# Dialysis Dependent AKI: Conveyer Belt vs Personalized Care?


Charuhas V. Thakar, MD

Robert G. Luke Endowed Chair in Nephrology

Professor of Medicine

Director, Division of Nephrology, University of Cincinnati

Chief, Renal Section, Cincinnati VA Healthcare System


UNIVERSITY OF Cincinnati

# Disclosures

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

UNIVERSITY OF Cincinnati

# 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 15th 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.

Started dialysis in chronic unit on Feb 1st 2023

- **Mr. Jones**

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 15th 2022.

Creatinine remained stable post-cath.

Progressed to ESRD as expected.

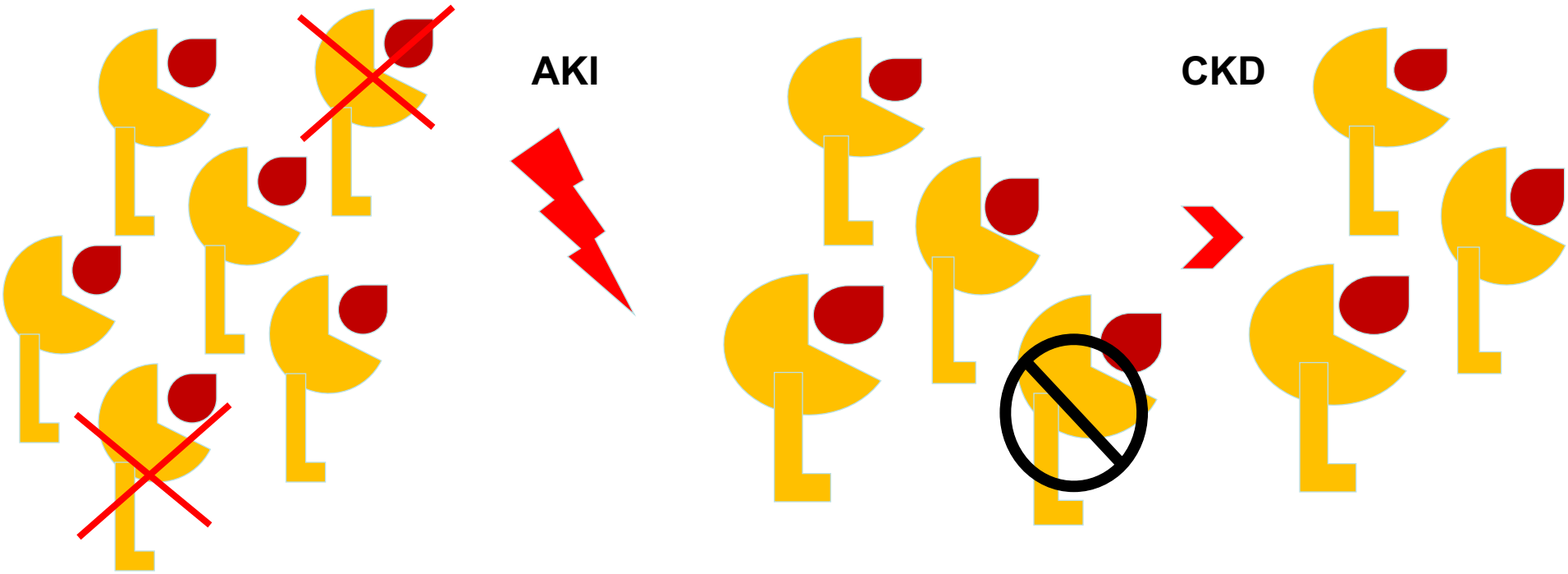
Started dialysis in chronic unit on Feb 1st 2023

# The Dialysis Conveyer Belt


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

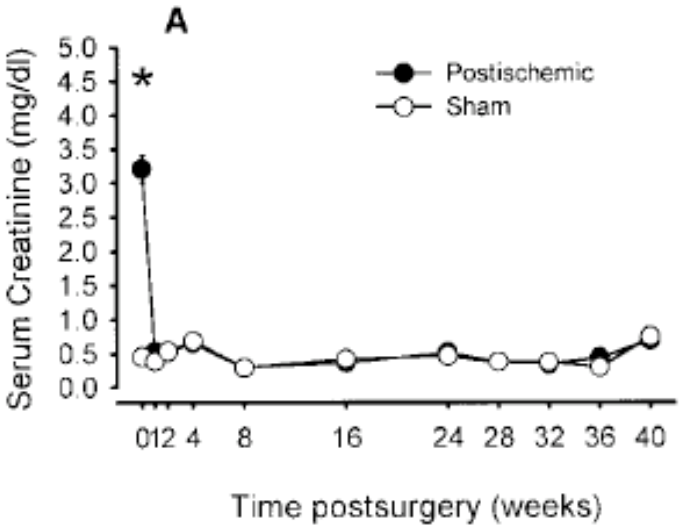
UNIVERSITY OF Cincinnati

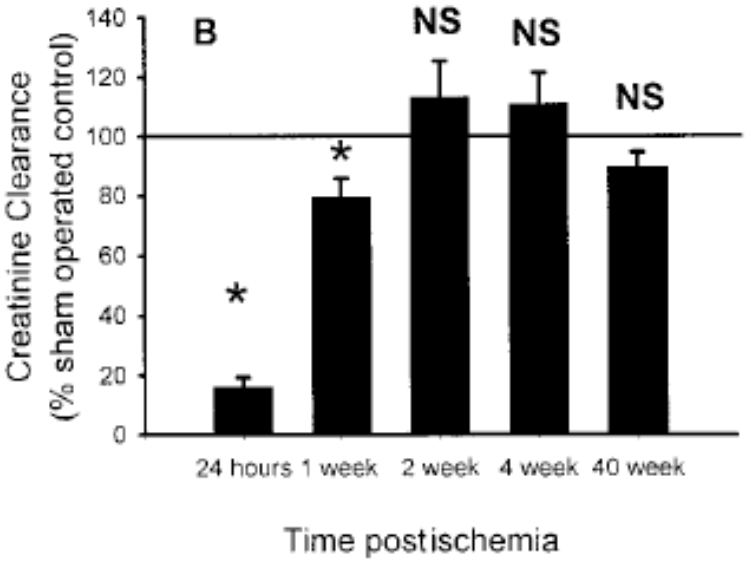
# AKI to CKD: Causal Pathway?




UNIVERSITY OF Cincinnati

# “Normalization” of Creatinine post IRI

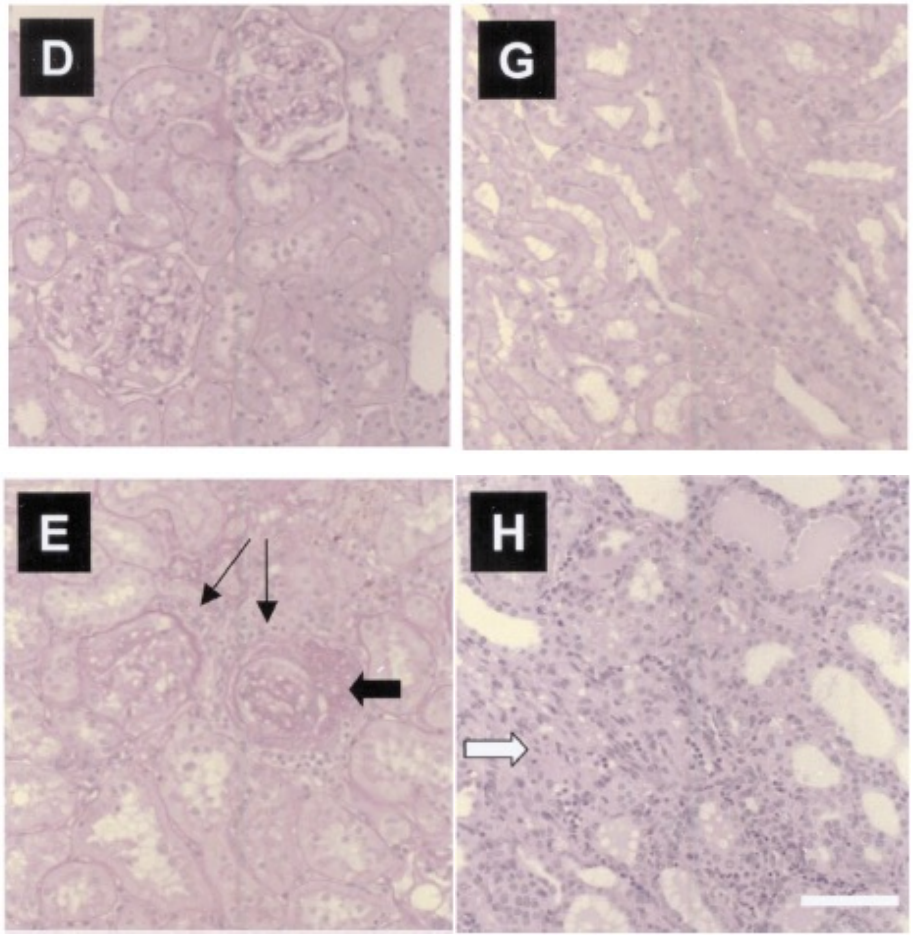



Basile, AJP, 2000

UNIVERSITY OF Cincinnati

# Microscopic Changes after IRI




40 Weeks

Sham

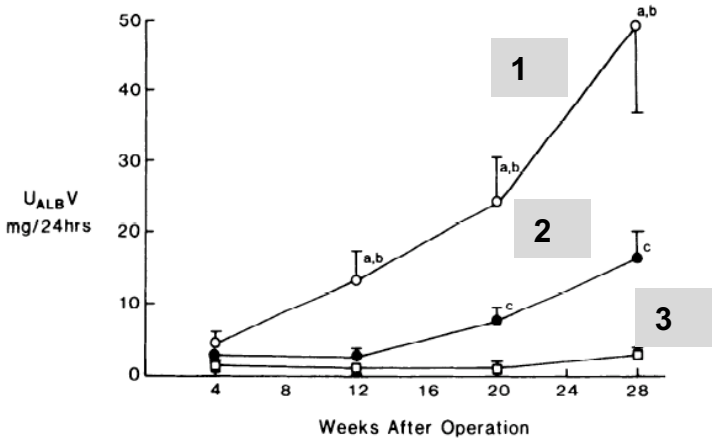
Post IRI

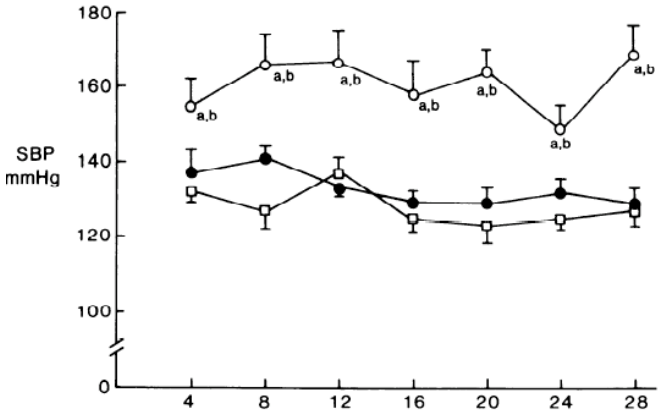
- Increased Pro-fibrotic activity
- Loss of capillary density
- Tubular Atrophy
- Glomerular Sclerosis

