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Periodic presumptive treatment for women with prevalent vaginal infections: secondary analysis of data from a randomized controlled trial

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To the Editor,

Bacterial vaginosis (BV), vulvovaginal candidiasis (VVC) and *Trichomonas vaginalis* (TV) are common vaginal infections associated with adverse reproductive health outcomes, including sexually transmitted infections (1-6). Their treatment is hindered by frequent recurrences and reinfection. Periodic presumptive treatment (PPT) has been evaluated as an alternative approach that involves providing antimicrobials to asymptomatic women to treat and potentially prevent these infections (7, 8).

We previously conducted a randomized trial to assess the effect of monthly oral PPT (2g metronidazole plus 150mg fluconazole) versus placebo administered for 12 months on the incidence of BV, VVC and TV among Kenyan female sex workers (FSWs) (7). The intervention reduced the incidence of BV by Nugent's score (hazard ratio [HR] = 0.55; 95% confidence interval [CI] 0.49–0.63). Since women with prevalent vaginal infections are likely to experience recurrences/reinfection (8, 9), we sought to test the hypothesis that the PPT effect would be greater among participants with a prevalent infection at enrollment. We used Andersen-Gill proportional hazards models to assess the intervention's effect on BV incidence stratified by baseline infection status. Each visit with BV was considered a 'new' event. We evaluated effect modification by baseline infection status using an interaction term and likelihood ratio (LR) test.

Among 310 women enrolled, 302 returned for 1 follow-up visit and 137 (45%) had one or more vaginal infections at enrollment; 105 (77%) BV, 32 (23%) VVC and 6 (4%) TV. There

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were 62/151 (41%) participants with a baseline infection in the intervention arm versus 75/151 (50%) in the placebo arm. BV incidence among participants with a baseline infection was 294/100 person-years (py) in the intervention arm versus 522/100 py in the placebo arm (HR=0.55; 95% CI 0.41–0.76). Among those without a baseline infection, BV incidence was 141/100 py in the intervention arm versus 202/100 py in the placebo arm (HR=0.71; 95% CI 0.47–1.09). There was no evidence of effect modification by baseline infection status (LR test $P=0.11$).

The reduction in BV episodes with the intervention versus placebo was greater among participants with a baseline infection (228/100 py) compared to those without (61/100 py). For participants without a baseline infection, the number needed to treat (NNT) was 16.7 compared to 4.4 among those with a baseline infection. This ~4-fold difference in NNT suggests that while the intervention was similarly effective in both subgroups, more BV episodes could be averted if PPT were targeted towards women with a prevalent infection. Findings were similar when stratified by baseline BV status.

Data for this secondary analysis were collected as part of a randomized trial that had high retention and regularly measured biological outcomes, enabling a more precise assessment of the vaginal environment. Generalizability of our findings may be limited by behavioral characteristics unique to FSWs, including differences in sexual activity, condom use and intravaginal practices. Our findings suggest that targeting PPT to women with prevalent vaginal infections is the most efficient approach to reducing BV incidence. These results will be useful in designing future trials to improve vaginal health.

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