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Authors

Lee, Bruce Y

McGlone, Sarah M

Wong, Kim F

et al.

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Modeling the Spread of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Outbreaks throughout the Hospitals in Orange County, California

Bruce Y. Lee, MD, MBA[1], **Sarah M. McGlone, MPH**[1], **Kim F. Wong, PhD**[1], **S. Levent Yilmaz, PhD**[1], **Taliser R. Avery, BS, MS**[2], **Yeohan Song, BS**[1], **Richard Christie, PhD**[1], **Stephen Eubank, PhD**[3], **Shawn T. Brown, PhD**[1,4], **Joshua M. Epstein, PhD**[5], **Jon I. Parker, MS**[5], **Donald S. Burke, MD**[1], **Richard Platt, MD, MS**[2], and **Susan S. Huang, MD, MPH**[6]

[1]University of Pittsburgh, Pittsburgh, Pennsylvania [2]Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, Massachusetts [3]Virginia Bioinformatics Institute, Blacksburg, Virginia [4]Pittsburgh Supercomputing Center, Pittsburgh, Pennsylvania [5]Johns Hopkins University, Baltimore, Maryland [6]School of Medicine, University of California, Irvine, California

Abstract

Background—Since hospitals in a region often share patients, an outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) infection in one hospital could affect other hospitals.

Methods—Using extensive data collected from Orange County (OC), California, we developed a detailed agent-based model to represent patient movement among all OC hospitals. Experiments simulated MRSA outbreaks in various wards, institutions, and regions. Sensitivity analysis varied lengths of stay, intraward transmission coefficients (β), MRSA loss rate, probability of patient transfer or readmission, and time to readmission.

Results—Each simulated outbreak eventually affected all of the hospitals in the network, with effects depending on the outbreak size and location. Increasing MRSA prevalence at a single hospital (from 5% to 15%) resulted in a 2.9% average increase in relative prevalence at all other hospitals (ranging from no effect to 46.4%). Single-hospital intensive care unit outbreaks (modeled increase from 5% to 15%) caused a 1.4% average relative increase in all other OC hospitals (ranging from no effect to 12.7%).

Conclusion—MRSA outbreaks may rarely be confined to a single hospital but instead may affect all of the hospitals in a region. This suggests that prevention and control strategies and policies should account for the interconnectedness of health care facilities.

To date, most studies of methicillin-resistant *Staphylococcus aureus* (MRSA), which represents a continuing public health and health care system problem, have focused on individual or, at most, small groups of hospitals.[1-10] Since a majority of MRSA-colonized individuals are asymptomatic and colonization can persist for substantial durations,[11] endemic or epidemic changes in MRSA levels in one hospital could potentially affect MRSA levels in other hospitals. Numerous prior studies have reported MRSA outbreaks in health care settings and have often described intra- and interward transmission.[3-9] Reports

Address correspondence to Bruce Y. Lee, MD, MBA, University of Pittsburgh, 200 Meyran Avenue, Suite 200, Pittsburgh, PA 15213 (BYL1@pitt.edu)..

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have occasionally included transmission between affiliated health care facilities,[1,2,10] but regional evaluations are lacking. We sought to model the impact that a MRSA outbreak in one hospital has on all of the other hospitals in a single large metropolitan county where substantial interfacility patient sharing has been demonstrated previously.[12,13]

Methods

We constructed an agent-based model (ABM) to represent patient flow throughout all adult acute care hospitals in Orange County (OC), California, which together serve a population of 3.1 million people. The model included detailed representations of each hospital and allowed us to explore the effects of different sized hospital-level and ward-level outbreaks at various locations.

Population Data Sources

We incorporated hospital-specific data from several sources. First, detailed data on annual adult admissions and hospital length of stay (LOS) distributions came from 2006 patient-level hospitalization data from all OC hospitals.[14] Second, prior published work provided detailed matrices on how OC hospitals share patients as both direct interfacility transfers and discharges and readmissions following an intervening stay at home or another location.[12] Third, we obtained previously collected information about the number, size, volume, and average patient LOS within hospital intensive care units (ICUs) from prior county-wide healthcare facility surveys.[15]

Model Structure

Our ABM represented adult inpatients in all 29 acute care adult inpatient facilities. Each computer agent represented a virtual person (ie, a patient) who had a MRSA infection status of either positive or negative and who was moving among the general community and hospitals each simulated day.