Basile, AJP, 2001

UNIVERSITY OF Cincinnati

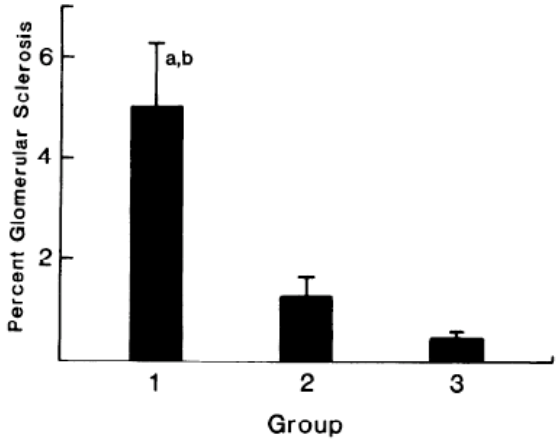
# AKI: Proteinuria and Neurohormonal




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

Meyer & Renkke, AJP, 1988

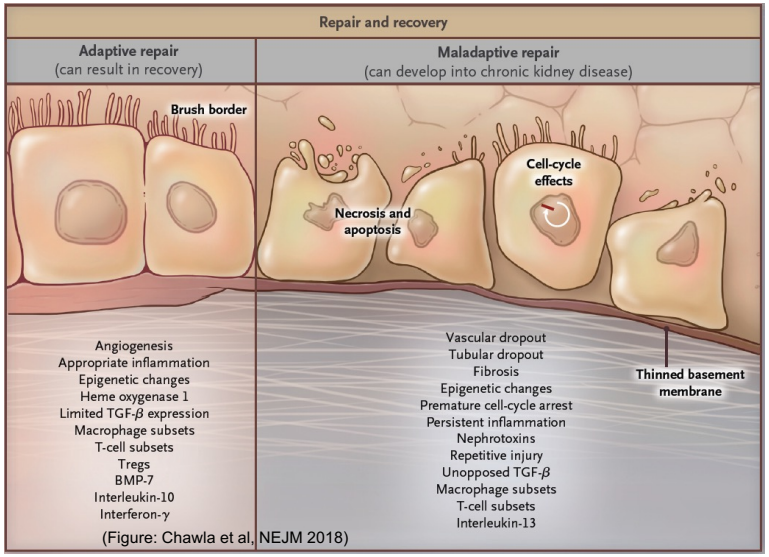



UNIVERSITY OF Cincinnati

# AKI → CKD

**Susceptibility:**
**Co-morbidity**
**Age**
**Drugs/toxins**

AKI Episode

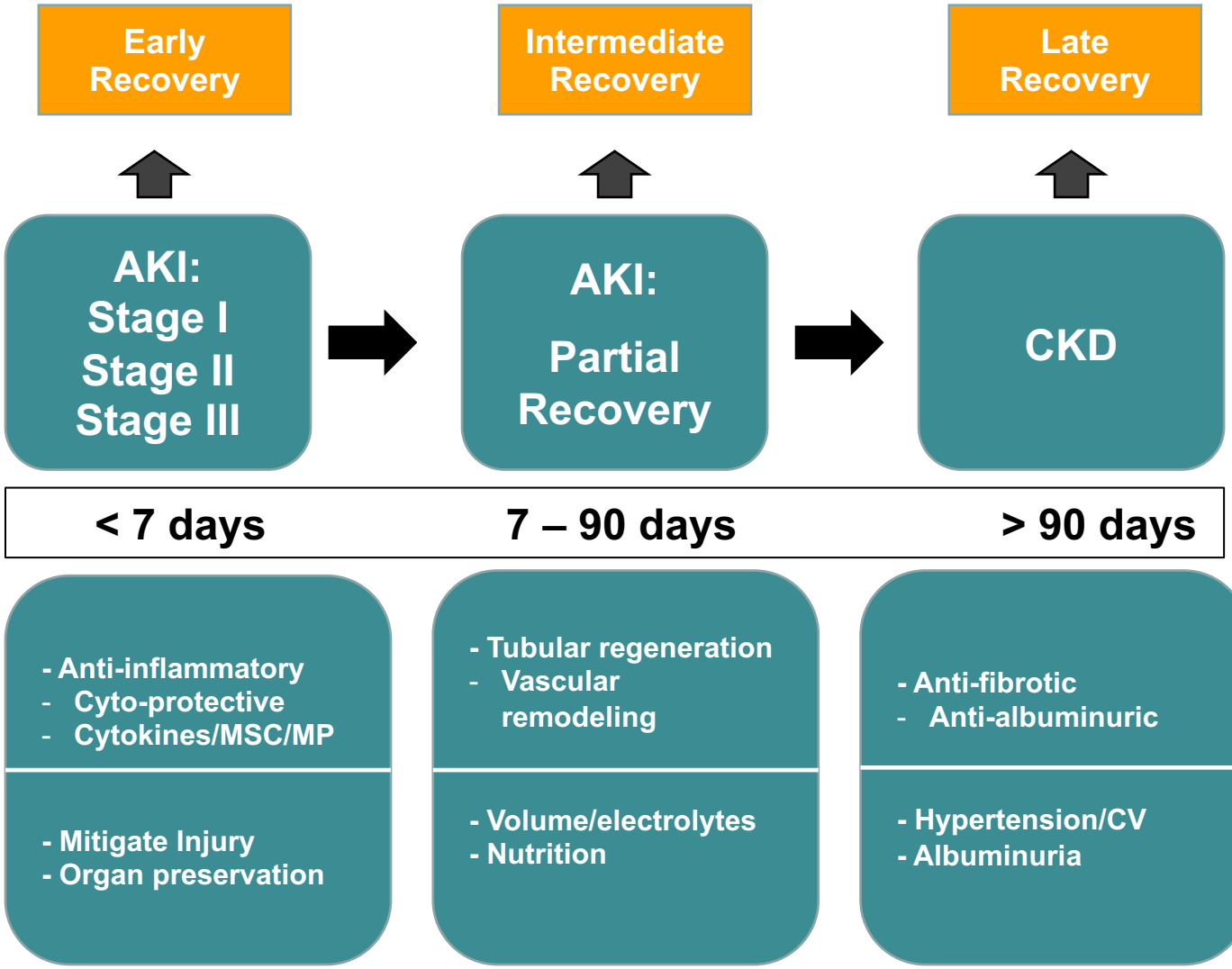


(Figure: Chawla et al, NEJM 2018)

- Tissue Fibrosis
- Albuminuria
- Increased Blood Pressure
- Neuro-hormonal adaptation

Pro-inflammatory State: Kidney and Beyond

UNIVERSITY OF Cincinnati




UNIVERSITY OF Cincinnati

# Rufous Hummingbird

# AKI-Dialysis and ESRD Risk

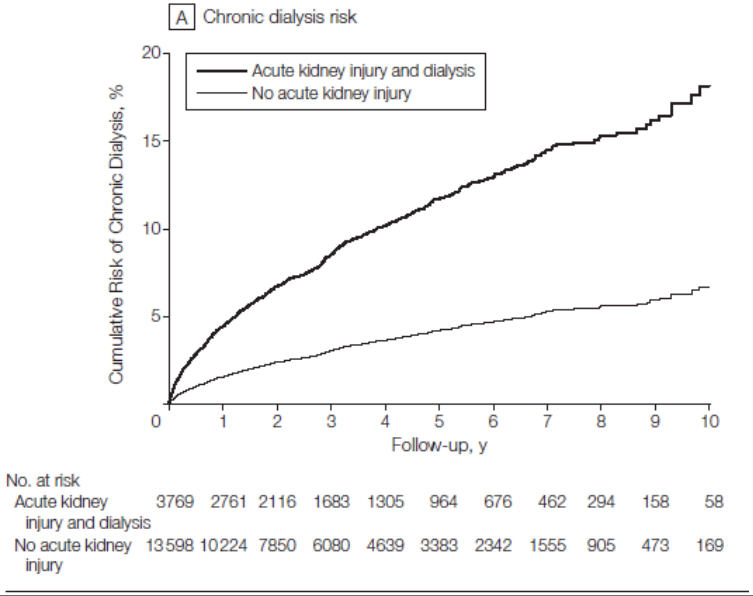


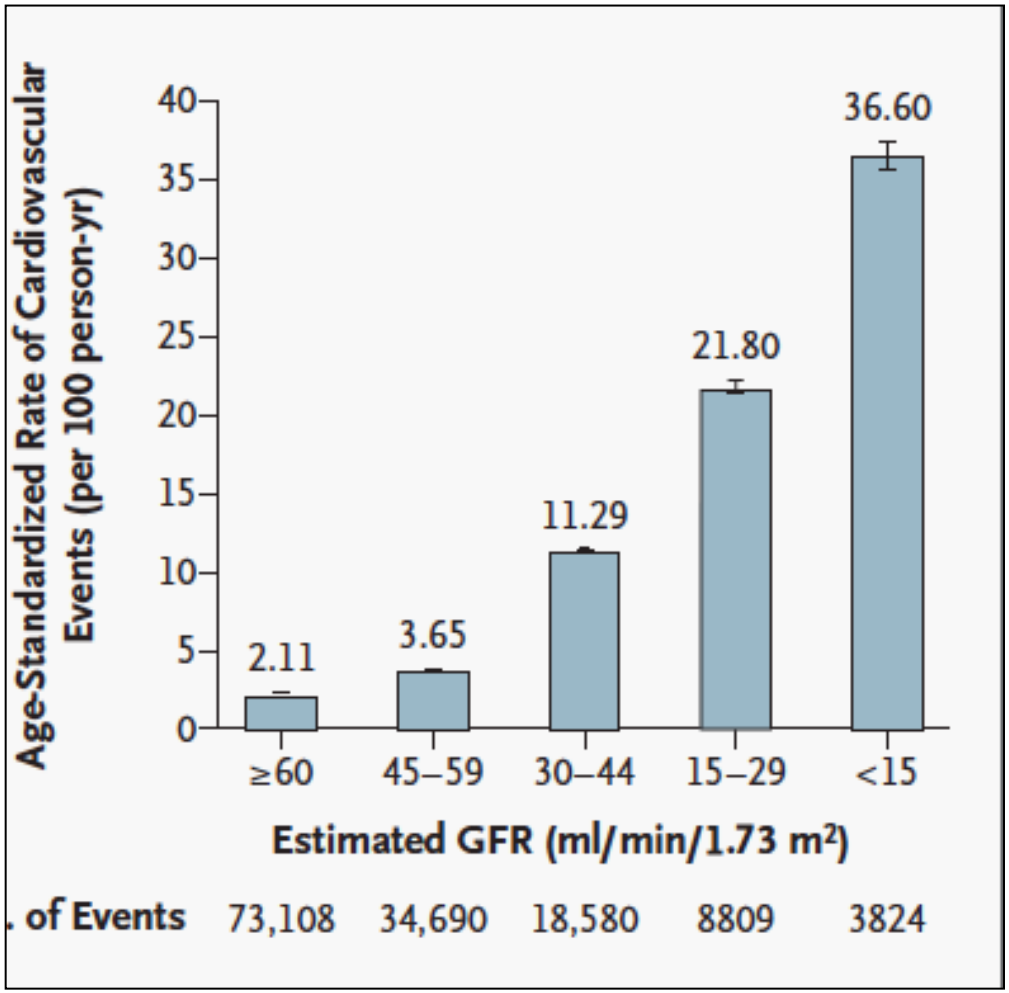

**Table 2.** Risk of Chronic Dialysis and All-Cause Mortality by Group

| | Acute Kidney Injury and Dialysis at Index Hospitalization (n = 3769) | | Without Acute Kidney Injury or Dialysis at Index Hospitalization (n = 13 598) | |
|---|---|---|---|---|
| Outcome | 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

