National Center for Emerging and Zoonotic Infectious Diseases

Mathematical Modeling to Inform Containment

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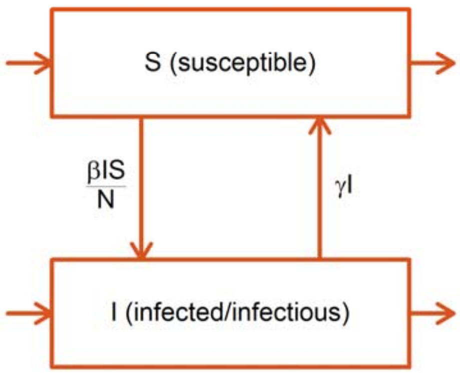
What can a simple mathematical model do?

- Make best use of sparse information
- Make predictions based on averages
- Incorporate information from multiple and disparate data sources
- Dynamically change as more information becomes available
- Complement traditional epidemiologic and outbreak response practices

What can’t a simple mathematical model do?

- Operate on its own: needs to be complemented by traditional epidemiologic and outbreak response practices, and local expertise
- Operate as a static model: needs to be updated with new information and rerun

Modeling transmission in hospitals



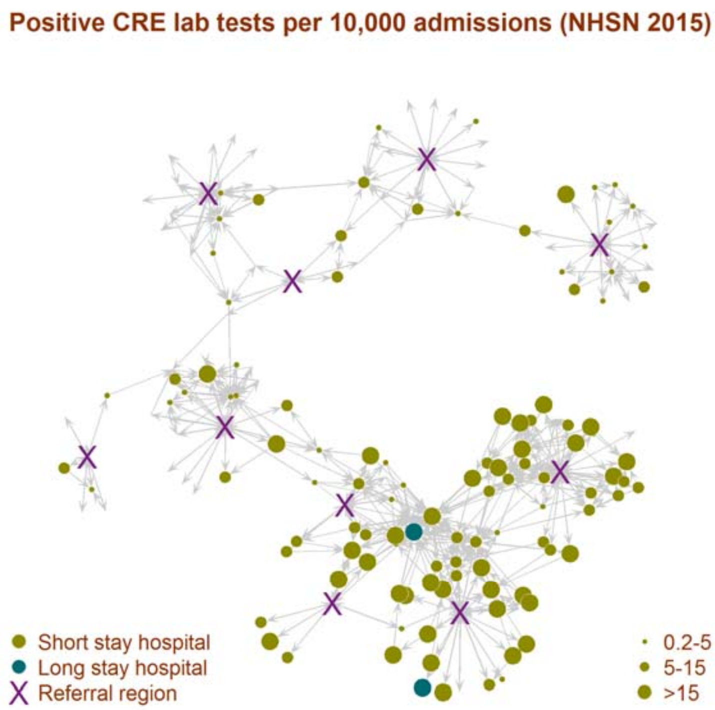
Susceptible – infectious/infected – susceptible (SIS) model

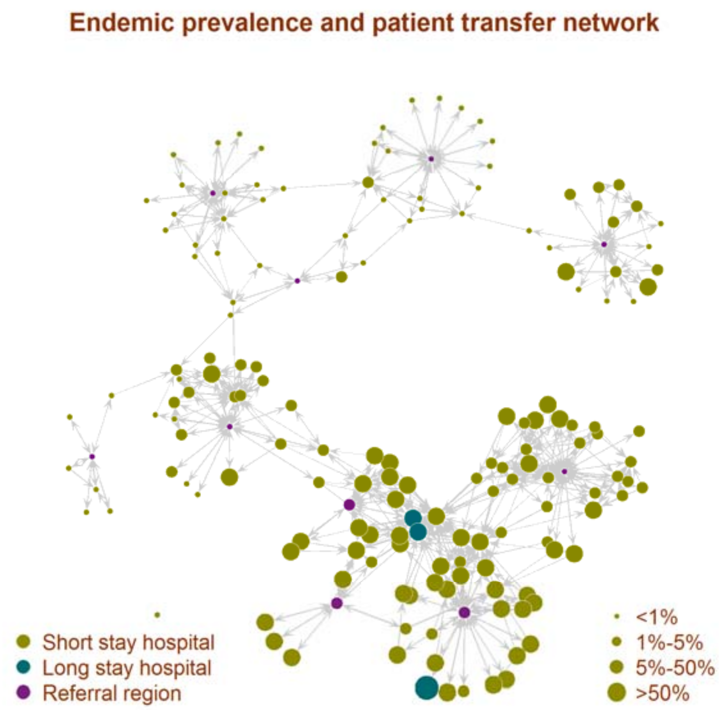
- Incidence depends on prevalence
- Infectious persons are discharged or transferred, or recover to susceptibles

