How to Choose Target Facilities in a Region to Implement Carbapenem-resistant Enterobacteriaceae Control Measures

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Background. When trying to control regional spread of antibiotic-resistant pathogens such as carbapenem-resistant Enterobacteriaceae (CRE), decision makers must choose the highest-yield facilities to target for interventions. The question is, with limited resources, how best to choose these facilities.

Methods. Using our Regional Healthcare Ecosystem Analyst-generated agent-based model of all Chicago metropolitan area inpatient facilities, we simulated the spread of CRE and different ways of choosing facilities to apply a prevention bundle (screening, chlorhexidine gluconate bathing, hand hygiene, geographic separation, and patient registry) to a resource-limited 1686 inpatient beds.

Results. Randomly selecting facilities did not impact prevalence, but averted 620 new carriers and 175 infections, saving \$6.3 million in total costs compared to no intervention. Selecting facilities by type (eg, long-term acute care hospitals) yielded a 16.1% relative prevalence decrease, preventing 1960 cases and 558 infections, saving \$62.4 million more than random selection. Choosing the largest facilities was better than random selection, but not better than by type. Selecting by considering connections to other facilities (ie, highest volume of discharge patients) yielded a 9.5% relative prevalence decrease, preventing 1580 cases and 470 infections, and saving \$51.6 million more than random selection. Selecting facilities using a combination of these metrics yielded the greatest reduction (19.0% relative prevalence decrease, preventing 1840 cases and 554 infections, saving \$59.6 million compared with random selection).

Conclusions. While choosing target facilities based on single metrics (eg, most inpatient beds, most connections to other facilities) achieved better control than randomly choosing facilities, more effective targeting occurred when considering how these and other factors (eg, patient length of stay, care for higher-risk patients) interacted as a system.

Keywords. modeling; intervention; targets; regional approaches; antibiotic resistance.

As resources are often limited, it may not always be possible (or feasible) for all healthcare facilities in a region to implement particular interventions of interest (eg, surveillance, decolonization, patient registries) to control the spread of antibiotic-resistant bacteria. Therefore, decision makers such as public health officials, policymakers, and hospital administrators may have to choose in which facilities to implement these interventions to provide the highest yield. The question then is how to choose these facilities?

One way might be to allow facilities to choose for themselves, which would either end with a random selection or those facilities that happen to have the most resources. Another way

would be to use a single metric, such as facility bed capacity, assuming that the largest facilities would have the most influence throughout the region. However, as our network analyses have shown, the largest facilities are not necessarily the most connected by patient sharing [1, 2]. Therefore, a third way may be to use network analyses to identify the most connected facilities.

It is not clear whether any of these possibilities are enough or if more information needs to be considered. Our previous work has demonstrated how healthcare facilities in a region form a complex system, and that the spread of pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenem-resistant Enterobacteriaceae (CRE), and vancomycin-resistant *Enterococcus* can be unpredictable without understanding this system [3–9]. Studies have also shown how coordinated efforts among facilities in a region can achieve better control of MRSA and CRE than facilities working independently [6, 7, 10, 11]. However, there is a dearth of studies evaluating different facility-targeting strategies. Therefore, to help identify an ideal group of facilities in which

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to intervene, we utilized our Regional Healthcare Ecosystem Analyst (RHEA)–generated agent-based model (ABM) of the Chicago metropolitan area to simulate the spread of CRE and the implementation of control measures in groupings of target facilities identified by various strategies.

METHODS

RHEA–Chicago Model

Using our previously described RHEA software [3–6, 10–13] and adapting our CRE clinical outcomes model [14], we generated an ABM of all 462 Chicago metropolitan–area [15] healthcare facilities serving adult inpatients (90 acute care hospitals, 9 long-term acute care hospitals [LTACHs], 351 skilled nursing facilities [SNFs], and 12 skilled nursing facilities that care for ventilator-dependent patients [vSNFs], covering parts of Illinois, Wisconsin, and Indiana).