Figure 1 depicts our model's general structure. Each hospital consisted of general wards and ICUs (if applicable). To standardize our model, each ICU had 12 beds, each long-term acute care (LTAC) ward had 10 beds, and each general ward had 20 beds. For example, if a hospital had a total of 100 beds including 20 ICU beds, the simulated hospital consisted of 2 10-bed ICUs and 4 20-bed general wards. Upon admission, a patient had a probability of entering either an ICU or a general ward. The patient stayed in that ward for a certain LOS, which was drawn from a ward-specific probability distribution (Table 1). After the assigned LOS lapsed, a patient in a general ward was either discharged back into the community or transferred to another hospital on the basis of probabilities derived from our patient flow data.[12] After each assigned ICU LOS lapsed, ICU patients transferred to a general ward for the remainder of their assigned hospital stay. Discharged patients had a probability of being readmitted or staying in the community that was based on hospital-specific data regarding patient readmission to any OC hospital within 1 year of discharge. Patients who tested positive for MRSA had a relative 30% increase in the probability of readmission to a hospital, which is consistent with previous findings.[16] Time to readmission (ie, direct transfer or readmission after an intervening stay at home or elsewhere) also drew from hospital-specific data. Whether a readmitted patient went to the same or a different hospital was based on our detailed interfacility patient-sharing data matrices.[12]

Transmission Model

MRSA transmission occurred within each hospital's general wards and ICUs, where patients mixed homogeneously. Other than the transfer of ICU patients to general wards, no mixing occurred between wards. The following equation determined the number of patients who

had test results that were positive for MRSA for the first time in each ward each day: number of new MRSA-positive test results in ward = βSI + (number of patients with MRSA that enter ward) – (number of patients with MRSA that leave ward). Specifically, defining $I(t)$ as the number of infectious patients (ie, MRSA colonized or infected) in the ward at the start of day t, $S(t)$ as the number of susceptible patients (ie, noncarriers of MRSA) in the ward at the start of day t, β as the transmission coefficient (which is parameterized for each hospital to generate a 1% incidence in the general wards, a 2% incidence in LTAC wards, and a 3% incidence in ICUs; Table 1), $C(t)$ as the number of MRSA-positive patients entering the ward at the end of day t, and $G(t)$ as the number of MRSA-positive patients leaving the ward at the end of day t, the equation is $I(t+1) - I(t) = \beta(S(t)I(t)) + C(t) - G(t)$, representing uniform mixing of susceptible and infective patients over the course of day t, plus net infective entrants at the end of day t.

Our initial baseline scenario assumed that patients who had positive test results for MRSA retained carriage indefinitely. Additional scenarios introduced MRSA carriage loss over time, with MRSA carriage duration drawn from a distribution based on published estimates.[17-20] One-third of patients who had positive test results for MRSA had indefinite carriage,[21] and the remaining experienced a linear carriage loss (6-month half-life). The model tracked MRSA prevalence (ie, number of MRSA-positive patients over total number of patients in that ward) in each hospital each day.

Experimental Scenarios

Experiments systematically implemented the following scenarios to each OC hospital (unless stated otherwise) and assessed the impact on all other OC hospitals: a sustained single-hospital MRSA outbreak increased the MRSA prevalence (among admitted patients) indefinitely (from 5% to 15%) in 1 hospital at a time; a temporary single-hospital MRSA outbreak increased the MRSA prevalence for 3 months (from 5% to 15%) in 1 hospital at a time; a single-hospital MRSA major outbreak increased the MRSA prevalence substantially (from 5% to 50%) in 1 hospital at a time; a regional MRSA outbreak increased the MRSA prevalence in all hospitals in and around the City of Orange (5 hospitals) from 5% to 15%; and a single-hospital ICU MRSA outbreak increased the MRSA prevalence (from 5% to 15%) in all ICUs in a single hospital. This scenario was systematically performed for each hospital. Each experiment was run in the model until it reached equilibrium (4-year run-in time) before an outbreak was introduced. Sensitivity analyses explored the effects of varying patient LOS (1 day vs a hospital-specific LOS distribution) and duration of MRSA colonization (range, indefinite to 1 day).

