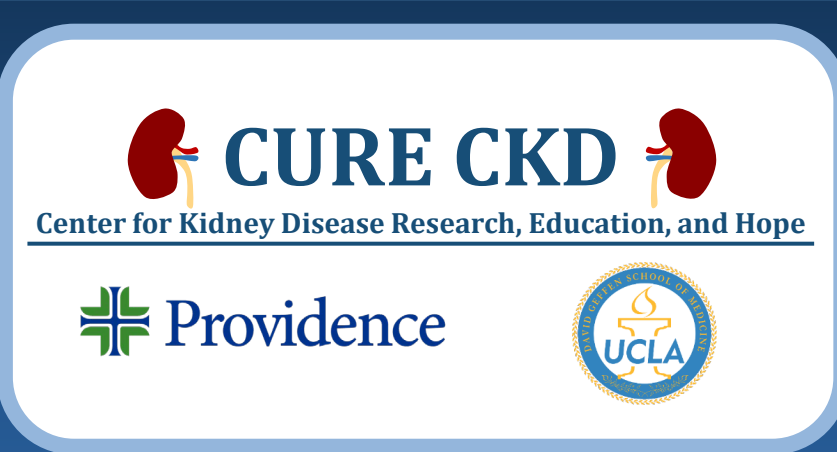


# Predictors of Progression to Kidney Failure in Patients with Focal Segmental Glomerulosclerosis

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## Background and Study Aim

Focal segmental glomerulosclerosis (FSGS) is a glomerular disease phenotype that often progresses to kidney failure. However, to risk stratify patients treated in usual clinical practice, predictors of progression are not well-delineated.

The study aim was to use real-world data to identify patients with FSGS and determine predictors of substantial estimated glomerular filtration rate (eGFR) decline, which is associated with a high risk of reaching kidney failure, or kidney failure.

## Methods

### Study Time Periods

- Entry: Date of FSGS identification between 2016-2020
- Baseline period: Date of FSGS identification through the next 180 days
- Follow-up period: After baseline period until study outcome or censorship for last eGFR measure calculated by CKD-EPI 2021

### Inclusion Criteria

- Data source is the CURE-CKD Registry based on electronic health records from Providence and UCLA Health<sup>1,2</sup>
- Adults, ≥18 years
- FSGS identified by ICD-10 diagnosis codes

### Exclusion Criteria

- Kidney failure before or during baseline period:
  - Baseline eGFR <15 mL/min/1.73 m<sup>2</sup>
  - Diagnosis code for kidney failure (ICD-10)
  - Procedure (ICD-9/10) or diagnosis (ICD-10) codes for dialysis
  - Procedure code for kidney transplant (ICD-9/10)
- No eGFR measurements during baseline or follow-up

### Outcomes

- Primary: Composite of ≥40% eGFR decline or kidney failure**
- Secondary:**
  - ≥40% eGFR decline: Indicator of high risk for kidney failure
  - Kidney failure:**
    - eGFR <15 mL/min/1.73 m<sup>2</sup>
    - Diagnosis code for kidney failure (ICD-10)
    - Procedure (ICD-9/10) or diagnosis code (ICD-10) for dialysis
    - Procedure code for kidney transplant (ICD-9/10)

### Statistical Analyses

- Kaplan-Meier survival estimates of time to first event for primary composite outcome and secondary outcomes
- Cox Proportional Hazard modeling to identify baseline predictors of primary composite outcome (N=325)
- Sensitivity: Macroalbuminuria (UACR >300 mg/g)/overt proteinuria (UPCR >0.5 g/g) status was added to the model for the subset of patients with available baseline measures (N=195)

