

MICROBICIDES:

Nice idea, but what are we doing for women now?

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Over the past decade, research into vaginal microbicides for HIV prevention has intensified. Investments have escalated rapidly as a product of intensive lobbying and scientific rationale that ostensibly seek to address female vulnerability to HIV through the development of a 'female controlled' HIV prevention technology.

This intensification, predominantly led by organisations headquartered in the global north, has included promotion of the idea that even a product with limited effectiveness would have an impact. In 2002, for example, the London School for Hygiene and Tropical Medicine modelled projected impacts of an assumed 60% effective first generation microbicide, calculating that 2.5 million infections would be averted over three years (Watts et al, 2002). The question as to whether or not a 60% effective technology could be effectively marketed for HIV prevention was not interrogated, but such modelling has given impetus to a sustained pursuit of microbicide technologies.

It is acknowledged that an effective and marketable microbicide is many years away. The potential for deadlines to be extended was underscored when the recent Phase III trial of a cellulose sulphate was terminated as a result of preliminary findings that use of the product was associated with increased risk of HIV infection. In a previous trial, involving around 800 sex workers in KwaZulu-Natal, nonoxonyl-9 was also found to increase the risk of HIV infection. The potential for further trial failures cannot be ruled out.

One immediate ethical implication is the need to re-consent all women on the remaining three phase III trials, to make them aware that products under trial may increase their risk to HIV infection. It is not clear as to whether this is being done?

In the context of current trials, if successful, the earliest that a moderately effective microbicide would be available is 2010, and it would take some years before the product is available in all countries. The potential for more effective products lies further into the future. There is no absolute certainty that a successful product will be found.

Investment in microbicide research

Investment in microbicides is substantial and is imbalanced in comparison to investments in the broader response to the epidemic. Table 1 illustrates the total investment in microbicides by public sector and philanthropic organisations over the period 2000-2005 – an investment that totals over US\$649,200,000 (HIV Vaccines and Microbicides Resource Tracking Working Group, 2005). The relative costs of this research into a single technology are high in comparison to funding of diverse contemporary HIV/AIDS interventions such as those of the Global Fund for HIV/AIDS, TB and Malaria (GFATM). For example, in the first five rounds of the GFATM some US\$1,337,290,793 was disbursed to sub-Saharan African countries for diversified HIV/AIDS and combined HIV/TB programmes (Global Fund, 2007). The

Table 1: Public sector and philanthropic investment in microbicides, 2000-2005

	2000	2001	2002	2003	2004	2005	Total
Public Sector							
US	\$34,600,000	\$61,300,000	\$75,300,000	\$78,800,000	\$92,000,000	\$99,300,000	\$441,300,000
Europe (incl EC)	\$700,000	\$400,000	\$5,000,000	\$10,600,000	\$29,900,000	\$37,800,000	\$84,400,000
Other (excl US, Europe)	\$300,000	\$100,000*	\$200,000	\$900,000	\$2,000,000	\$5,000,000	\$8,500,000
Multilaterals	\$100,000*	\$300,000	\$400,000	\$100,000*	\$200,000	\$200,000	\$1,300,000
	\$35,700,000	\$62,100,000	\$80,900,000	\$90,400,000	\$124,100,000	\$142,300,000	\$535,500,000
Philanthropic							
	\$29,400,000	\$3,400,000	\$24,800,000	\$16,900,000	\$18,100,000	\$21,100,000	\$113,700,000
Total	\$65,100,000	\$65,500,000	\$105,700,000	\$107,300,000	\$142,200,000	\$163,400,000	\$649,200,000
Total (ZAR @1:7)							4,544,400,000

* Estimated to be less than this amount. Source: HIV Vaccines and Microbicides Resource Tracking Working Group, 2005

comparative value of investment in microbicides is nearly half (48.5%) of this amount.

Requirements for intensified investment have also been articulated by various US-based microbicide lobbying groups as being US\$280 million per year over the next five years (International Partnership for Microbicides, 2005)

Microbicides and 'female control'

The broad argument made in global and local discourses about microbicides centre around the concept of 'female control' over HIV prevention via a vaginally inserted microbicide. This argument positions women as subordinate to men in sexual choice-making, and in decision-making about HIV prevention during sex – particularly a lack of control over choosing to use a male condom.

