**Effective and efficient prevention of HIV infection**

Global HIV-associated mortality has declined substantially in recent years, with the scale-up of antiretroviral therapy; but HIV-incidence has fallen by modest amounts and remains a staggering 2.1 million new infections every year.[1]

The limited effectiveness of HIV prevention efforts and the increased HIV survival is leading to continuously increasing number of people with living HIV infection worldwide. [2-6] This causes an enormous demand for accessible and affordable treatment, challenging health systems and universal health coverage attempts. [4, 7, 8]

The body of evidence on effective HIV prevention options [5, 6] has increased, although there are limited insights on why prevention works in some populations and why it fails in other groups. Also, information on the real-life cost-effectiveness of HIV-prevention strategies remains limited across the world, challenging policy makers in making decisions and public and private financing strategies. [7]

In the present issue of Lancet Infectious Diseases, Nichols and colleagues [9] report the attractiveness of preventive treatment strategies targeting men having sex with men (MSM). We know that pre-exposure prophylaxis (PrEP) with tenofovir and emtricitabine prevents HIV infections among highly sexually active men who have sex with men (MSM). PrEP is not approved nor reimbursed in most European countries, nor in most other settings. PrEP is given as prophylaxis, either regular daily treatment [5] or on an intermittent on-demand basis. Their study finds that PrEP is more cost-effective - in theory - when used on-demand at a €3,300 (Interquartile range €1,800-€6,400) per QALY gained as compared with daily treatment, at €14,300 (IQR €11,300-€20,900) at an 80% efficacy level. It finds that substantial decrease in drug prices could actually lead to net savings in health care costs. Their conclusion is that the two MSM prevention strategies are cost-effective and attractive given national cost-effectiveness standards (< €20,000).

The paper is well written and transparent on general methodology and on specific model assumptions, using extensive empirical data, taking into account formal appraisal guidance.[10] The findings on the costs and benefits around HIV prevention are plausible, yet they also urge comments on the feasibility, affordability and generalizability of PrEP as an attractive HIV prevention option. The authors assume a substantial (20%) positive 'snowballing' effect – prevention of subsequent infections among next partners after preventing a first infection. The efficacy is stated to be potentially largest among the most sexually active MSMs, yet in this group, HIV-incidence has remained stubbornly high across Europe and other regions. Also, little attention is paid to the need for the development of new PrEP medications if resistance increases with the use of PrEP on a large scale.

 The cost-effectiveness threshold value used in the study is likely too high for most countries. Even in a high-income country like The Netherlands, this threshold value (< €20,000) doesn't have a formally approved status in decision making. Here, the Minister of Health, with others, advocates a more comprehensive approach including multiple criteria, carefully.[11, 12] Also, in a comparative economic evaluation approach, one formally would compare the two options and their combination for the involved entire MSM population and not in two separate populations as presently done, leading to less favourable cost-effectiveness ratio’s. Lastly, even in the case of favourable cost-effectiveness results, the implicated total budget to promote mass use may be high while policy and other advocate groups argue that the budget should be saved for more urgent options. [6-8, 11]

 The recent systematic review[5] lists PrEP as one of the attractive HIV prevention options in a variety of global settings. Of course, the generalisability of the Dutch study findings is limited and more specific empirical evaluation and implementation research is needed across the globe to assess effectiveness and efficiency of HIV prevention. We now know that large-scale implementation of effective prevention strategies will be necessary to be able to measure population impact and to be able to reduce the already huge burden on the health systems and households without advanced health services and health financing mechanism. Nichole and colleagues[9] document that PrEP may be attractive. Implementation of HIV prevention will also need a continuation of strengthening demand and compliance, increased coverage, and affordable drugs at both the household and health system levels in all relevant settings.

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We declare no competing interests.

1. UNAIDS. *Global AIDS Update 2016*. 2016 [cited 2016 August 16th].

2. Garnett, G.P., et al., *Providing a conceptual framework for HIV prevention cascades and assessing feasibility of empirical measurement with data from east Zimbabwe: a case study.* Lancet HIV, 2016. **3**(7): p. e297-306.

3. Hargreaves, J.R., et al., *The HIV prevention cascade: integrating theories of epidemiological, behavioural, and social science into programme design and monitoring.* Lancet HIV, 2016. **3**(7): p. e318-22.

4. Isbell, M.T., et al., *We neglect primary HIV prevention at our peril.* Lancet HIV, 2016. **3**(7): p. e284-5.

5. Krishnaratne, S., et al., *Interventions to strengthen the HIV prevention cascade: a systematic review of reviews.* Lancet HIV, 2016. **3**(7): p. e307-17.

6. Smith, J.A., et al., *Maximising HIV prevention by balancing the opportunities of today with the promises of tomorrow: a modelling study.* Lancet HIV, 2016. **3**(7): p. e289-96.

7. Niessen, L.W. and J.A. Khan, *Universal access to medicines.* Lancet, 2016. **387**(10013): p. 9-11.

8. Niessen, L. and R. Stothard, *Equitable control of schistosomiasis and helminthiasis.* Lancet Infect Dis, 2016.

9. Nichols, B.E., et al., *Time to make PrEP for MSM broadly accessible? A cost-effectiveness analysis of PrEP for HIV-1 prevention in the Netherlands.* Lancet Infectious Diseases, 2016. **In press**.

10. Husereau, D., et al., *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)--explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force.* Value Health, 2013. **16**(2): p. 231-50.

11. Schippers, E.I., *Letter to Parliament on the Report on Cost-effectiveness in Practice*, in *826618-140666-Z*, Ministry of Health, Editor. 2015: The Hague.

12. Baltussen, R., et al., *Multi-criteria decision analysis to prioritize health interventions: Capitalizing on first experiences.* Health Policy, 2010. **96**(3): p. 262-4.