

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

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## 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  $\geq 60$  ml/min/1.73m<sup>2</sup> 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 renal impairment defined as an average eGFR of two consecutive tests  $< 60$  ml/min/1.73m<sup>2</sup>.
- 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,  $\geq 90$  ml/min/1.73m<sup>2</sup>); 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 60-90 ml/min/1.73m<sup>2</sup>, and 71.5%  $\geq 90$  ml/min/1.73m<sup>2</sup>.
- 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.

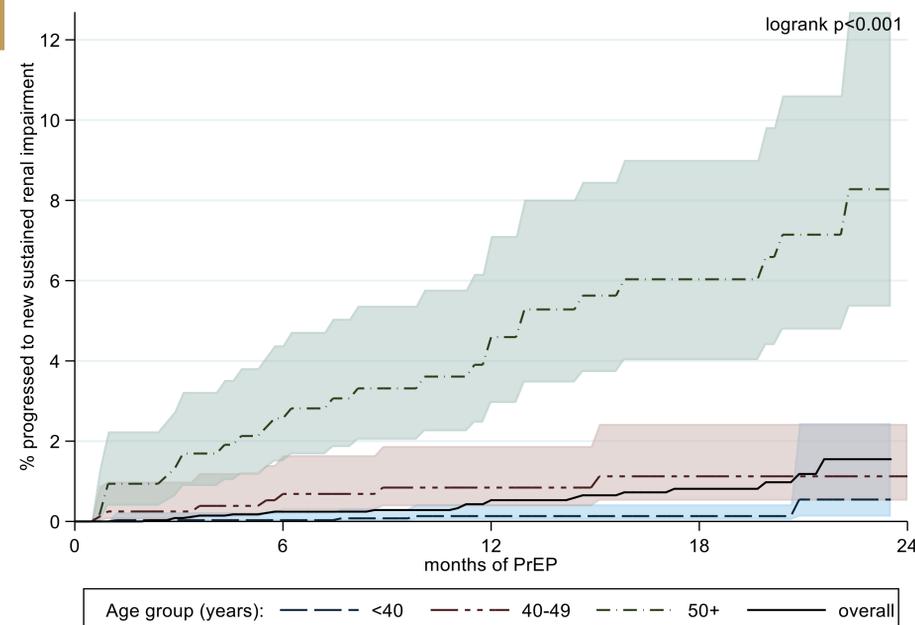


Figure: Progression to new sustained renal impairment (defined as an average eGFR of two consecutive tests  $< 60$  ml/min/1.73m<sup>2</sup>) by age group

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         |
|---|-----------|----------|-----------|----------------------|-----------|-------------------|-----------|-------------------|-----------|
| <b>All</b>                                      |           | 32       | 5.62      | 5.69 (4.03-8.05)     |           |                   |           |                   |           |
| <b>Baseline eGFR (ml/min/1.73m<sup>2</sup>)</b> | $\geq 90$ | 30       | 1.66      | 18.1 (12.7-25.9)     | $< 0.001$ | 1 (ref)           |           | 1 (ref)           |           |
|   | $< 90$    | 2        | 3.96      | 0.50 (0.13-2.02)     |           | 37.8 (8.97-159.6) | $< 0.001$ | 16.5 (3.86-70.6)  | $< 0.001$ |
| <b>Age group (years)</b>                        | $< 40$    | 2        | 3.55      | 0.56 (0.14-2.25)     | $< 0.001$ | 1 (ref)           |           | 1 (ref)           |           |
|   | 40-49     | 6        | 1.18      | 5.06 (2.28-11.3)     |           | 10.7 (2.12-54.2)  | 0.004     | 6.48 (1.26-33.38) | 0.025     |
|   | $\geq 50$ | 24       | 0.78      | 30.6 (20.5-45.7)     |           | 66.7 (15.2-293.3) | $< 0.001$ | 26.7 (5.90-119.9) | $< 0.001$ |
| <b>Recreational drug use</b>                    | 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     |                   |           |
| <b>HBV surface antigen positive</b>             | 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     |                   |           |
| <b>HCV antibody positive</b>                    | 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     |                   |           |
| <b>Medication possession ratio</b>              | $< 0.95$  | 8        | 2.15      | 3.72 (1.86-7.44)     | 0.067     | 1 (ref)           |           | 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.

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