In brief, each patient is represented by a computational agent, which, on a given day, can either carry or not carry CRE [15]. Each day, patients move from the community or other healthcare facilities into the various regional healthcare facilities. Each facility has a number of beds (matching actual facilities) and multiple units. Upon admission to a facility, a probability draw determines which unit the patient enters, while another facility- and unit-specific draw determines the patient's length of stay (LOS). CRE carriers have an additional LOS added to their LOS draw. Each day, patients mix homogeneously within units and carriers can transmit to noncarriers, using a unit- and facility-specific transmission coefficient (β): $\beta(\text{*})\text{susceptible patients}(\text{*})\text{infectious patients}$. When the LOS elapses, the patient is discharged and can either return to the community, transfer directly to another facility, or return to the community for a period before being readmitted to the same or another facility. Additionally, each carrier has a probability of CRE infection (25% [16, 17]), with a probability of being 1 of 4 types (bacteremia, intra-abdominal infection, pneumonia, or complicated urinary tract infection). Patients have probabilities of receiving different types of drug treatments, while additional tests and procedures are infection-specific. Each patient with a CRE infection has a probability of mortality based on their infection type, treatment received, and CRE-attributable mortality (35% [18]). Infected patients accrue associated costs and health effects. The [Supplementary Appendix](#) provides additional details, and [Supplementary Appendix Table 1](#) shows model inputs and sources.

Without CRE-specific interventions, only a fraction of CRE carriers (12%) are detected by clinical cultures. Known carriers are placed on contact precautions on admission to a hospital, LTACH, or vSNF for their LOS, and for 10 days in SNFs. Patients on contact precautions had a probability of remaining so upon transfer to other facilities (based on the likelihood of interfacility communication) and when readmitted to the same facility. Additionally, a fraction of non-CRE carriers and CRE carriers unknown to the institution are placed on contact

precautions for other reasons. Contact precautions attenuate transmission with 40% effectiveness (accounting for efficacy and staff compliance).

We modeled 2 interventions: an extensively drug-resistant organism (XDRO) registry [15] plus a CRE prevention bundle [19]. An XDRO registry is an electronic database that can track which patients are carrying antibiotic-resistant bacteria and can alert healthcare facilities when such a patient is admitted [20, 21]. The registry increased the fraction of CRE carriers identified and known by facility type. On admission, healthcare staff searched for each patient in the registry, with those identified as CRE positive placed on contact precautions. Additionally, newly identified carriers are added to the registry. The CRE prevention bundle consists of admission screening, daily chlorhexidine gluconate bathing, a hand hygiene campaign, and placing carriers in cohorts or private rooms [19], and was applied on admission by unit type: hospital ICUs, LTACHs (all units), vSNFs (skilled and ventilator units), or SNFs (all units). Screening consists of rectal screening with an associated sensitivity and specificity. Patients testing positive, regardless of carrier status (ie, true and false positives), are immediately placed on contact precautions. We assumed that the prevention bundle reduced incidence in a facility by 50% ([Supplementary Appendix](#)) [19].

Scenarios and Experiments

Our initial scenario assumed no intervention, whereas experimental scenarios consisted of implementing both the XDRO registry and CRE prevention bundle in various groups of target facilities, identified in different ways, up to a set bed limit. These methods ranged from those considering a single factor or characteristic that may be readily identified (ie, information is currently or readily available), to those considering one metric that accounts for more complicated factors/characteristics but may require data analysis, to methods considering a combination of single and/or complicated factors that may or may not require data analysis. [Table 1](#) describes these methods as well as the characteristics of facilities identified by these selection methods.

We normalized each group of target facilities by facility bed size, so that facilities were chosen up to a budget-limited 1686 beds (only intervening beds counted toward the limit). We did not allow for partial facility selection (all targeted units in a facility were included); thus, some groups had < 1686 intervening beds. Each method generated 2 groups of target facilities ([Table 1](#)): (1) All regional facilities ($N = 462$) were eligible for selection, and (2) we applied a geographic constraint to only select facilities within 13 miles of Rush University Medical Center in Chicago ($n = 161$). We applied this constraint to explore the impact of logistical considerations (eg, driving distance based on 1 hour of travel time in traffic) important for intervention planning and decision making.

