Global Campaign News – Issue #72
3 November 2006

Welcome to the *Global Campaign News*! The *Global Campaign News* is a forum for international exchange on microbicide activities and information with an aim to build a more informed and integrated movement for microbicide development and other prevention options against HIV and STIs. This and previous issues of *GC News* are available online at *http://www.global-campaign.org/gcarchives.htm*

In this issue:

Trials Watch

A closer look at incidence in microbicide effectiveness trials

Global

Several recent articles in GC News have made reference to "lower than anticipated HIV incidence" during effectiveness trials. Here, we take a closer look at what incidence means, why so many trials are seeing lower incidence rates than expected, and what the implications are for current and future trials.

Prevalence and incidence are two related, but different measures that describe the distribution of disease in a particular population. Prevalence is a measure of the number of total cases of a disease in a population at a certain moment in time For example, among women presenting for screening during a feasibility study at the Mtubatuba site in South Africa, the prevalence of pre-existing HIV infection was 50% (number of HIV positive women/number of total women being screened).

The incidence of disease is the number of *new* cases occurring in a population over a defined time interval. Incidence measures how quickly one sees new cases of infection or disease, whereas prevalence describes how many people total in a population are affected, regardless of *when* they become infected or sick. At the Mtubatuba site quoted above with a prevalence of 50% among screened women, the HIV incidence among those women enrolled was 12.6 infections per 100 person years. This means, among every 100 women they followed, 12 to 13 people became infected in the course of one year. [Note: the term "person-years" is a convention from epidemiology that allows researchers to annualize estimates of infection from individuals followed up for different lengths of time].

Thus it is possible to have situations of high prevalence but low incidence and vice versa. For example, the incidence of new cases of diabetes in a population may be only 1 per 1000 people per year (or 0.01% annually) but the prevalence of diabetes in a population could be 8 percent. The .01% incidence estimate includes only people

who were newly diagnosed with diabetes this year whereas the prevalence estimate includes these people as well as those already living with diabetes who were diagnosed in the past.

Likewise is it possible to have pockets of high HIV incidence (e.g. high rates of new HIV infections among intravenous drug users) in settings with an overall lower rate of HIV prevalence (e.g. less than 1 percent overall). Significantly, most measures of infection quoted by UNAIDS, National AIDS control authorities, and in the media are measures of HIV prevalence, not incidence.

Regrettably, there is no cheap, easy way to derive accurate estimates of HIV incidence. The most reliable way to establish incidence is to enroll HIV negative women in a cohort study and evaluate, using repeat HIV tests, the number of HIV infections that occur over time. For example, the Microbicide Development Programme conducted cohort "feasibility" studies to determine the incidence of HIV in the different populations being considered for inclusion in their current phase III trial of two concentrations of Pro2000. They found HIV incidence rates ranging from a low of 3.5 per 100 person-years in Mwanza, Tanzania to a high of 12.6 per 100 person-years in Mtubatuba, South Africa.

Cohort studies, however, are expensive to run and delay the start date of a potential trial for at least 6 months to a year while incidence data is being collected. In the interest of speed, some trial sponsors have tried to estimate the likely incidence in their participant population based on past prevalence estimates or data from previous studies about the observed ratio of prevalent to incident cases. As recent trial closures demonstrate, however, such approaches can yield misleading results. The field is currently discussing the pros and cons of different strategies for estimating the incidence of HIV.

Researchers in the Ghana Savvy trial estimated, for example, that there would be at least five infections per 100 person years of follow up in the placebo group (an HIV incidence rate of 5%), and that they would observe at least 66 incident infections during the trial. However, halfway through the study, an interim analysis found that only 17 total sero-conversions had occurred: nine on placebo and eight on *Savvy*. This translates into an HIV incidence of only 1.0% for *Savvy* and 1.1% for the placebo.

This incidence was dramatically lower than anyone anticipated, and the trial was closed on the recommendation of the Data Safety and Monitoring Board. Given the low rate of incident HIV infection observed, the DSMB concluded it would not be possible to recruit enough participants to answer the question of Savvy's effectiveness.