Model Parameterization

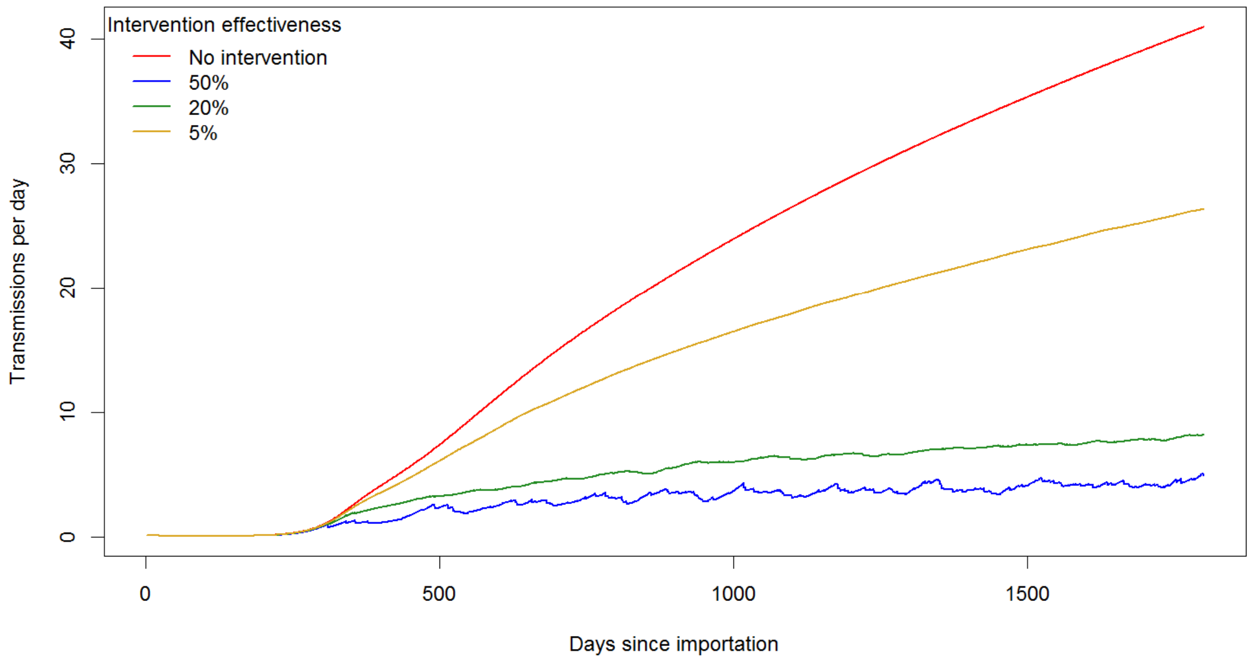
- Patient flow among healthcare facilities derived from Centers for Medicare & Medicaid Services data
  - Claims data and the Minimum Data Set (MDS)
- Facility type transmission parameter, β, estimated from NHSN CRE surveillance data
  - Corroborated by independent facility-level estimates in the literature

