Forecasting When, Where, and Possibly Why Outbreaks Are Likely to Occur

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(See the Major Article by Chan et al on pages 517–24.)

For centuries, infectious disease outbreaks have influenced not only geopolitical events and human migration [1] but also linguistic patterns and the development of different cultures [2]. Infectious diseases were the major drivers of morbidity and mortality throughout the world. However, over the past century, infectious diseases have been surpassed by chronic diseases in terms of their impact on morbidity and mortality: chronic diseases now cause 63% of deaths worldwide [3]. But not all parts of the world have benefited from the dramatic reductions in the morbidity and mortality attributable to infectious diseases. High-income countries have observed the greatest reductions. In many of these countries, decreases in infectious diseases were observed before major medical developments like the introduction of vaccines and antimicrobials. Instead these health improvements coincided with the widespread availability of clean water and improved sanitation, changes associated with economic development. In the current issue of Clinical Infectious Diseases, Chan et al explore the associations between measures of economic development and the likelihood of infectious disease outbreaks [4].

Considering multiple, easily obtained measures of economic development, Chan and colleagues find that the percentage of children vaccinated for measles and the number of telephone lines per 100 people are statistically associated with lower rates of infectious outbreaks. Here outbreaks are defined as either the first country to report cases, or, if that cannot be determined, the country with the most cases. However, it is important to stress that most of the variables they considered (eg, primary school enrollment, paved road density) are highly correlated with each other, and also with a “human development index” obtained from the United Nations [5]. Thus, regardless of the variables considered, the authors convincingly show that outbreaks can be partially explained and anticipated using publicly available information related to economic development and poverty. Importantly, Chan and colleagues, by focusing on forecasting, instead of merely reporting associations, move in the direction of understanding not only when and where outbreaks are most likely to occur, but maybe even why they occur.

An equally interesting finding of this paper relates to the factors not associated with a decrease in outbreaks. For example, the authors found that democracy was not an important predictor of infectious disease outbreaks in their model. Why? Findings from other investigations may help explain this result. Previous economic research has shown that “rule of law” (ie, fair implementation of laws and settling of disputes) is strongly associated with economic growth regardless of the political system [6]. In other words, democracy alone might not be enough. Indeed, in 1755 Adam Smith said that “a tolerable administration of justice” is needed “to carry a state to the highest degrees of opulence.” Three hundred years later, this same intervention may, at least in part, help decrease the occurrence of outbreaks.

Another interesting finding is that although the percentage of children vaccinated against measles was significant in their model, public health expenditure levels in general were not associated with a decrease in outbreaks. Perhaps, as the authors propose, health-associated financial aid to low-income countries may “displace” local spending on public health. They also suggest that in some cases aid may be used for unintended purposes.
Unfortunately, although we can provide vaccines and financial assistance to develop communications networks and vaccinate children, it is much more difficult to eliminate poverty in low-income countries and increase “rule of law.” Difficult as it is to raise incomes in low-income countries, it may be critical for detecting and controlling the spread of infectious diseases around the world. Outbreaks in lesser-developed parts of the world can affect the health and well-being of other countries. For example, Chan et al include outbreaks in North America (e.g., West Nile in the United States) spread from other parts of the world. Indeed, highlighting the “cost” of such outbreaks may help provide additional incentives for citizens in higher-income countries to subsidize not only public health infrastructure, but also economic development in general.

As Chan et al point out, their findings have limitations. First and foremost is the lack of available data. The data from the World Bank are, in some cases, notoriously sparse. Chan et al needed to impute missing data in many cases to complete their analysis. Also, many of the variables that might be important are not available: Accurate measures of rule of law, public corruption, private corruption, within-country price levels, and so on, are not as easy to measure as some of the variables considered in their model. Second, the authors also identify endogeneity problems inherent in this type of modeling. For example, if investment in public health is concentrated where the outbreaks are the worst or most likely to occur, increased public health investment might be associated with higher rates of outbreaks, at least in the short term.

Future work in this area should continue in at least 2 directions. First, better, more complete data are needed for both dependent and independent variables in such models. Furthermore, we need to determine which outbreaks are most important to anticipate. Clearly, not all outbreaks are the same in terms of their potential to impact morbidity and mortality. Nor are all outbreaks equal in terms of economic disruption. Such approaches are not only important for outbreaks, but also perhaps to control or reduce the emergence of antimicrobial resistance.

A second research goal should be to identify predictor variables for outbreaks that can be used as targets for interventions. Inferential techniques such as instrumental variables and exploiting natural experiments may help identify such targets. For example, the authors find that telephone lines are an important predictor. Building a large communications network may have some impact on outbreaks, but if we are to perform targeted interventions, we need to discover what is actually driving the outbreaks, not just what is associated with them. The identification and study of “outlier” countries may help find such causal factors to help answer why some low-income countries have more outbreaks than others. The majority of the outbreaks analyzed in this paper occur in low-income countries, but what truly differentiates low-income countries with large numbers of outbreaks from those with few? Geography undoubtedly plays a large role. The distribution of zoonotic infectious disease outbreaks is clearly not random. Chan et al recognize this and include the latitude of the country’s centroid in their model. Hot-spots do exist and in some cases economic development may actually drive outbreaks, at least for some period of time as people move into new areas and as more travel occurs between countries. More geospatial variables with data from longer periods of time may help generate answers and refine future models.

Regardless of the limitations of the available data, the work started by Chan et al should continue, in an effort to not only predict but also prevent future infectious disease outbreaks.

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