There are several possible explanations for the lower than expected incidence rates in effectiveness trials. The first is that the original estimate of HIV incidence could have been inaccurate, especially if not based on cohort data. As noted above, accurate estimates of incidence are difficult to come by. Also incidence can shift dramatically over time, especially in populations where men and women migrate frequently.

High rates of pregnancy among trial participants may also have contributed to lower rates of HIV acquisition. According to a presentation by Dr. Wes Rountree at M2006, women in the Ghana Savvy trial who discovered they were pregnant changed their sexual behavior in ways that reduced their risk of HIV. They engaged in sex less often, had fewer unprotected sex acts, and fewer partners. These behaviour changes together with high rates of pregnancy could partially account for the low rate of HIV incidence observed in the Savvy study.

Finally, just by participating in a prevention trial of this sort, a participant's risk of HIV acquisition may be diminished. Participants are getting the best available safer sex counseling and support, which is reinforced with every clinic visit. Participants also receive treatment for other sexually transmitted infections, which in turn indirectly decreases their risk of acquiring HIV. Thus, a good HIV prevention study itself can dramatically lower HIV incidence among participants. This is great news for the trial communities, but makes it more difficult to determine whether the candidate product is effective.

To address this issue, recruitment strategies are being modified to increase the likelihood of enrolling women at highest risk of HIV infection. Since younger women are often at the highest risk for new HIV infection, current efficacy trials are focusing on recruiting younger participants. Trial groups and sponsors are also working to explore the use of new assays and surveillance techniques to better estimate HIV incidence during screening and/or through pilot studies, in order to arrive at estimates of HIV incidence that are as accurate as possible.

For more information, and sources for this article, see:

Smart, T. *Microbicides 2006:* Are the microbicide clinical efficacy studies big enough? *NAM's aidsmap.org* Wednesday, May 10, 2006 full article at: http://www.aidsmap.com/en/news/DB107459-36CD-4868-9F24-0F36C4B00B88.asp

Skoler, S., Peterson, L., Cates, W. Our Current Microbicide Trials: Lessons Learned and To Be Learned, *The Microbicide Quarterly,* Jan-March 2006, Vol 4. No. 1. http://www.microbicide.org/microbicideinfo/reference/TMQ.Jan-Mar2006.FINAL.pdf

Cellulose sulfate trial updates from CONRAD

Global

CONRAD is currently making several adjustments to sites participating in the Phase 3 trial of cellulose sulfate (CS). The number of participants overall will remain the same. The changes in the trials are not a reflection of cellulose sulfate's safety or efficacy, but rather changes to accommodate lower than expected levels of HIV incidence. The decrease in certain regions indicates successful behavior modification due to counseling and condom use, and an intensive HIV/STI program for vulnerable women.

- ZIMBABWE: Beginning in February, CONRAD will initiate a Phase 3 trial of CS by enrolling 500 women at a site in Harare, Zimbabwe.
- SOUTH AFRICA: CONRAD is adding 500 women to a second clinic in Durban, South Africa in the first half of 2007.
- CHENNAI, INDIA: On 13 October 2006, enrollment in Chennai, India was halted due to a projected low HIV incidence in the region. All women enrolled will be followed as per protocol, i.e. for the duration of one year.
- BURKINA FASO: Initial plans to host a trial site of CS in Burkina Faso have also been halted due to HIV incidence rates projected to be as low as 1%.

Other trial sites are continuing per protocol i.e., Benin, Uganda, Bangalore, and the existing site in Durban. An independent data and monitoring committee will assess the data approximately half way through the trial which is expected to have an end date of 2009. For more information about the trials, please contact Lut Van Damme at lvandamme@conrad.org.

Science and research updates

Male genital hygiene affects risk of HIV infection

Excerpt reprinted from Reuters Health, 22 Sept 2006

Washing the penis regularly lowers the risk of HIV infection in uncircumcised men, and even among men who are circumcised, according to two papers in the Journal of Acquired Immune Deficiency Syndromes for September.

Male circumcision is associated with a reduced prevalence of HIV, according to Dr. Nigel O'Farrell, from Ealing Hospital in London, and colleagues. They now suggest that interventions to improve genital hygiene may also be effective in reducing HIV infection risk.

