



**NATIONAL CENTRE IN HIV
EPIDEMIOLOGY AND
CLINICAL RESEARCH**

Australian Biomedical Prevention and Microbicides Symposium

July 14 and 15, 2008

University of Sydney

Summary of Outcomes

Co-sponsored by:



**Global Campaign
FOR Microbicides**



Australian Government

AusAID

The Australian Federation of AIDS Organisations (AFAO) and the National Centre of HIV Epidemiology and Clinical Research (NCHECR) would like to thank the cosponsoring organisations for making this important symposium possible. In addition, we would like to acknowledge and thank the facilitators, panel presenters and event organisers.

List of Presenters

Jason Appleby	AFAO/Positive Life NSW
Jonathan Anderson	NCHECR, ASHM
Colin Batrouney	Victorian AIDS Council
Deborah Bateson	FPNSW
Louise Causer	NCHECR
Tony Cunningham	Westmead Millennium Institute
Basil Donovan	NCHECR
Janelle Fawkes	Scarlet Alliance
Andrew Grulich	NCHECR
Bridget Haire	AFAO
Elena Jeffreys	Scarlet Alliance
John Kaldor	NCHECR
Sue Kippax	NCHSR
Bebe Loff	Monash University
Maria McMahon	ACON
Lisa Maher	NCHECR
Jeremy Paull	Starpharma
Ian Ramshaw	Australian National University
Christina Richards	Independent health consultant
Michael Selgelid	Centre for Applied Philosophy and Ethics, ANU
Gilda Tachedjian	Burnet Institute
Dave Templeton	NCHECR
Handan Ward	NCHECR
David Wilson	NCHECR

PowerPoint presentations of most speakers are available. Please feel free to contact AFAO to obtain a copy.

Acronyms

ACON: Formerly the AIDS Council of New South Wales
AFAO: Australian Federation of AIDS Organisations
ANU: Australian National University
ASHM: Australasian Society of HIV Medicine
FPNSW: Family Planning New South Wales
NCHECR: National Centre in HIV Epidemiology and Clinical Research
NCHSR: National Centre in HIV Social Research

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Objectives

AFAO's policy position on HIV biomedical prevention is that research should take place in partnership with communities, information should be shared in a transparent and accountable manner. Any potential implementation of biomedical prevention technologies, should efficacy be established, must be very carefully negotiated with affected communities and positioned as an adjunct, rather than a replacement, to existing prevention interventions. Facilitating multi-sectoral conversation about biomedical prevention modalities is thus an important component of this work, and co-chairing the 2008 Australian Biomedical Prevention and Microbicides Symposium with the NCHECR was intended to realise this goal.

Symposium objectives were to:

- Provide an update on global microbicides and PrEP research, including emerging methodological challenges;
- Identify the possible PrEP research outcomes and plan for different scenarios;
- Identify research questions that will be unanswered by forthcoming phase III trial results;
- Consider issues of gender in the context of biomedical HIV prevention;
- Situate Australian research in a global context;
- Identify ways to conduct or support microbicides research in the Asia/Pacific region;
- Discuss the role of community and civil society in microbicide research; and,
- Establish objectives for a microbicides committee and ongoing work.

Australian Symposium on Microbicides and HIV Biomedical Prevention

On July 14 and 15, the second Australian Symposium on Microbicides and HIV Biomedical Prevention was held at the University of Sydney. There were 58 participants in attendance over the two days with representatives from (state) government, community, industry, and research.

PrEP

The first half-day segment of the program focused on pre-exposure prophylaxis (PrEP), which was situated in the context of the various prevention modalities that are undergoing investigation, together with those that have established efficacy (condoms, mother-to-child prevention packages, circumcision). The need for additional prevention options – particularly those that can be controlled by women and receptive sex partners – was highlighted.

Broad context-setting was followed by a detailed presentation on the cancelled PrEP trial in Cambodia. This accentuated the importance of collaboration with communities and the need for negotiation around fair compensation for trial-related harms and decent medical care for trial participants. It also raised the contentious issue that a partially effective HIV prevention tool, even if female-controlled, might have adverse consequences for people, particularly sex workers.

Whether PrEP could be an acceptable prevention intervention in Australia was then explored, using three hypothetical sets of trial results. Cost effectiveness, health promotion concerns, licensure issues, community demand and the potential imposition of PrEP upon sex workers were all discussed with relation to differing efficacy and side effect scenarios (90%, 60% or 30% efficacy, with side effects at 4%, 10% and under 2%, respectively). In summary, low-efficacy PrEP was rejected as something that would 'clutter and medicalise' people's lives, while high-efficacy PrEP was seen to offer benefits that would warrant complex strategic negotiations to ensure access for men at high risk of HIV. In them context of sex work, however, even high efficacy PrEP was seen as a potential threat that could undermine workplace condom culture.