Analyses included an assessment of changes in MRSA prevalence in each hospital over time following each outbreak, that is, a relative increase in MRSA prevalence from preoutbreak levels. We explored whether the impact of an outbreak was associated with the following:[13] hospital size (patient capacity), hospital in-degree (the total number of different hospitals that send patients to the given hospital), and hospital out-degree (the total number of different hospitals that receive patients from a given hospital).

Results

Outbreaks in different OC hospitals had varying effects on all other OC hospitals. The impact depended on the outbreak size and duration and the hospital size and connectedness (shared patients). In general, varying hospital LOSs and times to patient readmission had relatively little effect on the resulting prevalence changes.

Sustained Single-Hospital Outbreak

Figure 2 shows what happened to other hospitals over time after a single hospital experienced a MRSA outbreak (ie, an increase in prevalence from 5% to 15%). Following the outbreak, most other hospitals experienced an increase in prevalence and ultimately reached a new steady-state prevalence. For all but 3 hospitals, most of this increase occurred during the first 6 months following the outbreak, and it slowed considerably from 6 months to 1 year.

Figure 3 utilizes bubble maps to summarize the results of our experiments. Each column represents a single experiment. The number above each column indicates the hospital experiencing the outbreak. Each row in the column lists the relative change in prevalence from preoutbreak levels for all other OC hospitals. Overall, an outbreak that affected 15% of patients in one hospital led to a median increase in MRSA prevalence of 1.8% in all other OC hospitals. Increases were nonuniform across OC, with effects on other hospitals ranging from no effect to a 46.4% relative increase in MRSA prevalence when any other hospital experienced an outbreak. LTACs tended to experience the greatest relative percent change in prevalence: they were the most affected facility in 20 of the 29 outbreaks, with relative increases ranging from 0.5% to 46.4% (median, 3.1%). Conversely, LTAC outbreaks had relatively little effect on other OC hospitals (range, 0.9%–1.2%). Outbreaks in hospital 10 (the third largest in terms of bed capacity) resulted in the largest change throughout the network, with a median relative increase of 3.3% (range, 1.3%–46.4%). Among acute care facilities only, relative increases in prevalence of MRSA ranged from no effect to 14.2% (median, 1.5%).

Figure 4*A* shows that an outbreak's impact (median change in all other OC hospitals) correlated positively with the relevant hospital's bed capacity (correlation coefficient [r] = 0.71). Of the 12 single-hospital outbreaks that caused a median change of at least 2.0% across the network, 7 occurred in hospitals that had capacities of at least 200 patients. Only 2 hospitals that had capacities of at least 200 caused relative changes in network prevalence of less than 2.0%. On the other hand, as Figure 4*B* demonstrates, smaller hospitals tended to be more affected by outbreaks in other hospitals ($r = -0.51$); only 1 hospital with a capacity of at least 150 patients experienced a relative change of at least 2.0% when any other hospital had an outbreak. LTACs, which have smaller capacities, tended to be the most affected.

It took years to achieve new steady-state values across OC hospitals following a single-hospital outbreak (Figure 3; mean, 2,511 days), and only 13% of hospitals reached new steady states within 6 months (17% did so within 1 year). Nevertheless, most hospitals experienced 70% of outbreak effects within 6 months (22% of hospitals) or 1 year (62% of hospitals). There was no difference in time to steady state between LTACs and acute care hospitals.

Figure 4*C*, 4*D* reveals that the outbreak impact correlated somewhat with the hospital's degree. The higher the out-degree (ie, the total number of hospitals to which a given hospital sends patients) of the outbreak hospital, the greater the impact to the MRSA prevalence at other hospitals (Figure 4*C*). The greater the number of hospitals to which a given outbreak hospital sends patients, the larger the impact on the other hospitals ($r = 0.78$). In-degree (ie, the total number of hospitals from which a given hospital receives patients) correlated slightly with the relative change ($r = 0.45$) that a hospital experiences when there is an outbreak in any other OC hospital (Figure 4*D*); receiving patients from more hospitals resulted in a larger change in prevalence.

