Treatment as prevention: will it work?

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In the past two years, rapidly emerging new trial results have provided the scientific community and people living with human immunodeficiency virus (HIV) or acquired immune deficiency syndrome (AIDS) or at risk of infection, with welcome news. Interesting scientific evidence is accumulating for the effectiveness of biomedical interventions to prevent the transmission of HIV. Infected people may become less contagious when the viral load is suppressed by antiretroviral therapy (ART). In 2010, results from the Pre-Exposure Prophylaxis Initiative (iPreX) randomised controlled trial provided the first evidence that antiretroviral pre-exposure prophylaxis can reduce HIV incidence. In their study, Grant et al showed, that that daily oral antiretroviral medication reduced HIV incidence in HIV negative men who have sex with men (MSM) by 44% [1]. In July 2011, two studies from the United States, the TDF2 (tenofovir disoproxil fumarate and emtricitabine (TDF)) study and the Partners Pre-exposure study provided evidence that a daily oral dose of antiretroviral medication can reduce HIV acquisition among uninfected individuals exposed to the virus through heterosexual sex by at least 60% [2-3]. The randomised controlled HIV Prevention Trials Network study (HPTN 052) by Cohen et al demonstrated that earlier treatment (time of enrolment in study compared with CD₄ cell counts within or below 200-250 cells/mm³ or developing an AIDS defining illness) of HIV-infected persons with ART had both a clinical benefit for the infected individual and resulted in a 96% reduction in transmission to the uninfected sexual partner [4].

Early treatment for HIV, prevention of mother-to-child transmission, post-exposure prophylaxis, male circumcision, consistent condom use, behaviour change communication, microbicides, and possibly targeted pre-exposure prophylaxis are the most effective tools to prevent HIV transmission on individual and population levels [2-6]. Mathematical modelling studies indicated that early testing and early treatment of all individuals with HIV could effectively halt HIV transmission at the population level. Ecological studies have confirmed the effectiveness of the test and treat strategy in reducing HIV transmission and it appears to be bolstered further by HPTN 052 trial results [7-11].

New data on HIV in Europe in this issue by Likatavicius and Van de Laar demonstrate that HIV remains a public health problem in the European Union (EU) and European Economic Area (EEA) where more than 27,000 newly diagnosed HIV infections were reported during 2010 [12] (an increase of 4% compared with 2009). HIV diagnoses among men who have sex with men (MSM) have increased by 39% between 2004 and 2010, and represent 38% of the total HIV cases in the EU/EEA. New HIV diagnoses among injecting drug users (IDU) have declined by 44% since 2004, representing only 4% of cases in 2010. However, outbreaks of HIV in this group have been reported in some countries recently [13-14] and the prevalence of HIV and hepatitis C remains high as reported in this issue by Wiessing et al. [15]. The proportion of people diagnosed with a CD₄ cell count less than 350/mL (late diagnosis) [1, 16-17] is unacceptably high in Europe: almost half of the cases where a CD₄ cell count was available at the time of diagnosis. This suggests that individuals present late in the course of infection, cannot benefit from early treatment and are at risk of disease progression.

The potential and feasibility of treatment as prevention needs to be considered in light of the current epidemiological situation of HIV in Europe. For antiretroviral treatment to have a preventive effect, the HIV-positive individual's viral load must be suppressed to a very low level over time. Gardner et al. modelled the achievement of viral suppression by using the pre-requisite steps testing and diagnosis, linking to care, adherence to ART, and viral load suppression as the final outcome. They demonstrate that in order to achieve a sustained population-level reduction in viral load a high proportion of HIV-infected individuals must be i) diagnosed with HIV infection, ii) linked in a timely manner to HIV care, iii) retained in care, iv) placed on effective antiretroviral therapy and v) adherent life-long to this treatment [18]. The steps in this care cascade were reviewed and many individuals seem to drop out of at one of the steps. If all efforts would be maximised to 90% for all steps still only an estimated two-third of the cases would achieve viral suppression.

The care cascade points out key areas for programme and surveillance improvement within Europe. In addition to late testing and diagnosis of HIV, most Member States do not routinely monitor whether people tested positive for HIV are linked to care and, if so, whether they are retained in care. Monitoring access to and retention in care is particularly important for vulnerable populations among those living with HIV, including MSM, IDUs and migrants. Monitoring and surveillance systems should be adapted so that they track engagement in care more effectively and allow monitoring the impact of treatment on the course of the epidemic.

HIV testing, early diagnosis and access to early treatment have always been key strategies for HIV/AIDS prevention. New evidence for biomedical interventions is indeed promising and shows that knowledge of HIV status has now become the cornerstone for HIV prevention. However, the question arises as to whether the implementation of prevention treatment strategies is feasible and affordable as the trial results were obtained under optimised conditions. A recent cost-effectiveness study has highlighted that in addition to HIV testing and treatment substantial reductions in risk behaviour are still needed to contribute to substantial reductions in HIV transmission [19]. Treatment as prevention as an option in Europe is complicated by the fact that the HIV epidemic affects mostly socially vulnerable or marginalised groups who experience multiple barriers to accessing services and adhering to treatment. At the same time, a combination prevention toolkit is available with multiple effective programmatic, behavioural and structural interventions at different levels that can be tailored to local epidemics.

Interventions found to be consistently effective include condom provision, reduction of number of sex partners, partner notification services, needle and syringe exchange programmes, opioid substitution treatment, and behavioural change interventions [20-24]. At present there is little evidence that treatment as prevention works among MSM [25] and in light of the current epidemiological situation more efforts are needed to reverse the trend of sexually transmitted infections and HIV among MSM through combined measures. The evidence for harm reduction and prevention of communicable diseases in the field of drug use is overwhelming. A recently launched ECDC/EMCDDA guidance document brings together evidence and expert opinion and supports EU countries to reduce the burden of drug use as well as the burden of high prevalence of HIV, hepatitis B and C among IDUs [26]. It was launched at a critical moment when an outbreak of HIV among IDUs was reported [13]. In this issue, Pharris et al investigate recent outbreaks in Greece and Romania and assess the risk for HIV transmission among IDUs in Europe [27]. The analysis shows a heterogeneous pattern in with a potential risk for outbreaks in a number of countries where immediate action is warranted. It demonstrates the need for having adequate prevention services in place to prevent outbreaks of

HIV and hepatitis C. Outbreaks can be expected when drug using patterns change, the frequency of injection increases in combination with a low coverage of prevention services (including needle exchange programmes and opioids substitution treatment).

In the context of the Joint United Nations Programme on HIV/AIDS (UNAIDS) 2011 political declaration 'targets and elimination commitments' [28] to achieve zero new infections, no AIDS-related deaths and zero discrimination by 2015, we need to review the current HIV prevention strategies in Europe and to re-enforce the respective programmatic approach. With enough people in treatment, the treatment as prevention option will help to reduce HIV transmission however, there is as of yet no evidence that this will reverse HIV trends in Europe. To control the epidemic, primary and secondary prevention of HIV transmission remains crucial. To identify and apply the most effective prevention strategies to reduce the impact of HIV in Europe, there is an urgent need for better programmatic approach, involving a wide range of stakeholders including healthcare providers, civil society, those infected with HIV and prevention workers.

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