We thank Alison Morris-Gehring for her help coordinating this Series.

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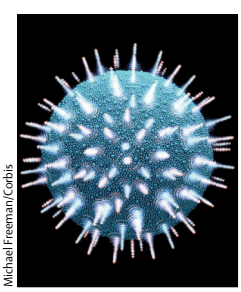
Pre-exposure prophylaxis works—it's time to deliver



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HIV

The science is now clear: oral pre-exposure prophylaxis (PrEP) with a coformulation of tenofovir disoproxil fumarate and emtricitabine (Truvada) significantly reduces the risk of HIV infection among individuals at high risk of HIV infection. The news that PrEP has shown consistent efficacy among those who take it as prescribed should be a cause for celebration, and galvanise action to ensure access to PrEP for those who could benefit the most. But almost 3 years since the US Food and Drug Administration approved tenofovir–emtricitabine for PrEP,[1] little is being done on implementation. With more than 2 million new HIV infections every year worldwide,[2] it is time for that to change.

Randomised controlled trials and open-label extension studies in many countries have shown the efficacy of daily oral PrEP in the populations at greatest risk for HIV infection, including men who have sex with men (MSM),[3,4] heterosexual women and men in HIV-discordant couples,[5,6] and people who inject drugs.[7] Most recently, at the 2015 Conference on Retroviruses and Opportunistic Infections, data from two additional studies, PROUD in the UK[8] and Ipergay in France and Canada,[9] were presented that showed similar, high efficacy of PrEP among MSM. In Ipergay, the use of tenofovir–emtricitabine on demand before and after sex reduced the risk of HIV infection by 86% among high-risk MSM.[9] A third study, the Partners Demonstration Project, which involved heterosexual HIV-discordant couples in Kenya and Uganda, showed that offering antiretroviral treatment to the infected partner and PrEP to the uninfected partner virtually eliminated the risk of HIV transmission.[10]

This evidence should prompt us to make PrEP available, quickly, to all those who could benefit. But global access to PrEP is extremely limited. The USA is the only country to have moved forwards with implementation of PrEP. The manufacturer of tenofovir–emtricitabine, Gilead Sciences, has applied for approval in several other countries, but regulatory authorities have generally been slow to act. PrEP demonstration projects exist, but most are fairly small and limited in scope.[11] The cost of PrEP scale-up is also a concern. Generic versions of Truvada are available in most middle-income and low-income countries, but, without additional donor support and new models for the provision of antiretrovirals, some countries seeking to expand access to PrEP would still be forced to make unfair trade-offs with other HIV prevention and treatment priorities.

The challenges are formidable. But as leaders of the International AIDS Society, and as practising HIV clinicians, epidemiologists, and researchers who work in diverse settings, we are committed to the principle that all people have a right to effective HIV prevention and treatment. Now that PrEP has been proven to work, we believe that expanding access to PrEP is not only sound public health policy but also a human rights imperative.

Nearly 15 years ago, widespread access to antiretroviral HIV treatment was the rallying call at the 2000 International AIDS Conference in Durban, South Africa. At that time, there were many sceptical voices, and arguments about feasibility, cost-effectiveness, and the ability of patients in poor countries to adhere to HIV therapy. These concerns were unfounded, and we are now on track to achieve the goal of providing

antiretroviral treatment to 15 million people by the end of 2015.[12] It is an extraordinary global health success story—one that few imagined possible at the time. Now, as we prepare to return to Durban for the 2016 21st International AIDS Conference, we once again face the challenge of scaling up access to a lifesaving intervention despite daunting barriers. But the global campaign to expand access to HIV treatment has proven that it can be done. By the time of the 2016 Durban conference, we challenge the world to act on several fronts to improve access to PrEP.

We believe that WHO should provide bolder leadership on PrEP. WHO needs to endorse PrEP unambiguously as an HIV prevention option for all populations at substantial risk of HIV infection, including women at risk and people who inject drugs, and issue comprehensive implementation guidance, as the US Centers for Disease Control and Prevention have done for the USA.[13]

Gilead Sciences and governments should work together to accelerate regulatory approval of tenofovir–emtricitabine as PrEP. Gilead should file for such approval in additional countries where PrEP could have a major impact, and regulatory authorities should provide expedited review. In addition, Gilead and its generic manufacturing and distribution partners should continue working to reduce the cost of tenofovir–emtricitabine globally with special attention to low-income and middle-income countries.

Governments, donors, and other stakeholders must work together to develop comprehensive strategies for the introduction of PrEP that are integrated into national health plans, as well as to ensure adequate funding for this method of HIV prevention. PrEP should be given a level of priority commensurate with its powerful evidence base. In many cases, new resources will need to be mobilised to pay for PrEP. However, implementation of PrEP should not come at the expense of other essential HIV or other key health programmes.

Human rights protections must be a central part of plans to make PrEP widely available. MSM, people who inject drugs, sex workers, and others must be able to seek PrEP without fear of discrimination, stigma, or legal penalties. Robust public education efforts will also be needed, not only to stimulate demand for PrEP but also to prevent misinformed opposition to PrEP.

Finally, operational research and the number and scope of demonstration projects need to be expanded so that remaining questions about PrEP implementation can be addressed, such as how to maximise uptake; support adherence, especially among women; expand access to adolescents; and integrate delivery of PrEP within health systems.

