HIV pre-exposure prophylaxis in injecting drug users

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Globally, there are an estimated 15·9 million injecting drug users, 3 million of whom have HIV.[1] The illicit nature of injection drug use and associated social stigma have created substantial challenges for HIV prevention in this group. Despite these obstacles, several programmes have shown that HIV transmission in injecting drug users can be prevented, stabilised, and even reversed with needle exchange programmes.[2] However, the HIV epidemic continues to grow in this high-risk population in some regions, particularly in eastern Europe, central Asia, and, since 2007, sub-Saharan Africa.[3] Much more needs to be done to reduce the continuing high rates of HIV transmission in injecting drug users.

Findings from a series of randomised placebo-controlled trials, viewed cumulatively, provide compelling evidence (figure) that antiretroviral pre-exposure prophylaxis (PrEP), when taken, is effective in preventing mother-to-child transmission of HIV,[4] sexual transmission in men who have sex with men, and sexual transmission between men and women.[5] In women, both oral and topical antiretrovirals have been shown to prevent sexual transmission. However, there is no rigorous evidence on whether PrEP is effective in preventing parenteral HIV transmission. In 2005, the US Centers for Disease Control and Prevention initiated the Bangkok Tenofovir Study to address this major gap and assess the efficacy of daily oral tenofovir disoproxyl fumarate (tenofovir) in preventing parenteral transmission of HIV.

In *The Lancet*, Kachit Choopanya and colleagues report the results of this important study.[6] They enrolled 2413 participants who reported injecting drugs within the previous 12 months and followed them up for a mean of 4·0 years. During follow-up, 50 participants acquired HIV: 17 were in the tenofovir group (HIV incidence=0·35 per 100 person-years) and 33 were in the placebo group (0·68 per 100 person-years), which

