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Interaction of mathematical modeling and social and behavioral HIV/AIDS research

Susan Cassels¹ and Steven M. Goodreau²

Susan Cassels: scassels@uw.edu

¹ Departments of Epidemiology & Global Health, 325 9th Ave, Box 359931, Seattle, WA 98104, Tel: (206) 897–1758

² Department of Anthropology, University of Washington

Abstract

1. Purpose of review—HIV is transmitted within complex biobehavioral systems. Mathematical modeling can provide insight to complex population-level outcomes of various behaviors measured at an individual-level.

2. Recent findings—HIV models in the social and behavioral sciences can be categorized in a number of ways; here, we consider two classes of applications common in the field generally, and in the last year in particular: (1) those that explore significant behavioral determinants of HIV disparities within and between populations; and (2) those that seek to evaluate the potential impact of specific social and behavioral interventions.

3. Summary—We discuss two overarching issues we see in the field: the need to further systematize effectiveness models of behavioral interventions, and the need for increasing investigation of the use of behavioral data in epidemic models. We believe that a recent initiative by the National Institutes of Health (NIH) will qualitatively change the relationships between epidemic modeling and sociobehavioral prevention research in the coming years.

Keywords

Interventions; effectiveness; behavioral data; parameterization

Introduction

Mathematical modeling has the power to substantially inform and enhance social and behavioral HIV prevention research. HIV, like all infectious diseases, is transmitted within complex biobehavioral systems. As a result, there are numerous examples of where the population-level outcomes of various behaviors cannot be determined intuitively from individual-level data, but where modeling can provide insight. For example, temporally overlapping relationships ("concurrency") and sexual role versatility have both been shown to potentially increase epidemic potential without disproportionately increasing individual risk [1, 2]. In other cases, modeling can clarify the overall effects of behaviors that have multiple countervailing impacts; for example, serosorting may decrease the contacts that an HIV-negative man has with known positives, but perversely increasing those he has with undiagnosed positives, who are more likely to be in the acute stage and highly infectious. Models are particularly useful at providing insight into potential impacts of behavioral interventions that are difficult or impossible to evaluate empirically for reasons of time, logistics, or ethics. Of course, for models to be useful, they must be based on good social and behavioral research.

HIV models in the social and behavioral sciences can be categorized in a number of ways; here, we consider two classes of applications: (1) those that explore significant behavioral determinants of HIV disparities within and between populations; and (2) those that seek to evaluate the potential impact of specific social and behavioral interventions. We briefly review publications from the last year in each of these categories while paying attention to model type and behavioral assumptions. We then discuss two overarching issues we see in the field: the need to further systematize effectiveness models of behavioral interventions, and the need for increasing bi-directionality of influence between social and behavioral HIV researchers and epidemic modelers. We end with a brief discussion of a recent initiative by the National Institutes of Health (NIH) that is likely to qualitatively change the relationships between epidemic modeling and sociobehavioral prevention research in the coming years.

Identifying important components of transmission systems

Since the groundbreaking modeling work on core groups [3, 4] and selective mixing [5–7], mathematical modeling has played an important role in identifying or suggesting important social and behavioral components of sexually transmitted infection (STI) transmission dynamics [8]. Recent work further explores the consequences of specific behaviors within and between populations. Below we review three recent papers that focus on a range of behaviors and populations, namely: partnership concurrency and assortative mixing by race in the United States (US); international migration in generalized epidemics; and widowhood in Zimbabwe.