Biomedical prevention

In the afternoon sessions, an overview of biomedical prevention research was provided, together with analysis of challenges including sample size calculations, adherence and product failure. The issue of new technologies facilitating HIV transmission, and the ethical and logistical consequences of this, was raised with regard to the microbicide products nonoxynol-9 and cellulose sulfate. Data from the recent Step vaccine trial - also halted because of increased transmission in the active product arm - was examined in detail by the Australian principal investigator, who argued that despite this significant setback, calls for HIV vaccine research to cease were misguided.

The role of circumcision for gay men and MSM in Australia, the potential for rectal microbicides and lessons that can be derived from the use of contraceptives that have application to the microbicide field were discussed in the mid-afternoon. New data showing some potential benefit from circumcision in men practicing insertive-only sex was presented, but the conclusion was that this section of the MSM populace was so tiny as to have minimal impact on incidence of HIV in Australian HIV. Safety, acceptability and separation of product use from sexual acts were among the issues raised from research into contraceptive vaginal devices that can be extrapolated to microbicides. Discussion of the potential social impacts of overt versus covert microbicide use, and the need for choice regarding whether or not an HIV prevention product has contraceptive action ensued. Regarding rectal microbicides, the importance of establishing rectal safety of vaginal products and of considering the role of anal sex in research aimed at heterosexual practices was emphasised in addition to the development of specific rectal products.

Vulnerability

Sex workers, people who inject drugs and the developing world context were the focus of this segment. The spectre of exploitation in international research was raised, with connections drawn between unrestricted foreign investment in South Africa and exploitative clinical research. The difference between occupational sex and recreational sex was emphasised by the Scarlet Alliance, with new, partially effective technologies posing a threat to established workplace cultures rather than offering useful choice. Meta-questions, such as whether new technologies will be available to those most at risk, and whether the burdens of biomedical prevention would be borne disproportionately by the disadvantaged, emerged in this session.

The day concluded with a spirited deconstruction of the argument that partner reduction and male circumcision are the only prevention modalities that ‘work’ in southern Africa.

Microbicides

Day Two began with an exposition of the sexual and reproductive health framework into which HIV prevention could be placed, and the argument was made that political will was the key factor both for improving women’s lives and increasing investment in microbicides. This was followed by a presentation from the Global Campaign for Microbicides outlining critical factors in microbicide advocacy, such as protecting the public interest, ensuring civil society engagement and keeping research accountable. The importance of government funding for microbicide research and development was emphasised.

In a presentation on mathematical modeling of microbicide impact, participants heard that widespread uptake of a moderately effective product is likely to have a greater epidemic impact than having a very high efficacy product, both for vaginal and rectal products. A further, paradoxical finding was that vaginal microbicides based on antiretroviral drugs may, under certain conditions, prevent more infections in men. This could occur as a result of women becoming infected while using the (partially effective) microbicide, then developing drug resistance as a result of continuing to use the product. A woman’s resistant virus, however, would be less fit and therefore less infectious than wild-type, potentially making infection of male partner/s less likely.

Regional opportunities and collaborations

Three key questions were posed regarding biomedical prevention research in the Asia-Pacific region: whether this research should take place and if so, what form it should take; and finally, what kind of role Australia should play. In addition, a presentation by NCHECR raised the issue of whether current microbicide safety studies are meaningful given the very short-term use of products.

With regard to the research collaborations taking place, a biostatistician from NCHECR discussed working with Gita Ramjee’s microbicide research group in South Africa. This was followed by a presentation from the University of Queensland that discussed AusAID-funded work on biomedical prevention in Papua New Guinea. The program was intended to assess acceptability, epidemiological impact and cost-effectiveness of male circumcision and other biomedical prevention technologies for future program implementation. Replete with hair-raising slides, this presentation highlighted the range of elaborate penile cutting practices that make the issue of circumcision particularly vexed in that country.

Australian pre-clinical and clinical research

The last four presentations focused on preclinical and clinical work on microbicide products under development in Australia. Starpharma reported on its unpublished studies of the safety of SPL7013 gel in men and sexually abstinent women, and made a case for products that have multiple disease targets, suggesting that the gel may be active against infections including herpes simplex and human papilloma virus as well as bacterial vaginosis. The Burnet Institute presented a pre-clinical testing algorithm for second generation microbicides, and argued that there is a funding shortfall for the translational research that is required to move potential products from the discovery

phase down the development path. This contention was supported by the delegate from ANU, who presented on a ‘natural’ microbicide – a peptide present in seminal fluid that has antimicrobial activity – which is not undergoing further development due to a lack of funding.

