

# Dialysis Dependent AKI: Conveyer Belt vs Personalized Care?

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# Disclosures

- Editorships
  - ASN, NKF, Springer
- Consulting
  - Teladoc, Vifor, NxStage
- DSMB/Steering Committees
  - Quark, Labcorp

# Objectives

- Describe pathophysiology of AKI and CKD connection
- Discuss epidemiological data supporting AKI and CKD connection
- Inform impact of AKI during transition to dialysis and beyond
- Discuss individualized models of care in ESRD based on AKI status

Hummingbirds of USA

# Story of Mr. Smith and Mr. Jones

- **Mr. Smith**

70 year old male with T2DM, with Stage III CKD with proteinuria developed stage II AKI on CKD post cardiac cath in September 2022.

Creatinine remained slightly higher than baseline.

On December 15<sup>th</sup> 2022 he underwent 2 vessel CABG; developed AKI on CKD and remained dialysis dependent post discharge.

Discharged to home with cardiac rehab but on dialysis.

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70 year old male with T2DM, and CKD Stage IV CKD with proteinuria.

Underwent outpatient cardiac cath with PTCA and DES to LAD and Circumflex in December 15<sup>th</sup> 2022.

Creatinine remained stable post-cath.

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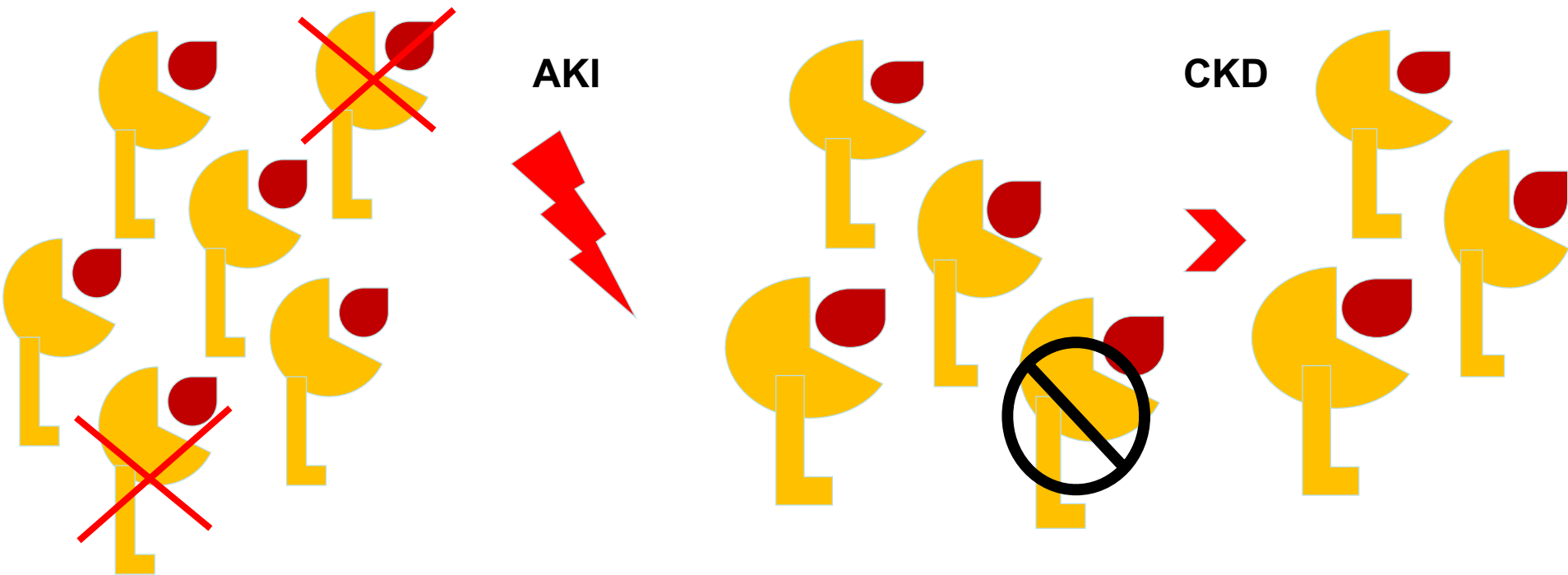
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**Should Mr. Smith and Mr. Jones receive the same dialysis care at FraVita Renal Care Inc.**

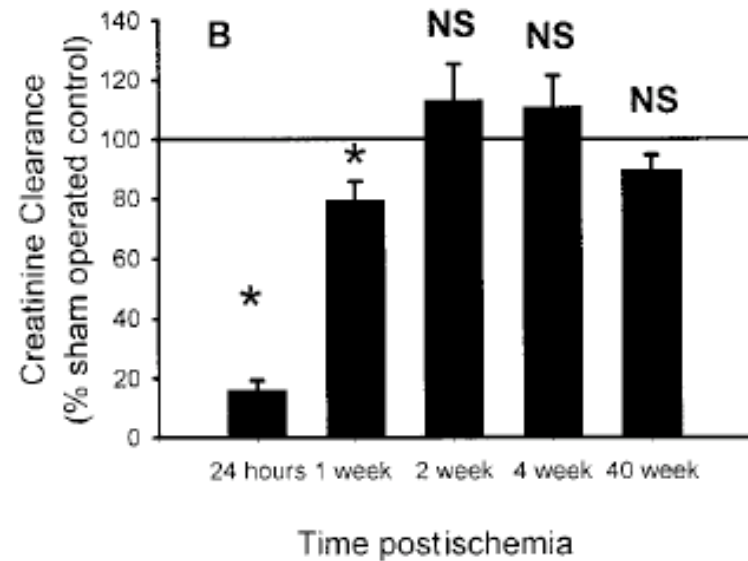
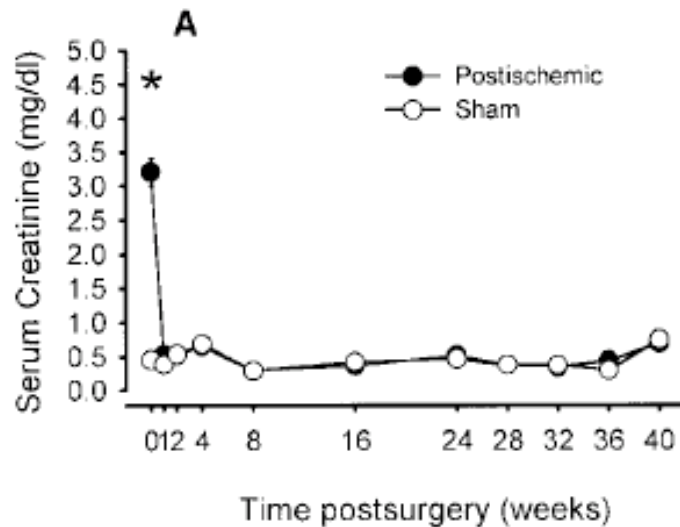
# The Dialysis Conveyer Belt



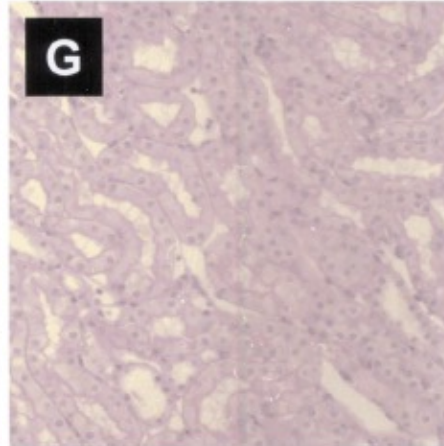
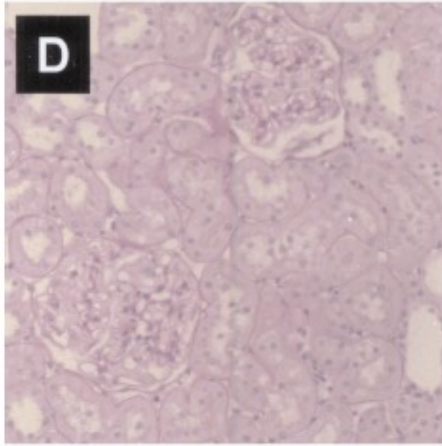
# AKI to CKD: Causal Pathway?



# “Normalization” of Creatinine post IRI

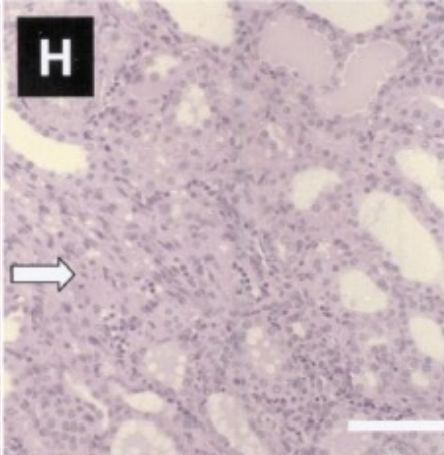
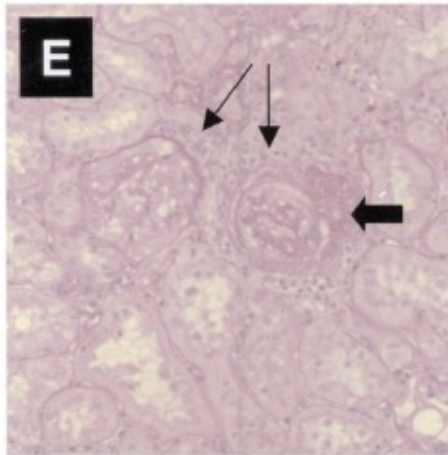


# Microscopic Changes after IRI



40 Weeks

Sham



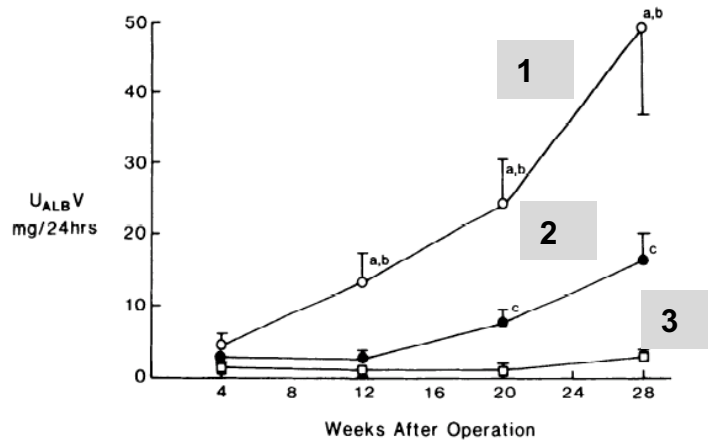
Post IRI

- Increased Pro-fibrotic activity
- Loss of capillary density
- Tubular Atrophy
- Glomerular Sclerosis

Basile, AJP, 2001

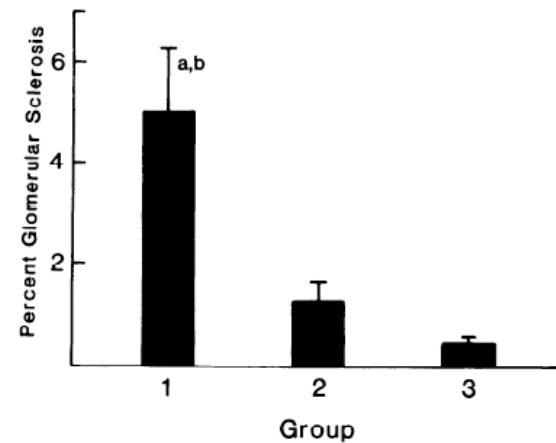
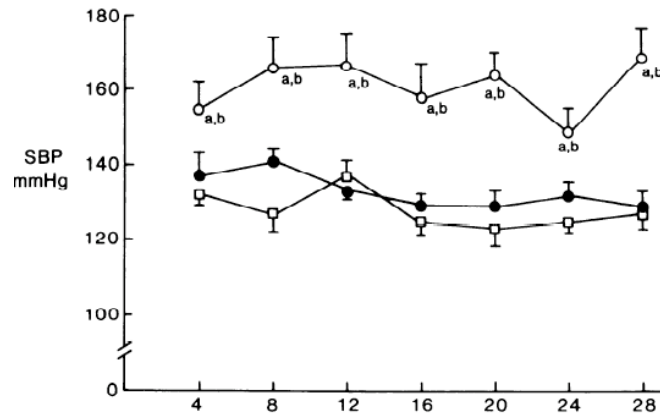