UNIVERSITY OF Cincinnati

# CKD: CV events and Hospitalizations

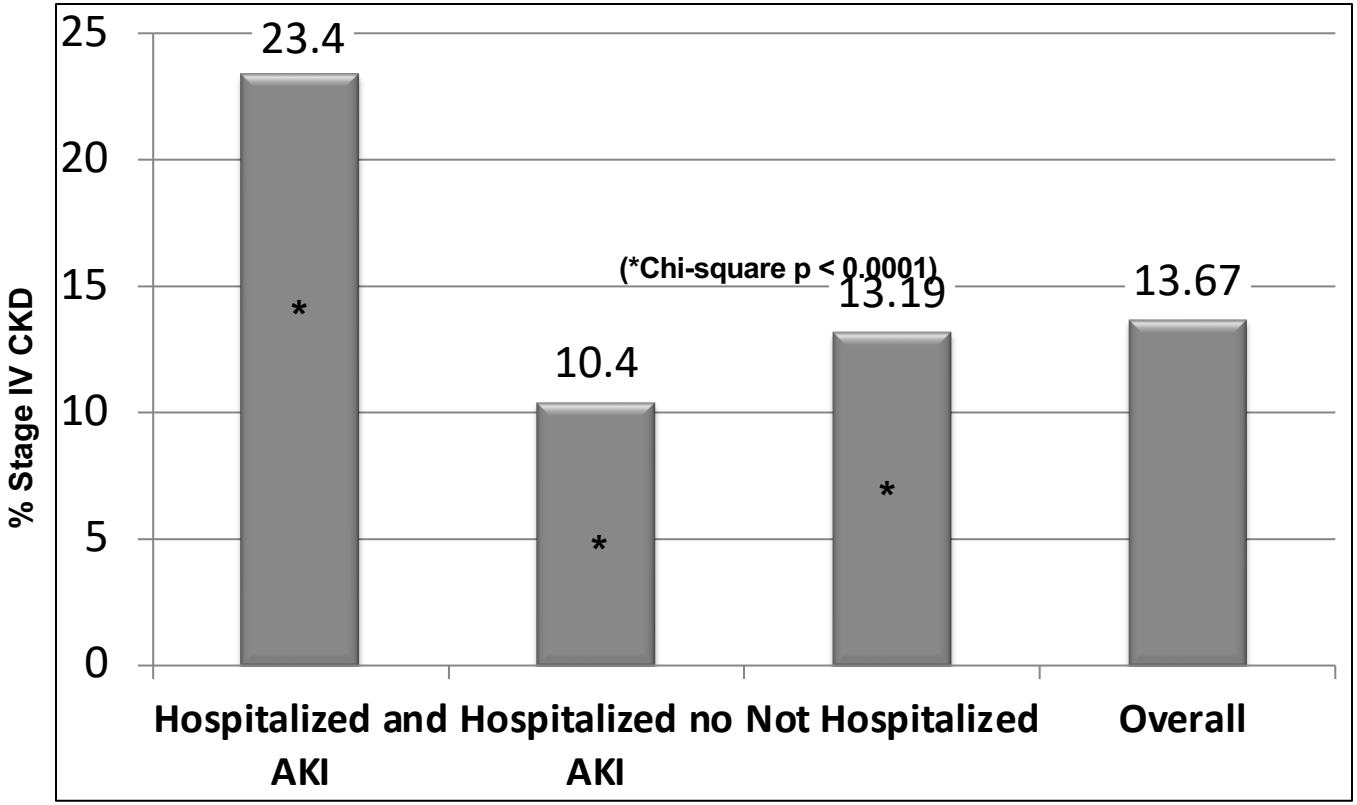



CV Events

Go et al, NEJM, 2004

UNIVERSITY OF Cincinnati

# Frequency of Stage IV CKD




(Thakar et al, CJASN, 2011)

UNIVERSITY OF Cincinnati

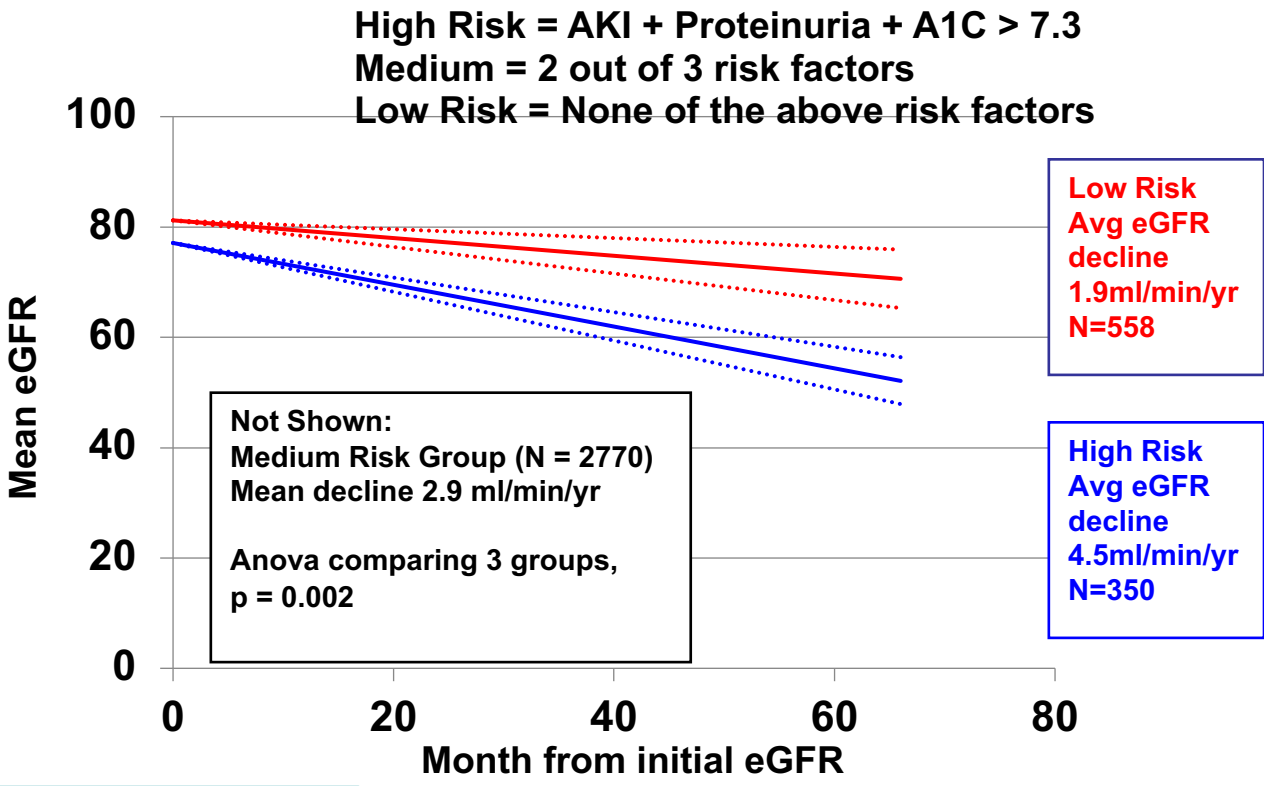
# Risk Factors of Stage IV CKD in DM

| Risk Factors | Hazard Ratio | 95% Confidence Interval |
|---|---|---|
| Age (in years) | 1.01 | 0.99, 1.02 |
| Sex (female *versus* male) | 2.65 | 1.40, 5.03 |
| Race (black *versus* 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)

UNIVERSITY OF Cincinnati

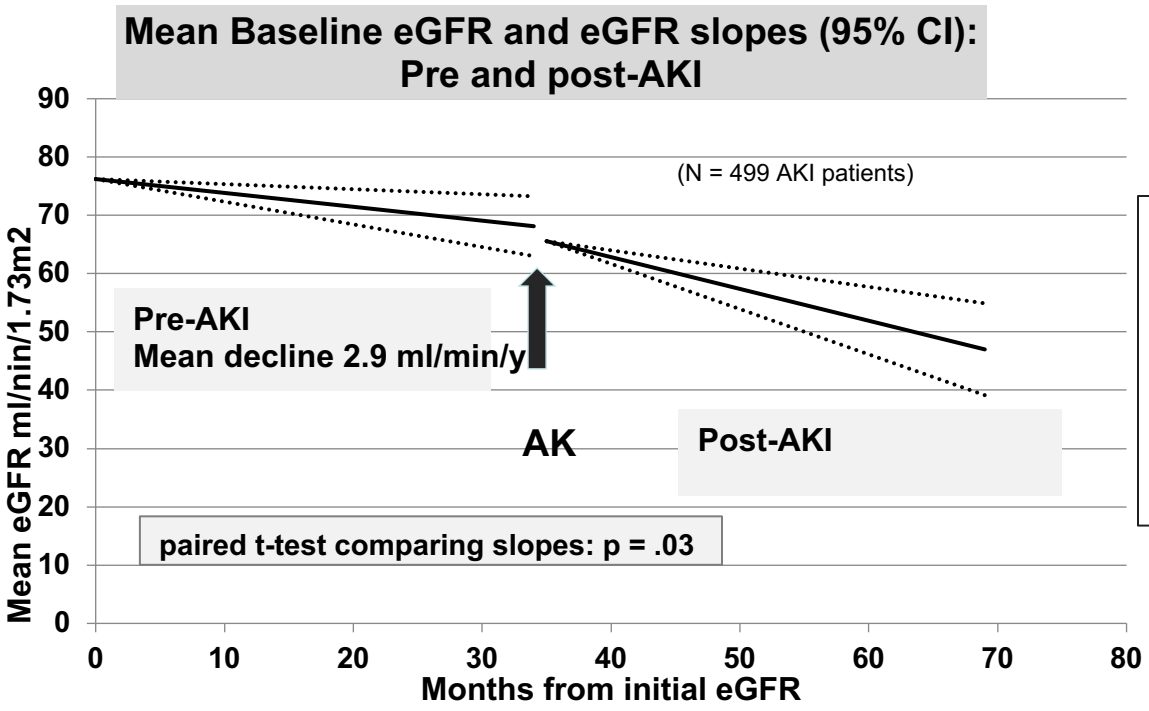
# HbA1C, Proteinuria and AKI: eGFR Decline Across Risk Groups




