Development of Predictive Models for Clinical and Utilization Outcomes of Chronic Kidney Disease in Patients with Type 2 Diabetes

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Background

Progression of chronic kidney disease (CKD) can signal risk of additional events and comorbidities that contribute to increasing healthcare costs. Most predictive models have evaluated risk of progression to end-stage kidney disease (ESKD) and mortality but not specifically in patients with type 2 diabetes (T2D).
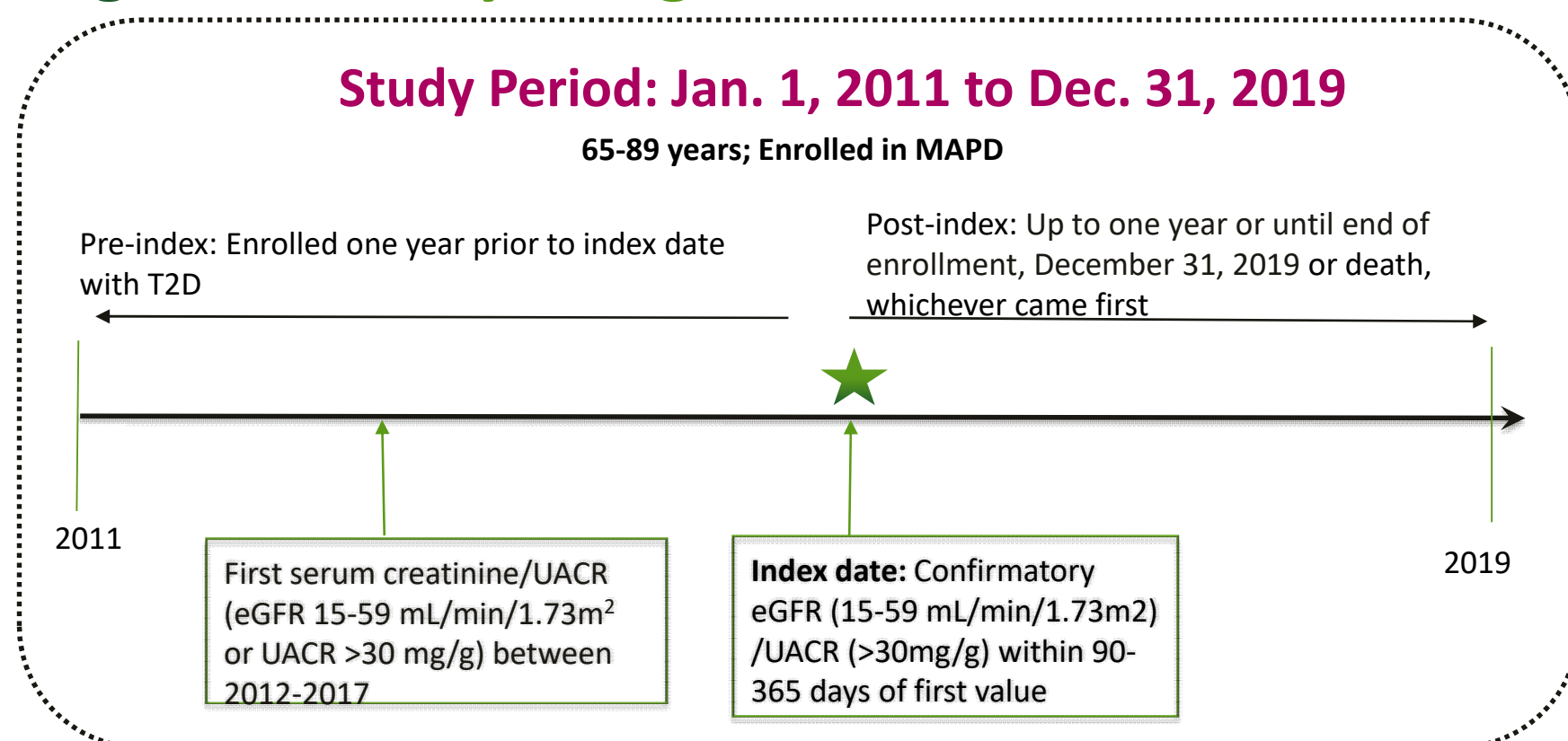
Objective

The purpose of this study was to develop predictive models for rapid progression of CKD, days out of the home, and high costs for patients with both CKD and T2D.