Simulation experiments consisted of 50 trials and simulated 3 years. The impact on CRE spread was the difference between

Table 1. Methods for Selecting Groups of Facilities to Target for Intervention and the Characteristics of Resulting Facility Groups Identified up to a Bed Limit (1686 Intervening Beds)

Method of Selecting Target Facilities	Description	Characteristics of Facility Groups to Target, Identified by Selection Method ^a		
		Eligible Facility Types	All Facilities Eligible (N = 462)	Geographic Constraint ^b (n = 161)
Random	Considers a single metric and does not require data or information about the facilities. Randomly selects facilities using a random number generator; although randomly picking facilities is not a practical strategy, it represents a situation in which various places implement measures in a noncohesive way.	Hospitals, LTACHs, SNFs, vSNFs	1660 intervening beds in 16 facilities (2 hospitals; 14 SNFs)	1646 intervening beds in 15 facilities (3 hospitals; 12 SNFs)
Type of facility	Considers a single factor using currently and/or readily available data. ^c Randomly chooses facilities of a particular level of care (eg, hospital, LTACH, vSNF, SNF), using a random number generator.	(1) Only hospitals (2) Only LTACHs (3) Only vSNFs	1626 beds in 63 hospitals 738 beds in 9 LTACHs 1528 beds in 12 vSNFs	1204 intervening beds in 36 hospitals 133 beds in 7 LTACHs 1057 beds in 9 vSNFs
Largest by bed size	Considers a single factor using currently and/or readily available data. ^c Chooses the largest facilities by bed size by ordering them from highest to lowest total number of beds.	Hospitals, LTACHs, SNFs, vSNFs	1674 intervening beds in 17 facilities (16 hospitals; 1 SNF)	1681 intervening beds in 13 facilities (10 hospitals; 3 SNFs)
Longest LOS	Considers a single factor using currently and/or readily available data. ^c Chooses those with the longest LOS by ordering facilities highest to lowest average patient LOS.	Hospitals, LTACHs, SNFs, vSNFs	1532 intervening beds in 13 SNFs	1524 intervening beds in 11 SNFs
Highest volume of discharged patients who are transferred or readmitted	Considers a more complex factor that requires calculations or analysis of data. ^d Chooses the facilities with the highest volume of discharged patients that are directly transferred to another facility and/or later readmitted to the same or another facility within a year.	Hospitals, LTACHs, SNFs, vSNFs	1682 intervening beds in 47 hospitals	1641 intervening beds in 40 facilities (36 hospitals; 2 LTACHs; 2 vSNFs)
Static network analysis	Considers a more complex factor that requires calculations or analysis of data. ^d Evaluated a facility's connections within the network. Measures a facility's beta-centrality which is the total potential influence of a facility in the network on others, both directly and indirectly, using valued data of degree and eigenvalues.	Hospitals, LTACHs, SNFs, vSNFs	1663 intervening beds in 40 facilities (39 hospitals; 1 SNF)	1681 intervening beds in 33 facilities (29 hospitals; 4 SNFs)
Care for high-acuity patients	Considers multiple factors using currently and/or readily available data. ^e Accounts for multiple characteristics such as facility types that care for patients with comorbidities that require a significant amount of care and longer patient LOS. Randomly chooses facilities (using a random number generator) that care for high-acuity patients.	ICUs, LTACHs, vSNFs	1551 intervening beds in 47 facilities (40 hospitals; 3 LTACHs; 4 vSNFs)	1604 intervening beds in 32 facilities (22 hospitals; 3 LTACHs; 6 vSNFs)
Combination of metrics	Considers multiple factors using currently and/or readily available data and may require calculations or analysis of data. ^{e,d} Combines several single and complex factors and targeted facilities that care for high-acuity patients, larger bed size, long average patient LOS, and have large number of discharged patients with another inpatient stay within 1 year; this method selected facilities that were commonly ranked high among the other lists.	Hospitals; LTACHs, SNFs, vSNFs	1681 intervening beds in 12 facilities (3 LTACHs; 9 vSNFs)	1686 intervening beds in 16 facilities (7 LTACHs; 9 vSNFs)

Abbreviations: ICU, intensive care unit; LOS, length of stay; LTACH, long-term acute care facility; SNF, skilled nursing facility; vSNF, skilled nursing facility with capacity to care for patients receiving mechanical ventilation.

^aIntervening beds included hospital ICUs, all units of LTACHs and SNFs, and skilled and ventilator units of vSNFs and were chosen up to a limit of 1686 intervening beds.

