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THE BODY COVERS: THE 15TH CONFERENCE ON RETROVIRUSES AND OPPORTUNISTIC INFECTIONS

## Expert Recommends "Prevention Cocktail" to Curb Epidemic of HIV Among U.S. Men Who Have Sex With Men

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*This is a transcript of a press conference that took place at CROI 2008, one of the most important HIV-related medical conferences of the year. In this transcript, Ronald Stall, M.D., of the University of Pittsburgh School of Public Health, examines the reasons behind the rebounding HIV epidemic among men who have sex with men in the United States -- and offers some ideas for how to stop it.<sup>1</sup>*



Ronald Stall, M.D.

Podcast coming soon!

**Ronald Stall:** Good afternoon. The conference asked me to do a literature review about what's driving the AIDS epidemic among gay men, MSM, in the United States. My talk will address three primary questions. The first is: Can HIV prevention work? The second is: Is it working on the community level? And the third is: What can we do to make things better?

The first question is easily answered. Can it work? The answer is yes. There have been two important meta-analyses that show that in randomized control trials, model HIV prevention programs reduce risk among gay men in very big ways. These studies have already been published, and give large effects sizes. For example, they include a 60% increase in using condoms for anal sex.

The next question: Are these programs actually working out in the real world? To answer this question, we turn to measures of HIV incidence among Americans and men throughout the industrialized world. We conducted an analysis, a systematic review of incidence estimates for MSM in Western Europe, the United States and Australia. The field tends to use proxy measures for incidence. That's because incidence estimates are very difficult and expensive to generate, and that may be especially the case among gay men. So you tend to see things in the literature about rising rates of unsafe sex, sexually transmitted infections, and so on.

The other problem with incidence estimates is that if you use any *one* estimate for a given city, it can't be generalized to a whole country, nor can it even be generalized to that city because of sampling issues. By using all of the incidence literature across the industrialized countries, we hope to miss or avoid many of the problems that emerge with proxy measures for incidence rates, or a stand-alone measure of incidence.

Our review, using very stringent review criteria, identified 20 different studies from 1995 to 2005, the protease era in Western Europe, North America and Australia, that yielded, in turn, 65 annualized incidence rates across this period.

On the international side, the rates of HIV incidence in Australia are significantly lower, at 1.1%, than we're seeing in North America or Europe, where those rates are about the same. The other interesting finding is that there were no increases or decreases in incidence rates among MSM in the industrialized countries from 1995 to 2000. Rates are not going up or down. The weighted mean incidence rate across all these countries is 2.5% per year.

Turning to the United States model: We looked at just the estimates for the United States. In community-based samples, which were the lowest rate of HIV incidence, compared to HIV alternative test sites or STD [sexually transmitted disease] samples, we calculated a mean incidence rate of about 2.4% per year.

The next thing we did was, we wanted to find out: What does 2.4% mean? What does 2.4%, in particular, mean over long periods of time? So we did a thought experiment, using a closed cohort of young gay men at the age of 18, none of whom were infected at 18, but calculated an incidence rate of infection of 2.4% per year as these men moved from age 20 to age 40. The model that we constructed yielded an estimate that at about age 25, about 15% of the men would be HIV positive; by age 35, about a third; and by age 40, about 41%.

The reason that we used the age of 40 as our cut-point is that AIDS was discovered a quarter of a century ago. These men would have had to have been, by definition, younger than 15 years of age. In addition, because we know that HIV incidence rates were stable from 1995 to the present, the vast majority of their sexual lives would have been in the context of this background incidence rate of about 2.4 or 2.5%.

