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Rarely Just About One Model: Multi-Model and Multi-Methodology Reasoning in Epidemic Modeling

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Abstract

In this paper, I argue that epidemic modeling of disease spreading involves both multi-model as well as multi-methodology reasoning. I demonstrate that epidemic modeling includes two different modeling methodologies: compartment and network modeling. Furthermore, within each of those methodologies, models are often constructed as structured groups of models, rather than as single models. I analyse the epistemic advantages of this mode of modeling, including complementary reasoning with different modeling methodologies and the ability to easily compare explanatory advantages of different models.

1. Introduction

Analyses of epidemiological modeling in philosophy of science can roughly be divided into two periods: (i) a pre-Covid-19 period, where such analyses focused on the underlying epistemology and the kind of causal explanations offered by risk factor models, often for noninfectious diseases (for example, Gani 1990; Broadbent 2009, 2011, 2013; Kincaid 2011), and (ii) a post-Covid-19 period, which saw an increased focus on epidemic models—for example, models of the spread of an infectious disease (for example, Rhodes et al. 2020; Iranzo and Pérez-González 2021; Northcott 2022). Notably, this distinction only tracks a shift in focus of the philosophical debate, not a shift in focus of epidemiology itself, where risk factor modeling and epidemic population modeling have coexisted, and continue to coexist, as active research foci. This paper will add a third consideration to those two areas of philosophical interest: the use of multiple epidemic models and multiple methodology in comparative reasoning to derive both general and specific explanations.

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1.1 Philosophical Analyses of Risk Factor Models

Pre-Covid-19 analyses of epidemiological modeling focus strongly on the need for epidemiological models to offer multicausal (rather than mono-causal) explanations for the development and spread of diseases. The underlying conception of a risk factor model is the specification of several risk factors and their relevant interactions.[1] Alex Broadbent (2009, 2011, 2013) comprehensively analyses the difficulties that arise in using such multifactorial risk models in deriving different kinds of explanations: in particular, he highlights that such models do not offer general explanations for why diseases occur in some people and not in others:

> When a risk factor for, say, diabetes is identified, the next question ought to be, "does this cause explain why some people get diabetes, and others don't?". The answer for known risk factors is "no," because risk factors are typically absent from some of the diseased cases to be explained, and also present in some healthy people. (Broadbent 2009, 307)

In other words, risk factor models lack the kind of mechanistic explanations one finds, for example, in physical models that offer a general explanation for each instance covered by the model (Broadbent 2011). This has been expressed by describing those models as "black box" models, which can be used to derive a causal hypothesis about the risk factors for developing a given disease without providing a fine-grained (mechanistic) causal explanation for how the disease develops in each given instance. It has also been recognized that risk factor models are nevertheless epistemically useful and enable the design of effective disease prevention measures—in particular, the design of public health interventions that summarily address certain risk factors. In particular, Broadbent (2011, 55–63) discusses the fact that there are numerous historical episodes where epidemiologists' willingness to view associated risk factors as causal explanations, even without knowledge of the exact causal mechanism behind those associations, has yielded practical benefits—for example, in the form of vaccinations or hygiene rules. It is also not uncommon that a causal mechanism is discovered after measures based on associative reasoning have already been implemented. Accordingly, Broadbent (2011) argues that such early transitions from risk factors to presumed causes are unproblematic as long as they do not prohibit an ongoing search for an underlying causal mechanism.

A second question of philosophical interest relates to the level of explanation offered by risk factor models. It can be argued that risk factor models are explanatory on the level of populations; that is, they offer an explanation for the overall rates of disease within a population. This explanation can even be viewed as mechanistical in that the interaction of different risk factors can be interpreted as a mechanism for those disease rates. Some philosophers of science (for example, Plutynski 2014) have argued that the question of which level of explanation offers a "good" explanation is not to be decided on general epistemic grounds but depends on the context in which this explanation is used (for example, in designing public health measures versus recommending individual medical treatment).

[1] I use the term "risk factor" to denote all factors influencing the risk to develop or contract a disease; that is, both factors that increase the risk and those that lower it.

In the context of this paper, it is important to recognize that these philosophical analyses of risk factor models are analyses of single-model reasoning; that is, they analyze how individual risk models can or should be used to derive causal explanations. In contrast, my analysis here focuses on multi-model and multi-methodology reasoning.

1.2 Philosophical Analyses of Epidemic Modeling

A review of post-Covid-19 papers on the epistemology of epidemiology shows that the focus of philosophers of science has shifted toward the question of how to choose the best epidemic population model for a given scenario. This is clearly, to some degree, a response to the public debate on Covid-19 modeling, which emphasized differences and "rivalries" between different modeling methodologies and models.

With respect to differences in methodology, Valeriano Iranzo and Saúl Pérez-González (2021) identify two coexisting modeling methodologies: compartment models and agent-based models. Compartment models divide the population into separate "compartments" of infected, susceptible, deceased, and other parts of a given population. The percentage of the population in each compartment then changes according to "flow rates," which are either modeled as constants in the model, or as more complicated, potentially time-dependent, functions. Agent-based models model the disease transmission between single individuals, usually by representing those individuals as nodes in a network whose contact with other individuals is represented as network connections/activation functions between different nodes. In contrast to risk factor models, both compartment and agent-based or network models explain the development of an epidemic with time—they offer an explanation for why a certain percentage of a population will have a certain disease status at a given point in time. The two different kinds of models and the explanations they offer are described in detail in sections 2 and 3, respectively.

Iranzo and Pérez-González (2021) conclude that the choice of modeling methodology should be influenced by the specifics of the target population and the aims of the policymakers—for example, compartment models are suitable for testing out population-level interventions such as vaccination programs, while agent-based models are suitable for testing social interventions targeted at influencing the relationships of smaller groups of people, such as lockdowns and partial isolations. In this paper, I recognize the same general methodological division between compartment models and network models. However, I focus on reasoning that combines the results from different methodologies; that is, on the complementary use of different methodologies, rather than of model choice.