Modeling spread across a network: the network structure





Modeled Regional Impact of the Containment Strategy



After detection of MDRO by clinical culture:

- Serial PPS, and infection control interventions at the index facility and at those most connected by transfer of infectious persons
- infection control interventions simulated as fractional reduction in transmission
- PPS continued fortnightly until two consecutive nulls

[CDC Interim Guidance for a Health Response to Contain Novel or Targeted Multidrug-resistant Organisms]

Identification of Priority Sites

Sentinel sites:

- Located where greatest amplification is expected
- Includes estimates of pathogen-specific dynamic parameters
- May be best suited for point prevalence surveys (PPS)

Central/bridge sites:

- Located on most frequented patient transfer pathways
- Does not include pathogen-specific information
- May be best suited for admission screening

Preliminary Findings: Identification of Sentinel Sites

- Analysis of a statewide network
  - Including hospitals, long-term acute care hospitals (LTACHs), and skilled nursing facilities (SNFs) stratified by ventilator use
- Identified 21 sentinel sites
  - 3 LTACHs and 18 ventilator SNFs
- These sites account for:
  - 2.2% of all facilities in the state
  - 1.0% of all admissions
  - 4.0% of patients in all facilities

Response: what happens after detection?

- Locations optimized for early detection may not be optimal for response
- An facility-based intervention to reduce transmissions may make some sentinel sites less sensitive!
- Once a novel pathogen is detected in a region, the best response may be adherence to containment guidelines and refinement of model to predict future spread

Next Steps

- Continue to refine the model as outbreaks progress and more is know about both the natural history of the infection of interest and where clinical cases have been identified
- Pilot a field study with sentinel sites identified via modeling?

Questions?

Thank you!

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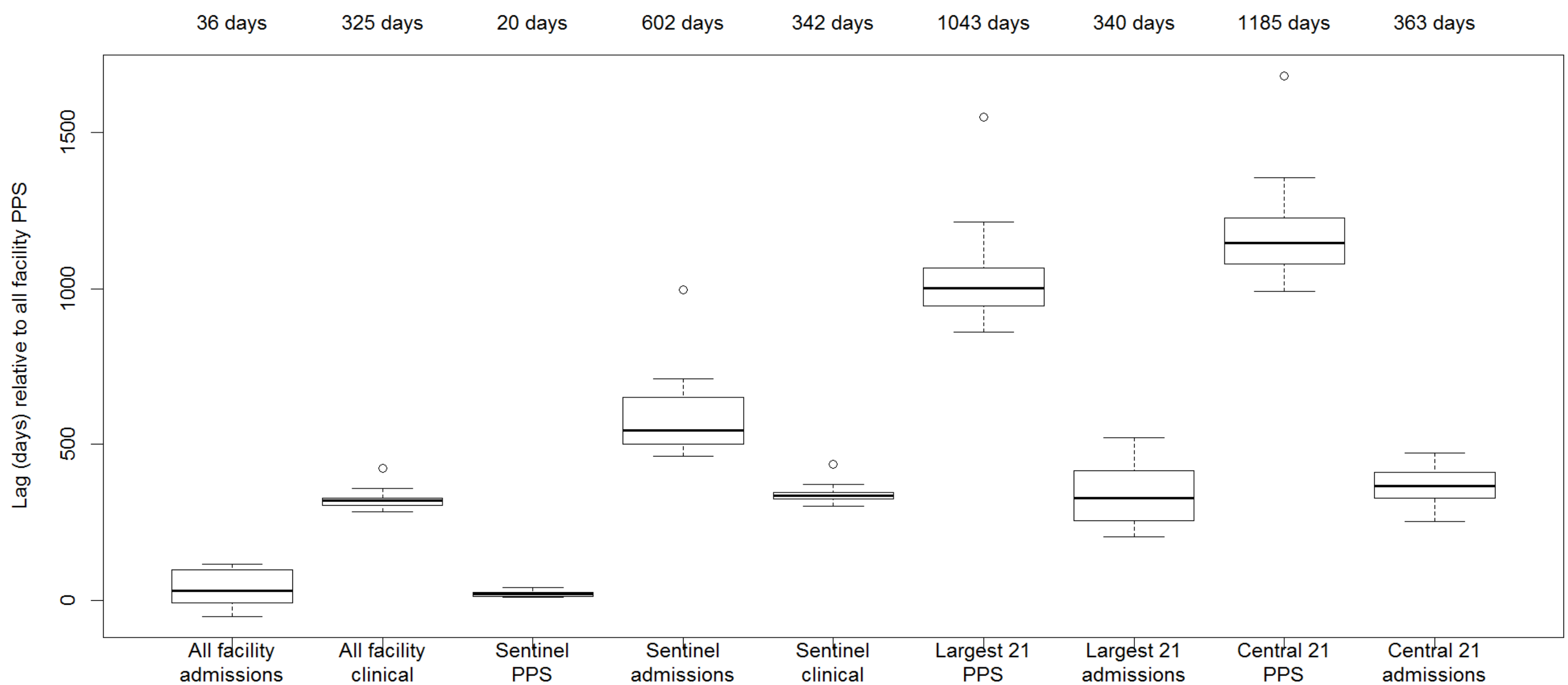
- Eleanor Adams
- Emily Lutterloh
- Monica Quinn