# AKI: Proteinuria and Neurohormonal Changes



Group 1 – Bilateral Segmental Infarct  
 Group 2 – Contralateral Nephrectomy  
 Group 3 – Sham operated

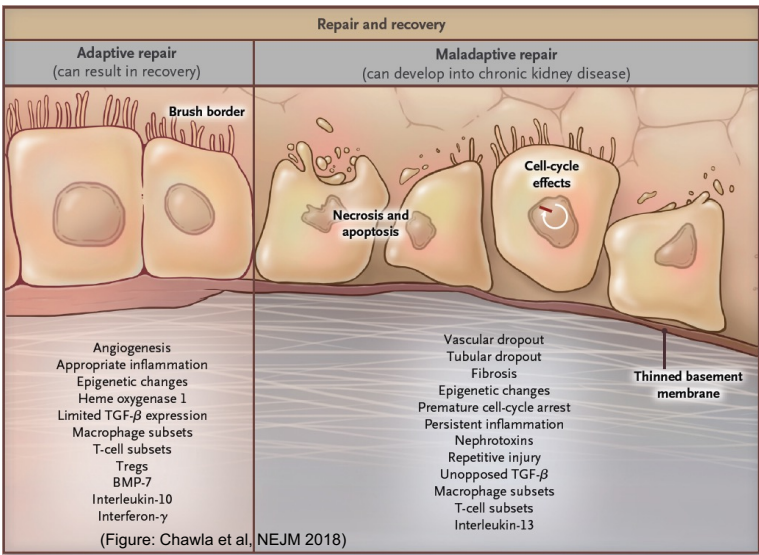
Meyer & Renke, AJP, 1988



# AKI → CKD

Susceptibility:  
Co-morbidity  
Age  
Drugs/toxins

AKI Episode



Tissue Fibrosis

Albuminuria

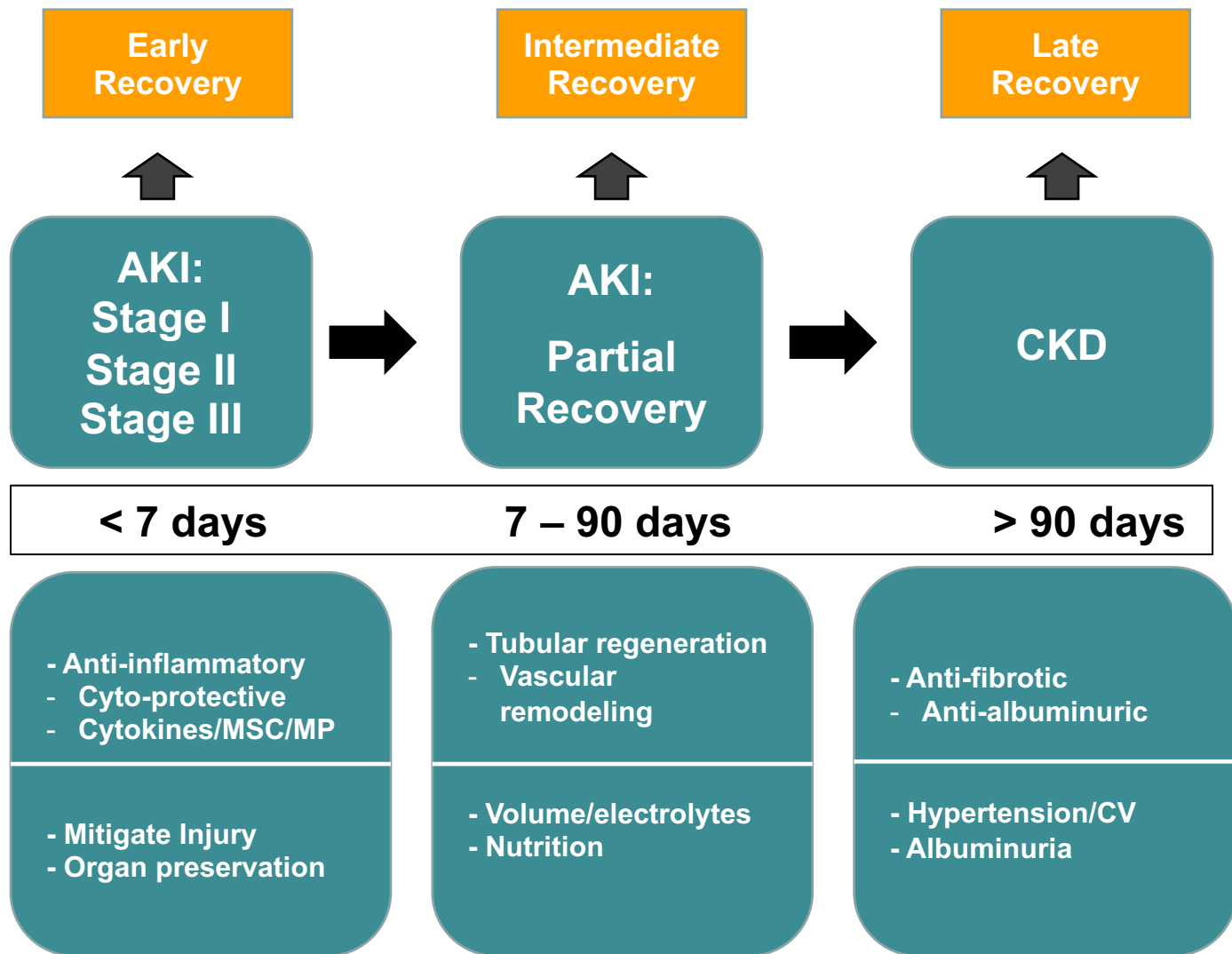
Increased Blood Pressure

Neuro-hormonal adaptation

Pro-inflammatory State:

Kidney and Beyond

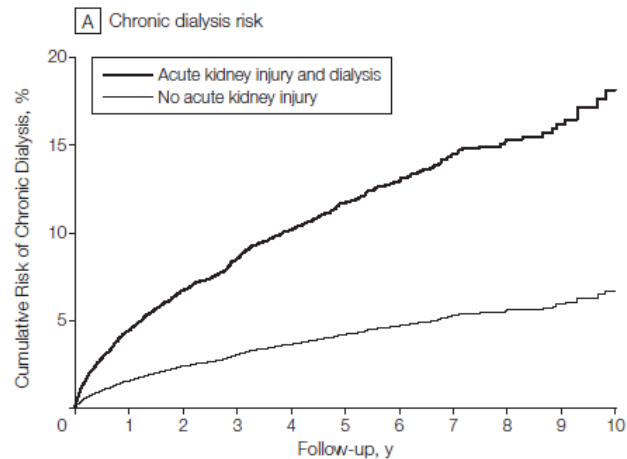




**Rufous Hummingbird**



# AKI-Dialysis and ESRD Risk



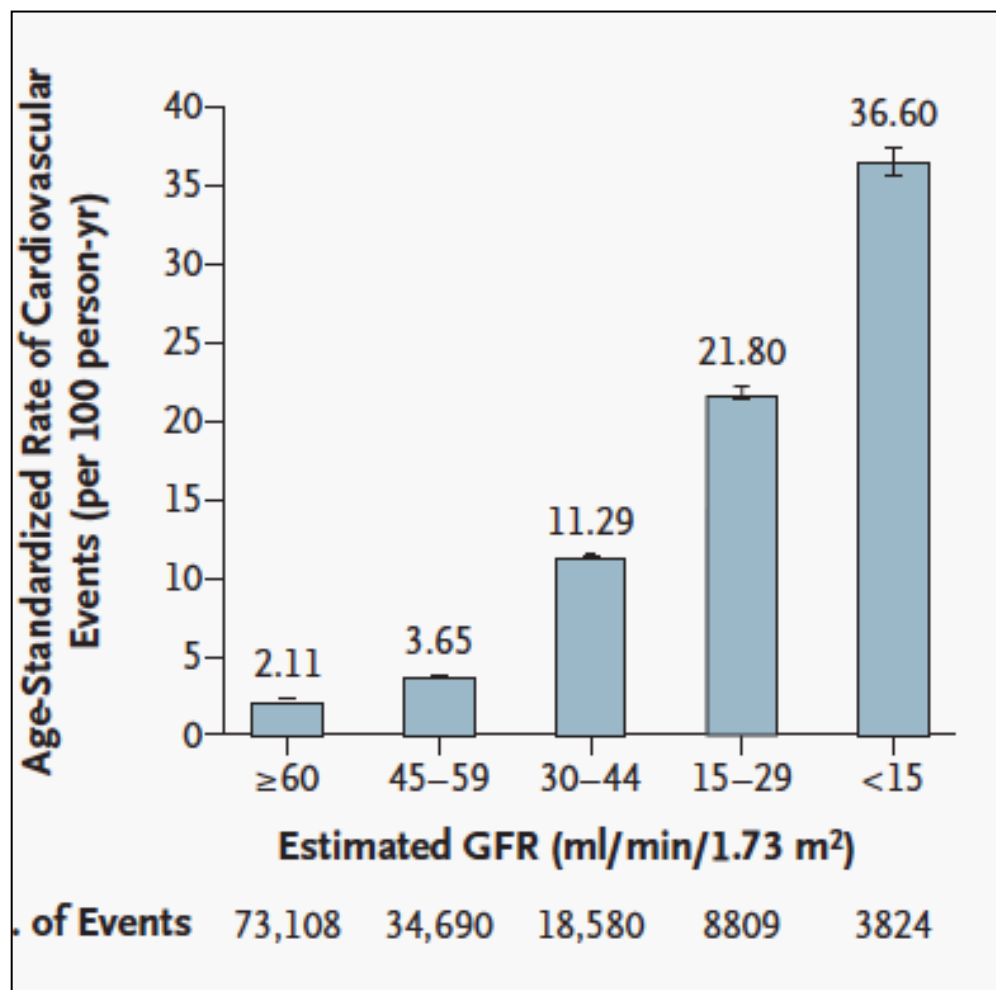
| No. at risk                      | 0     | 1     | 2    | 3    | 4    | 5    | 6    | 7    | 8   | 9   | 10  |
|----------------------------------|-------|-------|------|------|------|------|------|------|-----|-----|-----|
| Acute kidney injury and dialysis | 3769  | 2761  | 2116 | 1683 | 1305 | 964  | 676  | 462  | 294 | 158 | 58  |
| No acute kidney injury           | 13598 | 10224 | 7850 | 6080 | 4639 | 3383 | 2342 | 1555 | 905 | 473 | 169 |

**Table 2.** Risk of Chronic Dialysis and All-Cause Mortality by Group

| Outcome             | Acute Kidney Injury and Dialysis at Index Hospitalization (n = 3769) |                                     | Without Acute Kidney Injury or Dialysis at Index Hospitalization (n = 13 598) |                                     |
|---------------------|--|-------------------------------------|---|-------------------------------------|
|                     | No. of Events (%)  | Incidence Rate Per 100 Person-Years | No. of Events (%)   | Incidence Rate Per 100 Person-Years |
| Chronic dialysis    | 322 (8.5)  | 2.63                                | 403 (3.0)   | 0.91                                |
| All-cause mortality | 1311 (34.8)  | 10.10                               | 4884 (35.9)   | 10.83                               |

