The Crisis of AKI Follow-Up

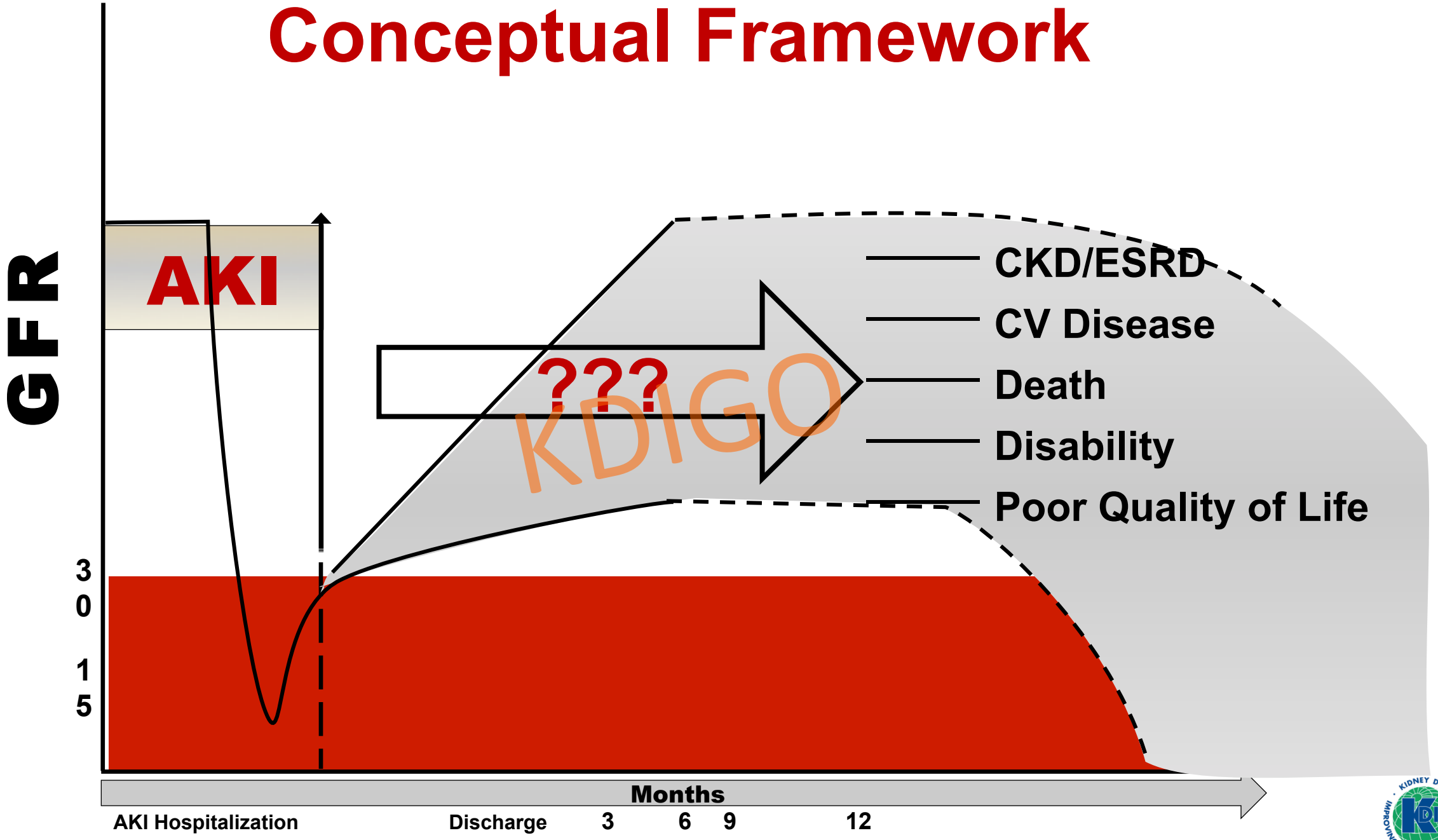
KDIGO Controversies Conference of Acute Kidney Injury
Rome, Italy 4/19

Eddie Siew, MD, MSCI
Associate Professor of Medicine
Vanderbilt Integrated Program for AKI Research (VIP-AKI)
Tennessee Valley Health Systems Veterans Affairs

DISCLOSURES

- Honorarium: Invited educational talk at DaVita Annual Physician Conference 3/2019
- Royalties: Author for UptoDate
- Scientific Advisory: Editorial Board CJASN
- Consulting Agreement: Akebia Therapeutics

Conceptual Framework



KDIGO 2012 Clinical Practice Recommendations for Post-AKI Care

2.3.4: Evaluate patients 3 months after AKI for resolution, new onset, or worsening of pre-existing CKD. (Not Graded)

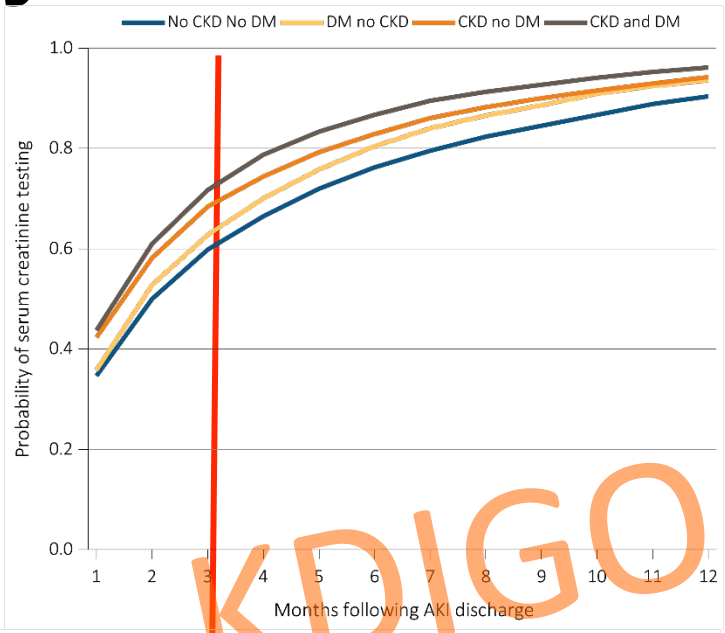
- **If patients have CKD, manage these patients as detailed in the KDOQI CKD Guideline (Guidelines 7–15). (Not Graded)**
- **If patients do not have CKD, consider them to be at increased risk for CKD and care for them as detailed in the KDOQI CKD Guideline 3 for patients at increased risk for CKD. (Not Graded)**

AKI Survivors vs Stable CKD: Apples and … Pears?

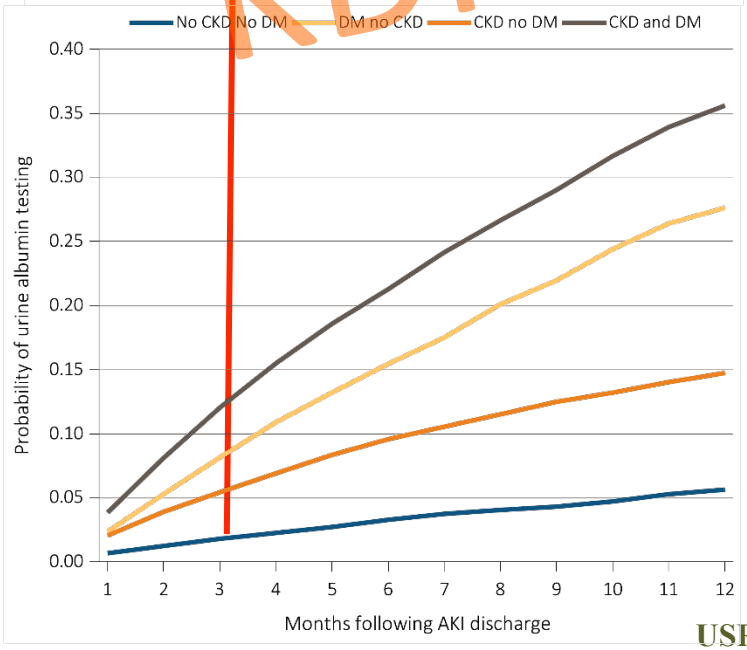
	Recent Hospitalized AKI	Stable CKD
Advanced Comorbidity/ Burden	↑↑	↑
Acute Organ Dysfunction	↑↑	-
Potential for Ongoing Recovery	↑	-
Susceptibility to future injury/ rehospitalizations/mortality	↑↑	↑
Susceptibility to nephrotoxins and adverse drug events (ADEs)	↑↑	↑
Inadequate Solute/Fluid Intake	↑	-
Poor Quality of Life/Frailty	↑↑	↑

