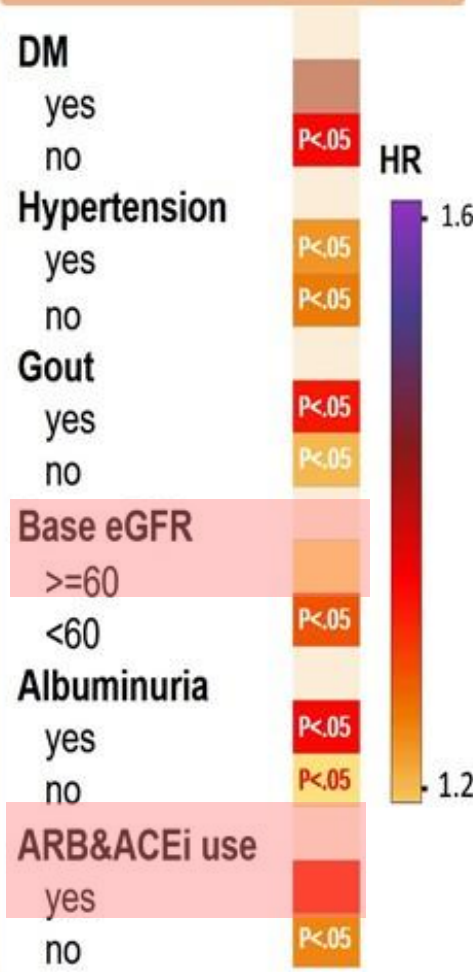
Mortality
Dip, 1.17
≥1.8, 1.31

win

Redialysis
Dip, 0.33
≥1.8, 2.26

MACE+ Mortality
Dip, 1.09
≥1.8, 1.31

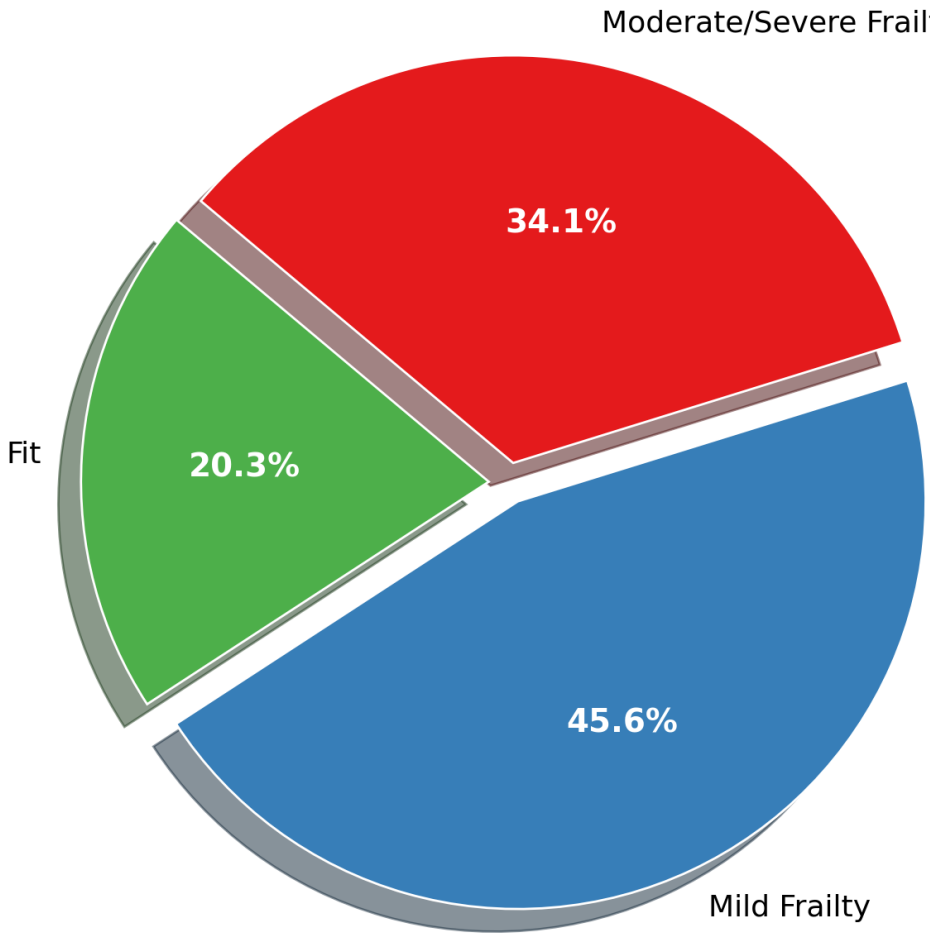
Sensitivity Analysis All-cause mortality



2025 Wu et al.

Frailty in AKD patients

N=18,763 AKD



79.7%

2025 Chen, Wu, unpublished data

The Frailty Factor: Your Risk After Acute Kidney Injury

FRAILTY
(MODERATE TO SEVERE)

HIGHER RISK OF DEATH

+17% Increased risk of all-cause mortality.

HIGHER RISK OF CARDIOVASCULAR EVENTS

+37% Increased risk of MACE (e.g., heart attack, stroke).

HIGHER RISK OF KIDNEY EVENTS

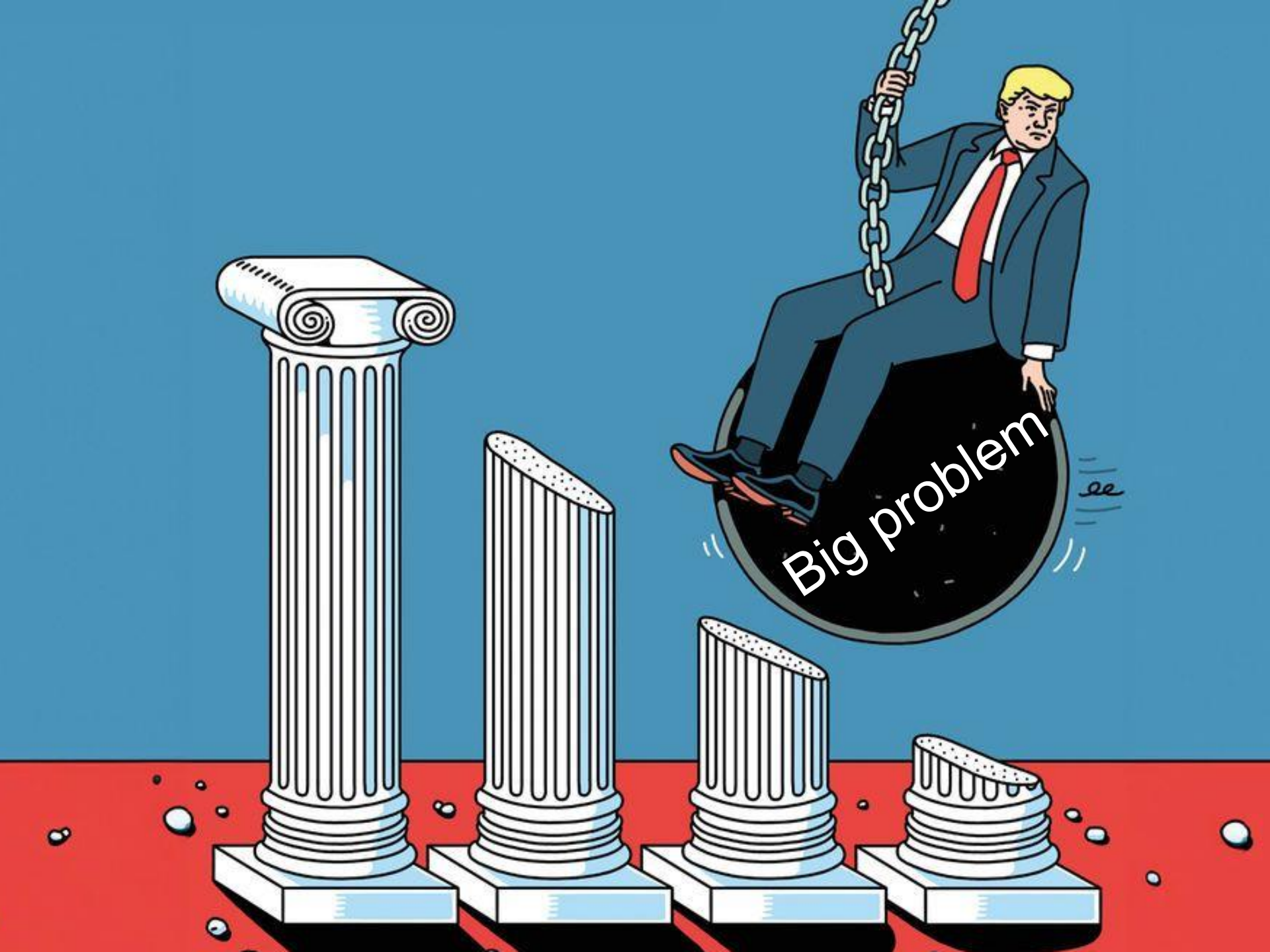
+ N/A Increased risk of MAKE (e.g., dialysis re-initiation).