We were kind of horrified that our model yielded prevalence estimates that high. And accordingly, we went back and looked at the largest samples published by the CDC [U.S. Centers for Disease Control and Prevention] of prevalence rates among men in the United States. The CDC just published, in 2005, a very large study of HIV prevalence rates, by age, in five American cities. What we find is that the model actually fits exactly what's going on in terms of HIV prevalence among gay men, at least in America's largest urban centers. This model that we are extrapolating based on the incidence rates, which culminates in an HIV prevalence rate of 40% at age 40, is not a prediction of something that may happen one day. We are describing epidemiological phenomena that are occurring all around us, and will continue to occur among young American men, if we do not find ways to lower HIV incidence rates further.

The last part of the talk focuses on how we can do a better job of HIV prevention. What I focus on are questions that gay men are asking about how to maintain sexual safety that are not being addressed by the proven programs that have yielded big effects sizes in randomized control trials. Among these are precise definitions of what is sexual safety nowadays, about maintenance of sexual safety over the long haul, about issues of community viral load.

For example, a very important analysis of African-American MSM by Greg Millett at the Centers for Disease Control showed that they actually engage in less risky behaviors than European-American gay men, and are less likely to use drugs. So if they're less risky and less likely to use drugs, where's all that virus coming from? Millett's answer, in a really wonderful analysis he did, showed that the rate of unknown HIV seropositivity -- [in addition to the] lack of access to antiretroviral care among African-American men who know that they are positive -- is so high that there is a much higher prevalence rate of men who are viremic in the population, which we call community viral load. In the context of men whose sexual access is limited by race, and whose sexual networks have such a high community viral load, even modest levels of sexual risk-taking can result in very high transmission rates, even though the men are doing the best they can to be sexually safe. So it's the context that matters with these guys, not their individual risk-taking behavior.

We also raised questions about the large investment that the United States has made in prevention science, but the challenge of getting this into the field so that community-based organizations can put this research to work. The amount of funding that's going into supporting HIV prevention in the United States is actually a rather small sliver of the entire budget. Holtgrave and colleagues at Johns Hopkins have shown that the amount that we're investing in HIV prevention only allows us to "run in place," in terms of winning the fight for HIV/AIDS prevention in the United States.

To summarize: What I've been able to show in the qualitative analysis is that there are multiple levels of prevention activity that are promoting risk among gay men, but that the interventions that we're using only operate at the level of the individual. They are not designed to operate in terms of context, [as in the case of] community viral load, or funding for getting prevention projects into the field, or policy, or treatment for comorbid conditions. Because we're only operating at one level, as opposed to the multiple levels that are driving risk, it's analogous to using AZT monotherapy to treat HIV infection: You can get effects sizes for short periods of time, but you cannot expect big effects for long periods of time.

I make an argument, and provide a design, for what I'm calling an "HIV prevention cocktail." What would a prevention cocktail look like? And how would we get this into the field? Those are the main points, but basically, at the HIV incidence rates we're already seeing in the published literature, we can expect an ongoing HIV epidemic among gay men that will yield high prevalence rates over time. The implications of this are so profound. We have got to find a smarter way to do HIV prevention in our country. Operating only at the level of the individual may not be the smartest

**Reporter #1:** What are the main points of your prevention cocktail?

**Ronald Stall:** I would help define what sexual risk is anymore. What are the risks of negotiated safety? What are the risks of positional strategies? Gay men are finding it difficult to use condoms every single time they have sex, for decades on end. This is true of men in general. The gay community has set up a whole series of strategies to allow men to dispense with condoms in particular kinds of relationships. But we don't have strong epidemiological data to show the long-term risks of these things.

The next point would be to continue with individual-level interventions, but to also mount interventions that would be at the level of context. For example, what would happen if we really did our best to enact strategies to diminish community viral load, particularly among African-American MSM communities? So that men who are positive are found, they are offered treatment for HIV infection, they are brought into the medical system, they are given help around maintaining sexual safety over long periods of time. So that the community viral loads in particularly vulnerable MSM communities are lowered. So that just a tiny little slip within the sexual networks of these communities does not result in HIV transmission.

Another point would be finding better ways to get proven HIV interventions into the field, so that the scientific investment that the United States has made, in terms of generating proven interventions, can actually be used by community-based organizations.