Kidney Surveillance after AKI

Serum Creatinine

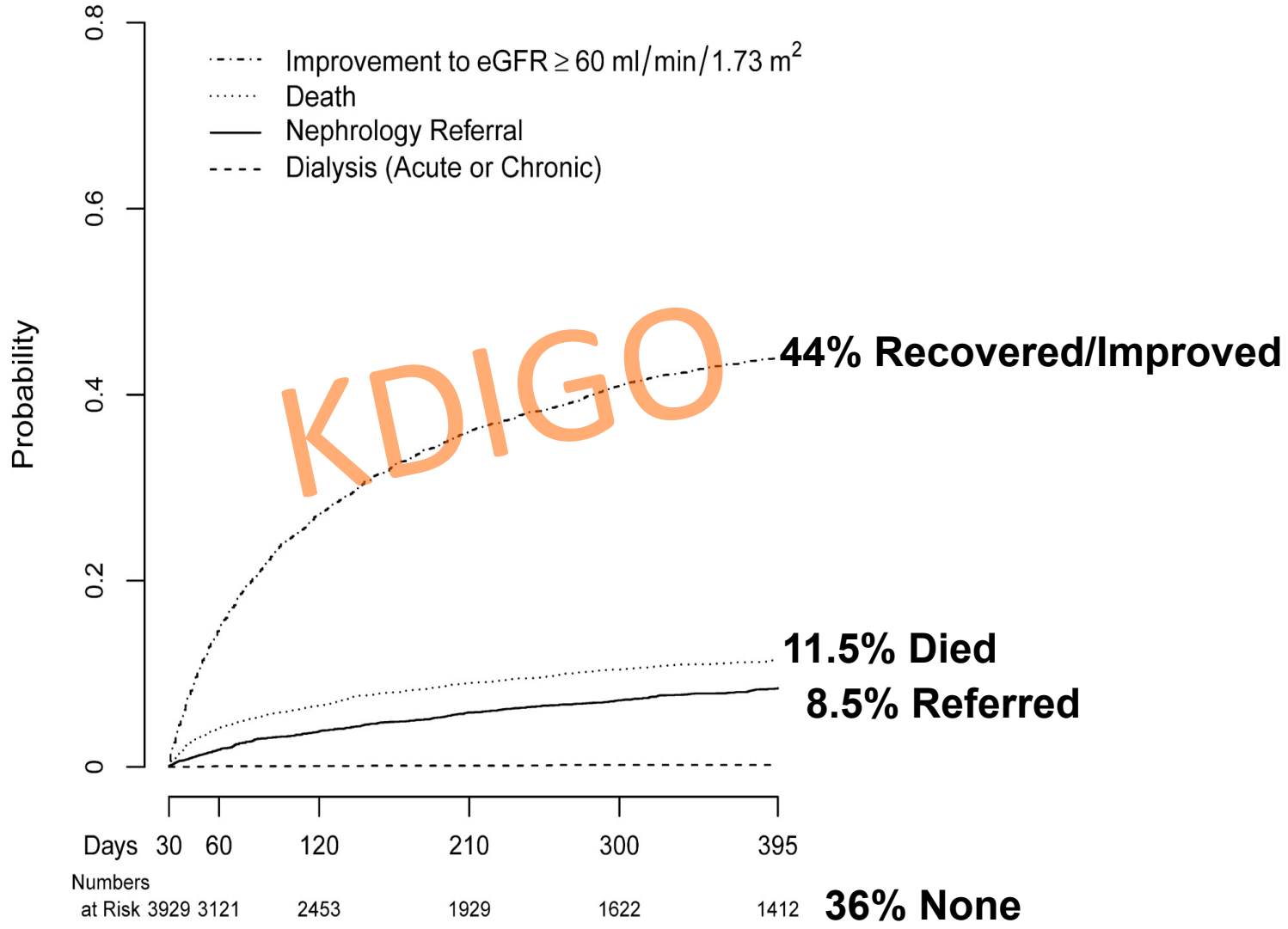


Albuminuria/ Proteinuria



USRDS 2015 ADR: Medicare AKI patients age 66 & older, 2012.

Outpatient Nephrology Referral Among Patients with eGFR <60 ml/min/1.73 m^2 After AKI



Siew et al. JASN 2012;23:305-312

Identifying Patients at High Risk

A Point values for each variable

Age, y	Points
<50	0
50-59	1
60-69	2
70-79	2
80-89	2
≥90	3

Sex	Points
Men	0
Women	3

Baseline SCr, mg/dL	Points
<0.6	0
0.6-<0.7	1
0.7-<0.8	1
0.8-<0.9	2
0.9-<1.0	2
1.0-<1.1	3
1.1-<1.2	3
1.2-<1.3	4
≥1.3	5

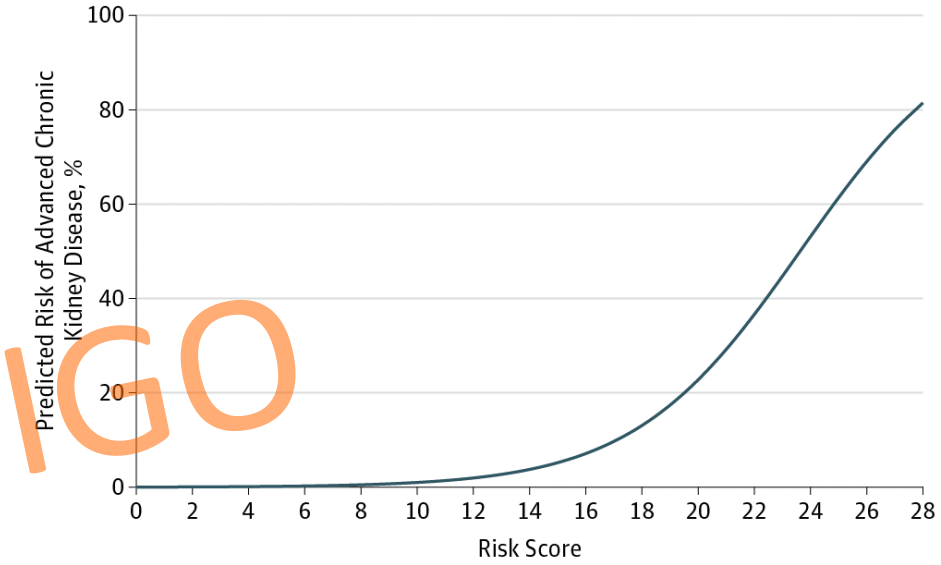
Albuminuria	Points
Normal	0
Mild	1
Heavy	3
Not measured	1

Acute kidney injury stage	Points
1	0
2	1
3	3

Discharge SCr, mg/dL	Points
<1.0	0
1.0-<1.3	3
1.3 -<1.6	6
1.6 -<1.9	7
≥ 1.9	11

Summation of Points:	
Age	+ _____
Sex	+ _____
Baseline serum creatinine value	+ _____
Albuminuria	+ _____
Acute kidney injury stage	+ _____
Discharge serum creatinine value	+ _____
Total Risk Score =	

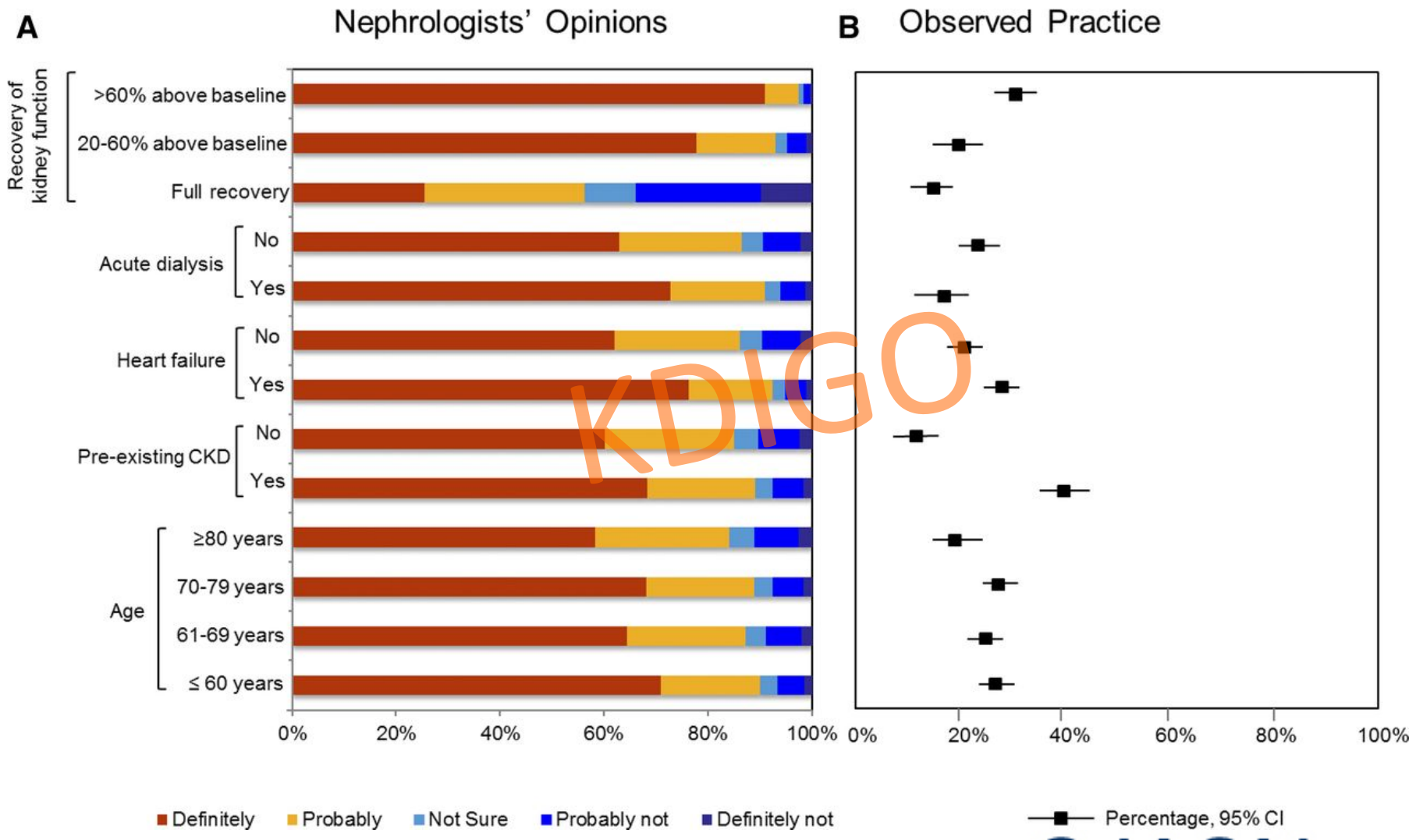
B Predicted risk of advanced chronic kidney disease



Total Risk Score	Predicted Risk of Advanced Chronic Kidney Disease, %	Percentage of Patients in Risk Category, %	
		Derivation Cohort	External Validation Cohort
1-8	<1	44.0	45.0
9-14	1-<5	43.6	43.8
15-17	5-<10	7.2	7.1
18-19	10-<20	2.5	2.1
≥20	≥20	2.7	2.0

James, MT et al. *JAMA* 2017; 318(19):1787-97

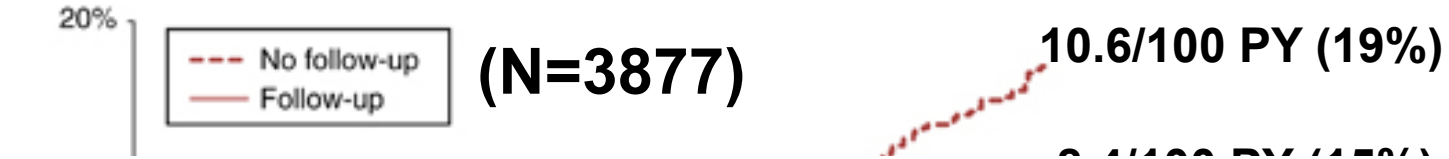
Disparity between Nephrologists' Opinions and Contemporary Practices for Follow-up after AKI Hospitalization.