Early mathematical models suggested that relational concurrency can dramatically increase the size of an epidemic, even without increasing the total number of partnerships in the population [1, 9]. Recent advances in dynamic network-based simulation models allow more nuanced examinations of the population-level effects of these behaviors, such as whether observed concurrency and partner mixing by race in the US could explain persistent racial differentials in HIV prevalence [10]**. This model considered the "reachable path" (modeling infectivity as 1, such that all serodiscordant contacts led to infection) under different behavioral scenarios. Although the biology was stylized, the behavior was parameterized using data on relational structure and timing (i.e. assortative mixing, concurrency, and partnership duration). The source data suggested that day-of-interview prevalence of concurrency was ~3 times higher for African-American men than Caucasian-American men, and that about 95% of relationships were same-race (black vs. white only). In their model, concurrency doubled the reachable path and produced a 2.6-fold racial disparity in epidemic potential [10]**. Two other articles either recently published or in press as of this review re-visit the concurrency hypothesis in light of increased knowledge of acute infection [11, 12]. Eaton et al. (2010) found that the growth rate and endemic prevalence of an HIV epidemic are heightened by increasing concurrency, and that primary infection amplifies the importance of relational concurrency [12]. Goodreau et al. [11], using data on prevalence and patterns of concurrency from Zimbabwe, find that an HIV epidemic can be sustained when both observed levels of concurrency and elevated transmissibility during acute infection were present; if either is eliminated, the epidemic dies out.

Other recent work has continued the thread of exploring the importance of behaviors among and between specific sub-populations to the epidemic as a whole. For instance, researchers from the Netherlands questioned whether international migration from high-endemic countries could significantly affect HIV prevalence among the general heterosexual population in low-endemic countries [13]. Their deterministic compartmental model found that migrants could not easily affect prevalence of HIV among Dutch natives, given moderate sexual risk behaviors, small numbers of migrants, and low rates of mixing with the native-born. However, immigration of HIV+ individuals accounted for a high proportion of

total infections in the Netherlands, since heterosexual transmission is occurring mostly within migrant communities [13]. Similar questions could be asked in many different contexts. Indeed, a simple multiplicative model was used to inform the recent decision to remove HIV infection from US immigration screening, concluding that there is a lack of evidence suggesting that immigration to the US significantly affects HIV incidence [14].

In some communities, widows and widowers may also be an important target population to reduce HIV transmission. One recent study [15] found that widows in Zimbabwe had high HIV prevalence (61% for widows; 54% for widowers), and widows were more likely than married women to have had >10 partners in the past 3 years. The study employed a deterministic compartmental model to illustrate the importance of widow behavior in ongoing HIV transmission, and compare the magnitude of the effect to other important behavioral risks and potential interventions. Dynamic simulations suggested that 8 - 17% of infections over 20 years could be attributed directly or indirectly to widow sexual activity.

Modeling social and behavioral interventions

Ultimately, the goal of mathematical modeling in social and behavioral research is not only to understand the nature of HIV transmission dynamics, but also to clarify how they can be most effectively targeted to prevent infections. Here we consider recent papers in three areas within this vein.

A recent modeling paper by a group at the World Health Organization provided a compelling scenario in which annual and universal HIV testing, and immediate antiretroviral therapy (ART) after diagnosis, could be an effective intervention [16]. There were many responses to the model regarding the modeling strategy and plausibility of the intervention. One paper revealed unintuitive effects of the proposed intervention under various scenarios about the timing of intervention, overall population risk, and rates of mixing [17]**. Results of their deterministic, compartmental model generally supported the conclusion that an aggressive test-and-treat strategy has the potential to substantially reduce HIV transmission. However, they also illustrate that in certain contexts similarly large reductions could be achieved with substantially less ambitious interventions. In other contexts, treatment strategies run the risk of extending the years of treatment per person without reducing incidence – simply exacerbating the problem while ART load increases. This model illustrates when and why the universal test and treat intervention might work, when it might fail, and when less effort might be required to obtain the same result.

