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# Pragmatic Open-Label Randomised Trial of Preexposure Prophylaxis: The PROUD Study

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Abstract Body:

Background: Randomised placebo-controlled trials have clearly demonstrated that tenofovir/emtricitabine (TDF/FTC), when taken regularly as PrEP, reduces the risk of HIV infection. However, there are concerns that this benefit might be counteracted by users of PrEP engaging in riskier sexual practices, increasing their chance of exposure to HIV and other STIs. This supports the need for pragmatic open-label randomised studies which mimic real-life clinical practice.

Methods: The PROUD study enrolled MSM from 13 sexual health clinics in England between 27Nov2012 and 30Apr2014. Eligibility criteria included a negative HIV test in the previous 4 weeks and reported condomless anal intercourse in the previous 90 days. MSM were randomised 1:1 to receive open-label daily TDF/FTC either immediately (IMM) or after a deferral (DEF) period of 12 months, and followed quarterly. Based on early demonstration of efficacy, the TSC/IDMC recommended on 13Oct2014 that all MSM in the deferral period be offered PrEP. All analyses are modified ITT (excluding 3 MSM with a reactive HIV test at baseline) based on person-years (PY) to the first HIV test after 48 weeks or after 13Oct2014, whichever was earlier.

Results: 545 MSM were randomised (276 IMM, 269 DEF). At baseline, median(IQR) age was 35(30-43) and 81% were white; median(IQR) number of anal sex partners in the previous 90 days was 10(4-20); 64% reported a diagnosed STI in the previous 12 months. 20 MSM (5 IMM, 15 DEF) had no HIV test after baseline; completeness of follow-up for HIV incidence was 91% (237/261 PY) for IMM and 89% (216/242 PY ) for DEF. Three HIV infections were observed in IMM (1.3/100 PY); 19 infections were observed in DEF (8.9/100 PY) despite 174 prescriptions of post-exposure prophylaxis (PEP). This yields a rate difference of 7.6/100 PY (90%CI 4.1-11.2) and a relative reduction of 86% (62-96%; P=0.0002). The proportion with a confirmed STI indicative of condomless anal intercourse (rectal chlamydia/gonorrhoea) was similar in IMM (29%) and DEF (27%) (P=0.50).

Conclusions: In this high incidence cohort, daily TDF/FTC conferred impressive protection against HIV, and higher than the levels previously observed in the placebo-controlled trials. Concerns that effectiveness would be undermined in a real-world setting were unfounded. There was no evidence of an increase in STIs in this population, although they were frequently reported in the year before enrolment.

This result strongly supports the use of PrEP among MSM who are at risk of HIV infection.