

Prospects for using pre-exposure prophylaxis to control the prevalence of HIV/AIDS in China

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ABSTRACT: Although important progress has been achieved in combating HIV/AIDS over the past 30 years, HIV/AIDS is still a serious threat to today's world. In China, figures on the incidence of this disease have painted a less than optimistic outlook. As the prevailing methods of preventing HIV/AIDS are all partially effective, novel and effective preventive interventions are needed in order to control the spread of the disease. Pre-exposure prophylaxis (PrEP) is one of the most promising prevention strategies and has garnered great attention worldwide. Current clinical trials on the efficacy and safety of this strategy have had some favorable results though major challenges around the world remain. Thus, China has taken an active part in the PrEP study to limit the prevalence of HIV/AIDS. This article describes the status of the PrEP study and discusses the opportunities and challenges encountered when implementing this strategy in China.

Keywords: Pre-exposure Prophylaxis (PrEP), HIV/AIDS, ethical dilemmas, financial capacity

Thirty years after its discovery, HIV/AIDS remains one of the world's most significant public health challenges, particularly in low- and middle-income countries. Recent data suggest that the levels of new infections worldwide remain high (about 2.6 million in 2009), although the overall growth of the global HIV/AIDS epidemic appears to have stabilized (1). The "prevention first" principle is broadly followed when controlling the prevalence of HIV/AIDS. However, the high incidence of HIV infection and partial effectiveness of current prevention strategies such as condom use, male circumcision, and distribution of sterile needles

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and injection equipment highlight the need for new and effective interventions to complement existing strategies. One preventive option currently being studied is pre-exposure prophylaxis (PrEP). PrEP refers to daily or intermittent administration of antiretroviral drugs (ARVs) such as tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) to protect high-risk HIV-negative individuals from infection. Satisfactory preclinical findings with regard to prevention of HIV infection by PrEP and confirmation of the long-term safety of ARVs used to treat AIDS (2,3) have fueled interest in using PrEP to prevent HIV infection in humans.

In China, the first AIDS case was reported in 1985, and the disease spread quickly in the 1990s. However, the scale of China's HIV/AIDS epidemic did not attract attention until 2003. Since then, annual morbidity and mortality rates have been showing obvious upward tendencies (Figure 1) (4). By October 31, 2009, a total of 319,877 individuals was reported to be HIV-positive; this figure included 102,323 cases of AIDS and 49,845 recorded deaths (5). By the end of 2009, approximately 740,000 individuals (range: 560,000-920,000) were estimated to be HIV-positive, with 48,000 new HIV infections (range: 41,000-55,000) in 2009 (5). Although the prevalence of HIV/AIDS in China remains low overall, pockets of greater prevalence among specific sub-populations and in some localities have appeared and the HIV/AIDS epidemic is spreading from high-risk groups to the general population. Since HIV/AIDS prevention and control remains crucial, universal, effective, and more accessible intervention strategies such as PrEP are

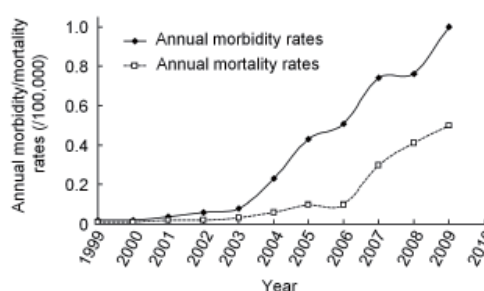


Figure 1. Morbidity and mortality rates of HIV/AIDS in the period of 1999-2009 in China.

urgently needed in China.

Among the modes of transmission of HIV, sexual transmission has become the fastest mode of transmission in China due to changing sexual behaviors and attitudes since China opened up to the outside world in the late 1970s (6). Of the new infections in 2009 in China, about three-fourths were transmitted through sexual contact, either heterosexual or homosexual (7). Female sex workers (FSW) and their clients and men who have sex with men (MSM) are the groups most vulnerable to HIV infection. Although condoms were effective in preventing HIV/AIDS and other sexually transmitted diseases, studies indicated that those high-risk populations had a low level of consistent condom use. Specifically, 60% of FSWs and 60-70% of MSMs in China did not use condoms consistently with their clients or sex partners (8,9). Common reasons for not using condoms were worries about loss of a partner's trust and reduced sensation (10). PrEP has numerous advantages in this regard, potentially allowing people access to treatment while not requiring discussion with one's partner and eliminating problems associated with physical and psychological factors. PrEP may play an important role in combating the prevalence of HIV/AIDS in China if it proves to be effective.

