Feasibility of identifying paediatric patients with chronic kidney disease and severe proteinuria using US electronic health records: A retrospective analysis and descriptive outcome assessment

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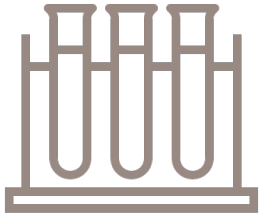
This observational analysis assesses the feasibility of identifying a real-world paediatric population with CKD and proteinuria by applying adapted selection criteria of the FIONA/FIONA OLE clinical trials to a US health records database

Eligible patients from the **US Optum electronic healthcare records (EHR) Database** (January 2013 to September 2021) were included:

Eligibility criteria

- Aged 6 months to 18 years at index
- ≥2 eGFR and ≥2 UPCR values indicating CKD stages 1–3 and severely increased proteinuria, respectively
  - Pairs of qualifying eGFR and UPCR values were separated by ≤89 days
  - 90–365 days gap between the first and second pairs of eGFR/UPCR values were required to ensure disease chronicity. The index date was the last qualifying laboratory value in the second pair

CKD and UPCR eligibility criteria by age group



Age		CKD stage*	UPCR (g/g)#
2 to <18 years		2 or 3	≥0.5
		1	≥1.0
6 months to <2 years	1 to <2	1, 2, or 3	
	6 months to <1 years	Serum creatinine ≤0.4 mg/dL	

ESKD composite endpoint‡

Defined as:
- eGFR <15 mL/min/1.73 m^2 sustained for ≥4 weeks
- Kidney transplantation
- Initiation of maintenance dialysis

and/or
- ≥1 inpatient or 2 outpatient diagnoses of ESKD

Other kidney disease outcomes and mortality‡

Incidences of:
- Components of ESKD composite
- Sustained >50% eGFR decline§
- Acute kidney injury
- All-cause mortality

These outcomes were reported for the overall population and stratified by the following subgroups:

- Index eGFR (<60 vs ≥60 ml/min/1.73 m^2)
- Index UPCR (≤1 or >1 g/g)

Outcomes were reported as cases per 100 patient years

*CKD stage 1: eGFR ≥90 ml/min/1.73 m^2; CKD stage 2: eGFR 60 to <90 ml/min/1.73 m^2; CKD stage 3: eGFR 30 to <60 ml/min/1.73 m^2; #values for UPCR correspond to severely increased proteinuria;
‡all outcomes were assessed as time to event outcomes; §defined as at least two valid decreases in eGFR >50% from baseline within ≥30 days and ≤90 days
eGFR, estimated glomerular filtration rate; CKD, chronic kidney disease; ESKD, end-stage kidney disease; UPCR, urine protein-creatinine ratio

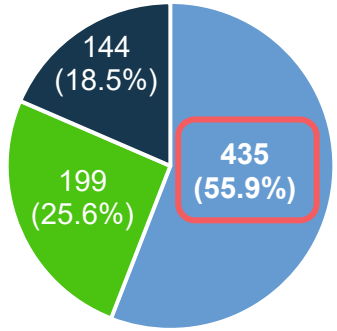
Baseline patient demographics from the US Optum EHR database were representative of a real-world population eligible for FIONA/FIONA OLE

Patient characteristic	N=778
Age, median (Q1–Q3)	**13 (9–15)**
Age group, n (%)	
6 months to <2 years	1 (0.13)
≥2 to <6 years	85 (10.93)
≥6 to <12 years	219 (28.15)
≥12 to <18 years	473 (60.80)
Female sex, n (%)	**371 (47.69)**
Race, n (%)	
African American	123 (15.81)
Asian	62 (7.97)
Caucasian	451 (57.97)
Other/unknown	142 (18.25)