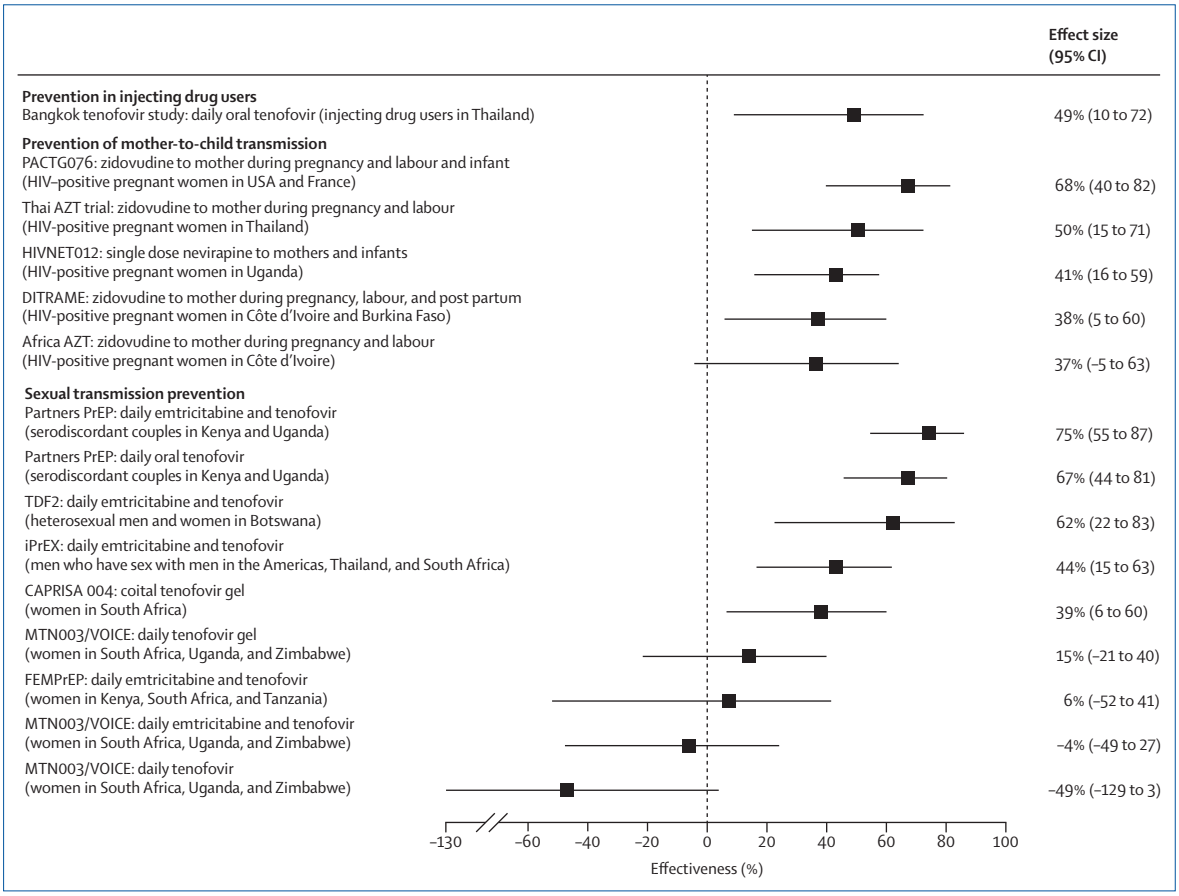

Figure: **Results of placebo-controlled randomised trials assessing the effectiveness of antiretroviral pre-exposure prophylaxis**

translates into 49% effectiveness of tenofovir (95% CI 9·6–72·2). Additional per-protocol and drug level analyses drew attention to the importance of adherence to achieve high levels of protection from PrEP.

Although findings from this study provide the evidence to show that PrEP is effective in preventing HIV infection in people who inject drugs, it is less clear as to whether the findings show that PrEP prevents parenteral transmission of HIV. People who inject drugs can acquire HIV through either unprotected sexual intercourse or sharing of needles and syringes. These two routes of HIV transmission are often linked epidemiologically. Not only do injecting drug users engage in unprotected sex, they might also engage in commercial sex to get money for drugs.

Because no biological marker exists to distinguish between HIV transmission that occurs through sex and that which occurs parenterally, all HIV infections during follow-up in this trial contribute to the overall efficacy measure. Tenofovir is known to be effective in preventing sexual transmission of HIV, so some fraction of the recorded 49% protection is probably due to prevention of sexual transmission, in view of the fact that the number of reports of multiple sexual partners decreased during follow-up. The extent of the remaining protection attributable to parenteral transmission is not known. However, although the participants in this trial were confirmed injecting drug users at enrolment, there were substantial reductions in reported levels of injecting drug use from enrolment to month 12 (from 63% to 23%) and needle-sharing (from 18% to 2%). These reductions continued—by 72 months, 18% reported injecting drugs and 1% reported needle-sharing. Furthermore, the investigators noted that the protective benefits of PrEP were evident only after the first 3 years of follow-up, by which time reported levels of injecting drug use and needle-sharing were low. Hence, it is not possible to make definitive conclusions about the efficacy of daily tenofovir for the prevention of parenteral transmission of HIV from these data. As a result, PrEP is not a replacement for politically sensitive needle exchange programmes to prevent parenteral transmission.

Even though questions remain about the extent to which PrEP can be effective in preventing either of the routes of transmission in this group, the overall result is that daily tenofovir does reduce HIV transmission in injecting drug users. The introduction of PrEP for HIV prevention in injecting drug users should be considered as an additional component to accompany other proven prevention strategies like needle exchange programmes, methadone programmes, promotion of safer sex and injecting practices, condoms, and HIV counselling and testing. PrEP as part of combination prevention in injecting drug users could make a useful contribution to the quest for an AIDS-free generation.

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SSAK was the co-principal investigator of the CAPRISA 004 tenofovir gel trial, and is a co-inventor on two pending patents of tenofovir gel against HSV-1 and HSV-2 with scientists from Gilead Sciences.

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