Implementing Regional Multidrug-resistant Organisms (MDROs) Prevention Bundles – Mathematical Modeling Methods and Findings

The information below is intended to provide an expanded model description and additional results and conclusions for prioritizing individual intervention components of bundled strategies to prevent the spread of novel and targeted multidrug-resistant organisms (MDROs). This information is intended for a technical audience and expands on the mathematical modeling results presented in *Regional Impact of Multidrug-resistant Organism Prevention Bundles Implemented by Facility Type: A Modeling Study*. These results informed the CDC's *Public Health Strategies to Prevent the Spread of Novel and Targeted Multidrug-resistant Organisms (MDROs)*. An interactive web-based application for individual regional healthcare networks is also available to provide results tailored to a jurisdiction's needs and interests.

The mathematical model builds on a previously published CDC model [1] that evaluated the *Interim Guidance for a Public Health Response to Contain Novel or Targeted Multidrug-resistant Organisms (MDROs)* [2] to now evaluate the effectiveness of proactively detecting individuals with MDROs and managing colonized and infected individuals with enhanced infection prevention and control (IPC) practices (e.g., isolation and Contact Precautions in acute care settings) to reduce their transmissibility to susceptible individuals. The updated model is parametrized with carbapenem-resistant Enterobacterales (CRE) disease characteristics and historical patient flow data in regional healthcare networks.

Model description

This simple multifacility susceptible-infectious-susceptible (SIS) model assumes N constant occupancy facilities (hospitals, nursing homes, the community) linked through patient transfer, where the prevalence v_a and v'_a of patients under normal and enhanced infection control, respectively, at facility a are governed by

$$\frac{dv_a}{dt} = (\beta_a v_a + \beta'_a v'_a)(1 - v_a - v'_a) - (\gamma + \frac{1}{\tau_a} + \frac{1}{t_{P,a}})v_a + \frac{1}{\tau_a}\sum_{b=1}^{N}\left(\frac{T_{ba}^{(00)} n_{ba}}{n_a} v_b + \frac{T_{ba}^{(10)} n_{ba}}{n_a} v'_b\right)$$

$$\frac{dv'_a}{dt} = \frac{1}{t_{P,a}} v_a - (\gamma + \frac{1}{\tau_a})v'_a + \frac{1}{\tau_a}\sum_{b=1}^{N}\left(\frac{T_{ba}^{(01)} n_{ba}}{n_a} v_b + \frac{T_{ba}^{(11)} n_{ba}}{n_a} v'_b\right)$$

Variables and parameters in the model

- v_a, v'_a: proportion of patients at facility a who are infected/infectious and under normal or enhanced infection control
- β_a, β'_a: transmissibility, at facility a, under normal and enhanced infection prevention and control (IPC)
- γ: recovery rate
- τ_a: mean length of stay at facility a
- $t_{P,a}$: testing periodicity (corresponding to periodic screening) or timescale, at facility a
- n_a, n_{ba}: admissions to facility a and transfers from facility b to facility a (aggregated over a year)
- $T_{ba}^{(10)}$, etc: proportion of the patients under enhanced infection control (first superscript, 1) at facility b transferred to facility a, who are placed under normal infection control (second superscript, 0) on admission at facility a; etc.

Patient flow network

The patient flow network is characterized by the facility-to-facility transfer tallies n_{ba}, the number of admissions (and discharges) n_a aggregated over a given time interval, and the average lengths of stay τ_a. The principal source for these quantities is the Centers for Medicare and Medicaid Services (CMS) patient-level fee-for-service claims data for CMS beneficiaries.

