Bugs and Bucks: Infectious Disease Persistence is a Matter of Economics**

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Summary

We live at a moment in history unprecedented with respect to both the breadth and quantity of resources available for the prevention and control of infectious diseases. Many communicable diseases of public health importance have exclusively human reservoirs, and can be made nontransmissible using readily available tools (e.g., vaccines, antimicrobials, and improved water and sewage treatment). In other words, we live in a time when it is (theoretically) within our power to actually eliminate or eradicate several infectious diseases of public health importance, and yet these diseases persist. It is proposed that the reasons for disease persistence in such situations relate primarily to phenomena that fall easily into frameworks already well studied and understood by economists. In this paper, “economics” is defined in its broad sense, as a discipline that seeks to understand the behaviors and choices of individuals and societies as they attempt to maximize their well-being through the production and distribution of “goods.” The “good” in question is the absence of morbidity and mortality from persistent infectious diseases. The failure to incorporate economic considerations into disease-control policy will result in suboptimal policy. Policy-relevant concepts include: (i) the concept of public goods (e.g., clean water, widespread vaccination) that produce environments and herd effects that benefit all members of a community and cannot be denied to anyone; (ii) the related concept of transmissibility of infection, and prevention of disease transmission, as key economic “externalities” that cannot be ignored when disease-policy decisions are made; and (iii) the fact that individuals with infectious disease, or at risk of infectious disease, are rational actors, and will behave and engage with one another in ways that can be described as economic “games.” Dissemination of knowledge related to these concepts, and tools and data that permit their incorporation into disease-control policy, represent a valuable opportunity to reduce the burden of persistent infectious diseases at local, national, and global levels.

Current realities

It is evident, from even a cursory evaluation of global statistics, there is a powerful economic undercurrent that must inform any discussion of the persistence of infectious diseases. Life expectancy, infant mortality, and the proportion of deaths attributable to infection all exhibit linear or log-linear relationships with per-capita gross domestic product (GDP). For example, as GDP increases, on average, there is a corresponding rise in life expectancy and a decrease in mortality rates (see Figure 1). While the mechanisms underlying this relationship are incompletely understood, it is clear that wealth translates into health at the national level, partly through elimination of infectious-disease threats.

Several key correlates of improved health and longevity include availability of infrastructure (e.g., to provide clean water and treat sewage), provision of basic health care and immunization, and development of systems to limit transmission of disease from animals to humans (e.g., via rabies prevention, and food-safety regulations/food inspection). All of these factors likely contributed to the epidemiological transition from infectious to chronic diseases as major drivers of mortality that occurred approximately a century ago in wealthy countries — with recent research suggesting that the largest single impact may have derived from reduced death from waterborne infection. However, successes in eliminating or markedly reducing morbidity from waterborne disease have not been replicated in many middle- and low-income countries, and indeed waterborne threats such as cholera have emerged in countries where they have not occurred previously. Similar observations can be made regarding vector-borne diseases such as malaria, once endemic but now rare in many high-income countries, including the United States. These diseases persist in low-income countries where the promise associated with control programs has been eroded by antimalarial-drug and pesticide resistance, and perhaps by climate change. In high-income countries, recent resurgences in vaccine-preventable diseases (including measles, mumps, rubella, and pertussis) have occurred, spurred in part by reduced vaccination levels that reflect public concerns about vaccine-adverse effects.

All of the aforementioned occurrences are driven, in part, by systems that have strong "economic" components. They have been facilitated by the failure of disease-control policy to consider such components, which include externalities (i.e., indirect effects that accrue due to the communicable nature of many infections), public goods (e.g., the "herd immunity" derived from vaccinating a sufficiently large proportion of the population), and "game behavior" (i.e., the tendency of members of the population to change their behavior based on their expectations of what others will do).

