Policy Brief

The promise of MICROBICIDES in future HIV prevention

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Background

In Malawi, Journalists Association Against AIDS (JournAIDS) with support from the International Partnership for Microbicides (IPM) is working on an advocacy project to raise awareness for the need for microbicides and other New Prevention Technologies (NPTs). The organization is also collaborating with fellows under an AVAC fellowship program. As part of maximizing the reach of the interventions, JournAIDS is also working with University of North Carolina (UNC) Project and Southern Africa AIDS Trust.

HIV prevalence amongst the 15-49 year old population in Malawi is at 10.6%, according to the most recent definitive population survey data for Malawi, the Malawi Demographic Health Survey (MDHS) 2010, referenced in the 2015-2020 Malawi National HIV Strategic Plan. The most recent estimates on the epidemic come from modelling using the UNAIDS SPECTRUM, which estimates the prevalence of HIV at 10.3% indicating a slight change in prevalence since 2010. The UNAIDS SPECTRUM further estimates that approximately 55,000 new infections will occur over the next year in Malawi[1]. More recent estimates from UNAIDS after modifying the prevailing models however, suggest the number of new infections to be much lower, between 26,000 and 36,000.

National sample survey data (DHS and BBS) and antenatal surveillance data indicate some heterogeneity in the epidemic. HIV prevalence in Malawi varies substantially over sex, age, urban-rural, geographic and socio-economic characteristics. Women are disproportionately impacted by HIV due to gender inequalities and low socio-economic status. Within the adult population there are also gender differences by age group: in women, prevalence is higher in ages 35-39 compared to ages 40–44 for men (noting that confidence intervals for these estimates are very wide due to small sample sizes).
Additionally, overall HIV prevalence is almost twice as much in urban communities (17.4%) compared to rural communities (9%).

Just like prevalence, the sub-population and locality variations described above for prevalence are most likely reflected in HIV incidence.

The 2010 MDHS estimates approximate very well the 2013 UNAIDS revised estimates which put incidence

[1]Joint United Nations Program on HIV/AIDS (UNAIDS) Malawi and National AIDS Commission Malawi. Modes of Transmission Analysis and HIV prevention Response. Distribution of new infections in Malawi 2013 and Recommendations for prevention strategies. 2014

amongst boys and girls aged 15 – 24 at 2.4% and 4.0% respectively[2], indicating that incidence in this population group has not been changing very much. It is conceivable that the current prevention strategy has significantly contributed to the changes in overall trends, but there is still need to reconcile the various estimates, preferably by conducting direct incidence estimation through population studies.

Although a range of prevention strategies exists such as condoms and partner reduction, they are not enough to stop the virus's spread. Many women are unable to negotiate condom use with their male partners and abstinence is not an option for women who are married, who want children or who are at risk of sexual violence. Furthermore, abstinence has been prove ineffective in young people.

Heterosexual sex is the primary mode by which HIV spreads in developing countries, and women have a heightened risk of infection due to a combination of biology and gender inequities. This is why women urgently need new HIV prevention strategies like microbicides that they can initiate themselves.

Summary: The Need for New Prevention Options

Defining microbicides and their importance

Microbicides are experimental medical products being developed to protect HIV-negative people from acquiring HIV during sex. Microbicides come in the form of gels, films, and even rings and are applied topically or inserted into the vagina. They are not yet available on the market for use in HIV prevention. Most microbicides contain antiretroviral (ARV) drugs used for HIV treatment that attack the virus at one of a number of points in the HIV life cycle. ARV medicines have extended and saved millions of lives across the globe — and these drugs are now being adapted to protect healthy adults from becoming infected with HIV. Multiple clinical trials have shown that ARVs can prevent infection when taken orally, in pill form, a prevention strategy known as PrEP (pre-exposure prophylaxis).

Some microbicides are being designed for women as vaginal products, and others in earlier development would be rectal products that both men and women could use. The International Partnership for Microbicides (IPM) and its partners such as Microbicides Trial Network (MTN) are focused on developing microbicides to protect women from HIV during sex with a male partner. Safe and effective microbicides could have a profound impact on the epidemic as part of a comprehensive prevention strategy that includes condoms, PrEP, treatment as prevention, male circumcision and one day, a vaccine.

Why Malawi urgently needs microbicides

Taking into serious consideration the fact that the HIV epidemic wears a female face, women are most affected by epidemic. Microbicides would give Malawian women and young girls a strong HIV prevention option as they will be able to decide on their reproductive health choices. Current HIV prevention options are not doing enough to slow the epidemic**.** The spread of HIV/AIDS continues to outpace the world's response to it: for every 3 people starting treatment in 2010, 5 people became newly infected. It is not feasible to treat our way to the end of AIDS.

Women and girls continue to bear the burden of the epidemic, especially in sub- Saharan Africa where approximately 6 in 10 HIV-infected adults are women. In some countries, HIV prevalence is three to eight times higher among women ages 15-24 than it is among men in the same age group. Current prevention strategies are therefore not enough to stop the spread of HIV —particularly among women.

The glimmer of hope is coming from microbicides

Decades of research into microbicides have resulted in proof-of-concept that ARV-based microbicides can offer women protection against HIV infection and potentially save millions of lives. In July 2010, the results announced from CAPRISA 004, a clinical trial in South Africa, showed that a vaginal gel containing the ARV *tenofovir* used around the time of sex reduces a women's risk of HIV by 39%.

However, subsequent trials looking at the microbicide gel were unable to confirm its efficacy because not

2 Joint United Nations Program on HIV/AIDS (UNAIDS) Malawi, May 2014 HIV estimates.

enough women in the trials used the candidate microbicide gel. For now, research into gels has been shelved, while longer-acting interventions requiring fewer acts of insertion are being studied.

