Nonetheless, there are signs that Muslim majority countries including those in the Middle East are beginning to address the HIV epidemic; many countries have recently developed national plans on HIV.[11] Parts of the Islamic world are also in the process of profound sociocultural transitions that are leading to increased tolerance and acceptance of practices such as premarital and extramarital sex.[12] What is often forgotten in the Islamic world's response to the HIV epidemic is that central in the teachings of Islam is the concept of compassion and justice. Muslims are encouraged to recite the phrase *Bismillah ir-rahman ir-rahim*, "In the name of Allah, most beneficent, most merciful", before undertaking any action—large or small.

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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 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

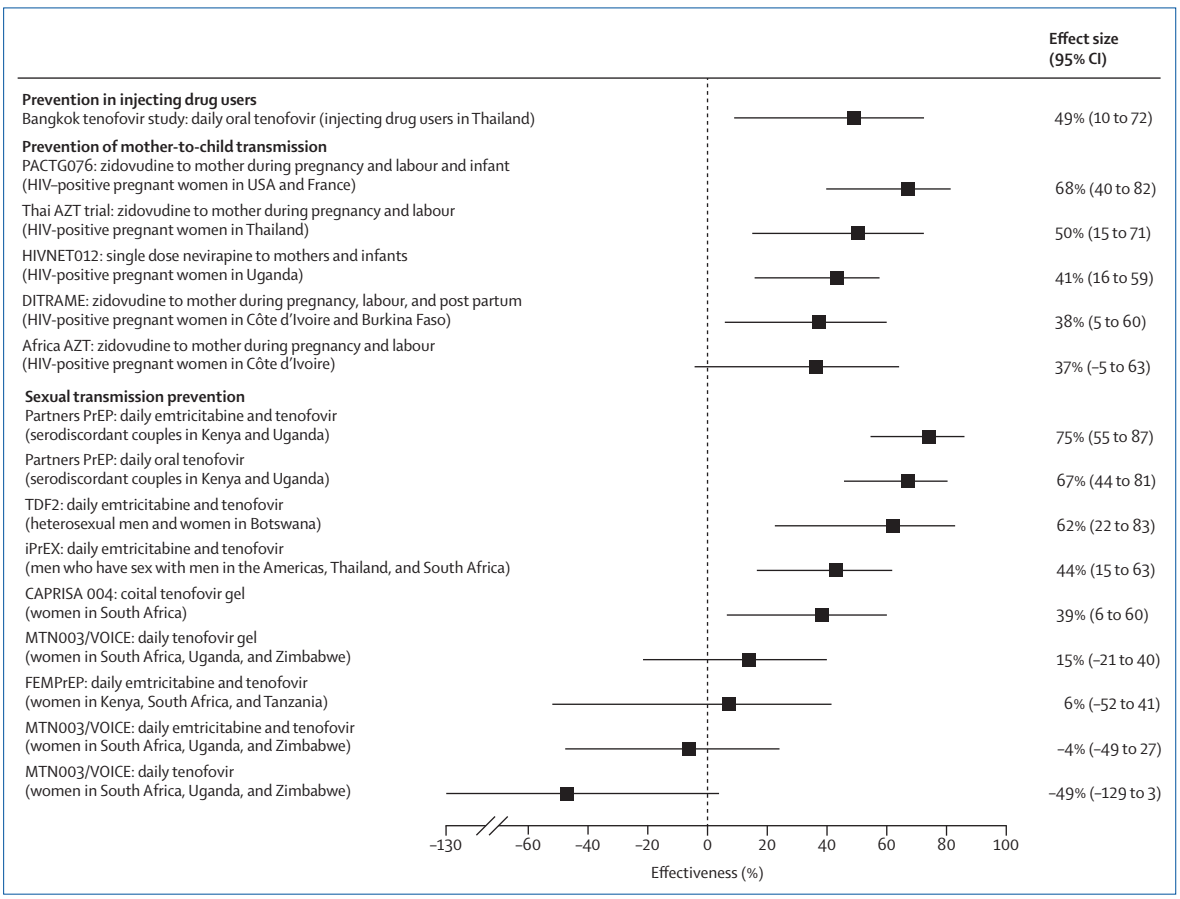

Figure: **Results of placebo-controlled randomised trials assessing the effectiveness of antiretroviral pre-exposure prophylaxis**

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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After first-line ART: towards an evidence-based SECOND-LINE


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Access to antiretroviral therapy in low-income and middle-income countries has been scaled-up effectively in the past decade; however, failure of the first-line regimen is increasing.[1] In *The Lancet*, the SECOND-LINE Study Group[2] provide a high-quality evidence-based strategy for safe and effective treatment of patients in whom first-line treatment has failed.[3] They did a randomised clinical trial to compare a WHO-recommended second-line treatment regimen—a ritonavir-boosted protease inhibitor (lopinavir) plus two or three nucleoside or nucleotide reverse transcriptase inhibitors (NtRTIs)—with a novel dual-treatment approach that combined ritonavir-boosted lopinavir with the integrase inhibitor raltegravir. The investigators showed that the efficacy of the new regimen was non-inferior to standard treatment: 223 (83%) of 270 patients in the raltegravir group versus 219 (81%) of 271 in the control group had a plasma viral load of less than 200 copies per mL at week 48 (difference 1·8%, 95% CI −4·7 to 8·3). No major safety issues emerged in either group. Patients who took raltegravir had significantly larger increases in CD4 T-cell count than patients who took the control regimen.

These findings are important because they show that the WHO-recommended second-line treatment is an efficacious rescue regimen. Furthermore, they suggest that the new regimen has equal efficacy, but with other potential advantages. First, use of a single treatment based on only two different compounds for all the patients failing first-line treatment will ease demand on drug supply and stocks. Second, simple regimens might enable treatment to be delivered by trained, but non-medical, health-care workers, improving access to HIV care in settings with limited resources.[4] Third, because the rescue treatment consists of two drugs from antiretroviral classes to which patients have not been previously exposed, genotypic resistance testing is not needed, saving time, money, and effort. Finally, the raltegravir regimen is likely to cause fewer toxic effects than NtRTI-based treatments.

Nevertheless, these advantages are counterbalanced by the higher cost of raltegravir—at present, it is prohibitively expensive in many low-income and middle-income countries. The study by Boyd and colleagues[2] provides a tradeoff, instead of settling for only what is readily available at a reasonable price in resource-constrained settings.[3] However, although the cost of raltegravir will hopefully drop owing to competition with other integrase inhibitors soon to be licensed, new mechanisms to provide wider access to raltegravir are needed if it is to be included in second-line regimens.

Progress in expanding HIV care in the past decade has been based on a public health approach, especially the introduction of a simple, effective, safe, and tolerable standardised first-line antiretroviral treatment regimen.[5] According to guidelines,[6] three regimens could be used sequentially, with exponentially increasing costs, in case