

## Is pericoital or peri-insemination preexposure prophylaxis effective human immunodeficiency prevention for vaginal exposures?

**TO THE EDITORS:** Safier et al<sup>1</sup> conclude that preexposure prophylaxis (PrEP) with oral emtricitabine and tenofovir disoproxil fumarate (FTC/TDF) dosed the day before, day of, and day after intrauterine insemination effectively achieves pregnancy in serodifferent (human immunodeficiency virus [HIV] +/HIV-) couples while avoiding HIV transmission. In this *Journal* in 2015, Mabileau et al<sup>2</sup> proposed similar PrEP dosing, “targeting fertile days” for serodifferent couples desiring pregnancy. However, this dosing schedule is not evidence-based, nor is it in accordance with guidelines.

The Centers for Disease Control and Prevention published PrEP guidelines in 2014, recommending PrEP for 20 days before vaginal exposure to effectively prevent HIV acquisition.<sup>3</sup> Although short courses of PrEP with pericoital dosing may be effective for rectal exposures,<sup>4</sup> this regimen is not recommended in the United States or for vaginal exposures. Oral TDF has low bioavailability; unabsorbed intractable medication may explain the 100-fold greater drug concentrations observed in rectal vs vaginal and cervical tissues.<sup>5</sup> Although rectally exposed individuals who use 4 or more FTC/TDF tablets weekly are protected fully,<sup>6,7</sup> in the Pre-exposure Prophylaxis Trial for HIV Prevention among African Women, or FEM-PrEP trial, 9% of vaginally exposed individuals who became infected had drug concentrations commensurate with the use of 4–5 tablets weekly.<sup>8</sup> Pharmacological modeling<sup>9</sup> supports Centers for Disease Control and Prevention guidelines that daily FTC/TDF dosing is required to protect fully against vaginal exposures.<sup>3</sup>

Although not referenced, Safier et al and Mabileau et al may have based their dosing strategies on the 2011 study by Vernazza et al,<sup>10</sup> in which the authors gave 2 doses of pericoital PrEP for serodifferent couples. This study’s success was likely due to concomitant use of treatment as prevention—treating HIV-positive partners with antiretroviral medications resulting in undetectable viral loads. In the studies of Safier et al, Mabileau et al, and Vernazza et al, male partners living with HIV were required to have undetectable viral loads; in fact, there has never been a case reported of penile–vaginal HIV transmission in the setting of an undetectable viral load. Therefore, in these studies, HIV prevention was due to treatment as prevention and not subtherapeutically dosed PrEP.

Oral FTC/TDF alone is a highly effective HIV prevention and safer conception method for vaginally exposed people adherent to daily dosing.<sup>11</sup> Treatment as prevention alone is also highly effective.<sup>11</sup> Intrauterine insemination with washed sperm alone is an additional highly effective safer conception strategy.<sup>12</sup> Couples may choose different safer conception methods based on risk

perception, fertility factors, care access, and personal preferences, necessitating multiple options. However, without new evidence, subtherapeutically dosed pericoital or peri-insemination PrEP is not an effective safer conception strategy for vaginally exposed individuals and should not be offered to serodifferent couples desiring pregnancy. ■

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