In the past year two models were simultaneously published to examine whether preferentially selecting sex partners with apparently concordant HIV status ("serosorting") is a useful prevention strategy. Serosorting remains a highly controversial intervention strategy for HIV-negatives even though it is widely practiced [18, 19]; thus modeling is an important tool to understand the unintuitive ways that serosorting behaviors may or may not be a part of a harm-reduction strategy. One found it to be partially effective in the context of Seattle, Washington [20], while the other suggested it may be a harmful strategy generally [21]. The results at first glance seemed contradictory, but the two modeled different populations, with Seattle having a much higher rate of testing than is found in many other locations. The models actually had similar conclusions: if the percent of MSM unaware of HIV infection was greater than 20% or if testing were less frequent than reported in the Seattle area, serosorting may be detrimental [22, 23]. Indeed, a recent report using data from 21 US cities found the prevalence of undiagnosed HIV infection among MSM to be well above 20% in most cities [24], suggesting that serosorting is not a good harm-reduction strategy for MSM in most communities. Interestingly, the report also suggests that the proportion unaware of

their infection is lowest in Seattle, at 15%; at this level, both models suggest that serosorting might be beneficial.

Behavioral modeling can also be important in biomedical interventions given the importance of issues like adherence, uptake, and risk compensation to long-term effectiveness. For vaginal microbicides, there was a need to understand how alternate sexual behaviors not targeted in microbicide trials could fuel transmission. Before the successful CAPRISA 004 randomised trial, which showed that a vaginal antiretroviral microbicide reduced risk of HIV infection by 39%, many trials of microbicides failed. McGowan and Taylor used a simple multiplicative model to suggest that receptive anal intercourse could significantly reduce the power of a study to detect whether microbicides were effective prevention intervention [25]*. Although this behavior was not always collected or reported in these trials (0.4 - 0.5% of women reported anal sex within the last 30 days in the CAPRISA trial), heterosexual anal intercourse is not uncommon. Their model predicts that if 2% of all acts were anal, and rectal transmission probability was 10 times higher than vaginal, effectiveness of a trial drops by 33% and power drops from 90% to 72% [25]*. Simple multiplicative models can be very useful for broad qualitative understanding of important determinants of a successful intervention [26, 27].

Finally, Reidy and Goodreau recently published a deterministic, compartmental model that evaluated the role of commercial sex venues (CSVs) in the HIV epidemic among MSM, using data from Seattle, Washington [28]. The uniqueness here lies in that they were able to consider the impacts of a structural intervention on community outcomes via individual behaviors. Approaches to regulating CSVs have been contentious issues since the very beginning of the HIV epidemic. However, modeling work on the impact of closure or other interventions has been hampered by the fact that it is difficult to know what men would do in the absence of such venues – have fewer contacts, move their contacts to other settings, or somewhere in between. The authors built their model around behavioral data collected by Reidy on patrons' activities in the CSVs and elsewhere that demonstrated that in the modern internet era, the same men tend to engage in much more risky behaviors when they use the internet to find partners than CSVs. All reasonable scenarios about reductions in contacts vs. replacements in contacts suggested that further closure of such venues would likely generate negligible effects on the epidemic or possibly increase it slightly. It should be noted that the modeling work was conditioned on the prevention activities that already occur in such settings; the potential impact of increasing or decreasing efforts currently placed on interventions within CSVs was not evaluated.

Future directions

Measuring effectiveness of social and behavioral interventions directly is often difficult or impossible, but mathematical modeling can theoretically test how scenarios of behavior change – incorporating coverage, impact and duration of intervention – affect HIV incidence. A few past models have specifically addressed effectiveness of behavioral interventions [29], but in our opinion more systematic work needs to be done in this field. Models of social and behavioral intervention effectiveness should include and systematically measure potential impacts of at least five behavioral components: 1) the proportion of the population that is receiving the intervention, 2) the proportion of the receiving population that adhere to the intervention, 3) the level of behavior change among adherers and non-adherers, 4) the duration of behavior change, and 5) the "set point" level of final behavior. Lastly, each of these components may systematically vary by sub-population (i.e. sex, age, race), and models of effectiveness should take account of these sub-populations if feasible.

