Moving towards zero new HIV infections: The importance of combination prevention

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Despite the availability of an extensive set of tools to stop transmission of HIV, there are still around 1.5 million new infections worldwide each year.[1] Interventions like increased condom use, less sexual partners, and more frequent testing for HIV are effective tools for preventing further transmission but they may be challenging to implement or adhere to. Also antiretroviral drugs prevent transmission. They can be used either as treatment of people with HIV, who cannot transmit HIV once their HIV-RNA has been adequately suppressed,[2] or as pre-exposure prophylaxis (PrEP) in people without HIV to prevent them from acquiring the virus.

Until now no single intervention is the silver bullet that will end transmission of HIV. Most likely, a combination of different interventions is needed. Which combination performs best in preventing HIV transmission in a given setting will depend on the characteristics of the HIV epidemic and on successful implementation of the interventions. Unfortunately, trials comparing different interventions are often impractical to conduct. Instead, mathematical models are better suited to explore the effectiveness of interventions. Such models capture the essential dynamics of the HIV epidemic in a mathematical framework, using parameters derived from observed data, and predict the effect of various interventions.

In *The Lancet Regional Health – Western Pacific*, Wang and colleagues use a mathematical model to quantify the effect of several behavioural and biomedical interventions on the HIV epidemic in men who have sex with men in Japan.[3] Their study builds on earlier work in which they used a similar model to forecast the effect of test-and-treat and PrEP in China and Japan.[4,5] Assuming interventions were implemented in 2022 the authors checked whether HIV incidence reached the threshold of elimination of transmission, defined as less than 1 per 1000 person-years, before 2050. HIV incidence among MSM is currently around 5 per 1000 person-years and without additional interventions the elimination target will not be reached. Two behavioural (reducing the number of sex partners in high-risk MSM, increased condom use) and two biomedical interventions (enhanced test-and-treat, introducing PrEP) were investigated at three different intensities, either separate or in combination.

Each of the four interventions by itself could achieve elimination of HIV transmission. However, this would involve large reductions in the number of sex partners or almost a doubling of the rate of condom use, which are both unrealistic to achieve. Enhancing test-and-treat would need annual testing rates to be at least 80%, which seem unlikely to be feasible as even in best performing countries like Australia testing rates are only around 70%.[6] PrEP appeared to be best suited to achieve elimination. The elimination target would already be reached if 10% of MSM used PrEP, and the effectiveness of PrEP can even be markedly improved if high-risk MSM, i.e., men with many sex partners, are prioritised.[7]

Whereas isolated interventions require large changes to reach the elimination threshold, relatively modest improvements suffice when combining interventions.[7] This study showed that a combination of the four interventions studied could eliminate HIV transmission within ten years, thereby preventing more than 80% of the expected new HIV infections under current policies. Importantly, the effect of enhanced testing and treatment as well as PrEP trumps that of behavioural interventions. This is good news because these biomedical prevention strategies are, at least in theory, relatively straightforward to achieve with changes in treatment guidelines and easier access to treatment and PrEP.

Nevertheless, significant hurdles remain on the road towards elimination. At the moment, people need to pay a third of their medication costs and PrEP is even not yet licensed yet, let alone reimbursed, in Japan.[8] Furthermore, enhanced test-and-treat reaches its maximum potential for preventing HIV transmission only if the time between HIV acquisition and diagnosis, currently approximately three years, is reduced to less than a year. This may require innovative strategies, as illustrated by a study in

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Amsterdam that showed that time between infection and viral suppression can be greatly reduced with increased awareness of acute HIV infection, targeted point-of-care testing, and same day linkage to care.[9]

This work illustrates the importance of combination prevention and provides guidance on which interventions should be prioritised. However, the study does not show which combination is most cost-effective. Future cost-effectiveness studies may convince policy makers to implement the necessary changes. All this, however, does not guarantee instant implementation of cost-effective or cost-saving interventions. In our own country, PrEP has been shown to be cost-saving at the current pricing,[10] but is still not freely available and, frustratingly, transmission of HIV still persists.

Contributors

Dr. Van Sighem wrote the original draft of the manuscript. Dr. Van der Valk revised the work and suggested critical edits. All authors have approved the final version of the manuscript.

Declaration of interests

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