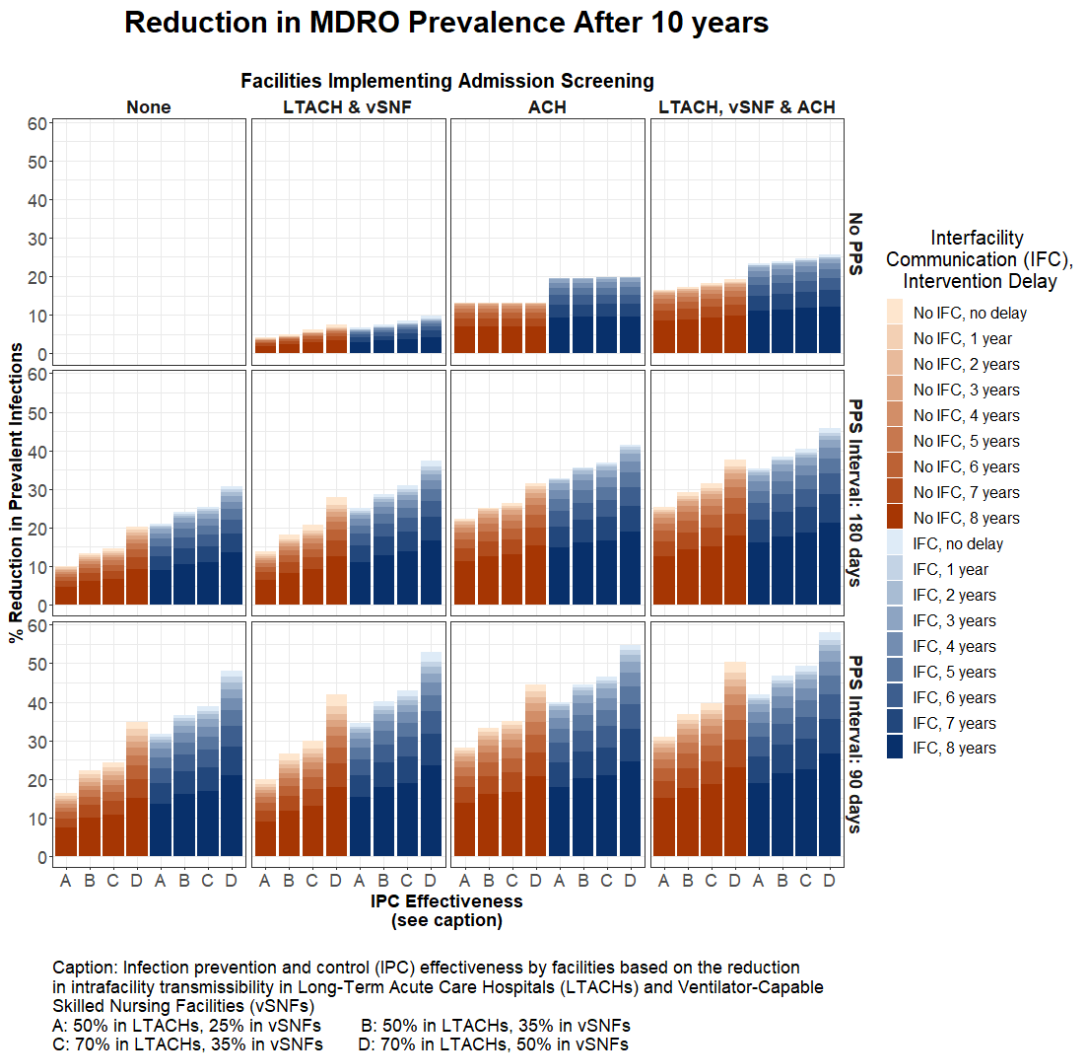
Table 1: Model parameters

Parameter	**Value**	**Source**
Disease parameters		
Recovery rate, γ	1/387 per day	Reference [3]
Transmissibility, β		
Acute care hospital (ACH) and Critical access hospital (CAH)	0.104 per day	Reference [1]
Long-term acute care hospitals (LTACH)	0.042 per day	Reference [1]
Ventilator-capable skilled nursing facility (vSNF)	0.02 per day	Estimated (NHSN, CMS claims)
Skilled nursing facilities (SNF)	0.0042 per day	Estimated (NHSN, CMS claims)
Other facilities and the community	0.001 per day	Estimated (NHSN, CMS claims)
Intervention parameters		
Point prevalence survey (PPS) periodicity, t_P	90 or 180 days	Informed estimate (CDC)
Admission screening	Patient transfer from an LTACH or vSNF to an ACH Patient transfer to an LTACH or vSNF	Informed estimate (CDC)
Transmissibility under enhanced IPC, β'		
ACH and CAH	0.0312 per day (-70%)	Reference [3, 4], Informed estimate (CDC)
LTACH	0.0126 per day (-70%), 0.021 per day (-50%)	Reference [3, 4], Informed estimate (CDC)
vSNF	0.01 per day (-50%), 0.013 per day (-35%), 0.015 per day (-25%)	Informed estimate (CDC)
SNF	0.00315 per day (-25%)	Informed estimate (CDC)
Other facilities and the community	0.001 per day (no change)	Informed estimate (CDC)
Interfacility communication	100% or 0%	

In the manuscript, we present the predicted prevalence reduction ten years into an outbreak with either no implementation delay or a three-year implementation delay following MDRO importation for different bundles of prevention interventions. We modeled interventions at levels that best represent practicable strategies health departments may use to slow the spread of MDROs. The effectiveness of targeted enhanced IPC practices for individuals with MDROs is based off previous literature and modeling [3, 4]. Interfacility communication is modeled as comprehensive (100% compliance) or unimplemented (0%).

