

Letter to the Editor

Data-Free Modeling of HIV Transmission in Sub-Saharan Africa

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To the Editor:

In 2004, we suggested that a major challenge to mathematical modelers was to “. . . construct a model that involves only penile–vaginal sex and that reproduces the epidemic curve seen in the 11 southern African nations that account for half of the disease on the African continent” (p. 786).¹ French et al² respond with a model that meets many of the specifications we detailed, and they also develop a model for HIV transmission through contaminated needles and syringes in healthcare settings. From their simulations, they conclude that an HIV epidemic based on sexual transmission was easy to start and sustain with estimates of transmission probabilities and partner change they deem “plausible.” In contrast, they argue that the transmission probabilities and number of injections with reused equipment required to generate an epidemic are “unfeasibly high.”

Although their modeling technique may be questioned, primarily for the limitations of compartment approaches, the most fundamental concern is their estimation of parameters. In their simulations, French and colleagues allow the per-contact heterosexual transmission probability to vary between 0.0025 to 0.015 (their Fig. 1). They cite an unpublished, privately communicated synthesis of transmission probabilities³ as the source for this range. However, the most rigorous estimate of the per-contact heterosexual transmission probability in sub-Saharan Africa is 0.0011 based on data from monogamous couples in Rakai, Uganda.⁴ This estimate is well below French and colleagues’ lower bound and below the level at which any epidemic could be produced in their model even with very high partner change rates. Transmission probability estimates derived from studies of prostitutes or their clients in sub-Saharan Africa have many uncontrolled confounders yet include values nearly an order of magnitude less than French and colleagues’ lower bound.⁵ Even the Rakai estimate of the sexual transmission probability may be exaggerated because sharing of syringes and razor blades (for making incisions to administer herbal medicines) within households is widespread in eastern and southern Africa.^{6–11} Such nonsexual blood exposures can act in concert with sexual exposures in married or cohabiting couples

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and have not been controlled for in published estimates of heterosexual transmission probabilities. Furthermore, estimated transmission probabilities based only on seroconversion in serodiscordant couples are biased upward, because 13% of couples in a Zambian cohort thought to have transmitted HIV within the partnership on similar grounds had genetically unrelated infections.¹²

French and colleagues also used estimates of sex partner change (1.5–4 new partners each year; their Fig. 1 and Table 1) much higher than observed in probability sample surveys of sub-Saharan Africans. The sources cited for their partner change estimates actually include no explicit basis for these estimates aside from “inspection” of unreferenced data¹³ and nonempiric values “to generate the scale of epidemic observed.”¹⁴ The number of sex partners in the prior year cannot be used to estimate annual sex partner change, because many partnerships, especially marriages, last longer than a year.

Publicly available data from the national probability sample household Demographic and Health Surveys (www.measuredhs.com) in 11 eastern and southern African countries indicate levels of partner change that are dramatically lower than the parameter estimates used by French and colleagues. A reasonable proxy measure of annual partner change is the number of nonmarital partners reported by men in the previous year (keeping in mind that sampled women consistently reported fewer partners than men). The mean for each survey is substantially below the lowest estimate examined by French and colleagues (Table 1). These surveys are current, but they concur with findings over the last 15 years.^{15,16}

Some similar problems obtain for the model proposed by French and colleagues for medical injections. In this case, French and colleagues use transmission probabilities for medical injections that encompass the range of published estimates.^{17,18} The problem here, rather, is that the topic has been inadequately studied. The proportion of used needles in medical settings that have detectable HIV varies from 0% in needles that had been boiled at several Ethiopian clinics¹⁹ to 33% of needles previously used by HIV-

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TABLE 1. Mean Number of Nonmarital Sex Partners in the Prior Year Reported by Male Respondents in the Demographic and Health Surveys* in Eastern and Southern Africa

Country	Year	N	Mean
Ethiopia	2000	2,607	0.23
Kenya	2003	3,573	0.37
Lesotho	2004	2,789	0.77
Malawi	2000	3,091	0.37
Mozambique	2003	2,893	0.78
Namibia	2000	2,929	0.82
Rwanda	2000	2,715	0.11
Tanzania	2003–2004	5,650	0.53
Uganda	2000–2001	1,961	0.34
Zambia	2001–2002	2,143	0.51
Zimbabwe	1999	2,607	0.41
French et al's range of average annual partner change	—	—	1.50–4.00

*Surveys involving national probability samples of adults (generally ages 15–49) residing in households and high response rates (www.measuredhs.com).

infected Cameroonians for intravenous injections.²⁰ Clearly, empiric experience is inadequate to understand where the true risk lies or to assess its heterogeneity or multiplicative effect on other modes of transmission. In addition, French and colleagues' allowing only one "spread" infection from a contaminated needle or syringe precludes the possibility of multiple infections arising from a single reused needle or syringe or from contaminated multidose medication vials and rinsing pans.¹⁷ Other types of blood exposures may also be involved with HIV transmission such as blood transfusion, dental procedures, circumcision, and induced abortion.

French and colleagues' model for heterosexual transmission is similar to prior modeling efforts for sub-Saharan Africa in which parameter estimates exceeded those in the empiric record.^{21–24} An important contribution of these efforts has been to demonstrate the level of sexual contact and sexual transmission that would actually be needed to "generate the scale of the epidemic observed." The disjunction between those parameters and the ones observed is cause for reconsideration.

The real value of mathematical models is in raising questions about the phenomenon modeled and identifying gaps in empiric knowledge.²⁵ Indeed, the modeling of HIV transmission in sub-Saharan Africa highlights important gaps in epidemiologic evidence. To determine modes of transmission with confidence, researchers should trace incident cases and uninfected controls' contacts about the full spectrum of time- and place-specific sexual and nonsexual exposures and sequence infected persons' HIV isolates.²⁶ Such strategies are the most informative and are usually the *first* used for investigating emerging infections,^{27–30} including HIV in the United States in the early 1980s^{31,32} as well as other endemic infections such as tuberculosis.^{33–35} In parallel with more comprehensive empiric evaluations, modelers might consider a more comprehensive, multifactorial approach. Not only are multiple modes and their interactions important, but the much discussed presence of adjuvants such as sexually transmitted infections (especially herpes simplex virus type 2)^{36,37} or of variable transmission probabilities such as the those potentially associated with the high viral loads of acute HIV infection^{38,39} need to be considered. For example, Gray and colleagues⁴⁰ constructed a model incorporating empirically based estimates of transmission probabilities and variable viral loads from their Rakai study⁴ to assess the impact of antiretroviral therapy and HIV vaccines on transmission.

Whatever questions may be raised, French and colleagues' simulations advance an important discussion and may serve as a stimulus to new investigations, both empiric and theoretical, that deal with an increasingly complex and recalcitrant problem.

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