With respect to choosing from different models within one modeling category, Robert Northcott (2022) distinguishes between two strategies that were evident during the Covid-19 pandemic: a commitment to one "master model," which is supposed to work for a great number of epidemic scenarios and is only minimally adapted for each new scenario, and contextual modeling, where each new scenario should prompt the choosing and/or development of a new model. Northcott (2022) concludes that during Covid-19 the use of a master model was less predictively successful than the use of newly developed, contextual models. Contextual models here refer to specific, relatively short-ranged models that can take into account the momentarily important parameters and variations between different scenarios—for example, the differences between a country with an aging and one with a young population. Instead of settling on one master model with a fixed algorithm and a

given number of updatable parameters, Northcott (2022) recommends a fluid approach that sets up new short-ranged, data-driven models for each new pandemic scenario:

> We know a lot more now than at the beginning of the Covid-19 pandemic, so both projections and policy responses are far better grounded than they were. But this welcome progress has not come from grand, one-size-fits-all models. Rather, it has come from a huge accumulation of knowledge gained by informal methods and by modeling that is empirically confirmed. (Northcott 2022, 17)

This paper adds to Northcott's identification of multi-model reasoning by investigating such reasoning in greater detail and demonstrating that different models are often ordered in structured groups, which allows specific comparisons between them. It also adds to Northcott's notion of flexible modeling by identifying other forms of multi-model and multi-methodology reasoning in epidemic modeling.

1.3 Model Construction and Model Explanation

There exists a large canon of literature on scientific modeling and accordingly a varied use of terminology (for a review, see Frigg and Hartmann 2020). In this section, I will briefly clarify the key concepts I will use to analyze epidemic modeling.

In the philosophical debate on scientific modeling, empirical data and scientific theory are often visualized as two vertically ordered levels, in which the theory is usually denoted as the top level and the empirical data as the bottom level (see, for example, Bokulich 2003, 610; Da Costa and French 2003, 55). There is currently significant disagreement about how the relationship among model, theory, and data should be construed (for a review of different approaches to this topic, see Frigg and Hartmann 2020, section 4.2). However, a common account views the model as being derived from the covering theory through a number of simplifications, idealizations, and abstractions, which are guided by knowledge about the empirical system the model is targeted toward.

A scientific model is, then, viewed as an entity located somewhere between these two levels. This spatial metaphor can be extended to distinguish two different kinds of *model construction: vertically* from top-level theory and bottom-level data and *horizontally* from already existing models (Bokulich 2003, 2015). This categorization of model construction has been chosen because it allows us to break down the eventual construction of model groups into vertical construction steps, which draw upon data and theory, and horizontal construction steps, which predominantly draw upon existing models. While this framework is useful in the given context, it is not the only viable conceptualization of model construction (for a template approach, see Knuuttila and García Deister 2019; for a perspectival approach, see Massimi and McCoy 2020).

There is currently no consensus account of the epistemic functions of scientific models but most authors base their analyses on the general premise that models should provide *explanations* and/or *predictions* about phenomena of scientific interest. The taxonomy of explanations I use is based on drawing two general distinctions: between *causal* and *noncausal* explanations (Bokulich 2017; Reutlinger and Saatsi 2018; Jansson 2020); and, within causal explanations, between possible and actual explanations (Bokulich 2014). Causal explanations are explanations that specify the causal processes underlying a

particular phenomenon while noncausal explanations do not reference causes but rely on other epistemically relevant features, often the mathematical structure of a given description of the phenomenon. It is possible to develop an even finer-grained taxonomy of causal explanations, by distinguishing between those that specify only an *initial cause* and those that provide a *causal mechanism* (Salmon 1984). The focus in this paper is very much on epidemic models that provide a causal mechanism rather than an identification of causes. This is due to the fact that this paper does not focus on the strand of statistical epidemiology modeling geared toward identifying risk factors (section 1.1) but rather on the one that models the spreading of a disease through a given population (section 1.2).

Within the class of causal explanations, one can also distinguishes between *possible* and *actual* explanations. A possible explanation must be consistent with the relevant known facts and should ideally generate enough additional predictions to distinguish it from a mere "just so" (post-hoc) story. In contrast, according to Alisa Bokulich (2014, 324), more is required of an actual explanation: scientists will only be willing to accept one of many possible explanations as an actual explanation if there exists sufficient additional evidence that the proposed mechanism (or nonmechanistic cause) actually operates in the model's target system. The additional evidence needed for the acceptance of a possible model explanation as an actual one can come from a variety of sources—such as by making the model less idealized, simplified, or abstract, or by gathering additional empirical data from the target system. The distinction between actual and possible explanations is one of credence by the relevant scientific community and is relative to the overall epistemic scenario the model is being evaluated in.

2. Hierarchies of Compartment Models

Since the early twentieth century, the standard models used in epidemiology to model the spread of diseases through different populations are compartmental models (for a brief history of the use of these models, see Brauer, Castillo-Chavez, and Feng 2019, 5–7). Compartmental models are based on the assumption that during an epidemic members of a given population can be divided into a set number of categories based on their infection status. Within these models, each category is conceptualized as a "compartment," which contains the members of the population with the corresponding infection status; the dynamics of the model then consist of an exchange of members among different compartments as the infection status of those individuals changes.

2.1 Construction of Hierarchies of Compartment Models

In this section, I discuss the construction of hierarchies of compartment models. First, I discuss an idealized, integrated construction process, as laid out in textbooks such as Fred Brauer, Carlos Castillo-Chavez, and Zhilan Feng's *Mathematical Models in Epidemiology* (2019). I then discuss how hierarchies are constructed and used in the context of the scientific publication process, where authors seldom have the space or inclination to develop a whole group of models but nevertheless view the smaller sets of models they put forward as part of a hierarchy of models. The simplest epidemic compartment model is the SIR (susceptible-infectious-removed) model (for a derivation of this model, see Brauer, Castillo-Chavez, and Feng 2019, 23; 30–34), which contains three compartments: a

compartment that contains the number *S* of individuals that are susceptible to the disease but not currently infected; a compartment that contains the number *I* of currently infected individuals; and a compartment that contains the number *R* of individuals who have been permanently removed from the infectious population, by acquiring immunity or through death. The dynamics of the model are then derived by specifying how the numbers *S, I,* and *R* change over time. The construction of this model is vertical (section 1.3): it requires the practitioner to prepare a suitable description of the target system, as well as to draw upon existing theoretical knowledge of population dynamics. For example, Brauer, Castillo-Chavez, and Feng (2019, 26–27) give the following prepared description of a very simple SI(R)-model:

(i) The rate of new infections is given by mass action incidence.
(ii) Infectives leave the infective class at a rate αI per unit time and return to the susceptible class.
(iii) There is no entry into or departure from the population.
(iv) There are no disease deaths, and the total population size is a constant *N*.