Figure 1 depicts the modeled reduction in MDRO prevalence in the Illinois network of facilities ten years following MDRO importation and compares combinations of intervention delays and intervention levels to an unmitigated (i.e., no intervention) scenario. The intervention delays modeled are 0 through 8 years in annual increments. The intervention layers include point prevalence surveys (PPS) at ventilator-capable skilled nursing facilities (vSNFs) and long-term acute care hospitals (LTACHs) (every 90 days, 180 days, or not implemented); admission screening (at acute care hospitals (ACHs) on patients transferred from LTACHs or vSNFs [ACH], at LTACHs or vSNFs on all patients [LTACH & vSNF], at ACHs on patients transferred from LTACHs or vSNFs and at LTACHs or vSNFs on all patients [LTACH, vSNF & ACH], or not implemented [none]); interfacility communication (100% compliance or not implemented); and enhanced IPC practices (reducing transmissibility in LTACHs by 50% or 70%, in vSNFs by 25%, 35%, or 50%, in skilled nursing facilities by 25%, and in ACH and critical access hospitals by 70%).

Figure 1: Illinois network, all intervention scenarios



In Figure 1, we show the modeling results for combinations of interventions across the Illinois patient transfer network. Each intervention bar is shaded by the delay between MDRO introduction to a region and intervention start time; each shade represents the incremental benefit (reduction in prevalence) attributable to implementing interventions one year earlier than the next. Interventions are classified as: 1. detection and tracking of infectious individuals (i.e., admission screening, PPS, and interfacility communication), and 2. prevention of onward transmission from detected or tracked infectious individuals through enhanced IPC practices. Detection of MDROs through colonization screening has a large impact on prevalence reduction. Overall, increased PPS frequency in influential facilities (e.g.,

vSNFs and LTACHS) and admission screening in more facilities (from an LTACH or vSNF to an ACH, and all admissions to LTACHs and vSNFs) results in the greatest predicted regional prevalence reductions for each IPC effectiveness level and intervention delay.