Scientific opportunities and challenges

Mathematical modeling approaches that are commonly employed with "complex systems" have been in relatively wide use for the study of infectious diseases since the 1920s. Such models are useful tools for explaining and predicting the response of epidemics to control efforts, and explicitly treat disease transmission effects as economic externalities. Such models represent the risk of infection in an individual in a population as a function of infection prevalence in contacts, but also as a function of the population's "immune status" and herd immunity. Herd immunity becomes a "public good" because it is shared by all individuals in the population. However, the application of disease models to public health policy is a fairly recent development, and there is relatively limited understanding of the concepts that underlie these models among front-line public health professionals. This results in a misdirected focus and suboptimal programmatic approaches. For example, the public health community focuses on the role of vaccines in protecting the vaccinated individual rather than the "herd." In the context of disease resurgence (e.g., the recent mumps epidemics that have struck North America and Europe), public health messaging recommends that young adults should be boosted for their own protection. With endemic diseases, such as influenza, public health messages focus on direct protection by immunization, rather than the (often more substantial) indirect protections produced by wide-scale immunization coverage. Models project that immunization of younger individuals, at less risk of severe outcomes from influenza but more likely to spread the disease as well as respond to vaccination, is actually a far superior influenza-vaccination strategy than the targeting of older individuals currently advocated by North American public health authorities. Such model projections have more recently been validated by randomized trials. As such, enhancing the understanding of such concepts as externalities and public goods, as well as improving the availability and acceptance of tools for system-dynamic modeling in public health, could provide innovative and more successful approaches to disease prevention and control policy.

However, although system dynamics models do explicitly capture externalities and public goods such as herd immunity, such models have only more recently begun to capture behavioral responses to disease risk (e.g., hiding, fleeing, and engaging in risky behavior due to a decrease in perceived risk). Recent work suggests that behaviors and associated changes in movement and contact patterns may provide the key to persistence of diseases (e.g., syphilis) and to the "waves" characteristics of epidemics and pandemics. Furthermore, rational actors, whether individuals, institutions, or governments, will behave in a manner that anticipates the actions of others (whether by free riding on herd immunity, or failing to invest in disease control due to concerns that others will not do the same), leading to suboptimal "Nash equilibria." In the context of immunization, Nash equilibrium refers to the phenomenon whereby as a disease approaches elimination due to high vaccine coverage, the (near-term) risk associated with the vaccine itself will inevitably begin to outweigh the (near-term) risk of infection and illness. This will lead rational parents to pull back from immunization of their children, on the assumption that other parents will continue to immunize (i.e., creating a free ridership problem). Nash equilibria can also be identified for systems in which neighboring jurisdictions or hospitals must invest to control disease; actors may free ride on successful neighbors, while high-performing countries may defund their efforts if disease is simply reimported from poorly performing neighbors. A key and as-yet-unanswered question is the degree to which changing risk perception by policy makers drives increases or decreases in disease-control funding, which could result in oscillation in disease prevalence independent of other systematic changes. Thus, there are emerging scientific opportunities related to the measurement of such changes in behavior, risk perception, and motivation in response to epidemics, both at the level of individuals and at the level of governments and decision makers. Furthermore, emerging social media and telecommunications technologies make it possible to measure and anticipate behavioral drivers of disease persistence (via mining of Twitter feeds, or by using cell-phone towers to measure movement patterns in epidemic regions).

Policy issues

- Public health and disease-control experts need to understand that issues of free ridership and Nash equilibria appear frequently <u>as a consequence of the success of programs</u>. Training programs for epidemiologists and public health physicians need to teach adaptability and responsiveness as core components of disease-control programs; a corollary is that disease-control programs need to be conceptualized and taught as <u>works in progress</u> that are not static over time. **Proposed leads:** Many of these concepts are already taught in economics curricula. Universities, schools of public health, and training programs (e.g., U.S. Centers for Disease Control and Prevention [CDC] Epidemic Intelligence Service) need to establish trans-disciplinary links necessary to integrate such concepts into training activities.