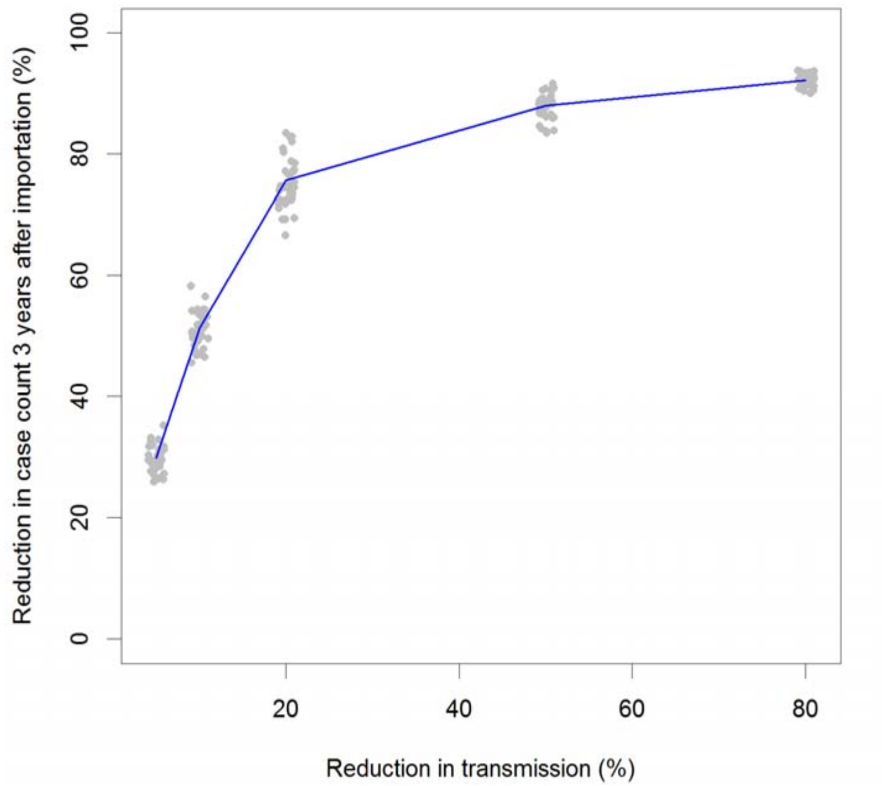
- Patricia Barrett
- Rebecca Greeley
- Jason Mehr