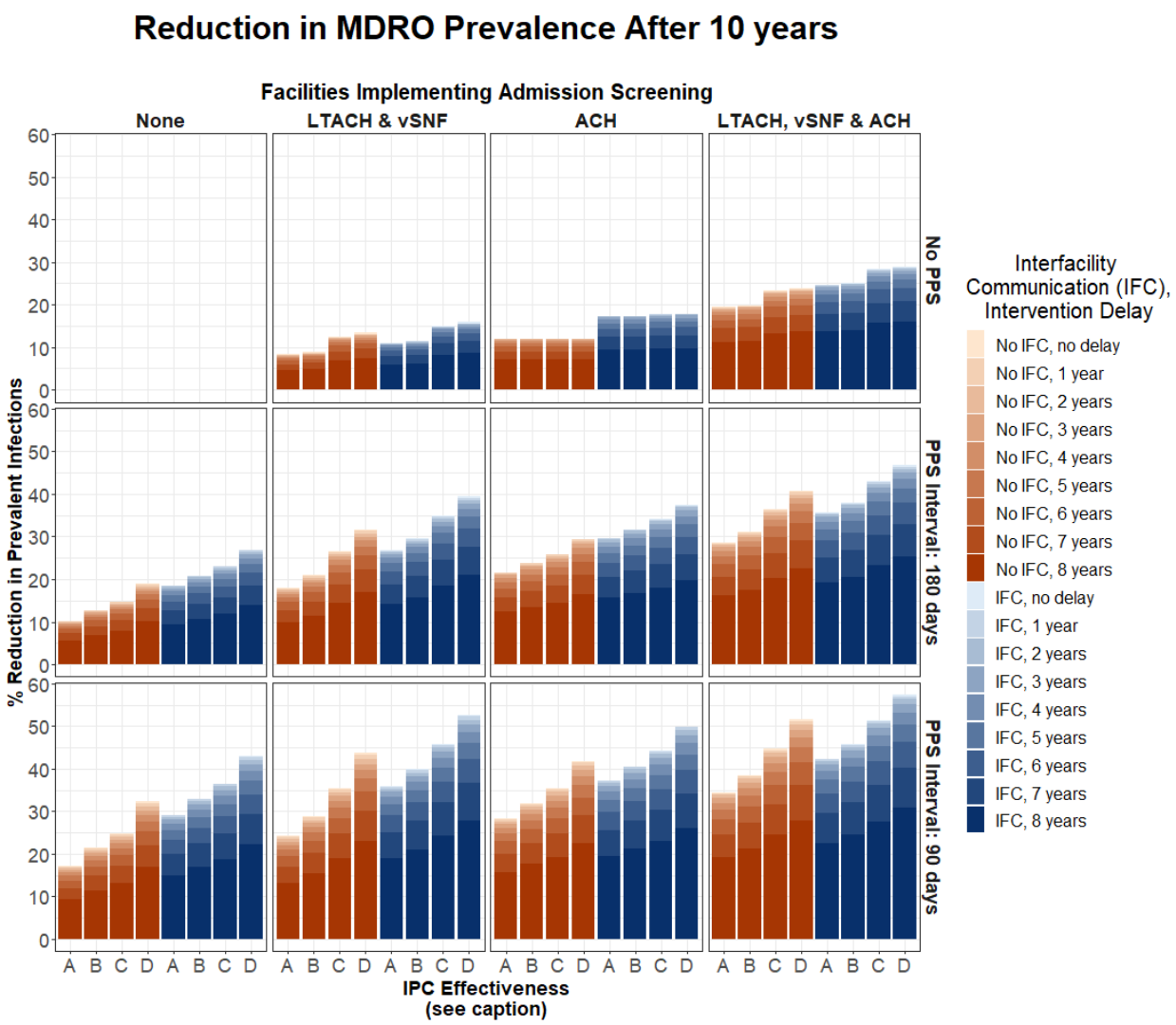
Comparing scenarios of all interventions minus admission screening and all interventions minus PPS allows for comparisons of their predicted relative impacts in the model. PPS in influential facilities (LTACHs and vSNFs) at both intervals assessed (90 and 180 days) performed without admission screening is predicted to have equal or better reduction than performing admission screening without complementary PPS. Among admission screening scenarios assessed, screening all patients transferred from an LTACH or vSNF (regardless of mechanical ventilation status) on admission to ACHs reduces regional prevalence more than screening all admissions to LTACHs and vSNFs. Combined admission screening of individuals transferring from an LTACH or vSNF to an ACH, and all admissions to LTACHs and vSNFs only resulted in marginally greater reductions than admission screening of individuals transferring from an LTACH or vSNF to an ACH alone. Based on the above findings, periodic PPS in vSNF and LTACH, combined with admission screening at ACHs for transfers from LTACHs and vSNFs, are likely to be highly effective approaches to detect individuals colonized with an MDRO. An intervention to improve interfacility communication (i.e., notification of patient MDRO status at transitions of care) as modeled reduces prevalence, especially in ACHs, but not to the same degree as colonization screening interventions. Therefore, initiatives to improve interfacility communication (e.g., creation of patient safety information exchanges) should be considered adjunct measures to other interventions to detect individuals with MDROs, such as PPS and admission screening.

Coupling detection and tracking with prevention of onward transmission through good adherence to enhanced IPC practices is predicted to result in the largest prevalence reductions among the intervention bundles assessed. Modest increases in the effectiveness of enhanced IPC practices in vSNFs

(e.g., increase from 25% effective to 35% or 50% effective) and LTACHs (increase from 50% effective to 70% effective) are predicted to decrease prevalence regionally.

Figures 2-4 present the same bundle combinations as Figure 1, implemented using data from three different transfer network regions (California (Los Angeles and Orange Counties, California), New Jersey, and New York) to compare intervention effectiveness across regions with diverse healthcare facility compositions. Each network has varying numbers of influential and highly connected facilities, but they all present similar prevalence reductions following the introduction of interventions.

