HIV incidence was low in Choopanya and colleagues' study (33 of 1209 participants), probably due to few people sharing needles and injecting drugs. With 48·9% reduction in HIV incidence,[1] more than half of patients will not be protected despite tenofovir pre-exposure prophylaxis. Moreover, injecting drug users usually have poor treatment adherence, which could result in suboptimal tenofovir plasma concentration. These factors might contribute to the development of tenofovir drug resistance.

Finally, social and economic issues should not be overlooked. If the cost of tenofovir is too high, it is not certain that injecting drug users will buy tenofovir for HIV prevention; if tenofovir is free, there is a risk of creating a parallel market.

We declare that we have no conflicts of interest.

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1 Choopanya K, Martin M, Suntharasamai P, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet* 2013; **381:** 2083–90.
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HIV prevention among injecting drug users is difficult for many reasons including illegality of drug use, marginalisation, and political and social opposition to needle-syringe programmes and opioid substitution therapy. Pre-exposure prophylaxis might be an alternative prevention approach.

Pre-exposure prophylaxis can reduce transmission among injecting drug users, as shown in the Bangkok Tenofovir Study.[1] This result raises questions including whether implementation to scale is acceptable and feasible, whether similar or adequate effectiveness will be achieved when delivered to scale, and whether such implementation is likely to be cost-effective compared with alternative approaches. Results of studies have indicated that pre-exposure prophylaxis is not necessarily cost-effective in some groups.[2]

The cost-effectiveness of pre-exposure prophylaxis for injecting drug users will vary according to HIV incidence among the people targeted and with the cost of prophylaxis. A wide range of incidence levels have been reported among injecting drug users, but 1–10 HIV infections per 100 person-years is a range representative of most settings. The annual per-person cost of tenofovir for pre-exposure prophylaxis in high-income settings such as the USA is US$1212–9036.[2] Depending on a country's gross national income and HIV prevalence, tenofovir for pre-exposure prophylaxis might be available at a discounted annual per-person cost of $207–365.[3] In some countries, generic tenofovir is available, with an annual course for one person costing $57–87.[3]

We calculated the ratio of the cost of pre-exposure prophylaxis to the number of infections averted on the basis of the range of representative incidence levels and costs in different settings. Assuming that the measured efficacy of pre-exposure prophylaxis among injecting drug users in the Bankgok study (48·9%)[1] is maintained with broader scale-up outside of a trial setting, in high-income countries the cost per HIV infection averted would be $24 785–1 847 853; the cost per infection averted would be $4 233–74 642 when discounted tenofovir is available; and $1166–17 791 when generic tenofovir is available. These simple estimates do not take into account site or personnel costs, or the health-care costs avoided by preventing HIV infections. These estimates also do not include the possibility of risk compensation, which might increase the rate of risk behaviour in injecting drug users who understand that treatment can reduce the probability of transmission.

Needle–syringe programmes are more cost-effective than these calculated cost-effectiveness ratios for pre-exposure prophylaxis. The cost per HIV infection averted by needle–syringe programmes is estimated to be $13 000–1 056 034 in high-income settings,[4] and $138–9 537 in countries where discounted tenofovir is available.[5]

The effectiveness of pre-exposure prophylaxis in populations injecting drugs would depend on attainment of adequate coverage and on sufficiently high adherence to maintain individual efficacy. The coverage of antiretroviral therapy among HIV-positive injecting drug users is less than 1% in many countries. Coverage of antiretrovirals among HIV-negative injecting drug users would be expected to be substantially lower. Therefore, because of expected low coverage and unimpressive cost-effectiveness ratios, we believe that pre-exposure prophylaxis is unlikely to be widely used for HIV prevention in injecting drug users.

We declare that we have no conflicts of interest.

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Authors' reply

Michael Hudgens and Stephen Cole, and William Miller and colleagues note that the Kaplan-Meier estimates[1] for the two groups were similar for the first 36 months of follow-up; however, a formal test for the proportional hazards assumption found that efficacy did not differ by time on study (p=0·15). Additionally, there is no biological reason to expect an absence of short-term benefit, and results from other pre-exposure prophylaxis trials do not lend support to this assumption.[2-4] We did the test for equal probability at 60 months using trial data and found 52% efficacy (95% CI 10–75, p=0·02).

Regarding risk behaviour, results of studies done in people who inject drugs in the same clinics in Bangkok showed strong associations between injecting drugs and HIV infection, but sexual activity did not increase the risk of HIV infection, and further analysis of risk data from the Bangkok Tenofovir Study[5] has shown that young age, sharing needles, and incarceration were independent risk factors for incident HIV infection; whereas sexual activity was not associated with HIV infection.[5] Participant randomisation ensures the efficacy result was due to the intervention, once daily oral tenofovir provided with a package of HIV prevention strategies.

Like Hu Zhiliang and Yang Yongfeng, we believe that close monitoring of HIV status will be an important component of HIV prevention strategies using pre-exposure prophylaxis. The antiretroviral resistance data from trials thus far are reassuring: in the four studies[1-4] that have shown efficacy, no resistance to the antiretrovirals used was detected among participants who became infected during follow-up.

We agree with Andrew Craig and colleagues that individuals and policy makers will need to consider cost when deciding which HIV prevention method or combination of methods to use. We note that the incremental cost of providing pre-exposure prophylaxis in settings where HIV-prevention services are available would be relatively small, and targeting individuals at highest risk of HIV infection would decrease the cost per infection averted. Data from trials suggest that when pre-exposure prophylaxis is provided with a package of HIV prevention services, HIV-associated risk behavior will decrease rather than increase.[1-4] Nonetheless, it will be important to monitor for risk compensation in future pre-exposure prophylaxis projects.

Additional work is needed to establish how best to implement pre-exposure prophylaxis in conjunction with other proven prevention measures among people who inject drugs, including: how to support adherence, assessing the cost of pre-exposure prophylaxis, and determining appropriate venues for pre-exposure prophylaxis delivery. Nonetheless, for people who will not or cannot stop injecting drugs, pre-exposure prophylaxis might provide an important new HIV prevention method to complement other available prevention strategies.

We declare that we have no conflict of interest.

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First case of *E anophelis* outbreak in an intensive-care unit


Xu Zijian/Xinhua Press/Corbis

The hospital infection-control team at the National University Hospital of Singapore identified three patients in the cardiothoracic intensive-care unit (ICU) and two patients from the surgical ICU that were colonised with *Elizabethkingia* during a 3 week period in 2012.[1] The *Elizabethkingia* strains were identified as *Elizabethkingia meningoseptica* on the basis of matrix-assisted laser desorption-ionisation time-of-flight mass spectrometry analysis. The five patients, who were ventilated via tracheostomy and had central venous catheters in situ, received multiple courses of broad-spectrum antibiotics. Before isolation of *Elizabethkingia*, three of the patients had underlying solid-organ malignancy, one patient had multiple abdominal surgeries, two patients underwent thoracic surgery, and one patient was on extracorporeal membrane oxygenation. After isolation of the *Elizabethkingia* strain, all patients were treated with intravenous piperacillin and tazobactam, co-trimoxazole, or levofloxacin, either alone or in combination. Three of the five patients died during their