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Structural sensitivity in HIV modeling: A case study of vaccination

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ABSTRACT

Structural assumptions in infectious disease models, such as the choice of network or compartmental model type or the inclusion of different types of heterogeneity across individuals, might affect model predictions as much as or more than the choice of input parameters. We explore the potential implications of structural assumptions on HIV model predictions and policy conclusions. We illustrate the value of inference robustness assessment through a case study of the effects of a hypothetical HIV vaccine in multiple population subgroups over eight related transmission models, which we sequentially modify to vary over two dimensions: parameter complexity (e.g., the inclusion of age and HCV comorbidity) and contact/simulation complexity (e.g., aggregated compartmental vs. individual/disaggregated compartmental vs. network models). We find that estimates of HIV incidence reductions from network models and individual compartmental models vary, but those differences are overwhelmed by the differences in HIV incidence between such models and the aggregated compartmental models (which aggregate groups of individuals into compartments). Complexities such as age structure appear to buffer the effects of aggregation and increase the threshold of net vaccine effectiveness at which aggregated models begin to overestimate reductions. The differences introduced by parameter complexity in estimated incidence reduction also translate into substantial differences in cost-effectiveness estimates. Parameter complexity does not appear to play a consistent role in differentiating the projections of network models.

1. Introduction

A guiding principle in public health modeling stipulates that a model should be only as complex as is necessary. Some argue that, “Unnecessary complexity … is almost as undesirable as over-simplification” (Basu & Andrews, 2013; Grassly & Fraser, 2008), yet there is little consensus as to what qualifies as “necessary.” A model should be simple but “not so simple that realistic violation of simplifying assumptions will change an inference” (Koopman, 2005). As a field, we have not yet

Abbreviations: PWID, people who inject drugs; MSM, men who have sex with men; PWUD, people who abuse but do not inject drugs; HIV, human immunodeficiency virus; HCV, hepatitis C virus; NSP, needle/syringe exchange program; SAT, substance abuse treatment.

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adopted a consistent evaluation of model complexity nor a protocol for structural sensitivity analysis; consequently, although taxonomies can provide guidance (Brennan, Chick, & Davies, 2006), structural choices for models are often chosen based on guesswork, intuition, and computational convenience. While most single-model studies can thoroughly assess first-order uncertainty (i.e., model sensitivity to input values), they cannot address second-order uncertainty (i.e., how structural assumptions and the construction of the model itself influence model behavior).

Although there is no consensus about *how* to address structural sensitivity, there is a growing consensus that it is an essential component of sensitivity analysis that *should* be addressed (Basu & Andrews, 2013; Bilcke, Beutels, Brisson, & Jit, 2011; Bojke, Claxton, Sculpher, & Palmer, 2009; Caro, Briggs, Siebert, & Kuntz, 2012; Jackson, Bojke, Thompson, Claxton, & Sharples, 2011; Suen, Goldhaber-Fiebert, & Brandeau, 2017). Consortia of modeling groups like CISNET (the Cancer Intervention and Surveillance Modeling Network) and the Mt. Hood Diabetes Challenge Network have made it common practice to collect and compare predictions across models that vary in scope, parameters, and structure (e.g., Eaton et al., 2012; van de Vijver et al., 2013). Bilcke et al. (2011) propose a standardized framework for addressing and presenting structural uncertainty in decision-analytic models, and Jackson et al. (2011) advocate for a comprehensive model that includes all possible parameters, which can then be pruned back to explore different simplifying assumptions.

In infectious disease modeling, a number of researchers have studied the effect of contact structure assumptions on epidemic control (Bansal, Grenfell, & Meyers, 2007; Hamilton, Handcock, & Morris, 2008; Huppert & Katriel, 2013; Kong, Wang, Han, & Cao, 2016). For instance, Bansal et al. (2007) characterize the "epidemiological distance" between network models and homogeneous-mixing compartmental models and Hamilton et al. (2008) explore how the properties of network degree distributions affect their ability to replicate disease propagation. The majority of such analyses use stylized examples to illustrate how different structural make-up affects model prediction and fitting to epidemics but they do not translate these differences into policy implications.

In the policy context, Rahmandad and Sterman (2008) compare multiple agent-based models with varying network structures to a dynamic compartmental model, all calibrated to the same targets, and Suen et al. (2017) analyze intervention effects for compartmental epidemic models with different levels of risk stratification. Both studies find that modeling choices may lead to different policy choices. Other infectious disease modeling studies have called for diversifying contact structures to improve modeling accuracy (Chick, Adams, & Koopman, 2000; Hellard et al., 2014; Scott, Hellard, & McBryde, 2016) and improve understanding of models' predictive capacities (Lee et al., 2017) or for adding individual heterogeneity to reduce predictive bias (Monteiro et al., 2016). Some studies compare parameter complexity across models with otherwise similar compartmental structure (Silal, Little, Barnes, & White, 2016) or compare the outcomes of simple compartmental models to the predictions of more complex models (White et al., 2009), demonstrating that models can and should be as simple as possible.

These are mostly isolated analyses; researchers have not employed a consistent framework for categorizing the exploration of structural assumptions in infectious disease modeling. Many studies point out the overwhelming use of dynamic compartmental models when evaluating policies and emphasize the important role of network effects in disease spread (Dombrowski et al., 2017; Hellard et al., 2014; Koopman, 2004; Scott et al., 2016) but do not offer further insight into when the use of various structures might be more or less appropriate or even how one might establish such criteria.

Towards this goal, Koopman develops a structural taxonomy for transmission models (Koopman, 2004; Koopman, Jacquez, & Chick, 2001) and a systematized approach, inference robustness assessment, for isolating the effects of structural choices in a model (Koopman, 2005, 2007; Koopman, Singh, & Ionides, 2016). Inference robustness assessment tests the validity of a given structural assumption, and the inference it produces, by relaxing that assumption gradually over a family of linked models. The experiment is thus designed to explicitly assess the extent to which inferences are robust to simplifying assumptions.

In this paper, we present a case study focused on HIV modeling that utilizes some of the key concepts of inference robustness assessment. Our case study compares the effects of a hypothetical HIV vaccine in multiple subpopulations over eight related transmission models, all calibrated to the HIV epidemic in King County, Washington, which we sequentially modified to vary over two dimensions: parameter complexity (e.g., the inclusion of age and hepatitis C virus (HCV) comorbidity) and contact/simulation complexity (e.g., compartmental vs. network models).

The introduction of an HIV vaccine could radically shift HIV control policy, and infectious disease modelers can play an important role in informing policy makers about population-level effectiveness and cost-effectiveness. As of June 2017, multiple ongoing HIV vaccine trials were in the phase II stage (Choi et al., 2016; National Institutes of Health, 2017). No model-based study of vaccine effectiveness or cost-effectiveness analysis has addressed structural uncertainty (Adamson, Dimitrov, Devine, & Barnabas, 2017). Additionally, no study that we are aware of has applied the principles of inference robustness assessment in infectious disease modeling, nor has any study that we are aware of compared models along the dimensions of parameter and contact complexity simultaneously.

In Section 2 we describe our modeling approach. In Section 3 we present the results of our analyses. We conclude with discussion in Section 4.

2. Methods

2.1. Overview

Fig. 1 provides a schematic overview of the eight models in our case study, organized according to the two dimensions of contact/simulation complexity and parameter complexity. Section 2.2 discusses each model in detail and Table 1 summarizes