Adding MRSA carriage loss attenuated outbreak effects. An increase in prevalence from 5% to 15% effected a median change of 1.0% (range, no effect to 62.5%) on the network. MRSA loss resulted in a 44% decrease in the relative change in MRSA prevalence for the entire network (median relative change, 1.0% vs 1.8%).

Temporary Single-Hospital Outbreak

Figure 5 shows how MRSA prevalence changed following a 3-month outbreak in 2 example hospitals (16 and 17). The impact manifested and peaked within 6 months of the outbreak start but did not persist, as the prevalence of MRSA colonization returned to near-preoutbreak levels in about 1 year.

Single-Hospital Major Outbreak

Figure 6 summarizes the results of a more dramatic single-hospital outbreak (an increase in MRSA prevalence from 5% to 50%) leading to a 5.6% median relative change throughout the network (range, 0.6%–212.0%). LTACs experienced the most change from outbreaks that occurred elsewhere but had the least impact on the network when experiencing outbreaks themselves. While time to steady state often took years to achieve (an average of 1,885 days, with 7% of hospitals reaching a new steady state in 6 months), most hospitals experienced 70% of outbreak effects within 1 year (52% of hospitals). There was no difference between LTACs and acute care hospitals in time to steady state.

Regional MRSA Outbreak

A concerted outbreak (an increase in MRSA prevalence from 5% to 15%) affecting all 5 hospitals located in the City of Orange resulted in a median 7.3% relative increase (range, 3.0%–58.3%) throughout the rest of OC. A major outbreak (an increase in MRSA prevalence from 5% to 50%) led to a median 30.5% relative increase (range, 11.1%–258.6%). Again, LTACs manifested among the highest relative percent changes. The impact did not appear to correlate with physical distance from the City of Orange.

Single-Hospital ICU MRSA Outbreak

Even an outbreak in a single hospital's ICUs affected hospitals throughout OC, causing a median 1.10% relative change in all other OC hospitals (range, no effect to 12.7%). LTACs experienced the greatest relative change in prevalence in 89% of ICU outbreaks.

Discussion

Our study emphasizes the substantial interconnectivity via patient sharing that exists among OC hospitals and that even a MRSA outbreak modeled in a single hospital's ICUs eventually percolated throughout OC. Moreover, the connections are rather heterogeneous: a MRSA outbreak may not necessarily spread proximally but instead could spread by leaps and bounds. The effects depend on outbreak size and location and may not fully manifest immediately, often taking 6 months to 1 year. In general, outbreaks in larger and more connected hospitals have more wide-ranging effects, although this correlation is not perfect. Changing hospital LOSs did not appreciably change our results.

These findings have multiple implications. First, every MRSA outbreak, regardless of location (ie, even in a single ICU), is not simply the concern of a single hospital but is potentially a regional concern. In other words, hospitals are not "islands" but rather parts of a complex system. It may be important for all hospitals to be aware of any outbreak that occurs in their given region. Sharing infection control information can help other hospitals to prepare for potential dissemination of an outbreak. Hospitals may enhance the monitoring

of patients transferred from a hospital experiencing an outbreak. Hospitals experiencing an outbreak may want to limit patient transfers or decolonize patients before discharge.

Second, a perceived MRSA outbreak in one hospital may be the result of practices or situations in another. While a hospital's infection control specialists may be searching for the source of an outbreak in their hospital, the culprit could actually be miles away. Therefore, hospitals may benefit from sharing not only epidemiological information but also infection control policy and practice information to help coordinate efforts.

Third, hospitals should understand their connections with other hospitals and realize the implications of establishing or severing connections. In other words, while fiscal or service reasons may drive patient sharing, hospitals may want to anticipate and prepare for the infection control implications of changes in patient sharing. Knowing patient movement patterns (eg, via information systems) could benefit hospitals and infection control strategies and practices. Furthermore, hospitals may want to consider potential infection control implications when forming relationships with other facilities.