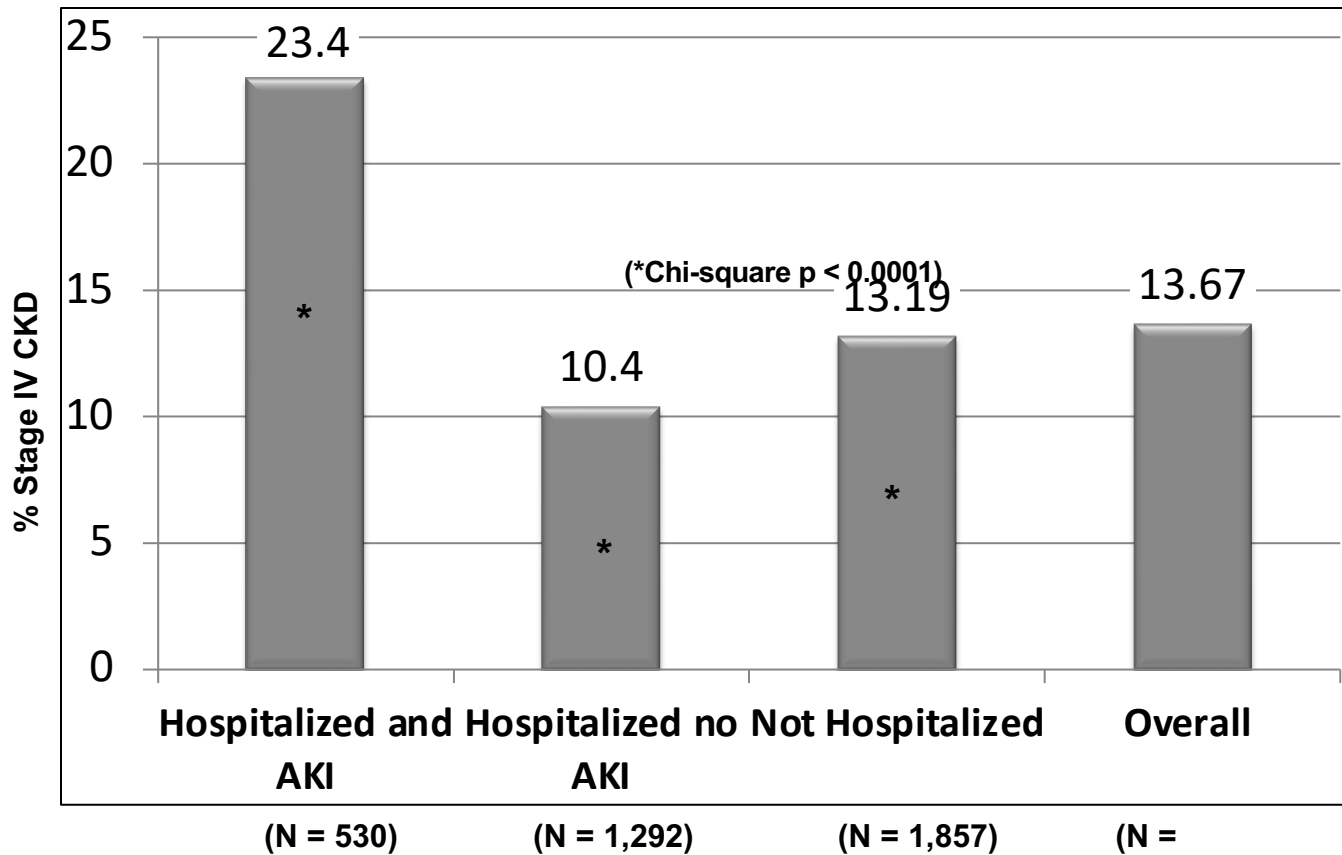
Wald et al, JAMA, 09

# CKD: CV events and Hospitalizations



CV Events

# Frequency of Stage IV CKD



(Thakar et al, CJASN; 2011)

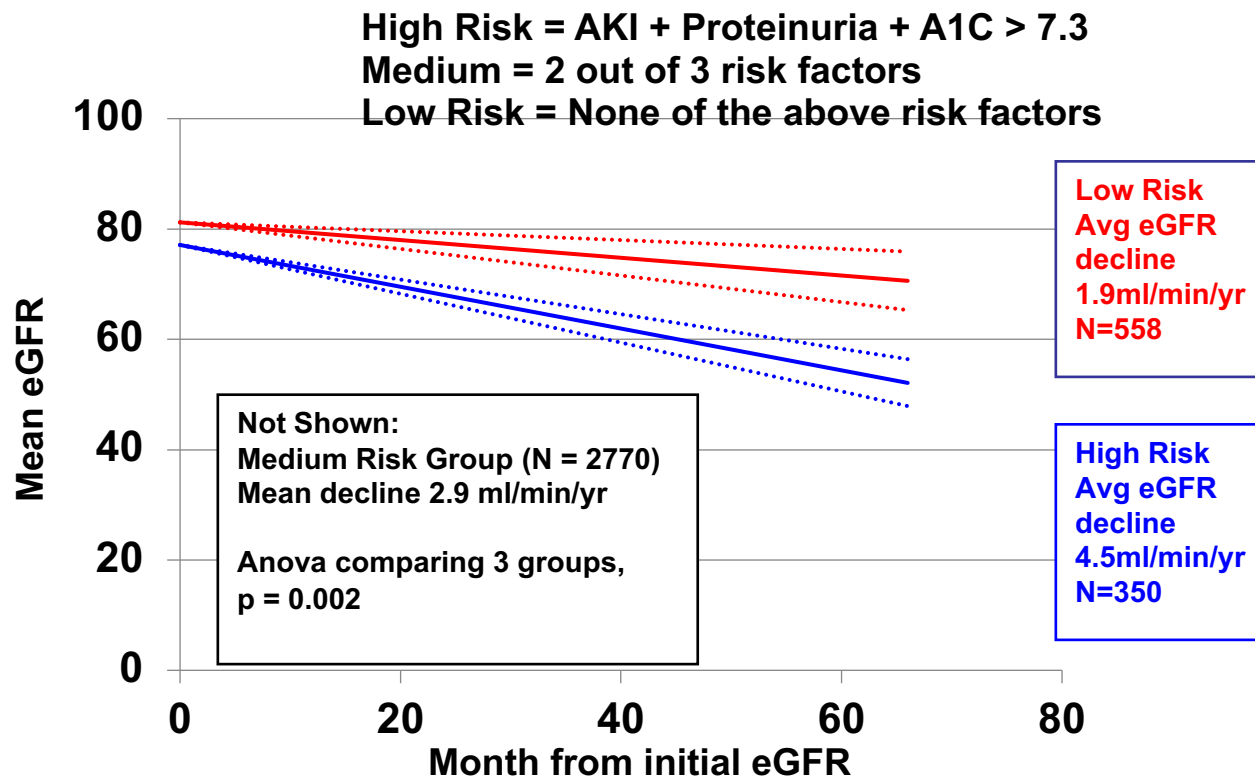
# Risk Factors of Stage IV CKD in DM

| Risk Factors                            | Hazard Ratio | 95% Confidence Interval |
|---|--------------|-------------------------|
| Age (in years)                          | 1.01         | 0.99, 1.02              |
| Sex (female <i>versus</i> male)         | 2.65         | 1.40, 5.03              |
| Race (black <i>versus</i> non-black)    | 0.91         | 0.71, 1.24              |
| Baseline creatinine (per unit increase) | 8.59         | 6.07, 12.15             |
| Obesity                                 | 0.72         | 0.52, 0.98              |
| Hypertension                            | 1.82         | 1.41, 2.37              |
| Proteinuria                             | 3.54         | 2.47, 5.08              |
| AKI                                     | 3.56         | 2.76, 4.61              |
| Number of episodes                      |              |                         |
| AKI (each episode, up to three)         | 2.02         | 1.78, 2.30              |

(Thakar et al, CJASN, 2011)