Clinical trials on the efficacy and safety of PrEP in preventing HIV infection have been carried out around the world and some have had positive results (11). Oral administration of TDF and FTC daily to HIV-seronegative men or transgender women who had sex with men in Peru, Ecuador, South Africa, Brazil, Thailand, and the United States led to a 44% reduction in the incidence of HIV in those subjects (12). Another completed study on sexually active, HIV-uninfected 18- to 40-year-old women in South Africa indicated that a 39% overall reduction in HIV acquisition was achieved by giving tenofovir 1% vaginal gel (13). In spite of those inspiring outcomes, some trials were halted due to the obstacles encountered (14). The most important issue involved is the ethical dilemma. Currently, most PrEP clinical trials are conducted in poor parts of the world such as Africa and Latin America, whereas funding for those trials is from developed countries in Europe and the US. The concern is that intervention measures are inadequately implemented to safeguard the rights and interests of vulnerable groups.

Capitalizing on the potential for PrEP to prevent HIV transmission, China has actively studied PrEP. Since a PrEP study is a complex and costly project, stable and continuous funding is vital. In this regard, China launched a Major State Science & Technology Special Project entitled "Feasibility Study on Use of PrEP to Reduce New HIV Infections in High-risk Groups of Western China". The project was allocated ¥10 million yuan in funding and was undertaken by Chongqing Medical University, Guangxi Medical University, and Xinjiang Medical University in 2009. Project participants

include MSMs, FSWs, and HIV-negative sex partners of HIV-infected individuals. Project researchers are from various fields and have focused on issues associated with ethics, prospects for use of PrEP, and drugs to prevent infection as might arise in the implementation process. In the early phase, a volunteer-based, anonymous, one-on-one survey of 762 subjects in Urumqi and Kelamayi of Xinjiang Uyghur Autonomous Region was conducted to assess the acceptability of PrEP strategy among FSWs in Xinjiang. Of the subjects, 69.29% were willing to undergo PrEP, but the FSWs had concerns about drug safety, effectiveness, and cost (15). This study found that a PrEP strategy was acceptable to FSWs in Xinjiang and laid the groundwork for future research.

As a new biomedical approach to HIV prevention, PrEP has the potential to become a powerful tool and may be an important addition to the prevention toolbox. But this prevention strategy is not without challenges. First, principles of human understanding and respect for the human rights of subjects should be adhered to from start to finish during PrEP clinical trials. Fundamental ethics, including respect, justice, non-maleficence, and beneficence, have to be put above study aims. In addition, subjects' rights to life, health, privacy, and free choice should be protected. The second challenge is the safety of long-term use of ARVs by healthy people. Although the safety and tolerance of TDF and FTC has been confirmed studies on HIV-positive animals and humans, more studies should be performed to investigate the toxic or adverse effects of longer exposure to these drugs in HIV-negative individuals. In addition, the resistance of HIV to ARVs should be monitored. Since completely preventing HIV infection through use of the PrEP strategy seems impossible, problems with drug selection should be resolved once individuals undergoing PrEP are accidentally infected and drug resistance occurs. The third challenge is the economy's capacity to allow use of PrEP. Because of the high-cost of ARVs, PrEP may be one of the most expensive strategies to prevent HIV. In China, HIV high-risk populations that take drugs or behave promiscuously are mainly on the fringes of society and reside in economically undeveloped districts or rural areas. In the current trial phase, access to ARVs is free. If the PrEP strategy proves effective and its scale is expanded, however, these drugs will not be available to most of the people who need them if they are not free. Given that fact, affordability of medicines might be the decisive factor guiding the adoption of the PrEP strategy. Thus, as clinical trials of this strategy continue the government should be acting as a public health decision-maker to resolve the contradiction between individuals' financial capabilities and their right to health. Issues like ensuring consistent and continuous project funding and allocating limited resources should be thoroughly investigated in order to facilitate the adoption of a PrEP strategy.

Thus far, the verdict is out on whether PrEP will be the most effective strategy for preventing HIV/AIDS. Ongoing and future trials will answer this question. One fact that must not be forgotten, should PrEP prove to be safe and effective, is that such a strategy is only a precautionary measure and is not a substitute of effective prevention strategies currently in practice. Integration of PrEP into an overall care platform may be the right way to go. With scientific data mounting, preparations for the possible roll-out of PrEP must be made should the strategy prove efficacious.

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