Methods

- **Study Design:** Retrospective observational study
- **Data Source:** Administrative claims data from a national health plan
- **Inclusion and Exclusion Criteria:**
  - With an estimated glomerular filtration rate (eGFR) measure of 15-59 mL/min/1.73m² or urine albumin-to-creatinine ratio (UACR) ≥ 30 mg/g between January 1, 2012 and December 31, 2017; the second or confirmatory eGFR 15-59 mL/min/1.73m² or UACR ≥30 mg/g within 90-365 days of the first value was identified and set as the index date.
  - 65-89 years of age
  - Diagnosed with T2D prior to the index date and enrolled in a Medicare Advantage prescription drug (MAPD) plan for at least 12 months pre-index and post-index period.
  - Excluded: stage V CKD/kidney failure (diagnosis or eGFR<15 mL/min/1.73m²), ESKD based on diagnosis, dialysis or renal transplant, or type 1 diabetes during the pre-index period.
- **Outcomes:** Measured during one year post-index
  - *Rapid progression of CKD:* Sustained decrease in eGFR >5 mL/min/1.73 m² per year
  - *Days out of the home:* Total number of days spent in hospitals, long term care facilities including skilled nursing facilities, inpatient rehabilitation facilities and observation stays plus 0.75 (based on 18 hours of 24 hour period) times number of days with emergency department (ED) visit plus 0.0835 (based on 2 hours of 24 hour period) times number of days with outpatient visits.
  - *Total (medical + pharmacy) health care costs (75-90 percentile)*
- **Statistical Analyses:**
  - Descriptive analysis
  - LASSO technique was used to identify predictors to be retained in the final models followed by logistic regression to generate parameter estimates and model performance statistics.
  - Inverse probability censoring weighting to account for the varying follow-up time.

Figure 1. Study design

Study Period: Jan. 1, 2011 to Dec. 31, 2019

65-89 years; Enrolled in MAPD

Pre-index: Enrolled one year prior to index date with T2D

Post-index: Up to one year or until end of enrollment, December 31, 2019 or death, whichever came first

2011 — 2019

First serum creatinine/UACR (eGFR 15-59 mL/min/1.73m² or UACR >30 mg/g) between 2012-2017

Index date: Confirmatory eGFR (15-59 mL/min/1.73m2) /UACR (>30mg/g) within 90-365 days of first value

eGFR, estimated glomerular filtration rate; UACR, urine to albumin creatinine ratio; MAPD, Medicare Advantage Prescription Drug.

Results

Patient population
- A total of 169,876 patients were identified based on the inclusion/exclusion criteria.

Baseline characteristics
- The overall average age was 75 years and the majority of patients were white (76.3%) and female (53.5%), which was generally similar across outcomes (rapid progression, ≥2% days out of the home, high [>75th percentile] healthcare costs).
- A higher proportion of patients with the outcomes were low income subsidy (LIS) or dual eligible (DE).
- A higher proportion of patients with the outcomes had higher comorbidity. Among patients with UACR or HbA1c values available, patients with the outcomes generally had higher UACR and HbA1c. (Table 1)

