post-surgical care guidelines to personalize and optimize care to reduce infections following appendectomy.



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2439. The role of positive externalities in economic evaluations of new antibiotics: modeling the impact of reduced transmission in healthcare facilities Richard Nelson, PhD1; Matthew H. Samore, MD2;

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Background. Positive externalities - beneficial spillover effects enjoyed by individuals who are not the primary consumers of a good - are rarely considered in cost-effectiveness analyses (CEAs) of antimicrobial drugs that could reduce person-to-person transmission of the target pathogen. We developed a compartmental model to simulate the effect of 2 hypothetical antibiotics targeting carbapenem-resistant Enterobacteriaceae (CRE) among hospital inpatients: one that treats bloodstream infections (BSIs) and one that decolonizes carriers. We assessed the contribution of positive externalities to the results of CEAs of these 2 antibiotics in the model.

Methods. Our model tracked patients according to CRE carriage, clinical infection, and detection status. Rates of CRE acquisition depended on transmissibility of carriers in different states and were calibrated to data from long-term acute care hospitals. For the BSI treatment scenario we assumed the new drug would decrease the death rate and transmissibility of patients after CRE BSI onset. For the decolonization scenario we assumed the new drug would increase clearance of CRE carriage after clinical detection. For each scenario, we quantified the drug's effect on the number of BSIs

and deaths among patients receiving the drug (direct effect) and among all patients (total effect, i.e., direct plus indirect effect) compared with usual care. For the CEAs, the effectiveness outcome was life-years (LYs) gained and we assumed the new drug cost of \$4,000 per dose and cost of a CRE BSI of \$24,788.

Results. For both the BSI treatment and decolonization scenarios, the total effect of introducing the new drug was greater than the direct effect alone, indicating the existence of positive externalities. Relative to usual care, the new drug led to a decrease in incremental cost and an increase in incremental effectiveness (see Figures 1 and 2).

The inclusion of positive externalities in CEAs can have important Conclusion. effects on whether these new antibiotics are deemed cost-effective, due to their potential for interrupting chains of transmission. In our model, the inclusion of these effects reduced the incremental cost and increased the incremental effectiveness of these antibiotics.

Figure 1: Results from cost-effectiveness analysis of treating drug vs. usual care including only direct effects and both direct and indirect effects under different assumptions of % of patients importing CRE



Note: labels for each data point in the graph indicate the % of patients importing CRE

Assumptions

ssumptions Cost of drug = \$4,000 Cost of CRE infection = \$24,788 Discounted LYs lost from infection-related death = 5

Figure 2: Results from cost-effectiveness analysis of decolonizing drug vs. usual care including only direct effects and both direct and indirect effects under different assumptions of % of patients importing CRE



Note: labels for each data point in the graph indicate the % of patients importing CRE Assumptions Cost of drug = \$4,000

Cost of CRE infection = \$24,788

Discounted LYs lost from infection-related death = 5

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2440. Using a geospatially explicit agent-based model of a regional healthcare network to assess varied antibiotic risk on Clostridioides difficile infection incidence Sarah Rhea, DVM, MPH, PhD¹; Kasey Jones, MS¹; Georgiy Bobashev, PhD¹; Breda Munoz, PhD¹; James Rineer, MS¹; Rainer Hilscher, PhD¹; Lauren DiBiase, MS²; Emily Sickbert-Bennett, PhD, MS²; David J. Weber, MD, MPH³; ¹RTI International, Research Triangle Park, North Carolina; ²UNC Health Care, Chapel Hill, North Carolina; ³University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

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Background. Different antibiotic classes are associated with different Clostridioides difficile infection (CDI) risk. The impact of varied antibiotic risk on CDI incidence can be explored using agent-based models (ABMs). ABMs can simulate complete systems (e.g., regional healthcare networks) comprised of discrete, unique agents (e.g., patients) which can be represented using a synthetic population, or model-generated representation of the population. We used an ABM of a North Carolina (NC) regional healthcare network to assess the impact of increasing antibiotic risk ratios (RRs) across network locations on healthcare-associated (HA) and community-associated (CA) CDI incidence.

Methods. The ABM describes CDI acquisition and patient movement across 14 network locations (i.e., nodes) (11 short-term acute care hospitals, 1 long-term acute care hospital, 1 nursing home, and the community). We used a sample of 2 million synthetic NC residents as ABM microdata. We updated agent states (i.e., location, antibiotic exposure, *C. difficile* colonization, CDI status) daily. We applied antibiotic RRs of 1, 5, 8.9 (original model RR), 15, and 20 to agents across the network to simulate varied risk corresponding to different antibiotic classes. We determined network HA-CDI and CA-CDI incidence and percent mean change for each RR.

Results. In this simulation study, HA-CDI incidence increased with increasing antibiotic risk, ranging from 11.3 to 81.4 HA-CDI cases/100,000 person-years for antibiotic RRs of 1 to 20, respectively. On average, the per unit increase in antibiotic RR was 33% for HA-CDI and 6% for CA-CDI (figure).

Conclusion. We used a geospatially explicit ABM to simulate increasing antibiotic risk, corresponding to different antibiotic classes, and to explore the impact on CDI incidence. The per unit increase in antibiotic risk was greater for HA-CDI than CA-CDI due to the higher probability of receiving antibiotics and higher concentration of agents with other CDI risk factors in the healthcare facilities of the ABM. These types of analyses, which demonstrate the interconnectedness of network healthcare facilities and the associated community served by the network, might help inform targeted antibiotic stewardship efforts in certain network locations.



