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An international collaboration to compare mathematical models of the potential impact of HIV treatment on new HIV infections in South Africa

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The rapid scale-up of antiretroviral therapy (ART) in sub-Saharan Africa in recent years has been an unprecedented public health success, already averting millions of deaths across the continent (1). In South Africa alone, an estimated 1.79 million people were receiving ART as of mid-2011 (2), and at least half a million more will begin treatment in the coming year. In addition to the therapeutic benefits of preventing AIDS and death amongst individuals infected with HIV, increasing evidence has demonstrated that individuals receiving ART who are virally suppressed are unlikely to transmit HIV to uninfected sexual partners (3).

This finding has created a great deal of enthusiasm for the idea of "HIV treatment as prevention" in which expanded access to ART for people living with HIV is a central component of strategies to substantially reduce the number of new HIV infections in coming years, and eventually end the HIV epidemic. Many mathematical models have been developed to simulate the potential impact and cost-effectiveness of different HIV treatment intervention strategies, with several focused specifically on South Africa. The most influential of these models, co-authored by SACEMA scientist Brian Williams, suggested that a strategy in which all adults are tested for HIV annually and begin ART as soon as they are found to be HIV-infected could reduce HIV prevalence in South Africa to below 1% within 50 years (4). Other mathematical models have investigated the impact of HIV treatment as prevention in combination with other prevention strategies or other guidelines for HIV treatment provision, such as the impact of treating individuals after their CD4 count falls below 350 cells/μL, in line with current national guidelines. Generally, all models have predicted positive prevention benefits of HIV treatment, but directly comparing the results of different models has been challenging because each model has been used to answer different questions and has reported different key outcomes.

In November 2011, the HIV Modelling Consortium convened a meeting at the Stellenbosch Institute for Advanced Studies with over 50 mathematical modellers, epidemiologists, biomedical researchers, and national and international HIV policy experts to discuss key topics related to modelling the impact of HIV treatment. The HIV Modelling Consortium (http://www.hivmodelling.org), coordinated by a secretariat jointly based at Imperial College London and SACEMA, is a project funded by the Bill and Melinda Gates Foundation that aims to help improve scientific support for decision making by co-coordinating a wide range of research activities in mathematically modelling the HIV epidemic. Previous topics taken on by the consortium include methods for understanding sources of HIV infection and the risk of the spread of drug resistance due to pre-exposure prophylaxis (PrEP). In the near future, workshops will be held concerning estimating HIV incidence and the use of models in clinical trials.

One key aim of the November meeting was to understand the extent to which different mathematical models agree about the potential impact of HIV treatment. To address this, the Modelling Consortium secretariat invited all mathematical modellers with an existing mathematical model of the impact of HIV treatment in South Africa to participate in a model comparison exercise in which each of the models would simulate a standardised set of HIV intervention scenarios and report common metrics of intervention impact.

Twelve independent mathematical models were included in the model comparison exercise. The collaboration brought together 19 mathematical modellers from eleven different institutions on three continents. The models of treatment as prevention in South Africa vary substantially in structure, level of complexity, and parameterization. However, each model was capable of estimating the impact of treatment on HIV incidence, and each is already being used to contribute to the international policy debates around the most effective use of HIV treatment.

The HIV treatment intervention scenarios considered by the models systematically varied the

