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Major Article

Dynamic transmission models for economic analysis applied to health care-associated infections: A review of the literature

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Background: Cost-effectiveness analyses are an important methodology in assessing whether a health care technology is suitable for widespread adoption. Common models used by economists, such as decision trees and Markov models, are appropriate for noninfectious diseases where treatment and exposure are independent. Diseases whose treatment and exposure are dependent require dynamic models to incorporate the nonlinear transmission effect. Two different types of models are often used for dynamic cost-effectiveness analyses: compartmental models and individual models. In this methodology-focused literature review, we describe each model type and summarize the literature associated with each using the example of health care-associated infections (HAIs).
Methods: We conducted a review of the literature to identify dynamic cost-effectiveness analyses that examined interventions to prevent or treat HAIs. To be included in the review, studies needed to have each of 3 necessary components: involve economics, such as cost-effectiveness analysis and evidence of economic theory, use a dynamic transmission model, and examine HAIs.
Results: Of the 9 articles published between 2005 and 2016 that met criteria to be included in our study, 3 used compartmental models and 6 used individual models.
Conclusions: Very few published studies exist that use dynamic transmission models to conduct economic analyses related to HAIs and even fewer studies have used these models to perform cost-effectiveness analyses.

Economics is the study of how individuals or groups of individuals use limited resources to satisfy their unlimited wants. In other words, it is the study of choices in the face of scarcity. In health care, economic evaluation often takes the form of cost-effectiveness analysis (CEA). CEAs compare the costs and benefits of 2 or more strategies and can be useful for policy and decision making by presenting detailed information on the consequences of different decisions. Other types of economic analyses in health care exist, including cost analyses (ie, analyses that focus solely on costs rather than both costs and effectiveness) and studies that examine the types of choices faced by health care decision makers.

Although they can be performed using statistical models, economic analyses are often conducted using simulation models because the data necessary for statistical analysis simply do not exist. This may be because 1 or more of the strategies being compared are hypothetical in nature. Models are a simplified representation of a real-world phenomenon and can be useful if that real-world phenomenon is complex or costly or time-consuming to perform. They are essentially a list of mathematical operations that dictate the behavior of simulated individuals in a predefined setting. Input parameters for economic simulation models can be obtained through a number of different sources, including published data or statistical analyses of randomized control trials or administrative data.[1]

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It is important to use the most appropriate model for the task at hand because the type of model chosen can have a substantial influence on the results of an economic evaluation.[2,3] In other words, for a health economic evaluation to be as useful as possible to decision makers, the modeling approach should coincide with the condition of interest. The most common model types are decision trees or Markov models, both of which assume that there is no interaction between patients and that the probability of patient exposure to a disease is constant over time. These assumptions are reasonable for noncommunicable diseases and thus these models are appropriate in most settings. However, the spread of infectious diseases is affected by the amount of contact individuals have. In addition, interventions for infectious diseases are designed to reduce transmission or progression from exposure to infection, or reduce duration of symptoms. These interventions will therefore influence not only whether treated individuals become sick (direct effect) but also whether other individuals will be exposed to the disease (indirect effect). Models that take into account these transmission effects are called dynamic models because the risk, or force, of infection changes over time.[4] Dynamic models are necessary for CEAs that evaluate interventions that affect a pathogen's ecology[5,6] or transmission.[7,8] Although these 2 scenarios are common for CEAs in the realm of infectious diseases, there are situations in which static models are acceptable.[4] For example, dynamic models are not necessary if the population of interest makes up a small subset of the overall population, such as vaccinations for travelers. In addition, static models may be acceptable if most of the treatment effects are direct with only a small proportion being indirect.

Dynamic models fall into 2 main categories: compartmental and individual models. To model the progression of a disease through a population in a compartmental model, individuals within that population are often categorized into different groups based on certain characteristics related to their experience with the infectious agent. One such example is a so-called SEIR model, a common type of compartmental model that examines individuals who may be susceptible (S) to, exposed (E) to, or infected (I) by the disease or removed (R) from the population via immunity or death. A system of differential equations governs transitions between the compartments. Compartmental models take a top-down approach, meaning that the characteristics of the system define the average behavior of the individuals in each compartment.