A recently published paper on the efficacy of a behavioral intervention in the US helps illustrate this point. Many Men Many Voices (3MV) is a behavioral HIV/STI prevention intervention for black MSM [30]. A randomized trial measured the efficacy of the 3MV intervention; it led to overall reductions in unprotected anal intercourse with casual partners and increases in self-reported HIV testing, but the results varied by type of partner and time of follow-up. Some results were seen only at three months, others only at six months. This suggests that some behaviors are adopted readily, but may fade with time, while others may take longer to adopt but potentially have more staying power. Even before this efficacy study, the 3MV intervention was included in the CDC's Diffusion of Effective Behavioral Interventions (DEBIs) program. These CDC-funded intervention programs are a cornerstone of HIV prevention in the US. However, before additional money is spent on these interventions, we should be able to predict how likely these interventions will reduce HIV incidence in the long term outside of the more rarefied trial setting. Modeling work that considers ranges of potential long-term scenarios can help.

Another key area for advancing the field is in greater consideration and evaluation for the usage of behavioral data in models. Models are only as good as the behavioral assumptions on which they are based. Although all models must necessarily make assumptions, there is certainly a wide range both in how closely models adhere to existing behavioral data for the population of interest, and in how specific assumptions may impact key findings. We believe the promise of modeling could be greatly enhanced by increased integration between modelers and sociobehavioral researchers. Specifically, having modelers work more closely with sociobehavioral researchers from the outset to ensure that the ways in which they convert existing sociobehavioral data into model structure and parameters seems appropriate.

A concrete example involves models on the epidemiology of HIV in sub-Saharan Africa. For example, one paper described above [15] includes in its assumptions that 10% of the married or remarried-population resides permanently in the highest sexual activity class, having on average 17.4 new sexual partners per year. The process by which these numbers were derived from data is an elaborate one, and the magnitude of this high activity group is what enables the epidemic to be maintained in the model. This is not an outlier; compartmental models of HIV transmission in Africa typically entail similar assumptions about high-sexual activity groups (often 5–10% of the population) who each have hundreds or thousands of lifetime sexual partners [31, 32]. The lack of connection between the resulting numbers and observed data have been highlighted [33], and even used to argue for modes of transmission other than sexual [34]. Others argue that it simply reflects a limitation of the compartmental modeling framework to explicitly capture network properties such as relational concurrency and degree distributions, which are what actually drive the epidemic [35]. This is not an arcane debate, but rather a crucial, and currently raging one, for understanding the epidemiology of HIV in sub-Saharan Africa and evaluating potential interventions [35-40].

A core aspect of this debate revolves around issues of the proper relationships between modeling and sociobehavioral research. The majority of this paper focuses on the role that modeling plays in sociobehavioral HIV research; but equally important is how sociobehavioral research informs modeling. The example above refers to how sociobehavioral research is imperative in parameterizing models, but a true collaboration between sociobehavioral researchers and modelers requires effort throughout the scientific process. Sociobehavioral research should identify modeling questions, influence model structure, and translate results to communities and governments as well. With a two-way interaction, mathematical models are more likely to be realistic, relevant, and appropriate for

the setting, and can be an important component of a comprehensive HIV prevention strategy.

Conclusion

At least one recent initiative indicates that the integration of modeling and sociobehavioral and prevention research will likely increase in the future. In 2008, NIH sent out a request for proposals for the "Methods for Prevention Packages Program" (MP3), funded six projects focusing on HIV prevention in different populations around the world, and has since renewed the request. The program has the specific goal of integrating modeling into the very earliest, and all subsequent, stages of intervention trials. There is also a focus on "combination interventions" that have multiple modalities, and a charge to consider variations in intervention targeting, adherence, uptake, and effectiveness among members of the population. As a result, epidemic modeling will need to expand in complexity to consider actors with a far richer set of individual characteristics than has been typical within a single epidemic model thus far. We will hopefully see a greater level of communication and shared understanding between modelers and behavioral researchers.

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