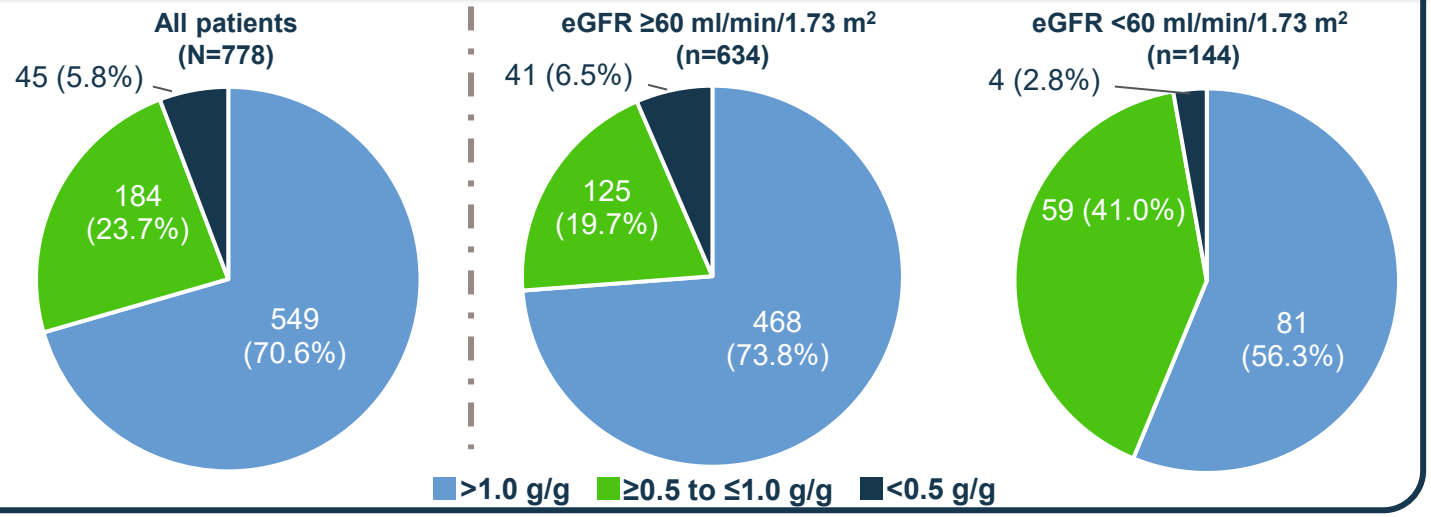
Comorbidity	N=778 (%)
Hypertension	**213 (27.38)**
Anaemia	**92 (11.83)**
Growth retardation	**55 (7.07)**
Hyperlipidaemia	40 (5.14)
Diabetes mellitus	22 (2.83)
Congenital heart malformation	19 (2.44)
Metabolic bone diseases	10 (1.29)

Prescription drugs	N =778 (%)
Antihypertensives*	**413 (53.08)**
ACE inhibitors	**350 (44.99)**
ARBs	**66 (8.48)**
Corticosteroids	**380 (48.84)**
DMARDs/immunosuppresives#	**303 (38.95)**
Anti-infectives	183 (23.52)
Diuretics	86 (11.05)
Antiarrhythmics (class II)	33 (4.24)
Erythropoiesis stimulating drugs	8 (1.03)

CKD staging at index (N=778)‡§



UPCR at index§



*Excluding diuretics, including ACE inhibitors and ARBs; #excluding corticosteroids;
‡only one patient with CKD stage 4 (eGFR <30 ml/min/1.73 m²) is included in CKD Stage 3 and 4; §data have been rounded to one decimal point and may consequently add up to >100%
ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; DMARD, disease-modifying antirheumatic drug; Q, quartile

Reported incidence rates of ESKD and kidney disease-related outcomes demonstrated disease progression for paediatric patients with CKD

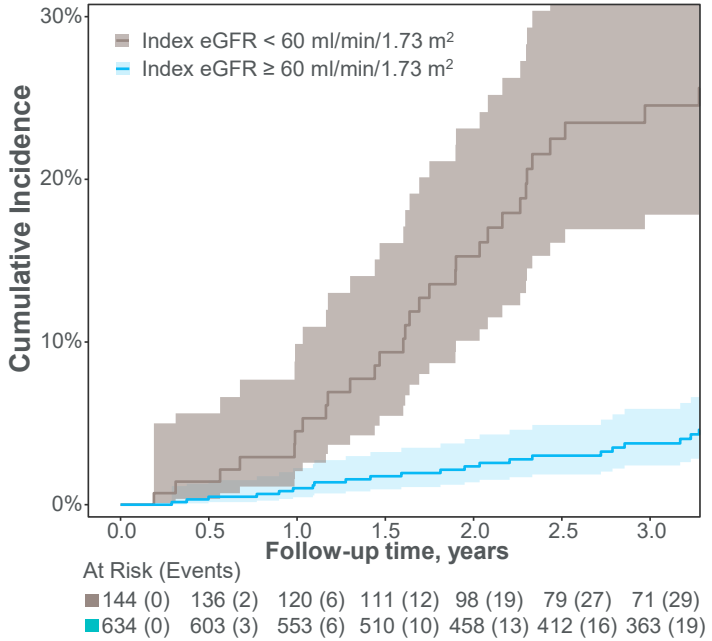
778 paediatric patients were included with a median follow-up duration of 3.8 years