Longer-acting microbicides, such as monthly vaginal rings containing the ARV *dapivirine,* are in advanced clinical development, while combination products, such as those combining two or more ARVs or an ARV with a contraceptive, are in earlier stages of development.

Malawi should invest in microbicide research

Currently, in Malawi, only the University of North Carolina (UNC) based in Lilongwe and the John Hopkins University in Blantyre are pioneering clinical trials in microbicides and other New Prevention Technologies (NPTs). IPM's ASPIRE trial looking at the vaginal ring is taking place in Malawi, among other countries. It is crucial that stakeholders within the national HIV response implementing the 2015-2020 National HIV Prevention Strategy and the 2015-2020 National HIV Strategic Plan ensure that the research agenda in NPTs and microbicides is strengthened. Currently research seems to be very weak as there are only a few institutions involved in such type of research.

While 2010 experienced a 5 percent increase in total global investment in microbicide research over 2009, [3] the $247 million funding levels in 2010 are still well below the annual $300 million amount recommended by experts to ensure an optimal research effort. As a result, promising microbicide research avenues are at risk of moving at a much slower pace than is warranted by the seriousness of the epidemic.

The Clinical Trial Process

The safety and efficacy issues

All microbicide candidate products must go through a rigorous program of laboratory screening and testing to ensure that they have an adequate safety profile before being tested in humans. Once a microbicide candidate satisfactorily passes these tests and additional safety tests in animals, it can be advanced through a series of human clinical trials. Clinical trials are carried out sequentially, first to determine the safety of the product (no significant side effects occurred) and then to test its efficacy (the ability of the product to prevent HIV infection).
Initial safety trials involve small numbers of women who participate under carefully controlled clinical conditions. Larger safety trials involving a wider range of women over longer periods are then conducted to gain broader safety data. Efficacy trials are then performed to test the ability of the microbicide to prevent HIV infection. These trials involve large numbers (hundreds to thousands) of women, and need to be conducted in locations where new HIV infections are occurring at a high rate. This allows researchers to better assess the difference in infection rates between those women who use the active microbicide and those who use a placebo.

Developing safe and effective microbicides for women in developing countries promises to be one of the great public health accomplishments of our generation.

Addressing ethical issues in clinical trials

All clinical trials, including microbicide trials, must be conducted according to international and national regulatory and ethics guidelines to protect trial participants' well-being, and guarantee the ethical and scientific integrity of the results.

Informed consent is the cornerstone of ethical trial conduct. Clinical research teams must ensure that all participants in microbicide trials have freely given their informed consent based on a clear understanding of the trial, including the risks and benefits of trial participation. The informed consent process must be consistent with International Conference on Harmonization Good Clinical Practice and local country guidelines. Informed consent is an ongoing process that requires periodic and ongoing discussions with participants to ensure their continued understanding of the trial.

3 HIV Vaccines and Microbicides Resource Tracking Working Group, "Capitalizing on Scientific Progress: Investment in HIV Prevention R&D in 2010",2011

In addition, as part of the standard of care guidelines for clinical trials, participants are provided with ongoing HIV and STI risk-reduction counseling, condoms, pre- and post-HIV test counseling, family planning counseling and treatment for curable STIs that are identified. Participants are also referred for support, care and treatment in the event that they become infected with HIV or require medical attention for any other condition.

Looking into IPM's vaginal ring

In general, vaginal rings provide slow, controlled release of drugs over extended periods of time. IPM's microbicide ring is a novel formulation. It is made out of a flexible silicone material with the ARV drug dapivirine dispersed uniformly throughout a matrix ring. In clinical studies to date, the dapivirine ring has demonstrated a good safety profile and has been well-tolerated among study populations. It has also been shown to successfully deliver the drug locally for a month or longer, with low systemic absorption. IPM began developing dapivirine as a microbicide in 2004 through a royalty-free licensing agreement with Janssen Sciences Ireland UC. This license has since been expanded to a worldwide rights agreement.

Key Policy Recommendations

- Malawi HIV researchers, scientists, CSOs and relevant stakeholders urgently need to come together to develop a microbicide research and implementation agenda. The National Research Council, National Health Sciences Research Committee (NHSRC), National AIDS Commission (NAC) and the Ministry of Health should agree on a national roadmap on microbicide and NPTs research and preparation for scale up. This is important because at present there seems to be a disjointed research agenda, hence harmonization of the research initiatives is very critical if Malawi is to reduce the brunt of the HIV epidemic.

- Microbicides will be critical to any comprehensive response to HIV/AIDS — one that takes into account the disproportionate impact of the epidemic on women — and a much needed tool in promoting women's sexual and reproductive health and well-being. Science has shown that ARVs can prevent HIV infection and save lives.

- We appeal to donors involved in financing microbicides and NPT research to provide more financial support towards HIV research especially in the field of microbicides. Realizing that potential and promises from microbicide clinical trials they require continued financial resources and political will to deliver promising innovations to the women who need them. Offering safe and effective microbicides for women in developing countries promises to be one of the great public health accomplishments of our generation.

- There is a need to develop an information and communication hub in Malawi to communicate effectively to the Malawi's general public on NPTs and microbicides. At the moment there is a huge knowledge gap and lack of awareness on HIV clinical trials, this status quo creates a room for rumours, misconceptions and a general lack of understanding on how clinical trials are conducted which could negatively impact on the research agenda. For instance the Ministry of Health, CSOs and the National Research Council could run adverts on TV, radio and popularize NPTs and microbicides across the local print and electronic media.

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