ASSESS FRAILTY TO IMPROVE CARE

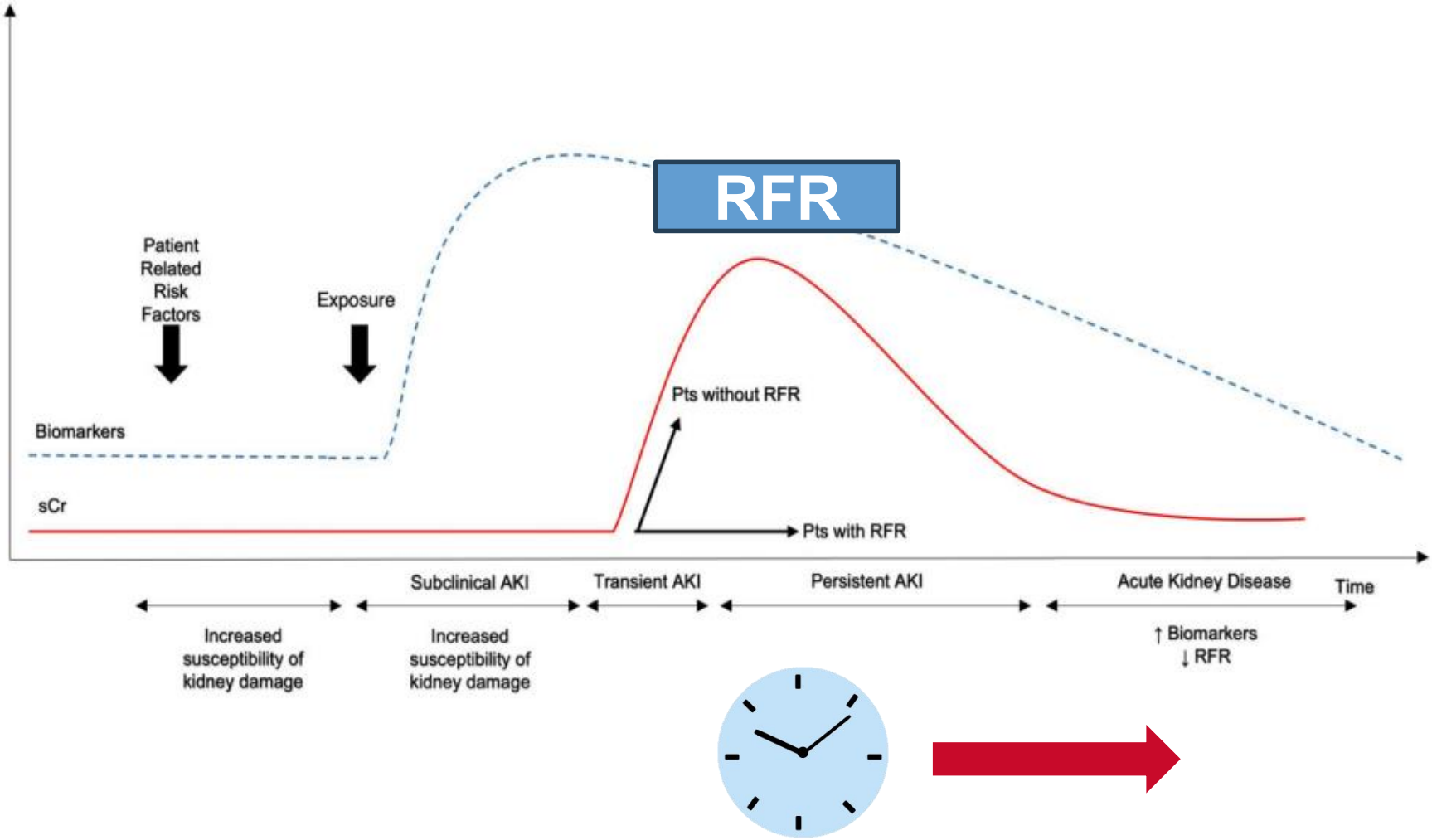
18,763

Retrospective cohort study
AKI requiring dialysis, 2015-2022
Frailty (Fit, mild, moderate or severe)

2025 Chen, Wu, unpublished data


Big problem

AKD and kidney function reserve



Clinical Kidney Journal, 2023, vol. 16, no. 11, 1813–1823

Kidney Risks of Contrast Media After Severe AKI

CONTRAST INCREASES KIDNEY EVENT RISK

+37%
Redialysis Hazard
After statistical adjustment

+11%
Persistent Dysfunction Hazard
After statistical adjustment

A NEW eGFR RISK THRESHOLD

1

36
mL/min/1.73 m²

Risk surges below this eGFR in contrast-exposed patients

Much higher than unexposed patients (22.8)

RISK IS HIGHEST SOON AFTER RECOVERY

The greatest risk occurs when contrast is given shortly after

2

HIGHEST RISK — 70 Days

Dialayis Stops

Risk Declines

CERTAIN PATIENTS MORE VULNERABLE

CKD Pre-existing Chronic Kidney Disease

Taking ACEIs/ARBs

3 **Amplified excess risk of persistent dysfunction**

23,263 after AKI-D (mean age, 69.6 years; 58.5 % men), 1 551 (6.7 %) contrast

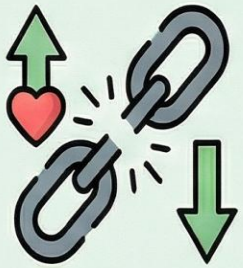
Lin , Wu et al , 2026 submission,

Metformin After Severe Kidney Injury: A Lifesaver?

11,576 patients (mean age 69.5, 44.7% male), 3,487 (30.1%) Male

LOWER RISK OF DEATH

1

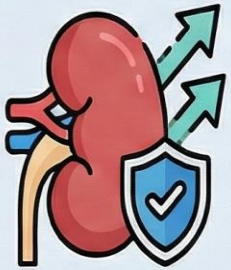


11% LOWER RISK

of all-cause mortality
mpared to non-users.

BETTER KIDNEY OUTCOMES

2



22% LOWER RISK

of major kidney events,

31% LOWER RISK

of needing dialysis again.

NO INCREASED ACIDOSIS RISK

NO SIGNIFICANT INCREASE

in the risk of metabolic acidosis, a primary safety concern.

Chiang , Wu et al , 2026 submission,

The traditional Four Pillars of AKD Therapy

Four Pillars of AKD Therapy, Bundle Protection,

A total of 22,566 patients with AKI-D (mean age 68.2 years; 58.9% male

AKD: The CKM Risk Accelerator

BEFORE AKD: Scattered Risks

Cardiovascular Disease (3.0%)

Chronic Kidney Disease (7.5%)

Diabetes (6.8%)

SCATTERED RISKS: Only **1.5%** have all three

Metabolic issues often a primary driver of risk.

AKD EVENT

Cardiovascular Disease (30.6% - 10x Increase)

Chronic Kidney Disease (63.0% - 8x Increase)

Diabetes (34.2% - 5x Increase)

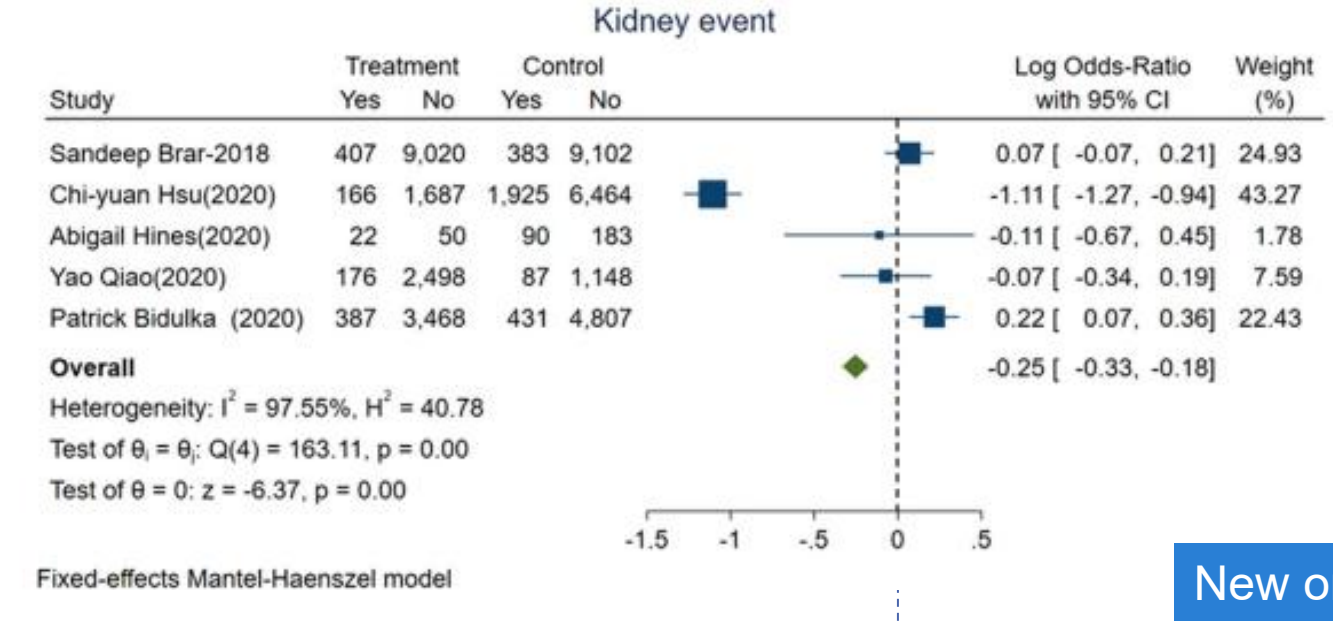
DANGEROUS CLUSTER: **11.4%**

The Kidney becomes the core driver, CKM accelerating cardiovascular and metabolic decline.

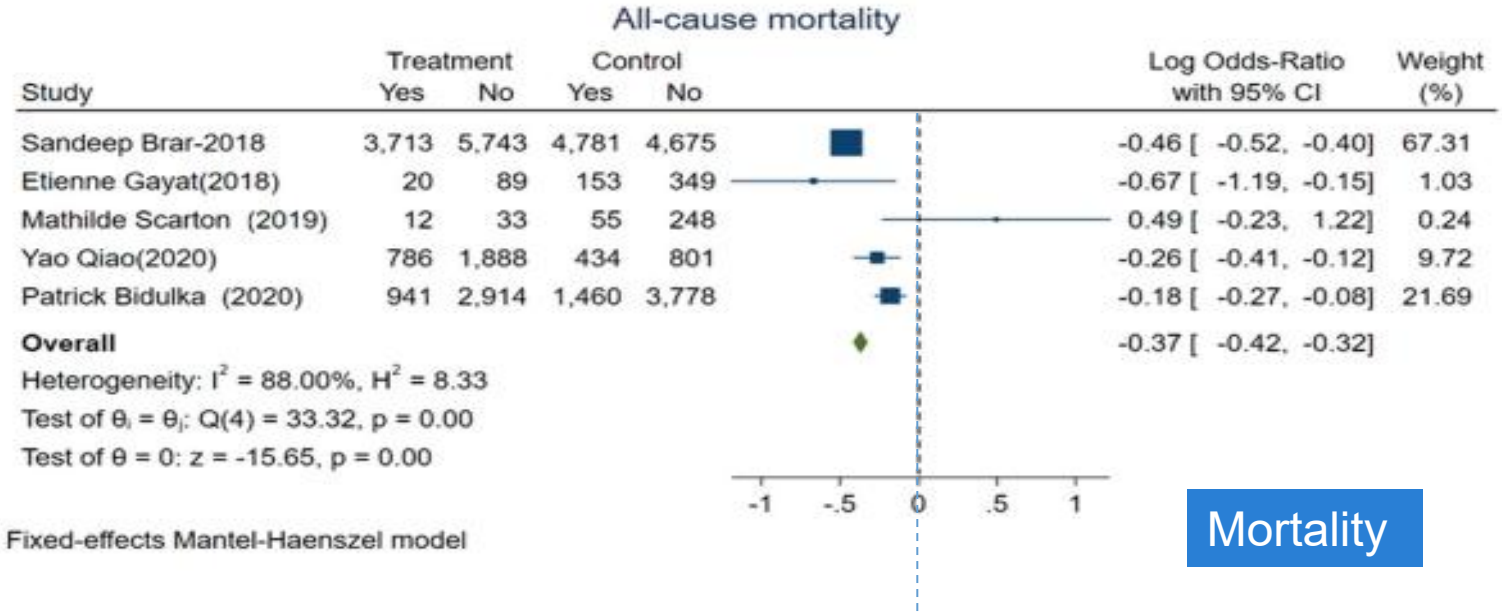
2025 Sung, Wu, unpublished data

Source: Aggarwal R, et al. *JAMA*. 2024

AKD aided by the use of ACEi/ARB



New onset AKI



Mortality

July 2021 | Volume 12 | Article 665250 Chen JY et al. Front. Pharmacol., 20 July 2021 |