Divya J. Karsanji et al. CJASN 2017;12:1753-1761

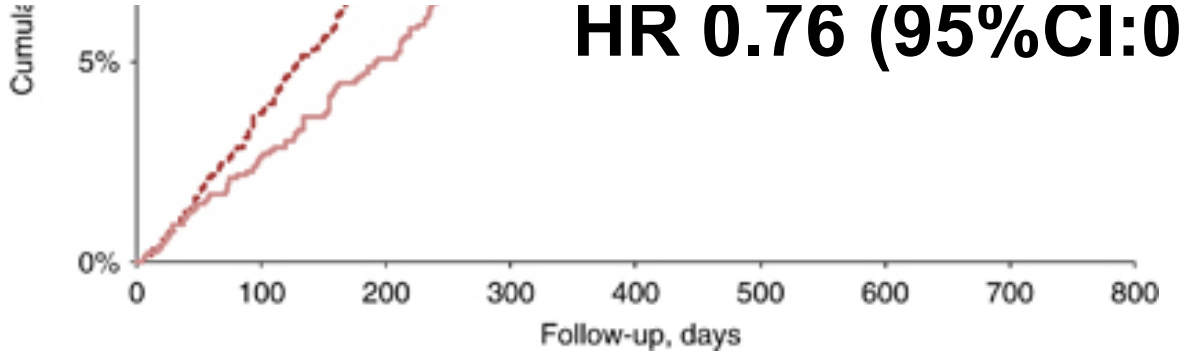
CJASN

Nephrology Referral Associates with Improved Survival After Dialysis-Requiring AKI



Is this Real?

What is Driving this?

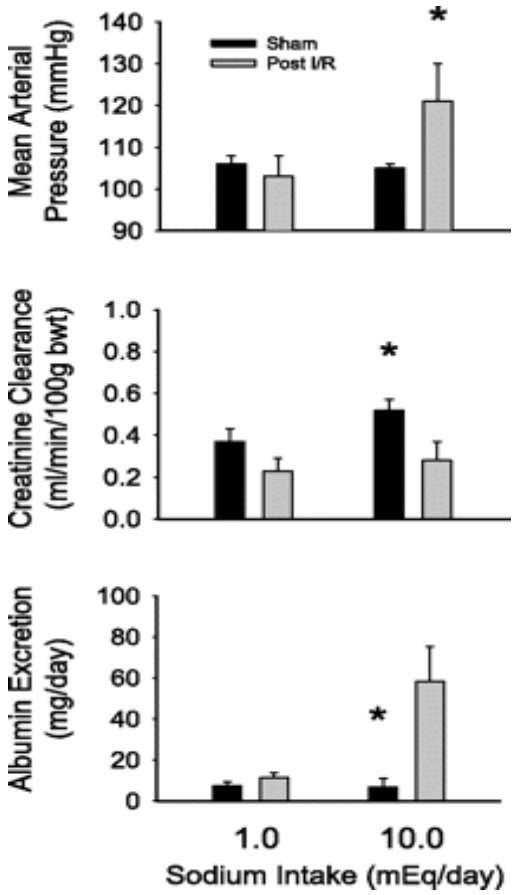


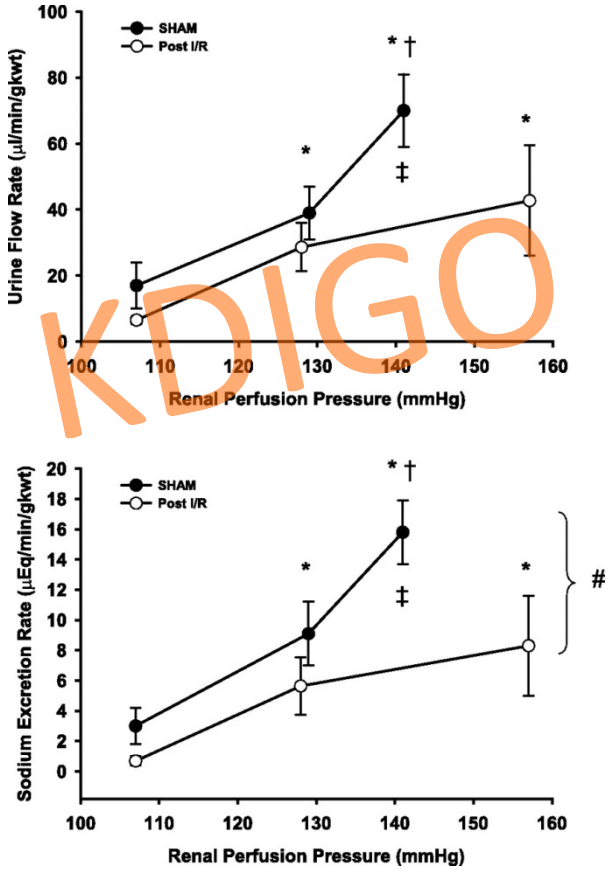
HR 0.76 (95%CI:0.62-93)

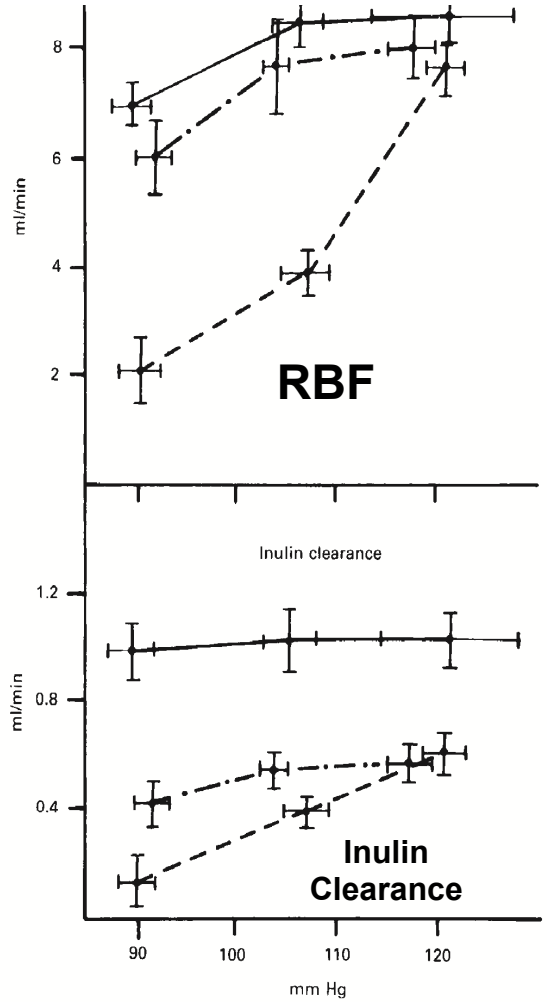
Harel *Kidney Int* 2013; 83:901-08

Actionable Factors that may Modify Long-term Risk?

AKI Causes Salt Sensitivity of Blood Pressure, Predisposes to Proteinuria, and Loss of Autoregulation



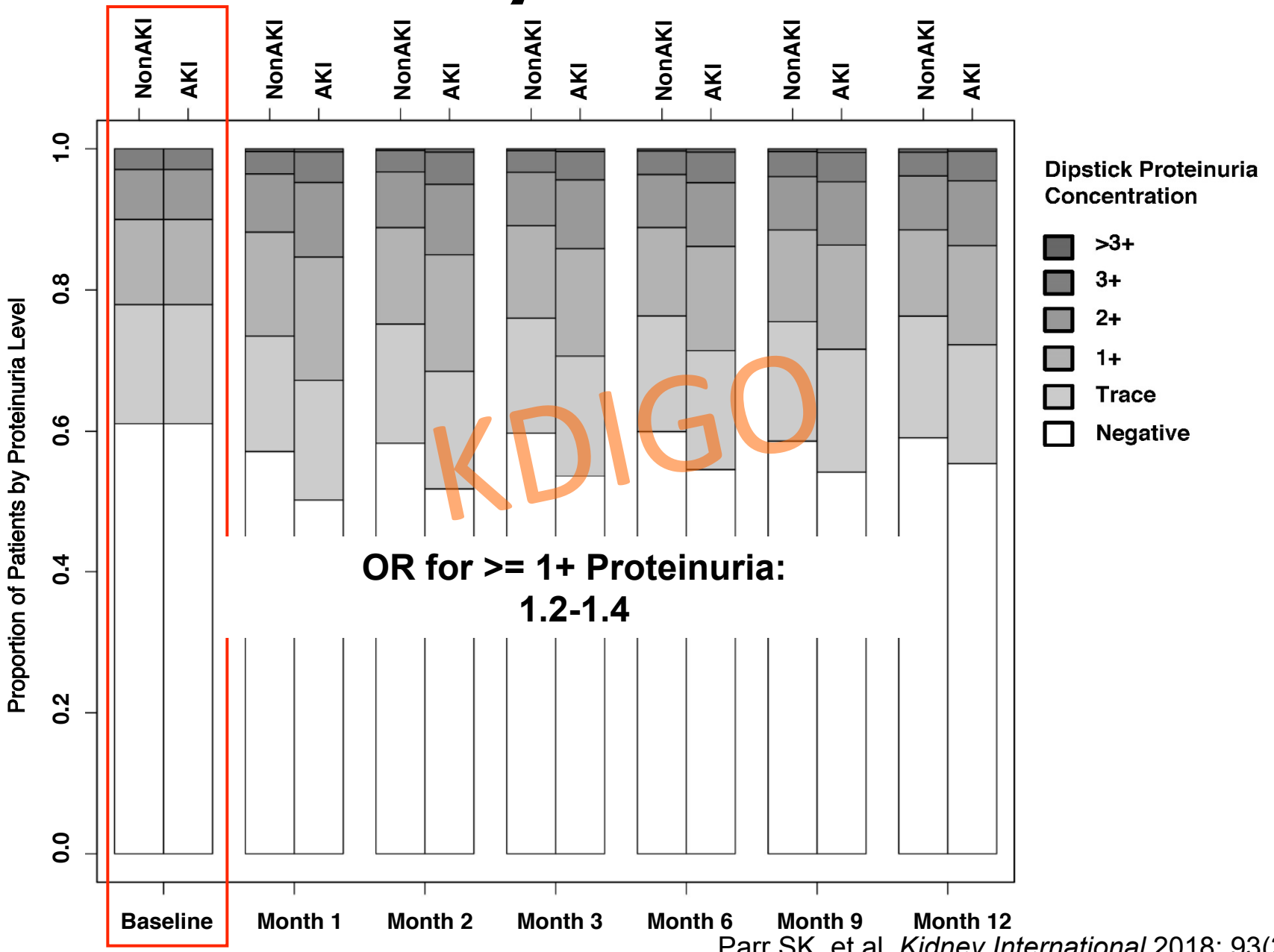




Pechman, K. R. et al. Am J Physiol Regul Integr Comp Physiol 297: R1358-R1363 2009