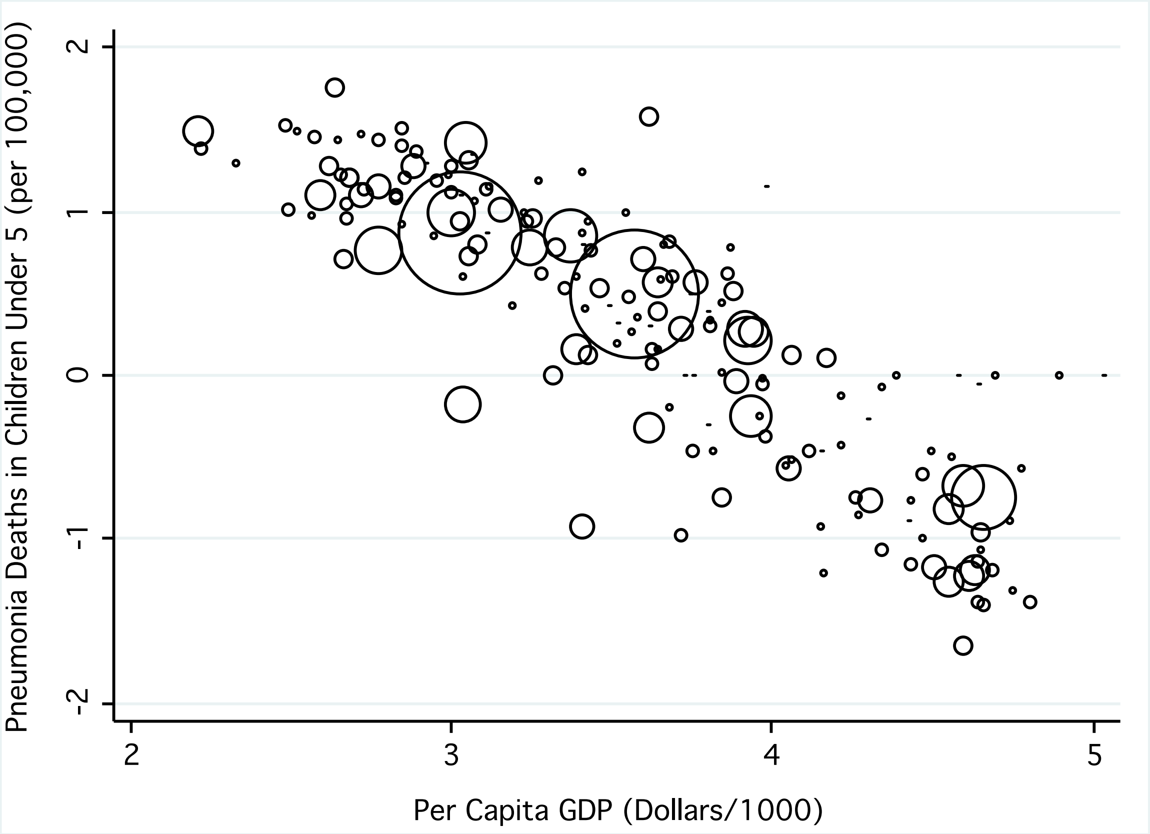
- Tools for modeling, interpretation, and analysis of infectious disease-control programs as <u>complex systems</u> must be made more readily accessible and user-friendly to front-line public health personnel. **Proposed leads:** Universities can foster training as part and parcel of core public health teaching; industry can work to meet the need for user-friendly software resources designed for use in the field. Such software resources also need to have graphical interfaces that facilitate the translation of model projections into easy-to-understand applets and graphs. Government agencies should adopt these tools.

- There needs to be improved understanding of how changes in disease prevalence drive downstream changes in the funding of disease-control programs, and to what extent such changes might be important drivers of disease persistence. **Proposed lead:** As this represents an informational need that lies at the intersection of social-science research and applied public health, partnerships between agencies that fund social science and health-policy research and agencies that would be the beneficiaries of such knowledge should be explored.

- Issues of personal privacy and confidentiality need to be reconciled with public good so that emerging electronic-data sources can be used to capture information on human migration, contact networks, and behavioral responses to epidemics and outbreaks. **Proposed leads:** National and regional governments need to review appropriate uses of extant electronic-data resources for protection of public health, and consider legislative and regulatory changes that balance privacy rights against potential contributions to population health.

