A Field Evaluation of Point-of-Care Creatinine Testing Within a Large PrEP Implementation Program in Western Kenya

To the Editors:

Programmatic scale-up of pre-exposure prophylaxis (PrEP) is progressing with nearly 400,000 PrEP initiations worldwide as of October 2018. The World Health Organization (WHO) recommends creatinine (Cr) testing before starting PrEP, quarterly during PrEP use for the first 12 months, and then annually thereafter. This recommendation is based on labeling requirements that tenofovir disoproxil fumarate–based PrEP has to be used only in persons with normal renal function and rare experience with renal complications among HIV-infected persons using tenofovir disoproxil fumarate as part of HIV treatment. Initial PrEP trials all tested renal function using serum Cr before starting PrEP and at least quarterly during PrEP use. Abnormal renal function results were very rare in PrEP trials and generally returned to normal after stopping PrEP. In high-income settings, where laboratory-based Cr testing is widely available, PrEP programs have found low rates of ineligibility and discontinuation based on renal function and toxicity.

In low- and middle-income countries (LMICs), PrEP programs are often located in decentralized settings without laboratory capacity to conduct Cr analysis; in such settings, Cr testing could be a barrier to PrEP initiation. In Kenya, the national PrEP guidelines recommend, but do not require, assessing creatinine clearance (CrCl) at PrEP initiation only if the clinic has laboratory capacity to do so. As programmatic PrEP delivery rolls out across LMICs with high HIV burden, it is unknown whether Cr testing is essential to assure safe PrEP use. Point-of-care (POC) machines could increase Cr testing accessibility, and previous evaluations have found feasibility in using validated POC Cr testing machines within LMICs for renal monitoring among obstetric patients and people living with HIV.

To date, no study has systematically evaluated POC Cr testing within the context of programmatic PrEP delivery in LMICs. We evaluated feasibility and utility of POC Cr testing for PrEP initiation within a large PrEP implementation program in Western Kenya. From June 2017 to December 2018, HIV-uninfected women seeking routine antenatal care (ANC), postnatal care (PNC), and family planning (FP) services were screened per national PrEP guidelines at 16 facilities in Kisumu, Kenya, as part of the PrEP Implementation for Young Women and Adolescents (PrIYA) Program. Before PrEP initiation, nurses measured height and weight, conducted Cr serum testing using validated Xpress StatSensor POC machines (Nova Biomedical Cooperation, Waltham, MA), and estimated CrCl by the Cockcroft–Gault equation using a mobile application (MDCalc). If a single estimated CrCl measurement was below the normal range (<50 mL/min according to Korean PrEP guidelines), the test was repeated before excluding that client from PrEP services. Daily quality control checks were run on the StatSensor POC machines with high-, low-, and normal-range control substances. All control substances and StatSensor strips were stored in refrigerators procured and maintained by the program. In a subset, we evaluated CrCl results, the cost per test, and time to receive a result for the POC test compared with standard laboratory methods (Roche Cobas c111 Analyzer; Roche Diagnostics, Indianapolis, IN). To perform the comparison, we conducted POC testing and laboratory methods on the same day among all women initiating PrEP at 1 facility over a 4-month period. Venous blood for laboratory testing was collected at the same time as POC testing. The Bland–Altman method was used to calculate the mean difference in estimated Cr between POC and laboratory-based measures.

Overall, 4169 women interested in initiating PrEP were evaluated for PrEP medical eligibility and received POC Cr testing: 1680 (40.3%) from ANC, 2101 (50.4%) PNC, and 388 (9.3%) FP. The median age was 24 years [interquartile range (IQR) 21–28], and 205 (5%) women were aged 18 years younger. The overall median estimated CrCl was 99 mL/min (IQR 82–119): 113 mL/min (IQR 98–132) for ANC clients, 111 mL/min (IQR 93–130) for PNC, and 99 mL/min (IQR 82–120) for FP. Few women had estimated CrCl less than the CrCl cutoff for PrEP ineligibility of <50 mL/min specified in the Kenyan national guidelines: 8/4169 (0.2%) overall, 1 (0.06%) from ANC, 5 (0.2%) PNC, and 2 (0.5%) FP. Using a slightly higher CrCl cutoff of <60 mL/min, overall 122 (3%) women had an estimated CrCl <60 mL/min, 4 (0.8%) from ANC, 91 (4.3%) PNC, and 17 (4.4%) FP. Among women with CrCl <60 mL/min, the median age was 25 years (IQR 23–30), the median height 161 centimeters (IQR 157–165), the median weight 53 kilograms (IQR 47–60), and the median Cr 106 μmol/L (IQR 97–124).