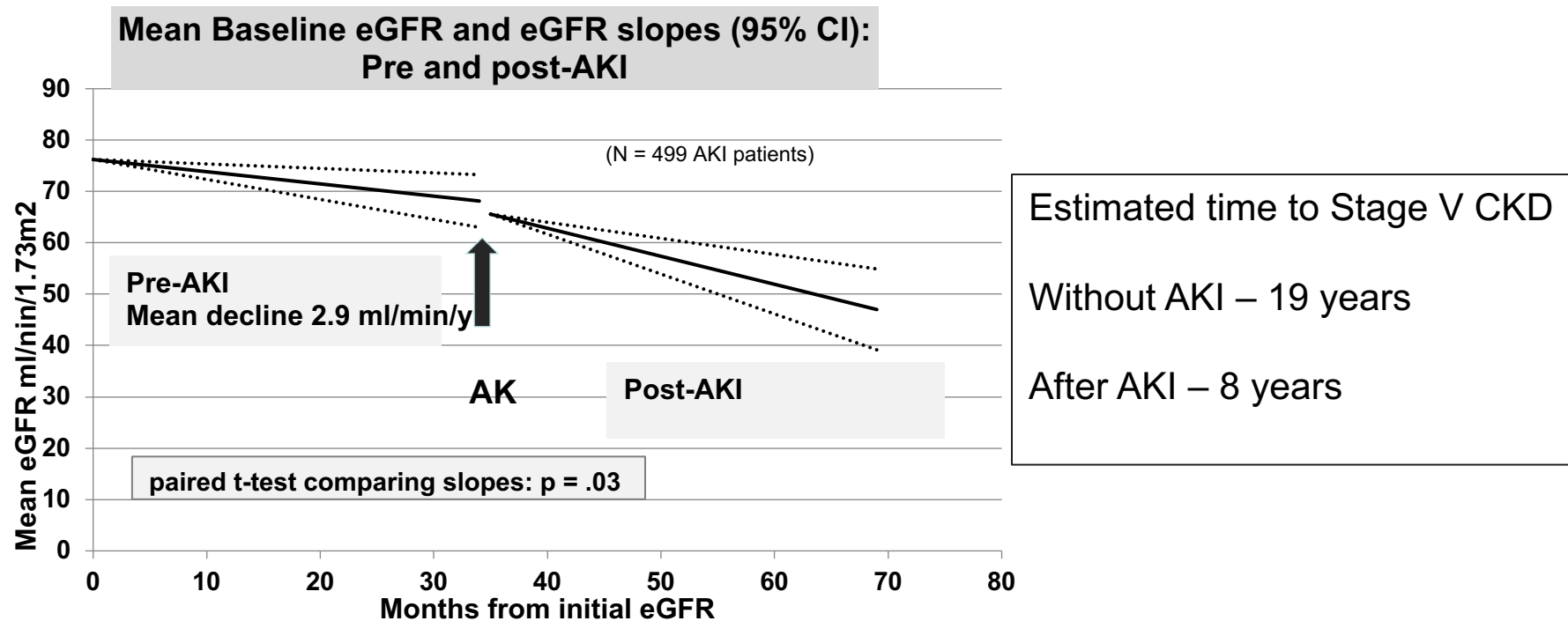


# HbA1C, Proteinuria and AKI: eGFR Decline Across Risk Groups



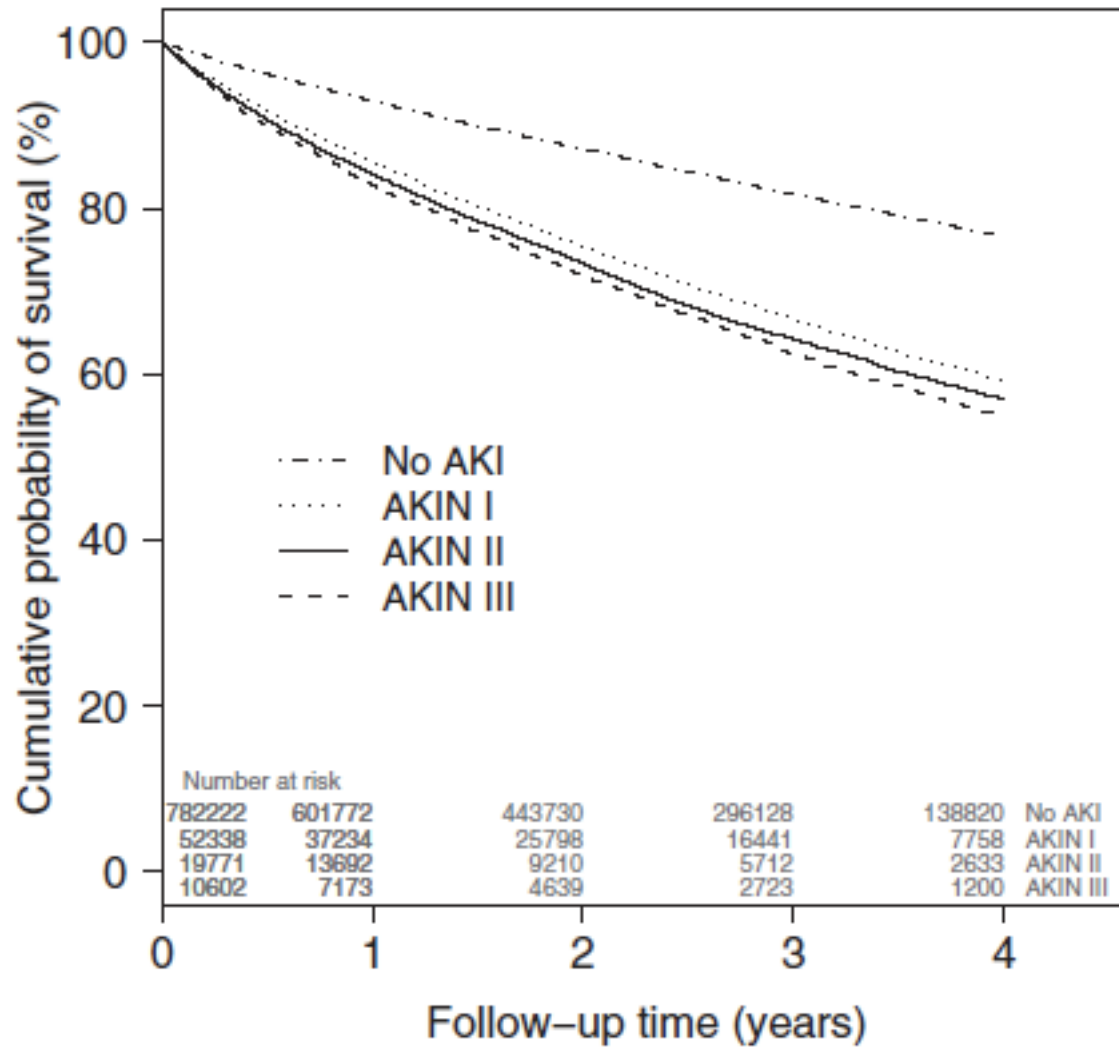
M. Sands & Thakar et al, ASN 2016

# AKI and eGFR Slopes in T2DM



M. Sands & Thakar et al, ASN 2016

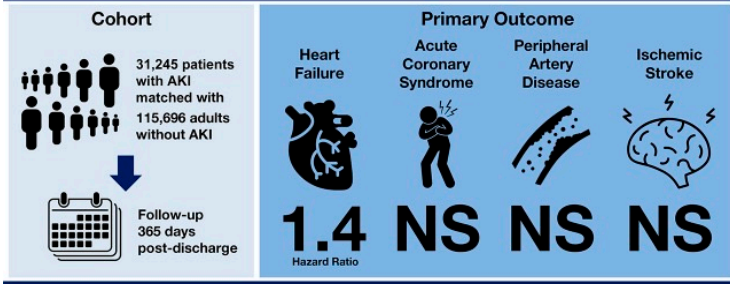
# Long-term Survival and AKI Severity



# AKI and Risk of New CHF

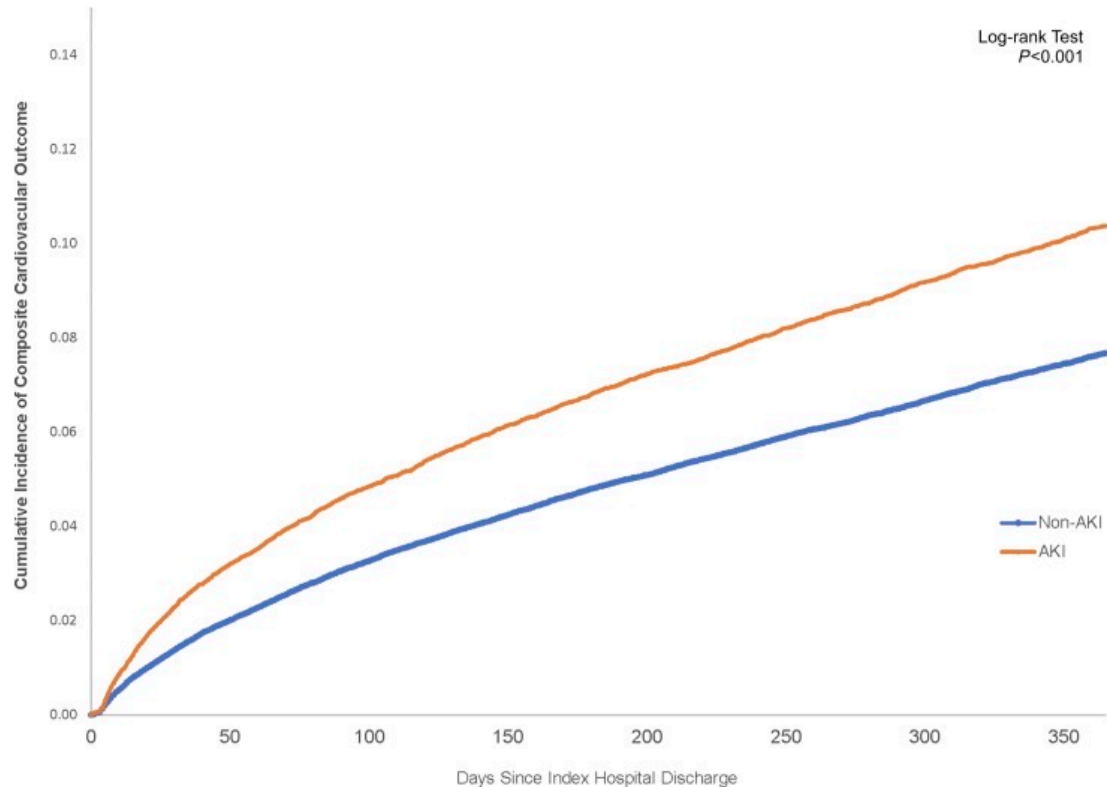
Is AKI associated with a higher risk of cardiovascular events 1-year after discharge?

CJASN  
CLINICAL JOURNAL OF AMERICAN SOCIETY OF NEPHROLOGY

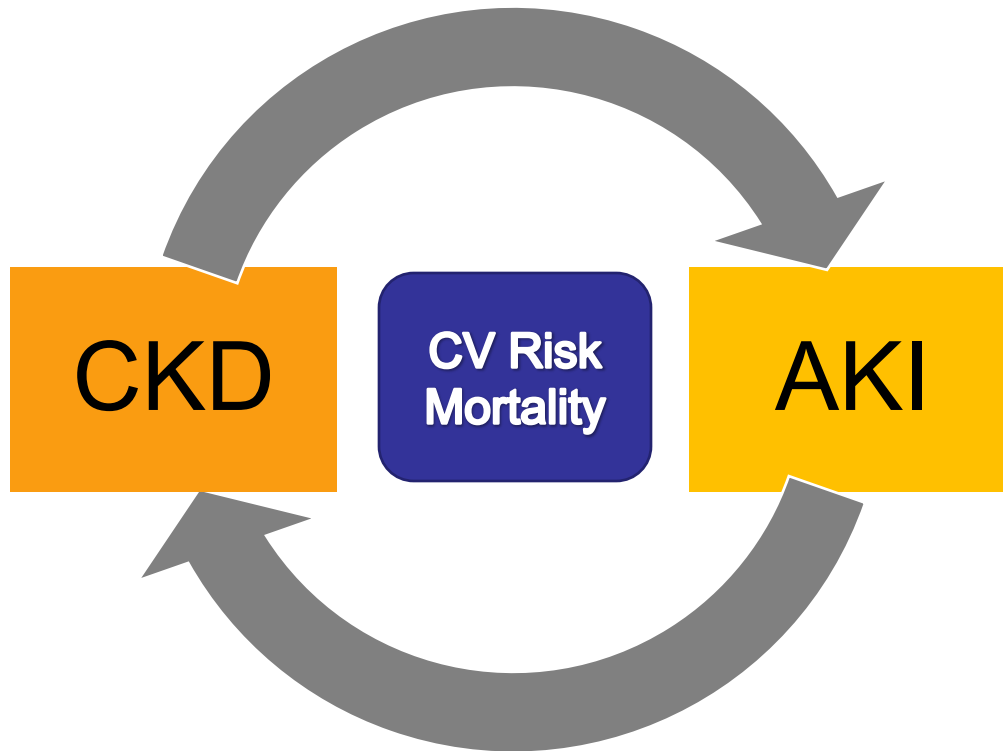


**Conclusions** AKI is independently associated with a higher risk of cardiovascular events, especially heart failure, after hospital discharge.

Alan Go, Chu-yuan Hsu, Jingrong Yang, Thida Tan, Sije Zheng, Juan Ordóñez, and Kathleen Liu. Acute Kidney Injury and Risk of Heart Failure and Atherosclerotic Events. CJASN doi: 10.2215/CJN.12591117.



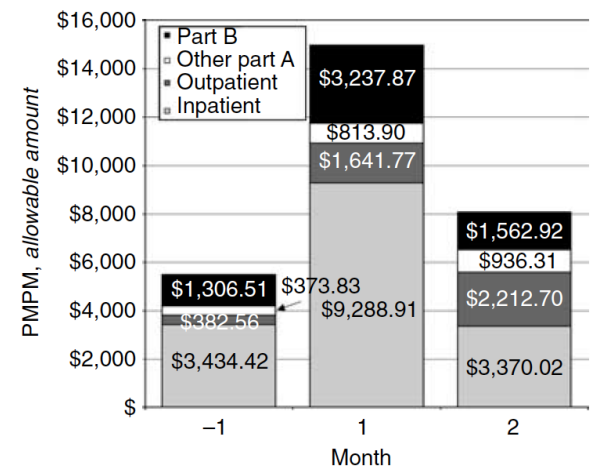
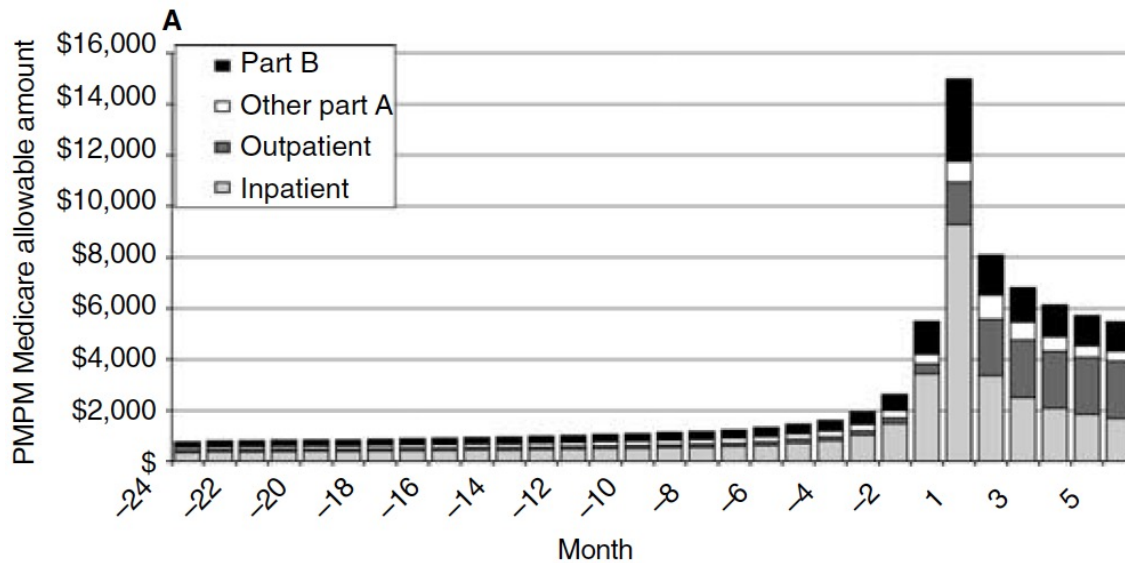
# AKI and CKD Link



Broad Billed Hummingbird



# Transition to ESRD



W St. Peter et al, KI 2004

# Some Key Statistics

- 70% -- Patients starting first treatment in hospital/Dialysis Dependent AKI
- 80% -- Patients starting first treatment with a catheter
- 46% -- Patients have never seen a nephrologist prior to ESRD initiation event



