

## Modelling the potential impact of an antiretroviral microbicide gel on the HIV epidemic in South Africa

**Eleanor Gouws - Advisor, Statistics, Modelling and Estimation;  
Epidemiology and Analysis Division, UNAIDS, Geneva, Switzerland**

**Brian Williams - Epidemiologist affiliated to SACEMA**

One of the major obstacles to preventing HIV-transmission has been the lack of an effective, female controlled method of prevention. Now, for the first time, a vaginal microbicide has been shown to reduce the risk of infection in women. CAPRISA 004 was a randomized placebo-controlled trial to assess the effectiveness and safety of a 1% vaginal gel formulation of tenofovir.<sup>1</sup> The results, released in 2010 at the XVIII International AIDS conference in Vienna, showed that women using the gel were 39% (95% CI: 6% to 60%) less likely to be infected with HIV than women using the placebo. There were no significant side effects, no increase in the overall adverse event rates, no tenofovir resistance in HIV seroconvertors, and the gel was found to be acceptable to the women in the trial.

To assess the public health and policy implications of this new method of control, a dynamical model of HIV transmission was used to determine the population level impact of the microbicide on the HIV epidemic in South Africa as well as the cost effectiveness of the gel, under a range of scenarios.<sup>2</sup> A compartmental model previously developed to explore the impact of medical male circumcision<sup>3</sup> was adapted for this study and fitted to trends in adult HIV prevalence. If the relative risk of HIV infection for a woman using the gel is  $RR$ , then the risk, averaged over male-to-female and female-to-male transmission, is

$$RR^* = \sqrt{RR}$$

and the average risk reduction at a coverage,  $c$ , is

$$RR_c = cRR^* + (1-c)$$

Using this expression to determine the reduction in transmission the dynamical model shows that the use of tenofovir gel could have a significant impact on the future course of the epidemic in South Africa. Compared to the baseline scenario in which tenofovir gel is not used, the model shows that consistent use of the gel in 80% or more of sexual encounters (high coverage) could prevent 2.33 (0.12 to 4.63) million or 21% of new HIV infections and avert 1.30 (0.07 to 2.42) million or 12% of AIDS related deaths over the next 20 years. Even at low coverage (gel use in 25% of

sexual encounters) it could prevent 0.5 (0.04 to 0.77) million or 4% of new HIV infections and avert 0.29 (0.02 to 0.44) million or 3% of AIDS related deaths over 20 years.

In the intervention trial the cost of the gel was US\$ 0.50 per application but most of the cost was for the applicator, not for the tenofovir. The estimated cost per infection averted at low gel coverage is then US\$2,392 (US\$562 to US\$4,222), or about 28% of the estimated life-time cost of providing ART to 1 person; whereas the cost per disability-adjusted life year (DALY) saved is US\$104 (US\$27 to US\$181) or about 2% of the estimated per capita gross national income per year. At high coverage, use of the gel is even more cost effective at US\$1,701 per infection averted and US\$74 per DALY saved. Furthermore, the cost-effectiveness of using tenofovir gel compares favorably with other prevention interventions. In countries where HIV incidence is lower than in southern Africa, the cost-effectiveness of tenofovir gel will be less favorable because the cost per infection averted rises as the incidence falls. However, in such settings, the impact of the gel on HIV incidence would be increased if targeted at women at high risk of infection such as sex workers.

The CAPRISA study provides the first evidence that the use of an antiretroviral drug in the form of a microbicide gel can significantly reduce the risk of HIV infection among women. The mathematical modelling shows that even at low coverage it could have a substantial population level impact and in southern Africa, where HIV incidence is high, it will be highly cost effective. While the results of the CAPRISA trial need to be confirmed by further research to meet the requirements for licensure by FDA and other regulatory bodies, the findings are an important and exciting step forward for HIV prevention. Used in combination with other prevention methods, such as male circumcision, condom promotion and HIV testing and treatment, we may finally begin to bring the epidemic under control.

**Eleanor Gouws**, Advisor, Statistics, Modelling and Estimation; Epidemiology and Analysis Division, UNAIDS, Geneva, Switzerland. Areas of interest:

epidemiology, biostatistics, infectious diseases, estimating the impact of HIV in countries. *gouwse@unaids.org*

**Brian Williams**, Epidemiologist affiliated to SACEMA. Area of research interest: mathematical biology. *williamsbg@me.com*

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