M. Sands & Thakar et al, ASN 2016

UNIVERSITY OF Cincinnati

# AKI and eGFR Slopes in T2DM




M. Sands & Thakar et al, ASN 2016

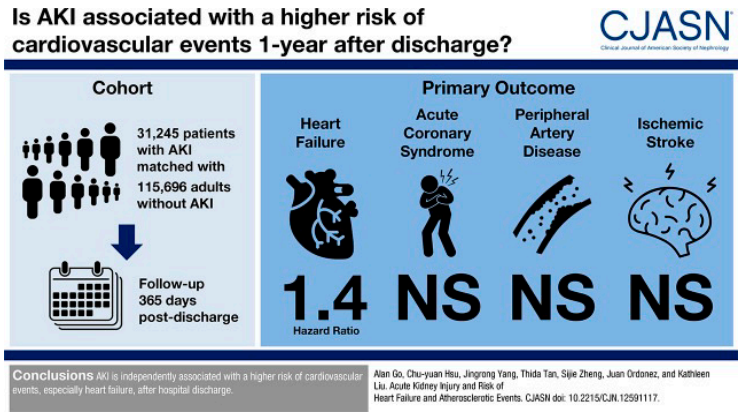
Estimated time to Stage V CKD

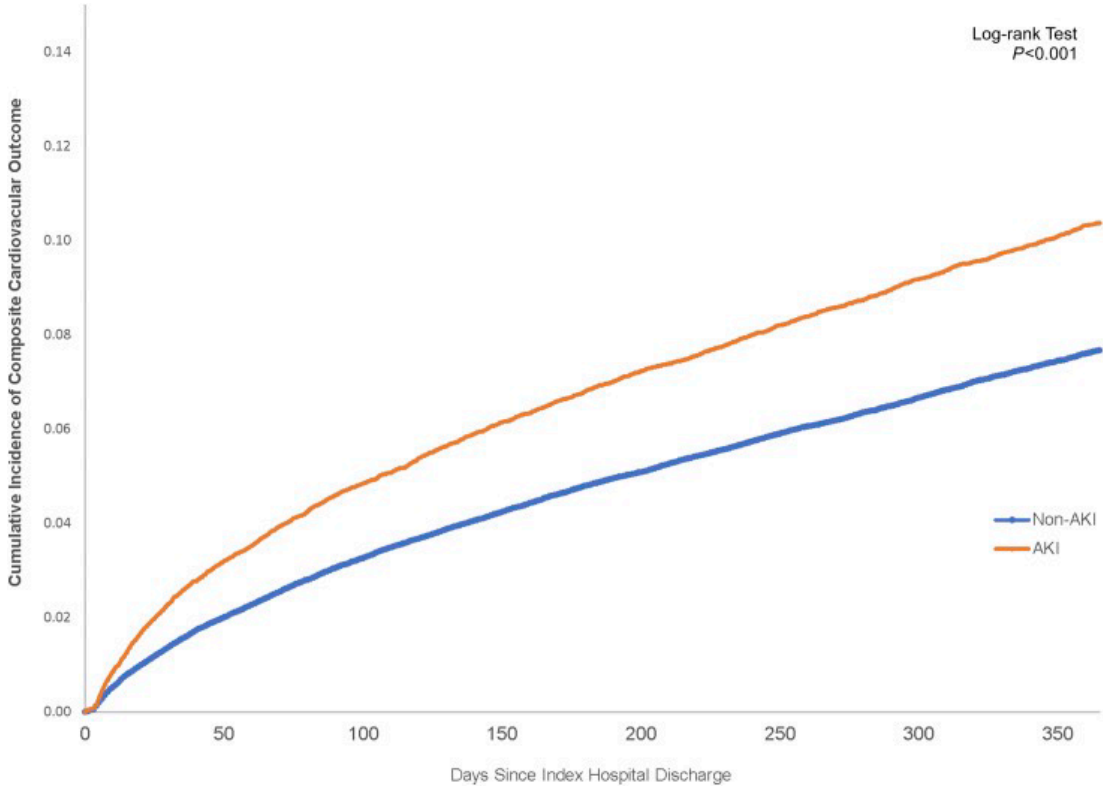
Without AKI – 19 years

After AKI – 8 years

UNIVERSITY OF Cincinnati

# AKI and Risk of New CHF

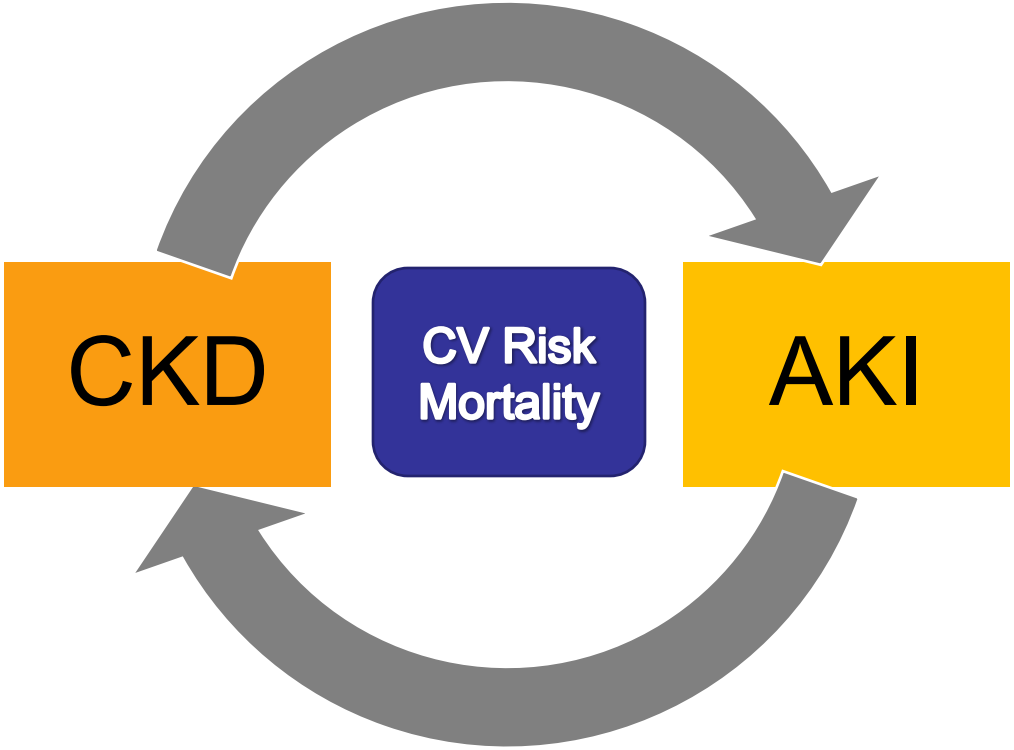



Alan Go et al, CJASN 2018

UNIVERSITY OF Cincinnati

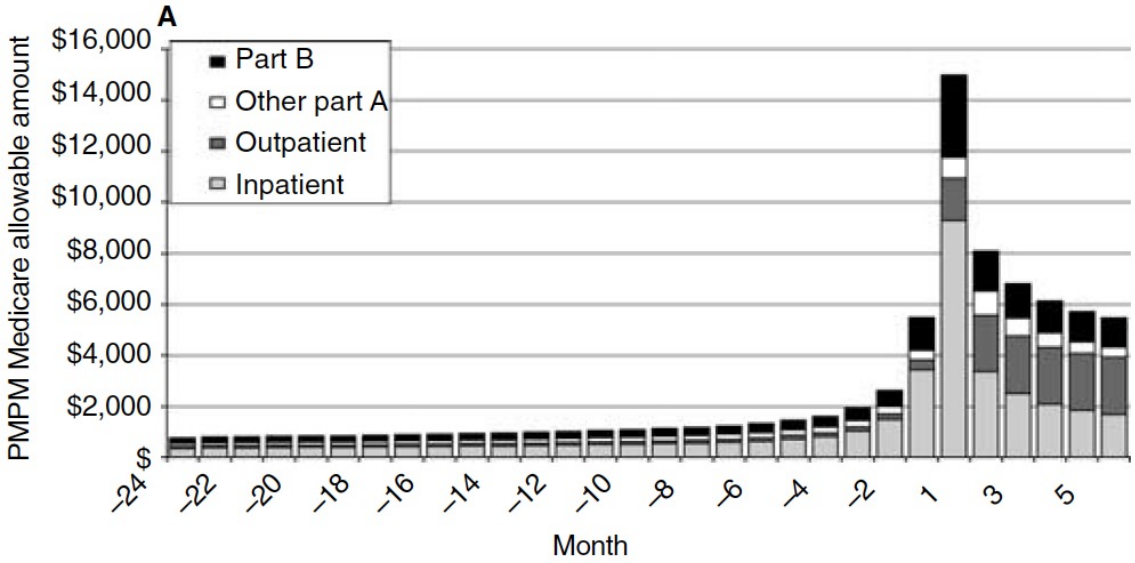
# AKI and CKD Link

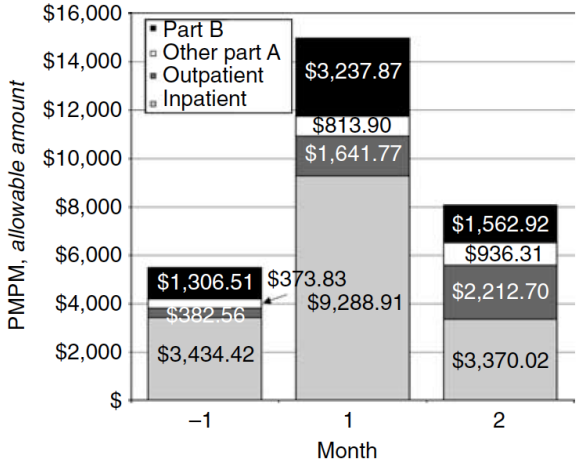



UNIVERSITY OF Cincinnati

Broad Billed Hummingbird

# Transition to ESRD



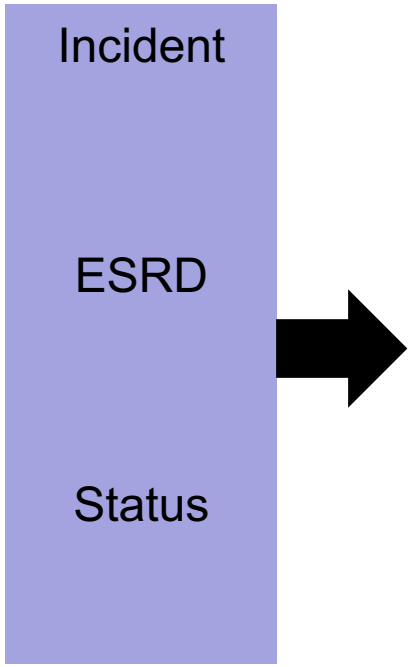

W St. Peter et al, KI 2004

UNIVERSITY OF Cincinnati

# Some Key Statistics

- 70% -- Patients starting first treatment in hospital
- 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

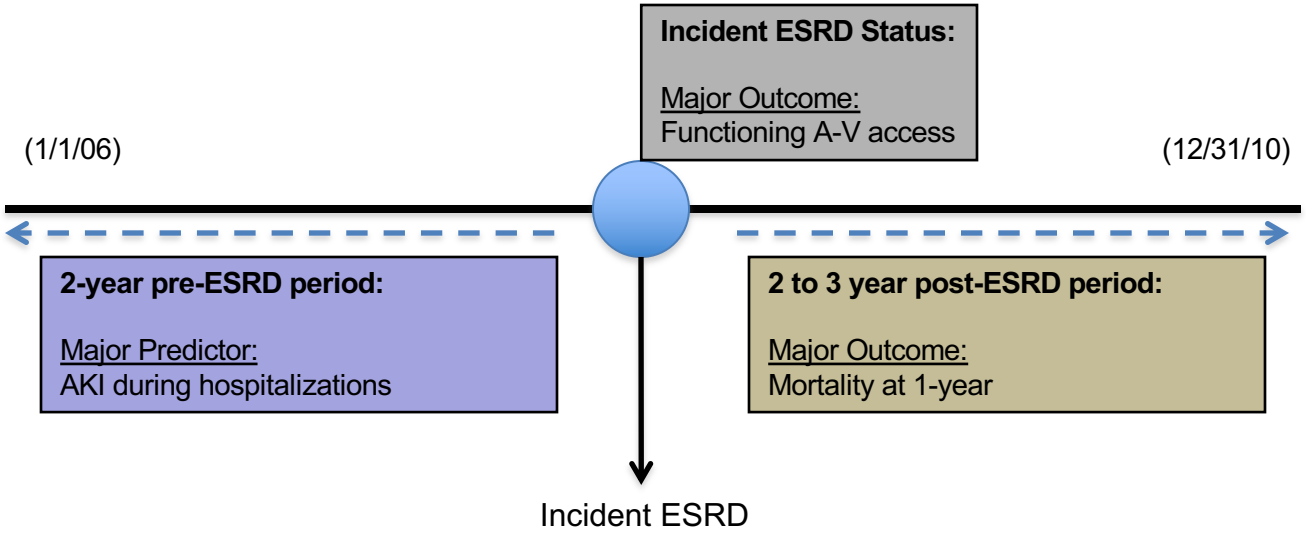
Transplant Status

# AKI and ESRD Link

- AKI during CKD journey accelerates CKD
  - Does pre ESRD AKI episodes change ESRD outcome?