Reduction in UPCR, 6 months post-index date:*
- 38.3% patients experienced ≥30% reduction
- 38.2% patients experienced <30% reduction

Outcome incidence rates reported as cases per 100 PYs (95% CI)#

	All patients N=778	Index eGFR ≥60 ml/min/1.73 m² n=634	Index eGFR <60 ml/min/1.73 m² n=144
ESKD composite endpoint†	**2.68 (2.11–3.34)**	**1.32 (0.89–1.84)**	**9.35 (6.82–12.4)**
Kidney disease-related outcomes			
Acute kidney injury	6.52 (5.56–7.57)	5.69 (4.71–6.78)	10.36 (7.61–13.64)
Kidney transplantation	1.58 (1.16–2.09)	0.67 (0.38–1.06)	5.73 (3.87–8.07)
Dialysis	0.80 (0.51–1.17)	0.33 (0.14–0.63)	2.77 (1.58–4.39)
ESKD diagnosis	2.20 (1.71–2.82)	0.92 (0.58–1.37)	8.58 (6.18–11.48)
Sustained >50% eGFR decline‡	1.69 (1.25–2.22)	1.28 (0.87–1.81)	3.45 (2.07–5.27)
All-cause mortality	0.23 (0.09–0.45)	0.21 (0.07–0.45)	0.32 (0.04–1.03)

Time to event ESKD composite endpoint:§ By index eGFR



Subgroup analyses showed incidence rates were **numerically greater** for patients with index eGFR <60 ml/min/1.73 m² compared with those with an index eGFR ≥60 ml/min/1.73 m²

*Data unavailable for 23.5% patients; #median of 3.8 years; ‡defined as at least two valid decreases in eGFR >50% from baseline within ≥30 days and ≤90 days; §eGFR <15 mL/min/1.73 m² sustained for ≥4 weeks, kidney transplantation, dialysis and/or ≥1 inpatient or 2 outpatient reports of ESKD. CI, confidence interval

CKD in children has significant long-term effects on growth and development, quality of life, and lifespan[1]

At present, there are **no treatments approved** for delaying CKD progression in this heterogenous paediatric population

Clinical paediatric development programme for finerenone in children with CKD

FIONA

6-month, placebo-controlled study to investigate the safety, efficacy, PK and PD of finerenone[2]

FIONA OLE

18-month, single-arm, open-label safety extension study to investigate long-term safety of finerenone[3]

The present observational study aims to assess **the feasibility of identifying a real-world paediatric population** with CKD and proteinuria **by applying adapted selection criteria** of the FIONA/FIONA OLE clinical trials **to US Optum EHR** to report:

- Baseline characteristics and change in UPCR within 6 months of index
- Kidney-disease outcomes and all-cause mortality