Table 1. Baseline clinical characteristics by outcome

	Rapid progression		Days out of the home		Healthcare costs		
	Yes	No	≥ 2% of days*	< 2% of days*	>90th percentile	75-90th percentile	<75th percentile
N	12,743	157,133	27,773	142,103	16,987	25,481	127,408
Row %	7.5%	92.5%	16.3%	83.7%	10.0%	15.0%	75.0%
Elixhauser, mean [SD]	5.5 (2.8)	4.8 (2.6)	6.0 (2.9)	4.6 (2.5)	6.5 (3.1)	5.7 (2.8)	4.4 (2.3)
Confirmatory eGFR, mL/min/1.73 m², mean [SD]	49.7 (8.8)	47.7 (9.7)	45.9 (10.7)	48.3 (9.4)	45.4 (11.0)	46.5 (10.3)	48.5 (9.3)
UACR Results, n (%)							
<30 mg/g	2,426 (19.0%)	32,424 (20.6%)	4,403 (15.9%)	30,447 (21.4%)	2,360 (13.9%)	4,267 (16.7%)	28,223 (22.2%)
30-299 mg/g	1,448 (11.4%)	32,058 (20.4%)	4,847 (17.5%)	28,659 (20.2%)	2,792 (16.4%)	4,606 (18.1%)	26,108 (20.5%)
≥300 mg/g	720 (5.7%)	7,411 (4.7%)	1,564 (5.6%)	6,567 (4.6%)	1,000 (5.9%)	1,378 (5.4%)	5,753 (4.5%)
Missing	8,149 (63.9%)	85,240 (54.2%)	16,959 (61.1%)	76,430 (53.8%)	10,835 (63.8%)	15,230 (59.8%)	67,324 (52.8%)
HbA1c Results, n (%)							
<8.0%	8,933 (70.1%)	112,807 (71.8%)	18,462 (66.5%)	103,278 (72.7%)	10,841 (63.8%)	16,892 (66.3%)	94,007 (73.8%)
≥8.0%	2,096 (16.4%)	25,047 (15.9%)	4,819 (17.4%)	22,324 (15.7%)	3,018 (17.8%)	4,606 (18.1%)	19,519 (15.3%)
Missing	1,714 (13.5%)	19,279 (12.3%)	4,492 (16.2%)	16,501 (11.6%)	3,128 (18.4%)	3,983 (15.6%)	13,882 (10.9%)

*2% corresponds to 7 out of 365 days.

SD, standard deviation; IQR, interquartile range; LIS, low income subsidy; DE, dual eligible; eGFR, estimated glomerular filtration rate; UACR, urine to albumin creatinine ratio; HbA1c, hemoglobin A1c.

Model performance statistics (Table 2)
- The range of C-statistics across models was 0.694 to 0.745 and sensitivity ranged from 60.2% to 82.7%.

Table 2. Model performance statistics

	Rapid progression	Days out of the home	High cost (75-90th percentile)
C-statistic	0.694	0.708	0.682
Sensitivity	82.7%	60.2%	65.3%

Risk factors associated with rapid progression (Figure 1)
- Elevated UACR, LIS/DE status, select comorbidities, select cardiovascular and diabetes medication use, and high number of physician office visits were significantly associated with increased odds of rapid progression.
- The results for the variable baseline eGFR must be interpreted with caution as patients with lower eGFR at baseline have less opportunity to progress rapidly than those whose eGFR is higher at baseline.

Risk factors associated with days out of the home (Figure 2)
- Elevated UACR was significantly associated with increased odds of days out of home.
- Similarly, LIS/DE status, select comorbidities, select cardiovascular and diabetes and medical use and increased physician encounters were also significantly associated with higher days out of the home.

Risk factors associated with high cost (75th-90th Percentile)
- Elevated UACR and low eGFR was significantly associated with total costs in the 75-90th percentile. Similarly, select comorbidities (e.g., CHF, COPD, complicated diabetes), select cardiovascular and diabetes medication use, inpatient hospitalizations, emergency department encounter, and increased physician encounters were also significantly associated with higher total costs.