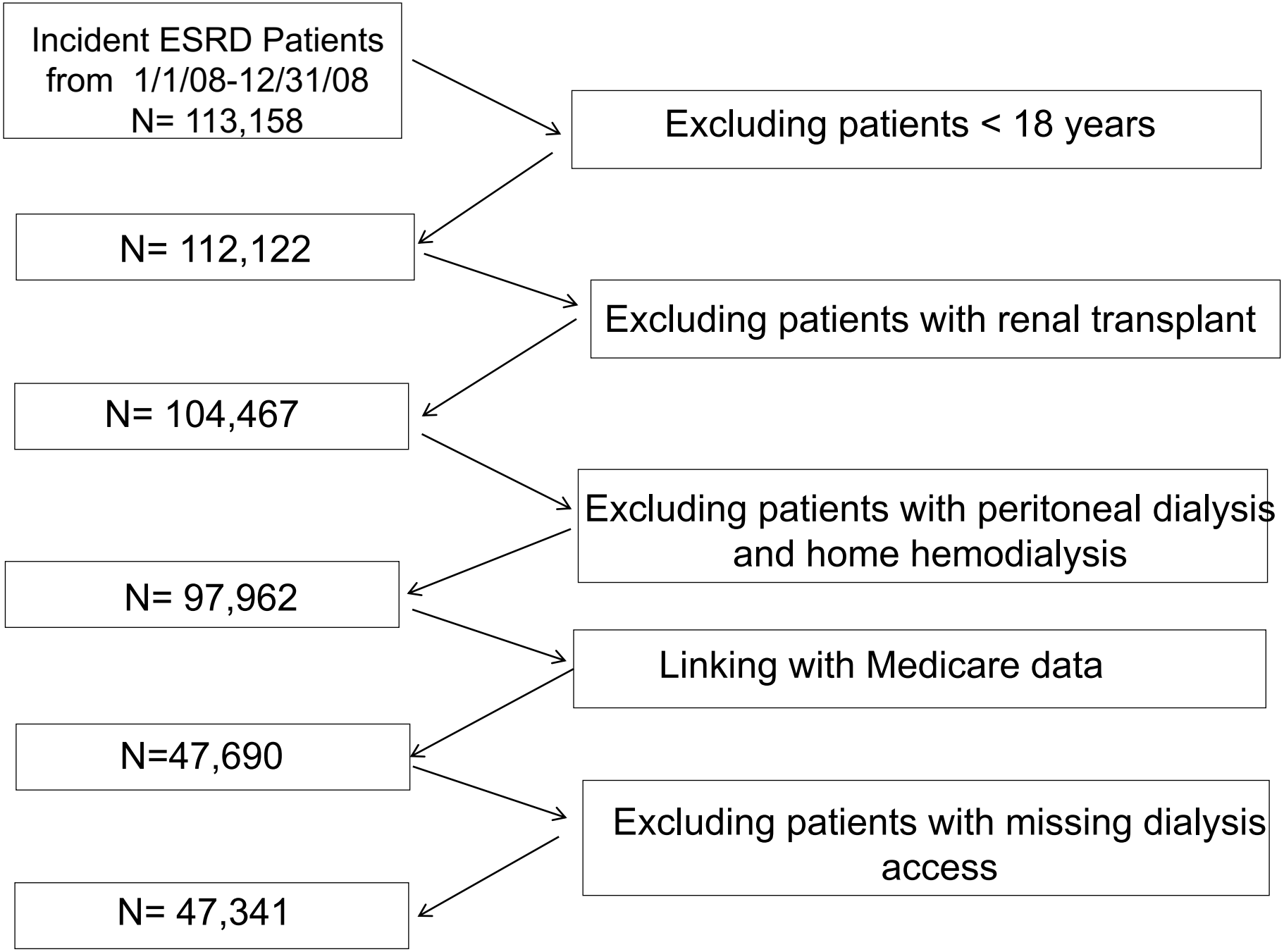
- Dialysis Dependent AKI in advanced CKD
  - Pre-2017:
    - Unable to get reimbursed in chronic programs
    - Stayed in the hospitals
    - Misclassified as “ESRD” if dialysis dependent at 15-30 days
  - Post-2017:
    - Payment for AKI dialysis possible
    - Relatively small numbers in ESRD units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

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




Lee et al, AJN 2018

UNIVERSITY OF Cincinnati




Lee et al, AJN 2018

## 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.

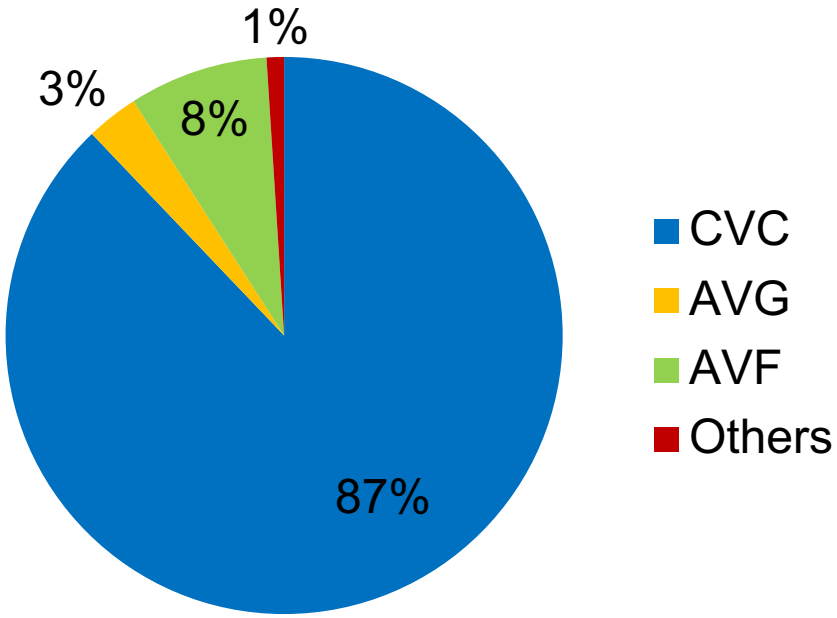
Lee T, Shah S, Leonard AC, Parikh P, Thakar CV, Acute Kidney Injury before Dialysis Initiation Predicts Adverse Outcomes in Hemodialysis Patients. Am J Nephrol 2018; 47: 427-434