Figure 1:

Incidence of pneumonia-related death in children as a function of per-capita gross domestic product, 2008–2009 data. Bubble sizes are proportional to countries' populations.



*** A policy position paper prepared for presentation at the conference on Emerging and Persistent Infectious Diseases (EPID): Focus on Prevention convened by the Institute on Science for Global Policy (ISGP June 5–8, 2011, at the Estancia La Jolla Hotel, San Diego, California.*

The following summary is based on notes recorded by the ISGP staff during the not-for-attribution debate of the policy position paper prepared by Dr. David Fisman (see above). Dr. Fisman initiated the debate with a 5-minute statement of his views and then actively engaged the conference participants, including other authors, throughout the remainder

of the 90-minute period. This Debate Summary represents the ISGP's best effort to accurately capture the comments offered and questions posed by all participants, as well as those responses made by Dr. Fisman. Given the not-for-attribution format of the debate, the views comprising this summary do not necessarily represent the views of Dr. Fisman, as evidenced by his policy position paper. Rather, it is, and should be read as, an overview of the areas of agreement and disagreement that emerged from all those participating in the critical debate.

Debate conclusions

- Mathematical models are important tools for researchers and policy makers addressing infectious diseases since they can help explain the spread of disease, clarify the impact of public health interventions, and aid in conveying complex ideas to lay audiences. Obviously, however, given their dependence on the quality of the input data and creativity of the models themselves, their predictions do not come with absolute certainty. Regulation, peer review, and the sharing of best practices should be instigated to increase the accuracy of models and the confidence in their usage.

- Researchers and policy makers within mainstream public health need to include models in their infectious disease control efforts. Incorporating training and courses into the curricula of public health schools, and for those already working in public health fields, can strengthen both the effectiveness of research and policy decisions.

- It is necessary to communicate to policy makers and public health professionals not only the general benefits of mathematical models, but also specific examples of economic concepts such as "Nash equilibria" and "free ridership " for use in modeling of infectious diseases. At present, these economic concepts are insufficiently taken into account in infectious disease control strategies and policies.

- Mobile phones and social media provide innovative ways to more accurately predict and track infectious disease spread. Researchers need to harness the data driven by such emerging technologies to construct mathematical models for disease prediction, including accounting for sociobehavioral factors. Efforts to collect and incorporate sociobehavioral data should be expanded.

- The challenges facing policy makers to continually balance the public good derived from controlling infectious diseases *writ large* against protecting the rights of individuals to accept or reject vaccination, and to maintain personal anonymity requires a greater understanding of the relative importance of societal factors influencing the appearance and spread of infectious diseases.

Current realities

In the study of infectious diseases, mathematical models are valuable tools for (i) understanding their scientific basis, (ii) predicting how they spread, (iii) demonstrating the impact of interventions, and (iv) aiding in communicating complex concepts among scientists, policy makers, and the public (e.g., through illustrative charts and diagrams). It was agreed that models are not crystal balls that foretell the future (i.e., they cannot predict what will occur with absolute confidence). It was strongly argued that, despite inherent imperfections, models can be effective tools for managing risk and uncertainty. However, it was also argued that the practical application of models to real-world scenarios is limited by their inability to provide wholesale assurances. Examples were presented where mathematical models failed to accurately predict an event and were used to convey a false level of certainty.

There was consensus that mathematical models, used in public health and other disciplines, vary in quality. Such variations are due to differences in the accuracy and availability of data inputs, as well as the precision of the models themselves. As a result, the application of models has resulted in both positive and negative consequences.

Minor disagreement was voiced concerning the simplicity of models. While some contended that models are too complicated to be useful to a lay audience, others countered that models can be conveyed with varying degrees of complexity appropriate for different audiences. For example, it was asserted that analogies and illustrations can be used to distill and convey the outcomes of models so that they can be comprehended by non-experts. It was further argued that only knowledge of simple math (e.g., addition and subtraction) is needed to understand most mathematical models.