Extra slides

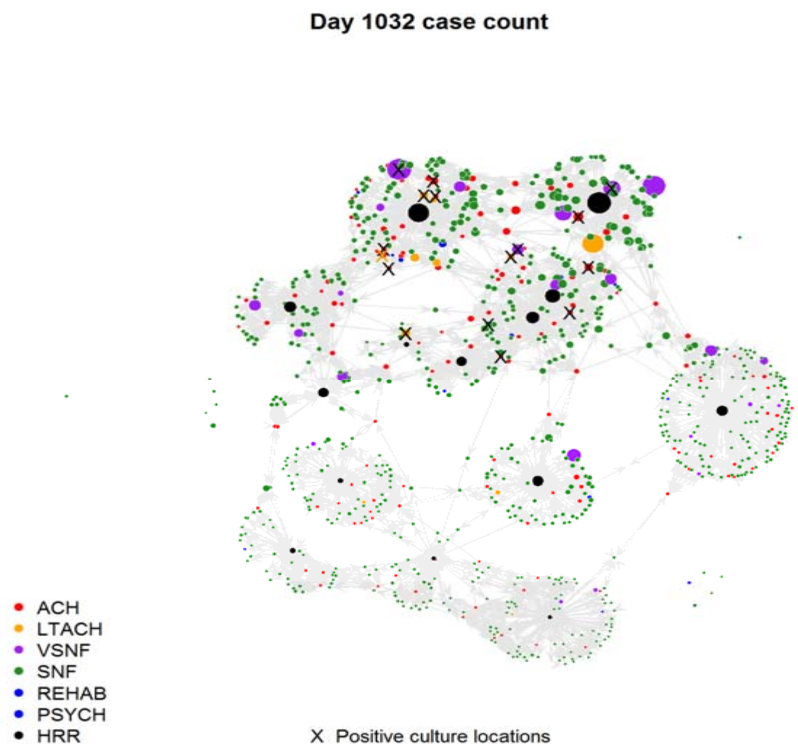
Comparing lags among detection strategies

