Relationship Between 24-hr Urinary Oxalate and Incident Chronic Kidney Disease Among Patients with and without Underlying Gastrointestinal Disease

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Disclosures

- Marja Puurunen, Caroline Kurtz, Richard Riese and Aoife Brennan are employees of Synlogic Inc.
- Gary Curhan is an employee of OM1, Section editor for UpToDate, and consultant for Allena Pharmaceuticals
- Michael Behling is an employee of OM1
- James McDougall is a consultant to Synlogic Inc.

Background

- Urinary oxalate is potentially toxic to the kidney

- Hyperoxaluria may result from:
  - intake of high oxalate foods
  - enhanced intestinal absorption
  - malabsorptive GI disorders such as: Crohn’s disease, short bowel syndrome, gastric bypass surgery, and chronic pancreatitis.

- Hyperoxaluria has been associated with adverse renal outcomes, including chronic kidney disease (CKD), but larger studies are needed.

Methods

- Longitudinal retrospective observational cohort study in US
- Patients who had completed at least one 24-hr urine collection between 1/2013 and 12/2020 were eligible for inclusion
- Data from a multi-source data cloud containing deterministically linked, de-identified, individual-level healthcare claims and electronic medical records (EMR) was used
- CKD and malabsorption were defined by the presence of relevant ICD 9/10 or CPT codes
- Patients with CKD at baseline were excluded from incident analysis
- Association between categories of urine oxalate (UOx) and incident CKD was modeled using logistic regression

Study Population

- Entry into the study was triggered by available data from at least one 24-hr urine collection
- Total number of adults identified: 764,860

- *Cohort 1*: 447,958 adults with at least 6 months of baseline and 6 months of follow-up data
  - Median follow-up: 37 months (IQR: 20, 56)
  - N=426,896 of Cohort 1 had no evidence of CKD (based on eGFR values and ICD codes) at baseline and were included in the incident analysis

- *Cohort 2*: 12,522 adults (2.8%) who had an underlying malabsorptive condition preceding index urine