Whilst the argument of gender power imbalances may be supported through research, it does not follow that the factors inherent in female disempowerment over sexual choice-making and HIV prevention are readily addressed by microbicide technology. Covert use of microbicides in contexts of established relationships is unlikely to be sustainable, given that microbicides are likely to alter the sensation of sex, and discovery of covert microbicide use may accentuate risk of partner violence (Woodson, 2004). Covert use is also made more complex by the unplanned nature of sexual intercourse and the desire for intimacy and sharing in established relationships. In the context of established relationships such as marital and cohabiting relationships, covert use is problematic (Mantell et al, 2005).

It should also be noted that the concept of 'female control' advanced in arguments for microbicides is not a radical vision of 'female control', but rather, simply a vision where women potentially have greater control over prevention-related choice-making in relation to sexual intercourse.

One might ask: Does this vision of 'female empowerment' simply preserve the status quo of severely skewed gender power relationships? Specifically, should women be encouraged to stay in a relationship

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if their choice over HIV prevention so apparently and obviously compromised? Should microbicide research be so aggressively funded, when they potentially do little more than smooth over the cracks of female disempowerment in established sexual relationships? With this question in mind, it is relevant to consider whether assumed male dominance over barrier-method choice-making is immovable.

Male condoms

In South Africa, a great deal of progress has been made in expanding condom availability through efficient distribution logistics, which, in combination with widespread promotion, has seen overall year-on-year increases in condom use. Proportions of females reporting condom use at last sex are relatively high, and this proportion has increased in the 25-49 year age group over time (Table 2). In a context where males are more likely to use condoms because they are more likely to engage in higher risk sex (for example higher likelihood of having two or more partners in the past year and in the last month: Shisana et al, 2005) – the actual gap in male and female condom use may be smaller than it appears at first glance. This opens up the possibility that in the context of the advanced South African epidemic, condom use during sex has become normalized to the extent that there are not severe gender-power disparities in choosing to use a condom for HIV prevention.

Table 2: Reported condom use at last sex, 2002 and 2005

Condom use at last sex	Male	Female	Male/Female Proportion
2002			
Age 15-24	57%	46%	0.8
Age 25-49	27%	20%	0.7
2005			
Age 15-24	73%	56%	0.8
Age 25-49	35%	29%	0.8

Source: Shisana et al, 2002; 2005

Female Condoms

Female condoms are an existing and effective female-controlled barrier method for HIV prevention and have been available since the late 1990s (Vijayakumar et al, 2006). Whilst female condoms are as effective for HIV prevention, they are more complex to use than male condoms.

Female condoms have however been found to be acceptable to a proportion of women, with higher levels of acceptability amongst high-risk women such as commercial sex workers (Mantell & Hoffman, 2006). In a year-long study, adding female condoms to the prevention method mix of high HIV risk Zambian couples was found to reduce unprotected sex from 42% to 10% (Musuba et al, 1998).

Whilst female condoms cost \$0.58 per unit in public sector programming, in comparison to \$0.05 for male condoms, the product is considered cost-effective for HIV and STI prevention programming, particularly if the offset costs of HIV infection are taken into account (Marseille et al, 2001; Gutierrez et al, 2004). A lower cost female condom has also been developed and is pending approval. The female condom has been available in South Africa on a limited basis at selected clinics, with 2.4 million female condoms being procured in 2005. A cost-effectiveness analysis by Dowdy et al (2007) estimated that 16.6 million female condoms were procured, 10,000 HIV infections would be prevented in South Africa.

Investments in future expectations of an effective microbicide technology are distinctly imbalanced in relation to investments in female condoms, which are effective for HIV prevention and are available and programmable now. Is such skewed investment justified? Why has the world, and South Africa ignored the potential for the application of a technology that addresses a reasonable proportion of the gender power issues and risk factors of HIV infection prevention, which microbicide technologies set out to address?

Prevalence amongst SA women

By mid 2006 there were 2,810,000 women aged 15-49 estimated to be living with HIV in South Africa (Dorrington et al, 2006).