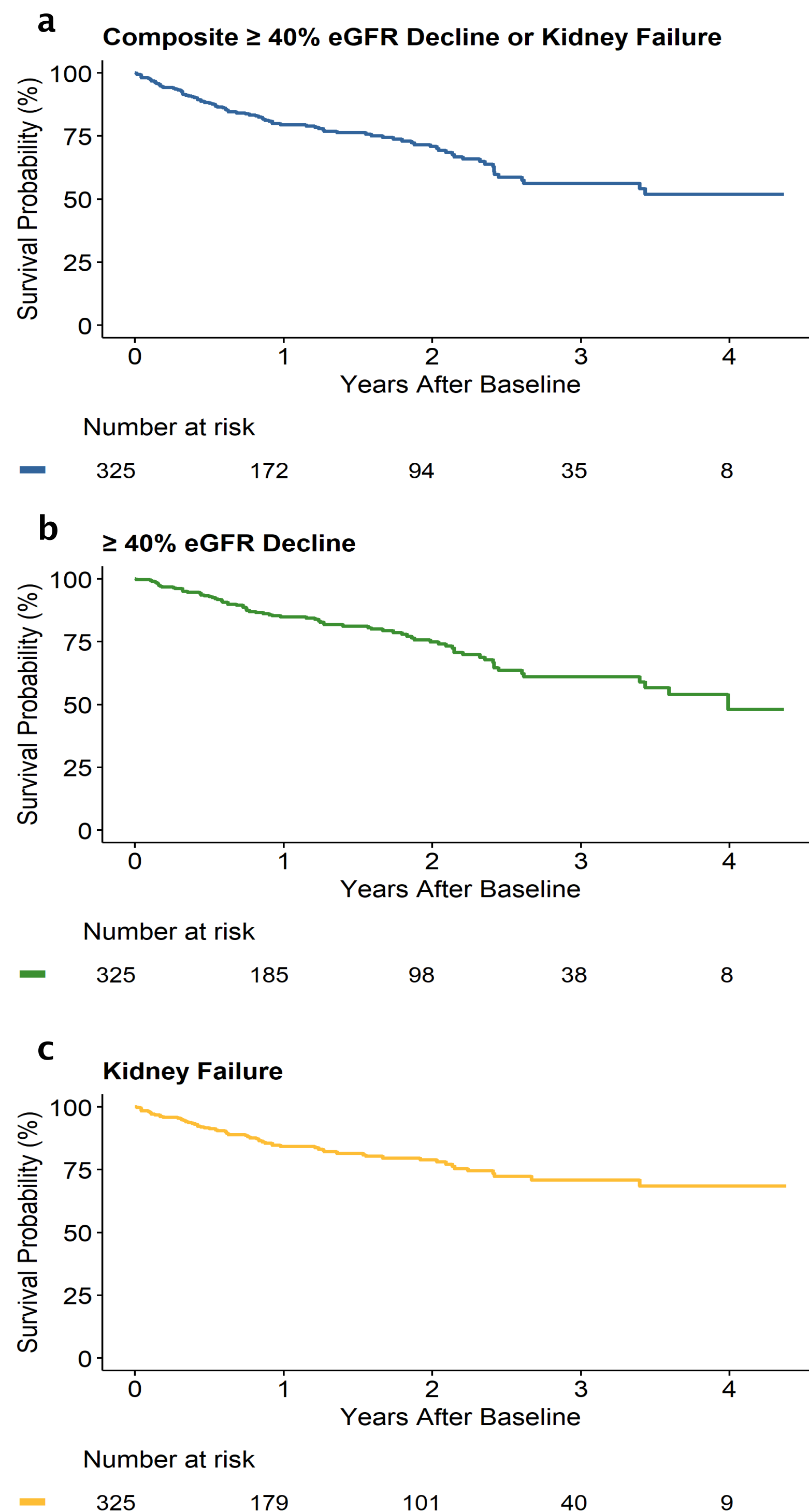
**Table 1.** Characteristics of Patients with FSGS, 2016-2020 (N=325)

Demographics	
<b>Sex, n (%)</b>	
Men	175 (53.8)
Women	150 (46.2)
<b>Race and ethnicity, n (%)</b>	
American Indian or Alaska Native	5 (1.5)
Asian	49 (15.1)
Black	33 (10.2)
Hispanic or Latino(a)	12 (3.7)
Native Hawaiian or Pacific Islander	4 (1.2)
White	168 (51.7)
Other <sup>a</sup>	46 (14.2)
Missing	8 (2.5)
<b>Age, y, mean, SD</b>	51, 17
<b>Primary health insurance, n (%)</b>	
Medicare	81 (24.9)
Medicaid	26 (8.0)
Commercial	177 (54.5)
Uninsured	5 (1.5)
Missing	36 (11.1)
Baseline Medications	
ACE inhibitor/ARB	216 (66.5)
Calcineurin inhibitor	52 (16.0)
Glucocorticoid	115 (35.4)
Baseline Clinical Characteristics	
<b>Hypertension, n (%)</b>	276 (84.9)
<b>Diabetes, n (%)</b>	112 (34.5)
<b>eGFR, mL/min/1.73 m<sup>2</sup></b>	
n (%)	325 (100.0)
mean, SD	58.4, 29.1
CKD Stage 1-2: ≥60, n (%)	139 (42.8)
CKD Stage 3a: 45-59, n (%)	57 (17.5)
CKD Stage 3b: 30-44, n (%)	61 (18.8)
CKD Stage 4: 15-29, n (%)	68 (20.9)
<b>HbA1c, %</b>	
n (diabetes) (%)	68 (60.7)
mean, SD	7.0, 1.2
<b>UACR, mg/g</b>	
n (%)	109 (33.5)
median (IQR)	939 (156-2134)
<b>UPCR, g/g</b>	
n (%)	106 (32.6)
median (IQR)	1.8 (1.0-3.5)