We compared estimated Cr and CrCl using duplicate POC and laboratory-based measures in a subset of women (n = 70) initiating PrEP within ANC (n = 34), PNC (n = 25) and FP clinics (n = 11). Among women with both POC and laboratory-based Cr results available (n = 70), the mean difference in estimated Cr between POC and laboratory-based tests from Bland–Altman validity
analysis was 29.6 μmol/L (Fig. 1A). CrCl using POC testing was 89 mL/min (IQR 81–112) compared with 149 mL/min (IQR 120–184) using laboratory-based methods (P < 0.001); no CrCl results were <60 mL/min with either test in this subset of women. A similar trend of lower CrCl using POC testing compared with laboratory-based methods was observed by the pregnancy status and trimester of pregnancy (Fig. 1B). POC Cr testing took a median of 1 minute (IQR 0–1) to receive Cr results and cost USD 4.5 per test. By contrast, laboratory-based results took a median of 3.5 hours (IQR 2.5–4.5) for the receipt of results and cost USD 5 per test.

We found implementation of POC Cr testing was feasible during PrEP initiation visits within high-volume maternal child health and FP settings in Kisumu, Kenya. PrEP ineligibility due to low CrCl was rare (<1% based on Kenyan
guidelines) among screened women, and POC creatinine testing took approximately 1 minute to receive results. In a subset of women with both POC and laboratory-based Cr results available, POC testing performed more conservatively than laboratory-based testing. This is similar to previous reports from validation studies among nonpregnant/postpartum populations that found higher blood Cr levels using Xpress StatSensor POC machines, which would translate to lower estimated CrCl. More programmatic data are needed on longitudinal safety monitoring of sustained PrEP users within LMICs’ settings.

In settings where CrCl is required by national guidelines or where POC testing is unavailable, Cr testing may require significant time, cost, and laboratory capacity within already constrained health systems. We found few women of reproductive age had CrCL <60 mL/min. Many PrEP programs have high rates of early PrEP discontinuation. Given the rarity of medical ineligibility, low rates of sustained PrEP use, and safety of shorter-term PrEP, our data suggest that not mandating Cr testing at PrEP initiation will generally be a safe decision. Cr testing among individuals who sustain PrEP use for >1 month may be one way to focus laboratory resources. In addition, as new PrEP agents become available that have less potential for causing kidney injury, such as tenofovir alafenamide, which is currently being tested for PrEP (clinicaltrials.gov #NCT02842086), the need for Cr testing before PrEP initiation might be further reduced.

Our evaluation of POC Cr testing focused on PrEP initiation visits; therefore, we are unable to comprehensively evaluate the utility of Cr testing at follow-up visits among sustained PrEP users. Our cost and time do not account for staffing, training, or other elements that a formal cost-effectiveness analysis of POC versus laboratory-based Cr testing would include. We also used the Cockcroft-Gault equation to estimate CrCl, which is influenced by the body weight and body mass index, and was initially calibrated among nonadolescents outside of African settings. Future evaluations could include more robust measurements of the glomerular filtration rate that perform better at extremes.

In summary, it was feasible to implement POC Cr testing during PrEP delivery within high-volume maternal child health and FP settings, and ineligibility due to low CrCl was rare among screened women. PrEP programs could consider conducting Cr testing at follow-up to reduce Cr testing–related time, costs, and inconvenience.

ACKNOWLEDGMENTS
The authors thank the PrYa study team and clients for their time and contributions. The authors thank the Kenyan Ministry of Health nationally and the Kisu County Department of Health, as well as the facility heads and in-charges for their collaboration.

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