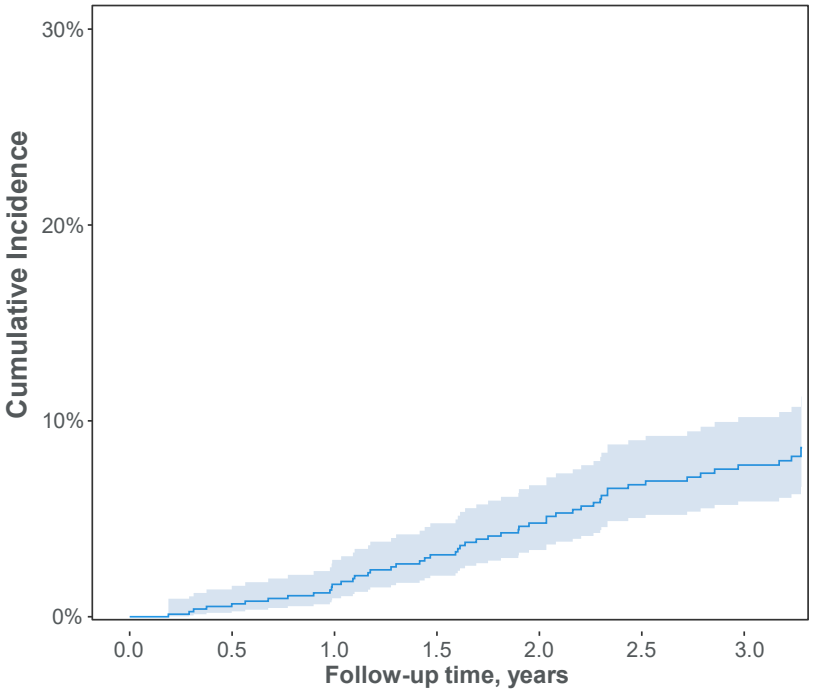
The use of real-world data to characterise the paediatric CKD population could provide useful insights to complement the findings of FIONA and FIONA OLE

PD, pharmacodynamics; PK, pharmacokinetics

1. Becherucci F, *et al. Clin Kidney J* 2016;9:583–591; 2. Bayer. https://clinicaltrials.gov/study/NCT05196035 (accessed 05 July 2024); 3. Bayer. https://clinicaltrials.gov/study/NCT05457283 (accessed 05 July 2024)

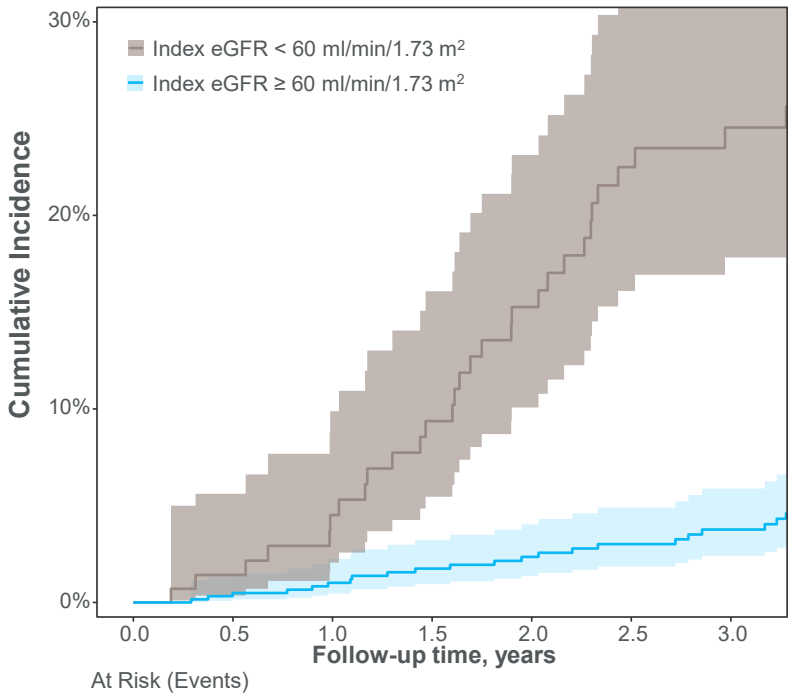
Risk for progression to ESKD in paediatric patients with CKD

