



The mission of the CFAR is to provide a multidisciplinary environment that promotes basic, clinical, behavioral and translational research in the prevention, detection and treatment of HIV infection.

#### NEWS BRIEF:

-To hear about the HPTN 052 study from Dr. Cohen, listen to his WUNC interview at: [http://wunc.org/tsot/archive/HIV\\_and\\_Sex.mp3/view](http://wunc.org/tsot/archive/HIV_and_Sex.mp3/view)

-Watch Dr. Cohen speak on the study at the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention (July, 2011 in Rome, Italy): <http://www.youtube.com/watch?v=P3DP0ntJfOs>

#### Our Issue Contributors:

**-Dr. Stuart Rennie** is Research Assistant Professor in Social Medicine and co-Chair of UNC's IRB for social and behavioral research. His current teaching and research interests focus on research ethics, public health ethics and medical ethics, particularly in the context of the developing world.

**-Dr. Christopher Hurt** is Clinical Assistant Professor in the Division of Infectious Diseases at UNC. His research interests include acute HIV infection, transmission of antiretroviral drug resistance, HIV phylogenetics, spatial epidemiology, and substance use's impact on HIV risk.

**-Dr. Ronald Strauss** is the Executive Associate Provost and Chief International Officer at UNC. He has held appointments in the School of Dentistry's department of dental ecology, the School of Medicine's department of social medicine, and the School of Public Health's department of epidemiology. He also serves as a dental clinician and advisor for the UNC Craniofacial Center.

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# Center for AIDS Research

## University of North Carolina at Chapel Hill

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### HPTN 052 Study Opens New Doors for HIV/AIDS Treatment Plans and Care

Dr. Myron Cohen, associate director of the UNC Center for AIDS Research, has had a very busy 30 years working in the field of HIV/AIDS medicine. As a Distinguished Professor of Medicine, Public Health, and Microbiology and Immunology at the University of North Carolina at Chapel Hill, he travels, sees patients, and leads research projects that explore the transmission and prevention of transmission of HIV, with a special focus on the role played by STD co-infections. Dr. Cohen received an NIH MERIT award in 2005 and is the author of more than 400 written scholarly works. He also received the Thomas Parran Award in 2005 for lifetime achievement in STD research from the American STD Association. He has extensive experience conducting research in countries such as Malawi, Africa and China. Dr. Cohen is the Chairman of the Scientific Advisory Board of the China CIPRA (at the China CDC) and is co-director of an NIH Ellison Fellowship Program at the National STD Center in Nanjing China.

At this summer's Global AIDS Conference in Rome, Dr. Cohen presented a paper on the HPTN 052 study, entitled "A Randomized Trial to Evaluate the Effectiveness of Antiretroviral Therapy Plus HIV Primary Care versus HIV Primary Care Alone to Prevent the Sexual Transmission of HIV-1 in Serodiscordant Couples". The study was a multi-site, randomized trial designed to "determine the effectiveness of two treatment strategies in preventing the sexual transmission of HIV in HIV-

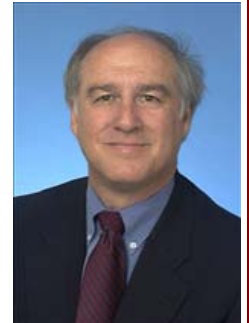
serodiscordant couples" (1).

According to the HIV Prevention Trials Network website, data from Africa and Thailand collected during the study shows that there is "a correlation between HIV viral load (blood levels) and HIV transmission. Specifically, the higher the viral load in the blood, the more likely the chance for transmission. Antiretroviral therapy (ART) reduces the viral load in the blood, as well as in genital secretions (for men and women), and the drugs can be detected in semen and vaginal and cervical secretions" (1). What this information implies is that taking ART "may make HIV-infected people less contagious" (1). These findings suggest that by taking ART, HIV positive persons could engage in sexual behaviors and still protect their partners from HIV infection.

This study has been met with media frenzy, and Cohen has been in high demand around the globe to speak about these incredible findings that could change the way that ART is prescribed and used. These results could serve as the starting point for a great shift in our current methods of ARV drug prescription and use.

