A. Personal Statement

I have a combination of field experiences and theoretical analysis capacities that prepare me for a role on the WHO HIV vaccine committee. From 1969 through 1986 I dedicated myself to advancing practical field epidemiology in the United States and in developing countries. During that time I had PAHO consulting positions in Chile, Bolivia, Uruguay, and Colombia. I served as a WHO consultant in smallpox eradication in India directing eradication efforts in Azamgarh district U.P. I spent 4 years developing innovative surveillance programs in Cali, Colombia within the local health department. And under US CDC and Mexican Secretariate of Health auspices, I developed innovative surveillance programs and trained a group of epidemiologists who went on to make those programs the cornerstone of highly successful disease control efforts in Mexico. In the US during that time I served as EIS officer and acting state epidemiologist in the state of Washington and I worked to supplement State of Michigan Surveillance programs with University of Michigan research programs and personnel.

Upon returning from Mexico in 1986 I dedicated myself to “developing theory that serves public health”. I made the decision to do that because in all of my work in Latin America, Asia, and the US I realized that the theoretical foundations for public health actions needed a firmer footing in infection transmission system theory, models, and data. Infection control actions were too often being undertaken with only a vague understanding of system effects on transmission dynamics. My collaborations with Ira Longini, who I supported both in Cali and at Michigan after he got his PhD, helped me develop a vision as to where infection transmission system analyses needed to go. I initially decided in 1986 to focus on HIV for building the needed theoretical foundation since I thought that having a definable contact was important. Although I continued to work on enteric and respiratory infection transmission systems and how vaccines worked with such systems, back in the late 80’s contact was defined in too abstract a manner for enteric and respiratory infection transmission systems to serve as model systems that could be related well to data. After a few years most of my research was directed to infections other than HIV. But now I am wholly rededicated to this infection.

Our initial work with HIV pointed out that acute infection played a crucial role in the transmission system. Nearly twenty years after that work, however, we are still ignorant about which cases are generating HIV transmissions. Cohen’s NEJM review this year graphed four papers that were relevant to how much transmission was coming from MSM during acute infection. Two of those were my work. But those two were only expressions of compatible ranges. Our great ignorance about who is doing the infecting is easy to understand. We diagnose infection long after it occurs and we don’t identify who the source case is. But I am happy to say that new stronger theory, new analytic methods, and above all, new data from deep sequencing viruses are giving us greatly increased power to determine the characteristics of the source cases of HIV infection. It is not our work with the Montreal data that is opening up this new knowledge. It is data from Michigan that is making the difference. The new methods will appear in Jan 2012 in Genetics by Erik Volz. These allow us to infer how many transmissions are coming from people who are diagnosed or undiagnosed, in different stages of infection, or are between different age, race, and geographic groups. Those new methods can calculate likelihoods for any coalescent given any transmission system model.

This is highly relevant to evaluation of HIV vaccines and decisions as to how to use HIV vaccines with different characteristics. The HIV transmission system has many complexities that markedly affect the assessment of vaccine effects. These complexities include patterns of partnership duration and concurrency, patterns of insertive and receptive behaviors, group specific contact patterns, and patterns of sex and partnership
formation by individuals over time. If vaccine effects are evaluated from trial populations experiencing these effects but where they are not integrated into the analysis, important vaccine effects could be missed. If the analytic models wrongly specify these effects, distortion of estimated effects will occur. The key to making good inferences in such a situation is to correctly assess the robustness of the inferences made to model misspecification and to formulate estimators that are robust.

In recent conference presentations we have demonstrated these effects. Two of those are now almost in press. Another from the recent Epidemics conference in Boston is in a state of revision and not yet submitted. What we have shown is that most MSM exhibit volatile or episodic risk behaviors. This volatility or episodic risk has strong effects on population risks, fraction of transmissions from acute infection, and the potential for vaccines with different effects on natural history of infection or transmissibility of any resulting infections to alter population transmission patterns. Most importantly, it makes the pattern of genetic relatedness in HIV strains provide a strong signal as to how vaccination has altered population transmission patterns. The signal should be far clearer that what would be perceived with current vaccine trial designs that are far more expensive.

While I do hope to play a significant role with the young people who are carrying on this work, I think my role as a senior investigator is more important at higher levels, such as on this WHO Vaccine committee. I think it could be important for this committee to be served by someone with both the long term understanding of HIV transmission system theories that I have as well as the understanding of the transmission system estimation of effects that I have. My service on QUIVER was a learning experience that has better prepared me to make positive contributions at this level.

B. Positions and Honors

Positions and Employment
1970-1972 Pediatrics residence at Harbor General Hospital, Los Angeles, CA.
1974 WHO consultant with the smallpox eradication program in India.
1975-1978 Diarrheal disease and nutrition investigations in Cali, Columbia with a position in the local health department and as a visiting scientist with CIDEIM.
1978-1983 Assistant Professor of Epidemiology, University of Michigan.
1983-1991 Associate Professor at the University of Michigan.
1984-1986 CDC fellow establishing a national field epidemiology and investigation service in Mexico
1991- Present Full Professor, Department of Epidemiology, University of Michigan.
1995- Present Founding member U of M Center for the Study of Complex Systems

Honors
1994 Howard Temin prize for best paper in Journal of AIDS
2005 Ken Rothman prize for best paper in Epidemiology

C. Selected relevant peer-reviewed publications (in chronological order out of about 150)


D. Research Support

Ongoing Research Support

NIH 04/01/08-06/30/13
“HIV Risk Dynamics, Genetics Patterns and Control”

The major goal of this project is to develop new methods to use HIV sequences from a population to help infer key transmission system parameters such as transmission rates by time since infection as well as the expected outcomes given different policies for infection control. Sequences gathered under the Quebec genotyping program are to be analyzed using these methods in order to inform particular policy decisions such as switching to early treatment.

Role: Principal Investigator

NIH 07/01/11-06/30/13
Supplement to study deep sequences as a basis for HIV surveillance and for use in the methods developed by Volz to estimate fractions of transmissions from different classes of individuals by fitting coalescent models