Kelleher, SP, et al. Conger. KI 1987

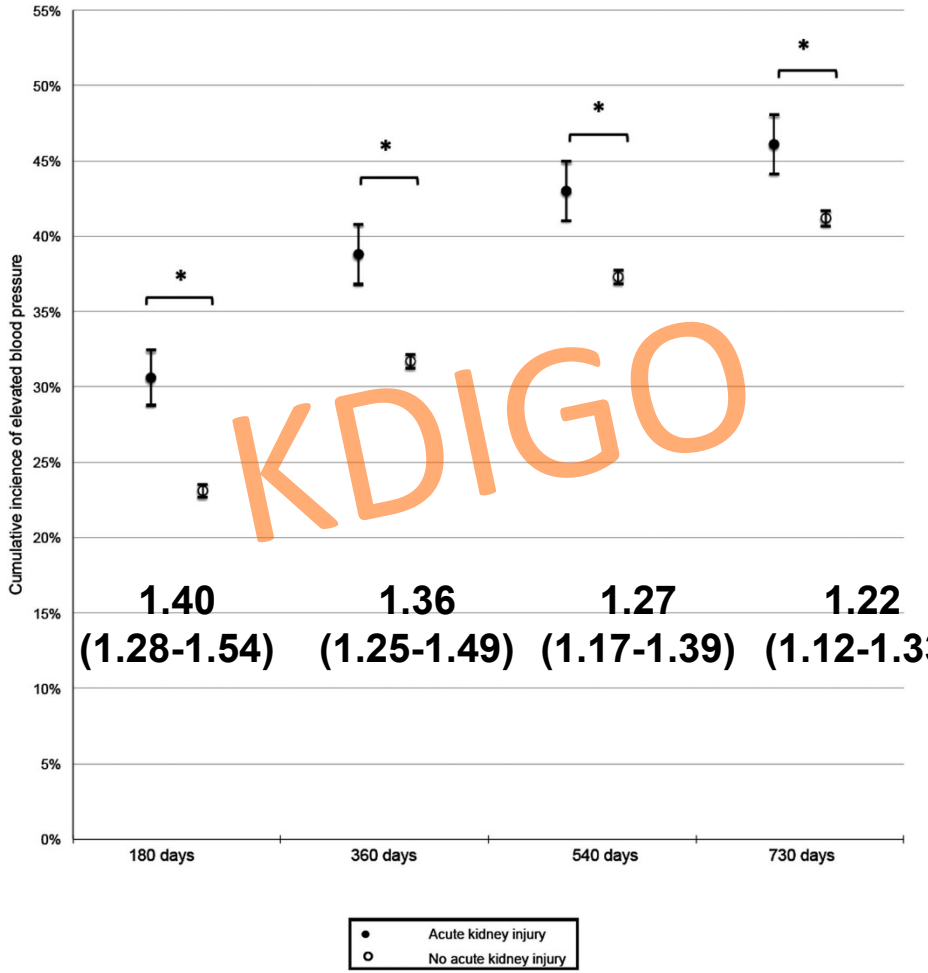
Proteinuria May Worsen after AKI



Parr SK, et al. *Kidney International* 2018: 93(2):460-469

HYPERTENSION MAY BE A POTENTIAL MEDIATOR OF CV AND KIDNEY OUTCOMES FOLLOWING AKI (N=2451 +AKI/41,160 -AKI)

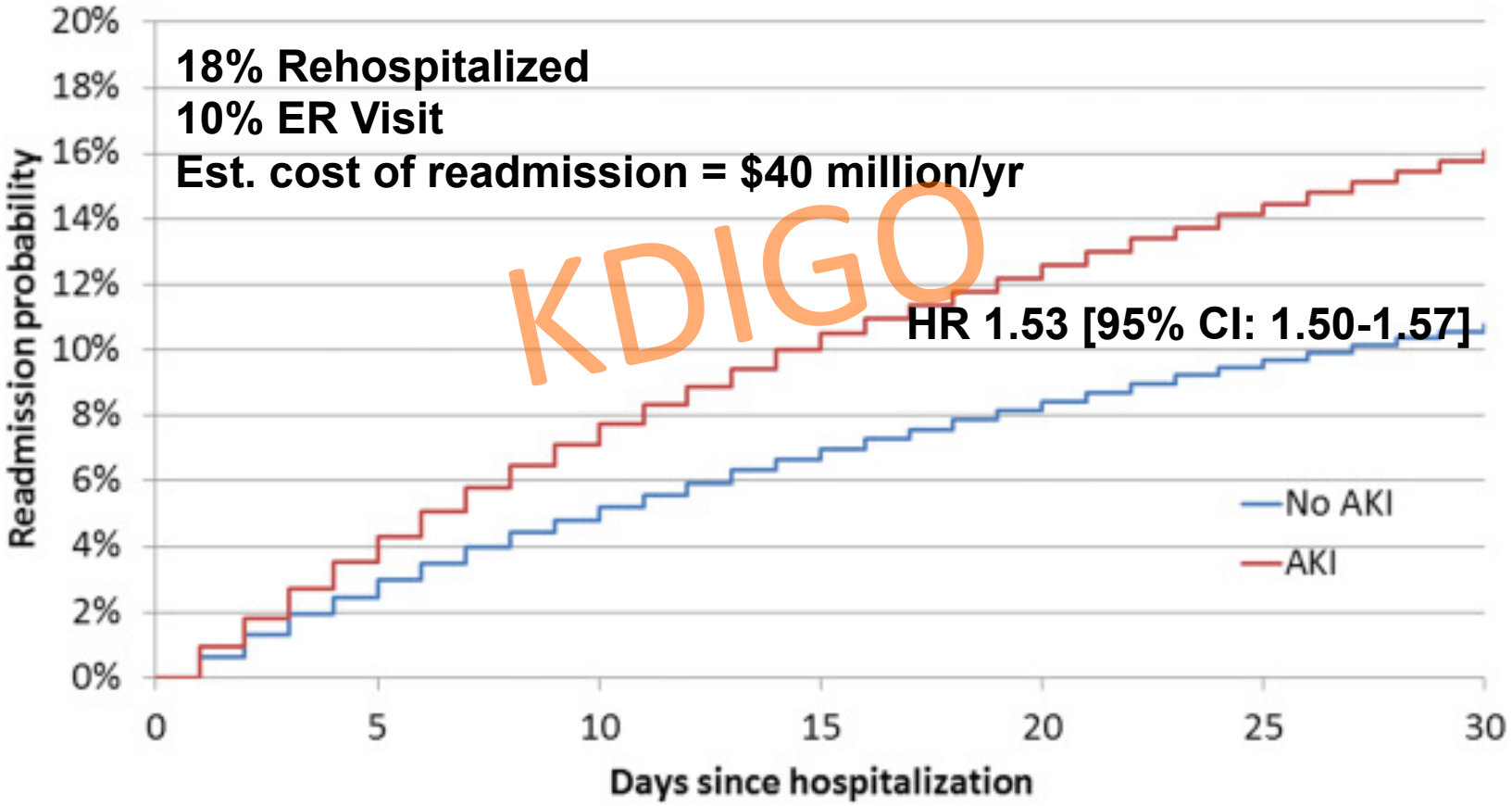
Adjusted OR for HTN:



Adjusted for age at index hospitalization, sex, race, body mass index, last ambulatory systolic and diastolic BP measurements, smoking status, diabetes mellitus, chronic heart failure, coronary heart disease, last ambulatory eGFR, and proteinuria.

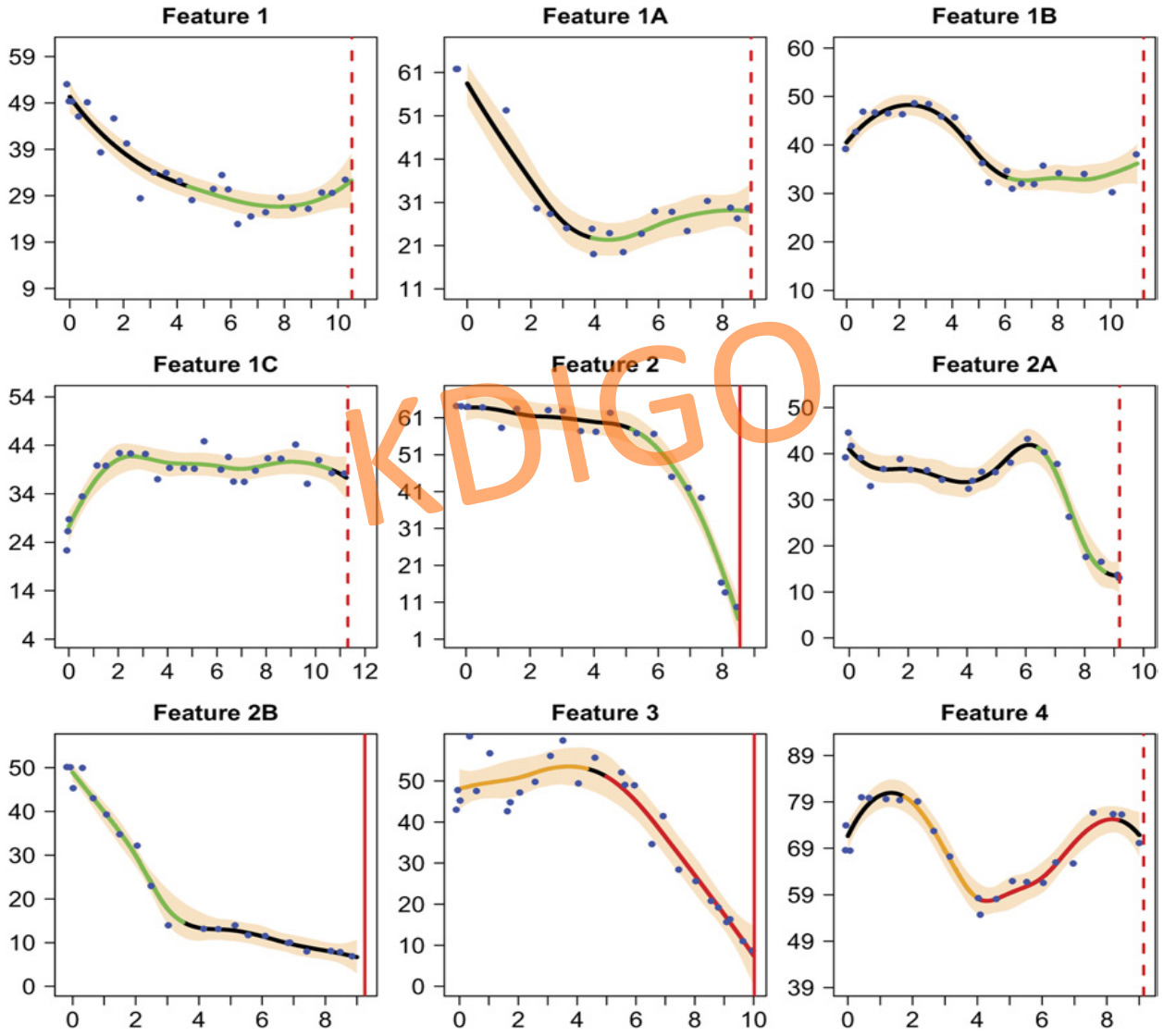
Chi-yuan Hsu et al. JASN doi:10.1681/ASN.2014111114