Outcome of GLP-1RA users in CKD

Study Design

systematic review and meta-analysis
GLP-1RA vs. **placebo**
RCTs ~ May 25, 2024

- **Glycemic control trials:** LIRA-RENAL, AWARD-7, PIONEER 5
- **CVOTs:** SUSTAIN-6, LEADER, HARMONY, PIONEER 6, REWIND, EXSCEL, FREEDOM-CVO, SELECT
- **Renal outcome trials:** FLOW

baseline **eGFR <60** cc/min/1.73m^2

17,996

Findings

Composite renal outcome

10 trials, n=15,164

OR 0.85 (0.77-0.94)

GRADE ⊕⊕⊕⊕ High

Composite CV outcome

11 trials, n=16,368

OR 0.86 (0.74-0.99)

GRADE ⊕⊕⊕⊖ Moderate

All-cause mortality

7 trials, n=11,949

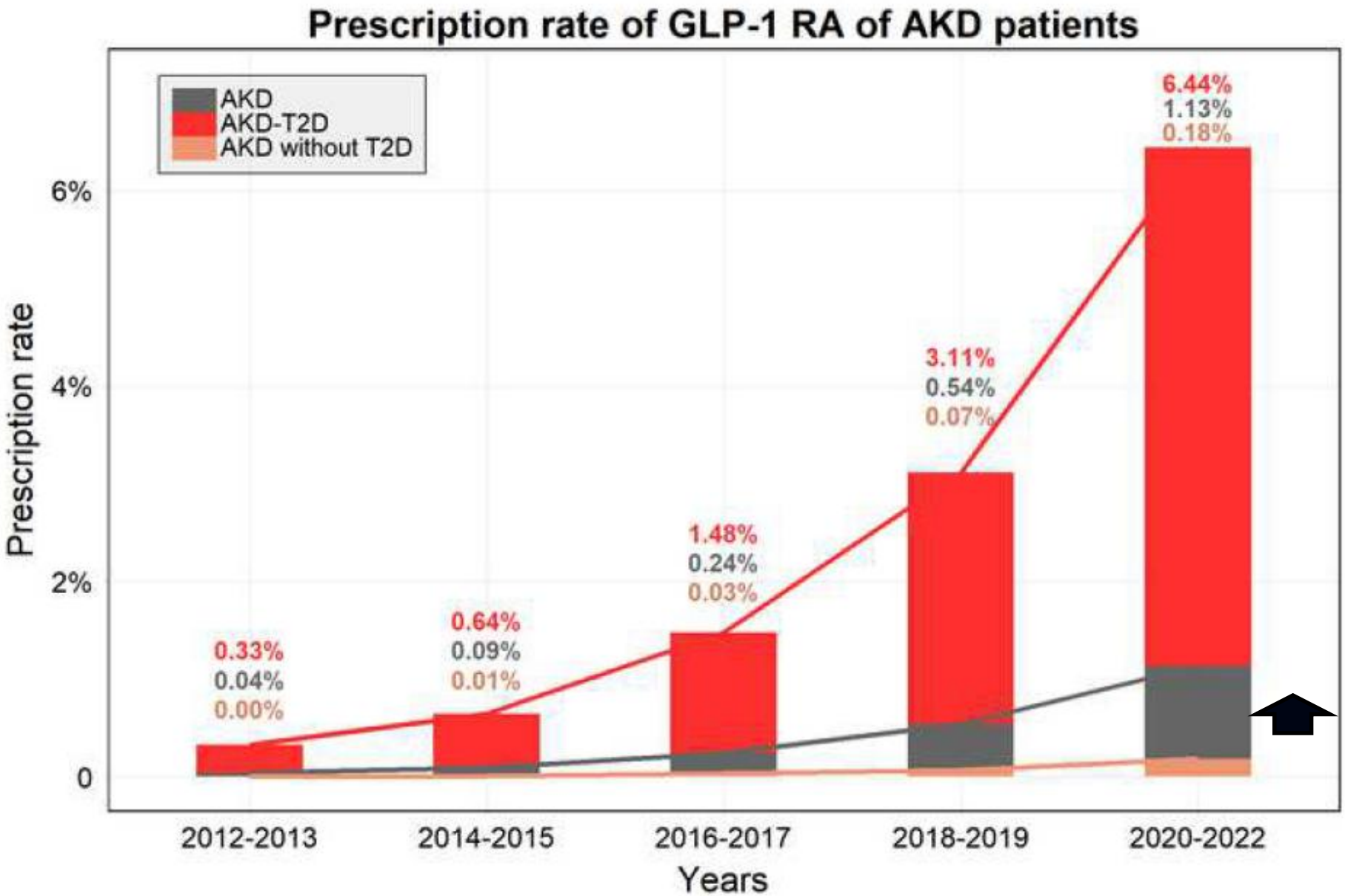
OR 0.77 (0.60-0.98)

GRADE ⊕⊕⊕⊖ Moderate

Sensitivity analysis: restricting to human GLP-1 backbone trials

composite renal	**OR 0.83 (0.75-0.92)**
all-cause mortality	**OR 0.70 (0.55-0.89)**
composite CV	**OR 0.78 (0.70-0.87)**