Specifically, they theorized that the presence of subpreputial penile wetness would increase risk, and that washing to keep the area under the foreskin dry would reduce risk. They define penile wetness as "the observation of a diffuse homogenous film of moisture on the surface of the glans and coronal sulcus).

Their study included 386 uncircumcised men residing in or near Durban, South Africa, who were free of genital ulceration or urethral discharge.

Clinicians who examined the men observed that half had some degree of wetness around the glans and coronal sulcus. Approximately 80% were judged to be slightly wet, 19% as wet, and 2% as very wet.

In contrast, only one of 36 circumcised men they examined had wetness.

Factors associated with penile wetness were younger age, low level of attained education, low income, higher lifetime numbers of sexual partners and not washing after sex.

The prevalence of HIV infection was 66.3% among men with penile wetness, versus 45.9% in those with no wetness. After adjusting for HIV predictors and confounders, the adjusted odds ratio (OR) for HIV infection was 2.27 when comparing men with wetness versus those who were dry. The degree of wetness did not affect the risk.

The authors note that the HIV prevalence among uncircumcised men without penile wetness was close to that of circumcised men (42.9%).

Although many of the factors associated with penile wetness were poverty-related, Dr. O'Farrell's group suggests that "information, education, and communication programs at a number of levels would be needed: for instance, encouraging washing related to sexual activity - precoital or postcoital or as an everyday life skill."

In the second Journal report, Dr. King K. Holmes, from Harborview Medical Center in Seattle, and associates interviewed 150 men living in Kenya regarding socioeconomic status and hygiene practices; 15% were HIV positive, and 97% were circumcised.

Components of hygiene associated with risk included amount of time spent in a bath (more than 10 minutes) and bathing immediately after sex.

Multivariate analysis revealed three independent risk factors for HIV infection: previous treatment for a serious illness (OR = 5.1, p = 0.02), circumcision (OR = 0.12, p = 0.04) and genital hygiene (OR = 0.41, p = 0.03).

J Acquir Immune Defic Syndr 2006;43:69-77,117-118.

Advocacy in Action

International Rectal Microbicides Working Group establishes steering committee

Global

Launched in 2005 by the AIDS Foundation of Chicago, CHAMP, and the Canadian AIDS Society with five people, the International Rectal Microbicides Working Group (IRMWG) is now a coalition of nearly 320 advocates, scientists, and policy makers from 33 countries working to advance the research and development agenda of rectal microbicides. In October, the IRWMG formally established its first steering committee with representatives from ten countries demonstrating a wide variety of experience, skill sets and backgrounds.

The steering committee members include:

Jonathan Berger, Braamfontein/South Africa
Manju Chatani, Accra/Ghana
Julie Davids, Providence, RI/USA
Jerome Galea, Lima/Peru
Dr. Pamina Gorbach, Los Angeles/USA
Bridget Haire, Sydney/Australia
Anuchit Jittrathanakul, Bangkok/Thailand
Dr. Rowena Johnston, New York City/USA
Rick Jones, Amsterdam/Netherlands
Jeremy Kwan, Kuala Lumpur/Malaysia
MarcAndre LeBlanc, Ottawa/Canada
Dr. Ken Mayer, Boston/USA
Dr. Ian McGowan, Los Angeles/USA
Kim Mulji, London/UK
Jim Pickett, Chicago/USA
John Shaw, San Francisco/USA
Roy Wadia, Vancouver/Canada

The IRMWG's mission is to promote and facilitate the ethical research and development of safe, effective, inexpensive and easy to use rectal microbicides for all those that need them. Homophobia, stigma, and a lack of awareness as well as resources have hindered the advancement of the rectal research agenda, but the IRMWG has brought much needed energy and focus to this area of work.

For up-to-date information and informational resources on rectal microbicides and the IRWMG, please visit www.lifelube.org. If you'd like to join the working group and sign up for its moderated listserve, please contact Jim Pickett at jpickett@aidschicago.org.