1 in 5 Patients with AKI Are Re-Hospitalized Within 30 Days (N=111,778 Matched Pairs)



Silver, SA et al. Am J Med 2016; Oct (epub)

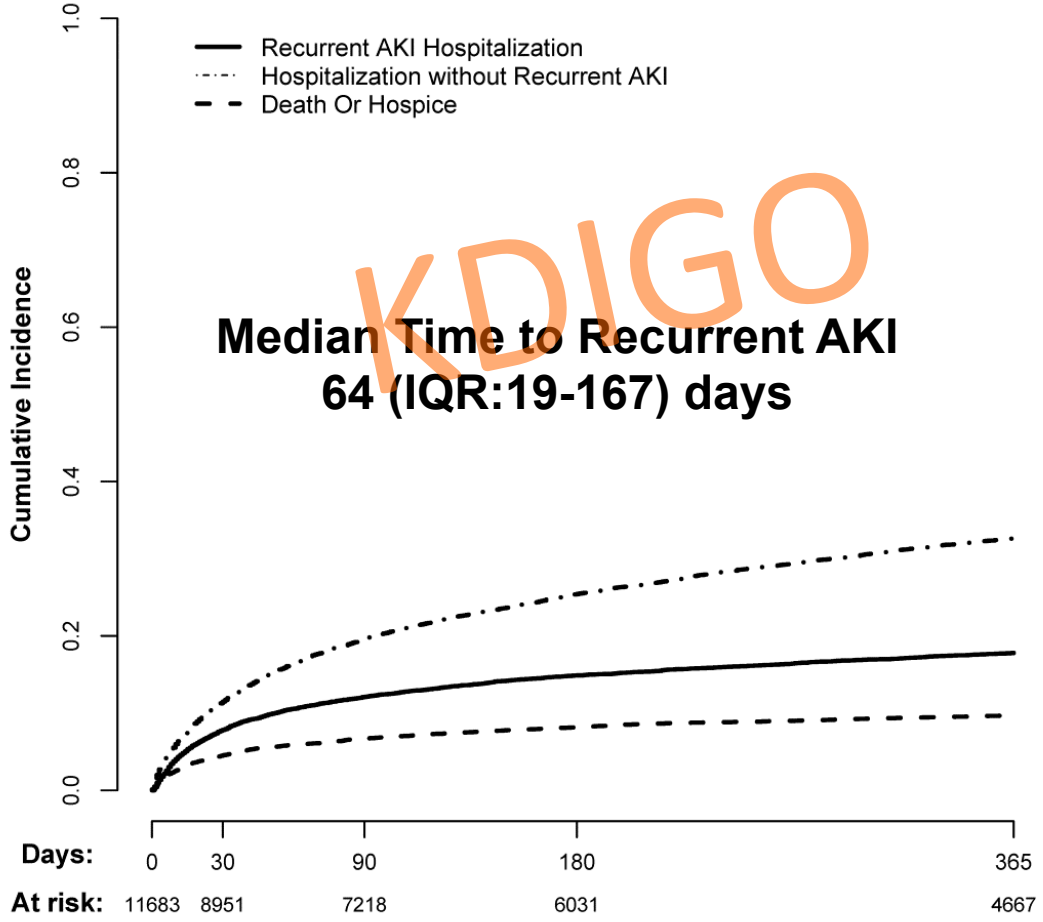
CKD Progression is Often NOT Linear (N=846)



Li, et al. AJKD 2012: 59(4):504-12

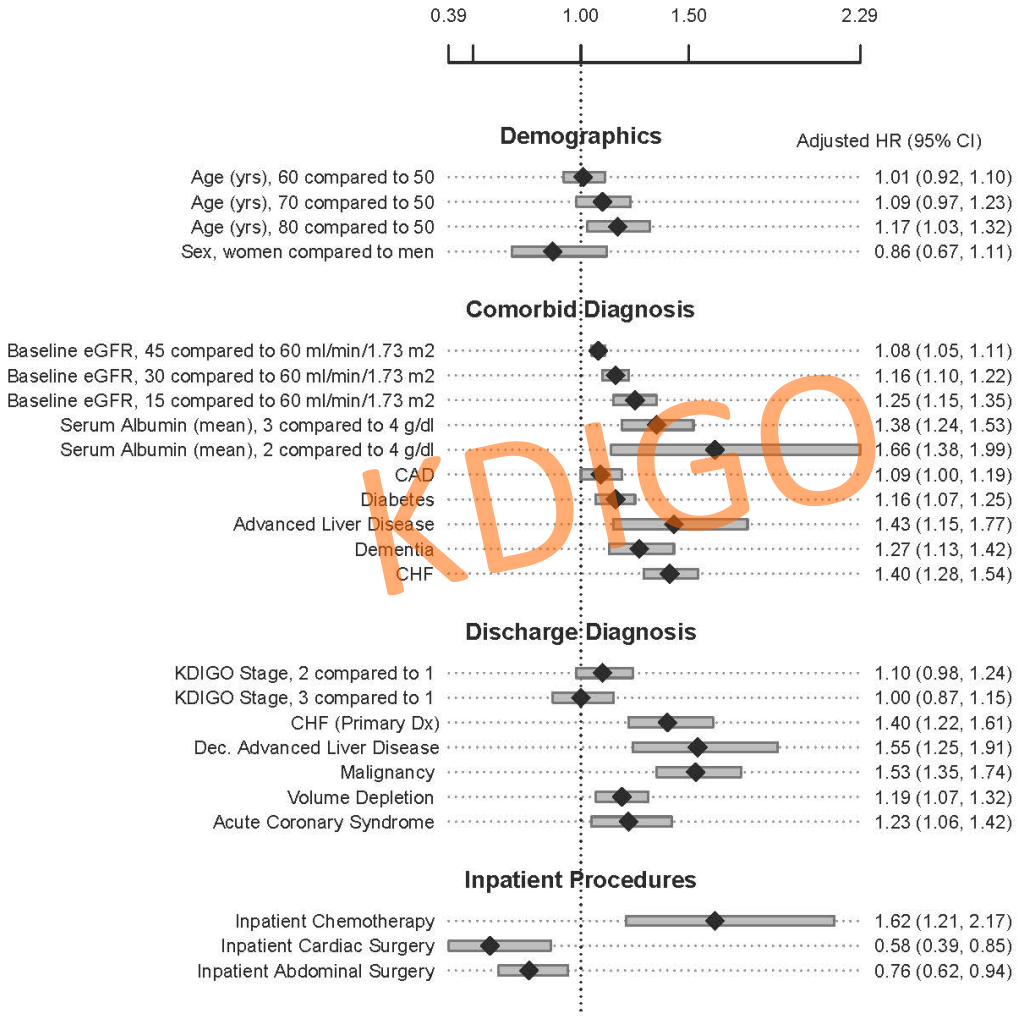
AKI Survivors are at High Risk For Recurrent AKI (N=11,683)

49% Rehospitalized at least once
25% With at least one episode of recurrent AKI
23% Died