There was considerable debate regarding the extent to which mathematical models are currently being used in infectious disease research and public health efforts. On one side, it was argued that models have been regarded as exotic or unusual, are not widely available, and are rarely taken into account in public health decisions. Others, however, suggested that their usage is actually fairly common. The debate concluded that the use of mathematical models varies considerably across fields of study. In human health, for instance, models have been employed more routinely than in disease ecology. It was also noted that models may be used for research and decision-making within some countries more than others, although no specific examples were provided.

There was strong agreement that economic concepts such as Nash equilibria and free ridership are insufficiently taken into account in infectious disease control strategies and policies. These concepts may have negative implications for the effectiveness of certain interventions (e.g., vaccination strategies). The concept of Nash equilibria was illustrated by the fact that public attitudes toward vaccines are related not only to perceived risks associated with the targeted disease, but also to the perceived risk of the vaccine itself; an individual is therefore more likely to accept the risks accompanying a specific vaccine when the risks associated with the corresponding disease are perceived to be high. For example, because of the devastating effects of polio in the 1950s, many societies were willing to be vaccinated with a new polio vaccine even though the vaccine sometimes produced negative side effects (e.g., paralysis). In terms of free ridership, it was noted that this problem becomes most apparent as vaccine uptake for a specific disease increases and the risks of contracting that disease correspondingly decrease. In this situation, individuals may feel that the risks associated with the vaccine outweigh the benefits and therefore choose to capitalize on the herd immunity that is provided by the large number of people who do receive the vaccine.

It was recognized that individual- and country-level responses to problems associated with infectious diseases are influenced by factors such as culture and socioeconomic status. Despite growing acceptance of the importance of these factors in shaping disease control strategies and outcomes, sociobehavioral responses to infectious disease risks have been underutilized as data for mathematical models. Moreover, it was noted that there is a deficiency in wider understanding and research related to why variations in sociobehavioral responses exist.

Surveillance was widely recognized as a crucial component of infectious disease prevention. However, it was asserted that current surveillance techniques are insufficiently multimodal because they do not take into account enough data sources and some types of data are heavily underrepresented (e.g., there is a dearth of information related to behavioral responses within data collection efforts). Reliance on only one information source was purported to increase the likelihood of erroneous models. For example, the modeling program Google Flu Trends was noted to have limited success when used in isolation of additional data because it does not take into account changes in behavior associated with disease threat.

Debate took place over the suggestion that individuals, governments, and institutions must be regarded as rational actors in relation to disease control and response. The premise underpinning this view was that individuals will behave in ways that anticipate how they expect others to behave. The question arose as to whether behavior in response to infectious diseases can always be regarded as strictly rational.

The relationship between a country's health and a country's wealth was also discussed in detail. There was consensus that, with a few exceptions (e.g., in the 1950s, China experienced a rapid rise in life expectancy while wealth remained low), there is a tight link between a country's level of wealth and health outcomes. However, this link encompasses complex factors and it is challenging to determine causality from any one factor. Differing views were expressed as to whether wealth translates into health or vice versa. It was contended that whether wealth leads to health or health leads to wealth is an important distinction to more carefully understand since it has implications for policy decisions.

Scientific opportunities and challenges

A significant challenge to increasing the uptake of mathematical models for use in infectious disease research and policy decisions is the difficulty in ensuring the accuracy of the results. There was consensus that the development of a robust system for peer review and validation of models, as well as setting guidelines and sharing best practices among modelers, would provide the requisite substantiation necessary to establish better confidence in models. For example, it was argued that policy makers would likely feel more secure in relying on the recommendations generated by models if they were better evaluated in terms of the risk of unexpected outcomes. Policy makers are obviously concerned that they, rather than the modelers, are likely to be blamed for unexpected outcomes.

There was consensus that the increasing utilization and availability of technologies (e.g., mobile phones and social media) provide important opportunities for the use and improvement of mathematical models in disease control. In Haiti, for example, mobile phone data were used to predict the spread of cholera far more accurately than traditional projection methods. However, it was argued that existing technologies have not been leveraged to their potential. Opportunities to incorporate technologies from other disciplines (e.g., oil drilling and hedge funds) into infectious disease modeling were also highlighted.