Individual simulation models differ from compartmental models in that they model the behavior of individuals rather than groups of individuals. Discrete event simulations[9] and agent-based models are 2 types of individual models.[10] In discrete event simulations, individuals typically compete for scarce resources where queues are important, such as wait times in emergency rooms[11] or organ transplantation[12] or large-scale viral outbreaks such as pandemic influenza[13,14] or smallpox.[15] Discrete event simulations have been used for infectious disease applications such as pandemic influenza containment strategies. Like compartmental models, discrete event simulations are also considered top-down. Agent-based simulation models, on the other hand, are considered bottom-up models in which the behaviors of the agents dictate the system-level characteristics. Agents in agent-based models are individuals who behave according to certain rules dictated by their situation and outlined by the modeler. In a hospital setting, agents can be patients, health care workers (HCWs), or visitors and these agents are capable of interacting with one another and transmitting disease.

Mathematical models of disease transmission are complex and computationally intensive. This may be a reason that, despite being well-recognized as the most appropriate modeling method for interventions related to infectious diseases, dynamic models are still quite rare in economic analyses. In fact, recent review articles have found that only 11% of 209 economic evaluations of vaccination programs[3] and only 5% of 55 economic evaluations of *Chlamydia trachomatis* interventions have used dynamic models.[16] A recent review focused on mathematical transmission models of health care-associated infections (HAIs) in general and only briefly touched on economic analyses.[17]

The purpose of this article is to review the published literature that uses these models to evaluate strategies for reducing and preventing transmission of HAIs. Reviewing these published articles will help to determine the extent to which these models are used as well as to identify areas of focus for future research in this area.

METHODS

We conducted a review of the published literature to identify studies that conducted economic analyses using dynamic models applied to HAIs. We searched PubMed for English-language, nonreview articles published between January 1, 2000, and December 31, 2016, for these terms: economics: *economic*, *cost*, *cost-effectiveness*; dynamic model: *dynamic*, *agent-based model*, *compartmental model*, *transmission model*; and HAIs: *nosocomial infection*, *health care-associated infection*, *hospital-acquired infection*, *hospital infection*. Articles ultimately selected for our review needed to have at least 1 of each of these 3 components. In other words, our goal was to find published articles that used dynamic simulation models to examine concepts related to health economics within the realm of HAIs. We also included articles identified by van Kleef et al[17] in the above-mentioned systematic review of mathematical transmission models of HAIs. With the identified studies in hand, we extracted information from each regarding the infectious pathogen(s) included in the study, the type of dynamic model used, the hospital setting (ie, ICU only and entire hospital), the type of economic analysis, the HAI prevention intervention being considered, and the findings from the study.

RESULTS

Literature search results

Figure 1 describes the results of our search strategy. Our literature search retrieved 216 articles. We reviewed the titles and abstracts of these articles and selected 18 for full-text review. Of these, 9 were removed due to lack of 1 of the 3 necessary components described above or due to the exclusion criteria. This resulted in 9 articles to be included in the final review. Highlights of these articles are shown in Table 1 and the articles are summarized below.

Compartmental models

Smith et al[18] explored the dynamics of a hypothetical epidemic of antibiotic-resistant bacteria that spans multiple hospitals. The authors created a mathematical model based on a set of differential equations that govern how antibiotic-resistant infections can spread from 1 facility to another by sharing patients. Investments in a hypothetical infection control strategy can decrease the number of newly infected individuals. The authors found that each individual hospital's incentives to invest in infection control resources depend on the proportion of patients who import antibiotic-resistant bacteria as well as the infection control investments made by nearby institutions. As hospitals share patients, there is an incentive to free-ride off of the infection control investments that others have made. This free-riding action becomes more attractive as the number of hospitals increases. The authors conclude that regional coordination of infection control efforts is necessary to prevent these perverse incentives.