Forward planning

The remainder of the afternoon was broken up into two sections. A small panel consisting of an epidemiologist, a basic scientist and a health consultant each examined and provided critique of recommendations from the previous year’s symposium. Two key issues emerged from this discussion: firstly, whether advocacy for microbicides should be separate from advocacy for other biomedical prevention technologies and secondly, how to balance any fledgling advocacy movement with the demands of retaining adequate funding for core business in the current political environment.

Robust debate ensued. While one participant was keen on keeping microbicides separate, the overwhelming consensus was that microbicides should be considered as one of several biomedical prevention strategies. It was gratifying that participants considered seriously their capacity to contribute to an effort that would necessarily be small, tightly defined and targeted at achievable outcomes.

A steering committee was not nominated as part of the business of the meeting; however, the need for such a body to form, define itself and set goals was evident.

Outcomes

The objectives laid out for this symposium were reached to varying degrees. Please see comments below on how each objective was reached.

To provide an update on global microbicides and PrEP research, including emerging methodological challenges

This objective was achieved, by means of clear and comprehensive presentations detailing the range of biomedical prevention modalities, the state-of-play with regard to where the research is at and when results are expected, and discussing the challenges and trial closures. Much thanks is due to the NCHECR staff and specifically to John Kaldor for being so committed to this aspect of the program.

Identify the possible PrEP research outcomes and plan for different scenarios

There was excellent participant feedback on this section of the program, with several delegates commenting favourably on the process. PrEP is generally seen as the biomedical prevention technology most likely to have direct application in Australia and several delegates opted to come to the PrEP scenario section alone. The excellent facilitation of Jonathan Anderson was critical to the success of this segment.

Identify research questions that will be unanswered by forthcoming phase III trial results

Panelists in the PrEP scenarios identified the efficacy of episodic PrEP as a question that will remain unanswered when the next PrEP efficacy data is released. Other questions such as dosing and body size were not specifically mentioned, though issues of potentially increased toxicity for people who fall outside the ideal health status of the ‘healthy human trial participant’ were mentioned.

Consider issues of gender in the context of biomedical HIV prevention

This was imperfectly achieved. Different genital anatomy was discussed, as was the role of the anus in both heterosexual and homosexual sex, but the emphasis was decidedly biomedical so the social meaning of gender was largely ignored. This was due to the difficulty finding speakers who felt able to address the questions.

Situate Australian research in a global context

Speakers from NCHECR realised this objective.

Identify ways to conduct or support microbicides research in the Asia/Pacific region

It was a matter of questions being asked as to how this should be done rather than answers supplied, so while this has not been achieved, the conversation has begun.

Discuss the role of community and civil society in microbicide research

Presentations from Scarlet and AFAO achieved this aim, together with the subsequent discussions.

Establish objectives for a microbicides committee and ongoing work

This meeting clarified that there is a context for further microbicide advocacy – within a broader biomedical prevention framework – and some support for developing an agenda. It was also clear, though, that there was something of a leadership vacuum regarding taking this forward.

Challenges & Lessons Learned

The loss of support from the Australian Reproductive Health Alliance (ARHA) was a major stumbling block to organising this meeting. In 2007, ARHA was the principle organiser of the first symposium and undertook to carry the project forward. Subsequently it lost a major funding source, had to reassess priorities, and dropped microbicide advocacy from its agenda. AFAO and NCHECR picked up the pieces and carried the project forward, but much of the learning from the initial symposium was lost in the process and many wheels re-invented. This is a problem with situating responsibility within a single, relatively fragile organisation rather than distributing it more broadly.

Australia is also arguably better placed to provide leadership and capacity development in the MSM epidemics in the region, given the history of HIV in Australia, than a broader focus on general population sexual and reproductive health. This is not to reject the possibility of supporting a SRH focus, but to acknowledge the political reality that shapes Australia's efforts into the Asia-Pacific region.

Plans for Dissemination

The report from the symposium will be posted on the AFAO website and a copy of the report will be sent to all participants, as well as those who expressed an interest but were unable to attend. The results of the first symposium and the activities of the Australian campaign could also be presented at the upcoming IAS conference through an external meeting or reception for all interested delegates.

Concluding Remarks

Microbicide advocacy is going to be a difficult ‘sell’ in the Australia, given the concentration of the local epidemic among homosexual men, our small population and the structure of research funding. There is, however, significant interest and some demonstrated commitment to pursuing some form of advocacy in this area, though this is likely to encompass other forms of biomedical prevention in addition to microbicides. Australia has a capable research community that is already involved in microbicide research and development. It has a vibrant AIDS sector that has been recognized for its efforts in HIV prevention both domestically and within the Asia-Pacific region. What is needed at this point is a group of committed individuals with sound institutional backing to provide leadership and coordination to help take Australia’s contribution to the next level.