This issue of our CFAR newsletter explores the possible ethical, clinical, and research implications of the HPTN 052 study. It includes several opinion pieces from members of our CFAR team and their thoughts on how this study could change the way we approach HIV/AIDS healthcare, prevention, education, and treatment in the future.

(1) [http://www.hptn.org/research\\_studies/hptn052.asp](http://www.hptn.org/research_studies/hptn052.asp)



### The Big Questions: Ethical Issues Inspired by the HPTN 052 Study by Dr. Stuart Rennie

This month, we asked Dr. Stuart Rennie, ethicist and HIV/AIDS researcher at UNC-CH, to share his thoughts on ethical issues that may stem from the newly released HPTN 052 study results. He shared these very thought-provoking questions with us:

**Clinical Questions:** Doctors armed with the knowledge of HPTN 052 are faced with something of a dilemma. When should their patients start ARVs? On the one hand, if they start them early, before the patient's immune system is compromised, is that decision really in that patient's interest? HPTN 052 showed there are some clinical benefits to the early initiation of treatment, but these have to be weighed against countervailing factors such as the possibility of drug resistance and drug side-effects. On the other hand, waiting until the patient has a lower CD4 count before initiating treatment will increase risks to that

person's (seronegative) sexual partner(s). On the internet, there are already worries expressed that 'treatment as prevention' will lead to clinicians treat HIV-positive persons more as disease vectors than as patients. Overall, HPTN 052 will force physicians to make some ethically tricky decisions in particular cases.

**Research Questions:** The ethics of some ongoing research studies on HIV prevention may be seriously affected by the results of HPTN 052. For example, some PREP studies involve serodiscordant couples. If the results of HPTN 052 are taken into account, then providing treatment to some of those HIV+ persons (depending on their CD4 count) should be the standard of care/prevention. It would seem to follow that the design of those studies is now unethical, according to the Declaration of Helsinki, or at least the design is open to debate. One could also go further,

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and ask if PREP studies make sense anymore post-HPTN 052. Why bother giving ARVs to seronegatives as an HIV prevention strategy? Why not just give all HIV+ persons ARVs early, so their at-risk partners do not get infected?

Health Policy Questions: Many ethical problems will be confronted when translating the results of HPTN 052 into policy. In theory, if all HIV+ persons were put on ARVs early worldwide, there would be a massive decrease in new HIV infections. In practice, it has taken decades to increase access to those who desperately need ARVs, especially in resource-poor countries. Despite decades of effort, the rates of HIV testing are still very low in many settings. The state of health infrastructure in many countries is fragile, including shortages of competent health care professionals. Given all this, and the current economic crisis, how can we reasonably expect rollout of early initiation of ARV treatment to have an impact as a prevention strategy? Who is going to pay for all this? Besides cost, there are questions of equity. Since we already can't give ARVs to everyone who needs it, now that we know more about treatment as prevention, we face some difficult rationing decisions. When distributing ARVs, should we give priority to those more likely to transmit the virus to others? That may seem justified from a public health perspective, but what about those who need ARVs but are less likely to transmit the virus, such as HIV-positive children and faithful HIV-positive sexual partners. In addition, there is the problem of coercion: should the policy on early initiation of ARVs be voluntary? Should patients be allowed to refuse early treatment if they do not want it? There are good (ethical) reasons to make the policy voluntary, but those in public health may want to limit the potential for refusal in order to have the greatest epidemiological impact.

These are all extremely important questions and issues raised by Dr. Rennie, and the UNC CFAR looks forward to an active dialogue among clinicians, researchers, and the community in the months to come on these topics.

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### A Study of Huge Magnitude: Thoughts on HPTN 052 from Dr. Christopher Hurt

The United Nations estimates that in 2009, 2.6 million new HIV infections occurred worldwide. In order to combat the spread of the HIV pandemic, a variety of behavioral and biomedical interventions have been proposed, but combinations of the two seem to hold the greatest promise for the future. UNC has long been a leader in studying the dynamics of the sexual spread of HIV (and other STIs) among both heterosexuals and men who have sex with men. Critical basic science and translational research by current and former UNC investigators examined the relationship between blood and semen viral loads during chronic and acute infection, and laid the groundwork for what has evolved into the "treatment as prevention" strategy. This approach posits that broad antiretroviral utilization by HIV-infected persons can reduce infectiousness to others, thus reducing overall incidence. Ecological and cohort data supported this concept, but it remained unproven – until now.