Notably, assumptions (iii) and (iv) imply that the *R* compartment is dormant; that is, the model is effectively a two-compartment SI model. The notion of mass action incidence is a general notion about the number of contacts that members of different compartments will have with one another: it assumes that the number of contacts between members is proportional to the overall population size; that is, βN. From this prepared description and the general theory about population dynamics, a set of two differential equations is derived:

$$S' = -\beta SI + \alpha I \quad (1a)$$
$$I' = \beta SI - \alpha I, \quad (1b)$$

where *S'* and *I'* denote the time derivatives of *S* and *I,* respectively, and $N = S + I$ (viz. assumption (iv)) has been used to eliminate the total population number *N* from the equation. It is easily apparent that the construction of this simple compartmental model constitutes an excellent example of vertical model construction.

However, the majority of compartmental model construction in epidemic modeling is not one of *ab initio* derivation of the model from covering theory and assumptions about the target system. Instead, it consists of the extension of existing simple models into more sophisticated ones. This requires successively amending the prepared description and drawing on additional bits of theoretical knowledge. For example, the simple SI model (1a–1b) can be transformed into a real SIR model by adding a compartment *R* for individuals that have been removed from the population (Brauer, Castillo-Chavez, and Feng 2019, 30). To hold the total population number constant, it is further assumed that the removal rate and the birth rate are equal. From the existing SI-model (1a–1b) and these amendments to the prepared description, the following SIR model (2a–2c) is derived:

$$S' = -\beta SI + \mu(I + R) \quad (2a)$$
$$I' = \beta SI - \alpha I - \mu I \quad (2b)$$
$$R' = \alpha I - \mu R, \quad (2c)$$

where μ is the population's death/birth rate.

The number and configurations of additional models that can be added to such a hierarchy of compartment models is virtually infinite. However, a prominent methodology of constructing such hierarchies is the successive addition of further compartments to a given model, or the subdivision of existing compartments to capture different strains of a disease (Brauer, Castillo-Chavez, and Feng 2019, 49–52). For example, the SIR model described above can be extended into a SEIR-model (Brauer, Castillo-Chavez, and Feng 2019, 64) through the addition of a fourth compartment *E,* which contains those members of the population that have been exposed to the infection but are not symptomatic or infectious yet. Even more sophisticated variations are the SLAIR-model (Brauer, Castillo-Chavez, and Feng 2019, 133–135), which adds compartments for individuals at a latent (*L*) and asymptomatic (*A*) stage of the disease, respectively, or the SEQIHR-model (Brauer, Castillo-Chavez, and Feng 2019, 134–236), which adds compartments for quarantined (*Q*) and for hospitalized (*H*) members of the population to the SEIR model. The process of creating a hierarchy of models through successive extensions of the prepared description of a given target system is highly variable: beyond successively adding compartments, a range of hierarchies can also be constructed by adding assumptions about the distribution of transmission rates within the population—for example, by making the proportionality constants β and μ dependent on a range of relevant variables and by making these functions successively more sophisticated (Brauer, Castillo-Chavez, and Feng 2019, chapter 13). The process of constructing a hierarchy of epidemic models through systematic changes to the prepared description is depicted diagrammatically in Figure 1.

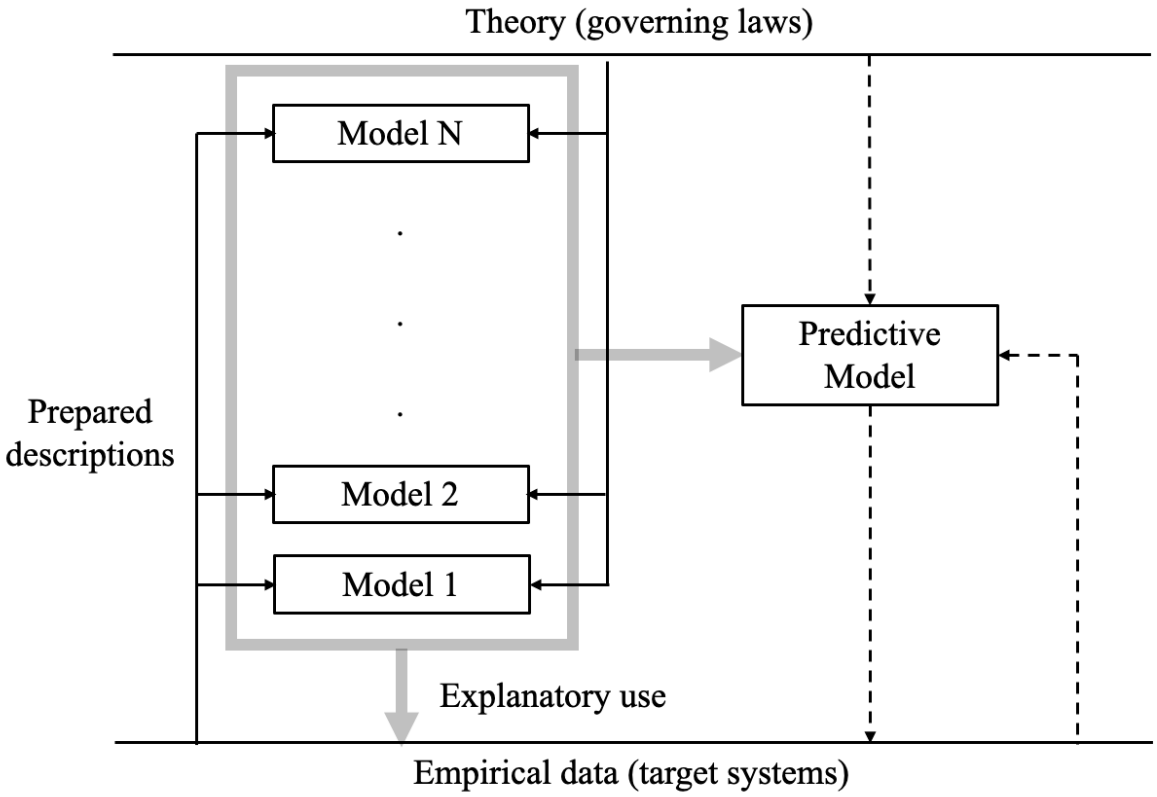

Figure 1. Hierarchies of models in epidemic modeling.