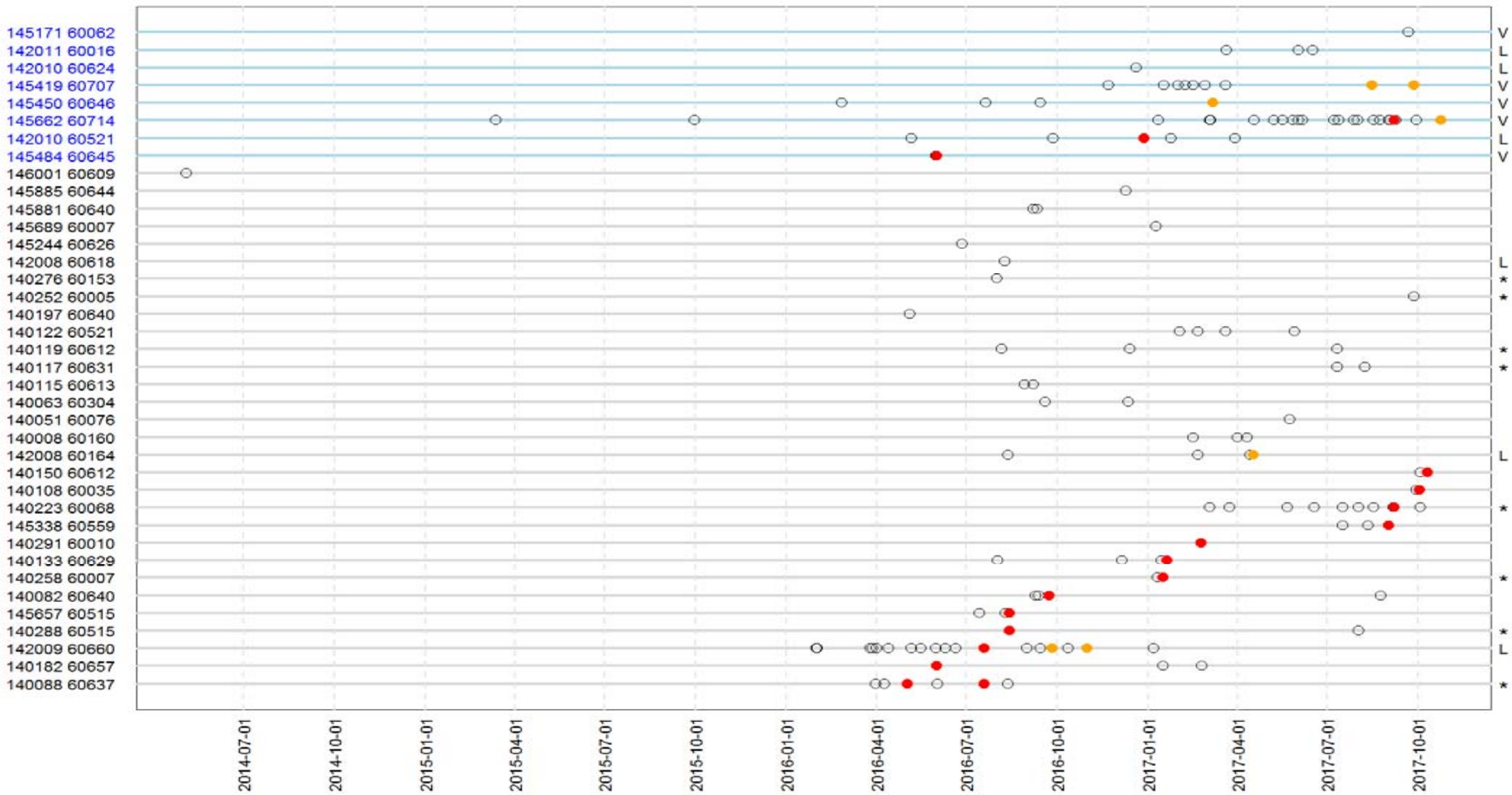


Estimated Relative Reduction in MDRO Transmission



Estimating spread of *C auris* in Illinois





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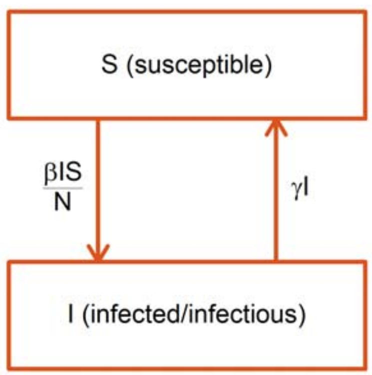
Mathematical Modeling: Transmission of Disease

- Simplified representation of transmission of pathogens + disease processes
  - Involves the systematic deconstruction of the mechanisms of transmissions
    - Explicitly describe simplifying assumptions
    - Systematically conduct experiments to quantify influence
- Mathematical representation
  - Improves technical dialogue
  - Clarifies thinking
  - Allows pros and cons of a program to be quantified

