

# Network Models, Patient Transfers, and Infection Control

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(See the Major Article by Ray et al on pages 889–93.)

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Residents of long-term care facilities are at high risk for acquiring multidrug-resistant organisms [1–5]. These individuals are often admitted to acute-care hospitals, promoting the propagation of multidrug-resistant (and other) infections to other patients. Thus, hospital transfers represent an important potential point of intervention, where informed decisions can be made to control the spread of multidrug-resistant organisms, if only one could sufficiently understand the complex interactions that enable the spread of infections. Ray et al's article "Spread of Carbapenem-Resistant Enterobacteriaceae Among Illinois Healthcare Facilities: The Role of Patient Sharing" in the current issue of *Clinical Infectious Diseases* uses a model constructed from healthcare data to help elucidate the relationship between multidrug-resistant organisms and the sharing of patients between long-term care facilities and acute-care hospitals [6].

Scientists and engineers use models to understand the behavior of complex systems in many fields. Obviously, any resulting model-based predictions are only as good as their underlying models are faithful to reality; in general, finer-grained models support more refined predictions. In epidemiology, relatively coarse epidemiological models based on random mixing (ie, the assumption

that every member of the population is at similar risk) have long been used to predict how infections spread across large populations [7]. In reality, interactions between healthcare workers are not uniformly random [8], individual healthcare workers come into contact with diverse sets of patients [9–11], and some hospitals are much more likely to transfer patients to or from other hospitals [12]. These inconsistencies with the underlying model assumptions may compromise the effectiveness of interventions based on that model. For example, vaccinating a particular subset of healthcare workers (ie, those who are more densely connected with patients and other healthcare workers) may be much more effective than vaccinating healthcare workers selected at random [8]. In addition, increasing hand-hygiene adherence may be much more important among healthcare workers with more direct contact with patients [9, 13], and networks via peer effects may even influence healthcare worker behavior [14]. Thus, random mixing models do a poor job of predicting both how infections spread within and across hospital facilities and how effective a particular intervention meant to prevent, halt, or slow the spread of an infection might be. As a consequence, interventions designed to interrupt the spread of multidrug-resistant organisms may be much more effective if patterns of connectivity between healthcare and long-term care facilities are explicitly considered in the design of the intervention.

Ray et al clearly show that a higher volume of transfers between long-term care facilities and hospitals is associated with higher rates of extensively drug-resistant

organisms (XRDOs), providing much needed empirical evidence for the importance of considering long-term care facilities when designing infection-control practices in closely associated hospitals. The authors highlight the importance for the infection-control community to gain not only a greater understanding of the flow of patients between facilities but also the need for a framework to understand how potential interventions may be affected by patient transfers. Thus, while Ray et al focus on patients "shared" between long-term care facilities and hospitals, the implication that hospital transfers amplify the spread of healthcare-associated infections extends well beyond the facilities considered.

Of course, the association between hospital XRDO rates and transfer volumes described by Ray et al may not actually be caused by the transfers. The associations observed could be due to unconsidered factors such as (unmeasured) severity of illness or the patient's transfer history prior to the present transfer. Hospitals with higher XRDO rates may receive a greater volume of transfers from long-term care facilities or may admit more critically ill and/or frail patients, both of whom are more likely to acquire XRDOs. In addition, as Ray et al were unable to adjust for the direction of patient transfers, additional work should examine the direction of transfers, patient transfer history, severity of illness, and similar elements. Even so, the causation that Ray et al propose is surely epidemiologically plausible. Simmering et al showed that indgree (defined as the number of hospitals from which transfer patients are accepted into a specific hospital) was significantly associated with *Clostridium difficile* rates, even

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after controlling for both hospital and patient characteristics [12]. Given the importance of networks in the spread of a wide range of infections [15], it seems reasonable that the transfer effects posited by Ray et al are indeed likely to be important even after considering other explanations.

The authors' findings highlight how important it is that infection-control efforts consider more than what is going on locally at a particular hospital. This notion is not new to healthcare epidemiology nor are efforts to coordinate responses among facilities [16]. Yet research supporting the importance of these so-called network effects (ie, patterns of interfacility transfers) on the spread of healthcare-associated infections has lagged behind research on similar network effects underlying the spread of, for example, sexually transmitted diseases [17, 18]. Moreover, much work remains to be done on the development and implementation of interventions purposefully designed to address or, better still, exploit the properties of the specific network of hospital transfers. For example, using a game-theoretic approach, Miller et al showed that because infections can spread among institutions, screening policies should be set at the regional level and efforts to control infections by individual hospitals may fail because they cannot control what happens at connected hospitals [19]. However, before we can consider the role of centralized decision-making or regional strategies, we need a much better understanding of the role, extent, and influence that transfers have on defining precisely where the regional boundaries may lie. In fact, the boundaries implicitly defined by the network of hospital transfers may or may not correspond to geopolitical boundaries, so efforts to design interventions based on city, county, or state levels may fail simply because they do not exploit the more natural boundaries of the facility-transfer network.

Finally, even if the association between transfers and XDRO rates described by Ray et al eventually proves not to be causal,

their findings still have profound implications for infectious disease surveillance efforts. While surveillance is the cornerstone of public health, such efforts are often colored by convenience sampling, where surveillance sites are recruited based on their willingness to participate rather than on any grand design plan [20–22]. Instead, given a set of surveillance site candidates, a limited set of participating sites should be chosen so as to optimize some designed outcome (eg, obtaining more timely estimates of disease activity or obtaining more reliable estimates). Ray et al's findings illustrate how the decision to include or not include hospitals that share greater proportions of patients with long-term care facilities may have profound implications when estimating the prevalence of XDROs at a population level.

In conclusion, the thoughtful work by Ray et al highlights the need for a greater understanding of the role that hospital transfers play in infection control. More to the point, the authors' use of mathematical models or, more specifically, network models fit to surveillance data illustrates how such data analytic techniques can guide the development of effective interventions to improve this particular healthcare outcome. Better surveillance systems for XDROs and other infectious diseases, coupled with additional work to clarify the patterns implicit in these data, can help determine what the most effective interventions are likely to be and where they should be best applied, thereby making the best use of what are inevitably scarce resources.

#### Note

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