To evaluate the reliability and consistency of our findings, we performed several ad hoc analyses. We found no significant changes in treatment effect in subgroup analyses by CD4 count, HIV viral load, use of antiretroviral therapy, RPR titer, or syphilis stage.

In terms of Jarisch-Herxheimer (JH) reactions, we would like to clarify that our study was not designed to address the incidence of these reactions. This is in contrast with rates reported in studies where investigators were actively looking for symptoms and signs [8, 9], including subtle ones, suggestive of JH reactions. Although we did not record any severe cases of JH reactions, we did not systematically inquire of patients about this at the time of treatment. As we did not use any standardized symptoms checklists of JH reactions at the 3-month follow-up, it is plausible that some patients might have developed a mild reaction but considered it not sufficiently severe to be mentioned to study members. The patients had standard instructions to contact the clinic immediately in the event of medical issues, and none did.

Note

Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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Redefining Human Immunodeficiency Virus (HIV) Preexposure Prophylaxis Failures

To the Editor—Failures of daily oral human immunodeficiency virus (HIV) preexposure prophylaxis (PrEP) with tenofovir disoproxil fumarate/emtricitabine are rare, with only 3 HIV seroconversions documented among patients adherent to PrEP at the time of infection [1–3]. However, PrEP failures could be defined more broadly as HIV infections that occur at any point along the PrEP continuum of care [4]. Here, we describe HIV infections among individuals who sought or were referred for PrEP within the Kaiser Permanente Northern California (KPNC) healthcare system.

KPNC provides comprehensive medical services to 4.1 million members; the KPNC PrEP program has been described previously [5]. In this analysis, we included KPNC members with patient- or provider-initiated referrals for PrEP from July 2012 through February 2017, as identified from outpatient encounter and referral data. Duration of PrEP use was estimated from first pharmacy fill to last day of PrEP in possession, regardless of gaps between fills. HIV infections were identified using the KPNC HIV registry. End of follow-up was the earliest of health plan disenrollment, HIV diagnosis in KPNC, or 28 February 2017.

We identified 7124 individuals who sought or were referred for PrEP. Of those, 26 (0.4%) were diagnosed with HIV infection during assessment for PrEP eligibility. Of the remaining 7098 individuals, 4991 (70%) started PrEP and 2107 (30%) did not start PrEP. Of the 2107 who did not start PrEP, 22 were later diagnosed with HIV infection, corresponding with an incidence rate of 1.1 per 100 person-years (95% confidence interval [CI], 0.7–1.7). Of the 4991 who started PrEP, there were no HIV infections during 5104 person-years of PrEP use (mean duration of use, 12.4 months; upper limit of 1-sided 97.5% CI, 0.1). Of 1303 (26%) who no longer had PrEP in possession at the end of follow-up, 11 were diagnosed with HIV infection between the last supply of PrEP and the end of follow-up, corresponding with an incidence rate of 1.3 per 100 person-years (95% CI, 0.8–2.4).

We identified no HIV infections during more than 5000 person-years of PrEP use, consistent with the high adherence previously observed in this setting [5]. However, HIV infections were identified among individuals who were being assessed for PrEP eligibility (ie, late to access PrEP), who sought or were referred for PrEP but did not start (ie, failure to initiate PrEP), or who discontinued PrEP (ie, failure to be retained in PrEP care). Strategies are critically needed to ensure that patients start, restart, or continue PrEP during periods of risk for HIV acquisition.

Notes

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Performance of Rapid Diagnostic Testing in Patients with Suspected Malaria in Cambodia, a Low-Endemicity Country Aiming for Malaria Elimination

To the Editor—We read with interest the article by Ranadive et al [1] assessing the performance of malaria rapid diagnostic testing (RDT) vs polymerase chain reaction (PCR) in Swaziland, a low-transmission country aiming at elimination. Through a large regional data set collected from 37 health facilities over 2 years, they demonstrated the poor sensitivity of RDT (First Response Malaria Ag P. falciparum HRP-2 Detection Rapid Card Test, Premier Medical) for *Plasmodium falciparum* (*Pf*) diagnosis (51.7%), due to a high proportion of low-density infections among symptomatic subjects (54/162 [33.3%]), along with a low positive predictive value (PPV) (67.3% for all samples and 62.3% for ≥100 parasites/μL samples), due to the high proportion of false positivity (32.4%). To overcome some of the limitations of the study (eg, the decision to include only 10% of negative RDTs samples), the authors called for more inclusive analyses.

We would like to share our ongoing experience in Chey Saen district (population 22 499, 27 villages), Preah Vihear province, Cambodia [2]. The district is served by 3 health centers, 2 health posts, and 28 village malaria workers. In 2014, the *Pf* prevalence detected by PCR was estimated at 0.73‰ [3]. The incidence of symptomatic *Pf* infections in 2016 was 3.6‰. Since 2014, a network of malaria RDT providers has been supported and trained by Médecins Sans Frontières, in providing national guidelines treatment and in the RDT use (SD FK80 p.f/P.v Malaria Antigen Rapid Test, Standard Diagnostics). Since October 2015, the network is routinely collecting filter paper blood spots for subsequent qualitative and quantitative (using parasite density-calibrated controls) real-time PCR diagnosis (Institut Pasteur in Cambodia) [2, 4].

We conducted an overall analysis of the data collected between October 2015 and March 2017. A total of 4382 patients with suspected malaria were tested with both RDT and PCR. Of the 168 PCR-positive *Pf* samples, 23.8% (40/168) had a parasite density <100/μL.

Table 1 displays all RDT and PCR results either including (n = 4382) or excluding samples with parasitemia <100/μL (n = 4342). The false-positive and false-negative rates were 11.0% (15/136) and 1.1% (47/4246), respectively. The sensitivity of RDT (vs PCR) was 72.0% (95% confidence interval [CI], 64.5%–78.5%), compared to 90.6% (95% CI, 83.8%–94.8%) after exclusion of low parasitemia samples. The negative predictive value increased from 98.9% to 99.7% when low-density samples were excluded. In both analyses, specificity was 99.7%, and the PPV scored 89.0% and 88.5%, respectively. Low parasitemia was the main reason for false-negative RDT

Table 1. Comparison of Rapid Diagnostic Test (RDT) and Polymerase Chain Reaction (PCR) Results Among All Samples and Samples From High Density (≥100 Parasites/μL) Infections—Diagnostic accuracy of RDTs Versus PCR as Gold Standard

	PCR Positive, No.	PCR Negative, No.	Total, No.	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
All samples							
RDT positive	121	15	136				
RDT negative	47	4199	4246				
Total	168	4214	4382				
RDT accuracy				72.0 (64.5–78.5)	99.7 (99.4–99.8)	89.0 (82.2–93.5)	98.9 (98.5–99.2)
Excluding samples with parasite density <100/μL							
RDT positive	116	15	131				
RDT negative	12	4199	4211				
Total	128	4214	4342				
RDT accuracy				90.6 (83.8–94.8)	99.7 (99.4–99.8)	88.5 (81.5–93.2)	99.7 (99.5–99.8)

Abbreviations: CI, confidence interval; NPV, negative predictive value; PCR, polymerase chain reaction; PPV, positive predictive value; RDT, rapid diagnostic test.