Fourth, since the impact of an outbreak can be far reaching and take time to manifest, patience and perseverance may be important for those tracking, preparing for, or responding to an outbreak. For example, if a connected hospital experiences a large outbreak, public health officials and hospital administrators may want to maintain heightened infection surveillance and control measures for an extended period of time.

Fifth, changing LOSs did not appear to substantially impact our MRSA results. This is a useful finding, as there has been considerable debate over the implications of shortening or lengthening LOSs.

Sixth, since the prevalence of MRSA in a community can affect the prevalence of MRSA in hospitals that admit patients from that community, increases of MRSA prevalence in a community can manifest as "outbreaks." Therefore, hospitals may want to be aware of what is occurring in the community and nursing homes.

Finally, our findings emphasize systems thinking when considering MRSA and its control. Appropriate surveillance and interventions may require the coordination of various hospitals and efforts that span multiple organizations. Perhaps a central organization could coordinate infection control activities throughout a county.

Our study advances the existing literature by using more extensive real-world data and detailed representations of the structure of and transmission within each hospital. To our knowledge, it is the most extensive study of its kind in the United States. Some studies have examined networks of hospitals on a smaller scale, with theoretical representations of hospitals, or in other countries with different health systems.[11,22-25]

Although our model was based on extensive data from OC, the interconnectedness of hospitals in OC and our findings are likely not unique and could be applicable to other regions. A recent paper by Donker et al[23] utilized referral data from the Dutch national medical register to model a hospital network in the Netherlands. While the US health care system differs from that of the Netherlands, our findings were similar. They also showed long times to achieve steady state for all hospitals in the network (up to 10 years) and that prevalence was related to the extent of a hospital's referral patterns (ie, degree). Our study took further steps by building a more detailed hospital structure (including wards and ICUs) and transmission model, incorporating additional elements such as a MRSA loss rate, performing more sensitivity analyses, and showing the MRSA prevalence effects of an outbreak by hospital, outbreak size, and location. Also, our model included patient sharing

that occurred beyond referrals (eg, patients choosing to use other hospitals). Future studies could explore other hospitals in the United States and other countries to confirm our findings.

Limitations

Models that include everything are not helpful. Hence, Einstein admonished that models be made as simple as possible, but no simpler. Accordingly, a number of factors were excluded, though they are suitable topics for future research. Our study focused on adults and did not include pediatric hospitals or long-term chronic care facilities (ie, nursing homes [not included in the Office of Statewide Health Planning and Development]) or their patients. However, a hospital outbreak could have originated in the transfer of a nursing home patient. Although a vast majority (86%) of patients stay within OC for hospital care, some do cross county lines. While the Office of Statewide Health Planning and Development database is quite comprehensive, no database can capture every single patient, especially those who are undocumented. Finally, it is unclear how generalizable our findings may be to other counties, although a large diversity of hospital types and sizes were represented.

Conclusion

Our results show that a MRSA outbreak, even in a single hospital's ICU, can affect all the hospitals in a region. These effects may depend on outbreak size and location and often take time to fully manifest. Generally, outbreaks in larger and more connected hospitals affect a greater number of hospitals to a greater extent. Our results suggest that surveillance, prevention, and control strategies and policies should account for the interconnectedness of health care facilities. Future models may include representations of nursing homes.

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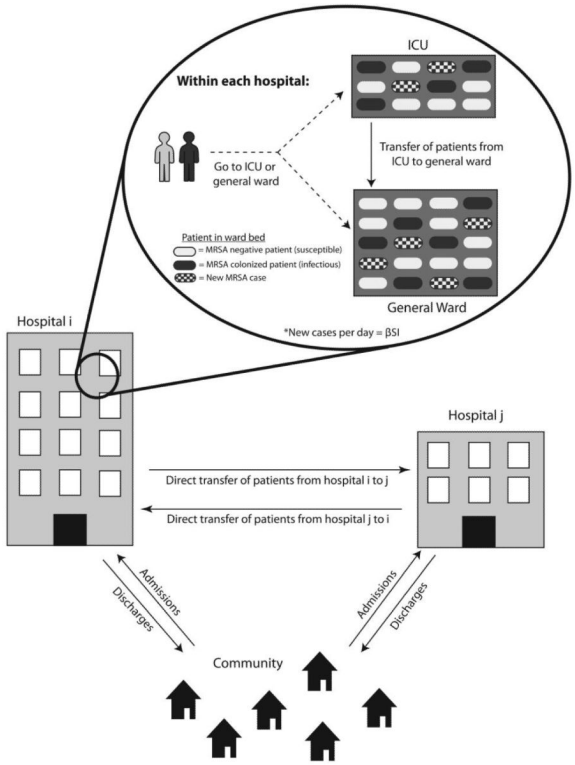

Figure 1.
Schematic flow of patients within the network and transmission.

