

**Background:** There is an urgent need to improve our understanding of the mucosal immunopathogenesis of HIV acquisition in the female genital tract, particularly in high-risk women such as female sex workers (FSWs). Cervical biopsy samples offer technical advantages over cytobrush sampling, but there are concerns that this might increase HIV acquisition, particularly if healing is slow and/or women do not abstain from sex during healing. **Methodology/Principal Findings:** Cervical biopsy samples and cervico-vaginal swabs for co-infection diagnostics, prostate specific antigen (PSA) and immune studies were collected from 59 women, including HIV seropositive and HIV-exposed seronegative (HESN) FSWs as well as lower risk women from Nairobi, Kenya. A clinical-demographic questionnaire was administered and women were instructed to avoid sexual intercourse, douching and the insertion of tampons for 14 days. All participants underwent a repeat exam to assess healing within the 14 days, and had HIV diagnostics at six months. Cervical sampling was well tolerated, and 82% of participants had healed macroscopically by 5 days. Both self-report and PSA screening suggested high levels of compliance with pre- and post-procedure abstinence. Delayed healing was associated with vulvovaginal candidiasis (VVC) and HESN status. At six-month follow up all low-risk and HESN participants remained HIV seronegative. **Conclusion:** Cervical biopsy sampling is a safe and well-tolerated method to obtain cervical biopsies in this context, particularly if participants with VVC are excluded. As healing could be delayed up to 11 days, it is important to support (both financially and with rigorous counseling) a period of post-procedure abstinence to minimize HIV risk.