^bOnly facilities within a 13-mile radius of Rush University Medical Center were eligible for selection.

^cData can be from national and state databases or state reports (eg, hospital profiles, annual bed reports).

^dData can be from national and state hospital databases and national and state long-term care databases that include information on discharges (eg, Centers for Medicare and Medicaid Services' minimum data set, Medicare Provider Analysis and Review [MEDPAR] limited data set, Medicaid Analytic eXtract Data).

intervention and no-intervention scenarios. We evaluated the impact regionwide and within Cook County, in which the city of Chicago is located and where facilities have a higher prevalence than others in the region (based on surveillance data [22]). For each scenario, we calculated the incremental cost-effectiveness ratio (ICER) as:

$$\text{ICER} = \frac{(\text{Cost}_{\text{CRE Intervention}} - \text{Cost}_{\text{No CRE Intervention}})}{(\text{Health Effects}_{\text{No CRE Intervention}} - \text{Health Effects}_{\text{CRE Intervention}})}$$

where health effects were measured in quality-adjusted life years (QALYs). The CRE intervention was considered cost-effective if ICERs were $\leq \$50\,000/\text{QALY}$ saved and economically dominant if saving costs and providing health benefits.

RESULTS

No Intervention

Figure 1 shows the prevalence of CRE carriage regionwide and within Cook County over time. Regionwide, there were 12 740 new carriers over the 3-year period in the absence of CRE-specific interventions which resulted in 3186 infections and 383 CRE-attributable deaths, costing \$326 million in total direct and indirect (ie, societal) costs (Table 2).

Targeting Facilities Randomly

While prevalence decreased by a relative 2.1% regionwide compared to no intervention after 3 years when all facilities were eligible, there was no impact when geographically constrained (Figure 1). Figure 2 shows the cumulative number of new carriers over the 3-year period. When all facilities were eligible, there were 12 120 new carriers that resulted in 3011 infections (Table 2). Intervention costs were greater than the generated cost savings from averted cases, thus resulting in higher overall costs ($\leq \$11.4$ million more) compared to no intervention, except from the societal perspective. When geographically constrained, targeting random facilities was not cost-effective (Table 3).

Targeting Facilities by Type

Randomly targeting by facility type was better than targeting randomly, and targeting LTACHs resulted in larger gains than targeting either hospital ICUs or vSNFs (Figures 1 and 2 and Table 3). Targeting LTACHs decreased the prevalence of carriage by a relative 17% and 22% regionwide and within Cook County, respectively, regardless of constraints. Targeting vSNFs resulted in the second-largest reductions, except when all facilities were eligible, in which case targeting ICUs resulted in a larger decrease in prevalence (Figure 1A). As vSNFs have a higher CRE prevalence, targeting these facilities resulted in larger gains than targeting ICUs. Of all selection methods, targeting LTACHs resulted in the largest indirect benefits in nonparticipating facilities when limited geographically (Figure 3). Targeting all LTACHs when geographically constrained averted 3049 new carriers, 741

infections, and 89 deaths; saved $\leq \$70.2$ million (Table 2); and was dominant under all conditions tested (Table 3).

Targeting the Largest Facilities by Bed Size

Intervening in the largest facilities had little impact on the prevalence of carriage (Figure 1), with a 2.3% relative reduction regionwide (2.3% in Cook County) compared to no intervention after 3 years, without geographic constraints. Compared to no intervention and randomly targeting facilities, there were small gains in decreasing transmission regionwide; however, better gains were achieved when targeting LTACHs or vSNFs (Figure 2). Regionwide, there were more infections and deaths when targeting the largest facilities than when targeting by type (Table 2). Compared to no intervention, targeting the largest facilities generated cost savings only when all facilities were eligible (Table 2) and was cost-effective under some conditions (Table 3).

Targeting Facilities With the Longest Length of Stay

This method favored the selection of SNFs and had little to no impact on carriage prevalence and transmission regionwide or within Cook County compared to no intervention (Figures 1–3 and Table 3). While averting CRE infections and deaths (Table 2), the savings generated were less than the intervention costs and were not cost-effective from any perspective (Table 3).