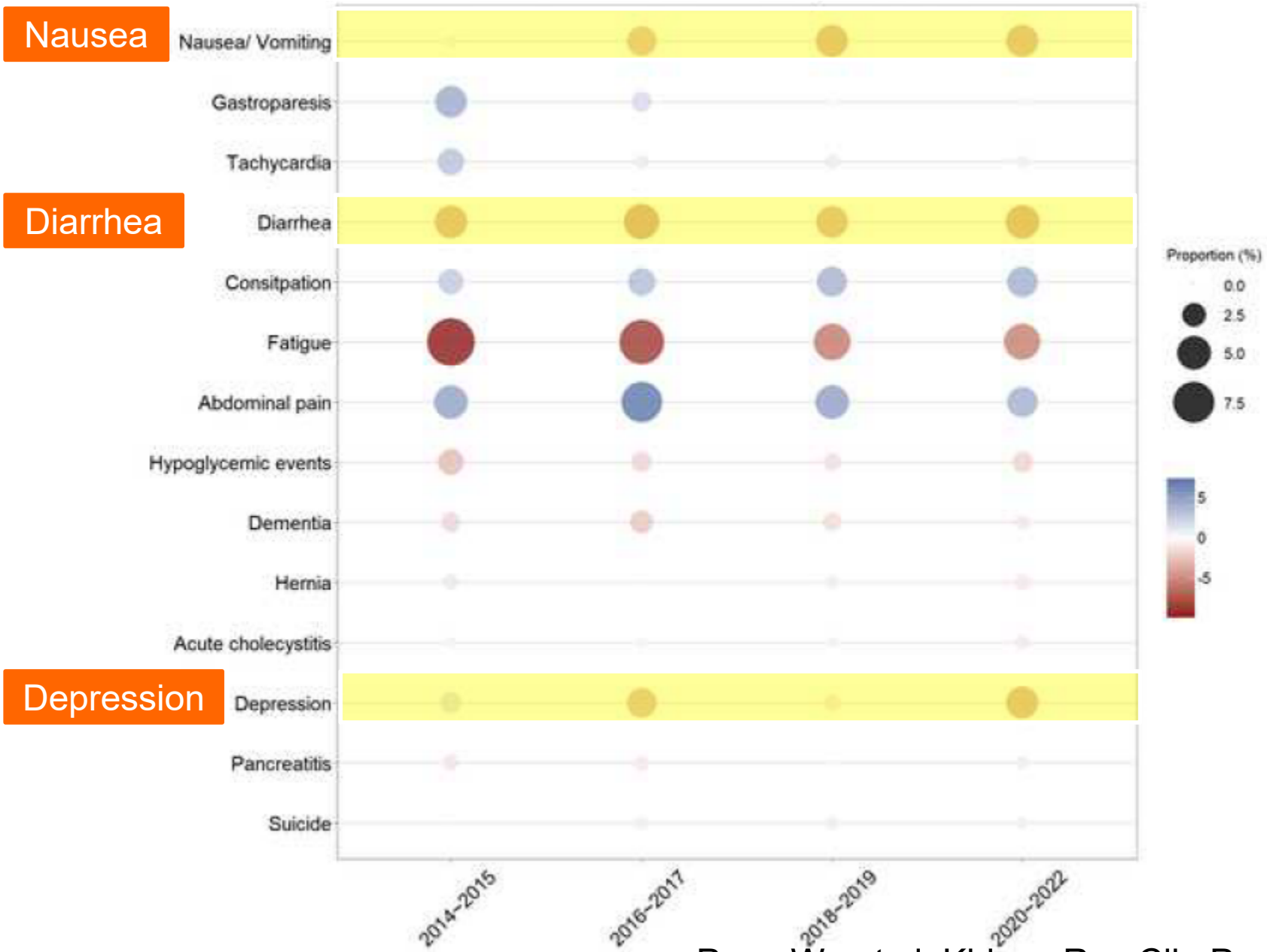
Am J Kidney Dis 2025 Jan 23:S0272



1,095,318 AKD patients, stratified by T2D status
8,334 (0.8%) received GLP-1 RAs

Pan , Wu et al.
Kidney Res Clin Pract. 2025

Years Difference of GLP-1 RA temporal time change



Pan , Wu et al. Kidney Res Clin Pract. 2025

nature communications

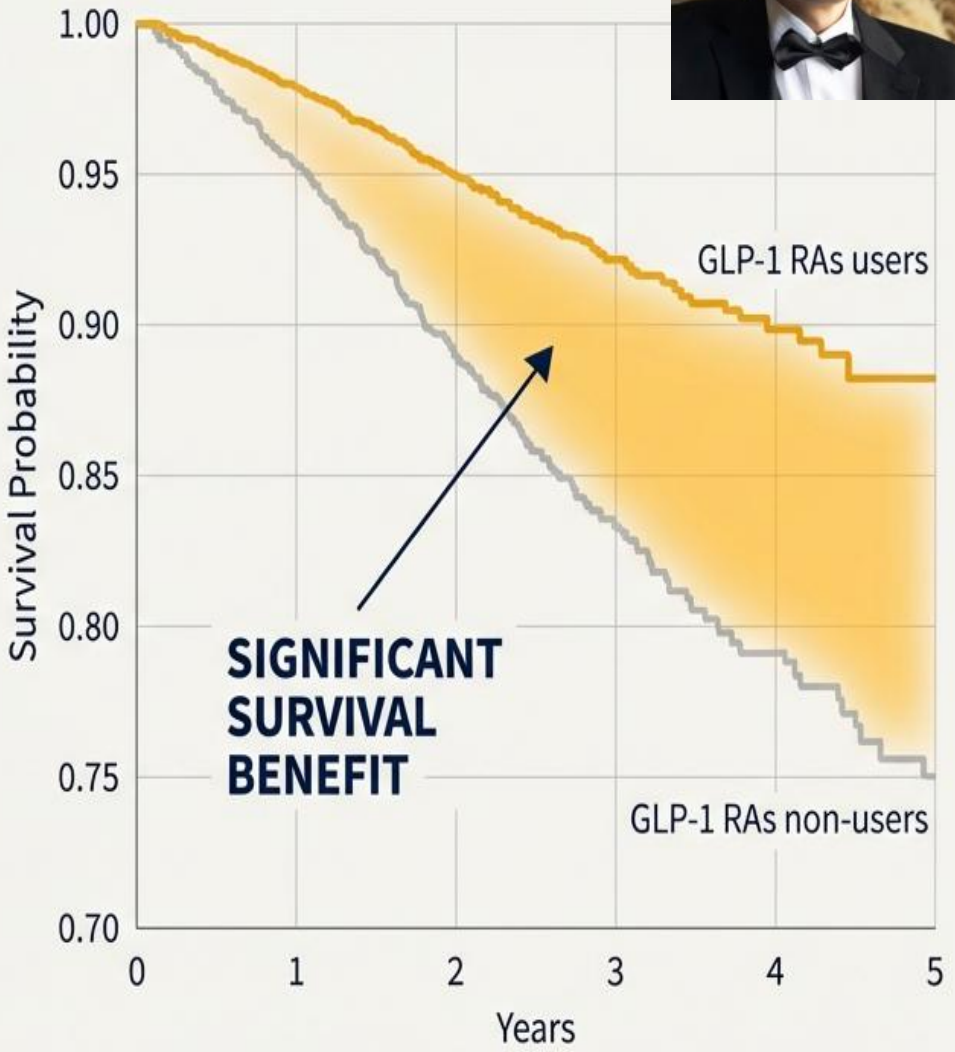
A New Therapeutic Avenue: GLP-1 RAs in Acute Kidney Disease

First real-world evidence shows GLP-1 RAs dramatically improve outcomes in type 2 diabetes patients with acute kidney disease.

43% lower all-cause mortality

12% lower major adverse cardiac events (MACE)

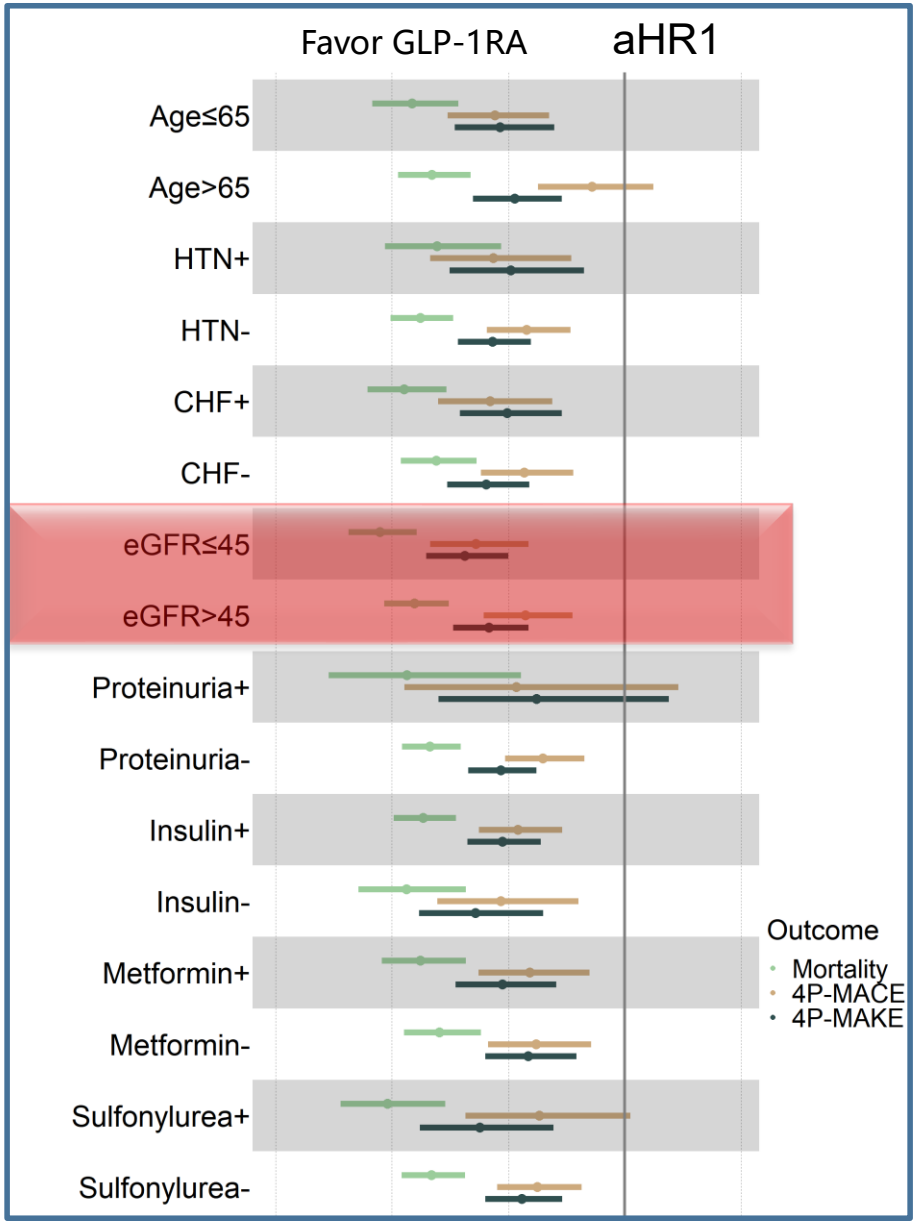
27% lower major adverse kidney events (MAKE)

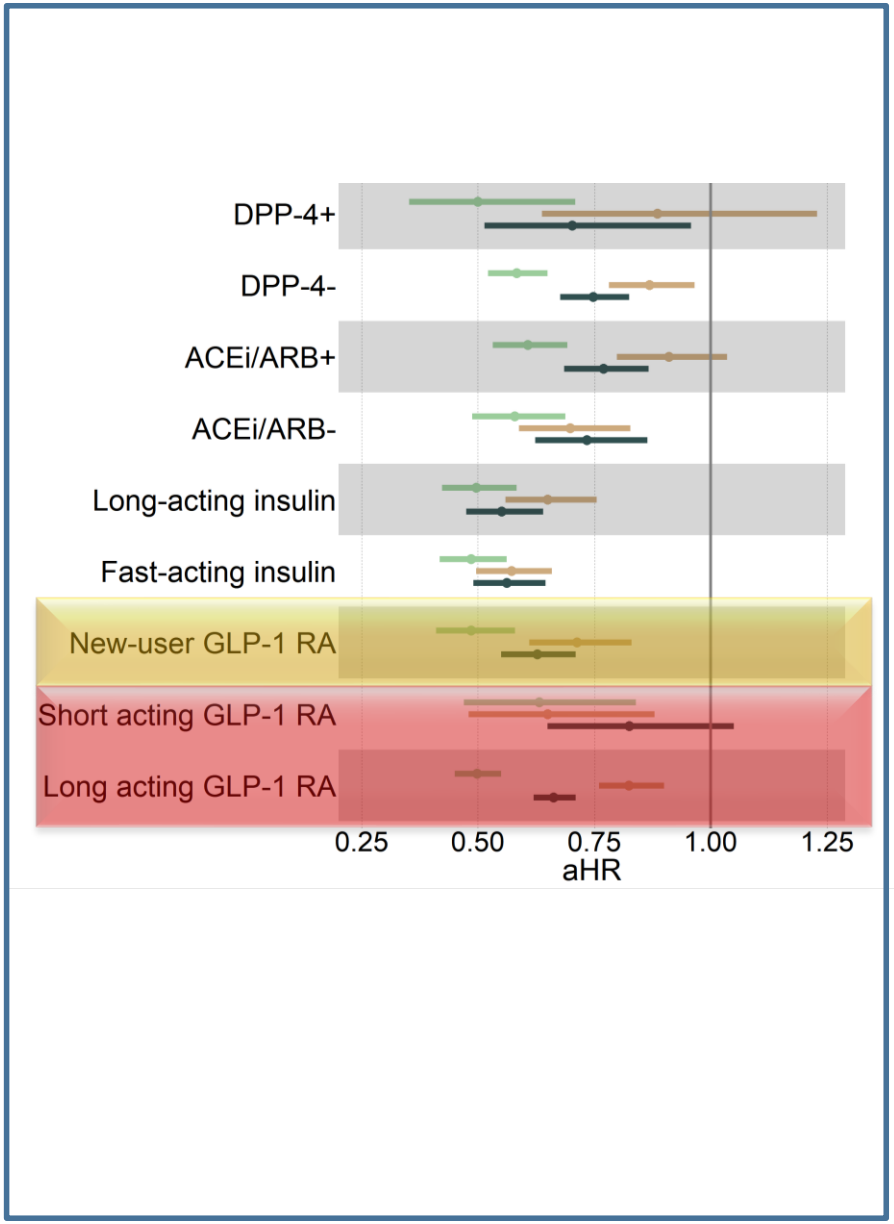


N= 15880

4.5%
2.2 years

Pan HC, et al., 2024, *Nature Communications*





Pan, Wu, *Nature Communication*, 2024

GLP-1RA during at Dialysis Commencement

TriNetX database

Worldwide, real-time healthcare data from over 250 millions de-identified patients

January 2015 to May 2023

82041 patients

Type 2 diabetes & initializing dialysis > 3 months

GLP-1 receptor agonist (1685, 2.1%) vs.
Long-acting insulin (32750)

Propensity score matching

N = 1682 in each group
Median follow up: 1.4 years

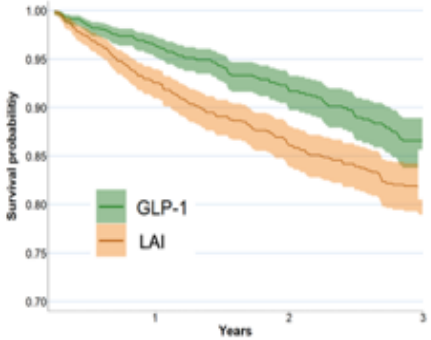
Outcomes:

All-cause mortality 37% ↓

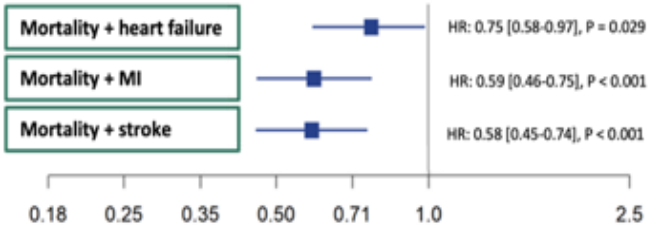
MACE 35% ↓

MAKE 25% ↓

Kaplan-Meier Curve:



Specificity analysis:



Conclusion:
Our findings underscore the protective effects of GLP-1 RA in mortality, cardiovascular and renal outcomes, as well as the safety profile in diabetic patients at the initiation of dialysis.