For far too long, the world has accepted the notion that breakthroughs in health will take years, if not decades, to reach low-income countries. After a period of unprecedented progress on HIV prevention, treatment, and other challenges, we know it is not only necessary, but possible, to pick up the pace. PrEP is a powerful addition to our HIV prevention arsenal, and can save many lives. We need to take action now to put the strong and consistent evidence of PrEP efficacy into practice.

For the **21st International AIDS Conference** see http://www.aids2016.org/

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CB and FB-S declare no competing interests. L-GB has received Truvada for PrEP from Gilead to conduct a demonstration project in adolescents in South Africa. AP was chair of the data safety monitoring board for PROUD but has no competing interests with PrEP, and has participated in advisory boards and educational events sponsored by Gilead that were not related to PrEP; he and his institution have received grants for research in HIV-infected patients from Gilead that were not related to PrEP.

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Corticosteroids and pneumonia: time to change practice

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Pneumonia is characterised by lung inflammation, with fluid filling the alveoli and preventing adequate oxygenation of the body, and can be acquired in the community or in hospital. In 2013, about one million children died from pneumonia, which was the leading cause of death in children aged 5 years or younger.[1] Annually, 15 adults per 1000 visit a doctor for symptoms of community-acquired pneumonia.[2] In 2013, lower respiratory tract infections caused 2·7 million deaths.[1] Although the epidemiological burden of community-acquired pneumonia is highest in patients aged 65 years or older, the disease incurs substantial morbidity and health-care costs in working-age adults.[3]

Management of this disorder relies mainly on empirical antibiotic treatment, and so far no adjunct therapy is recommended.[4] In *The Lancet*, Claudine Angela Blum and colleagues[5] report that 7-day treatment with 50 mg oral prednisone daily hastened recovery and hospital discharge in adults with community-acquired pneumonia of any severity.[5] Compared with controls (who received placebo), clinical stability was achieved 1·4 days earlier in the corticosteroid-treated patients (3·0 days in the prednisone group *vs* 4·4 days in the control group; hazard ratio [HR] 1·33, 95% CI 1·15–1·50), who subsequently spent 1 day less in hospital. Treatment with prednisone was well tolerated except for transient mild-to-moderate hyperglycaemia (76 [19%] *vs* 43 [11%]; OR 1·96, 95% CI 1·31–2·93). This trial was appropriately designed to minimise selection bias and possible confounding, and powered to show the efficacy of corticosteroids convincingly.

See Online for appendix

The favourable benefit-to-risk ratio noted with corticosteroids in this trial is in line with findings from trials done in Egypt,[6] Italy,[7] Japan,[8] the Netherlands,[9] and Spain.[10] Only one trial[11] did not show benefit from corticosteroids. Data from five of these six trials accounting for 1379 adults with community-acquired pneumonia showed that adjunct treatment with corticosteroids reduced length of hospital stay (mean difference –1·10 days, 95% CI –1·86 to –0·34; figure), time on intravenous antibiotics (–0·69 days, –1·21 to –0·17, three trials, 1120 patients; appendix), and time to clinical stability (–1·41 days, –2·18 to –0·64; three trials, 1029 patients). In these trials, observed mortality of control patients in the short term ranged from 0% to 7% in patients not in the intensive care unit (ICU),[5,6,8,11] and from 15% to 30% in those in ICU.[7,9,10]

Corticosteroids might provide survival benefit for adults with community-acquired pneumonia requiring

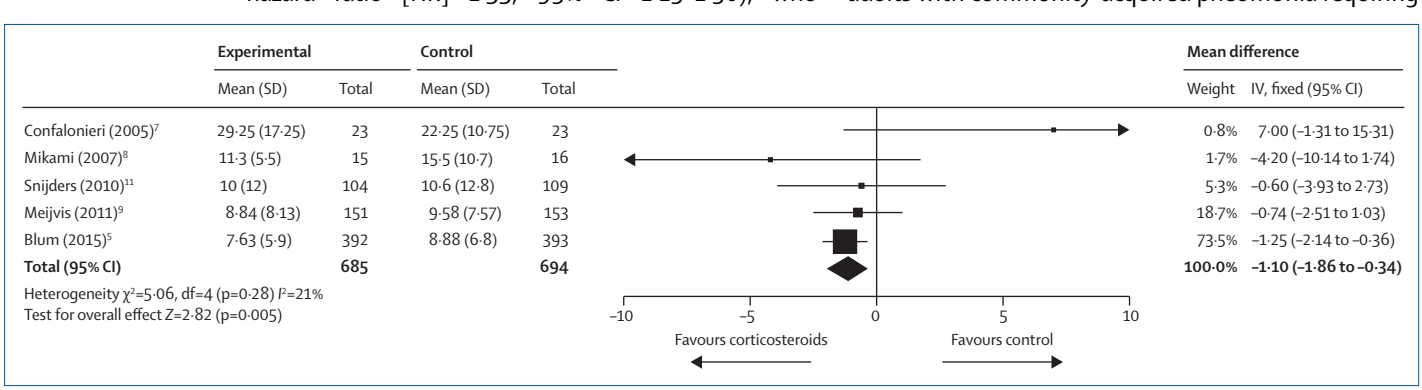

Figure: **Mean difference of length of hospital stay in adults admitted to hospital with community-acquired pneumonia who received corticosteroid treatment or placebo**
I calculated the pooled mean difference with a fixed-effects model and noted no heterogeneity for the analysis including all trials. In the forest plot, for each individual trial, the mean difference is represented as a black square in the centre of the black line corresponding to the 95% CI; the size of the black square is proportional to trial's weight.