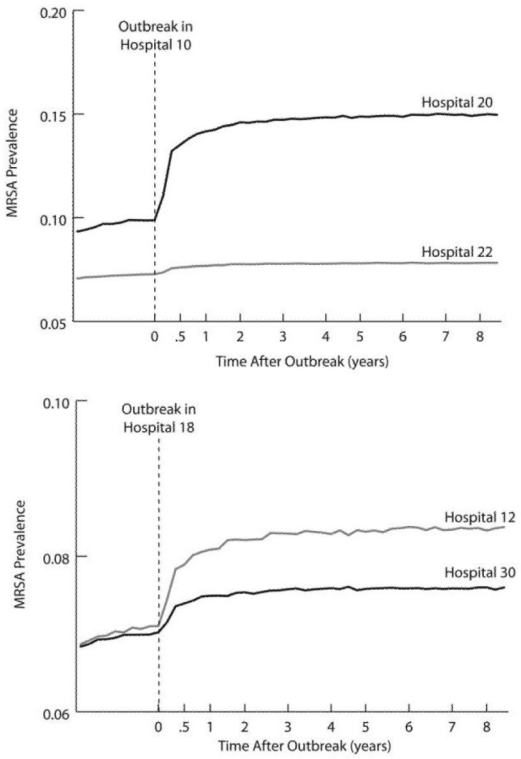

Figure 2.
Effects of outbreak on other hospitals over time.

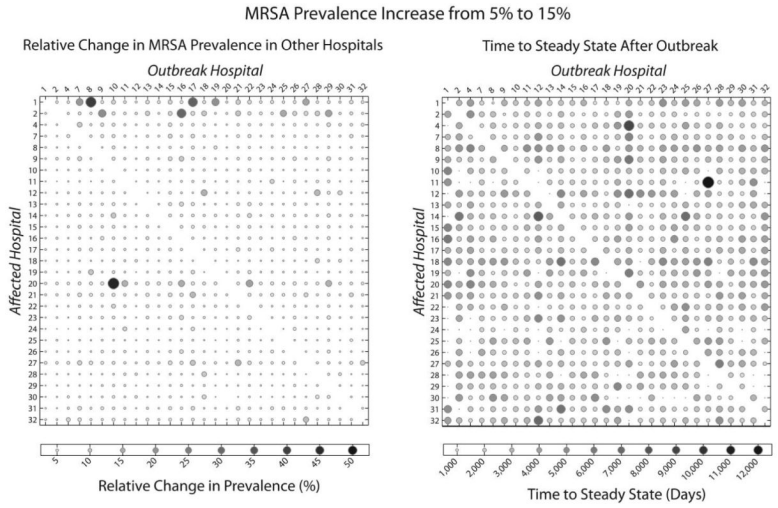

Figure 3.

Bubble maps for hospital-specific lengths of stay, with increased probability of transfer and delayed readmission, for a 15% increase in prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA). Each column represents a single experiment. The number above each column indicates the hospital experiencing the outbreak. Each row in the column lists the relative change in prevalence from preoutbreak levels for all other Orange County hospitals.