Targeting Facilities With the Highest Volume of Discharged Patients Who Are Transferred or Readmitted

Targeting facilities with the highest volume of patients who are directly transferred or later readmitted to the same or another facility resulted in substantial gains compared to targeting by size and, in some circumstances, facility type (Figures 1–3). Compared to no intervention, regionwide prevalence decreased by a relative 11.4%, with 2489 fewer new carriers when all facilities were eligible, and by 12.1%, with 2279 fewer new carriers when limited geographically. In Cook County, prevalence decreased by a relative 7.9% when all facilities were eligible (19.5% when limited geographically). Targeting this way averted 578–644 infections and 69–77 deaths regionwide, generating cost savings from all perspectives (Table 2).

Targeting Facilities by Static Network Analysis

Although targeting facilities by their beta-centrality resulted in better gains than targeting random facilities or the largest by bed size, it did not provide as many gains as targeting by type or volume of discharged patients who are transferred or readmitted (Figures 1–3). Savings in direct medical costs and productivity losses were outweighed by intervention costs and often did not provide overall cost savings (Table 2).

Targeting Facilities That Care for High-acuity Patients

Targeting facilities that care for high-acuity patients decreased prevalence regionwide by a relative 11.5% and 10.9% (8.8% and

Figure 1. Median true prevalence of carbapenem-resistant Enterobacteriaceae (CRE) carriage over time when implementing an extensively drug-resistant organism (XDRO) registry plus CRE prevention bundle in various groups of target facilities identified by different selection methods in healthcare facilities regionwide when all facilities are eligible for selection (A), healthcare facilities regionwide with a geographic constraint (B), healthcare facilities in Cook County when all facilities are eligible for selection (C), or healthcare facilities in Cook County with a geographic constraint (D). Geographic constraint: Only facilities within a 13-mile radius of Rush University Medical Center were eligible for selection (n = 161). Abbreviations: LTACH, long-term acute care facility; vSNF, skilled nursing facility with capacity to care for patients receiving mechanical ventilation.

16.4% in Cook County) when all facilities were eligible and when limited geographically, respectively. Targeting facilities this way was comparable to targeting only vSNFs when limited geographically (Figures 2 and 3). This selection method averted ≤ 2001 new carriers and ≤ 561 infections, resulting in cost savings ($\leq \$48.3$ million) from all perspectives, except when limited geographically from the third-party payer perspective, which was cost-effective (Tables 2 and 3).

Targeting Facilities by a Combination of Metrics

Targeting facilities by combining metrics (which targeted LTACHs and vSNFs) yielded the largest reductions in prevalence and transmission (Figures 1–3) compared to all other selection methods (except for carriers regionwide with all facilities eligible;

Figure 2A). Compared to no intervention, prevalence decreased by a relative 20.7% regionwide (29.0% in Cook County) and 25.2% regionwide (35.0% in Cook County) when all facilities were eligible and when limited geographically, respectively. Targeting by combining metrics when geographically constrained averted 3792 new carriers (29.8% relative reduction) regionwide and 3386 (53.0% relative reduction) in Cook County (Figure 2). This method resulted in the largest direct impact (regardless of constraints), averting >2000 new carriers in participating facilities, and the largest and second-largest indirect impact in nonparticipating facilities (Figure 3). Targeting facilities by combining metrics averted ≤ 944 infections and 113 deaths regionwide, saving $\leq \$85.3$ million (Table 2), and was economically dominant from all perspectives (Table 3).

Table 2. Clinical and Economic Outcomes of Implementing an Extensively Drug-resistant Organism Registry (XDRO) Plus Carbapenem-resistant Enterobacteriaceae (CRE) Prevention Bundle in Various Groups of Target Facilities Identified by Different Selection Methods