The above description of the construction of hierarchies of models is based on the exposition of this process in textbooks such as Brauer, Castillo-Chavez, and Feng's *Mathematical Models in Epidemiology* (2019). In these textbooks, the construction is depicted as a conceptually unified process, where successive steps of adding a model to the hierarchy follow directly upon each other. However, the construction of new hierarchies of epidemic models usually takes place in a more distributed way through the addition of different models to a hierarchy by different research groups. Researchers will make available their model and its results through a research publication that references publications pertaining to prior models in the hierarchy; that is, either the discussion of such hierarchies in textbooks, or the presentation of relevant ancestor models in previous research publications.

Such research publications then likewise form a group that can be associated with the construction of one hierarchy of models. For example, M. de la Sen and A. Ibeas (2021, 2) present a SEIHAR model and reference as a source of ancestor models two textbook discussions of SIR hierarchies (Mollison 2003; Keeling and Rohani 2008); multiple prior research papers of SEIR models with different compartments—for example, a SVEIRS model by Xinyu, Song, Yu Jiang, and Huiming Wei, and a SIRVS model by Tailei Zhang (2015)—as well as several models with relevant parameter variations (for variations in the vaccination (V) rate, see De la Sen and Alonso-Quesada 2011, 2015). The hierarchy of models referenced through those sources is used to offer a set of core equations from which the new SEIHAR model is constructed by addition of compartments, as well as a choice of parameter configurations (De la Sen and Ibeas 2021, 4–8). The hierarchy of existing models thereby provides both the ancestor models from which the eventual model is constructed, as well as the context for its explanatory and predictive use (section 2.2).

2.2 Explanatory and Predictive Use of Hierarchies of Epidemic Models

Epidemic models in a hierarchy of models (section 2.1, Figure 1) can be used in two distinct ways: to provide and test possible explanations of disease developments; that is, to identify potential causal factors and the mechanisms governing the development an epidemic; and to provide predictions of the future development of a given epidemic scenario from an actual explanation. A major epistemic distinction between these two approaches is the fact that the explanatory use requires researchers to consider the whole hierarchy and to draw comparative conclusions about the models within it, while the predictive use requires further bottom-up adaptations of one model for a given specific scenario. The two ways of using hierarchies of epidemic models is also depicted in Figure 1.

The explanatory usefulness of model hierarchies in epidemics becomes immediately apparent if the process of adding compartments to a given model is understood as the successive addition of causal factors into the mechanistic explanation of the model's and target system's behavior. To wit: the behavior of the SI model is explained by the interaction of the infectious with the susceptible population variables (by a causal mechanism based on infection and susceptibility); the behavior of the SIR model is explained by the interactions of infectious, susceptible, and dormant (removed) population variables (by a causal mechanism based on infection, susceptibility, and removal); the behavior of the SEIR model is explained by the interactions of infectious, susceptible, dormant, and exposed population variables (by a causal mechanism based on infection, susceptibility, removal, and

exposure); and so on. In order to identify how each added causal factor influences the behavior, epidemic modelers must do two things: investigate the behavior for each model comprehensively—for a range of independent parameters—and compare the outcomes of different models to one another to gauge how the additional causal factors have changed the outcomes—identify which phenomenological features are best explained by which causal mechanism.

For example, Brauer, Castillo-Chavez, and Feng (2019, 26–30) provide an in-depth discussion of the behavior of the SI model for different parameter regimes and then follow up with a similar analysis of the SIR model (2019, 30–34). However, the most important conclusions about the causal role of removal in influencing the behavior of the SIR model are drawn in comparison to the well-analyzed SI-model. In this case, the comparison between the SI model and the SIR model indicates that removal is a relevant causal factor only for certain parameter regimes. In other words, only under certain conditions can a mechanism based on removal (and other causal factors) provide an explanation for the model's and target system's behavior. Similar discussions can be found elsewhere (for example, Brauer, Van den Driessche, and Wu 2008; Keeling and Rohani 2008). In research publications that add models to an existing hierarchy, such as De la Sen and Ibeas (2021) discussed above, a similar comparative investigation of explanatory factors takes place by referring to models in the same hierarchy—for example, by running their SEIHAR model with different compartments inactivated, such as removing the sub-compartment H containing hospitalized patients, and by applying or not applying vaccinations (De la Sen and Ibeas 2021, 18–27). The discussion of the relevance of different causal factors in the mechanism is therefore always a comparative one, based on comparative reasoning of the behavior of different models within a given hierarchy.

In contrast, the use of epidemic models to establish actual explanations and extend those into predictions appears to be a good example of the traditional epistemic function ascribed to single, vertically constructed models: the model provides an actual causal-mechanistic explanation for the behavior of the target system, and therefore one that can be used to make predictions about this system. As established in section 2.1, it seems apparent from the literature that epidemic models are usually initially constructed as hierarchies (for example, Brauer, Castillo-Chavez, and Feng 2019, chapters 2–3). If a predictive model is needed, then the epidemiologist must: (i) pick a particular model from a hierarchy; and (ii) perform further constructive tasks to make the model more applicable to the given scenario. Using the distinction between possible and actual explanations, this can be interpreted as transforming the possible explanations provided by the relatively general models in the hierarchy to an actual explanation for the given scenario. If one is reasonably sure that the model's dynamics explain the actual target system's behavior, one is justified in viewing the extrapolated behavior of the model system as predictive for that of the target system. In epidemic modeling, both the choice of a model to adapt for a specific scenario and the actual process of adaptation are strongly guided by considerations of the target system. With respect to the first choice, epidemiologists need to determine which causal factors and mechanisms will be significant for the given scenario; that is, which of the general models from a given hierarchy will be chosen for adaptation. For example, Brauer, Castillo-Chavez, and Feng describe the process of choosing a model for an influenza epidemic:

> Our starting point is the simple SIR model. Two aspects of influenza that are easily added are that there is an incubation period between infection and the appearance of symptoms, and that a significant fraction of people who are infected never develop symptoms but go through an asymptomatic period, during which they have some infectivity, and then recover and go to the removed compartment … Thus a model should contain the compartments S (susceptible), L (latent), I (infective), A (asymptomatic), and R (removed). (2019, 312)

Similarly, De la Sen and Ibeas (2021, 4) argue that their splitting of the usual single "infected" compartment *I* into hospitalized *H* and non-hospitalized *I* sub-compartments is justified by the fact that the model is intended to be used for the modeling of Covid-19 pandemics and that this particular disease shows the range of severity captured by the sub-compartments.