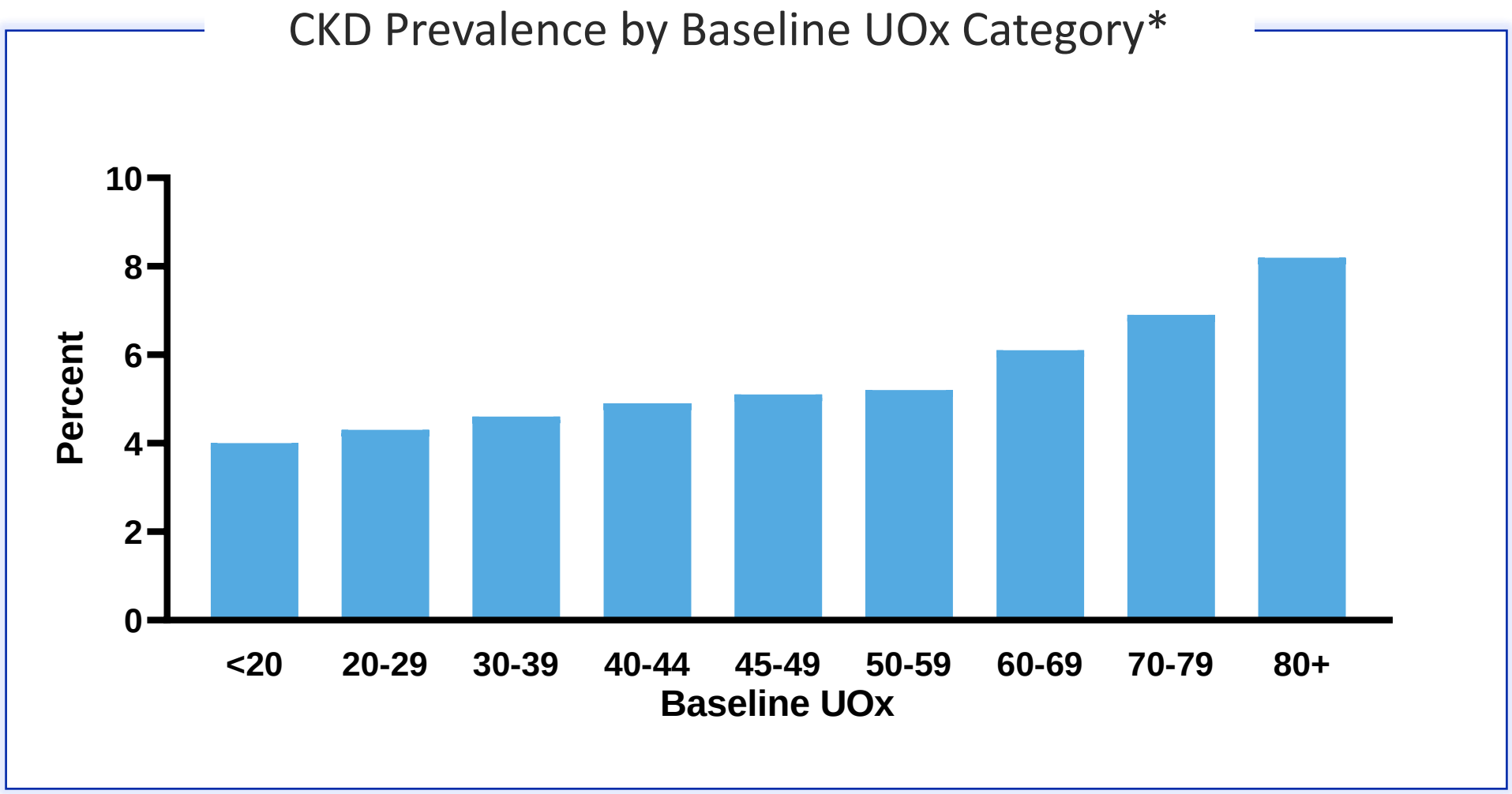
Results: Patient Characteristics

	Cohort 1 (Overall) N=447,958	Cohort 2 (Malabsorptive condition) N=12,522
Age, yr	55.4	54.3
Female	49.6%	58.0%
White race	93%	93%
BMI, kg/m^2	30.2	29.9
Charlson Comorbidity Index	2.3	2.8
Number of kidney stone events in the baseline period, median (IQR)	2 (0-5)	3 (1-7)
eGFR, ml/min/1.73 m^2	81.3	82.3

