PROUD Study Results 'Strongly Support' UK PrEP Use in New Paper

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The investigators behind the PROUD study, which found Truvada (tenofovir/emtricitabine) as pre-exposure prophylaxis (PrEP) reduced the risk of HIV infection by 86 percent among a group of high-risk men who have sex with men (MSM) in England, have published a paper outlining the finer details of the study in The Lancet. Initial results from the real-world study of PrEP were presented at a major medical conference in March.

PROUD was an open-label, randomized trial conducted at 13 sexual health clinics in England. The study recruited MSM who reported condomless intercourse with another man during the previous 90 days. A total of 544 MSM were enrolled in the study between November 2012 and April 2014, including 275 in the immediate group and 269 in the deferred group.

The participants were randomly assigned either to receive a PrEP prescription with instructions to take Truvada daily—the immediate group—or to wait a year to receive the medication—the deferred group.

The participants returned for follow-up every three months.

Respective median demographic details of the immediate and deferred groups were as follows: 35 years of age for both; 59 percent and 62 percent had a university degree; 59 percent and 62 percent reported engaging in "chemsex" (a British term for a major trend of MSM engaging in sex under the influence of certain sexually disinhibiting drugs) during the previous 90 days; 63 percent and 65 percent had been diagnosed with a sexually transmitted infection (STI) during the previous 90 days; and 35 percent and 37 percent had been prescribed post-exposure prophylaxis (PEP) during the previous year.

In October 2014, after analyzing the data to determine how well PrEP was preventing HIV, the trial's steering committee found that PrEP was working so well that it should be offered to all participants. The PROUD investigators did so, effectively ending the study, at least as it was initially designed.

At that time, the researchers had follow-up data for 243 (94 percent) of the 259 person-years participants contributed to the immediate group and 222 (90 percent) of the 245 person-years contributed by the deferred group members. Person-years are the cumulative amount of time all

participants have spent in a study follow-up period.

Three individuals in the immediate group contracted HIV, for a rate of 1.2 per 100 person-years. Twenty members of the deferred group contracted the virus, for a rate of 9 per 100 person-years, despite the fact that 85 members of the deferred group received 174 prescriptions for PEP during the study follow-up period. Six of the 20 deferred participants who contracted HIV received a total of 12 PEP prescriptions. Additionally, 12 members of the immediate group received a total of 14 PEP prescriptions.

The difference in the infection rate between the two groups meant that PrEP reduced the population-level risk of HIV by 86 percent in this study. This figure was much higher than the 44 percent and 50 percent effectiveness rates reported, respectively, in the 2010 iPrEx and 2014 iPrEx open-label extension (OLE) phase studies of PrEP among MSM. The PROUD study authors estimated that the true risk reduction figure for their study may be between 64 and 96 percent.

Of the three new HIV infections in the immediate group, one is believed to have pre-dated the start of PrEP. Neither of the other two men appeared to have been taking Truvada at the time they contracted the virus.

The researchers calculated that in a population of MSM with a similar level of risk for HIV as the PROUD participants (who were strikingly and, to the investigators, unexpectedly high risk), just 13 men would need to take PrEP for one year to prevent one infection among them. This is known at the number-needed-to-treat figure.

It appeared that the high success rate in this study was tied to good overall adherence to daily PrEP. All 52 people in the immediate group who were tested for tenofovir (one of the two drugs in Truvada) in their plasma had detectable levels of the drug. Average adherence to PrEP in both of the iPrEx studies was quite poor, likely explaining their lower overall success rates. Though cutting a group's HIV risk in half, as seen in iPrEx OLE, does not constitute a failure.

There were no serious drug reactions among the study participants. Otherwise, 28 adverse side effects, most commonly nausea, headache and joint pain (these reactions are not considered "serious"), resulted in participants interrupting their PrEP-taking. Thirteen of these episodes were judged to be Truvada-related.

Despite the fact that participants in the immediate group reported a greater rate of sexual risk-taking when compared with the deferred group, there was no statistically significant difference between the rate of STI acquisition between the two study groups. The overall STI rate in the immediate and deferred groups was a respective 57 percent and 50 percent. The rate of acquisition of rectal gonorrhea or syphilis, a relatively good proxy for condomless receptive anal intercourse, was 36 percent and 32 percent, respectively. Statistically, this latter pair of figures was essentially the same, meaning any difference between them could have occurred by chance. The study authors state in their paper that a study including a greater number of participants could have made more precise estimates about the differences in sexual risk-taking.

Six members of the study contracted hepatitis C virus (HCV), three in each group. Half of these men may have contracted hep C through injection drug use. One of the other men contracted hep C around the time of or shortly after acquiring HIV. Research has suggested that MSM are at risk of sexual acquisition of HCV, and that having HIV raises that risk.

In a group of over 600 MSM receiving PrEP from a San Francisco clinic, none of whom have contracted HIV, there has been two cases of apparent sexual acquisition of hepatitis C over a two-and-a-half year period. Half of these men contracted an STI during their first year, or partial first year, on PrEP. Forty-one percent reported using condoms less often since starting Truvada.

The PROUD researchers found evidence suggesting that the study's participants had self-selected to create a high-risk study population. In other words, high-risk MSM may be more likely to seek out PrEP—an encouraging sign for Truvada's capacity to reduce HIV incidence among MSM on the whole. Other studies, including iPrEX OLE and the study looking at the San Francisco clinic, have come to similar conclusions: that high-risk MSM are more likely to go on PrEP than lower-risk MSM.

The PROUD study authors concluded that their "findings strongly support the addition of PrEP to the standard of prevention" for at-risk MSM.

To read the study, click here.

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