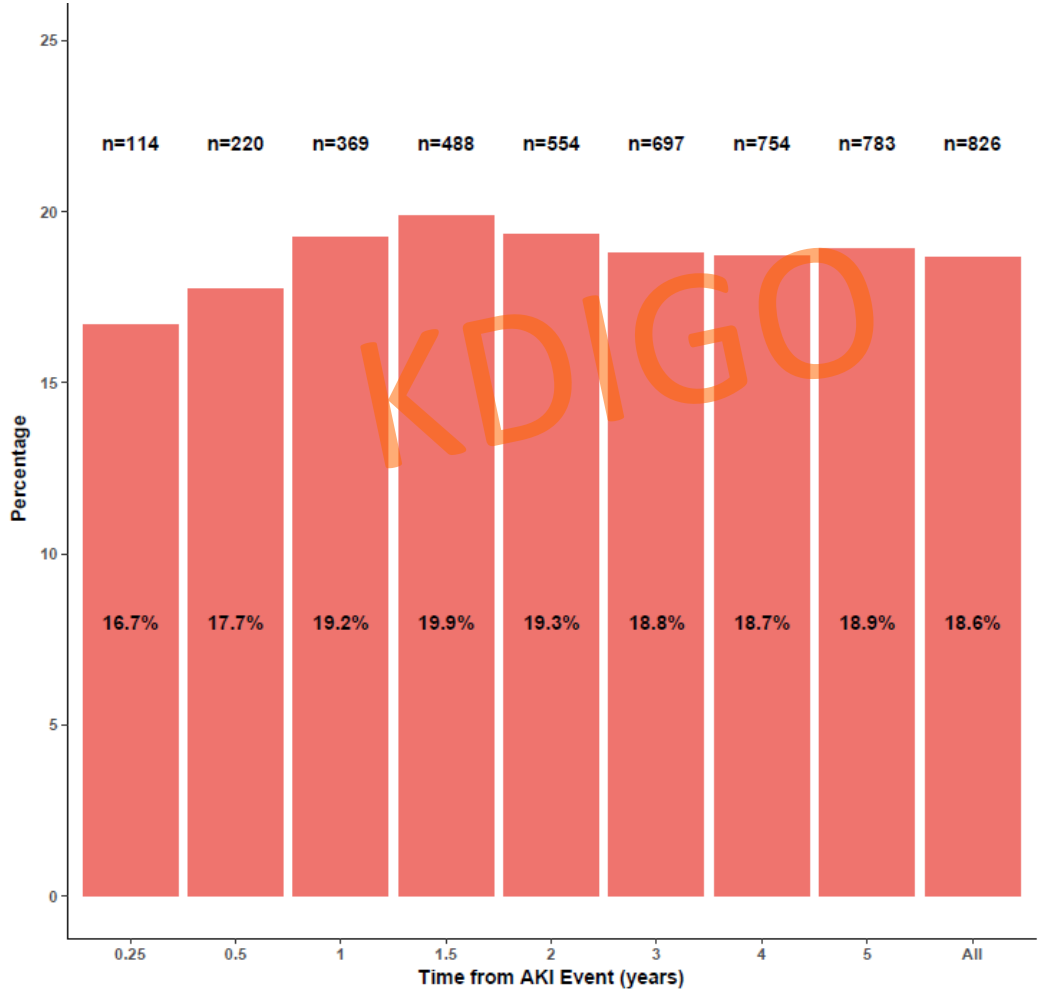
Siew ED, et al. *J Am Soc Nephrol* 2015

Risk Factors for Recurrent AKI Are Not Limited to Age and CKD



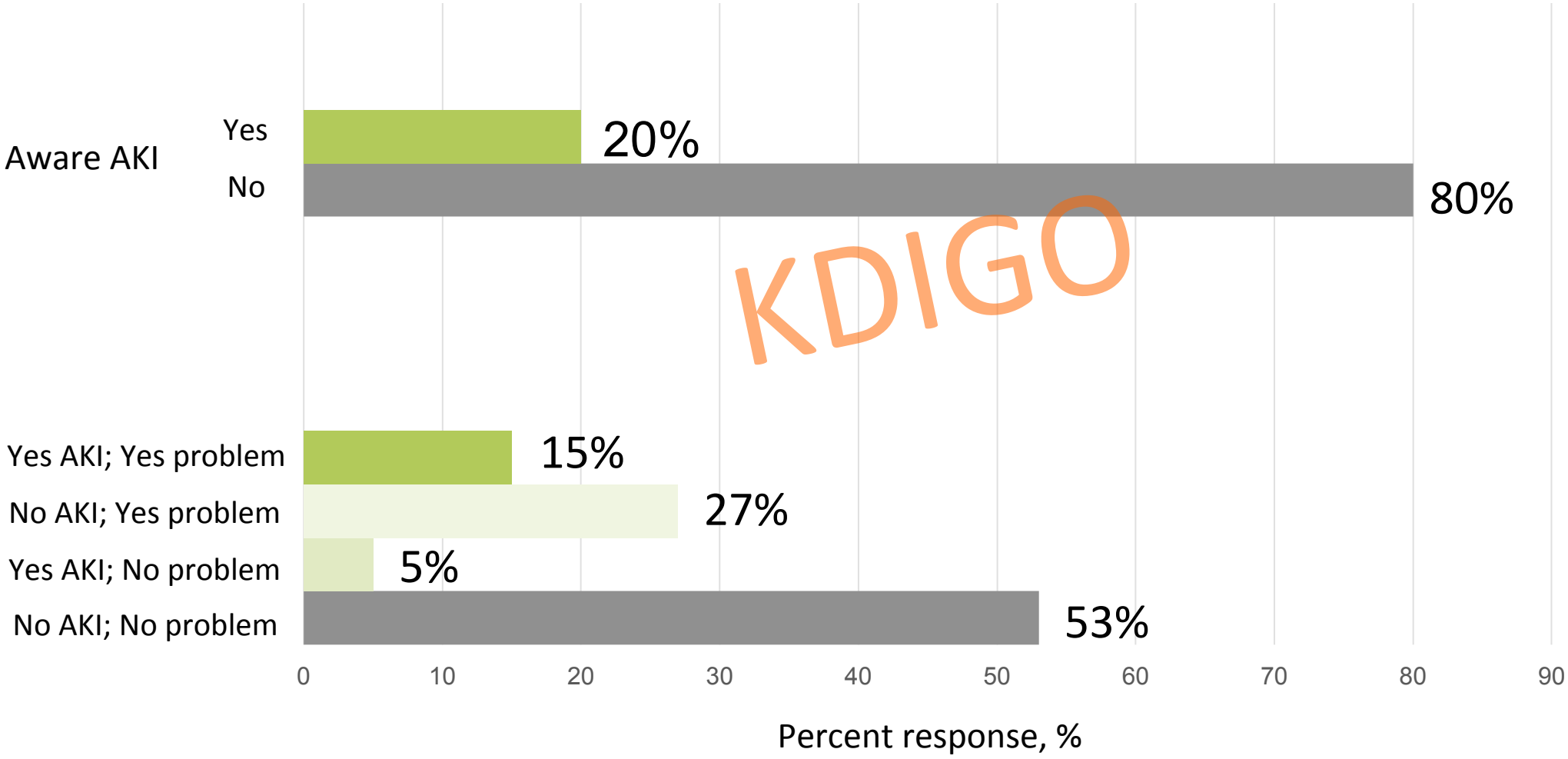
Siew ED, et al. *J Am Soc Nephrol 2015*

1 in 5 AKI Survivors Regularly Use NSAIDs in the Southern Community Cohort Study (N=826)



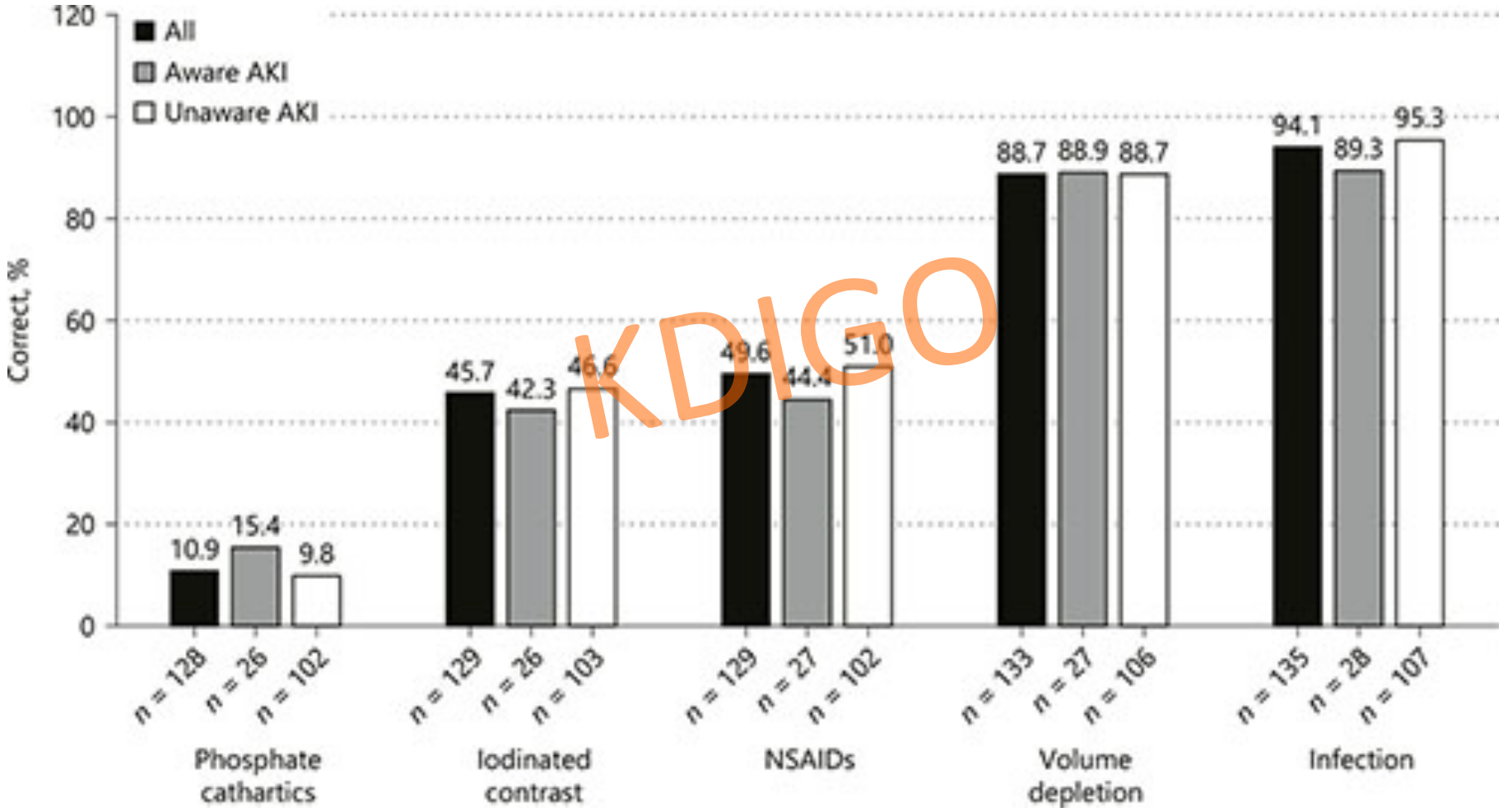
Lipworth, L et al. BMC Nephrology 2016, 17(1):189

Awareness of AKI or Having a Problem with Kidney Health Among Patients with KDIGO Stage II-III AKI (N=137)



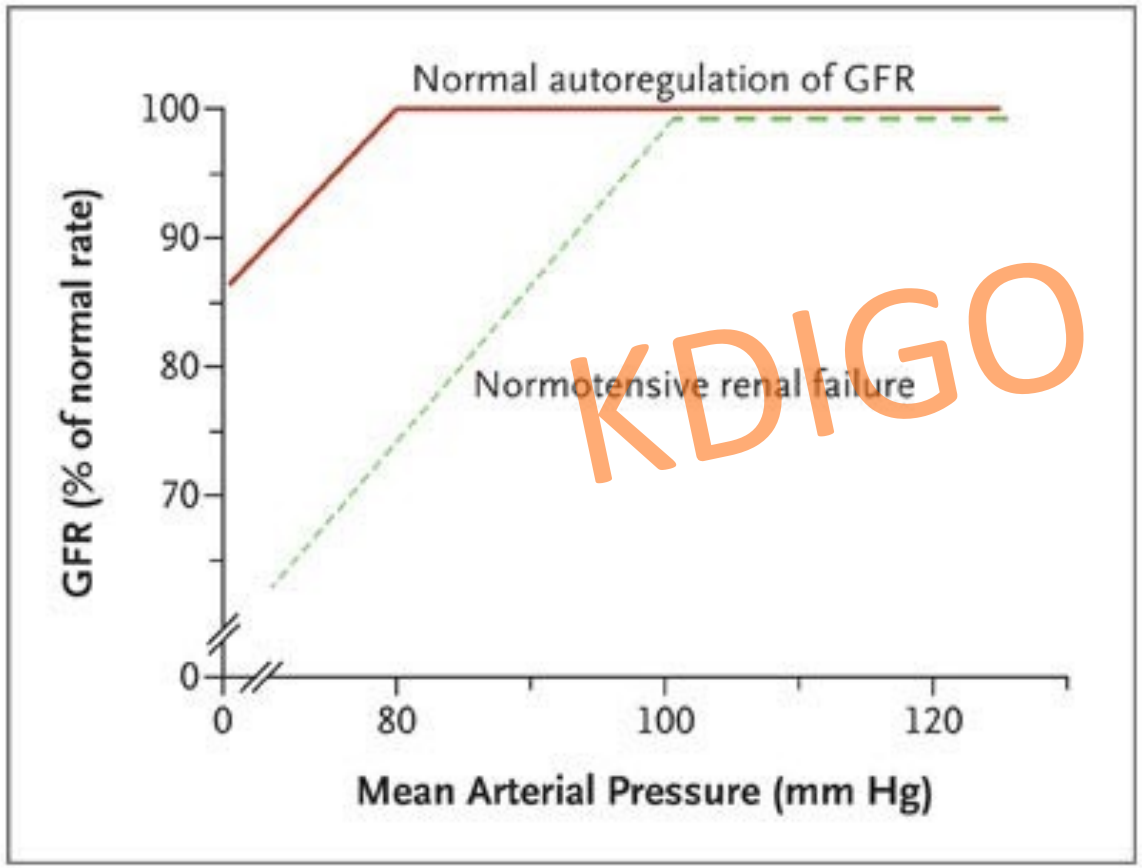
Siew, ED et al. Am J Nephrol 2019: 49:449-59

Knowledge of AKI Risk Factors Among Patients with AKI Stage II-III



Siew ED. Am J Nephrol 2019;49:449–45

Is Recurrent AKI Preventable?