Method for Selecting Target Facilities	CRE Infections, No.	CRE-Attributable Deaths, No.	OALYs Lost	XDRO Registry Plus CRE Prevention Bundle Costs	Total Cost (Millions, US Dollars)			Cost Savings (Millions, US Dollars)			Ranking of Methods (Greatest to Smallest Benefit)
					Hospital Perspective	Third-Party Payer Perspective	Societal Perspective	Hospital Perspective	Third-Party Payer Perspective	Societal Perspective	
No intervention	3186	383	4049	...	111.3 (111.0–111.6)	61.4 (61.2–61.5)	325.5 (324.7–326.4)	...	...	...	...
All facilities eligible (N = 462)											
Random	3011	362	3828	11.6 (11.6–11.6)	116.9 (116.6–117.2)	69.6 (69.5–69.8)	319.3 (318.4–320.1)	...	...	6.3	9
By type: hospitals	2612	314	3321	8.5 (8.4–8.5)	99.7 (99.5–99.9)	58.8 (68.7–58.9)	275.5 (274.8–276.1)	11.6	2.6	50.1	4
By type: LTACHs	2453	295	3117	6.3 (6.3–6.3)	92.0 (91.7–92.3)	53.5 (63.4–53.7)	256.9 (255.9–257.8)	19.3	7.8	68.7	1
By type: vSNFs	2896	348	3679	7.4 (7.4–7.4)	108.6 (108.3–108.8)	63.2 (63.0–63.3)	303.3 (302.5–304.0)	2.7	...	22.3	7
Largest facilities by bed size	2922	351	3714	8.1 (8.1–8.1)	110.2 (109.9–110.5)	64.4 (64.2–64.5)	306.7 (305.9–307.5)	1.1	...	18.9	8
Longest length of stay	3156	379	4010	8.3 (8.3–8.3)	118.6 (118.2–119.0)	69.1 (68.9–69.3)	330.8 (329.7–331.8)	...	...	...	10
Highest volume of discharged patients who are transferred or readmitted	2542	305	3230	7.9 (7.9–7.9)	96.7 (96.5–97.0)	56.9 (56.7–57.0)	267.7 (266.9–268.5)	14.5	4.5	57.9	3
Static network analysis: beta centrality	2836	341	3603	8.5 (8.5–8.5)	107.6 (107.4–107.9)	63.1 (63.0–63.3)	298.2 (297.6–298.9)	3.6	...	27.3	6
Care for high-acuity patients	2625	315	3337	8.9 (8.9–8.9)	100.7 (100.4–100.9)	59.5 (69.4–59.6)	277.2 (276.6–277.9)	10.6	1.9	48.3	5
Combination of metrics	2457	295	3122	8.7 (8.6–8.7)	94.6 (94.3–94.9)	56.0 (55.8–56.2)	259.7 (258.8–260.5)	16.7	5.4	65.9	2
Geographic constraint ^a (n = 161)											
Random	3125	375	3972	12.5 (12.5–12.5)	121.7 (121.4–122.0)	72.7 (72.6–72.9)	331.9 (331.1–332.7)	...	...	...	9
By type: hospitals	3035	364	3857	6.2 (6.2–6.2)	112.2 (111.9–112.5)	64.6 (64.5–64.8)	316.3 (315.6–317.1)	...	...	9.2	6
By type: LTACHs	2445	294	3107	5.5 (5.4–5.5)	90.9 (90.6–91.2)	52.5 (62.4–52.7)	255.3 (254.4–256.2)	20.4	8.8	70.2	2
By type: vSNFs	2853	343	3626	6.8 (6.8–6.8)	106.5 (106.2–106.8)	61.8 (61.6–61.9)	298.4 (297.6–299.3)	4.8	...	27.1	4
Largest facilities by bed size	3123	375	3969	9.5 (9.5–9.5)	118.6 (118.3–118.9)	69.6 (69.4–69.8)	328.6 (327.7–329.6)	...	...	...	8
Longest length of stay	3178	382	4039	9.8 (9.8–9.8)	120.9 (120.6–121.2)	71.0 (70.9–71.2)	334.7 (333.7–335.6)	...	...	...	10
Highest volume of discharged patients who are transferred or readmitted	2608	313	3314	9.0 (8.9–9.0)	100.1 (99.8–100.4)	59.2 (59.0–59.4)	275.5 (274.6–276.3)	11.2	2.2	50.1	3
Static network analysis: beta centrality	3020	363	3838	10.0 (10.0–10.0)	115.4 (115.1–115.7)	68.1 (68.0–68.3)	318.7 (317.9–319.5)	...	...	6.8	7
Care for high-acuity patients	2816	338	3579	11.5 (11.5–11.6)	109.9 (109.6–110.2)	65.8 (65.6–66.0)	299.3 (298.4–300.2)	1.4	...	26.2	5
Combination of metrics	2242	269	2850	11.1 (11.1–11.1)	89.5 (89.2–89.8)	54.3 (54.1–54.5)	240.3 (239.4–241.1)	21.8	7.1	85.3	1