# AKI and ESRD Link



## ESRD Care

Modality Choice

Residual function/Recovery

ESRD Care

Survival/Palliation

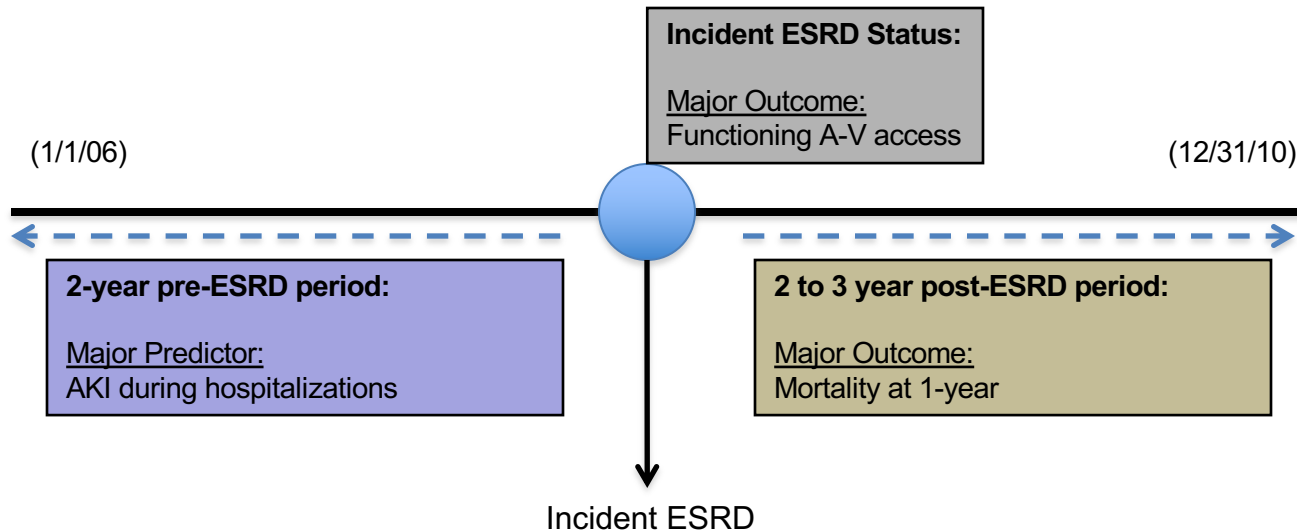
CV Risk

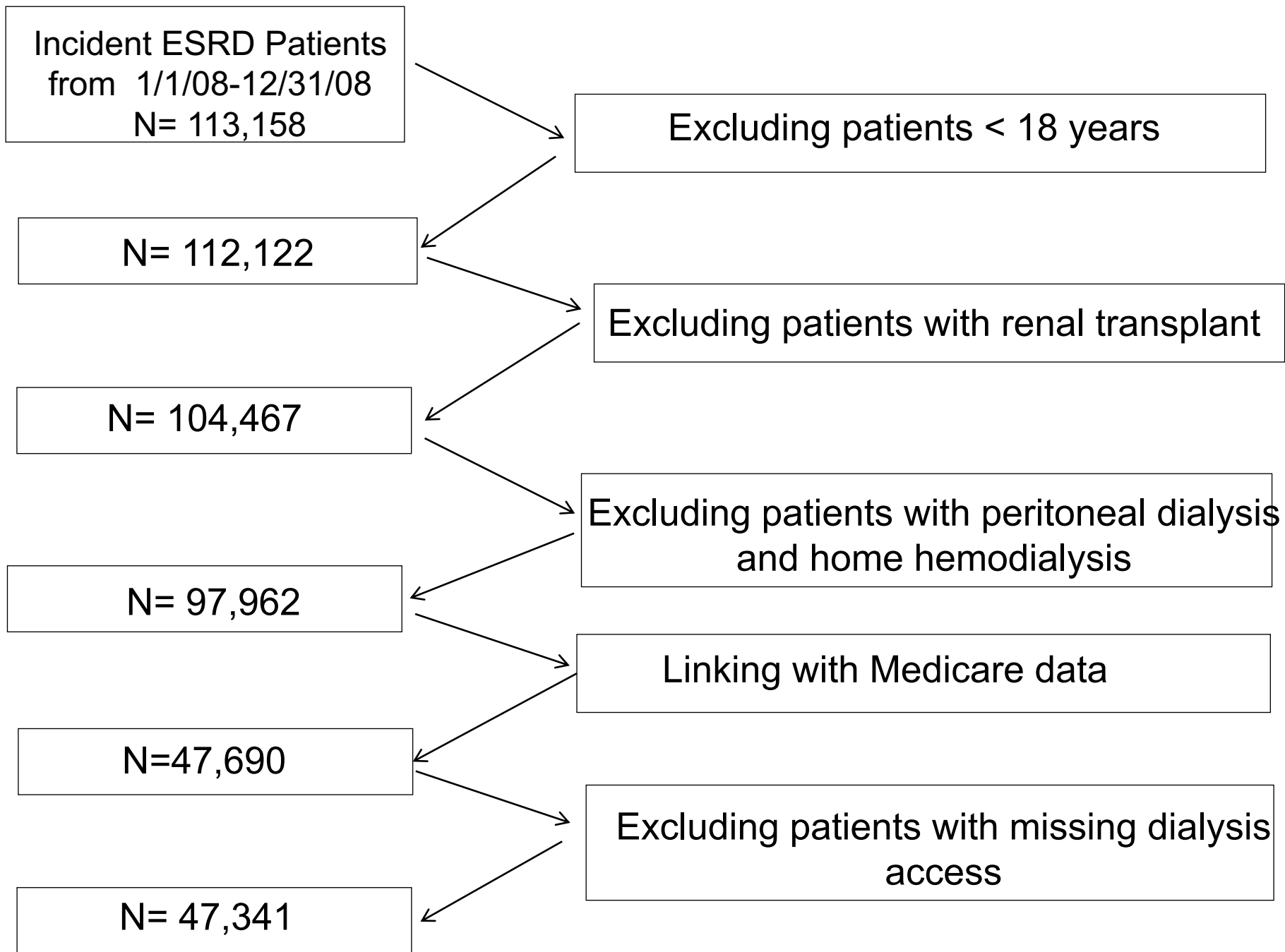
Transplant Status

# AKI and ESRD Link

- AKI during CKD journey accelerates CKD
  - Does Pre-ESRD AKI episodes influence survival after ESRD?
- Dialysis Dependent AKI in advanced CKD
  - Pre-2017:
    - Unable to get reimbursed in chronic programs
    - Stayed in the hospitals
    - Misclassified as “ESRD” if dialysis dependent at 15-30 days
  - Post-2017:
    - Payment for AKI dialysis possible
    - Relatively small numbers in ESRD units
    - Limited data hence no individualized care

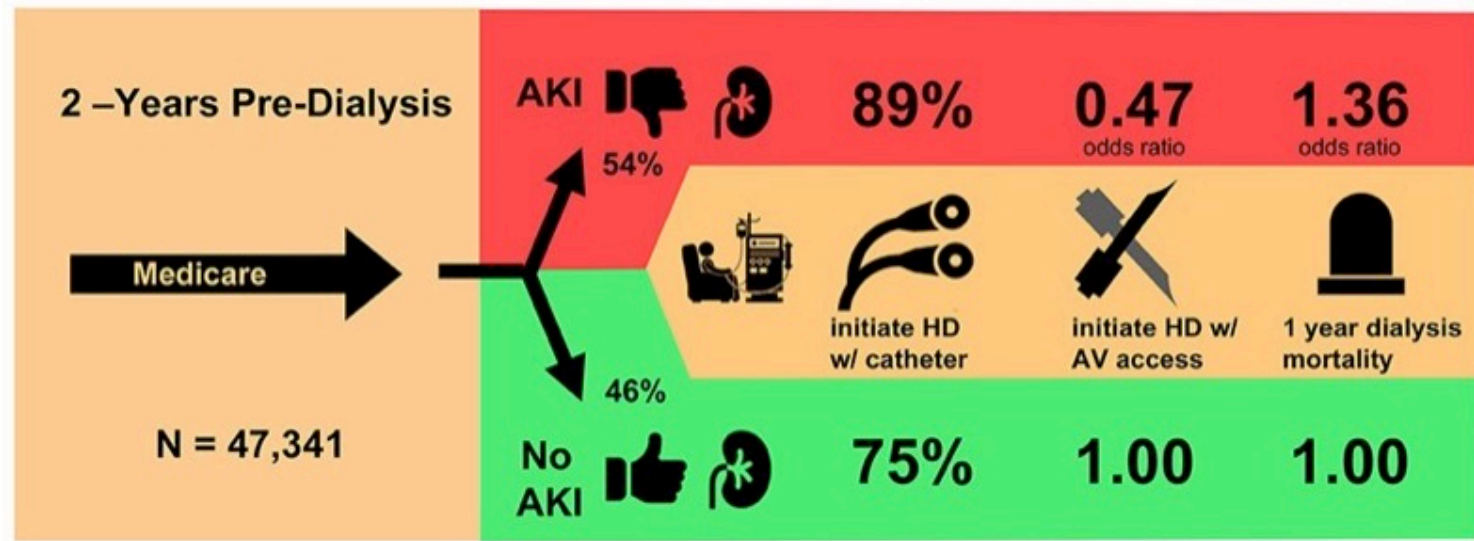
# Pre-ESRD AKI and Dialysis Outcomes: Time of Observation





Does AKI affect what happens to people when they subsequently start dialysis?

American Journal of **Nephrology**

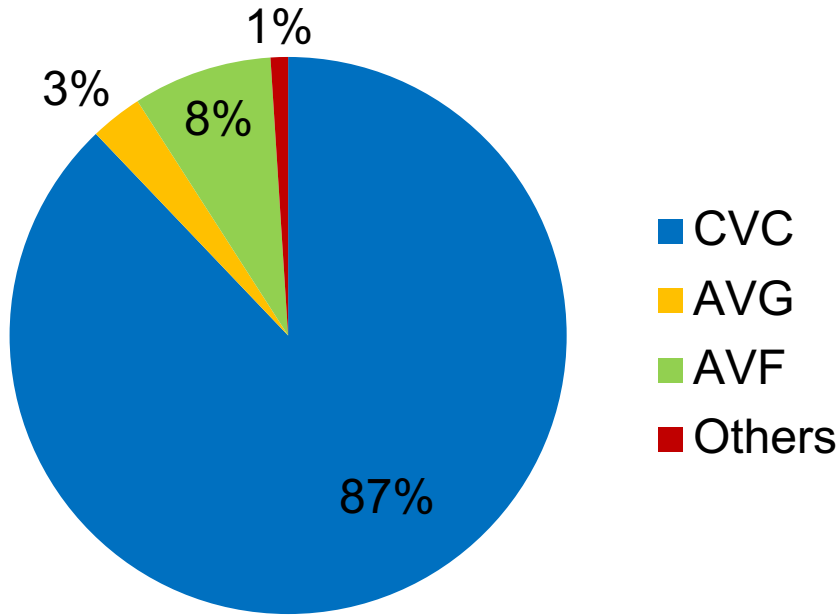


**Conclusion** An AKI event prior to initiating hemodialysis independently increases the risk of CVC use and predicts 1-year mortality.