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2441. Automated, Rapid Detection of Potential Healthcare-Acquired Infection Clusters Based on Microbiology And Patient Geotemporal Data

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Background. Whole-genome sequencing (WGS) has shown promise in identifying transmissions of healthcare-associated infections (HAIs), but it may be costly to sequence all potential HAIs. By automatically identifying samples likely to be HAIs, WGS can be focused on specific samples. We describe an algorithm that quickly identifies potential HAI clusters by analyzing patient geotemporal and pathogen microbiology data. This approach systematically triages potential HAI investigations to aid infection control professionals (ICPs) in their workflow.

Methods. This novel algorithm within Philips IntelliSpace Epidemiology scores the potential of transmission for pairs of infections. Inputs include microbiology (MB) data (genus- or species-level identification and antimicrobial susceptibility test results) and geotemporal (GT) data (timing of sample collection and shared location stays). From the resulting pairwise scores, clusters of potential HAIs are identified. Leveraging 9 months (June, 2018 – March, 2019) of data from a 900-bed US hospital (i.e., 2825 samples, 1814 patients and 13 organisms—of which a subset of 404 samples had WGS performed concomitantly with MB studies), we evaluated the extent to which this algorithm captures genetically similar sample pairs.

Results. Pairwise scores enrich for genetically similar samples when considering MB data only (odds ratio: 17.3), GT only (odds ratio: 6.1) and a combination of both (odds ratio: 19.8), with highly significant P-values for all ($P < 10^{-16}$). Considering MB only, 91% of samples group together in potential transmission clusters. With MB and GT data, this fraction drops to 24.6% (694 samples) forming 178 possible clusters, 173 of which contain fewer than ten samples each. The 5 larger clusters contain 40–64 samples each and span multiple units in the hospital.

Conclusion. The proposed system automatically suggests potential HAI clusters. By combining MB and GT data, the number of samples to review is reduced, enabling ICPs to focus their attention and sequencing efforts. By focusing on a targeted group of higher probability clusters, ICPs may be able to increase their efficiency and effectiveness in controlling the spread of HAIs—thus boosting potential for patient safety and amelioration of cost of care.

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2442. Detection of Prosthetic Hip and Knee Joint Infections Using Administrative Databases – A Validation Study

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Background. Forming large cohorts to study prosthetic joint infections (PJIs) is a challenge without an existing surgical registry, as is the case in Canada. Administrative databases are an option, yet PJI diagnostic codes are insensitive. There is a need to improve the detection of PJIs from within administrative databases.

Methods. Individuals who had a primary arthroplasty at four hospitals in Toronto, Canada from 2010 to 2016 were identified using Canadian Classification of Health Intervention codes (based on the International Classification of Disease, Tenth Revision). Each re-admission to the same hospital until December 31, 2016 was reviewed for the presence of a PJI. The performance characteristics (sensitivity, specificity, positive and negative predictive values) of combinations of diagnostic and procedure codes when compared with the gold standard of chart review were calculated. The primary outcome was the algorithm that maximized sensitivity and positive predictive value.

Results. 27,843 primary arthroplasties were performed with 8595 readmissions, of which 572 involved a PJI. Median follow-up was 1258 days (interquartile range (IQR) 614–1891 days), with median time to first re-admission of 352 days (IQR range 166–725 days). PJI codes exhibited a sensitivity of 0.86 (95% confidence interval (95% CI 0.83–0.89) and positive predictive value (PPV) of 0.89 (95% CI 0.86–0.92). The best performing algorithm is a combination of a PJI code or joint spacer insertion procedure code or insertion of a peripherally inserted central catheter along with an arthroplasty code (sensitivity 0.90, 95% CI 0.88–0.93 and PPV 0.89, 95% CI 0.86–0.91). Using timing from primary arthroplasty, spacer insertion codes and presence of a subsequent arthroplasty procedure code identified 68% (71/105) of first stage and 74% (108/146) of debridement with joint retention procedures during the first re-admission for a PJI.

Conclusion. Combinations of diagnosis and procedure codes can reliably identify PJIs from administrative databases. Individual orthopaedic procedure codes and timing from primary arthroplasty can inform the surgical procedure performed. This PJI detection algorithm could be used for PJI surveillance and research.

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2443. Impact of Antimicrobial Stewardship on the Incidence of Carbapenem-Resistant *Pseudomonas aeruginosa*: A Nonlinear Time-Series Analysis Approach to Identify Carpapenem Thresholds

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Background. To estimate the impact of antimicrobials stewardship in the temporary evolution of the Density Incidence of *Pseudomonas aeruginosa* resistant to carbapenems (DI_PaCRE).

Methods. In Modena Policlinico, a tertiary care hospital, from September 2014, universal rectal screening and antibiotic stewardship (ABS) focusing on carbapenem sparing strategy were introduced. We used the statistical approach already described (A nonlinear time-series analysis approach to identify thresholds in associations between population antibiotic use and rates of resistance. López-Lozano JM, et al. Nat Microbiol. 2019 Apr 8. doi: 10.1038/s41564-019-0410-0) in order to adjust a non-linear model (Multivariate Adaptive Regression Splines) looking for the identification and estimation of thresholds in the influence of the use of Carbapenems on the DI_PaCRE.

Results. We identified a threshold at 5.65 DDD/100 bed-days of Carbapenems (CarbUse). Indeed, above this threshold, for every increase of one DDD/100 bed-days, the DL_PaCRE increased by 0.15 new cases by 1000 bed-days. On the basis of our analyses, considering a typical course of 7 days of treatment, an average CarbUse of 6.5 DDD/100 bed-days in 2012 and 2013, for an average of 15000 monthly bed-days, means around 139 treated patients. In order to avoid the emergence of resistance, the