Another would be taking a good, hard look at the investment that we're making in prevention overall, and making a decision on the policy side as to whether this investment will generate the effects sizes that we need.

The final point would be to test what happens, to see whether or not the effects sizes we get by operating at multiple levels with the prevention cocktail are larger than when we operate only at the level of the individual.

Those are among the suggestions. There are others, as well.

**Reporter #2:** Did you see any relationship between post-exposure prophylaxis and reduction in transmission?

**Ronald Stall:** We didn't look at that.

**Reporter #3:** Are there any biomedical strategies that you have talked about with colleagues, or in research, that you would endorse?

**Ronald Stall:** The biomedical strategy that I think would make a lot of sense would be to try and do focused interventions that look at reducing community viral loads. HIV risk isn't just about our own individual behavior. It's about the level of HIV prevalence out in the communities in which we find our sexual partners; and the proportion of partners in those sexual networks that are viremic, and efficient transmitters. Effectively and efficiently finding HIV-positive people who are viremic and need to be brought into HIV treatment, and helping them maintain sexual safety over the long haul, would be an efficient use of our money. It's not just biology, and it's not just behavior; it's interventions that would conjoin the two.

By the way, on the Australian question: One of the interesting things is that the incidence rates of infection in Australia are 1.1%. If you do the same model that I did for the United States, the results you yield are that, by age 30, about 15% of the men would be positive, and by age 40, about 20% would be positive. So under conditions that have already been obtained in Australia among MSM communities, they would yield half the expected prevalence rates we're seeing in the United States, and one-third of what we're seeing among African-American MSM. We can clearly do a better job. I think we need to learn from our Australian colleagues, and invent some strategies that can help replicate these successes.

**Reporter #4:** Information was recently published about 30 Western countries and how they score in preventable death, and the U.S. came in last. Part of the rationale for that is our health care delivery system. HIV was not one of the

parameters in that study, but certainly HIV is preventable. If you can prevent HIV, you can prevent death from HIV.

I'm just wondering: In looking at other countries that do a better job in preventable death, what have they done in this same area that you're talking about, and how can we learn from them? And does it not all boil down to the way that urgent care and acute care and health care delivery in general is set up in our country? Is there any way it can be fixed, short of total restructuring of health care delivery?

**Ronald Stall:** Oh, dear. Well, I'm not running for President. [Laughter]

I think that's the question before us. How do we make it work despite our very low ranking in terms of outcomes? We're spending that money very inefficiently. We're spending among the highest costs of providing health care. Clearly something is wrong. And finding something to make the American health care system actually provide care to American people, help Americans stay healthy, and do so at less cost is, I think, the hundred million dollar question. If it were only a hundred million, that would be wonderful. Many people have worked on this. I don't have fast answers.

**Harold Jaffe:** Maybe I could ask the last question. Do you feel that the gay community -- and that's hard to define, obviously -- is as engaged in giving the same priority to prevention as it did earlier on [in the HIV epidemic]?

**Ronald Stall:** I think gay men are doing as well as any group of human beings could ever do, in view of the onslaught that's happened over the past quarter of a century due to this epidemic. Men are having a hard time staying consistently safe every single time we have sex. But that's true of all men. What we need to do is look at what's happening around contextual issues, and areas where we can help promote health among gay men that would increase the efficacy of our prevention efforts, and increase our ability to do a better job with HIV prevention. I don't think it's helpful to engage in a blaming-the-victim kind of analysis. There are much smarter ways to promote health in these communities than blaming victims.

## Footnote

1. Stall R, Friedman M, Marshal M, Wisniewski S. [What's driving the US epidemic in men who have sex with men](#). In: Program and abstracts of the 15th Conference on Retroviruses and Opportunistic Infections; February 3-6, 2008; Boston, Mass. Abstract 53.

*This transcript has been lightly edited for grammar and clarity.*

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