Lee T, Shah S, Leonard AC, Parikh P, Thakar CV, Acute Kidney Injury before Dialysis Initiation Predicts Adverse Outcomes in Hemodialysis Patients. Am J Nephrol 2018; 47: 427-434

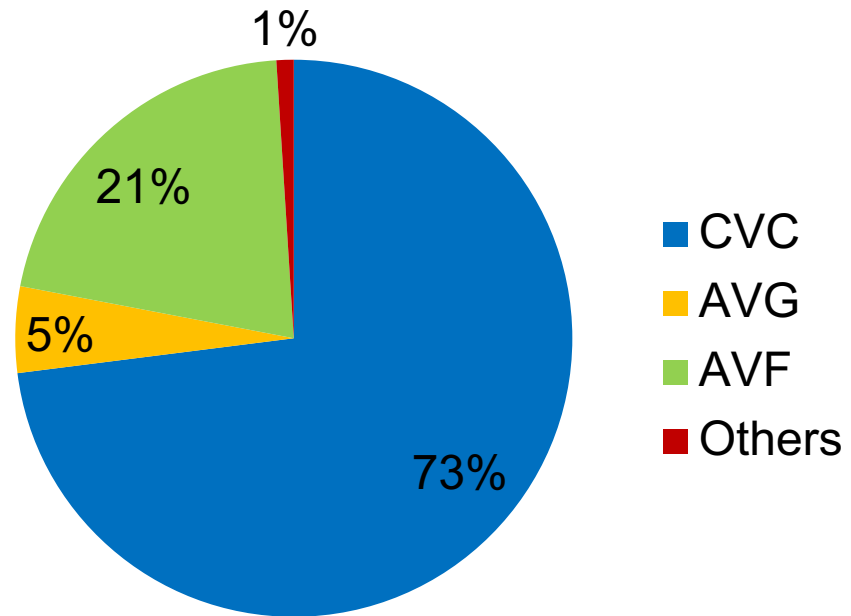
# Dialysis Access

## Pre-ESRD AKI



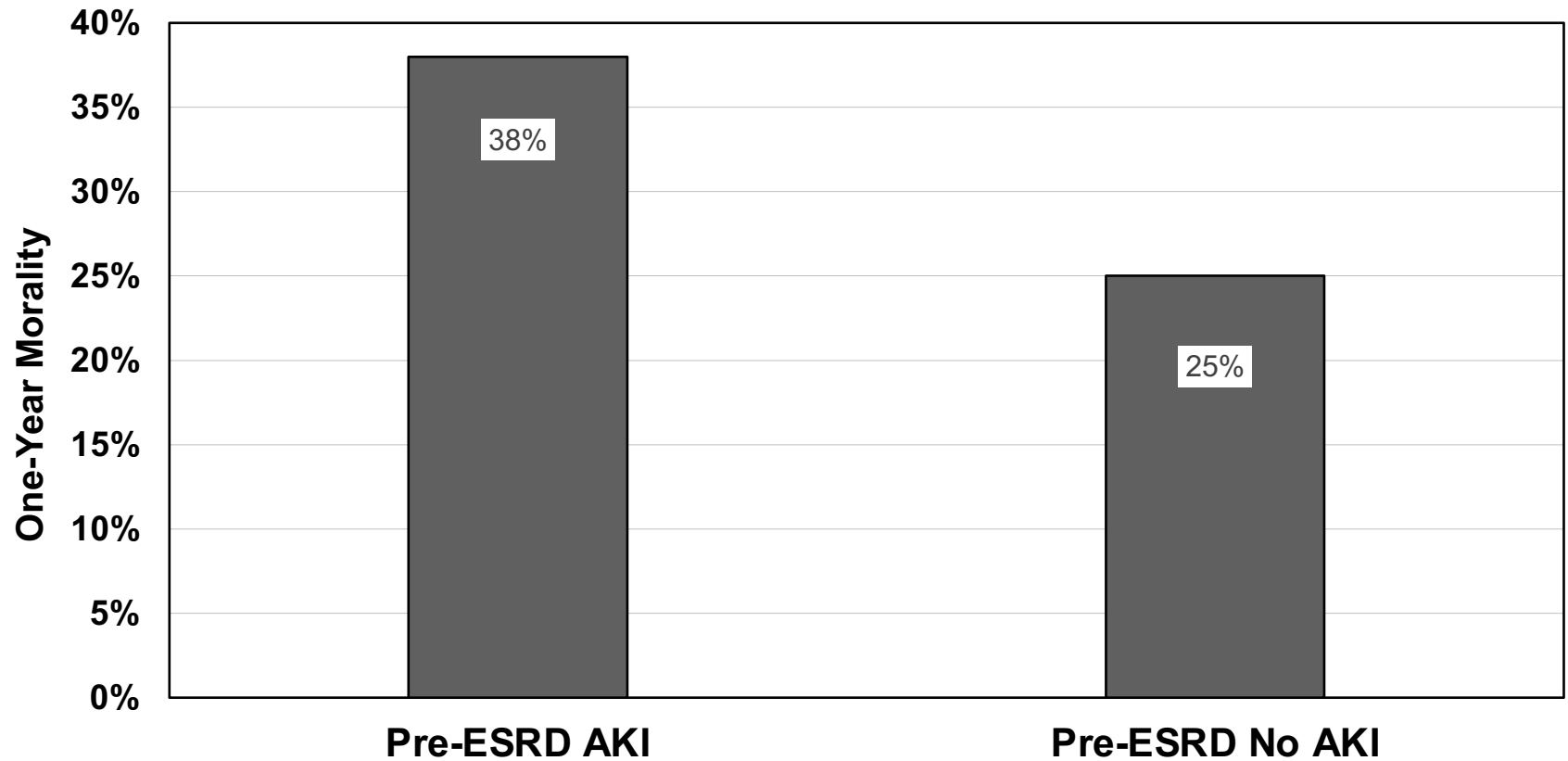
N = 25,607

## Pre-ESRD No AKI



N = 21,734

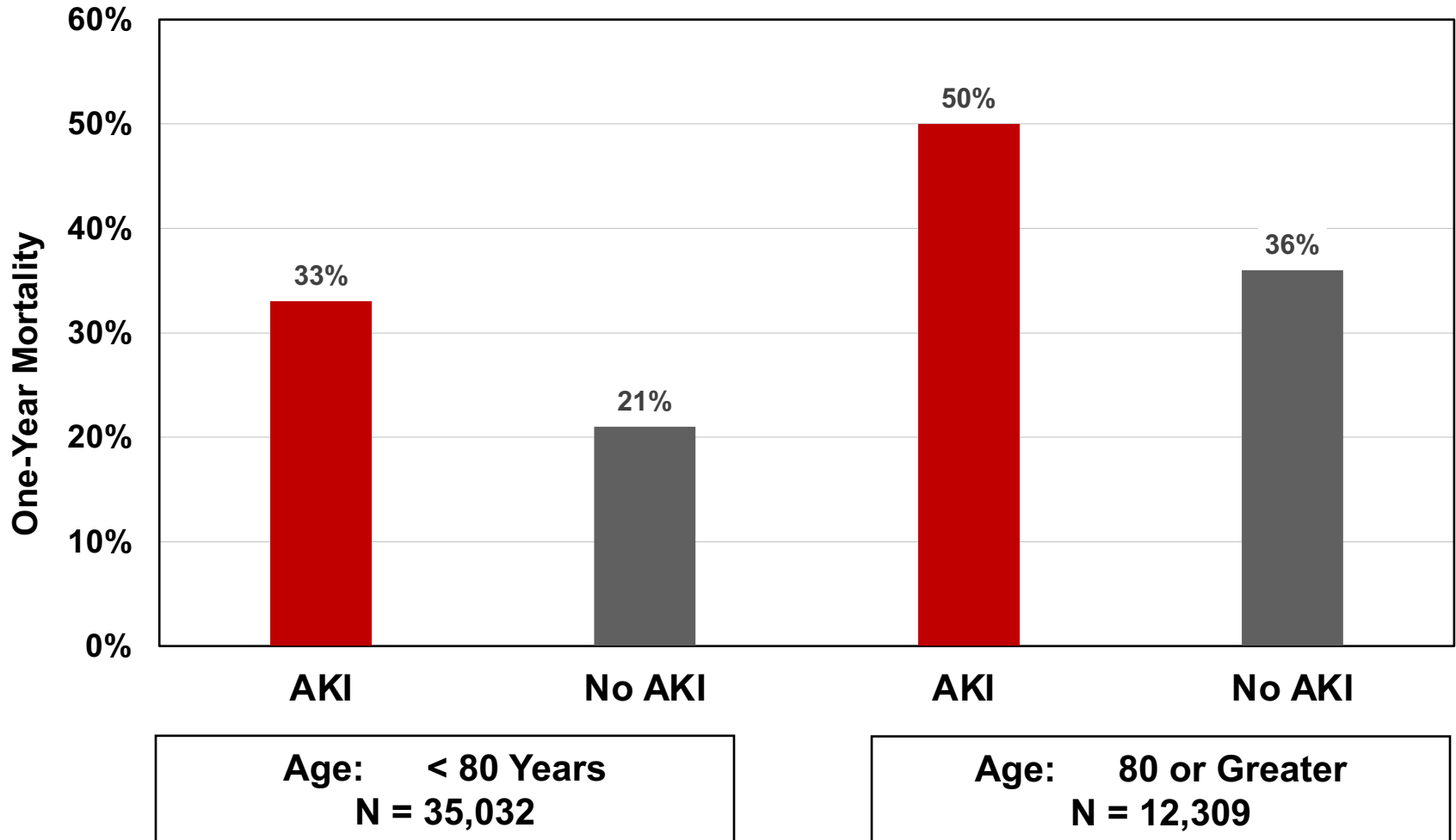
# One-Year Mortality After Incident ESRD



N = 25,607

N = 21,734

## ESRD: Mortality by Octogenarians Status





Anna's Hummingbird



# Dialysis Patients at LTAC

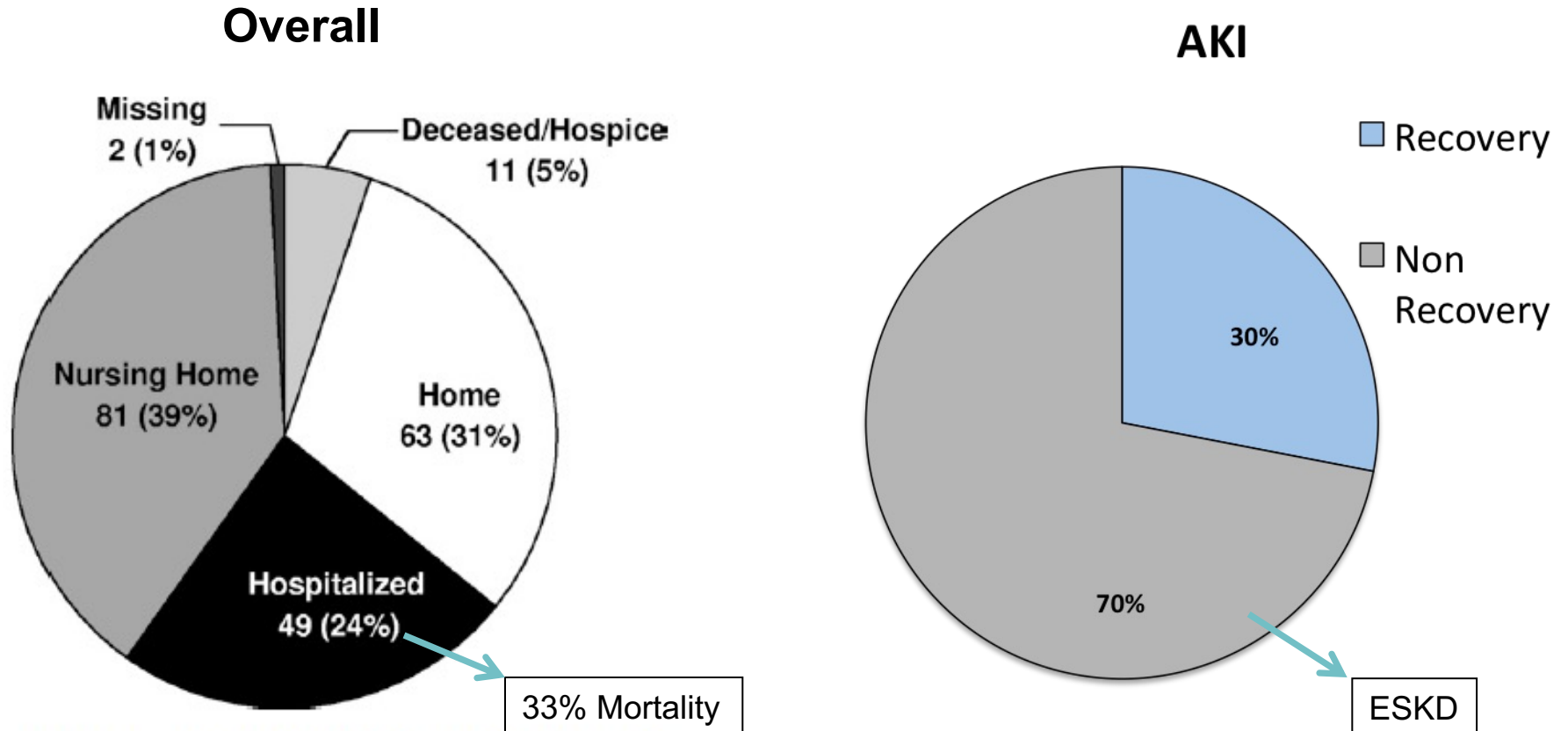
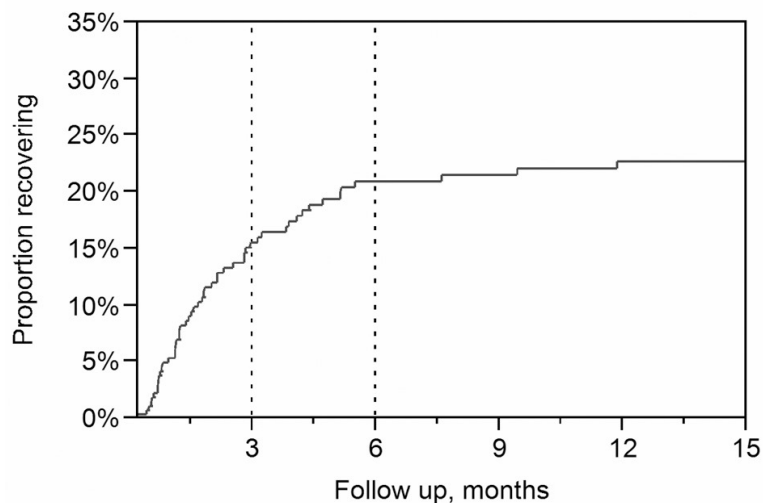


Figure 1. Disposition/outcomes of hemodialysis patients from long-term care hospitals.