Since the model for predictive use is chosen based on information about the causal mechanisms that are investigated using model hierarchies, the two epistemic uses of epidemic models—possibly explanatory and actually predictive—are not independent of each other. In particular, the more explanatory investigation of a given hierarchy has been undertaken, the easier it is for epidemiologists to choose appropriate models for predictive uses from this hierarchy.

Once a model for prediction has been chosen, it needs to be adapted to a specific target system. In epidemic modeling, this primary requires parametrization: the determination of specific numerical values for the independent constants in a model—for example, in the case of the SI and SIR models discussed above, the constants *a, b,* and *m*. This adaptation is based on further use of any available data about the target system: whatever information is available about the system's past behavior is used to estimate those values in a systematic way, which allows practitioners to judge how reliable these estimates are. Parametrization is a highly technical activity that usually requires various curve-fitting methodologies and can itself be regarded as a mathematical subfield (see, for example, Brauer, Castillo-Chavez, and Feng 2019, 334–337). Research papers presenting models therefore usually draw on separate publications devoted to the fitting of a given parameter for a given scenario. For example, De la Sen and Ibeas (2021, 18, table 1) use the results of ten other publications to fit their model for a Covid-19 scenario.

In the framework for analyzing model construction used here, such curve-fitting activities are classified as bottom-up constructions. Accordingly, the adaptation of the model for predictive use can be viewed as additional model construction; that is, a predominantly bottom-up step is added to the construction during which the prepared description of the model is extended to include the relevant numerical data for the curve fitting. As is evident in the example above, the bottom-up construction step is usually undertaken by several different research groups and can then be added to different general models from a given hierarchy.

The claim that predictive epidemic models are chosen and adapted from a hierarchy of models can be viewed as supporting Northcott's (2022) assertion that modeling can be rigidly focused on one model, or more fluidly switch between different ones (section 1.2): this can be interpreted as more or less frequent return to the hierarchy to choose a new model for a slightly different scenario. The existence of those hierarchies also explains why the fluid approach remains an effective epistemic strategy: the choice of a new model to

adapt to a concrete scenario does not have to be made without any prior knowledge of the options but from a structured list of well-explored options.

3. Repositories and Transfer of Epidemic Network Models

Modeling of disease transmission in epidemiology does not solely rely on compartment models (section 2); in addition, network models are also commonly used. While the configurations of these models are very different from those of compartment models, in this section, I demonstrate that modeling with epidemic network models also involves the construction of structured groups of models. However, instead of the hierarchies identified in the case of compartment models, these groups are best described as repositories (section 3.1). Given the different group structure, the epistemic functions of groups of network models are also different (section 3.2)—in particular, they predominantly provide either structural explanations or actual causal-mechanistic explanations (section 1.3).

3.1 Construction of Repositories of Network Models

In epidemic modeling, network models are used to model the early stages of an epidemic, when transmissions are still highly heterogeneously distributed throughout the population and when individual contact structures still have significant impacts on the development of the disease (Brauer, Van den Driessche, and Wu 2008, 133). Here, network models represent individuals (or small clusters of individuals) as nodes in the network and contacts between individuals as edges between the nodes. This methodology allows the model to capture the varying numbers of contacts between different individuals and to represent heterogeneous contact structures.

It is important to note here that this choice between models is epistemically more complex than reflected in this paragraph and that the standard field-internal argumentation (found in textbooks such as *Mathematical Epidemiology,* edited by Brauer, Van den Driessche, and Wu 2008), which is based on the distinction between early, heterogeneous transmissions and late, homogeneous transmissions, ignores the fact that this distinction itself is a simplification of the real situation, as pointed out by Pascal Crépey, Harold Noël, and Samuel Alizon (2022). The epistemic difficulties in drawing this distinction and their consequences for models choice is discussed in more detail in section 4.

While the initial choice of a network model approach (rather than compartmental modeling) is motivated by considerations of the target system at different time periods, the actual construction of epidemic network models relies both on horizontal and vertical model construction. In particular, epidemiologists are well aware that there exists a repository of well-studied network models from which they can pick candidate models for their own target systems. For example, Fred Brauer, Pauline Van den Driessche, and Jianhong Wu write: “The study of graphs originated with the abstract theory of Erdös and Rényi of the 1950s and 1960s … and has become important more recently in many areas, including social contacts and computer networks, as well as the spread of communicable diseases” (2008, 135).

Repositories of complex models—a class of models that is often taken to include network models—have been studied in Zuchowski (2019). They found that large repositories of network and cellular automata models without assigned target systems are constructed

through the systematic variation of the models' formalisms. The construction of such repositories is therefore a form of horizontal model construction. As the variation of the model's formalism can be automated, such repositories of models often contain many hundreds of models (for an example of the large-scale construction and cataloguing of cellular automata models, see Wolfram 2002). However, the repositories are not unstructured: further study usually goes into identifying subgroups of models with different dynamical and phenomenological properties—for example, in the case of network models, based either on the periodic or nonperiodic behavior of transmissions across the network, or on the geometry of the underlying network structure (Brandes and Erlebach 2005; Lewis 2009). The horizontal construction of large repositories of models is schematically depicted in Figure 2.

