

Renal Impairment in a Pre-exposure Prophylaxis Implementation Cohort in Australia

Hamish McManus^a, Douglas Drak^b, Jack E. Heron^c, Tobias Vickers^a, Stefanie Vaccher^a, Iryna Zablotska^d, Rebecca Guy^a, Benjamin Bavinton^a, Fengyi Jin^a, Andrew Grulich^a, Mark Bloch^e, Catherine C O'Connor^a and David M Gracey^{b,c,e} on behalf of the EPIC study team

^a The Kirby Institute, UNSW Sydney, Sydney, Australia; ^b University of Sydney, Camperdown, NSW, Australia; Renal Department, ^cRoyal Prince Alfred Hospital, Camperdown, NSW;

^d University of Sydney, Westmead, NSW, Australia; ^eHoldsworth House Medical Practice, Sydney, NSW, Australia

Background

- Co-formulated tenofovir disoproxil fumarate/emtricitabine is prescribed as pre-exposure prophylaxis (PrEP) to prevent HIV infection.
- Prior studies have found low incidence of new renal impairment in people taking PrEP but have been restricted to clinical trial settings.

Objectives

- To describe the rate of loss of renal function amongst HIV-negative patients receiving PrEP.
- To describe the relative contribution of risk factors for renal disease amongst HIV uninfected patients receiving PrEP enrolled in the EPIC trial in NSW.

Methods

- We included participants enrolled in the EPIC-NSW study with baseline eGFR \geq 60ml/min/1.73m² with more than one PrEP dispensing visit between 1 March 2016 and 30 April 2018, and no recorded prior PrEP use.
- Patients without eGFR monitoring were excluded.
- The primary outcome was new sustained of renal impairment defined as an average eGFR of two consecutive tests <60ml/min/1.73m².
- Risk of progression to new sustained renal impairment was estimated using the Kaplan-Meier method.
- Cox proportional hazards models stratified by study site were used to compare risk factors including baseline eGFR (60-90, \geq 90ml/min/1.73m²); age (<40, 40-49, \geq 50 years); recreational drug use; hepatitis B virus (HBV) and hepatitis C virus (HCV) infection status; and time-updated PrEP medication possession ratio (defined as the proportion of elapsed days covered by prior dispensed PrEP, and dichotomised in this study as <0.95, \geq 0.95).
- Significant covariates ($p<0.10$) were included in a multivariate model.

Results

- 5,868 participants were included, with over 5,620 person years (PY) of follow-up.
- 28.5% had baseline eGFR between 60-90ml/min/1.73m², and 71.5% \geq 90ml/min/1.73m².
- 65.9% of participants were aged <40 years; 19.4% were aged 40-49 years; and 14.7% were aged \geq 50 years.
- 47.0% had an average medication possession ratio <0.95; and 53.0% \geq 0.95.
- 19.6% reported recreational drug use.
- 10.4% had a positive HBV surface antigen.
- 1.2% had positive HCV serology.