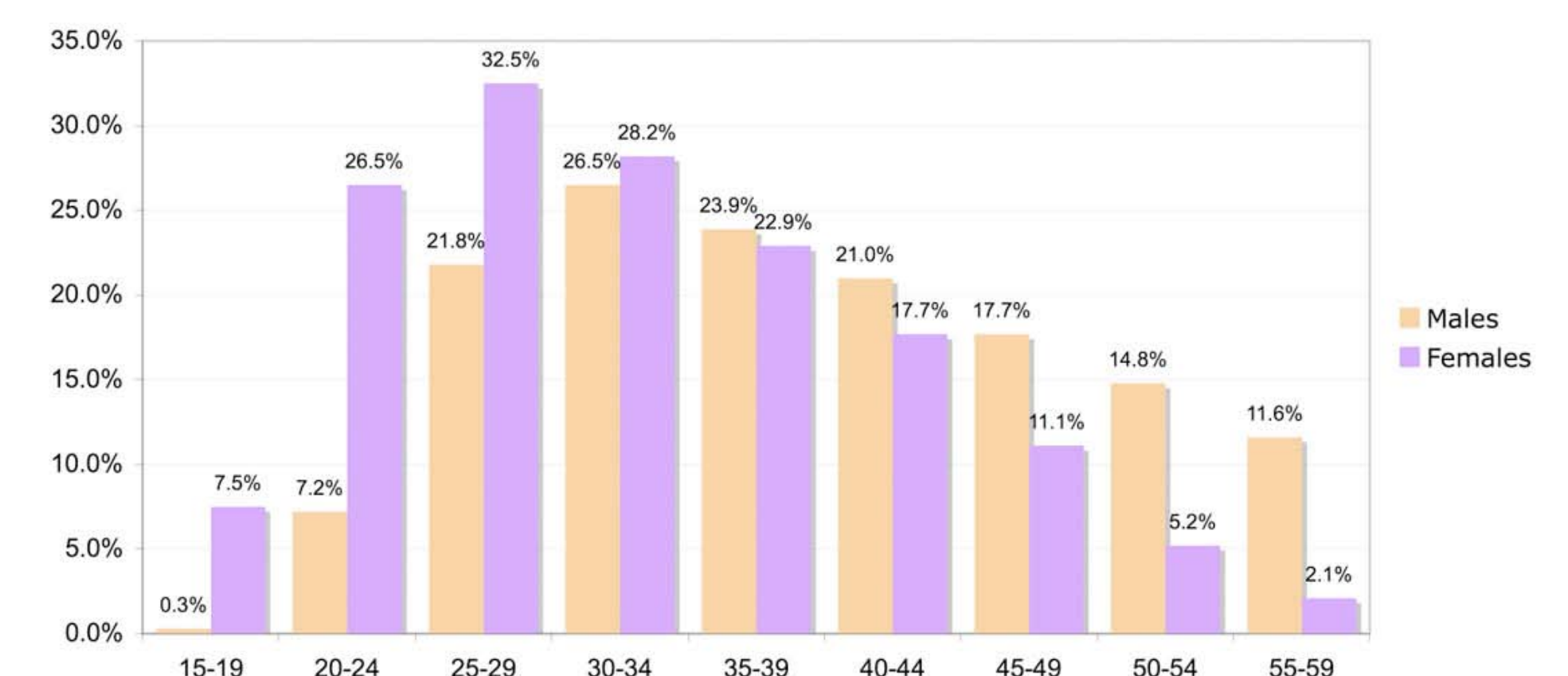
Data from the 2005 Nelson Mandela HSRC survey showed that the incidence of HIV peaked among women aged 20-29 years at 5.6%, more than six times the incidence found among men of the same age (0.9%).

Among youth aged 15-24 years, females account for 90% of recent HIV infections (Rehle et al, 2007). Using the ASSA 2003 projections, it is estimated that there will be approximately 3.9 million new HIV infections occurring in South Africa over the next seven years. If we conservatively estimate

Right: A list of completed, ongoing and planned microbicide trials in South Africa.