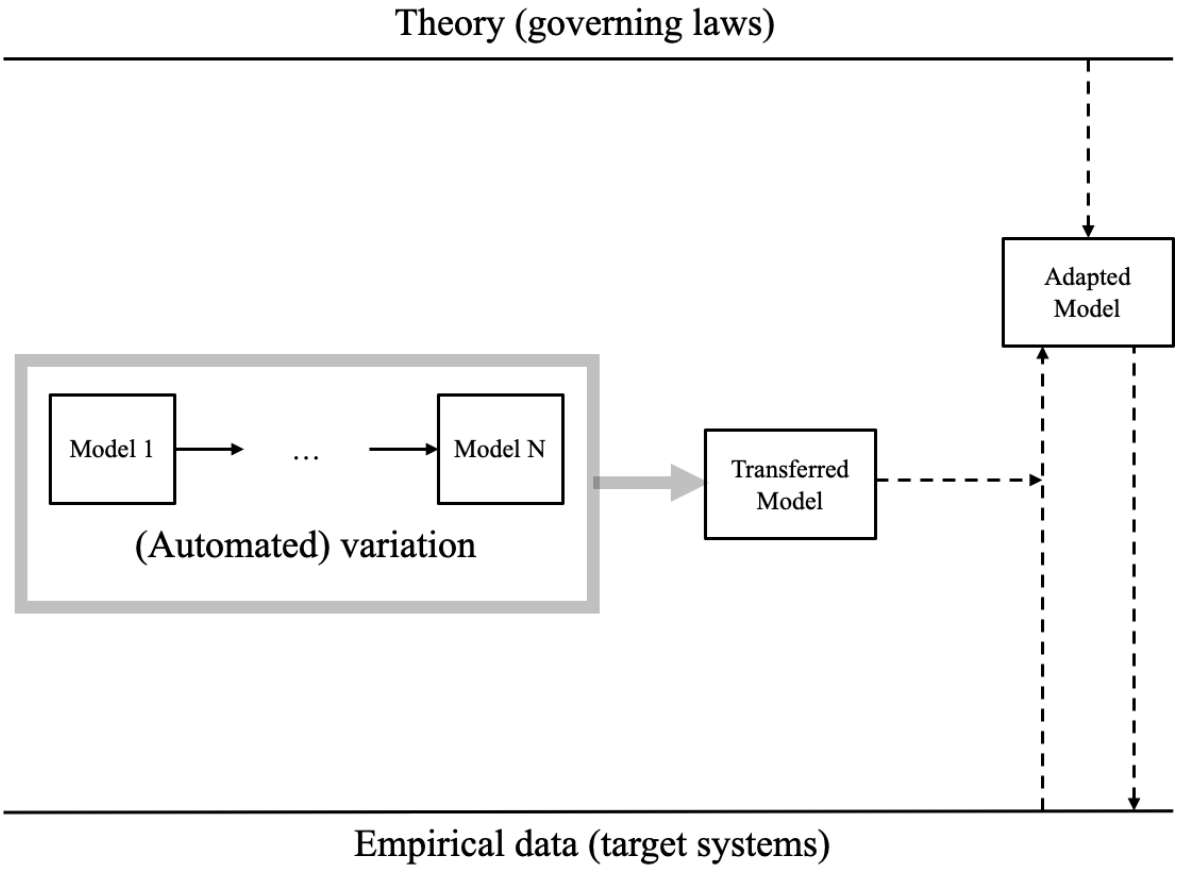

Figure 2. Repositories of models in epidemic modeling.

There exists a division of labor between different disciplines: the construction of large repositories of network models is largely done by mathematicians and computer scientists (Brandes and Erlebach 2005; Lewis 2009), while epidemiologists use those existing repositories to choose models suitable for transfer to their particular target systems. As was the case with hierarchies of models, the advantage of choosing from a set of well-studied "standard examples" (Brauer, Van den Driessche, and Wu 2008, 142) is that there exists a body of general knowledge about these models that the practitioner in a given subfield can draw upon (2008, 142–144) and that can guide the choice of a model to transfer from the

repository to the given target system. The information provided in these repositories can be described as noncausal structural explanations: they explain how a given mathematical structure leads to certain behavior of generic networks. Based on these structural explanations, epidemiologists can make informed choices about models with a mathematical structure that can (non-causally) explain the behavior observed in the target system they are interested in. The first step in the use of repositories in epidemic modeling is therefore a horizontal transfer of a model from the general repository to a specific epidemic target system. The horizontal transfer of a model to a new target system then requires the reinterpretation of the model's dynamics to fit this new scenario. In epidemic modeling, this usually consist of an interpretation of nodes as individuals in a population and of edges as indicating contacts between individuals. The transfer of models from the repository to specific epidemic target systems is also depicted schematically in Figure 2.

Following the horizontal transfer of a generic network model to represent the contact structure of a given population, epidemic-specific additions usually need to be added to the model. In a simple network model, these usually consist of a transmission function, which indicates how likely a given contact is to result in disease transmission, and a set of independent variables indicating the disease status of each individual (Brauer, Van den Driessche, and Wu 2008, 138–140). These additions to the transferred network model are constructed vertically: they are derived from considerations and assumptions about the target system and the covering epidemic theories. In fact, the reasoning behind defining functions for transmissibility and susceptibility on the network is very similar to that used to construct similar functions in compartment models (section 2.1). This vertical construction step is also depicted schematically in Figure 2. The construction of epidemic network models could therefore be described as "diagonal"—it starts with the choice and horizontal transfer of a network model from a large, horizontally constructed repository of such models. However, once such a model has been transferred, numerous vertically constructed additions and adaptations are added to it.

3.2 Structural, Explanatory, and Predictive Use of Epidemic Network Models

All three kinds of explanations—structural, possible, and actual (section 1.3)—are involved in the process of epidemic network modeling, as described in section 3.1. In the early stages of the modeling process, noncausal, structural explanations for certain network dynamics are established through the creation of network repositories. Once a generic network model has been transferred to and reinterpreted for a given target system, the resulting model provides a possible causal, mechanistic explanation for the given target system. Lastly, vertical constructions and specifications can transform this model into one that can provide an actual explanation and therefore can also be used to make load-bearing predictions.