1,680

Lai, Wu et al, **Cardiovasc Diabetol**, 2024 Jul 29;23(1):277

TRUMP
WILL
FIX IT!
HOME
GUEST
PERIOD
TRUMP WILL FIX IT
DREAM BIG AGAIN!

SGLT2i

KDIGO guideline

2024
Management in CKD

First-line drug therapy for most patients

SGLT2i
continue until dialysis or transplant

2022
Diabetic management in CKD

First-line drug therapy

SGLT2i
(Initiate eGFR ≥20; continue until dialysis or transplant)

2020
Diabetic management in CKD

First-line therapy

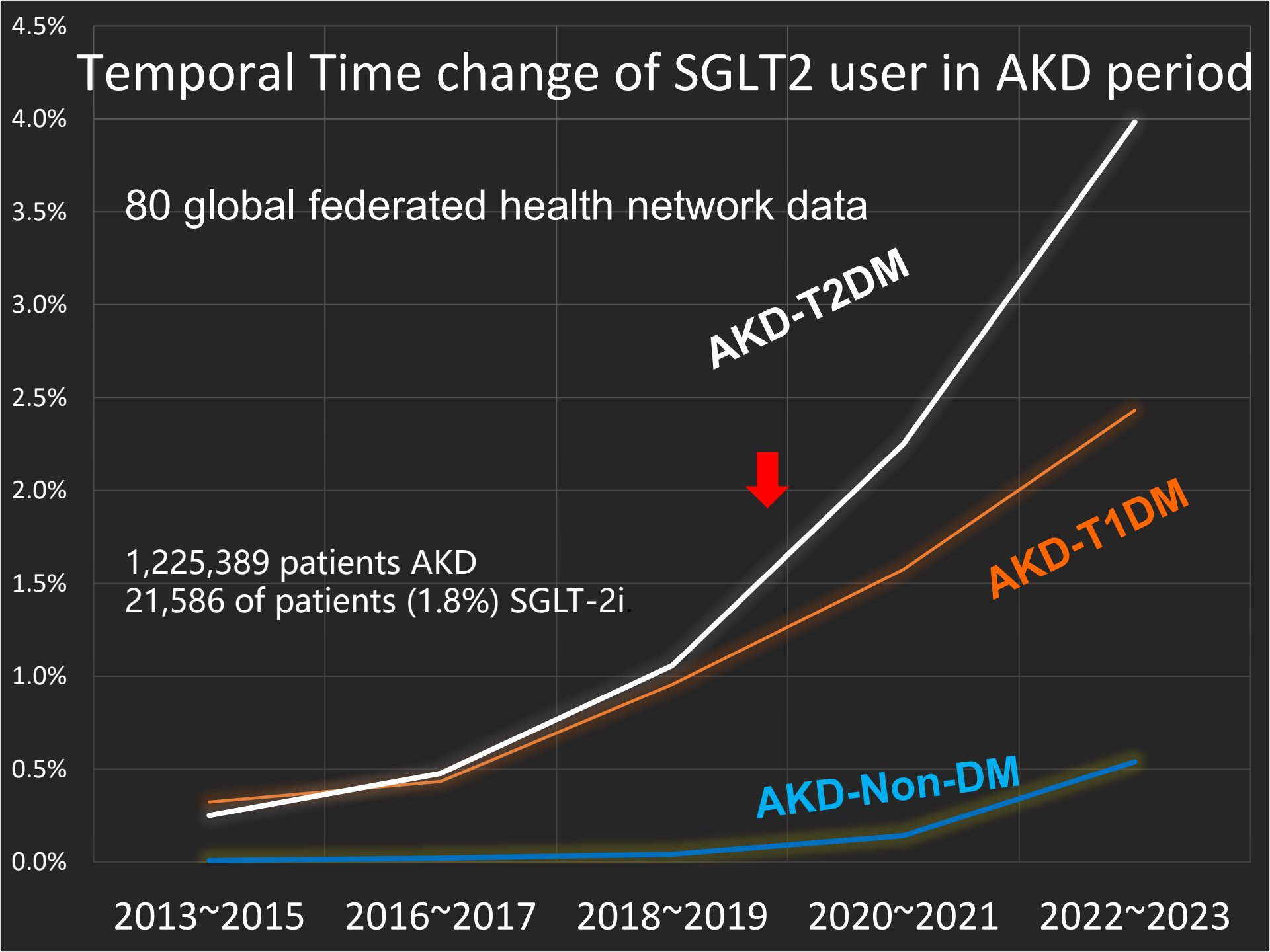
SGLT2 inhibitor

eGFR < 30 — Do not initiate

Dialysis — Discontinue

Kidney Int.. 2024;105(4s):S117-s314.

CKD, chronic kidney disease


Temporal Time change of SGLT2 user in AKD period
80 global federated health network data
1,225,389 patients AKD
21,586 of patients (1.8%) SGLT-2i
AKD-T2DM
AKD-T1DM
AKD-Non-DM
4.5%
4.0%
3.5%
3.0%
2.5%
2.0%
1.5%
1.0%
0.5%
0.0%
2013~2015
2016~2017
2018~2019
2020~2021
2022~2023

SGLT-2 Inhibitors: A Protective Link for Diabetes & Kidney Disease

Significant benefits in patients with type 2 diabetes and acute kidney disease, compared to non-use.

LOWER RISK OF DEATH

31%

LOWER RISK

of all-cause mortality.

FEWER MAJOR KIDNEY EVENTS

38%

LOWER RISK

of major adverse kidney events (MAKEs).

REDUCED CARDIAC EVENTS

25%

LOWER RISK

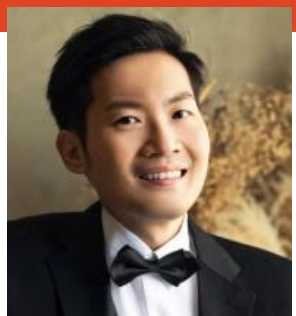
of major adverse cardiac events (MACEs).