Data are presented as mean (95% confidence interval) unless otherwise indicated. Costs are presented as net present value in millions of US dollars. Abbreviations: CRE, carbapenem-resistant Enterobacteriaceae; LTACH, long-term acute care facility; QALY, quality-adjusted life-year; US, United States; vSNF, skilled nursing facility with capacity to care for patients receiving mechanical ventilation; XDRO, extensively drug-resistant organism.

^aOnly facilities within a 13-mile radius of Rush University Medical Center were eligible for selection.

Figure 2. Total number of new carbapenem-resistant Enterobacteriaceae (CRE) carriers over 3 simulated years when implementing an extensively drug-resistant organism (XDRO) registry and CRE prevention bundle in different groups of target facilities identified in different ways regionwide when all facilities are eligible for selection (A), regionwide with a geographic constraint (B), Cook County when all facilities are eligible for selection (C), or Cook County with a geographic constraint (D). Box represents the interquartile range (25th and 75th percentile), the central line in each box is the median, and whiskers are the minimum and maximum across simulation trials. Geographic constraint: Only facilities within a 13-mile radius of Rush University Medical Center were eligible for selection (n = 161). Abbreviations: LTACH, long-term acute care facility; vSNF, skilled nursing facility with capacity to care for patients receiving mechanical ventilation.

Table 3. Incremental Cost-effectiveness Ratio of Implementing an Extensively Drug-resistant Organism Registry Plus Carbapenem-resistant Enterobacteriaceae Prevention Bundle in Various Groups of Target Facilities Identified by Different Selection Methods Compared to No Intervention Regionwide

Method for Selecting Target Facilities	All Facilities Eligible (N = 462)			Geographic Constraint ^a (n = 161)		
	Hospital Perspective	Third-Party Payer Perspective	Societal Perspective	Hospital Perspective	Third-Party Payer Perspective	Societal Perspective
Random	25 194	37 305	Dominant	135 784	147 989	82 968
By type: hospitals	Dominant	Dominant	Dominant	4858	17 076	Dominant
By type: LTACHs	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant
By type: vSNFs	Dominant	4919	Dominant	Dominant	927	Dominant
Largest facilities by bed size	Dominant	9002	Dominant	91 402	103 238	38 529
Longest length of stay	185 303	195 066	131 382	963 361	968 709	913 088
Highest volume of discharged patients who are transferred or readmitted	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant
Static network analysis: beta centrality	Dominant	3967	Dominant	19 498	32 028	Dominant
Care for high-acuity patients	Dominant	Dominant	Dominant	Dominant	9397	Dominant
Combination of metrics	Dominant	Dominant	Dominant	Dominant	Dominant	Dominant

Data are presented as United States dollars per quality-adjusted life-year (QALY) saved. Values ≤\$50 000/QALY saved are considered cost-effective. Dominant: less costly and more effective compared to no intervention.

Abbreviations: LTACH, long-term acute care facility; vSNF, skilled nursing facility with capacity to care for patients receiving mechanical ventilation.

^aOnly facilities within a 13-mile radius of Rush University Medical Center were eligible for selection.

DISCUSSION

Our results show that ideally, selection of healthcare facilities for CRE interventions should use a combination of metrics; it is

not enough to consider single factors alone. Targeting facilities using combined metrics resulted in the greatest CRE reductions and economic benefits as it accounted for the dynamics

Figure 3. Total median number of new carbapenem-resistant Enterobacteriaceae (CRE) carriers averted in targeted facilities (direct benefit) and nonparticipating facilities (indirect benefit) regionwide over 3 simulated years when implementing an extensively drug-resistant organism registry (XDRO) plus CRE prevention bundle in various groups of target facilities identified by different selection methods compared to no intervention when all facilities were eligible for selection (A) or geographically constrained (B). Geographic constraint: Only facilities within a 13-mile radius of Rush University Medical Center were eligible for selection. Abbreviations: LTACH, long-term acute care facility; vSNF, skilled nursing facility with capacity to care for patients receiving mechanical ventilation.