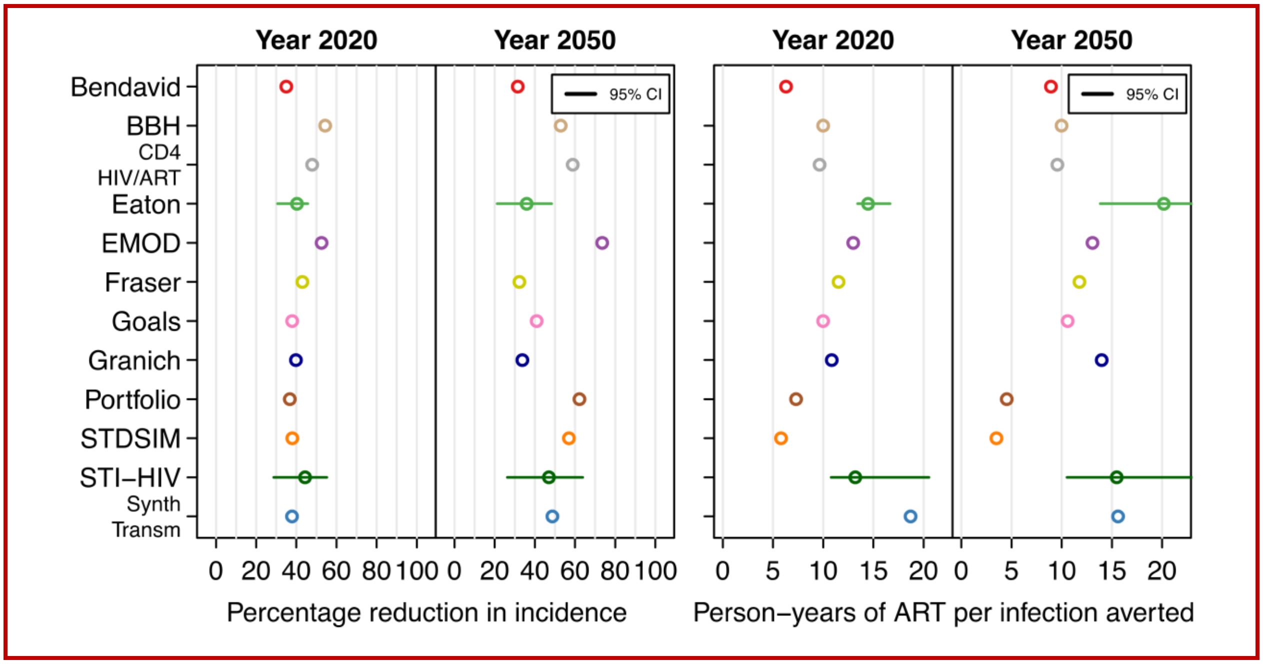

Figure 1: *The percentage reduction in HIV incidence and the cumulative number of person-years of ART provided per infection averted in years 2020 and 2050 across twelve independent mathematical models. Results are for an HIV treatment intervention strategy in which 80% of individuals have access to ART, HIV-infected individuals receive ART on average one year after their CD4 count falls below 350 cells/µL, and 85% of individuals are retained 3 years after starting treatment. HIV treatment is assumed to become available in the year 2012. The reduction in incidence is based on comparing the intervention to HIV incidence in an artificial counterfactual scenario in which no ART is provided.*

CD4 cell count threshold at which infected individuals are eligible to start treatment, the percentage of the population with access to ART, and the proportion remaining on ART three years after starting treatment. For a hypothetical intervention program in which 80% of individuals have access to ART, with treatment initiated on average one year after their CD4 cell count falls below 350 cells/µL and with 85% remaining on ART three years after, the models estimated that HIV incidence would be 35% to 53% lower after eight years than it would have been if no treatment was provided at all (Figure 1). This is significant as it shows that all models agree that substantial prevention benefits could be accrued by strong programs that implement the ART clinical guidelines.

The models were also used to estimate the impact of the existing ART programme in South Africa by simulating the actual number of people starting ART in South Africa during each year from 2001 to 2011. Based on this analysis, the models estimated that the HIV incidence rate in South Africa in 2011 may have been 17% to 32% lower than it would have been if no treatment had been provided. However, HIV prevalence is relatively similar to what would have been expected if treatment had not been provided, meaning that it has not been possible to observe declines in the epidemic using existing surveillance methods.

However, there was greater variation in the range of model predictions of the reduction in incidence over the long-term: from 32% to 74% reduction after almost forty years. There was also a large amount of variation in the models' estimates of the amount of ART provided for each HIV infection averted, one key determinant of the ultimate cost and cost-effectiveness of the intervention. For the same intervention scenario, estimates ranged across models from one infection averted for every 6 person-years of treatment provided to one infection averted for every 18 years of treatment provided. Following the presentation of the preliminary results of this investigation at the HIV Modelling Consortium meeting in Stellenbosch, the final results of the study were presented publicly as a poster at the 19th Conference on Retroviruses and Opportunistic Infections (5) and at the International HIV Treatment as Prevention Workshop. Encouraged by the success of this project and the enthusiasm for collaboration amongst HIV modellers, the HIV Modelling Consortium looks forward to organizing additional model comparisons in the future, including further work to understand differences in models of HIV treatment and other important topics in HIV modelling.

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For more information on the HIV Modelling Consortium or the meeting on HIV Treatment as Prevention, please see http://www.hivmodelling.org.

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