Lee et al, AJN 2018

UNIVERSITY OF Cincinnati

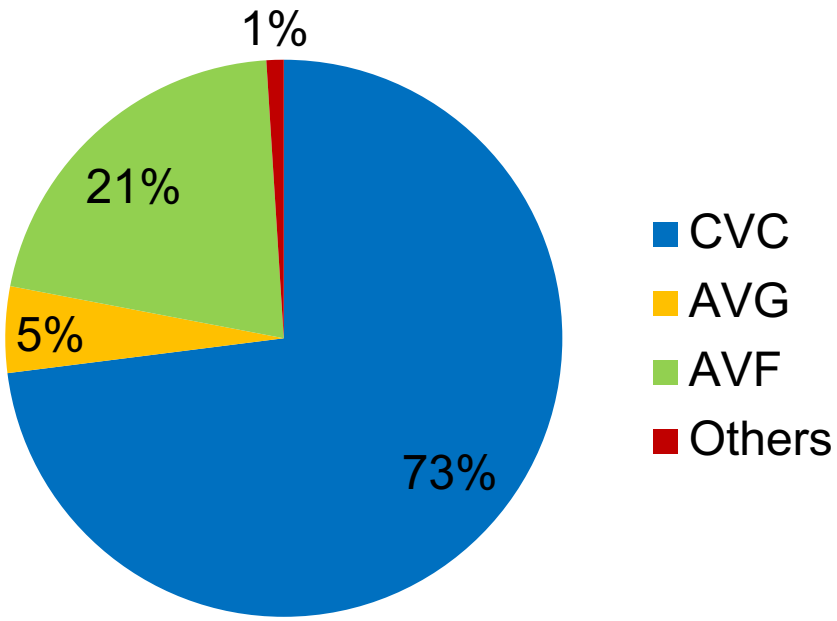
# Dialysis Access

## Pre-ESRD AKI




N = 25,607

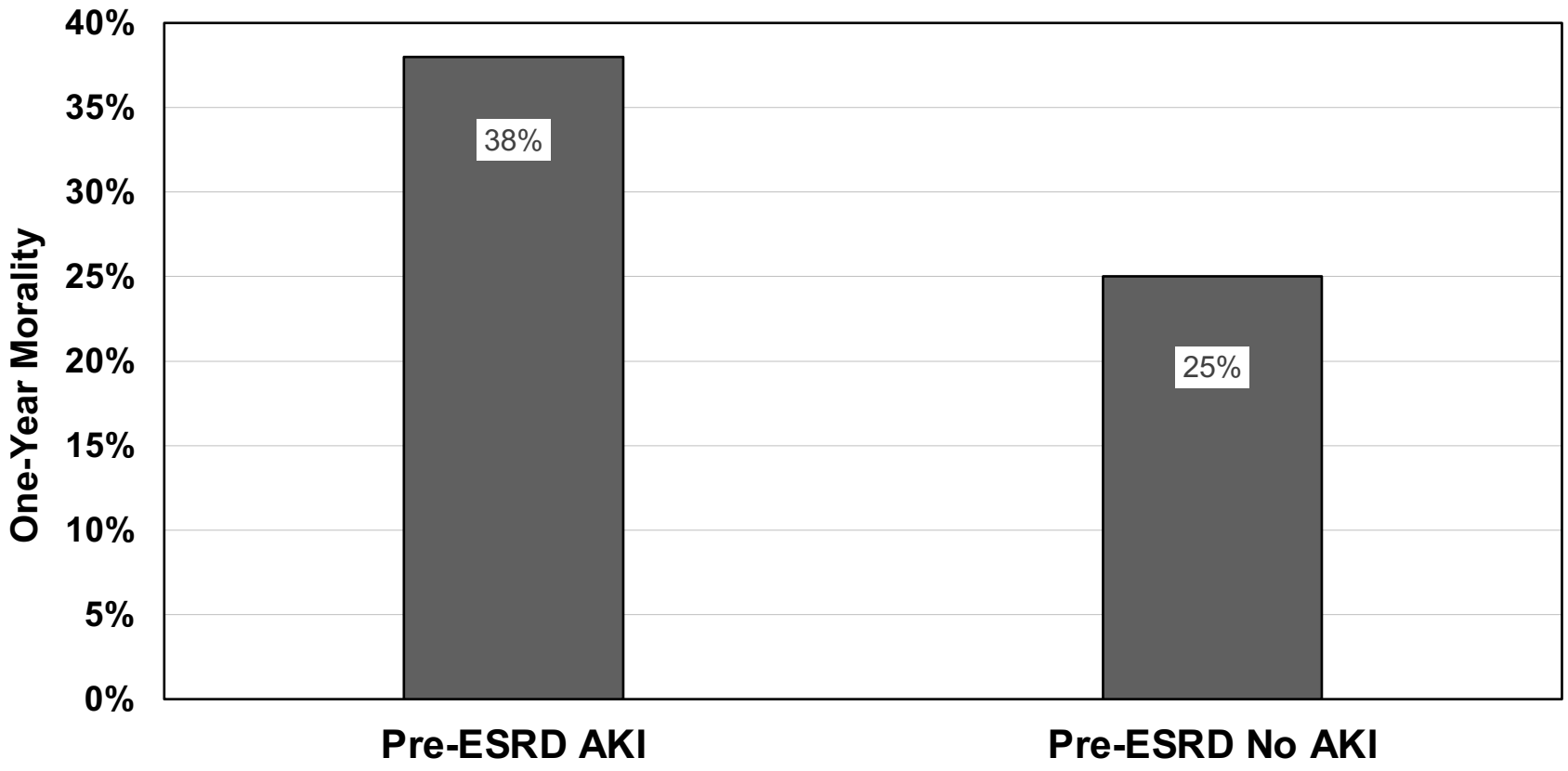
## Pre-ESRD No AKI




N = 21,734

UNIVERSITY OF Cincinnati

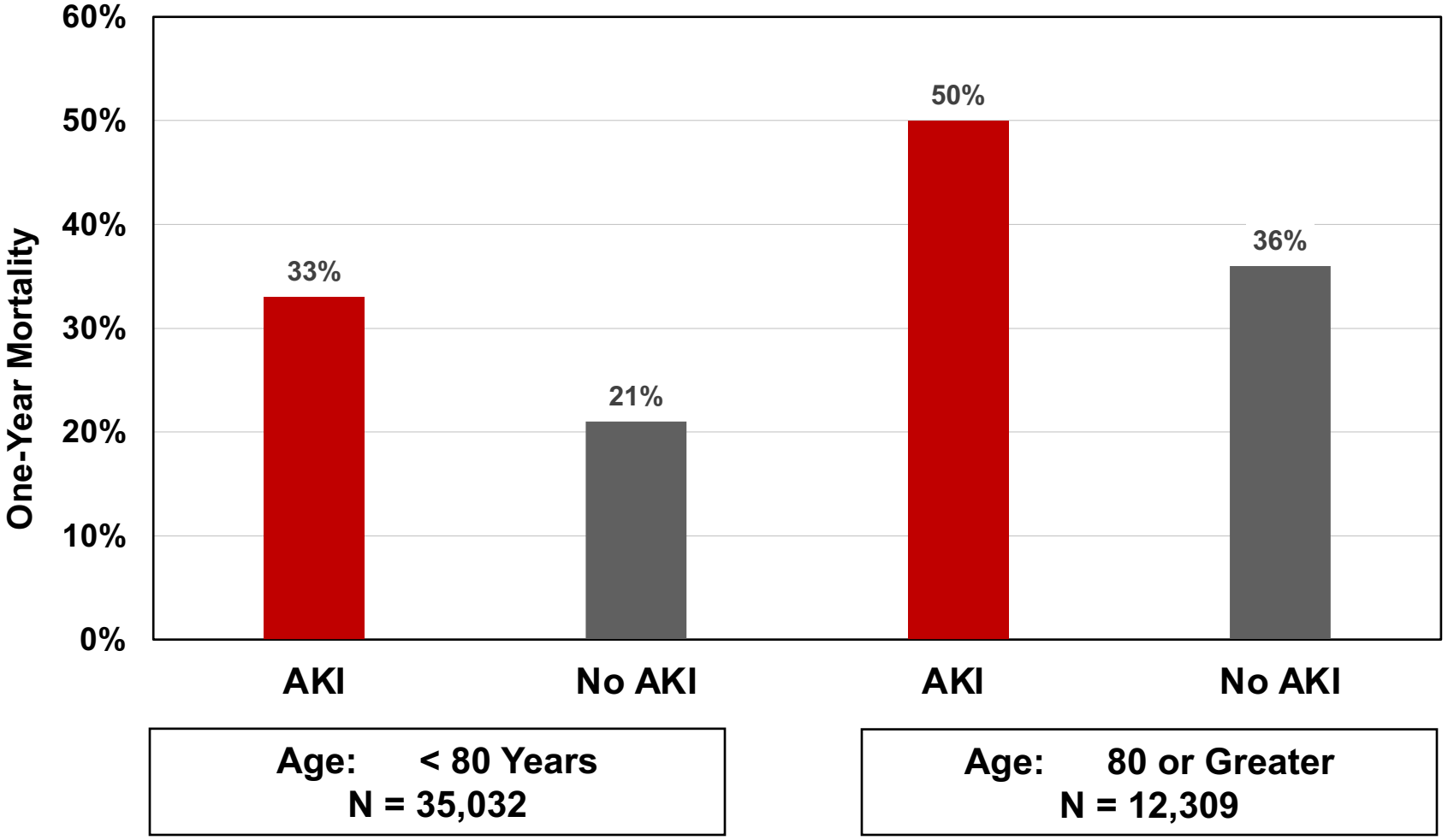
# One-Year Mortality After Incident ESRD




| N = 25,607 | N = 21,734 |
|---|---|

UNIVERSITY OF Cincinnati

# ESRD: Mortality by Octogenarians Status




UNIVERSITY OF Cincinnati

Anna’s Hummingbird

# Dialysis Patients at LTAC

## Overall

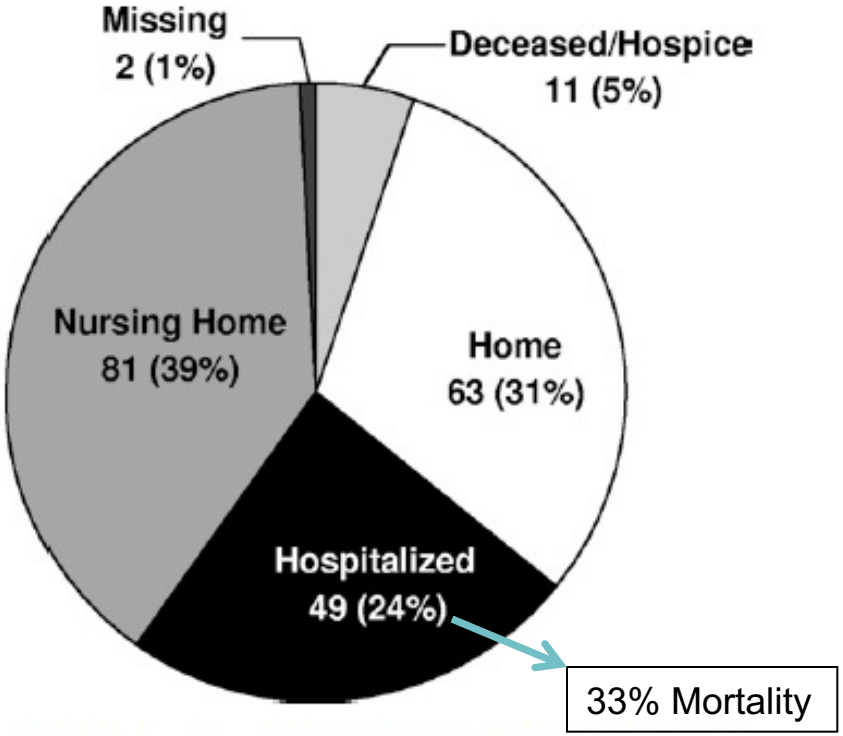
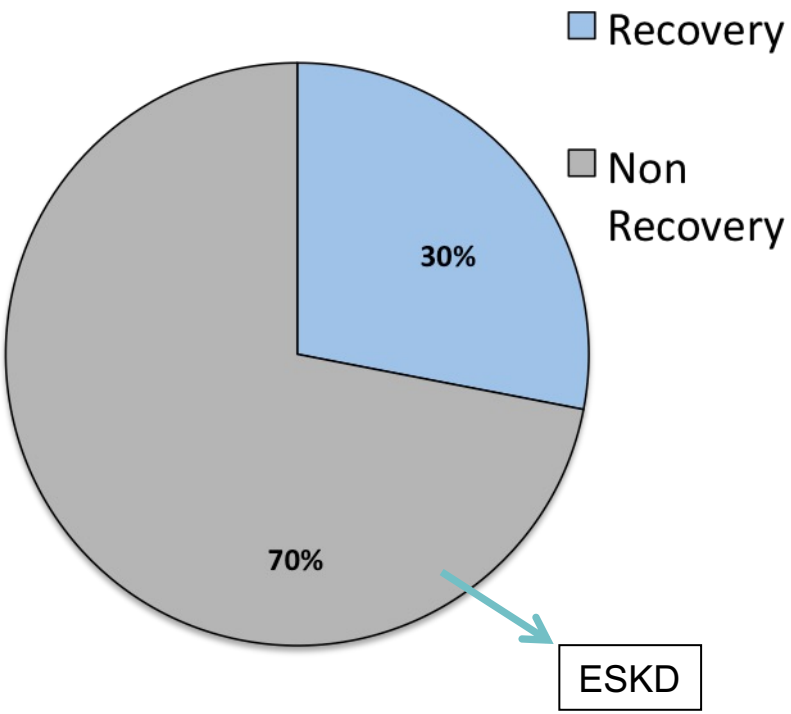