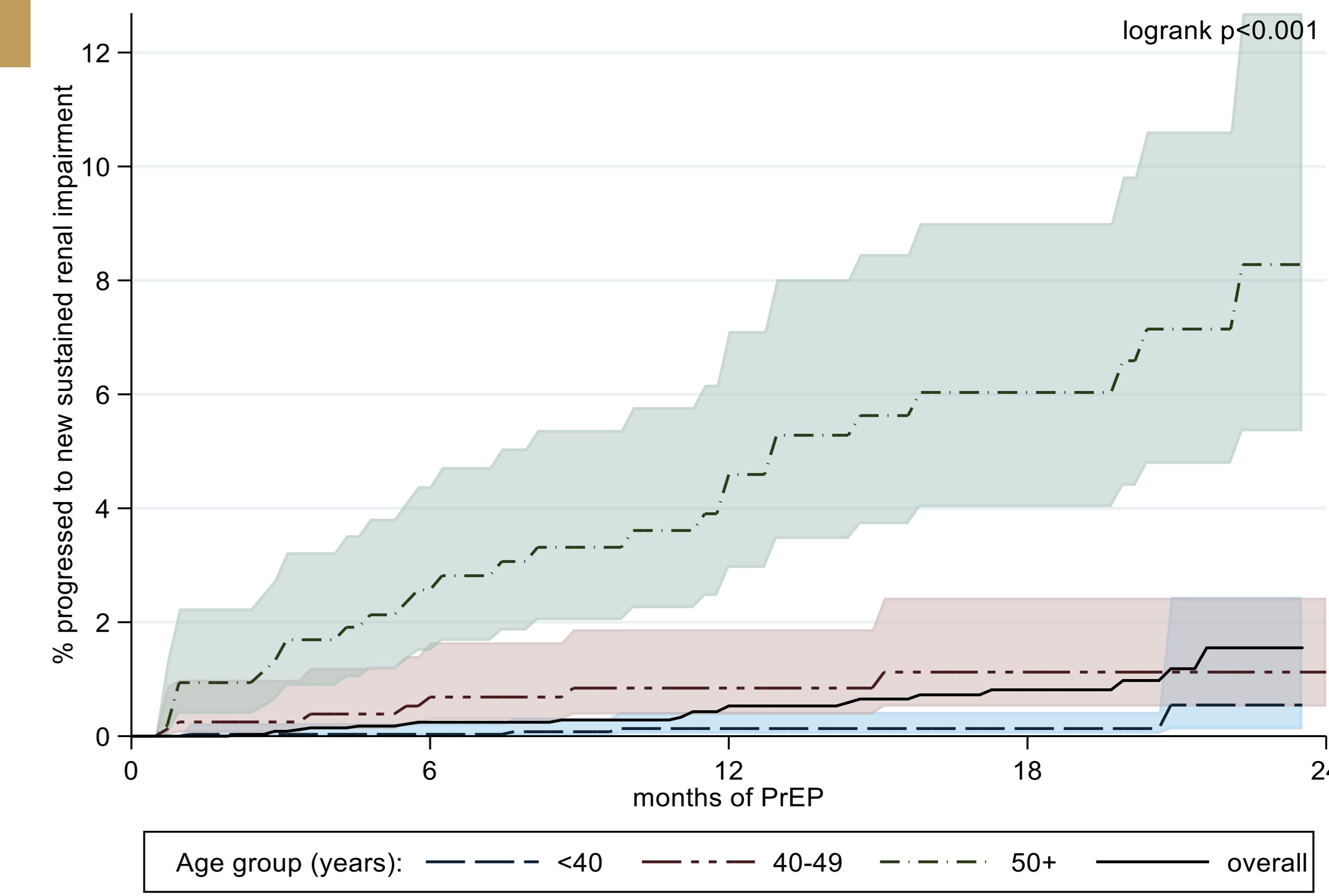


Figure: Progression to new sustained renal impairment (defined as an average eGFR of two consecutive tests <60ml/min/1.73m²) by age group

Table: renal impairment by risk factor

a. numbers and rates

b: Cox proportional hazards models

Characteristic	Category	Failures	PY (000s)	Rate/1000 PY (95%CI)	p	HR (95%CI)	p	MV HR (95%CI)	p
All		32	5.62	5.69 (4.03-8.05)		1 (ref)		1 (ref)	
Baseline eGFR (ml/min/1.73m ²)	\geq 90	30	1.66	18.1 (12.7-25.9)	<0.001	37.8 (8.97-159.6)	<0.001	16.5 (3.86-70.6)	<0.001
	<90	2	3.96	0.50 (0.13-2.02)		1 (ref)		1 (ref)	
Age group (years)	<40	2	3.55	0.56 (0.14-2.25)	<0.001	10.7 (2.12-54.2)	0.004	6.48 (1.26-33.38)	0.025
	40-49	6	1.18	5.06 (2.28-11.3)		66.7 (15.2-293.3)		26.7 (5.90-119.9)	
Recreational drug use	No	28	4.33	6.46 (4.46-9.36)	0.127	1 (ref)			
	Yes	4	1.29	3.11 (1.17-8.27)		0.45 (0.16-1.28)	0.135		
HBV surface antigen positive	No	28	5.05	5.54 (3.83-8.03)	0.578	1 (ref)			
	Yes	4	0.57	7.02 (2.63-18.7)		1.53 (0.44-5.29)	0.505		
HCV antibody positive	No	31	5.56	5.58 (3.92-7.93)	0.323	1 (ref)			
	Yes	1	0.06	15.8 (2.22-112.0)		3.03 (0.41-22.5)	0.277		
Medication possession ratio	<0.95	8	2.15	3.72 (1.86-7.44)	0.067	1 (ref)			
	0.95+	24	3.47	6.92 (4.64-10.32)		2.11 (0.93-4.81)	0.076	1.56 (0.68-3.58)	0.292

Conclusion

- In a large real-world PrEP cohort, risk of renal impairment increased over two years of PrEP, with older patients and those with pre-existing renal dysfunction at significantly higher risk.

Acknowledgements: EPIC-NSW site coordinators who recruited, enrolled and followed up study participants; EPIC-NSW site pharmacists who managed the study medication supply logistics at the site level and dispensed study medications to site personnel and study participants; Shawn Clackett of the Kirby Institute who provided administrative assistance; Dale Halliday of the New South Wales Ministry of Health who assisted with drug procurement, management of medication supply logistics at the study level, and other aspects of study conduct; Matthew Vaughan of ACON who assisted with study recruitment and communications with potential and actual participants; Jason Asselin at the Burnet Institute, who managed the ACCESS data extraction for the private sites. We thank Tobias Vickers and Denton Callander for assistance with ACCESS data extraction and analyses. Gilead Sciences provided 2000 person-years of Truvada for the study, and The New South Wales Ministry of Health funded the conduct of the study. The Kirby Institute is affiliated with the Faculty of Medicine, University of New South Wales and funded by the Australian Government of Health and Ageing.