Figure 1. Factors associated with rapid progression of CKD
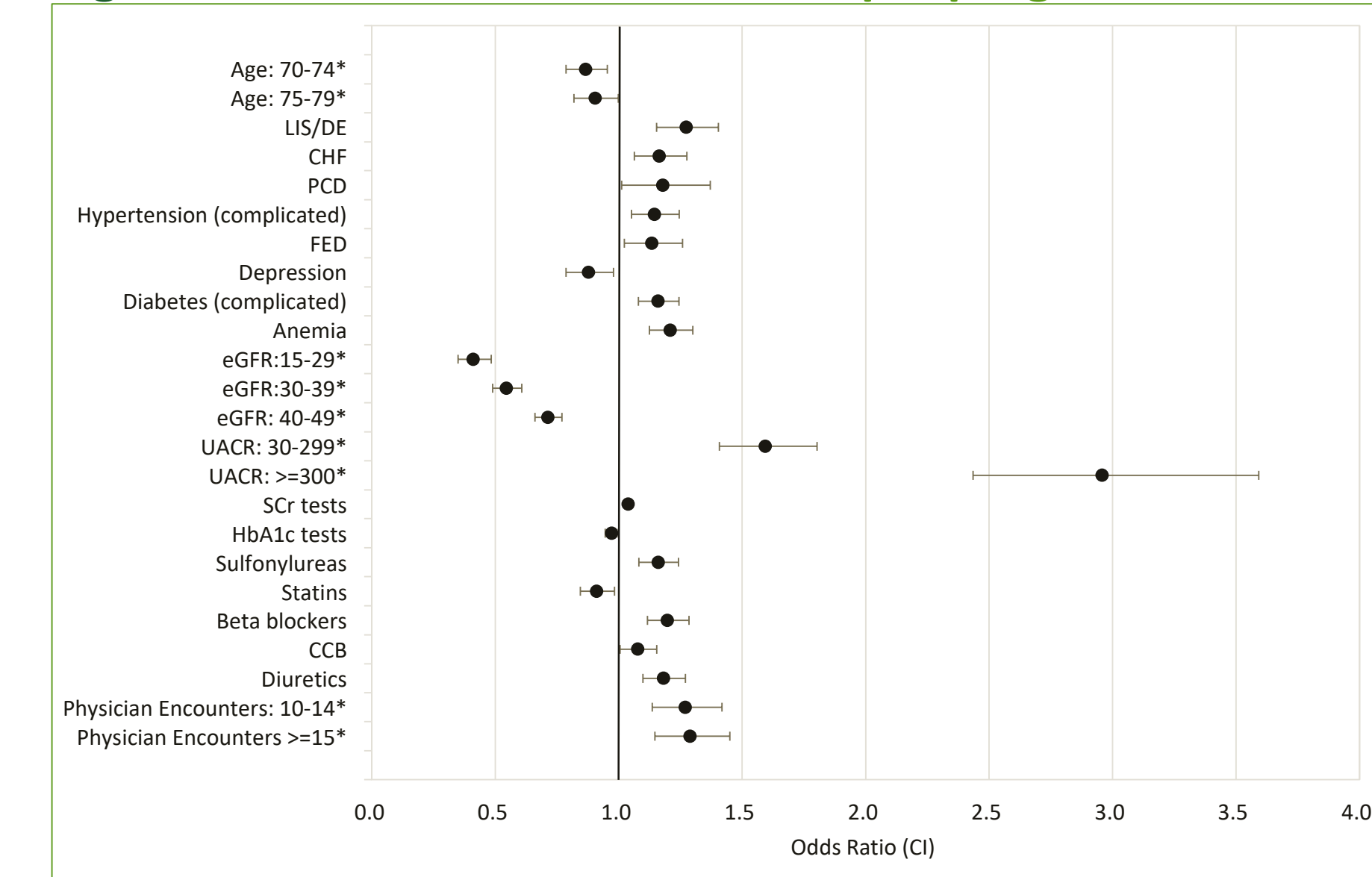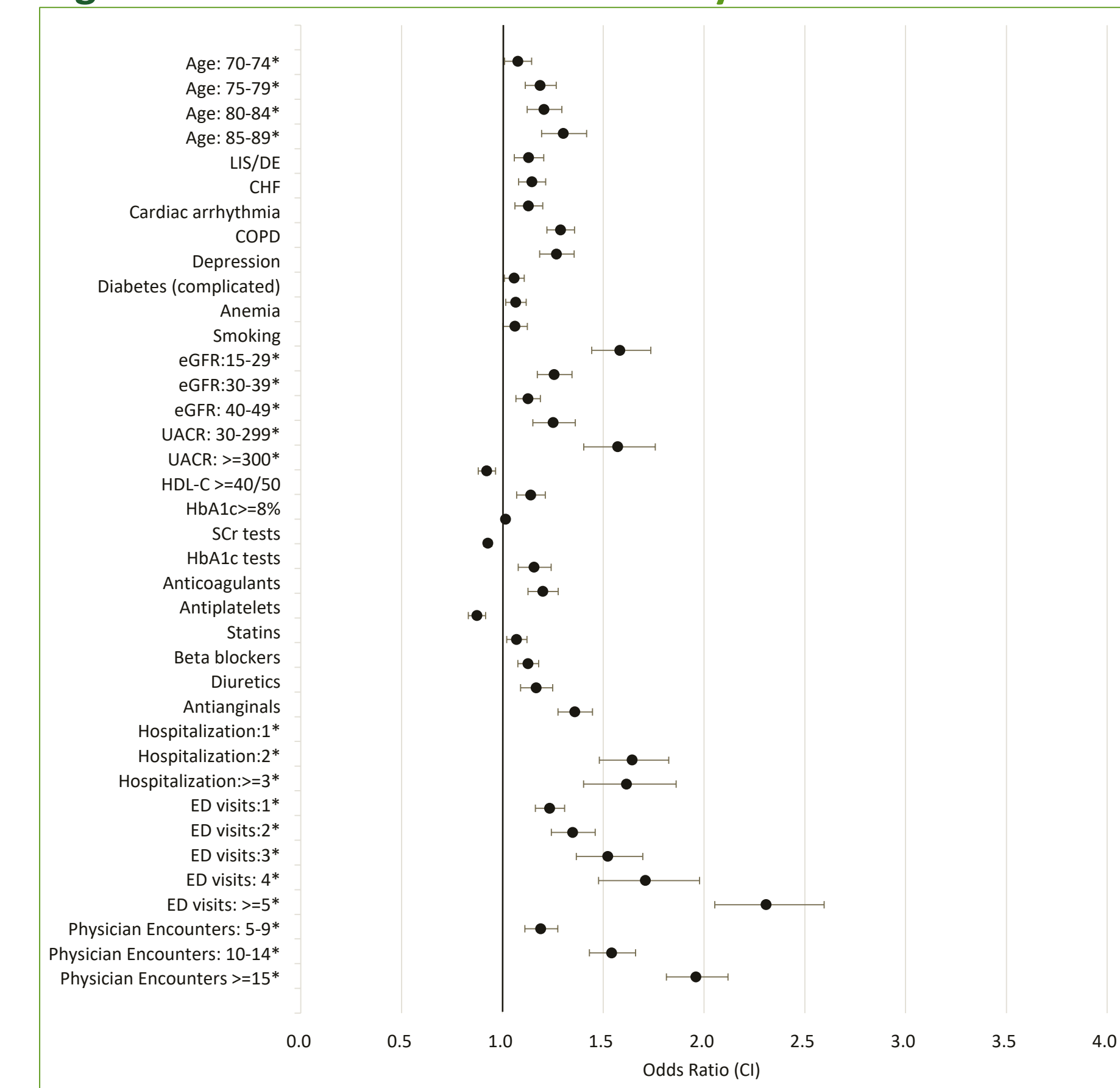