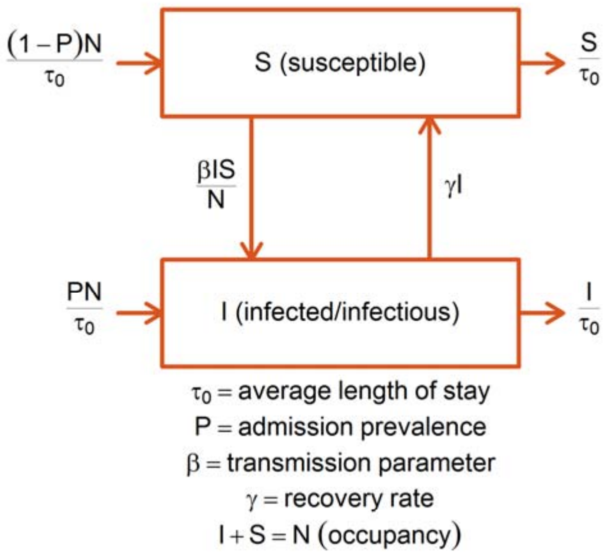
Modeling transmission in a hospital



Susceptible – infectious/infected – susceptible (SIS) model

- Incidence depends on prevalence

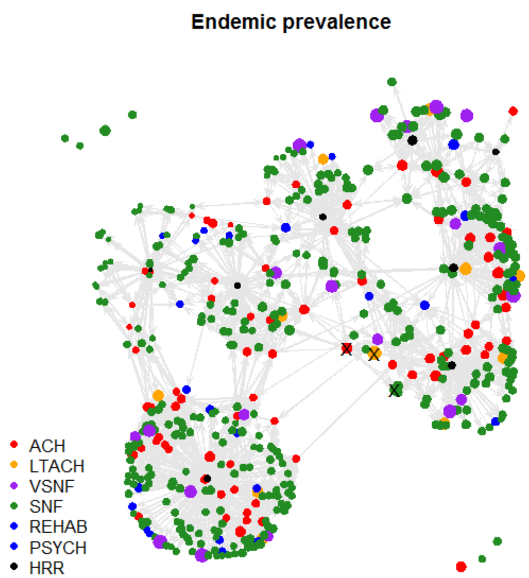
Modeling transmission in a hospital



Susceptible – infectious/infected – susceptible (SIS) model

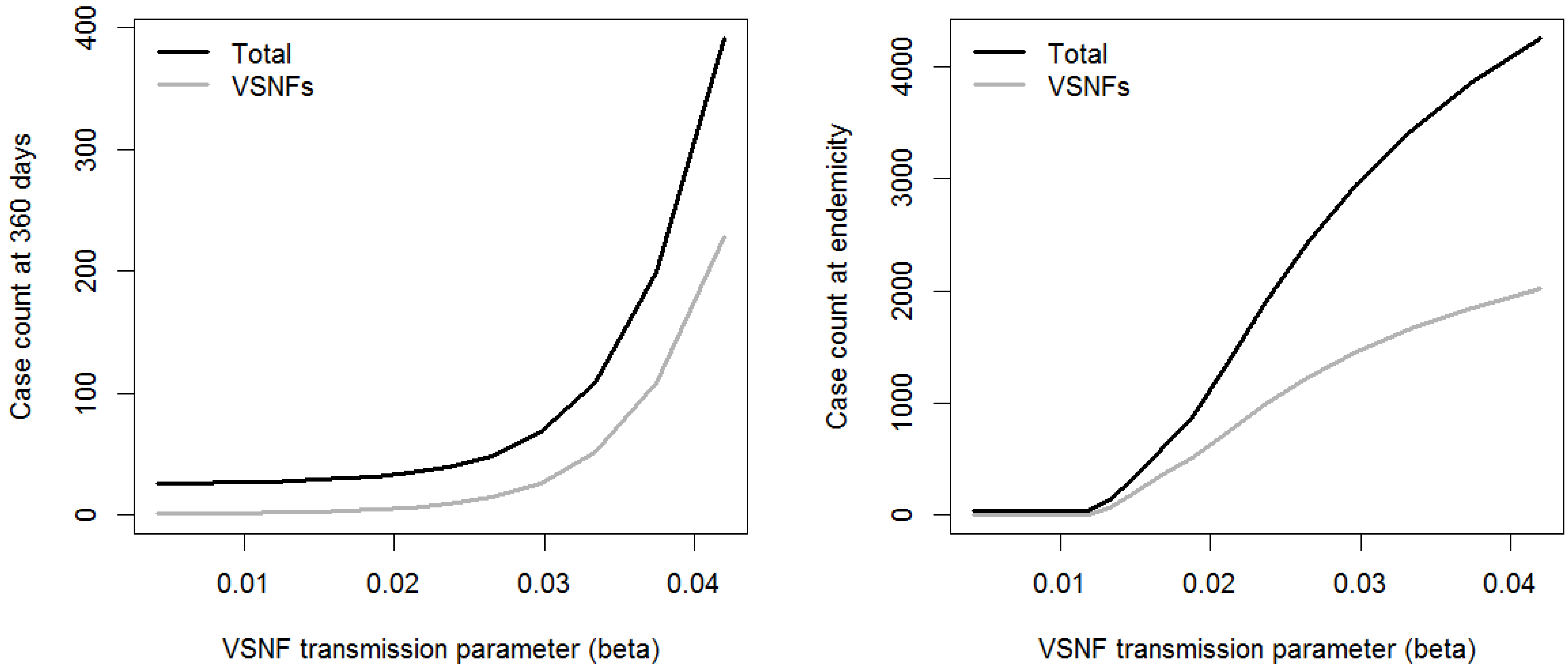
- Incidence depends on prevalence
- Infectious persons are discharged or transferred, or recover to susceptibles
- Reproduction number (R_0) = number of secondary cases from a primary case
- Hospital reproduction number = number of secondary cases from a primary case at a hospital ≈ transmission parameter X length of stay