Results: 24-Hr Urine Results

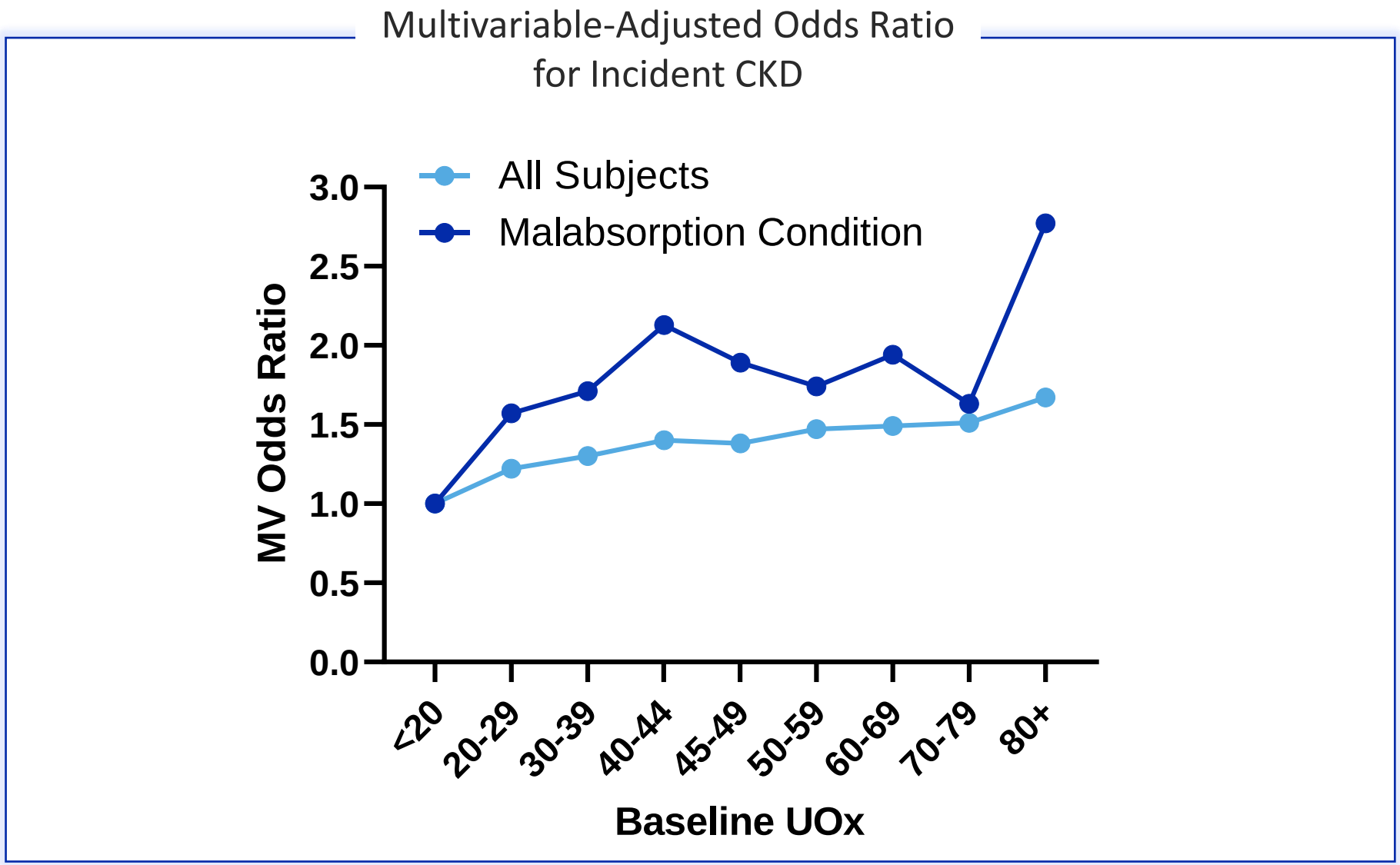
	Cohort 1 (Overall) N=447,958	Cohort 2 (Malabsorptive condition) N=12,522
Oxalate, mg/d	36.1	40.5
Calcium, mg/d	197	161
Citrate, mg/d	595	462
Creatinine, mg/d	1639	1497
Oxalate >= 40mg/d	31.0%	39.5%
Oxalate >=45 mg/d	21.0%	30.7%

Baseline Prevalence of CKD is Elevated with Increasing UOx and Underlying Malabsorptive Condition



*Analysis based on subpopulation of Cohort 1 with no CKD at baseline (N=426,896)

Risk for Incident CKD Increases with UOx Level and is Heightened with Underlying Malabsorption Condition



Conclusions

- This is the largest population-based study on the relationship of UOx and incident CKD to date
- Prevalence of CKD increased across categories of 24-hr urine oxalate
  - Prevalence of CKD was twice as high in patients with UOx >= 80 mg/d compared with < 20 mg/d
- Among patients without a history of CKD, higher urine oxalate is associated with higher risk of developing incident CKD
  - Risk is substantially higher among those with an underlying malabsorptive condition
- These data strongly support findings from smaller previous studies that higher urine oxalate may contribute to the risk of developing CKD
- Currently no pharmacological therapies targeted at UOx lowering are available. These data highlight an unmet medical need