For example, Matt J. Keeling and Pejman Rohani (2008, chapter 2) discuss how different network geometries can structurally explain the spread of diseases (or other distributing phenomena—for example, rumors) on those networks. For this investigation, no disease-specific details are necessary, and the chapter draws heavily on general results established in graph theory. However, the investigation is then extended into the derivation of a number of possible explanations for the spread of infection on relatively simple networks. Using these results, Keeling and Rohani (2008, chapter 3) then discuss the application of these results to "real networks," to models whose underlying network

structure is specific to a given target system and that will therefore provide actual explanations and predictions for this target system.

As was the case for modeling with hierarchies of compartment models (section 2.2), it is usually only in didactic texts like Keeling and Rohani's (2008) that we find all three variations of the use of repositories of models in epidemic modeling discussed in an integrated analysis. Research publications on epidemic network modeling usually present investigations that constitute a single stage in this process. The majority of research papers on network modeling can also be categorized as either investigating relatively general models to provide possible explanations (for example, Pastor-Satorras and Vespignani 2001; Newman 2002; Masuda and Holme 2017, chapter 12; Kiss, Miller, and Simon 2017, chapters 2–3), or using results from these general investigations to provide predictive models for specific scenarios (for example, Masuda and Holme 2017, chapter 14; Ferguson et al. 2005; Ferguson et al. 2006).

4. Multi-Methodology Reasoning Across Compartment and Network Domains

The coexistence of compartment (section 2) and network (section 3) models in epidemic modeling provides unique epistemic challenges. In particular, epidemiologists need to: (i) decide which of these methodologies is appropriate for a given target system (section 4.1); and (ii) relate the results from both methodologies to each other (section 4.2).

4.1 Choice of Modeling Methodology

The choice of model type is usually determined by judging the degree of actual heterogeneity in a given population's disease transmission—it is generally assumed that network models will be a better choice for the early stages of a disease outbreak, when transmission is highly heterogeneous and contact structures can still be captured relatively precisely (Brauer, Van den Driessche, and Wu 2008, 133). In the later stages of an epidemic, transmissions are assumed to be relatively homogeneous and the precise contact networks are more difficult to capture; therefore, compartment models will be a better choice. This distinction itself is based on a simplification and likely not applicable to severe pandemic scenarios, where people tend to change their behavior and social networks considerably throughout the course of the pandemic. For example, Jamie Bedson et al. write:

> Although this strong assumption is true for some diseases (for example, the common cold) or situations (for example, a boy's boarding school), the history of major epidemics demonstrates that microscale interactions between individuals are important. In practice, observed interactions reflect a range of social, cultural, political, economic and behavioural shifts over the course of a disease; they include both collective and individual behaviours and, most critically, they are dynamic and variable. (2021, 835)

Accordingly, an overreliance on compartment models to model the later stages of an epidemic can lead to considerable model errors, such as an underestimation of the effectiveness of local (county-level) interventions and a tendency to overestimate the final

epidemic size (Chowell et al. 2016). In response to an increasing recognition that the distinction between homogeneous and heterogeneous phases of a pandemic is problematic.

Even setting aside the difficulties of drawing a clear distinction between the homogeneous and heterogeneous transmission phases of an epidemic, arguments for why a particular type of model has been chosen for a particular purpose often rely on more complex epistemic reasoning. In particular, practitioners rely on the particular aims of their research project (explanatory or predictive purposes) and scenario-specific limitations (such as whether it is possible to achieve predictive accuracy at all) to justify their choice of modeling methodology. For example, in the context of the Covid-19 pandemic, network (or methodologically similar agent-based) models were used to investigate the effects of interventions that can only be captured in such models, such as travel restrictions and social distancing (Chang et al. 2020; Ando et al. 2021). Similarly, it can be argued that the influence of different vaccination rates or variations in disease status can best be captured by compartment models (De la Sen and Ibeas 2021). The reasoning behind choosing a particular model for a particular scenario therefore works on epistemic trade-offs: the ability to construct models that provide particular, causal-mechanistic explanations is weighted against the potential mismatches of the modeling technology to the anticipated spread of the disease. This also means that there are compartment models for the early stages of a disease outbreak and network models for the later stages of epidemics. It is therefore possible to have a coexisting set of different results and explanations from compartment and network models for the same target system, which further calls into question the assumption that modeling domains can be clearly distinguished and supports the need to integrate network and compartment modeling (section 4.2).

4.2 Integrating Network and Compartment Modeling

As discussed in section 4.1, the fact that it is difficult to clearly distinguish domains for each modeling methodology based on traditional distinctions, such as early/late phases of an epidemic or heterogeneous/homogeneous disease transmission, has led to demands from practitioners and policymakers for an "integrated" approach to modeling (Kretzschmar 2020; Bedson et al. 2021; Rose et al. 2021; Crépey, Noël, and Alizon 2022). Integrated modeling can take two general forms: (i) the complementary use of modeling results from compartment and network (and, if appropriate, other types of models) for integrated reasoning about disease scenarios; and (ii) the construction of integrated models that couple compartment and network algorithms. I now discuss the epistemic strengths and weaknesses of each of those approaches in turn.

Approach (i), the integrated reasoning with modeling results from different methodologies, is based on the notion that most modeling research projects will still commit to one of the methodologies but the results need to be coordinated and collected to allow holistic reasoning about a disease scenario that integrates results from many different models. As Mirjam Kretschmar (2020, 44) points out, this poses a logistic—and currently unresolved—challenge of making all the results available in a comparative format and of establishing academic institutions devoted to such integrated reasoning (such as a "central modeling unit" in large public health institutions) without siphoning off too many resources from individual modeling projects.

Beyond the logistic challenge of practically enabling integrated, cross-methodological reasoning in epidemic modeling, integrated reasoning also raises epistemic questions—most prominently, how to integrate potentially conflicting results and which models to give epistemic preference in such a scenario. A relatively straightforward way of integrating reasoning with potentially conflicting results from both network and compartment models is to insist that each modeling methodology addresses a different, complementary set of epistemic questions. For example, Alun L. Lloyd and Steve Valleika (2007) stress that network models can address questions about the influence of particular contact structures as well as of potential interventions into such structures, while compartment models are simply unable to provide information about such aspects of disease development. In contrast, due to the fact that they generally use fewer computational resources and can therefore be run for more iterations, compartment models can better answer questions about the long-term development of epidemics (Meehan et al. 2020). This approach of complementary reasoning appears common in epidemic modeling and many authors justify their choice of model or of modeling technology by reference to the kind of epidemiological question it is meant to address, often acknowledging that the "other" class of models addresses complementary questions that they cannot tackle in the given publication (see, for example, Newman 2002; Lloyd and Valleika 2007).