**Figure 1.** Disposition/outcomes of hemodialysis patients from long-term care hospitals.

## AKI



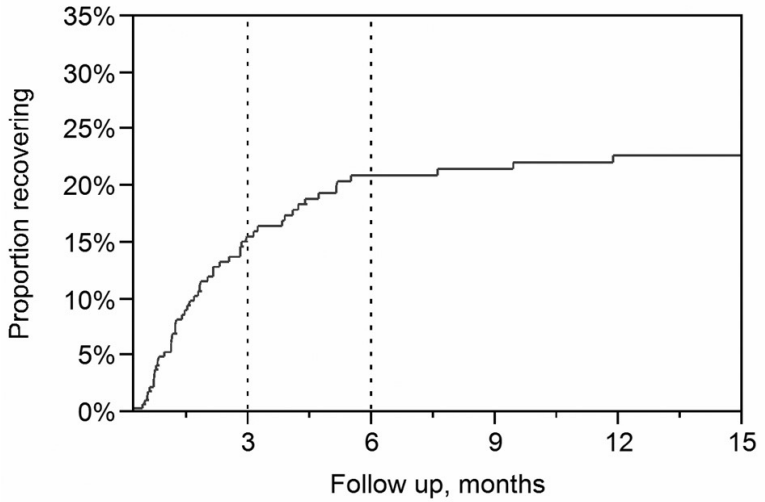

**N, 206 (~50% AKI)**

Thakar et al, AJKD, Feb 2010

UNIVERSITY OF Cincinnati

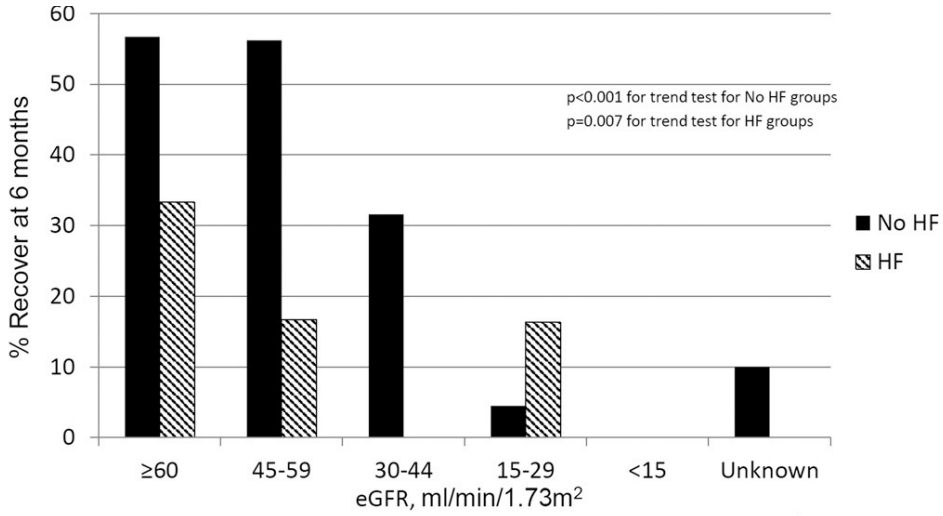
# Recovery Pattern in Dialysis Dependent AKI: Single Center

## 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

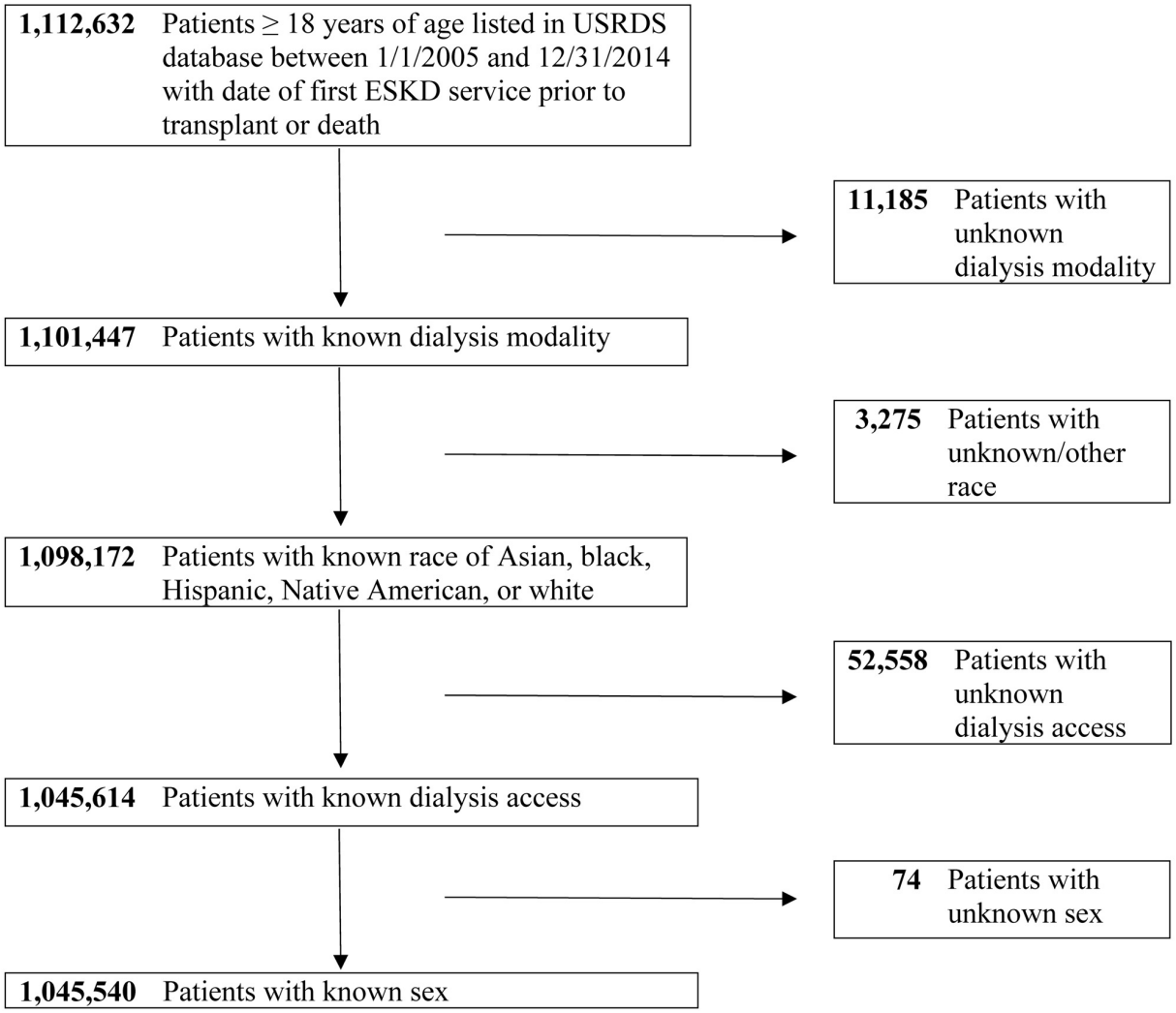



| Number of patients per subgroup: | | | | | | |
|---|---|---|---|---|---|---|
| **No HF** | 30 | 16 | 19 | 44 | 25 | 20 |
| **HF** | 12 | 12 | 21 | 43 | 31 | 8 |

LJ Hickson, AJKD 2015 Mayo Clinic Experience

UNIVERSITY OF Cincinnati

# AKI-ESRD: Cohort Derivation



# AKI-ESRD Key Findings

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

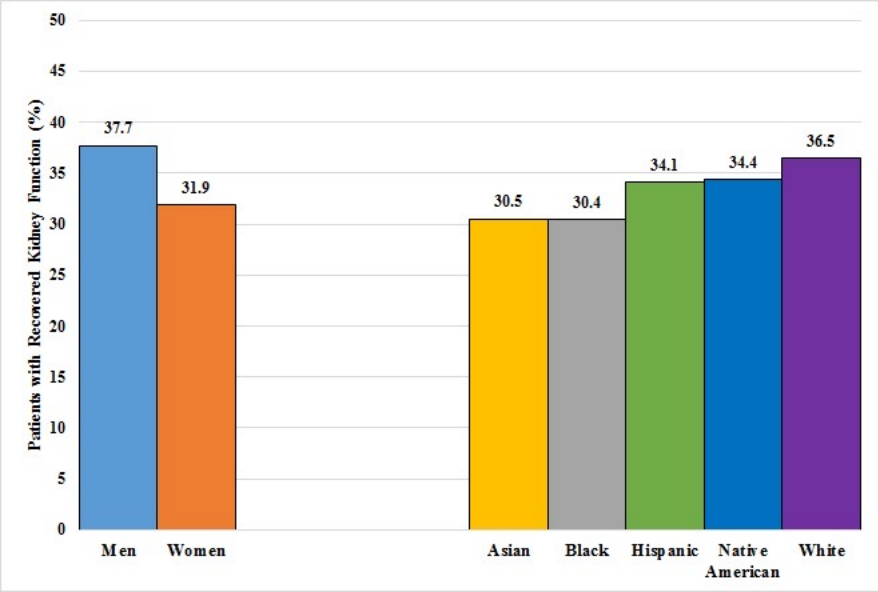
**Key Observations:**
AKI-ESRD – 3.1%
DM-ESRD – 46%
Other-ESRD – 50.9%

| 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% |

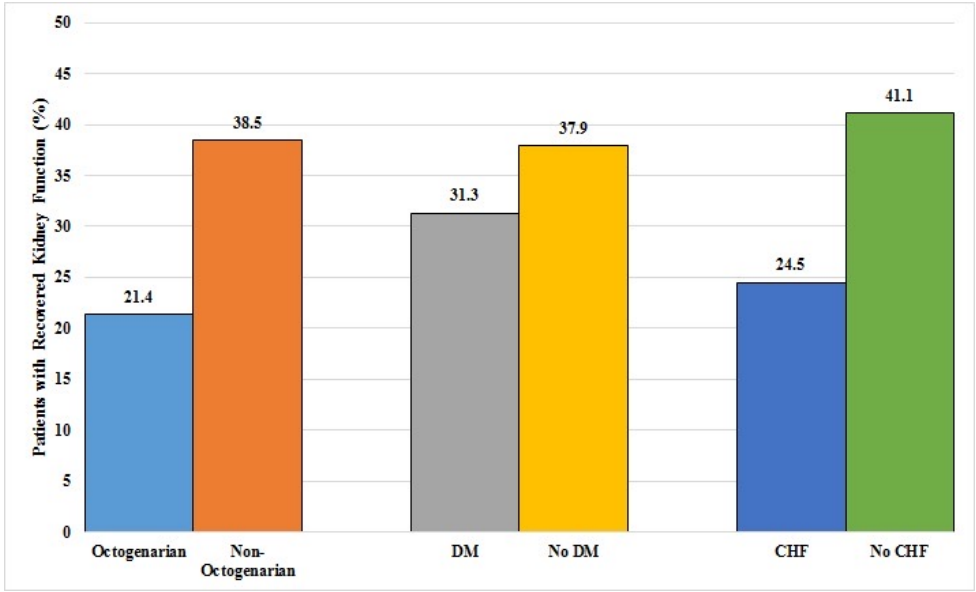
| Outcomes | AKI-ESRD Recovery | AKI-ESRD NonRecovery |
|---|---|---|
| 1 Year Mortality | 10.7% | 48.5% |