Time to event ESKD composite endpoint:*
All patients



At Risk	778	739	673	621	556	491	434
Events	0	5	12	22	32	43	48

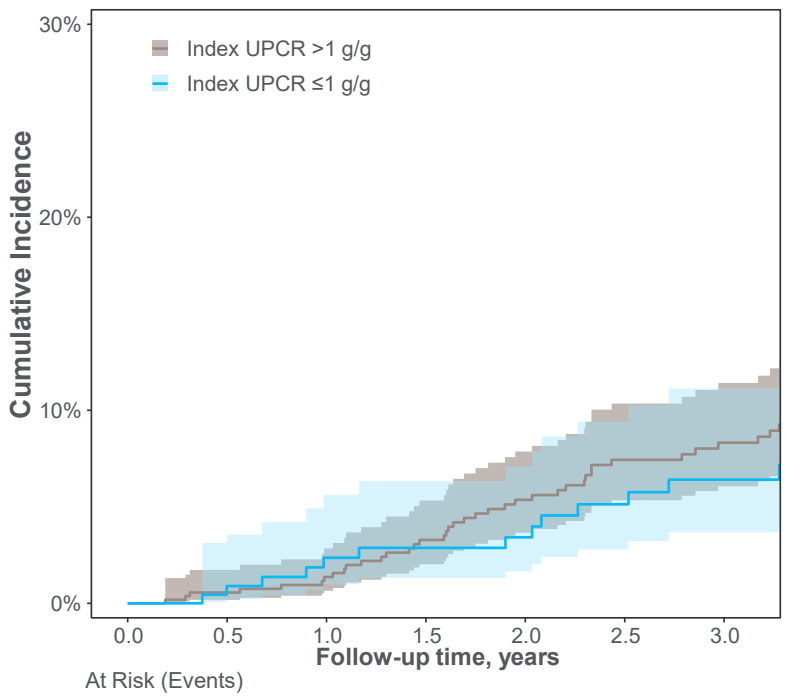
Time to event ESKD composite endpoint:*
By index eGFR



At Risk (Events)

144 (0)	136 (2)	120 (6)	111 (12)	98 (19)	79 (27)	71 (29)
634 (0)	603 (3)	553 (6)	510 (10)	458 (13)	412 (16)	363 (19)

Time to event ESKD composite endpoint:*
By index UPCR



At Risk (Events)

549 (0)	520 (3)	477 (7)	436 (16)	386 (25)	341 (33)	301 (36)
229 (0)	219 (2)	196 (5)	185 (6)	170 (7)	150 (10)	133 (12)

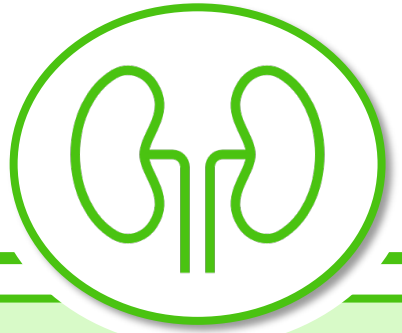
Paediatric patients with CKD are at relevant risk for CKD progression. Subgroup analyses suggest that patients with an index eGFR <60 ml/min/1.73 m^2 were at a greater risk of ESKD compared with those with an index eGFR ≥60 ml/min/1.73 $m^{2\#}$

*Sustained eGFR <15 mL/min/1.73 m^2, kidney transplantation, dialysis, and/or ≥1 inpatient or 2 outpatient reports of ESKD; #baseline differences between the two cohorts under comparison may exist; the results presented are descriptive

In conclusion, this study demonstrates…

…the feasibility of characterising a paediatric population with CKD and increased proteinuria using US Optum EHR data in a population similar to the FIONA/FIONA OLE study population

…considerable rates of disease progression over time and associated comorbidities, despite ongoing treatment, indicating the burden of CKD in children and the resulting unmet medical need in clinical practice



…that patients with more advanced CKD at index (eGFR <60 ml/min/1.73 m^2) appear to experience a greater incidence rate of ESKD* and are at a higher risk of kidney disease related-outcomes compared with those with eGFR ≥60 ml/min/1.73 m^2

Study limitations:

- Patient data from Optum EHR represent clinical practice in large, integrated healthcare delivery networks across the US; these findings may not be generalisable to other countries
- Patients may have received care from outside the provider network included in Optum EHR, potentially resulting in incompleteness of data during baseline and follow-up
- Data limitations and missingness may be more pronounced in healthier patients, owing to fewer HCP interactions and thus generating fewer data points. Including unhealthier patients in observational research may overestimate study outcomes compared with studies using more heterogeneous patient populations

*Composite outcome: eGFR <15 mL/min/1.73 m^2 sustained for ≥4 weeks, kidney transplantation, dialysis and/or ≥one inpatient or two outpatient reports of ESKD
HCP, healthcare professional