User: 5319
Non-user: 225047

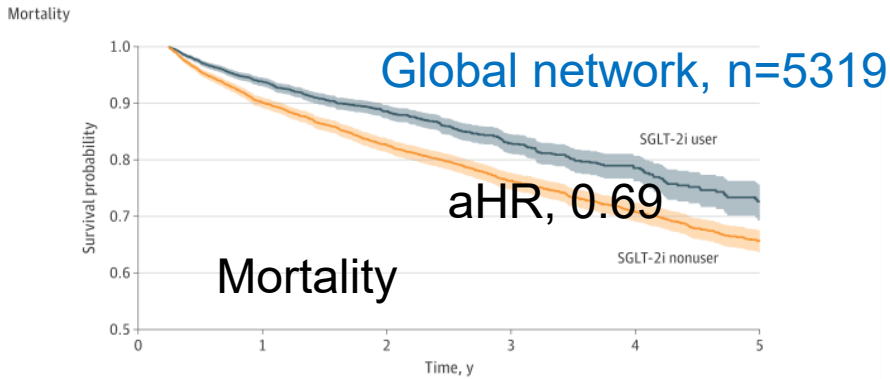
2.3%

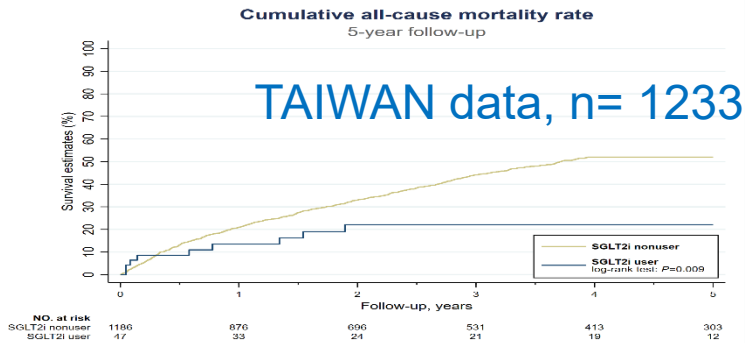
Propensity score matching

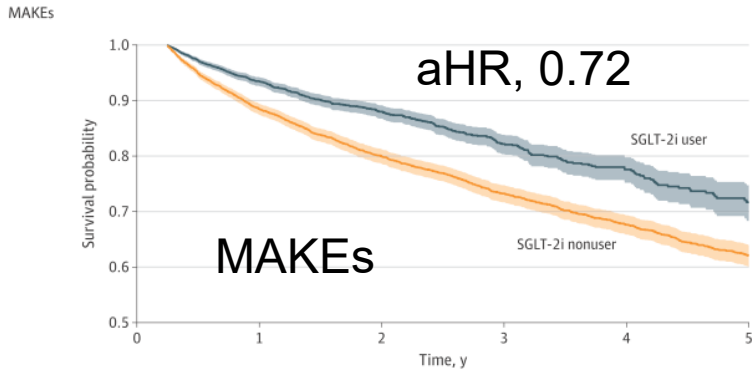
2024 Pan, Wu, JAMA Open

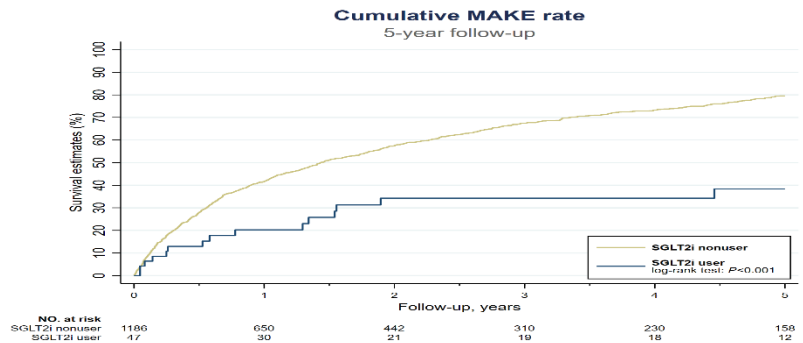


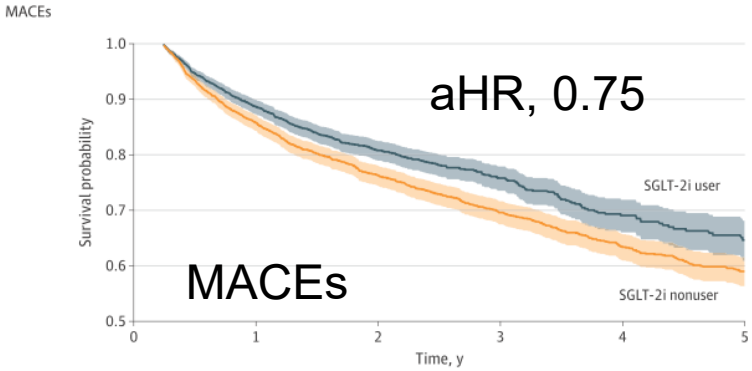
Outcomes following SGLT2i in AKD

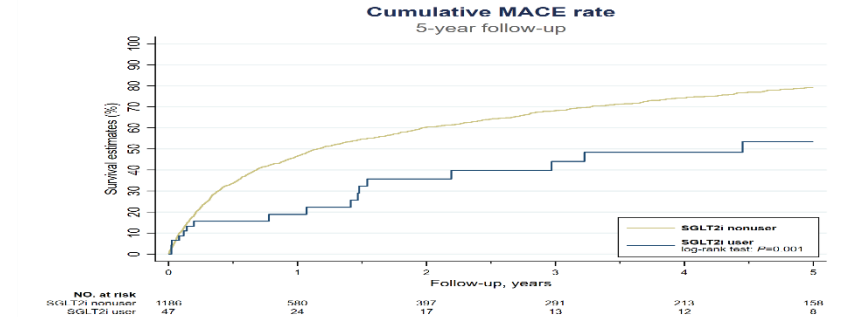












Pan, Wu et al

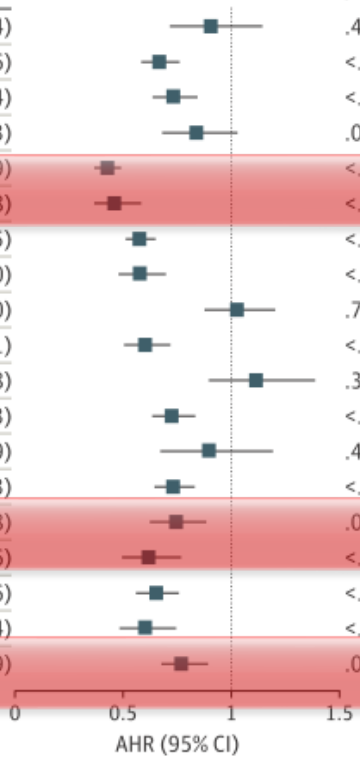
JAMA Network Open. 2024;7(1):e2350050.

Subgroup analysis SGLT-2 inhibitors

Mortality

A Mortality

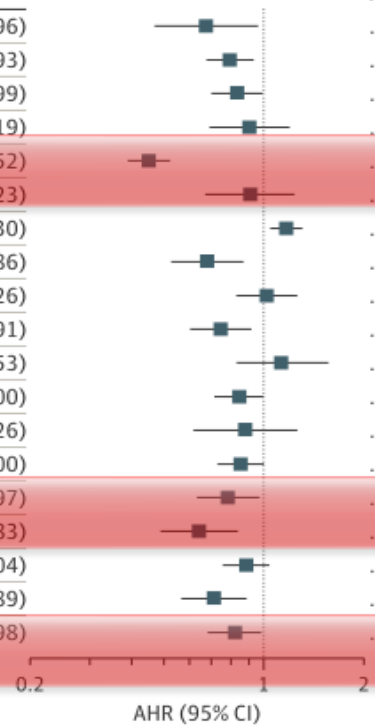
Subgroup	AHR (95% CI)	P value
HTN positive	0.91 (0.72-1.14)	.40
HTN negative	0.67 (0.59-0.76)	<.001
eGFR ≤45	0.73 (0.64-0.84)	<.001
eGFR >45	0.84 (0.68-1.03)	.09
eGFR ≤30	0.43 (0.37-0.49)	<.001
eGFR >30	0.46 (0.37-0.58)	<.001
Insulin positive	0.58 (0.52-0.65)	<.001
Insulin negative	0.58 (0.48-0.70)	<.001
Metformin positive	1.03 (0.88-1.20)	.75
Metformin negative	0.60 (0.51-0.71)	<.001
Sulfonylurea positive	1.12 (0.90-1.38)	.32
Sulfonylurea negative	0.73 (0.64-0.83)	<.001
DPP-4i positive	0.90 (0.68-1.19)	.45
DPP-4i negative	0.73 (0.65-0.83)	<.001
ACEI/ARB positive	0.75 (0.63-0.88)	.001
ACEI/ARB negative	0.62 (0.50-0.76)	<.001
Diuretics positive	0.65 (0.57-0.76)	<.001
Diuretics negative	0.60 (0.49-0.74)	<.001
New user	0.77 (0.68-0.89)	.01



MACE

C MACE

Subgroup	AHR (95% CI)	P value
HTN positive	0.67 (0.47-0.96)	.03
HTN negative	0.79 (0.67-0.93)	.005
eGFR ≤45	0.83 (0.70-0.99)	.04
eGFR >45	0.91 (0.69-1.19)	.48
eGFR ≤30	0.45 (0.39-0.52)	.001
eGFR >30	0.91 (0.67-1.23)	.55
Insulin positive	1.17 (1.05-1.30)	.004
Insulin negative	0.68 (0.53-0.86)	.002
Metformin positive	1.02 (0.83-1.26)	.83
Metformin negative	0.74 (0.60-0.91)	.005
Sulfonylurea positive	1.13 (0.83-1.53)	.43
Sulfonylurea negative	0.84 (0.71-1.00)	.05
DPP-4i positive	0.88 (0.62-1.26)	.49
DPP-4i negative	0.85 (0.73-1.00)	.05
ACEI/ARB positive	0.78 (0.63-0.97)	.02
ACEI/ARB negative	0.64 (0.49-0.83)	.001
Diuretics positive	0.89 (0.76-1.04)	.14
Diuretics negative	0.71 (0.57-0.89)	.002
New user	0.82 (0.68-0.98)	.03



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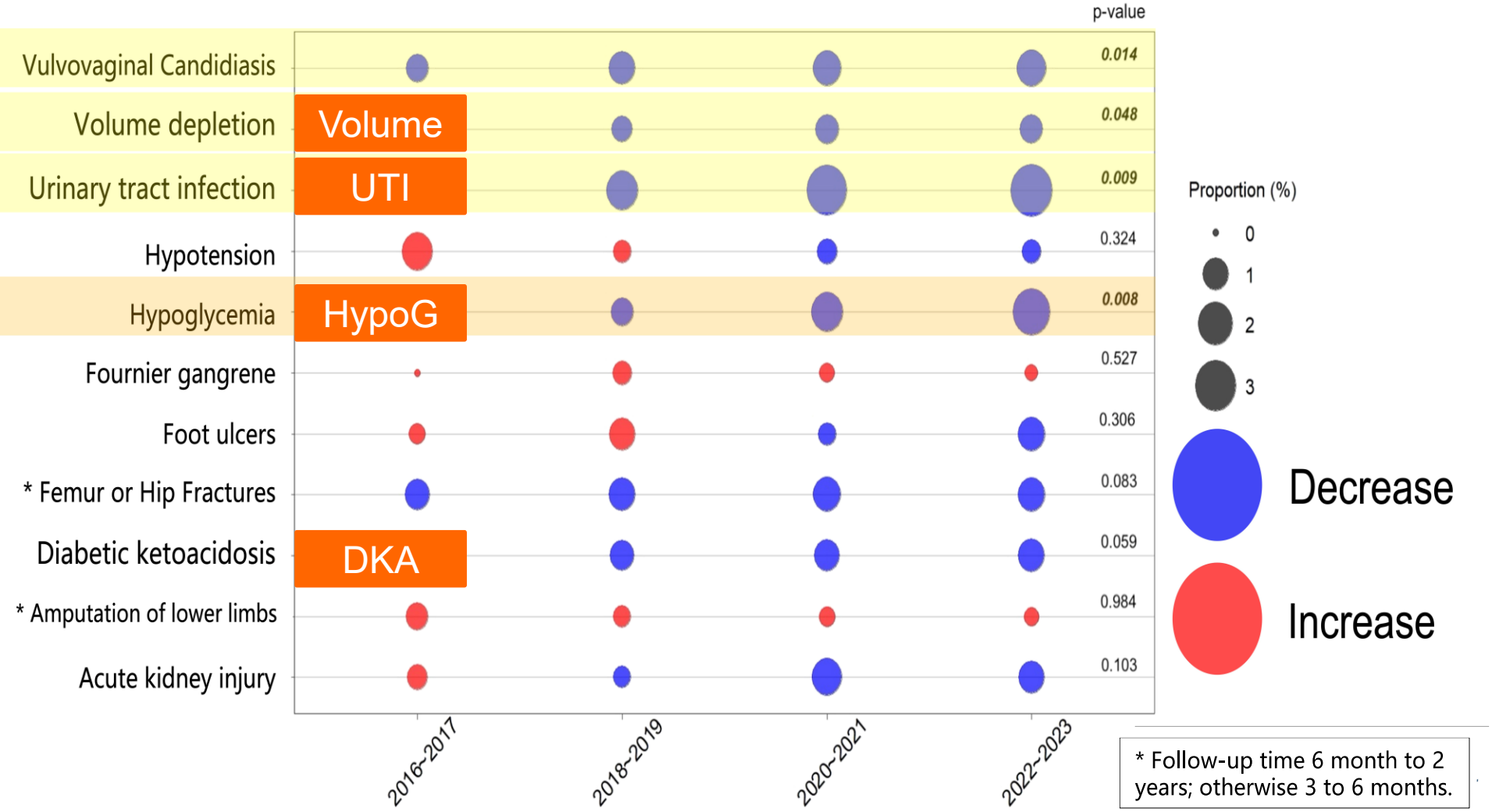
Yearly Differences in Incidence Rates of Adverse Events
AKD-SGLT2i-T2DM cohort



* Follow-up time 6 month to 2 years; otherwise 3 to 6 months.