Figure 2: California (Los Angeles County and Orange County) network



Caption: Infection prevention and control (IPC) effectiveness by facilities based on the reduction in intrafacility transmissibility in Long-Term Acute Care Hospitals (LTACHs) and Ventilator-Capable Skilled Nursing Facilities (vSNFs)
A: 50% in LTACHs, 25% in vSNFs B: 50% in LTACHs, 35% in vSNFs
C: 70% in LTACHs, 35% in vSNFs D: 70% in LTACHs, 50% in vSNFs

Figure 3:New Jersey network

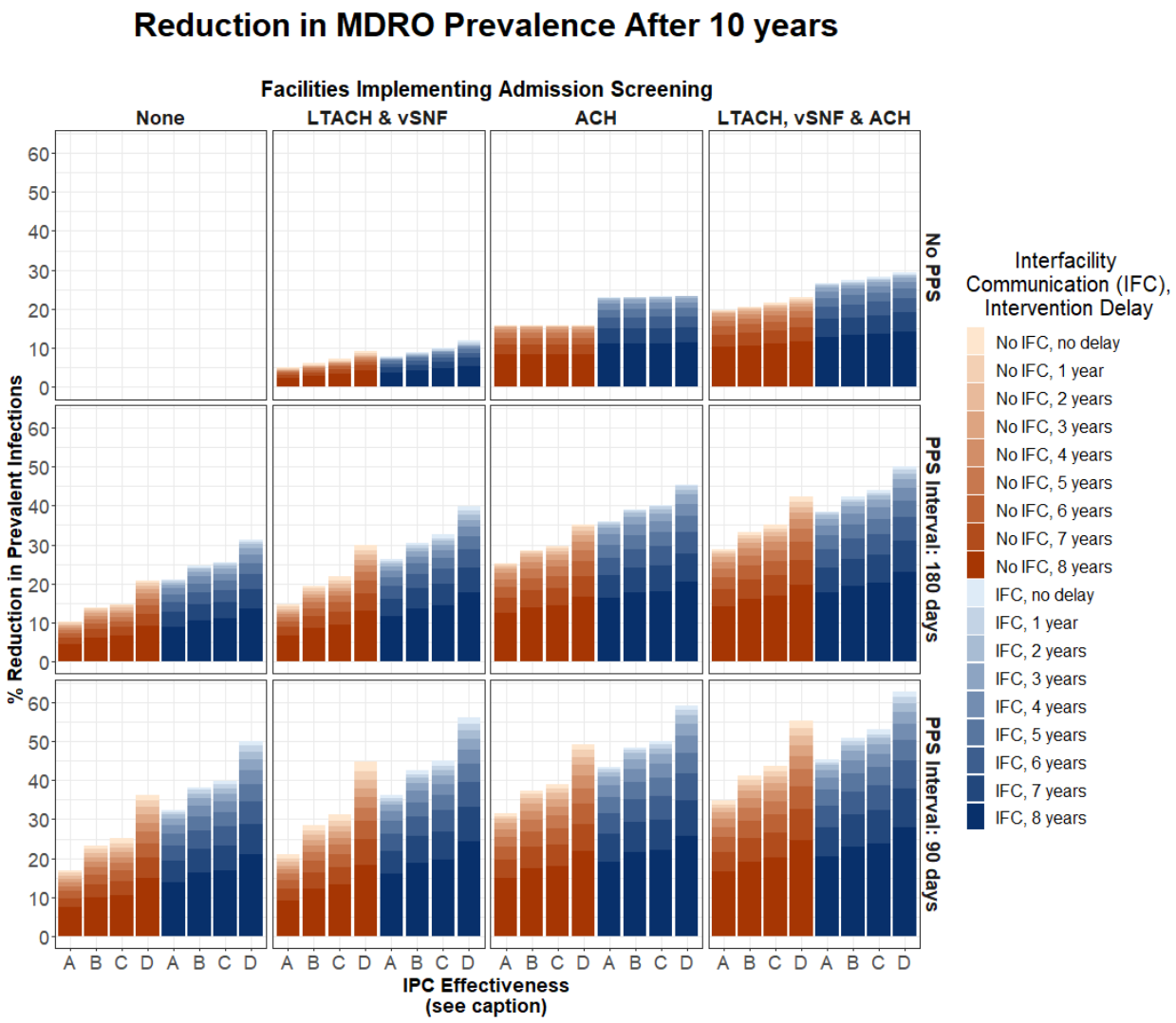


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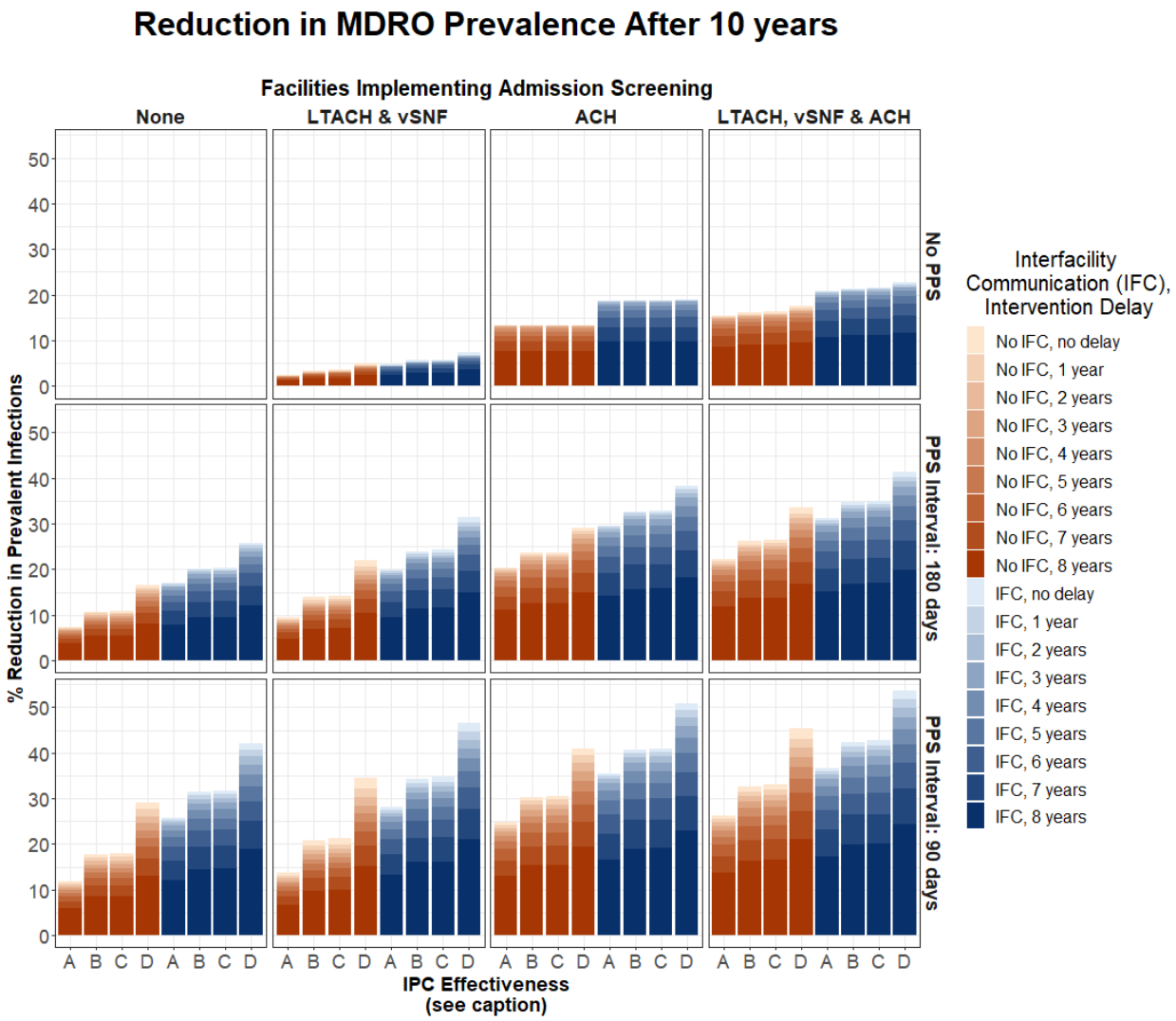
Figure 4: New York network



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References

1. Paul P, Slayton RB, Kallen AJ, Walters MS, Jernigan JA. Modeling regional transmission and containment of a healthcare-associated multidrug-resistant organism. Clinical Infectious Diseases 2020; 70(3): 388-94.

2. Centers for Disease Control and Prevention. Interim guidance for a public health response to contain novel or targeted multidrug-resistant organisms (MDROs). Atlanta, GA: US Department of Health and Human Services, 2017.
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