The ability to keep modeling domains separated by restricting each to a set of different epistemic questions and, therefore, a different set of causal-mechanistic explanations, works best if those explanations are treated as possible rather than actual explanations. If the work with different models is seen as investigating different possible sources of an epidemic, different modeling technologies can coexist without needing further integration as their results do not need to be seen as conflicting with one another. Further work to integrate compartment and network modeling is only needed if: (i) epidemiologists wish to investigate the interaction of network- and compartment-based causes; or (ii) the explanations provided by different models are treated as actual explanations and conflict with one another. In both didactic and research publication on epidemic modeling, those two scenarios appear to be exceptions; in other words, the vast majority of publications is targeted at deriving possible explanations and has therefore no need to expansively address conflicts with other models. This is also evident in the emerging literature on integrated reasoning with different models, which—as described above—emphasizes the need to foster dialogue between different modeling groups and to coordinate a collection of different results, rather than the resolution of conflicts between different results (Kretschmar 2020; Bedson et al. 2021).

Approach (ii) to integrated modeling—in particular, to integrated modeling with compartment and network models—is to combine both modeling methodologies in a single model. Such combined models can be constructed by linking several compartment models into a relatively small network—such as by assuming that each compartment model describes a region or community within which the disease spread is homogeneous and only modeling exchanges between those clusters (see, for example, Ferguson et al. 2005; Ferguson et al. 2006; Meng et al. 2021). The number of nodes in such networks of compartment models is therefore usually much smaller than those of individual-based networks. However, such models can be used to tackle questions that straddle the usual epistemic divide between the two modeling methodologies, such as how the interaction of regions with different vaccination rates influences the development of a pandemic.

Furthermore, coupling different compartment models for different regions allows the model to capture differences in the descriptive parameters for each region—for example, different age demographics in different areas of a country—and therefore make the model more specific for a given scenario (Ferguson et al. 2005; Ferguson et al. 2006; Meng et al. 2021).

However, the fact that those models allow many parameters to be fine-tuned for a given scenario, and therefore potentially to use the model as an actual explanation for a given scenario, brings with it several epistemic challenges. Firstly, models that couple network and compartment algorithms require input data on different spatial and/or temporal scales—for example, in the scenarios discussed above on the mobility between different regions and the vaccination rates within each region. This means that epidemiologists who construct and use integrated models need to have access to both traditional epidemiological data and social/behavioral data. Bedson et al. (2021) have therefore identified establishing access to behavioral data sets and establishing interdisciplinary knowledge exchange between epidemiologists and social scientists as one of the primary challenges of integrated modeling. Such interdisciplinary collaborations will also be necessary as each dataset will come with specific uncertainties and errors, which will need to be identified and taken into account when interpreting integrated models' results. It is likely that the interaction between different uncertainties in different sets of input data within an integrated model will be complex. Crépey, Noël, and Alizon (2022) have pointed out that the challenge of integrating data across methodologies and scales is one of the currently largely unaddressed challenges of integrated epidemic modeling.

Similarly, in the philosophy of science literature, there is a debate on the fact that computational models that integrate algorithms written to capture processes on different spatial or temporal scales usually contain additional bits of formalism to link those different bits of algorithm together, to translate between those different scales within the model (Winsberg 2010). These transitional parts of the formalism usually do not represent a physical process in the target system and are therefore interpreted as an additional source of errors in scale-transitional models. The debate about the problematic nature of such potential mathematical artifacts has focused on integrated models in climate science but, as Crépey, Noël, and Alizon (2022) have pointed out, is applicable to epidemic modeling as well. In particular, the need to have such translation algorithms introduces an epistemic trade-off situation: integrated models that are very exact, in the sense that they integrate many different processes on different scales, automatically introduce a source of error through the coupling algorithm used to achieve this integration. It is therefore not straightforwardly the case that integrated models offer more of an actual explanation for a given scenario. This needs to be ascertained for each model separately.

5. Conclusions

I have analyzed the construction and use of hierarchies of compartment models (section 2) and repositories of network models (section 3) in epidemic modeling. I have also analyzed integrated reasoning with different kinds of models (section 4). My analysis yields five core, novel insights, which are summarized below.

(i) Epidemic modeling is methodologically highly pluralistic in that it encompasses different modeling methodologies, different modes of model construction, and the use of models for different kinds of explanations.

(ii) Epidemic modeling often relies on reasoning with structured groups of models, rather than with single models. The groups of models constructed are different for each modeling methodology: vertically constructed hierarchies of compartment models (section 2) and horizontally constructed repositories of network models (section 3), respectively.

(iii) Different modeling methodologies are used complementarily in multi-model and multi-methodology reasoning. In contrast to what might be expected from the coexistence of two very different modeling methodologies, epidemiologists do not usually argue that one methodology should be used exclusively or is generally superior to the other (section 4). Instead, separate domains of application have been delineated—for example, network models are preferred for the modeling of the early stages of an epidemic and compartment models for the later stages. However, those distinctions are problematic and increasingly questioned by epidemiologists—see (v) below.

(iv) A focus on single, authoritative models is not generally characteristic of epidemic modeling. This indicates that the situation during the Covid-19 pandemic, as described by Northcott (2022), with a focus on identifying a single master model rather than a more flexible approach to modeling, is not generally characteristic of modeling in epidemiology. The epistemic advantages of multi-model and multi-methodology reasoning identified here (sections 2–4) also renders additional support to Northcott's (2022) claim that a focus on one master model is not the epistemically best modeling strategy in epidemiology.

(v) Integrated epidemic modeling comes with epistemic challenges that are yet to be resolved. As discussed in section 4, epidemiologists have increasingly become aware of the need to avoid simplistic demarcations of applicability and to systematically integrate different modeling methodologies, either through integrated reasoning or through the use of integrated models (section 4). The epistemic challenges that arise from such approaches are currently unresolved and can be viewed as one of the most important issues for epidemiologists to address in the future.

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