many hospitals have a limited capacity for provocative measures to obtain sputum due to enhanced infection control.[9] Although programmes might baulk at the increased costs and logistical constraints in implementing such universal testing, hospital management should coordinate with tuberculosis programmes to make available the funds, laboratory supplies, and personnel needed to make this possible. This practice change, along with additional investment in developing better tuberculosis diagnostics, would be a valuable step in transforming the hospital back to a place of healing for Vika and other clinically vulnerable individuals living with HIV.

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Real-world safety of pre-exposure prophylaxis for HIV

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In the decade since it was first approved, tenofovir-based pre-exposure prophylaxis (PrEP) has emerged as one of the most effective means of preventing the spread of HIV.[1,2] However, PrEP remains underused[3] and PrEP users tend to disengage from care over time.[4] There are many potential barriers to PrEP use in real-world settings, including associated costs to patients and clinics, the need for frequent follow up, and concerns about potential side-effects. Addressing these barriers might make PrEP more accessible to people at risk for HIV transmission as we work towards ending the HIV epidemic.

One barrier to PrEP implementation is the need for frequent monitoring of creatinine clearance due to the potential for kidney toxicity with tenofovir disoproxil fumarate. The WHO 2017 implementation tool for PrEP recommends obtaining blood creatinine every 6 months in all users of tenofovir disoproxil fumarate-based PrEP.[5] In *The Lancet HIV*, Robin Schaefer and colleagues[6] evaluated the effect of tenofovir disoproxil fumarate-based PrEP on kidney function in a real-world setting. The authors did a systematic review and meta-analysis of published literature as well as a meta-analysis of individual participant data from 17 PrEP implementation projects and two randomised controlled trials including longitudinal data from 14 368 PrEP users. Although tenofovir disoproxil fumarate-based PrEP was associated with increased risk of grade 1 and 2 or higher kidney adverse events, clinically significant declines in creatinine clearance of less than 60 mL/min were rare and occurred more commonly with increasing age and in people with baseline creatinine clearance of less than 90 mL/min. The increase in risk was most significant for people older than 50 years but was also notable for those older than 40 years. Important caveats acknowledged by the authors include a lack of data on PrEP adherence and relatively short follow-up (median 10 months, IQR 6–15, range 0–51). Highly adherent PrEP users had the greatest benefit but might also be at increased risk for kidney injury and other adverse effects of PrEP, particularly with long-term use. Longitudinal data were also more limited for women, with cisgender men making up more than three-quarters of the participant level meta-analysis sample.

We believe these findings help to identify subgroups that will benefit most from intensive monitoring of kidney function when taking tenofovir disoproxil

fumarate-based PrEP. With the recent approval of monthly cabotegravir for PrEP, these data also identify subgroups of PrEP users who might be better candidates for alternative forms of PrEP, including cabotegravir or emtricitabine with tenofovir alafenamide when available. However, the access too, and indications for, these alternative PrEP medications are limited. In turn, perhaps the recommendations for creatinine testing can be relaxed for younger patients with normal baseline kidney function, who are at low risk of PrEP-associated kidney toxicity. Reducing barriers to PrEP use among younger individuals would be especially beneficial because globally 82% of new HIV infections in 2020 occurred among people aged 15–49 years.[7] If we can target the subgroup of PrEP users who would benefit most from frequent creatinine testing this might reduce the cost, infrastructure, and frequent follow-up visits required for PrEP care. As a result, the barrier to entry into PrEP care and retention in PrEP care might be reduced for young healthy people at risk for HIV.

The results of Schaefer and colleagues have immediate implications for clinical practice and health policy. Clinicians can use these findings to discuss the small risks associated with tenofovir disoproxil fumarate-based oral PrEP with clients and advise clients on available PrEP options when available in their location. PrEP providers should revisit the risks and benefits with PrEP users who remain adherent to PrEP for periods longer than 12 months, given the paucity of data beyond that point. Similarly, these findings might lead to a change in the recommended frequency of laboratory testing in future PrEP treatment guidelines. The results of this study support the updated PrEP guidelines from the US Centers for Disease Control and Prevention, which now recommend creatinine clearance monitoring every 6 months only for people aged 50 years or older or with creatinine clearance of less than 90 mL/min at PrEP initiation, and every 12 months for other PrEP users.[8] Using real-world data to shape future PrEP programmes is an important step towards increasing PrEP accessibility and preventing the spread of HIV.

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Making PrEP easy

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As pre-exposure prophylaxis (PrEP) approaches its tenth birthday, there is much to celebrate. In populations with high PrEP coverage, HIV incidence is declining. PrEP use is associated with reduced anxiety[1] and increased intimacy, pleasure, and sexual satisfaction.[2] PrEP connects users to other prevention services and gives them a sense of control over their health.[3] PrEP is a biomedical win, with health benefits that extend well beyond HIV prevention.

Implementation, however, is a different story. In *The Lancet HIV*, Jing Zhang and colleagues report on an ambitious global systematic review and meta-analysis of PrEP adherence and reinitiation.[4] Across diverse regions and populations, discontinuation was common within the first 6 months of use—although many people reinitiated PrEP soon thereafter—and a substantial proportion of people who continued PrEP had suboptimal adherence. By Zhang and colleagues' estimates, fewer than one in three people who initiate PrEP are fully protected against HIV infection during the first 6 months of use.

Synthesising evidence on PrEP use worldwide is no small undertaking. As noted by Zhang and colleagues,