To our knowledge, this is the first well-documented case of Fanconi syndrome in an HIV uninfected man receiving HIV pre-exposure prophylaxis (PrEP).

**Objectives**: Renal dysfunction due to tenofovir disoproxil fumarate (TDF) is rare among individuals without HIV infection. We report an HIV uninfected man who developed reduced renal function and features of Fanconi syndrome while receiving TDF with emtricitabine (FTC) for HIV pre-exposure prophylaxis (PrEP).

**Methods**: Case report from a prospective study of PrEP with TDF-FTC (CCTG Study 595, NCT01761643). Eligible subjects were men who had sex with men or transgender women who were at increased risk of acquiring HIV infection. Individuals were excluded who had calculated creatinine clearance (CrCl) less than 60 mL/min by the Cockcroft-Gault formula, active hepatitis B, proteinuria 2+ or greater by dipstick, or use of other nephrotoxic drugs. Routine monitoring of serum creatinine was performed at entry, week 4, week 12, then every 12 weeks.

**Results**: A 49 year old white man with a history of kidney stones 7 years earlier and no ongoing medical problems or medication use initiated daily PrEP with TDF-FTC and had no subjective complaints while on drug. Routine monitoring at week 12 of treatment showed 25% fall in CrCl. Additional testing at week 12 revealed hypophosphatemia with renal phosphate wasting, consistent with Fanconi syndrome. TDF-FTC was discontinued and 4 weeks later there was improvement in CrCl with resolution of phosphate abnormalities. By week 24 (12 weeks off TDF-FTC), CrCl had risen to near baseline levels. He was not rechallenged and remained HIV negative throughout. Neither glycosuria, hematuria, nor proteinuria were detected by dipstick at any time point. No other similar cases were documented in CCTG 595 (N=400).

**Discussion**: Randomized trials have not documented an increase in renal tubular toxicity with TDF-FTC based PrEP compared to placebo. However, we report a clear and significant reversible impairment in renal function accompanied by hypophosphatemia and renal phosphate wasting in an HIV uninfected man receiving TDF/FTC. Clinicians should be aware that this complication may still occur when TDF is used in HIV uninfected individuals.