SGLT2i during Acute Dialysis Commencement

Study Population

Patients with T2DM who initiated dialysis

Excluding:

1. Any dialysis before the dialysis in 30 days
2. Death before index date
3. SGLT-2i usage before dialysis in 3 months

N= 49,762

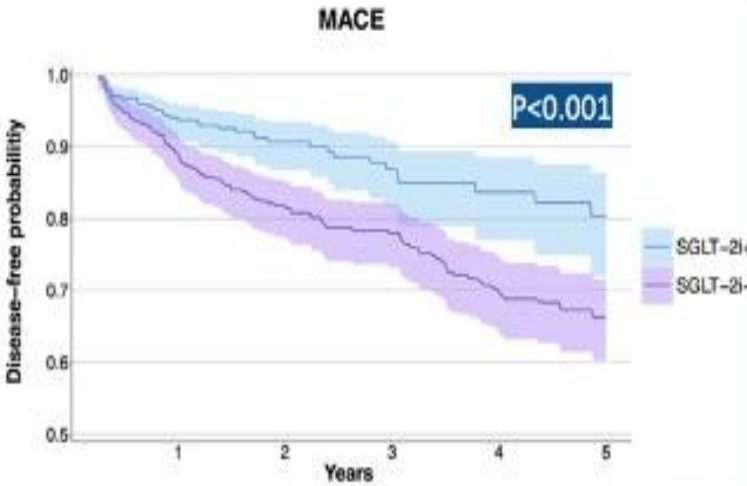
Median follow-up time: 2.0 years

Matched Cohort

PSM by age, gender, ethnicity, race, daily habits, comorbidities, BMI, and medications

771 SGLT-2i users

771 Non-users



Findings:

↓51% All-cause mortality

↓48% MACE

DKA

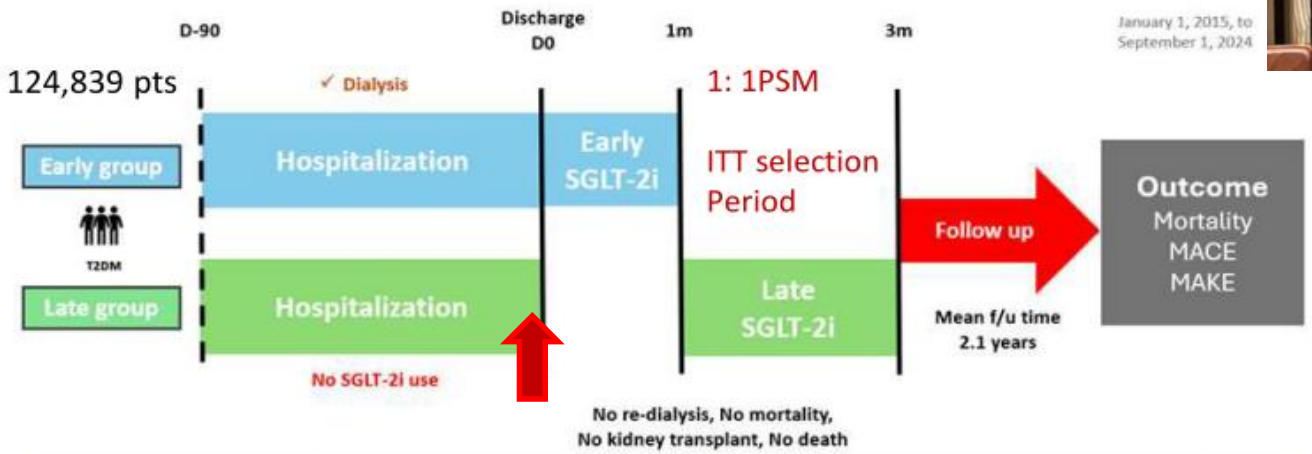
DKA, UTI/genital infection, hypoglycemia, dehydration, bone fracture, below-knee amputation, 90-day readmission