**N, 206 (~50% AKI)**

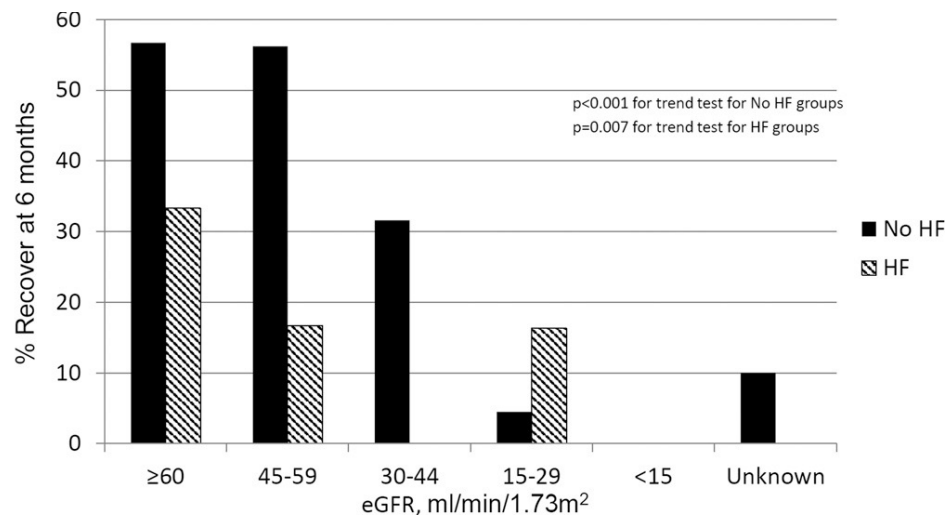
# Recovery Pattern in Dialysis Dependent AKI: Single Center

## Pattern



|                                 | Time Zero | 3 mo | 6 mo | 9 mo | 12 mo | 15 mo |
|---------------------------------|-----------|------|------|------|-------|-------|
| Total no. renal recovery events | 0         | 38   | 49   | 50   | 52    | 52    |
| No. at risk                     | 281       | 186  | 147  | 138  | 124   | 106   |

## Predictors



Number of patients per subgroup:

|       | ≥60 | 45-59 | 30-44 | 15-29 | <15 | Unknown |
|-------|-----|-------|-------|-------|-----|---------|
| No HF | 30  | 16    | 19    | 44    | 25  | 20      |
| HF    | 12  | 12    | 21    | 43    | 31  | 8       |

# AKI-Dialysis Recovery

Starting Cohort of  
Hospitalized AKI-D  
N = 2214  
Recovered: 905 (41%)

Baseline eGFR 15-29  
vs > 30

26% vs 47%

Hb < 12  
Recovery: 39%

39% vs 53%

Platelets < or >/= 150

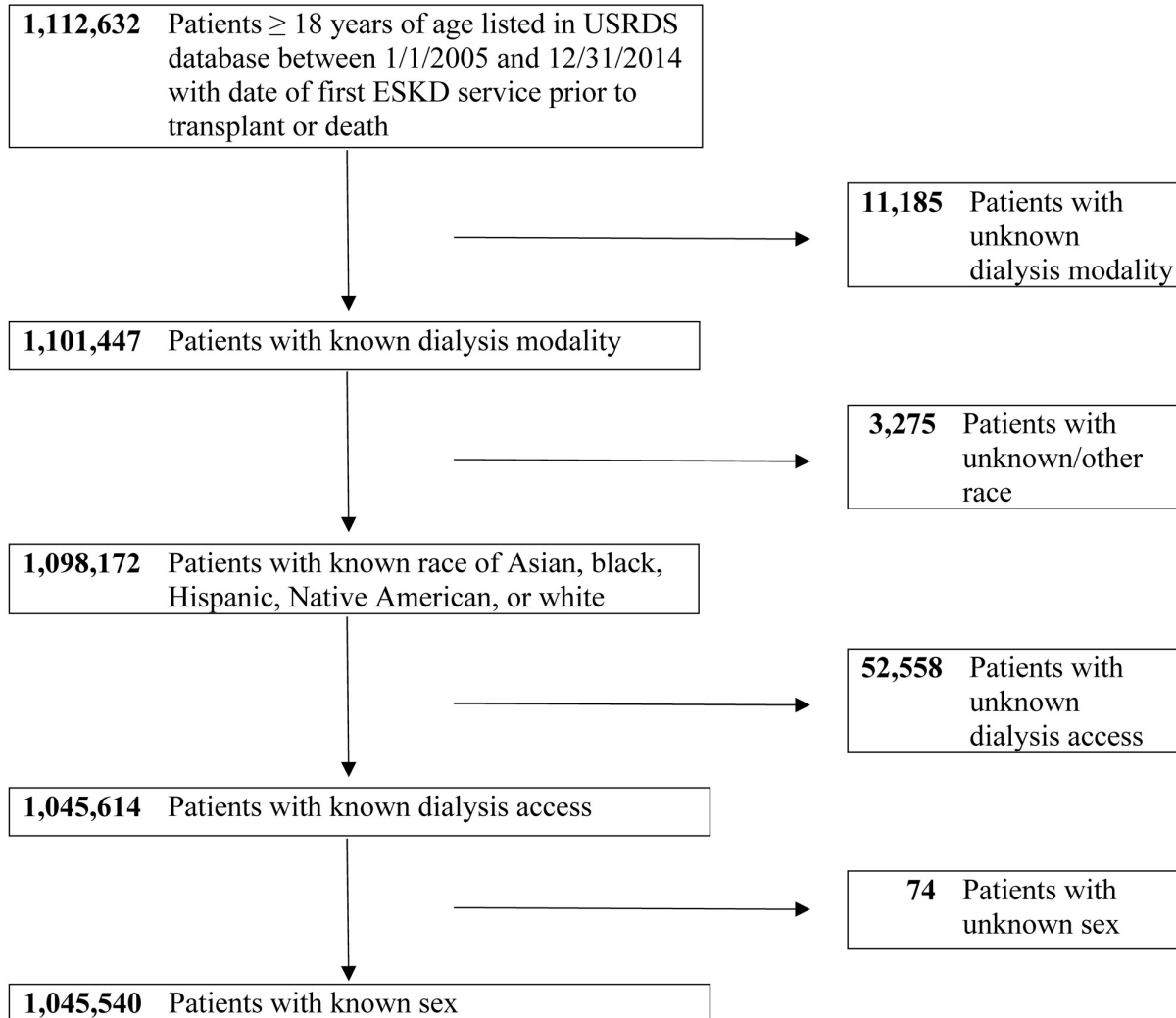
31% vs 42%

Diabetes No vs Yes

36% vs 42%

Lee BJ et al  
KI Reports 2019

# AKI-ESRD: Cohort Derivation



# AKI-ESRD Key Findings

## Cohort:

1.045 Million (2005 – 14)  
 Mean age 63 Years  
 Octogenarians 14.5%

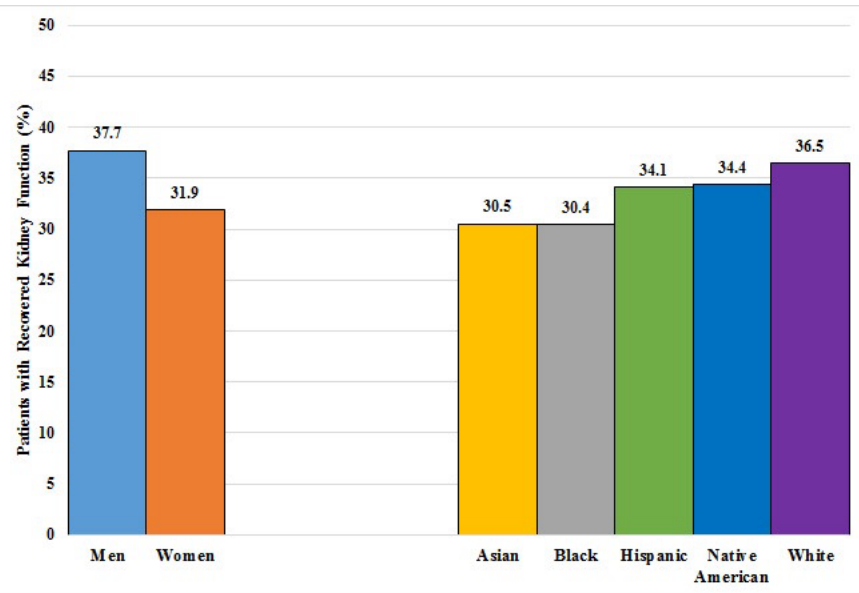
## Key Observations:

AKI-ESRD – 3.1%  
 DM-ESRD – 46%  
 Other-ESRD – 50.9%

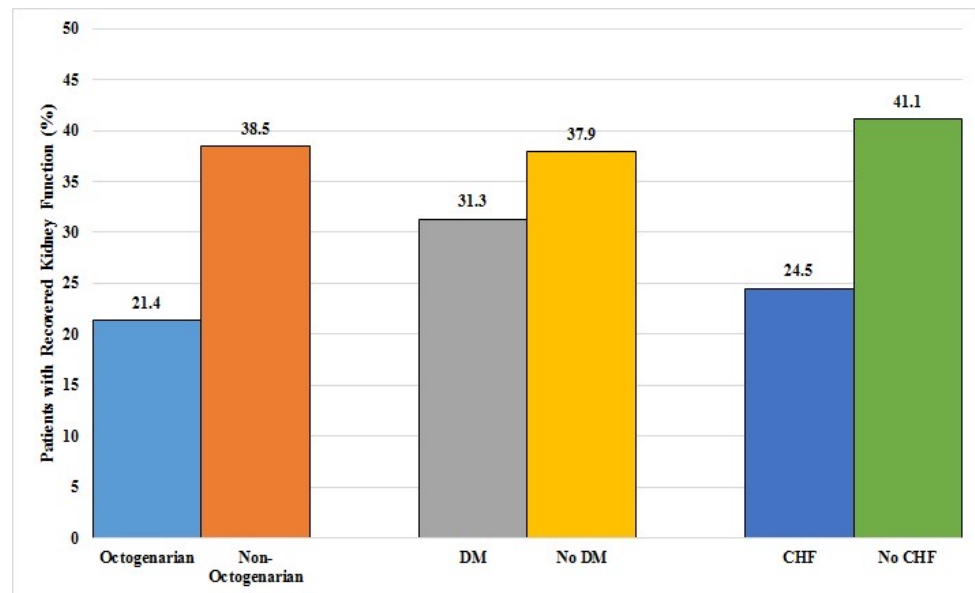
| Outcomes         | AKI-ESRD | Diabetic ESRD | Other ESRD |
|------------------|----------|---------------|------------|
| Renal Recovery   | 35.3%    | 4.0%          | 6.9%       |
| 90 day Mortality | 15.2%    | 6.5%          | 8.6%       |
| 1 year Mortality | 35.2%    | 19.8%         | 22.7%      |

| Outcomes         | AKI-ESRD Recovery | AKI-ESRD NonRecovery |
|------------------|-------------------|----------------------|
| 1 Year Mortality | 10.7%             | 48.5%                |