of the network and how many factors interact as a system. In the Chicago metropolitan region, the method selected LTACHs and vSNFs, which care for high-acuity patients, have longer LOS and greater bed size, and are highly connected to other facilities. These facility types have been identified to be important to CRE dissemination in Chicago [23–26]. Choosing facilities by combining metrics provided substantial benefits in both participating and nonparticipating facilities. By considering measures interacting as a system, selected facilities accounted for direct and indirect effects, and for reverberating effects regionwide not considered by other methods (eg, using single measures missed indirect effects in other facilities). Additionally, choosing targets when combining metrics provided substantial cost savings under all tested conditions.

Our work demonstrates how computational modeling can help identify which facilities in a region to target for intervention. Models can serve as “virtual laboratories” to test interventions in different groups of facilities, while considering dynamics that are important to pathogen spread and control. This can save time, effort, and resources, and can eliminate guesswork and uncertainty. Limited resources may restrict the ability of all facilities to participate; therefore, decision makers (eg, public health authorities, hospital administrators, infection control practitioners) need to know which and how to identify target facilities. Selecting facilities using readily available or simple factors (eg, convenience, geographic location, specific facility characteristics, or willingness) may not account for the complex interplay of patient sharing and subsequent disease spread between facilities. For example, random selection may target facilities that have little impact, intervene independently, or are willing to participate, but does not consider patient movement and LOS. Selecting large facilities is relatively straightforward, targeting facilities that see the most patients (typically with shorter LOS and higher patient turnover), but misses connections between facilities. Selecting by LOS does not account for patient sharing and may capture a lower patient volume. More complex metrics like network analyses can identify facilities central in the patient sharing network, but requires substantial data, and may not select facilities caring for high-risk patients. Combining multiple metrics can help overcome the weaknesses of individual single metrics, while incorporating their strengths, leading to a more complete and dynamic approach.

Our study also highlights the need for control strategies to fit a region. This requires complex measures and an understanding of how things work to adequately capture the complex nature and processes of regions. Without this information, using a single factor to identify targets for interventions may not be enough and could miss substantial indirect benefits. Different regions have different circumstances and considerations (eg, prevalence, facility types, or existing interventions) that can

be accounted for directly and indirectly when combining metrics. In this study, ideal targets consisted of LTACHs and vSNFs; however, not all regions may have these facilities and other facility types may be selected by this method. While geographic constraints had little impact on regionwide benefits when combining metrics in Chicago, these and other constraints (eg, financial) are important considerations to inform practical decision making when planning programs and interventions. Modeling can help elucidate these relationships, account for these considerations, and help decision makers consider their own local circumstances and constraints.

There are some limitations to this study. All models are simplifications of real life and cannot represent all events or outcomes [27]. We were limited to patient data from the Centers for Medicare and Medicaid Services, which may not represent the transfer patterns of all patients, as these patients tend to be older and present with more comorbidities. Additionally, not all regions may have LTACHs and vSNFs and therefore patient transfer patterns and subsequent pathogen spread may be different than that of the Chicago metropolitan area. Our model was calibrated to the most robust prevalence data available; however, limited facility-specific data may not capture all variability, and data showing how prevalence may change over time are lacking. We assumed a robust and constant intervention effectiveness; however, compliance with interventions is variable and may change over time [28–32] and as technology advances. While randomly choosing a small subset of 462 facilities has substantial variation, the group identified represents an average set of targets. With more SNFs than any other facility type, random targets primarily consist of SNFs when facilities have the same likelihood of selection. Our model assumes minimal community transmission. Our model did not directly account for antimicrobial resistance emerging from selective pressure from antibiotic use. Therefore, the assumption is that antibiotic use is reasonably similar across different facilities and would not affect which facilities should be targeted. Future experiments could explore what may happen if antibiotic use and selection pressure were different from facility to facility.

In summary, while choosing target facilities based on simple measures such as the facilities with the most inpatient beds or the ones most interconnected by network analyses achieved better control than simply randomly choosing from all facilities, in the Chicago metropolitan area, choosing facilities using a combination of metrics that accounted for the care of high-risk patients, LOS, bed size, and connectedness in the network achieved even better control.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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