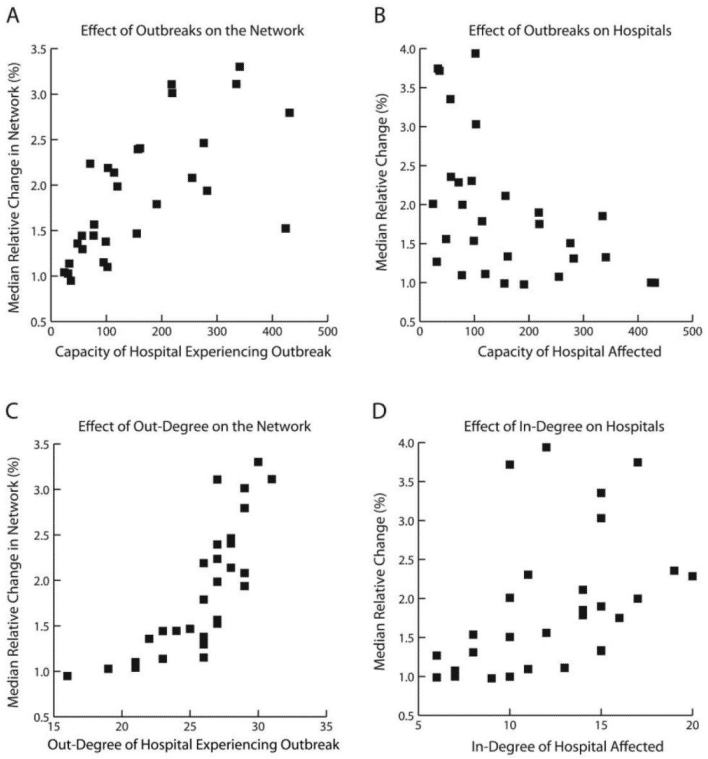

Figure 4.

Scatterplots of effects of (*A*) outbreaks on the network, (*B*) outbreaks on hospitals, (*C*) out-degree on the network (the total number of hospitals to which a given hospital sends patients), and (*D*) in-degree on hospitals (the total number of hospitals from which a given hospital receives patients).

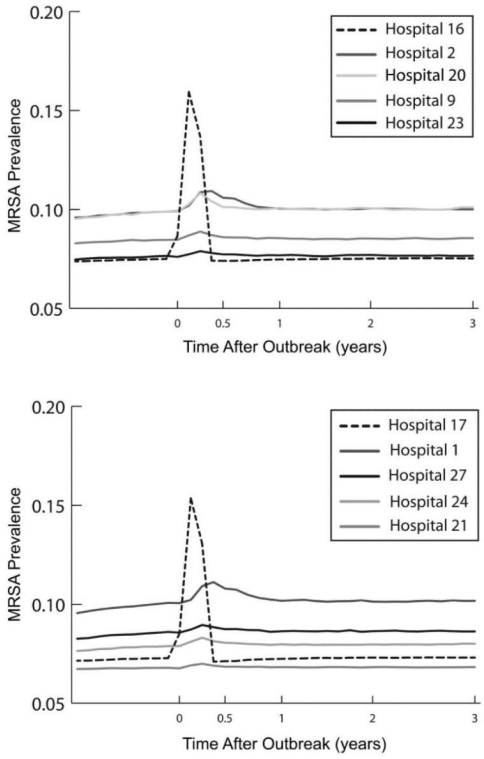

Figure 5.
Effects of a 3-month outbreak on other Orange County hospitals.

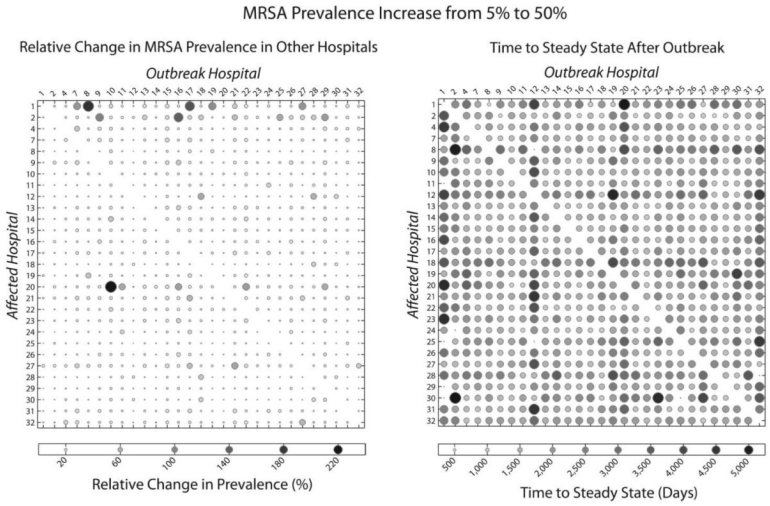

Figure 6.