Insights into the real-world application of administering SGLT-2is post-dialysis

Wang, Wu, et al. **Cardiovasc Diabetol**. 2025

SGLT2i after AKI-D, Time is Everything

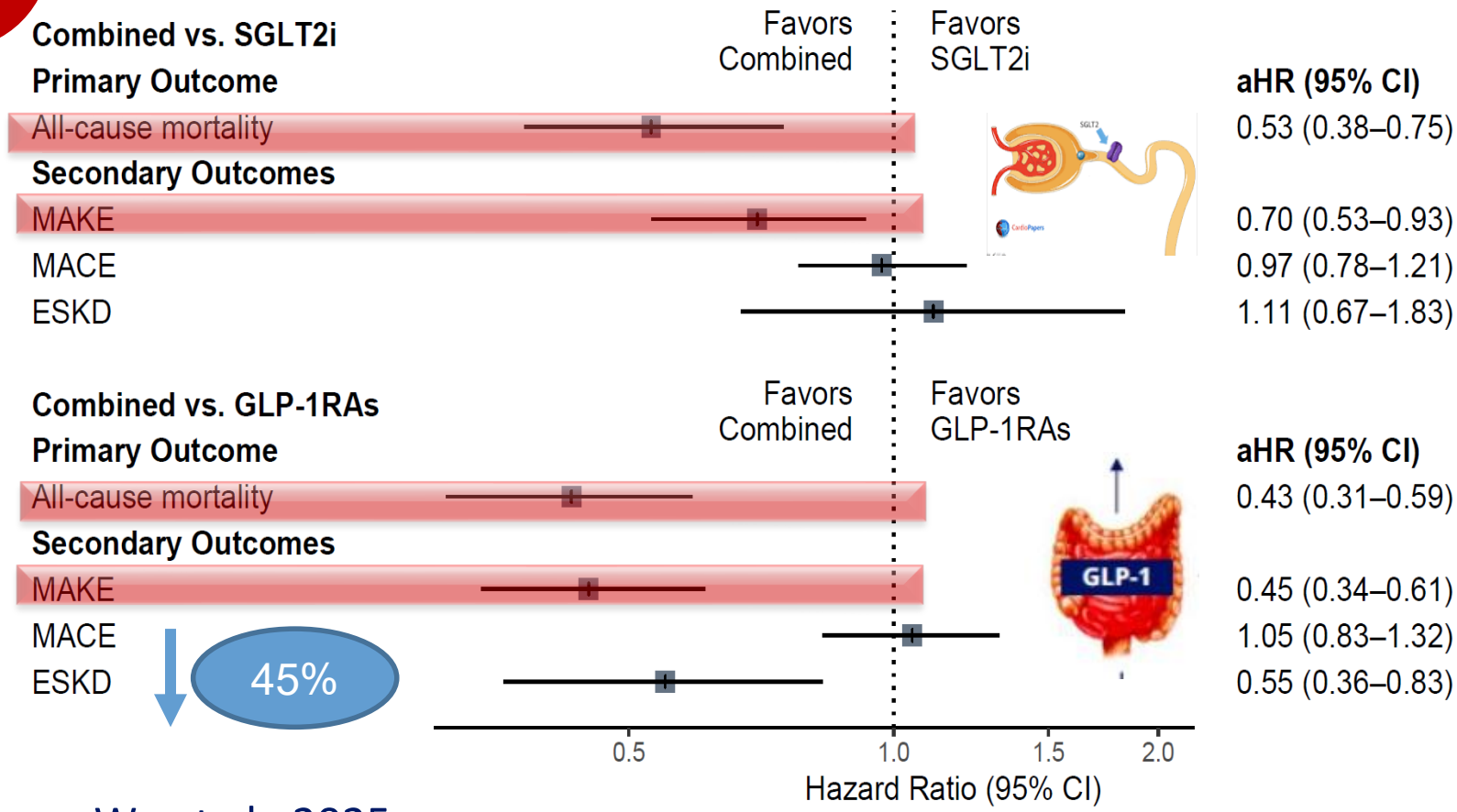
1



Chou, Wu et al, 2025 In Prepare

GLP-1 RA + SGLT2i combination in AKD patients

2



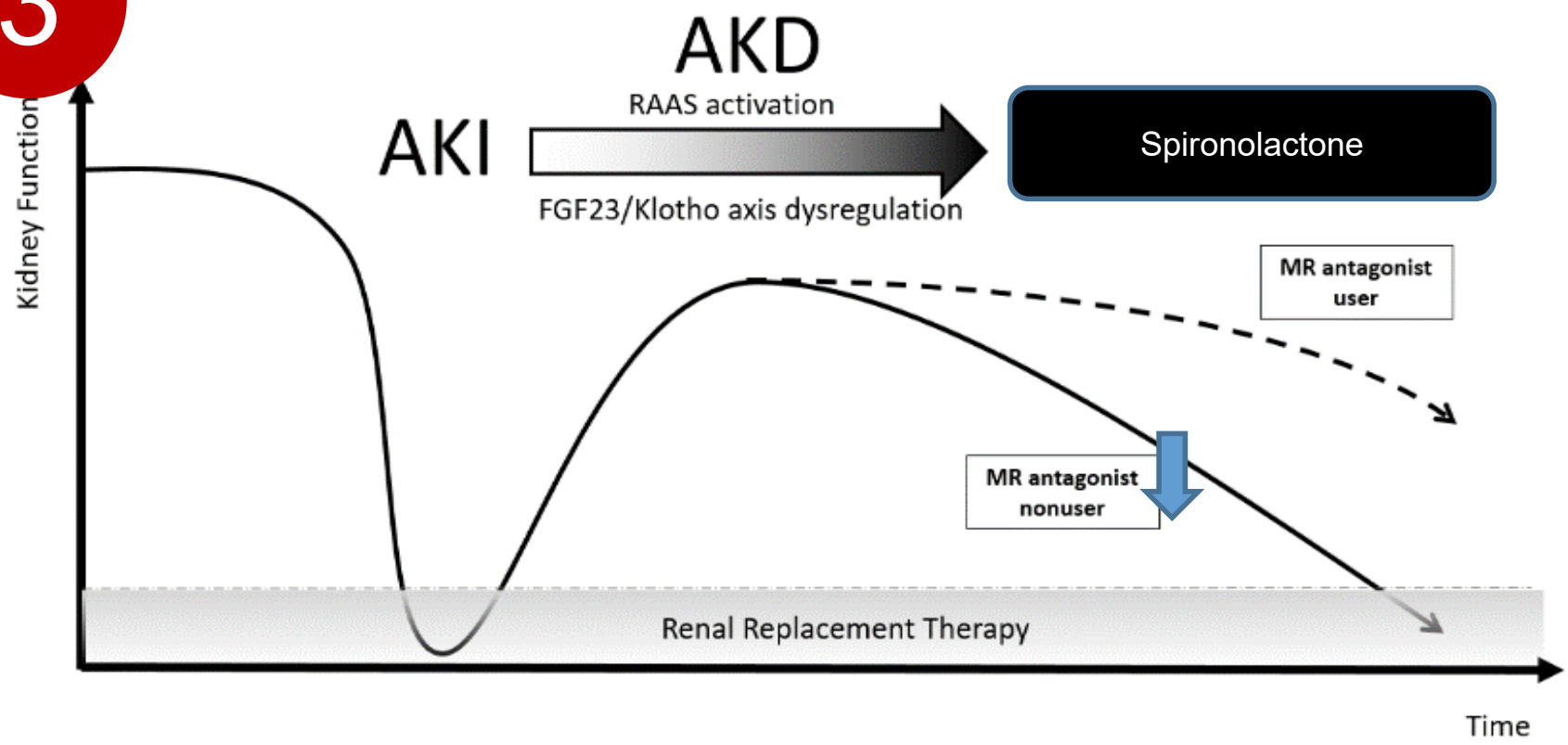
Chen , We et al , 2025

Diabetes Research and Clinical Practice

Hypoglycemia, DKA and Diabetic retinopathy

Spironolactone decrease re-dialysis at AKD

3

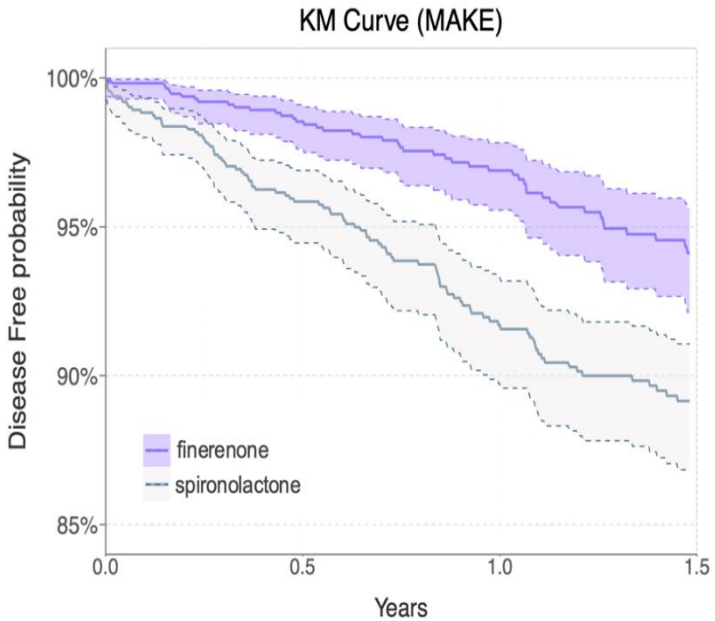


7,252 AKD patients with hypertension, 2,255 treated with spironolactone

NSARF

Lin YF et al , 2018 Journal of HTN

Finerenone vs Spironolactone for DKD : A Target Trial Emulation Study



MAKE : Number at risk(number event)

finerenone	1132(0)	1120(12)	1101(31)	1086(46)
spironolactone	1132(0)	1086(46)	1057(75)	1036(96)

in patients with Chronic Kidney Disease (CKD) and Type 2 Diabetes (T2D)

Exposure & Outcomes

Exposure

1,132 Finerenone

1,132 Spironolactone

Outcomes

Primary outcomes

Major adverse CV events (MACE)
Major adverse kidney events (MAKE)
All-cause mortality

Secondary outcome

Hyperkalemia
(serum potassium ≥ 5.5 mEq/L)

Results

Adjusted hazard ratio (aHR)

MACE
0.74 (95%CI, 0.58-0.94)

MAKE
0.47 (95%CI, 0.33-0.67)

Mortality
0.31 (95%CI, 0.21-0.45)

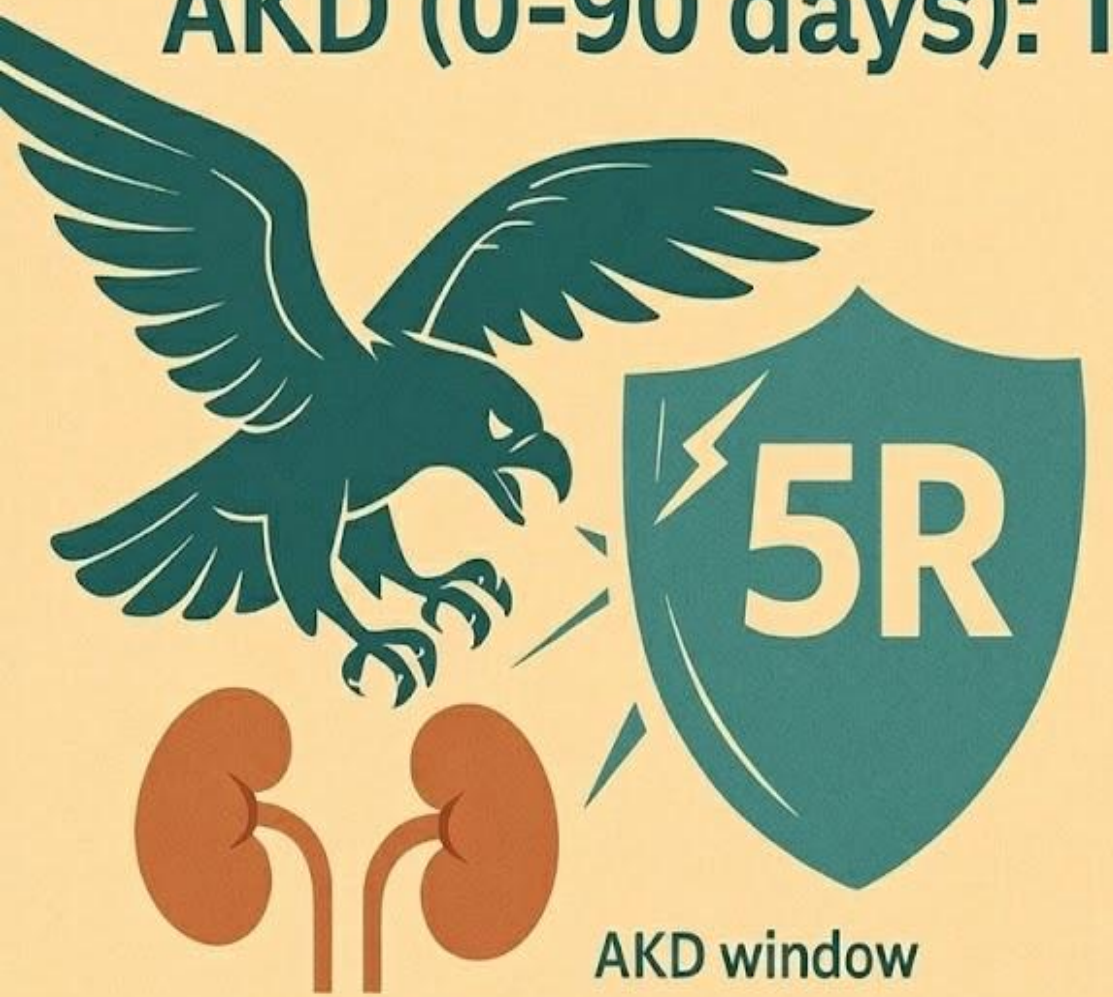
Hyperkalemia
17.2% vs 26.4%, P<0.001

18,314 patients with CKD and T2D, 1,345 initiated finerenone (mean 68.5 years; [59.4% and 16,969 initiated spironolactone

Wang , Wu et al
Nature communication, 2025

4 BP
Prometheus

AKD (0-90 days): The 5R Shield



- Recognition
- Risk assessment
- Response
- Rehabilitation
- Renal support

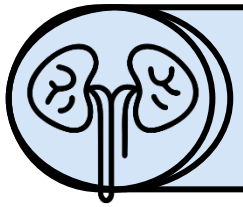
- BP, Proteinuria
- Sick Day
- Vaccination

MAKE
AKD
GREAT AGAIN!

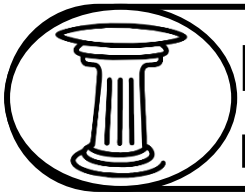
Risk and Outcomes of AKD

Vin-cent Wu, M.D.
dr.vincentwu@gmail.com

AKD drives dialysis and mortality



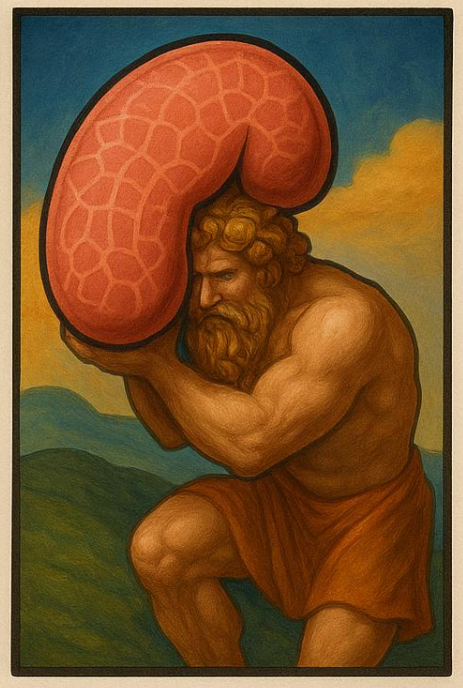
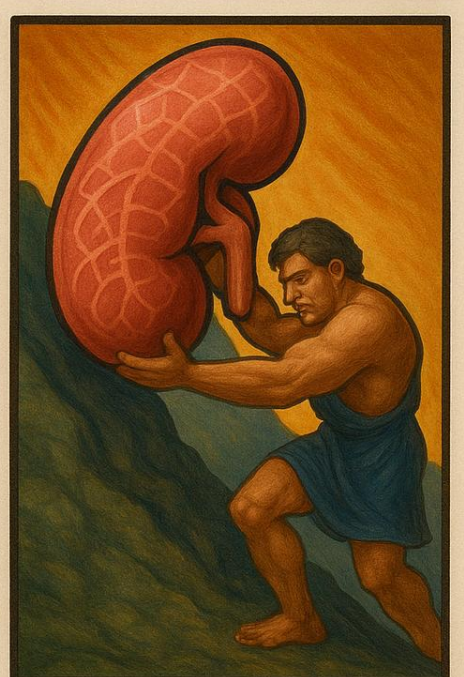
SGLT2i & GLP-1RA show promise in breaking the AKD–CKD link.



Four-pillar therapy (BP, bundle protection) reduces risk and saves lives.

Disconnect AKD from progression and mortality through **timely MDC**

Gratitude is extended to the invaluable assistance rendered by all~

NSARF

NTUH Surgery Intensive Care Unit Acute Renal Failure Group