New Resources

HIV in the Middle East: Links between Islam and HIV prevalence

Middle East

The 21 October issue of the British Medical Journal features an article on HIV in the Middle East by Carla Makhlouf Obermeyer, scientist at the World Health Organization. Obermeyer starts the article with the following statement: "Prevalence of HIV in the Middle East is low but there is no room for complacency. The problem of HIV in the Middle East has elicited contradictory expectations and responses. Denial ('Not in our region') characterised the early phases of the epidemic." The author reviews what is known about the HIV epidemic in the Middle East and north Africa region. Current estimates by WHO and UNAIDS show that prevalence in the Middle East and north Africa region is approximately .2%, though there are concentrated epidemics (prevalence of 5% or more) among intravenous drug users in Iran and Libya. Obermeyer then provides an excellent set of links to information resources from Ministries of Health and multilateral organizations on the subject. Finally, Obermeyer examines the extent to which lower prevalence can be attributed to cultural factors, particularly those related to the practice of Islam and to gender. The entire article is available at http://bmj.bmjjournals.com/cgi/content/full/333/7573/851

AIDS Research Therapy: Short report on the Microbicides 2006 conference

Global

AIDS Research Therapy has just published a report back from the Microbicides 2006 conference that took place in Cape Town from 23-26 April 2006. The report, penned by prominent actors in the field, provides short summaries of the presentations and discussion in each of the four tracks--basic science, clinical science, social and behavioural science, and community mobilisation and advocacy activities. The full article is available at: http://www.aidsrestherapy.com/content/3/1/25. This is an Open Access article which permits unrestricted use, distribution and reproduction in any medium, provided the original work is properly cited, so please do share the article with your colleagues!

In Memoriam

In Memory of Dan Dunable

North America

Dan Dunable, longtime Atlanta AIDS activist, HIV treatment educator and microbicides advocate, died unexpectedly at home on 4 October. He was 51.

Dan grew up in Wheeling, West Virginia, and received a BS in Business Administration from West Virginia University. After relocating to Atlanta in the late 1970s, he enjoyed a successful career in electronic sales with Macy's, becoming one of the retail giant's leading performers. His career evolved in the mid 1990s after he became a volunteer with Atlanta's AIDS Survival Project and was subsequently tapped to manage the agency's Treatment Education Department. Under his direction, it became the most influential and respected resource of its kind in the southeast United States.

Dan excelled as an advocate in HIV treatment education, regularly attending scientific conferences and publishing articles read by people all over the world. Over the years he had been a member of the Southeastern Gay Men's Health Summit and Positive Living Conference organizing committees and served on the AIDS Research Consortium of Atlanta (ARCA) and Emory Hope Clinic community advisory boards. Most recently, Dan had been a Research Specialist with the University of Connecticut's Atlanta-based Share Project.

Dan is survived by a brother, Kerry, and his mother, Ellen. He will be deeply missed by family and friends as well as the HIV/AIDS community, for whom he had been a generous, dedicated link to information and resources for over a decade.

"Dan supported the Georgia Campaign for Microbicides from the very beginning. He volunteered at many of our functions and attended meetings regularly. He knew that microbicides were the next big thing in prevention. I will miss his input, guidance, and friendship" stated Terri Wilder, coordinator of the Georgia Campaign for Microbicides.

A memorial fund to benefit Dan's favorite AIDS organizations has been established. Donations may be forwarded to BeautyAid, Inc., 781 Dalerose Avenue, Decatur, GA 30030. www.beautyaid.org.

Follow these links to read a more personal story about Dan in the Atlanta Journal Constitution and several articles that Dan wrote for The Body.
http://www.ajc.com/metro/content/metro/obits/stories/2006/10/13/1014metobdunable.html
http://www.thebody.com/asp/dunable.html

Visit Omololu Falobi's memorial website

Africa

A website designed in memory of Omololu Falobi has just been launched. The web address is www.omololuinourhearts.org. The site is part of efforts by Journalists Against AIDS (JAAIDS) Nigeria to keep Omololu's vision and works alive. Visitors can view some of Omololu's pictures, access abstracts, speeches and post tributes and condolences. JAAIDS intend to keep improving and updating the site daily. Please feel free to send them relevant materials to: jaaids@omololuinourhearts.org or kingsley@nigeria-aids.org.

A tribute space has also been created for Omololu at: http://omololu-falobi.blogspot.com thanks to Tim France and the HDNET team. You can also find a link to a video interview he gave during the AIDS 2006 conference in Toronto.

We welcome your input and contributions for future issues! Please send emails to: info@global-campaign.org.
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