# AKI-ESRD: Renal Recovery

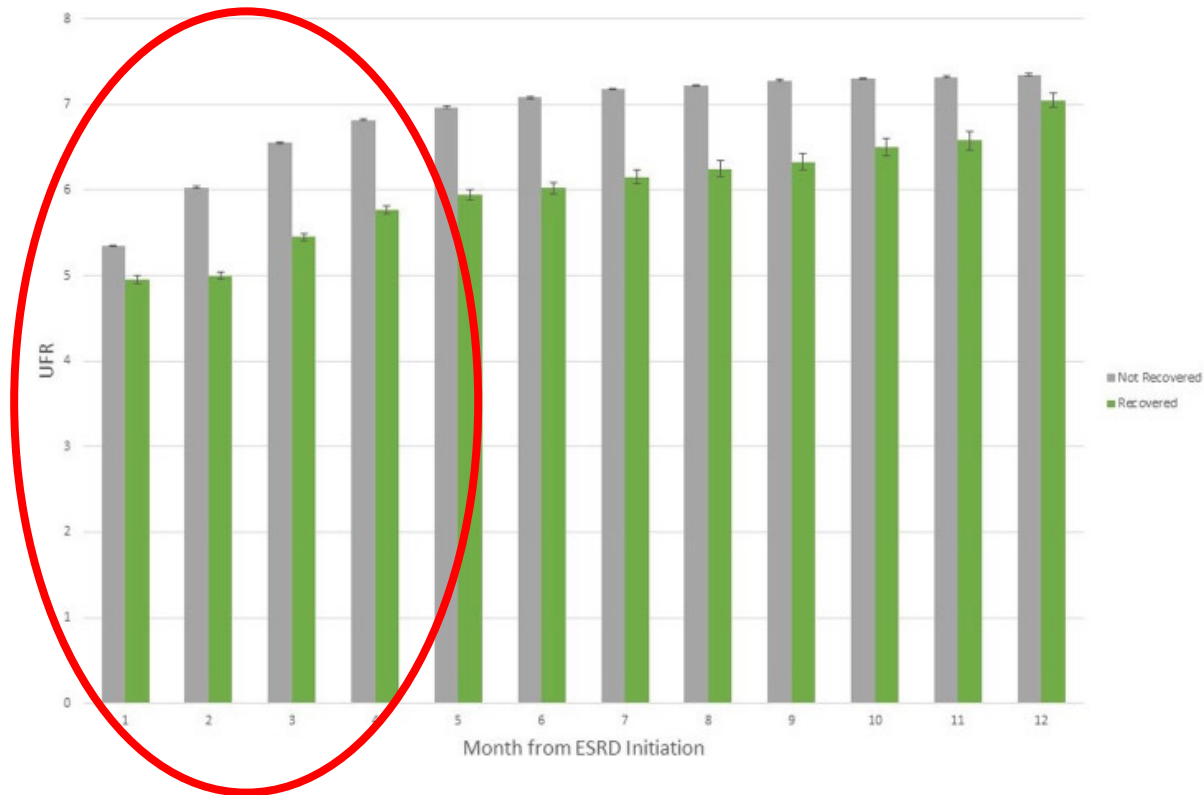


Gender & Race



Co-morbid Conditions

# Ultrafiltration Rate and Renal Recovery





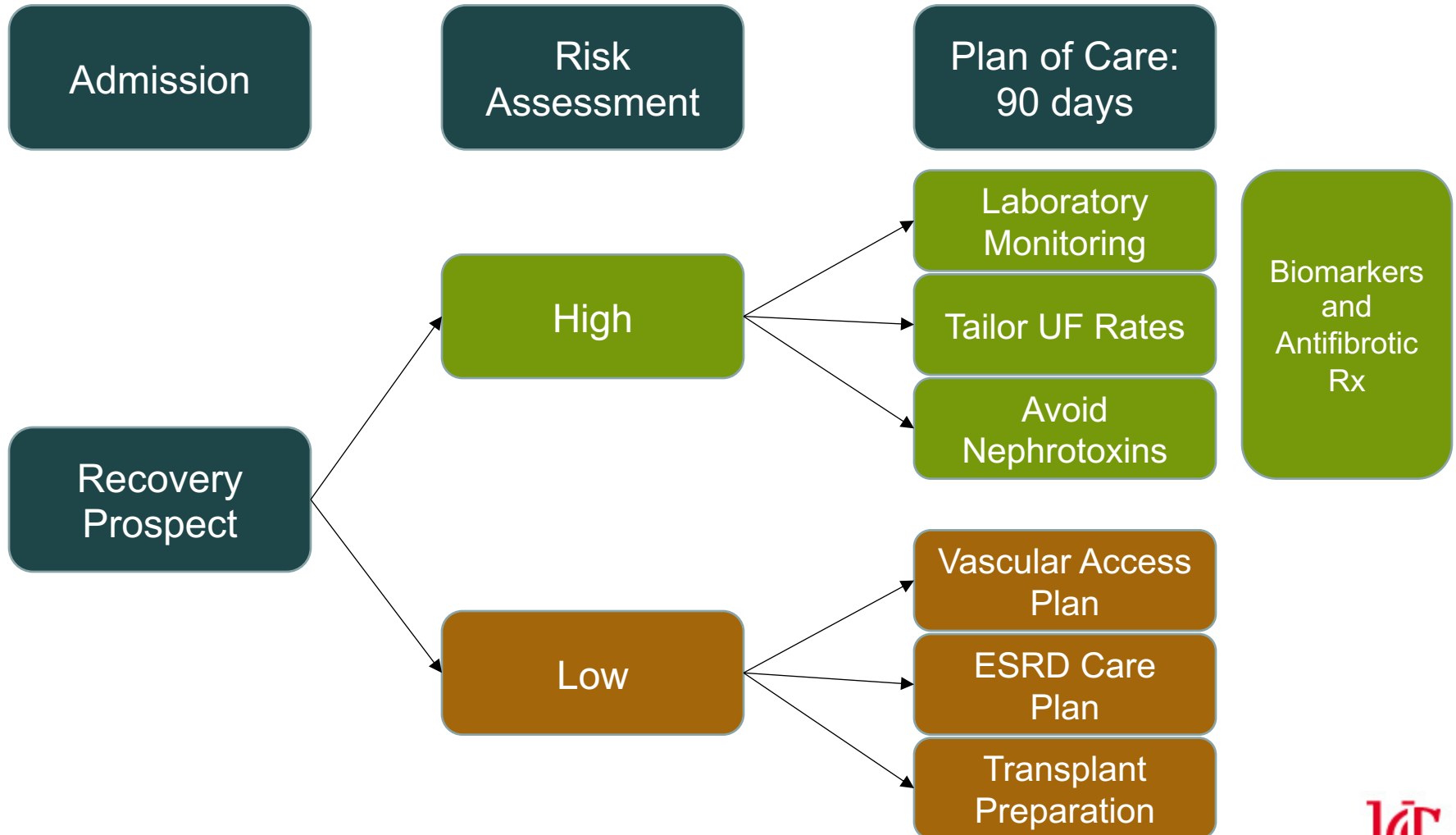
# Prescribing Patterns in Dialysis Dependent AKI

| 799 patients with DD-AKI | Week 1                    | 30 Days                   | P Value |
|--------------------------|---------------------------|---------------------------|---------|
| # Meds per patient       | 7.8 +/- 6.6<br>(median 5) | 14.4 +/- 8<br>(median 13) | <0.05   |
| Polypharmacy (> 10 meds) | 32.3%                     | 68%                       | <0.001  |

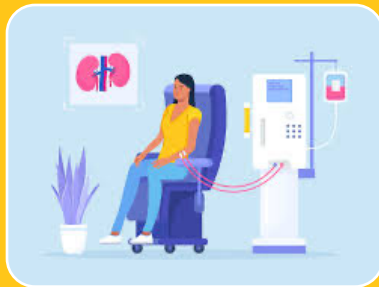
## Potentially Contraindicated Medications:

- Aminoglycosides
- NSAID
- Digoxin
- Rivaroxaban
- Metformin

# Triaging Care: Dialysis Dependent AKI



# AKI and ESRD Link: Implications



## Patient's Health

- Prognosis
- Recovery



## Dialysis Programs

- Care Planning
- Resources and Costs



## Healthcare Systems

- Acute Care
- Transplant Options

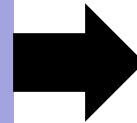
# AKI and ESRD Link



Incident

ESRD

Status



**ESRD Care**

Modality Choice

Residual function/Recovery

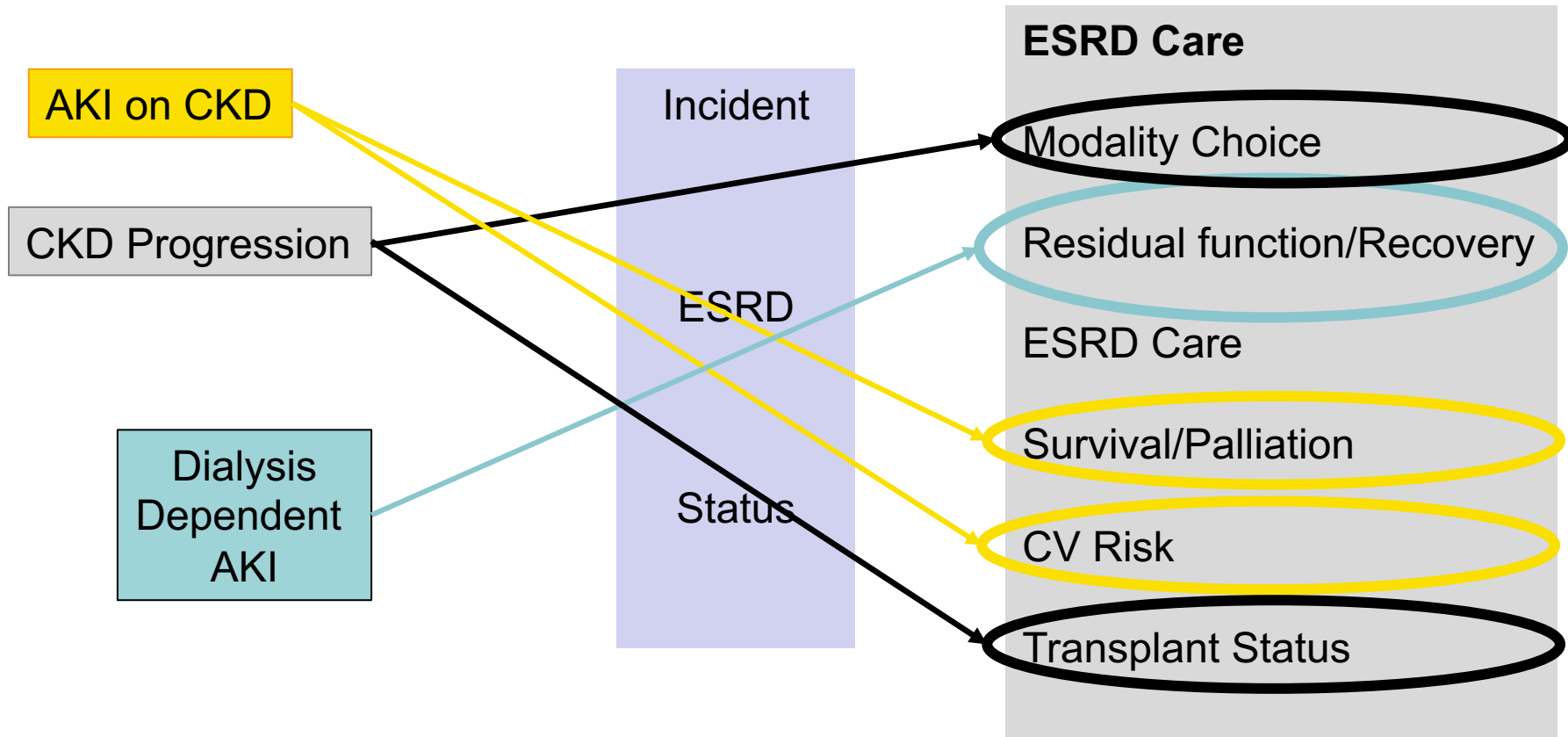
ESRD Care

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CV Risk

Transplant Status

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**Should Mr. Smith and Mr. Jones receive the same dialysis care at FraVita Renal Care Inc.?**

**I Hope They Don't!**

Thank You!



**Ruby Throated Hummingbird**