UNIVERSITY OF Cincinnati

# AKI-ESRD: Renal Recovery



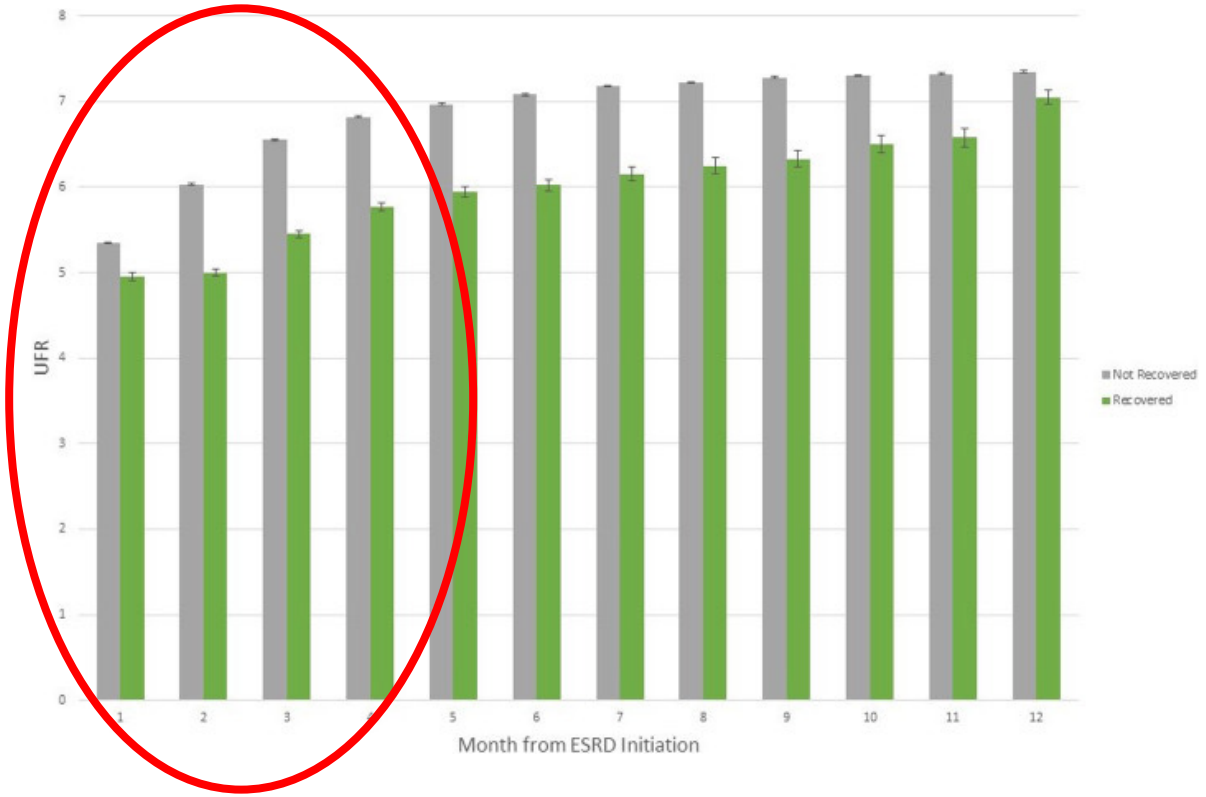

Gender & Race




Co-morbid Conditions

UNIVERSITY OF Cincinnati

# Ultrafiltration Rate and Renal Recovery




M. Santos et al, BMC Nephrology 2021

UNIVERSITY OF Cincinnati

# Prescribing Patterns in Dialysis Dependent AKI

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

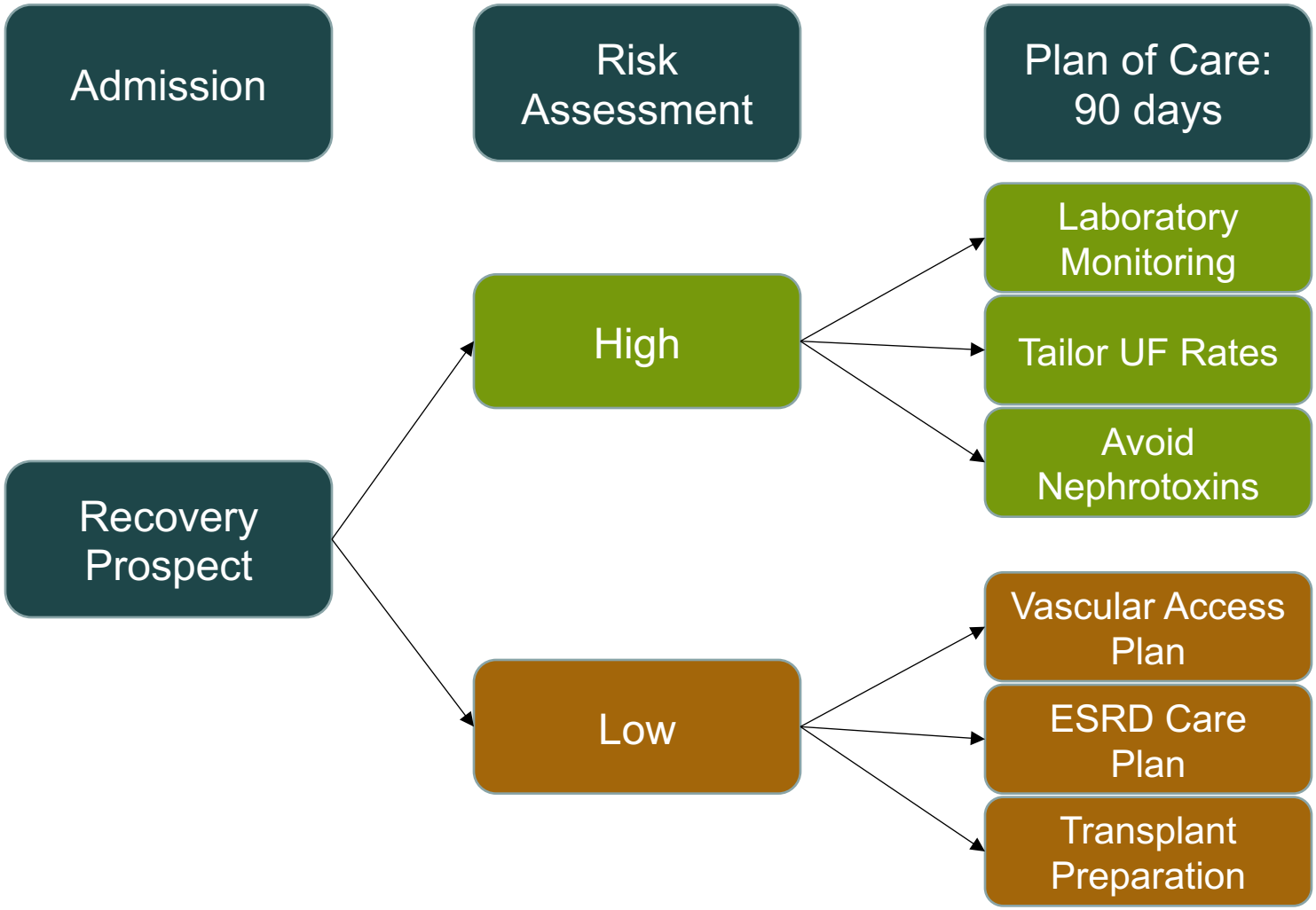
Potentially Contraindicated Medications:

- Aminoglycosides
- NSAID
- Digoxin
- Rivaroxaban
- Metformin

Manley et al, ASN 2019

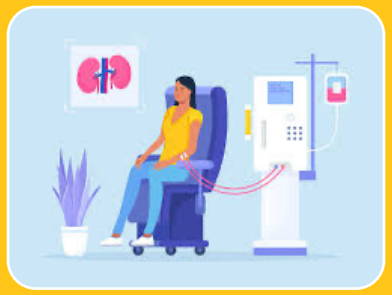
UNIVERSITY OF Cincinnati

# Triaging Care: Dialysis Dependent AKI




UNIVERSITY OF Cincinnati

# AKI and ESRD Link: Implications



| Patient's Health | Dialysis Programs | Healthcare Systems |
| --- | --- | --- |
| - Prognosis<br>- Recovery | - Care Planning<br>- Resources and Costs | - Acute Care<br>- Transplant Options |

UNIVERSITY OF Cincinnati

# AKI and ESRD Link


Incident

ESRD

Status

**ESRD Care**

Modality Choice

Residual function/Recovery

ESRD Care

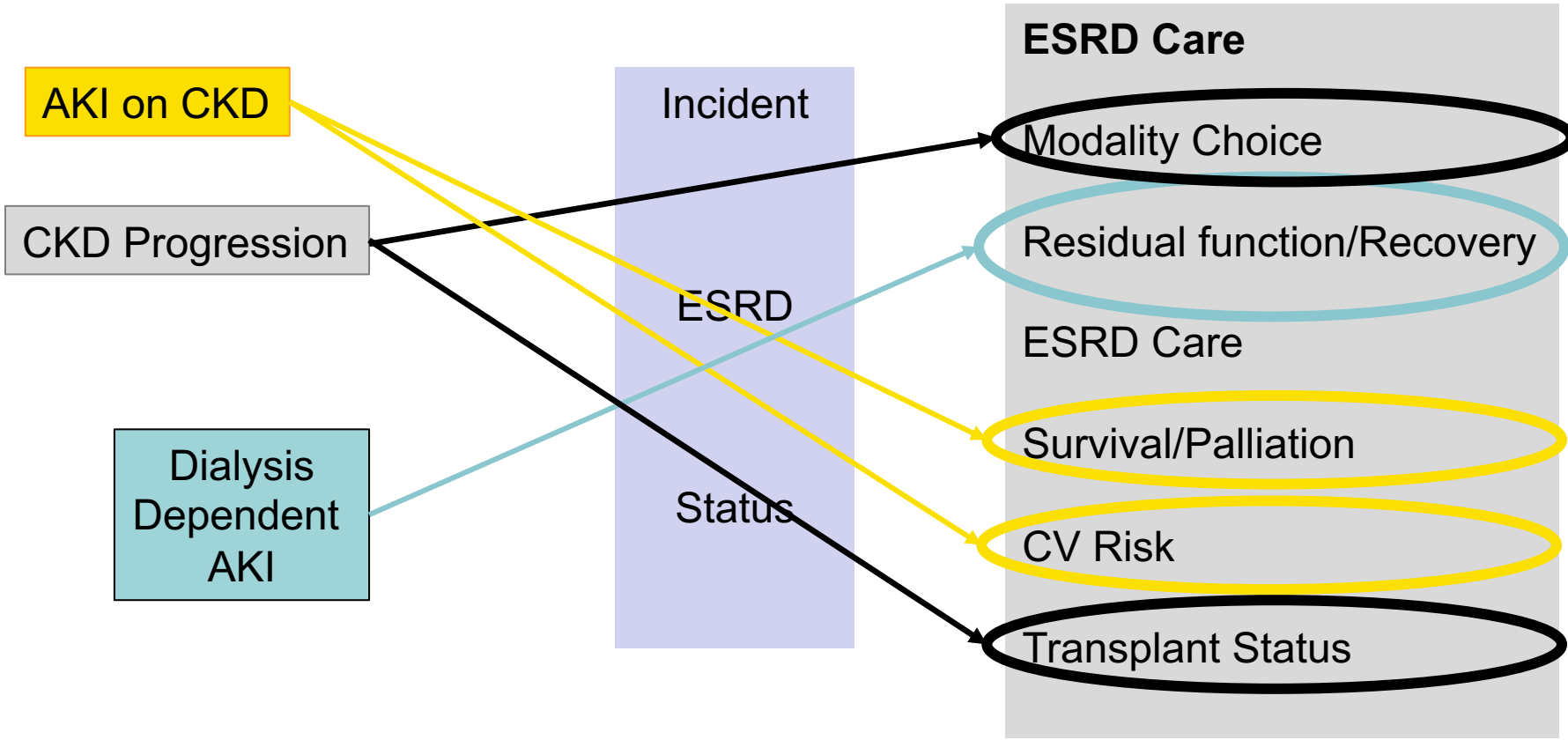
Survival/Palliation

CV Risk

Transplant Status

UNIVERSITY OF Cincinnati

# AKI and ESRD Link




UNIVERSITY OF Cincinnati

# 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 15th 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.

Started dialysis in chronic unit on Feb 1st 2023

- **Mr. Jones**

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 15th 2022.

Creatinine remained stable post-cath.

Progressed to ESRD as expected.

Started dialysis in chronic unit on Feb 1st 2023

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

**I Hope They Don't!**

**Ruby Throated Hummingbird**