- Nephrotoxin Avoidance
- Volume Management?
- Optimal BP?
- RAAS Inhibition?

Abeulo NEJM 2007; 357:797-805

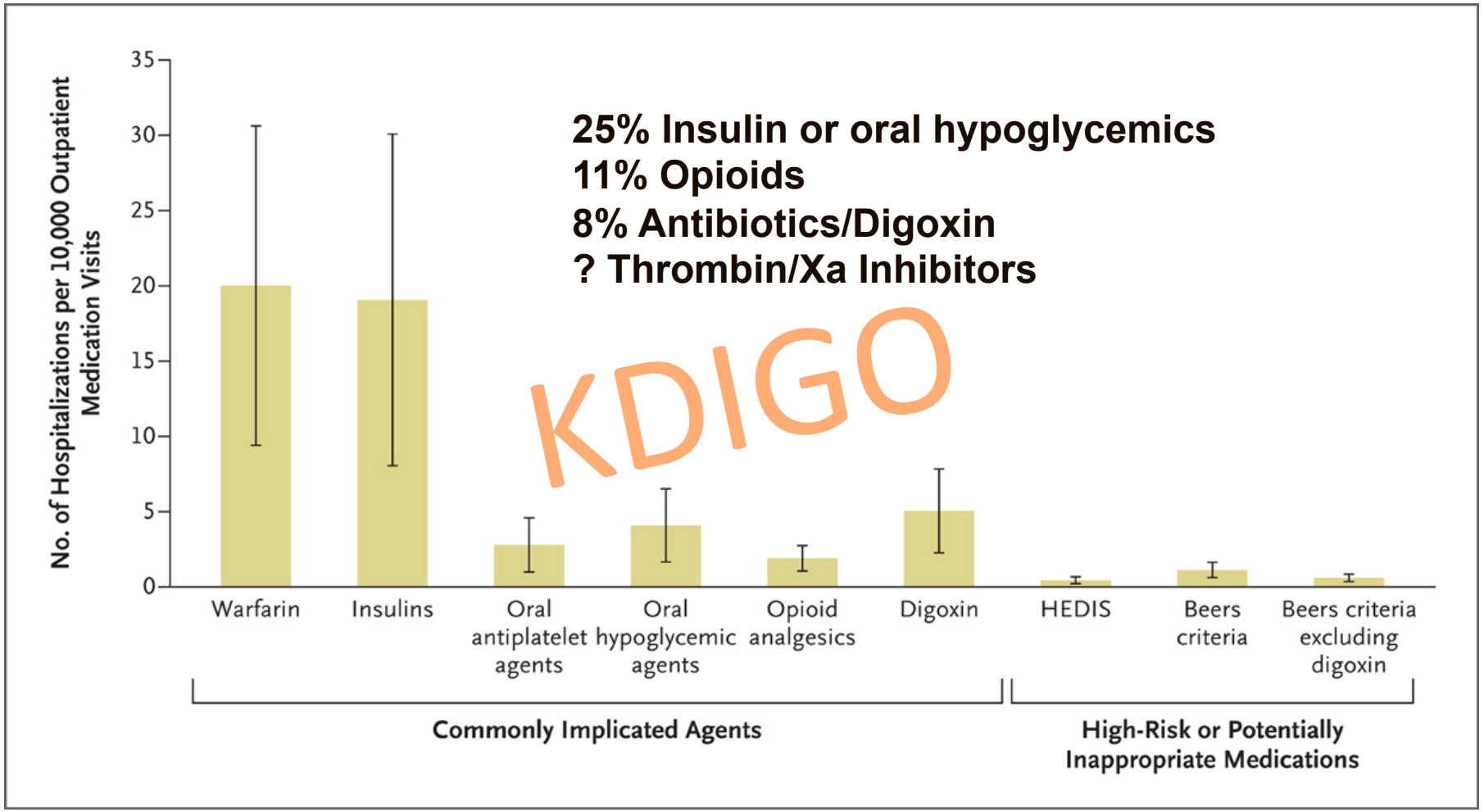
RAAS Inhibition post-AKI?

	#Events/#Patients	Crude HR	Adjusted HR
All-Cause Mortality	3713/9456 (39%)	0.89 (0.85-0.93)	0.85 (0.81-0.89)
Hospitalization for a renal cause	549/9414 (6%)	1.31 (1.15-1.49)	1.28 (1.12-1.46)
Acute renal failure	407/9427 (4%)	1.26 (1.09-1.46)	1.25 (1.08-1.46)
Hyperkalemia	73/9455 (<1%)	1.47 (1.08-2.29)	1.56 (1.07-2.27)

Brar, et al. JAMA Intern Med. 2018;178(12):1681-1690

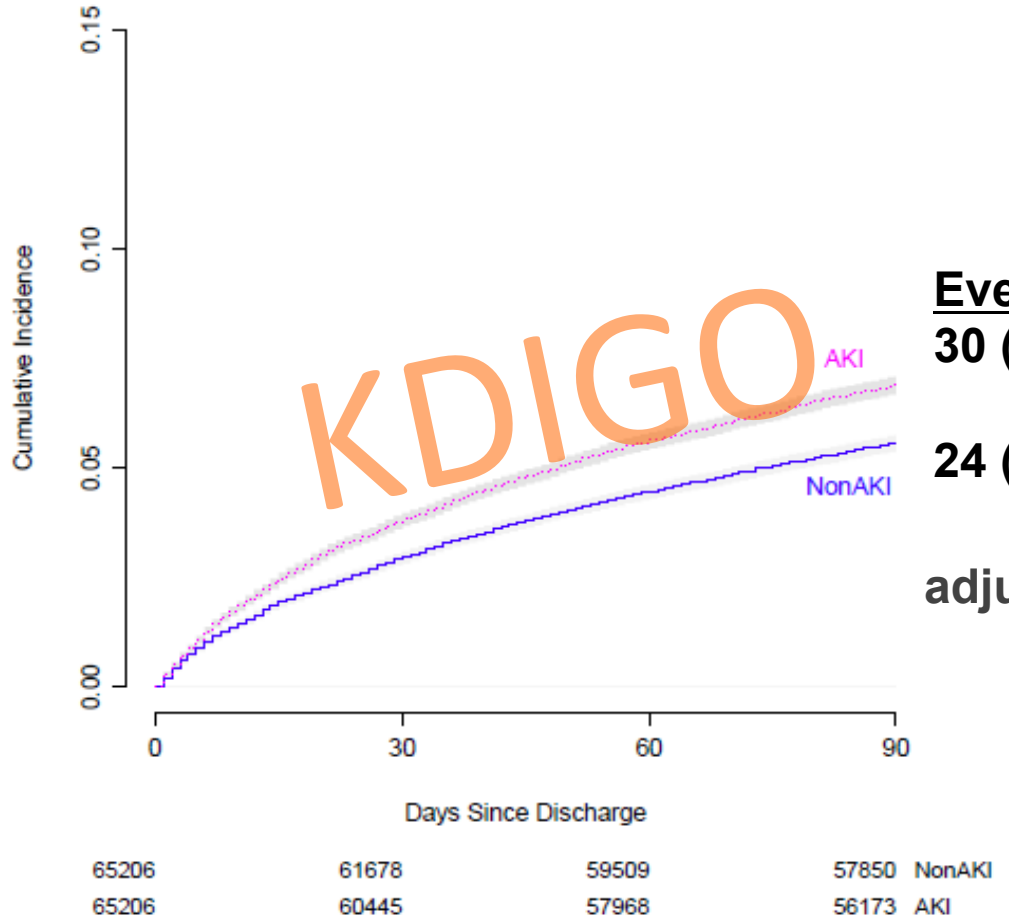
Other Outcomes of Interest?

Adverse Drug Events in Older U.S. Adults Tend to Involve Drugs Cleared by the Kidney



Budnitz DS et al. N Engl J Med 2011;365:2002-2012.

Risk of Hypoglycemia Among AKI Survivors with Diabetes (N=65K matched pairs)



Events per 100 PYs

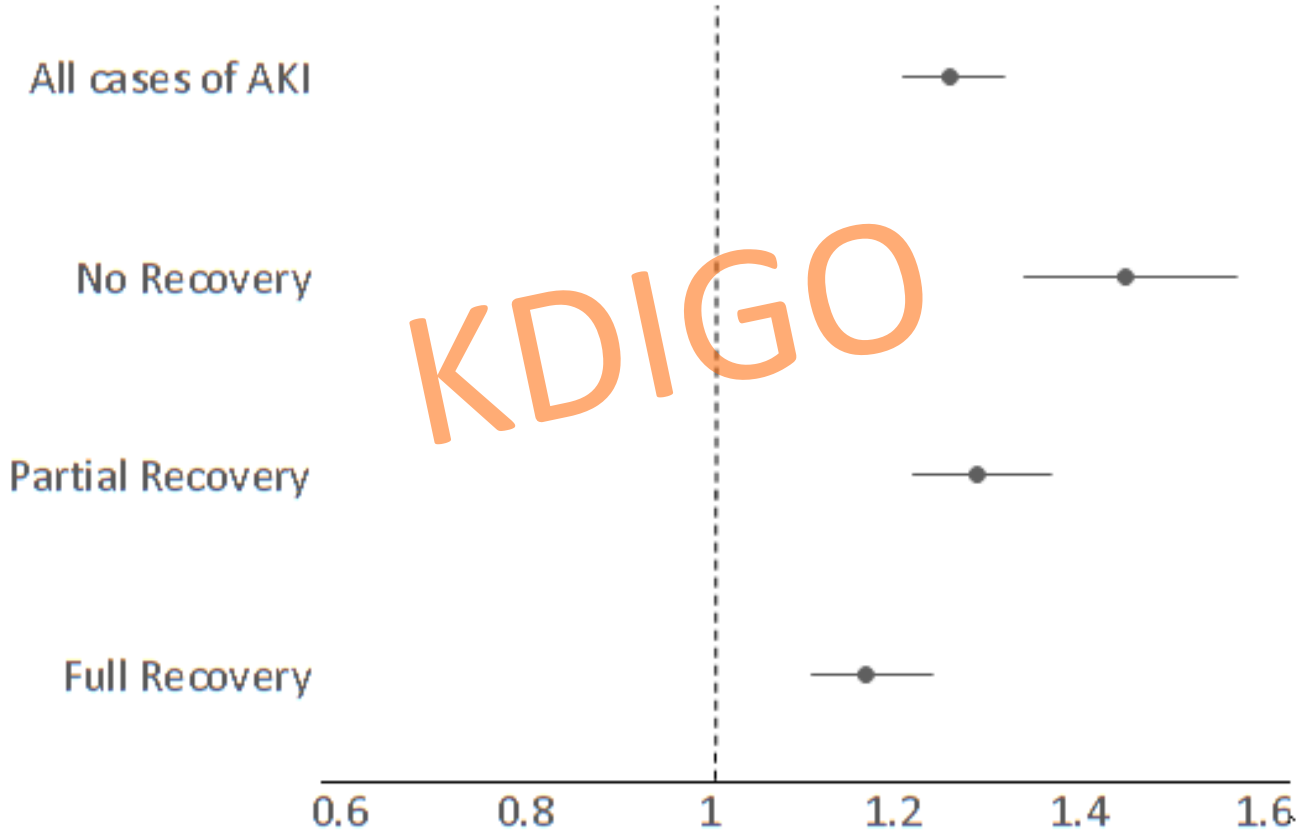
30 (29-30)