Bubble maps for hospital-specific lengths of stay, with increased probability of transfer and delayed readmission, for a 50% increase in prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA). Each column represents a single experiment. The number on the top of each column is the hospital experiencing the outbreak. Each row in the column lists the relative change in prevalence from preoutbreak levels for all other Orange County hospitals.

TABLE 1

Model Inputs and Hospital Parameters

				General ward		ICU	
Hospital	**2006 admissions**	**Mean LOS**	**Median LOS**	**LOS[a]**	**β**	**LOS[a]**	**β**
1	388	33.97	28.5	3.31 (0.70)	0.00033	1.84 (0.63)	0.00
2	949	39.29	25	3.25 (0.86)	0.00028	1.84 (0.63)	0.00
4	3,851	9.03	5	1.73 (0.81)	0.00047	1.84 (0.63)	0.0051
7	10,037	5.70	4	1.57 (0.69)	0.00046	1.25 (0.87)	0.011
8	17,613	5.83	4	1.55 (0.69)	0.00065	1.84 (0.63)	0.0053
9	4,580	5.65	4	1.40 (0.71)	0.00066	1.19 (0.89)	0.0067
10	26,872	4.64	4	1.40 (0.60)	0.00083	1.99 (0.58)	0.0070
11	11,215	3.89	3	1.24 (0.53)	0.0011	1.84 (0.63)	0.011
12	2,507	4.54	4	1.33 (0.59)	0.0012	1.84 (0.63)	0.00
13	10,285	4.03	3	1.30 (0.53)	0.00070	1.84 (0.63)	0.012
14	2,602	7.98	4	1.59 (0.72)	0.00063	0.91 (1.00)	0.011
15	18,023	6.79	4	1.49 (0.80)	0.00054	1.63 (0.72)	0.0060
16	18,980	5.31	4	1.47 (0.62)	0.00075	1.63 (0.72)	0.0064
17	16,446	4.83	4	1.37 (0.62)	0.00084	1.84 (0.63)	0.0085
18	19,231	4.84	4	1.38 (0.65)	0.00078	1.42 (0.80)	0.0076
19	4,082	4.28	4	1.28 (0.58)	0.0013	1.22 (0.88)	0.024
20	966	12.47	11	2.41 (0.50)	0.00034	1.84 (0.63)	0.0098
21	6,644	5.67	4	1.46 (0.72)	0.00062	2.54 (0.38)	0.0077
22	16,086	4.98	4	1.39 (0.69)	0.00062	1.84 (0.63)	0.0047
23	6,663	5.43	4	1.53 (0.64)	0.00047	1.57 (0.74)	0.012
24	16,465	4.24	3	1.28 (0.61)	0.00096	1.84 (0.63)	0.0058
25	10,740	5.25	4	1.46 (0.67)	0.00069	1.34 (0.83)	0.0088
26	13,152	4.63	4	1.33 (0.55)	0.00093	1.84 (0.63)	0.0059
27	3,135	6.47	5	1.62 (0.69)	0.00059	1.84 (0.63)	0.011
28	18,943	4.67	4	1.34 (0.58)	0.00090	1.84 (0.63)	0.0091
29	32,082	4.90	4	1.40 (0.60)	0.00081	1.84 (0.63)	0.0072
30	5,551	5.09	4	1.36 (0.67)	0.00094	1.54 (0.75)	0.022

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				General ward		ICU	
Hospital	**2006 admissions**	**Mean LOS**	**Median LOS**	**LOS[a]**	**β**	**LOS[a]**	**β**
31	5,658	5.03	4	1.41 (0.67)	0.00082	2.11 (0.53)	0.040
32	1,836	4.81	3	1.07 (0.46)	0.0015	2.99 (0.26)	0.00

NOTE. β, ward's transmission coefficient; ICU, intensive care unit; LOS, length of stay.

[a]Values are mean (SD) log-normal LOS.