Although technologies offer new opportunities, other data obstacles remain. Problems in accessing data (e.g., privacy issues) that are most useful for mathematical models were highlighted as a continuing challenge. Additionally, data integration issues were purported to decrease model efficacy. For example, it was recognized that the ability of Google Flu Trends to accurately model influenza disease spread has been limited by an insufficient variety of data inputs.

It was contended that the resurgence of a number of preventable diseases in more-wealthy countries caused by increased vaccination refusal (e.g., pertussis and measles) has presented an opportunity for concepts such as free ridership and herd immunity to be incorporated into infectious disease control strategies. It was strongly emphasized that, as a starting point, a considerable amount of work will need to be done to improve how such ideas are communicated to policy makers, the public health community, and the public.

Policy issues

Confidence in models for infectious diseases would be enhanced by the current efforts to improve the quality of the data input, to identify the best practices for the use of results, and to establish minimal acceptable standards for creation. There was strong agreement that it is necessary to establish a formal process for the peer review of models to ensure all models adhere to certain standards.

There was a call for mathematical models to be employed by researchers and policy makers in a variety of fields so that models are not solely the domain of a narrow group of mathematically centered individuals. It was recommended that rigor, as well as training in the development and application of models as tools for infectious disease control, should be widely instituted among researchers and policy makers. Success stories were used to highlight the feasibility of this approach. For example, grant requirements compelled a group of disease ecology experts to create a predictive model. This led to positive and transformational results for the team and the project.

Given the acknowledged importance of training researchers and policy makers to appropriately create and interpret models, it was suggested that public health degree programs include courses on models as part of their curricula. Additionally, it was emphasized that an informal educational process must be developed through which those working in public health can learn how to appropriately apply modeling and its results to their activities. Reaching out to individuals who are already in public health fields is of particular importance because public health agencies are currently uncertain about how to utilize models and their outcomes (particularly in areas such as resource allocation across departments and budgets).

There was general agreement that improving messaging concerning the value and limitation of models is imperative, both for promoting the use of mathematical modeling and for increasing vaccine uptake. The key messaging issues are: (i) that non-mathematicians can and should be trained to better use models, (ii) that carefully constructed models can be successfully used to manage disease risk, and (iii) that models can be effective tools for communicating with lay audiences when their outcomes are simplified (e.g., via visual images or analogies). On the topic of vaccines, it was contended that the public does not understand the concept of herd immunity as an externality. It was asserted that the public looks for credible messengers to guide them, but has not been adequately provided with the intellectual tools to make decisions about vaccine usage. It was conceded that it may be challenging to effectively convey the concepts and values underlying collective action, especially in countries that are guided by a credo of rugged individualism (e.g., the United States and Canada). However, the resurgence of diseases such as measles in more-wealthy countries may provide a window of opportunity for messaging related to the importance of vaccine uptake.

It was argued that social and attitudinal changes related to protecting the public good may sometimes be more effective than mandating rigid policies. For example, problems enforcing coercive laws (e.g. compulsory vaccination) were highlighted. It was argued that education (i.e., to change mindsets) is not only a better route to disease control but also preserves individual liberties.

The debate highlighted the need for policy makers to address potential conflicts between the public and private good. For example, it was noted that coercive public health policies may benefit the public (e.g., by lowering disease rates through mandatory vaccinations) while simultaneously infringing upon the decision-making rights of individuals. It was similarly noted that there is a fine line between the public and private good that must be navigated in the selection of data inputs for models. This is because the inclusion of sensitive data could improve the accuracy of models while concurrently infringing upon the privacy of individuals to maintain their anonymity.

Specific diseases should be targeted in the development and implementation of mathematical models because it is difficult, and generally less effective, to make recommendations that simultaneously address all infectious diseases. Influenza models were used to illustrate the potential success of a singular disease approach. Such models have demonstrated that there is a high likelihood that influenza mortality would decrease if children were given preferential vaccination treatment over the elderly. Using this model outcome, it was suggested that children should be the primary focus of the next influenza vaccination drive.