24 (23-24)

adjusted HR 1.26, 95% CI: 1.21-1.32

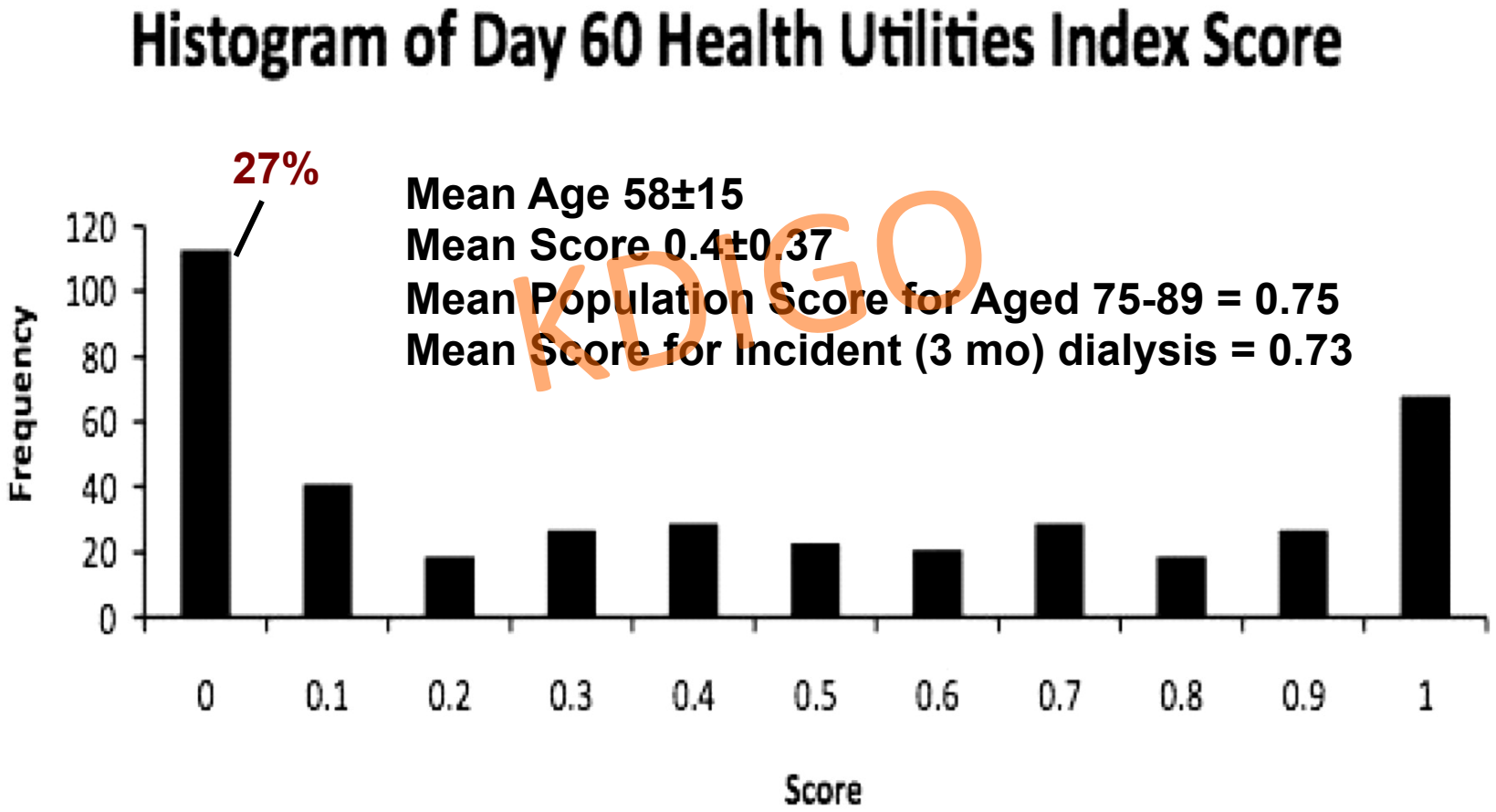
Hung, AM, et al. Diabetes Care 2018; 41(3) 503-12

Poor Recovery Increases Risk for Hypoglycemia After AKI Among Patients with Diabetes



Hung, AM, et al. Diabetes Care 2018; 41(3) 503-12

Health Utilities Index Scores are Low Among 60-day Survivors of the ATN Study(N=414)

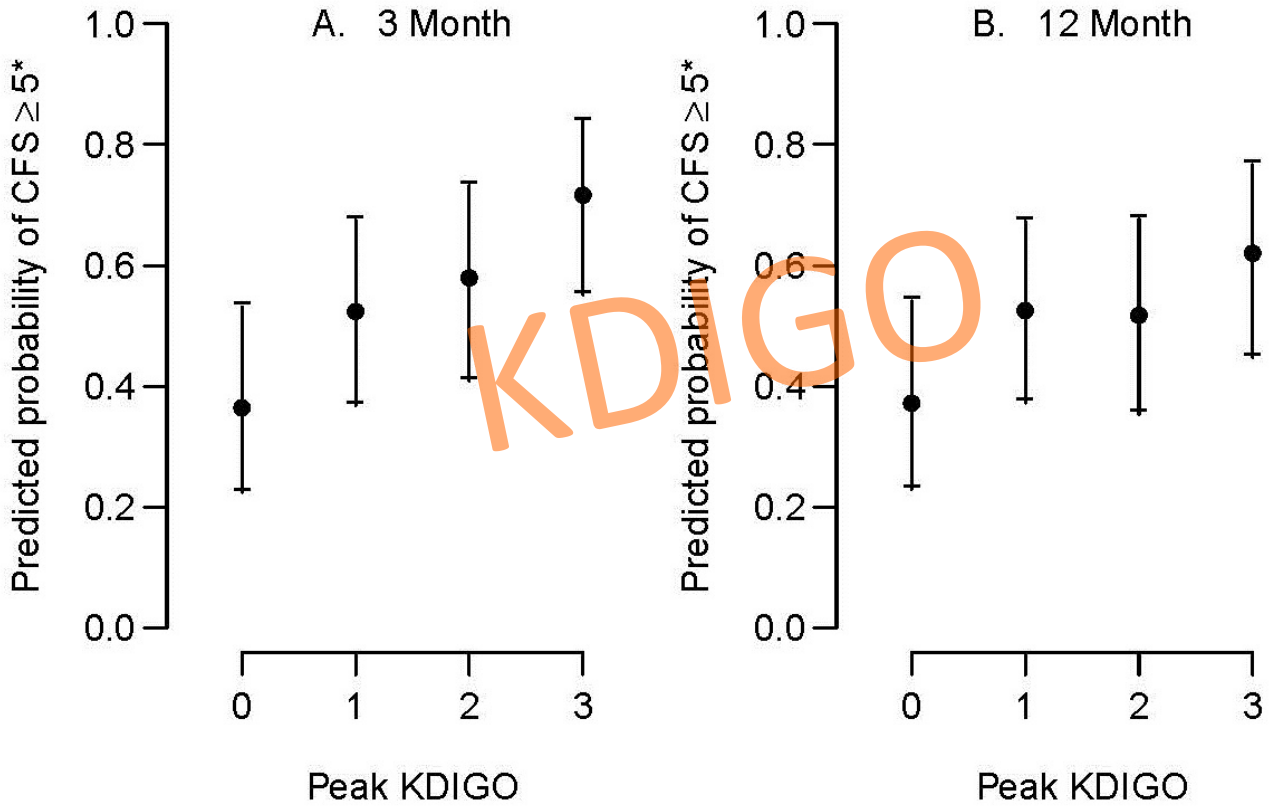


Johansen K L et al. CJASN 2010;5:1366-1372

Reasons to Address Long-Term Goals Following Hospitalization

- Risk of rehospitalization/death are high
- It will be an informed discussion
- Good opportunity to coordinate with PCP
- Other home caregivers more likely to be available and engaged
- Optimal time to listen for patient preferences and to engage in shared-decision making

Probability of Developing Frailty Increases with AKI Stage in Critically Ill (No AKI N=74, AKI N=243)



Abdel-Kader, K et al. *Crit Care Med* 2018; 46(5):e380-88

Transition to Chronic Dialysis– House Maintenance

PICC Line Use increasing

- 942,000 sold in US/annually

Sadfar N, Chest 2005; 128(2):489-95
Medtech Insight

Case Control Study, N=282 w/o nonrecovered AKI

- 120 non-AVF(catheter/AVG) vs. 162 AVF
- % PICC: 44.2% non-AVF vs. 19.7% in AVF, p< 0.001
- Adjusted OR for non-AVF 2.5 (1.2-5.4)
  Gender, vein/artery size, and any CVC

Ters, ME AJKD 2012; 60(4):601-608

Summary

- The number of AKI survivors is growing
- Survivors are at risk for future loss of kidney function, cardiovascular disease, death, and disability/poor QoL
- Proportion who follow-up with Nephrology is low

….BUT, Optimal Care Strategies Need to be Defined

Potential Domains to Improve Post-AKI Care

- Monitoring for recovery/recurrent AKI
- Identification and Referral for those at High Risk (duration, severity, ? Biomarkers/RFR)
- Recognition/Treatment of intermediate targets (proteinuria, BP)
- Prevention of Recurrent AKI/rehospitalizations (nephrotoxin use, ? blood pressure/volume/RAAS?), Adverse Drug Events
- **Critical Patient-Centered targets**: HrQOL/Frailty, symptom management, educational awareness, transitions to ESRD or conservative care, nutrition

Acknowledgements

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- Vanderbilt Center for Kidney Disease (VCKD)