<sup>a</sup>includes patients that did not identify with main census categories

## Results

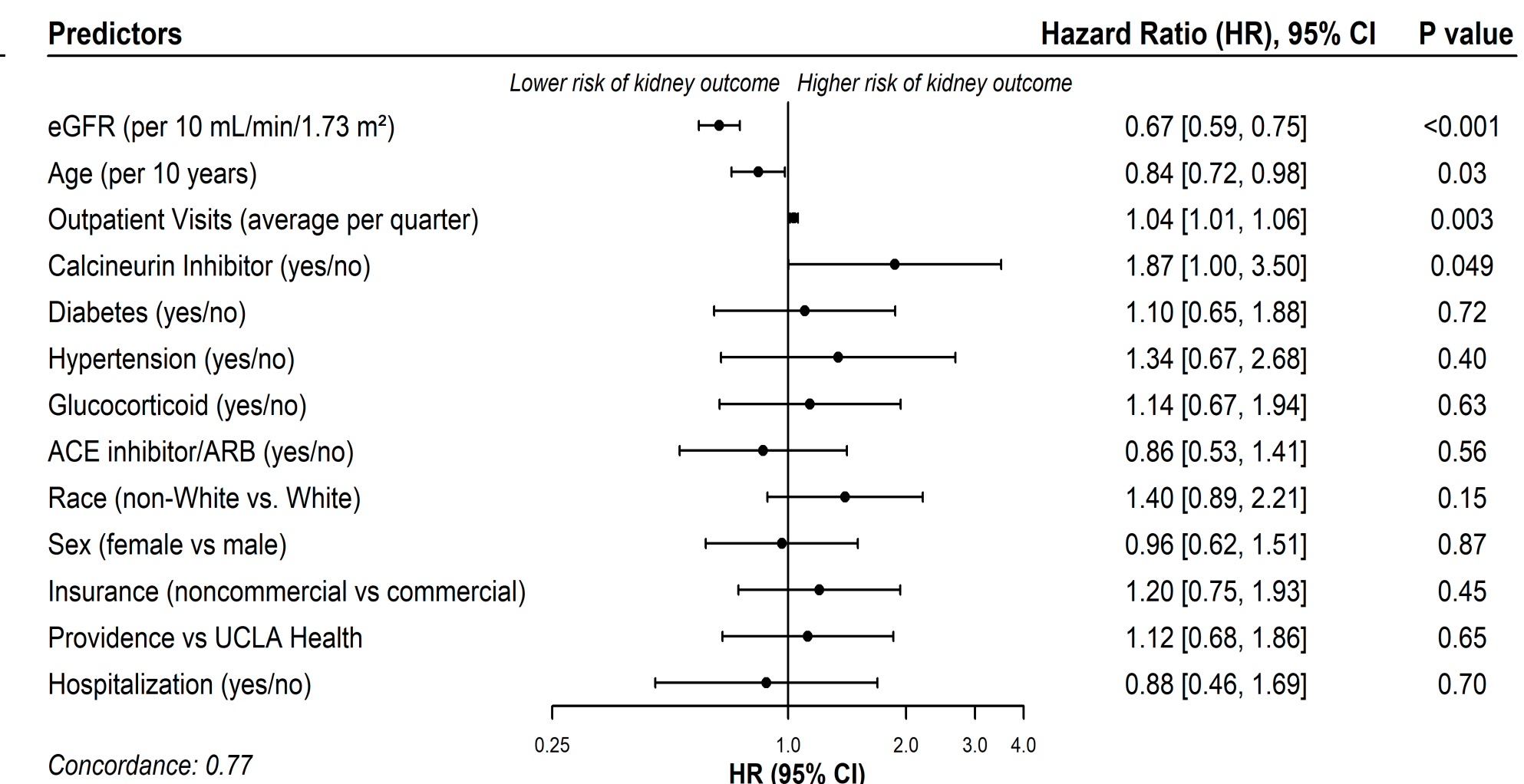
**Figure 1.** Kaplan-Meier Survival Analysis for (a) Composite ≥40% eGFR decline or kidney failure (b) ≥40% eGFR decline (c) kidney failure



## Outcomes Frequency

- Primary composite outcome ≥40% eGFR decline or kidney failure**
  - 88/325 (27.1%) reached a first event at a median of 1.2 years
- ≥40% eGFR Decline**
  - 75/325 (23.1%) total events
- Kidney Failure**
  - 61/325 (18.8%) total events
- In the presence of unmeasured competing risks (e.g., death) predictors are limited to the cause-specific hazard function

**Figure 2.** Predictors of Primary Composite Outcome of ≥40% eGFR Decline or Kidney Failure in Patients with FSGS (N=325)



## Sensitivity Analysis

- Macroalbuminuria/overt proteinuria (HR: 4.06, 95% CI: 1.34-12.34, p=0.01) was an independent predictor for the composite outcome
- Overall model stability persisted for other predictors

## Summary

- Real world patients with FSGS have high rates of ≥40% eGFR decline or kidney failure within a relatively short timeframe
- Younger patients and those with lower kidney function were at greater risk.
- More frequent outpatient visits and calcineurin inhibitor use may reflect bias by indication in higher risk patients

## Conclusions

Risks of progression to kidney failure are high in real world patients with FSGS treated in usual clinical practice.

Earlier detection, with particular attention to younger patients, is needed to detect FSGS when therapeutic strategies may be most beneficial.