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Debate: PreP is not an essential component of TasP

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At the 3rd International HIV Treatment as Prevention Workshop in Vancouver, Canada, in April 2013 I was asked to put forward the case that "Pre-Exposure Prophylaxis (PreP) is not an essential component of Treatment as Prevention (TasP)". Here I reproduce my argument and invite readers of the SACEMA Quarterly to express their own views on this important issue.

At the International AIDS Society meeting in Durban in the year 2000, Nelson Mandela said: "It is never my custom to use words lightly. If twenty-seven years in prison have done anything to us, it was to use the silence of solitude to make us understand how precious words are and how real speech is in its impact upon the way people live or die." The words we say, the guidelines that we write, the advice that we give, has a direct impact on peoples lives. We carry a heavy duty.

I have been asked to oppose the motion that PreP is an essential component of TasP, but we need to be clear as to what is at issue. First of all, by saying that PreP is an essential component of TasP we acknowledge that TasP has priority and the matter at hand is the role of PreP as a component of TasP. Secondly, by saying that PreP is an essential component of TasP we imply that without PreP TasP is unlikely to succeed in its goals and intentions. But in order to decide on the extent to which PreP is an essential component of TasP we need to be clear about what is it that we hope to achieve through the use of TasP. My job is to convince you that while PreP may be a useful, and even an important, addition to TasP it is by no means an essential component of TasP.

What is in the best interests of individual people?

The only way to save the lives of the 22 million or so people currently infected with HIV, who are not already on treatment with anti-retroviral drugs, is to make sure that they are able to start taking treatment well before they begin to develop life threatening, AIDS related infections. Indeed, if we want the best possible prognosis for individual people they should start treatment as soon as possible after they become infected. As public health practitioners we therefore have a moral duty and an ethical obligation to ensure that as many people as possible are given the opportunity to know their HIV status and to have immediate access to treatment. Furthermore, the only way to stop the epidemic is to ensure that as many HIV-positive people as possible start treatment as soon as possible and comply with their treatment as far as possible.

So the essential core of HIV-control must be universal access to life-saving anti-retroviral drugs for the immediate benefit of infected people and for the protection of their sexual or social partners.

Let me therefore restate the proposition and ask: for which people and under which circumstances might PreP be an important component of TasP? In doing this we must remember that all problems in public health are essentially problems in optimization and the important, and often difficult, thing is to decide what it is that we want to optimize.

For people who are already infected with HIV PreP is clearly not an option. In comparing the impact of PreP and TasP on individual people therefore, we are only concerned with those who are found to be HIV-negative when tested and we can offer them one of two options: continue to be tested regularly and if and when you become infected start treatment; or start PreP immediately and if and when you become infected, in spite of PreP, start treatment. What then do we want to optimize? I suggest that we should minimize the expected number of years that a particular person is likely to spend on treatment.

Now it is clear that if the incidence is very low, starting people on PreP will lead to many years of unnecessary treatment, and this will favour TasP; if the incidence is very high people will become infected very quickly under TasP but less quickly under PreP, fewer people will be infected, and those that are not infected can stop taking drugs when they are no longer at risk of infection so that this will favour TasP. In other words, we should favour PreP when the risk of infection is high and TasP when the risk of infection is low. The optimization question is then: where is the break-even point? Above what level of risk should we favour PreP over TasP and vice versa?

The calculation is not difficult to do but we need to make some assumptions (1). For the sake of the present discussion let us assume first that people are at high risk of infection for a period of ten years (2); second that, once infected, people on ART will live out a normal life (3), and third that PreP reduces the likelihood of being infected by about 60% (4-6). Then we can show that the break-even point occurs when the annual risk of infection is 6% per year (7); above 6% per year PreP is favoured; below 6% per year TasP is favoured.

Who then has a risk of infection that is greater than 6% per year? KwaZulu-Natal in South Africa is one of the worst affected places in the world and in

the year 2000 the risk of infection exceeded 6% in women between the ages of 15 and 37 (8); now, because the incidence has fallen, as a result of treatment, the risk of infection only exceeds 6% per year in women aged 20 to 27 years (9) and for them the difference between PreP and TasP in the number of person years that they can expect to have on treatment would be marginal. For particular risk groups the incidence of HIV may be higher so that, for example, commercial sex-workers in high prevalence settings may be better off if they start PreP before they become infected. An HIV-negative person in a discordant relationship may also be at high risk if their positive-partner is not on ART. I know women that are certain that their husbands have other sexual partners but they feel that they cannot ask them to use condoms. One might well advise them to take PreP. But these are relatively few in number and as treatment coverage increases, the incidence of HIV will fall, and the number of people for whom PreP should be recommended will also fall. We may therefore regard PreP as a useful, even important, option for certain people at high risk of infection, but this does not make it an essential component of TasP.

What is most important for public health?

In the long the aim must be to rid the world of the scourge of HIV (10) and we also need to consider the population-level or public health costs and benefits. In this regard we need to optimize the effectiveness, affordability, and cost-effectiveness of TasP and PreP. We know that TasP can reduce HIV incidence by 96% (11). If all those at risk were tested once a year, on average, and if we were able to achieve 90% coverage, the overall reduction in incidence under TasP would be 82%; enough to eliminate HIV in half of the sub-Saharan African countries and to reduce it to very low levels in all countries. We also know that PreP can reduce HIV incidence by about 60%. In sub-Saharan Africa the proportion of all infections that are in key-populations at high risk is less than about 30% and even in concentrated epidemics it is likely to be less than about 50%. If half of all of these high-risk sexual encounters were covered by PreP then the overall reduction in incidence would be about 20%, as compared to about 80% under TasP, so that the impact of TasP on the incidence of HIV would be four times greater than it would be under PreP. So TasP is considerably more effective than PreP.

Both TasP and PreP require a considerable up-front investment. However, there must be at least as many people at risk of HIV-infection as there are people infected with HIV. The initial investment under both TasP and PreP would therefore be about the same so that affordability does not favour either one.

In the long term TasP would either lead to, or come close to, eliminating HIV (12) so that the cost would fall to zero or very low levels while under PreP the prevalence might fall to about 25% of its current level and the world would have to spend several billion dollars a year for the indefinite future treating those people who TasP does not protect. In the long term TasP is considerably more cost-effective than PreP, or if you prefer, gives a much higher rate of return on the initial investment.

I would like to suggest therefore that a relatively small proportion of individual people, who are at especially high risk of infection, might be advised to take PreP for as long as they are at risk of infection and remain negative. From a public health point of view TasP is much more effective than PreP and offers a substantially better long-term investment. This leaves open a role for PreP as a useful addition to, but by no means an essential component of, TasP along with male circumcision, condom promotion, treatment of sexually transmitted infections and behaviour change programmes.

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