Sources:
www.mtnstopshiv.org
www.global-campaign.org
www.microbicide.org

Figure 1: Modelled HIV prevalence in South Africa by sex and age group, 2006



Source: Dorrington et al, 2006

that 60% of these will occur amongst women, this translates to 2.3 million female infections over the time period. The sheer number and scale of these infections is unlikely to be influenced any investment in microbicide technology development.

What are we doing for women now?

The vulnerability of girls and women to HIV in South Africa is disproportional. This vulnerability is a product of a range of intersecting biological, behavioural, cultural and socioeconomic factors that are not necessarily diminished by the introduction of a biotechnology that focuses only on reducing (but not eliminating) biological risk of HIV infection.

There has been little intensification of focus on the disproportional risks of HIV infection amongst girls and women in South Africa over the past decade, and whilst the 2007-2011 National Strategic Plan draws attention to female vulnerability, there is no specific programmatic focus identified to address this problem.

The contemporary milieu of vulnerability and risk of South African girls and women is starkly apparent yet poorly understood, and research in this sphere is dramatically underfunded. Whilst hope may be pinned on microbicides as a possible future panacea to this problem, there is an urgent need to take stock of the present, unclouded by imagined promises of future technologies.

Clearly, research into female vulnerability needs to be intensified with a view to developing pragmatic interventions that reduce the likelihood of HIV infection amongst both women and men. This includes shifting focus beyond dependence on biotechnologies for HIV prevention, with emphases on reduced exposure to sexual networks via strategies including delayed sexual debut, limiting partner turnover and avoiding concurrent sexual partnerships, being amongst the more obvious areas of focus. It would appear also that there is a need to intensify discourses about rights to protect oneself from HIV infection, and there is also potential to mobilise increasing awareness of HIV status that is occurring as a product of expanded availability and uptake of HIV testing. This includes provision of support for 'positive prevention' amongst people who test HIV positive.

It is time to ask some hard questions about the scale, direction and flow of HIV research funding. If there are further trial failures, will this be seen as a failure of 'proof of concept', or will research and funding simply be intensified? Can we ignore the urgent need to address incident infections amongst girls and women 'here and now'?

Clearly we have to use the resources we have at our disposal including existing technologies such as male and female condoms. But more than this, we need research investment to be directed towards the contemporary epidemic, and not towards imagined impacts of future technologies.

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Location	Candidate product	Sponsor	Phase	Status
Unidentified clinic, Johannesburg	ACIDFORM Amphora gel	CONRAD, USAID	Phase 1	Study and analysis completed
RHRU, Wits University, Johannesburg; Farnovs-Parexel Clinical Pharmacology Research Unit, Bloemfontein	Dapivirine (TMC 120)	International Partnership for Microbicides, Inc.	Phase 1/2	Clinical studies complete
Farnovs-Parexel Clinical Pharmacology Research Unit, Bloemfontein	Dapivirine (TMC 120)	International Partnership for Microbicides, Inc.	Phase 1	Clinical studies complete
UCT, Cape Town and MEDUNSA, Pretoria	Carraguard	Population Council CDC	Phase 2	Study and analysis completed
MRC, Durban; Unidentified, Johannesburg	PRO 2000	Division of AIDS, US National Institute of Allergy	Phase 1	Study and analysis completed
UCT, Gugulethu, MEDUNSA, Pretoria; MRC, Durban	Carraguard®	Population Council, USAID, Gates Foundation	Phase 3	Clinical studies completed
MRC, Hiabisa	BufferGel and 0.5% PRO 2000/5 Gel (P)	NIAD, Indevus, ReProtect	Phase 2/2B	Enrolling
Esselen Street Clinic, Johannesburg	Acylovir		Phase 3	Closed to accrual
RHRU, Wits University, Johannesburg; MRC, Durban; Africa Centre for Health and Population Studies, Mthubabab	PRO 2000	Indevus, MRC DFID Funder	Phase 3	Active recruitment
CAPRISA: Vulindlela, Durban Durban	Tenoflover/PMPA Gel	CAPRISA, USAID, LIFELab, Gilead, FHI, CONRAD	Phase 2/2B	Planned
UCT, Cape Town	Tenoflover/PMPA Gel	Microbicide Trials Network	Phase 2	Planned