Figure 2. Factors associated with days out of the home

LIS, low income subsidy; DE, dual eligible; CHF, congestive heart failure; PCD, pulmonary circulatory disorders; FED, fluid electrolyte disorders; eGFR, estimated glomerular filtration rate; UACR, urine to albumin creatinine ratio; HDL, high density lipoprotein cholesterol; SCr, serum creatinine; HbA1c, hemoglobin A1c; CCB, calcium channel blocker; ED, emergency department.
Reference groups: Age 65-69 years; UACR <30mg/g; Hospitalizations 0; ED 0; Physician encounters <5

Discussion

- Multiple factors were associated with increased risk for rapid progression, increased number of days out of the home and higher costs within one year; however, identifying and focusing efforts on the modifiable risk factors could improve outcomes.
- For example, UACR may be used as an additional or early indicator for decline in renal function which may be associated with poorer outcomes. Increased efforts for UACR monitoring, including potential remote or digital strategies, may be considered.
- Appropriate management of comorbidities and importantly T2D through disease management programs or other interventions may also be of benefit.

Conclusions

- The predictive models developed in this study can be potentially used as decision support tools for clinicians and payers, and the risk scores from these models can be applied to future outcomes studies focused on patients with T2D and CKD.

Limitations

- Common limitations in use of administrative claims: potential errors in coding, omissions in claims data, and unmeasured clinical, economic or behavioral factors.
- This study focused on patients enrolled in an MAPD in a large national health plan, and hence may not be generalizable to a younger population enrolled in commercial plans.
- This is a non-randomized study using data observed in a non-interventional setting and hence no causal inference can be ascertained.
- Missing clinical information: medical records and laboratory values (eGFR, UACR and HbA1c) were available only for a subset of patients.