

Pre-exposure Prophylaxis (PrEP) for HIV Infection and New Sexually Transmitted Infections: A Win-Win Opportunity?

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Pre-exposure prophylaxis (PrEP) significantly reduces the risk of HIV acquisition in patients exposed to a high risk of infection such as men who have sex with men (MSM), heterosexual couples, and people who inject drugs [1-3]. However, despite declines in new HIV diagnosis, bacterial sexual transmitted infections (STIs) among MSM have dramatically risen since the late 1990s [4,5].

This increase occurred concurrently with the introduction of effective PrEP, the advent of electronic mechanisms for meeting sex partners and population-level changes in sexual behavior, including increased numbers of sexual partners, increased condom-less anal sex, and increased recreational drug use including chem-sex. This substantial increase in STIs particularly in the MSM population suggests the potential increase of sexual risk behavior induced by PrEP through a risk compensation [6]. Risk compensation refers to an increase in risk-related behaviors when an intervention reduces perceptions of risk among individuals or a population.

While the IPERGAY [2] and PROUD [3] placebo-controlled studies demonstrated that there was no increase in the number of STIs in patients under PrEP, different studies [7-16] showed a significant increase of the prevalence of bacterial STIs (including *Treponema pallidum*, *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG)). A recent meta-analysis [17] including 17 open-label PrEP studies, demonstrated that the use of PrEP was associated with a moderate increase of new STIs in MSM (OR=1.24, 95% CI: 0.99-1.54), particularly rectal STIs (OR 1.39, 95% CI 1.03-1.87) and rectal CT infections (OR 1.59, 95% CI 1.19-2.13).

We recently conducted a multicenter, retrospective,

observational study [18] in three Sexual Health Clinics of northeast France from March 2017 to April 2019 to compare in a real-life setting the non-HIV STI incidence in an MSM patients population treated by PrEP to that of an MSM patient's population with no prophylactic treatment. PrEP was prescribed in MSM continuously every 3 months along with screening laboratory test for STI. Ninety-two male patients (41 MSM/PrEP+ versus 51 MSM/PrEP-) were included. The mean time of follow-up was 9 months \pm 5.5. The mean number of consultations was significantly higher in MSM/PrEP+ (4 ± 2.05 versus 3.2 ± 1.7 , $p=0.02$), as was the mean number of sexual partners over the last six months (26.2 ± 31.8 versus 8.6 ± 10.3 , $p=0.0004$). The proportion of patients who used a condom was similar in both groups. The frequency of STIs detected was similar between patients under PrEP (48.8%) and controls (58%, $p=0.60$). The mean number of STIs during follow-up was 1.40/patient (1.40 ± 0.68) in the MSM/PrEP+ group compared to 1.83/patient (1.83 ± 0.95) in MSM/PrEP- patients ($p=0.13$). The mean number of STIs per person-year was 1.13 in the MSM/PrEP+ group compared to 2.05 in the MSM/PrEP- control group ($p=0.14$). The risk of developing a new STI in MSM/PrEP+ patients during the follow-up (17%) was not significantly reduced compared to the MSM/PrEP- control group (Relative Risk=0.83; 95% CI=0.5621 to 1.223). NG infections were more common both in the MSM/PrEP+ patients (36% of all STIs) and the MSM/PrEP- patients (40%), followed by CT infections (32% and 29%) and syphilis (25% and 24%).

These rather reassuring results were recently confirmed by Morgan et al. [19]. They found a similar rate of bacterial STIs in MSM/PrEP+ patients compared to MSM/PrEP- patients. Furthermore, PrEP use was not associated with STIs among young MSM and transgender women despite

increased condom-less anal sex. The authors underlined the importance of surveillance, regular screening of other STIs, and messages on protection by condom and vaccinations in MSM/PrEP+ patients in order to prevent the still debatable increase of STIs.

The discrepancy of these results could not be explained by differences in sexual risk behaviors since PrEP use was associated with a higher number of sexual partners and an increase of condom-less sex as compared to MSM/PrEP-patients [18-22].

Our rather reassuring data suggest the importance of surveillance, regular screening of other STIs, and messages on protection by condom and vaccinations in MSM/PrEP+ patients in order to prevent the still debatable increase of STIs.

The fact that high risk sexual behaviors persist after starting PrEP, highlights the importance of ongoing, intensive sexual health screening and interventions [21]. Recent updated guidelines from the International Antiviral Society-USA (IAS-USA) group recommend STIs screening in MSM on PrEP every three months [23]. Furthermore, at-risk groups of MSM reporting higher PrEP adherence, multiple sexual partners, and inconsistent condom use following PrEP initiation should be closely monitored and managed with frequent free of cost STIs testing and intensive sexual health counseling, such as dedicated, condom-affirming counseling [21]. This seems to be essential to facilitate early STIs treatment and reduce further spread. A recent modeling study [24] found that while PrEP use may lead to increased STI incidence following individual-level behavior change, the timely diagnosis and short duration of STIs among PrEP users due to high screening frequency may also lead to an overall decrease in STIs prevalence and incidence.

Altogether these data suggest that PrEP may be considered not only as HIV prevention but as an opportunity for intensive sexual health counseling and screening to curb the rise of STIs [21].

Although there are recommendations of STI screening every 3-6 months for MSM using PrEP, substantial gaps still exist between CDC recommendations and current clinical practice. In a recent US study including HIV-negative MSM using PrEP, PrEP users in the Southeast were significantly less likely to be consistently screened for urogenital and rectal STIs during PrEP care [22]. Beside regular STI screening, at each 3-month visit, the patients should receive a reminder of the various prevention measures as well as the risks. The free availability of condoms should also be proposed.

In conclusion, PrEP has an important role in HIV prevention, and uncertainty over its effect on risk

compensation and STI incidence should not prevent it from being provided to people at high risk. To support effective PrEP programming, it is our opinion that a win-win strategy is urgently needed to implement new STIs control while continuing to expand PrEP use.

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