Earlier this year, the results of HPTN 052 were released, showing conclusively that the strategy of treatment as prevention works. This randomized, placebo-controlled study, chaired by our Infectious Diseases division chief, Dr. Myron Cohen, demonstrated that when the HIV-infected partner in a serodiscordant heterosexual couple is treated with antiretrovirals (ARVs), there is a 96% reduction in the risk of transmission to the uninfected partner. These results are clinically important for many reasons, but three warrant specific mention here. First, the magnitude of the effect was by no means subtle. Often in clinical research, the effect size is modest, leaving some question about whether or not it's worth it to implement the new treatment in practice. Here, with so large an effect, there is very little room to dither about efficacy. Second, it augments the data we already have about the benefits of having one's HIV infection controlled by ARV therapy. Large cohort studies like SMART and D:A:D have suggested that uncontrolled virus may predispose some HIV-infected persons to medical complications of chronic inflammation, such as premature coronary or cerebrovascular disease. While these prior data reflect individual-level effects of being treated, HPTN 052 shows the altruistic effects of therapy for others and for public health. For some patients (especially women) who put their loved ones' health before their own, the results may prove useful in discussions about the pros and cons of starting ARVs. Finally, 052 presents a powerful counterargument to proponents of pre-exposure prophylaxis (PrEP), another "treatment as prevention" strategy. Instead of treating persons already living with HIV, PrEP is used as primary prevention among those who are HIV-uninfected but at high risk for acquiring the virus. The preventive effect seen with the four PrEP major studies released to date (iPrEx, CAPRISA, TDF2, and Partners PrEP) has ranged between 40-80% – and much lower than the 96% seen in HPTN 052. It is clear that PrEP will have a specific niche in prevention – especially among marginalized, at-risk persons unable to negotiate for safer sex practices – but from a perspective of allocation of scarce resources, it makes much more sense to treat those already living with HIV than to provide medications to those not yet infected.

"Treatment as prevention" is not a panacea; it remains to be seen how these findings can be implemented on a large scale, and clearly we continue to have difficulties in this country with finding at-risk persons, testing them, and linking them to care. However, HPTN 052 provides critical evidence that those efforts have a potentially big payoff: reduction in the numbers of new HIV infections, and the beginning of the end of the pandemic.

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### "Couples Can Take Care of One Another" and more about HPTN 052 from Dr. Ronald Strauss

The HPTN 052 study has changed how HIV scientists, policy makers and clinicians approach HIV/AIDS prevention. In this study, individuals infected with HIV substantially lowered the chance that they would transmit the virus to their long-term uninfected sexual partners by taking antiretroviral medications early, while they were feeling healthy.

This was a large clinical study sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) and continues until 2015. The release of findings at the request of the data and safety monitoring board (DSMB) happened because the data was already indicating strongly that early antiretroviral medications taken by HIV-infected individuals quite dramatically reduced transmission to their uninfected partners.

Dr. Myron (Mike) Cohen directs the Institute for Global Health and Infectious Diseases at the University of North Carolina at Chapel Hill; he was the study Principal Investigator. This study also suggests that extrapulmonary tuberculosis can be reduced for the HIV infected participant by early antiretroviral treatment, as well.

One aspect of this study which is especially exciting to me is that it examines how couples – in long-term relationships – can help to avoid transmission and also can take care of one another. The study further supports that serodiscordant couples can have relationships in which transmission can be avoided. The implications for public health globally are enormous. We are so proud that a UNC scientist and a global team could implement a study that has changed how HIV will be understood and treated in the years to come.

To read more opinions on the HPTN 052 study, visit our CFAR CODE office blog at: <http://uncfcar.blogspot.com/>