Estimating spread of *C auris* in a U.S. state



- 75 ACHs, 11 LTACHs, 25 PSYCHs and REHABs, 349 SNFs and 20 VSNFs in 8 Dartmouth Atlas Hospital Referral Regions
- Transfer network created using MDS and CMS data
- VSNFs identified using MDS data , provider-of-service file 2016 and CMS supplied list
- Transmission parameters estimated at an LTACH from recent PPS study; others (except SNF and VSNF) borrowed from NHSN based estimates for CRE; SNF borrowed from published results for CRE
- Mortality among infected estimated from PPS study

Impact of transmission at VSNFs on outbreak dynamics



Why are LTACHs important?

- Virtually all LTACH admissions are transfers from acute care hospitals
  - Chicago CRE data: ACH prevalence & LTACH importation
    - LTACH importation rate >20%
    - ACH carrier prevalence in ICU's <4%
- Facility Transmission Threshold
  - Influenced by transmission rate parameter (β) and mean length of infectious period in facility, which is collinear with length of stay (LOS)
    - ACH: High β, short LOS
    - SNF: Low β, long LOS
    - LTACH: High β, long LOS
  - Pre-intervention, LTACH alone could sustain outbreak
  - Intervention LTACH below this critical threshold

Shared Healthcare Intervention to Eliminate Life-threatening Dissemination of MDROs in Orange County [SHIELD-OC]

- Demonstration of regional benefit from targeted approach to decolonization (reduction in MDRO infections and colonization)
  - CDC, CA Department of Public Health (CDPH), Orange County Health Care Agency (OCHCA), University of California, Irvine
- Mathematical modeling of patient movement used to identify likely higher transmission settings
- Targeted decolonization intervention
  - Chlorhexidine bathing
  - Iodophor nasal swabs
- Facility and community level impact measured by surveillance swabs in LTACs and NHs and reportable disease data on (CRE, MRSA, ESBLs, VRE)
  - Surveillance swabs at start and finish in both intervention and no intervention facilities to measure community-wide impact

Providing Regional Organizations with TEchniques to ConTrol MDROs [PROTECT] in Chicago.

- Builds on previous work in Chicago
  - Demonstration of impact on CRE infections among affiliated ACHs of decolonization in 4 high prevalence /transmission LTACs
  - XDRO registry, jointly administered by Chicago/IL DOH and Rush Epicenter personnel that maintains state registry of CRE colonized or infected persons, facilitating early contact precautions and decolonization when these patients are admitted to a facility
- Goals of PROTECT
  - Model how transmission of CRE could occur across a region of interconnected healthcare facilities
  - Assess the potential cost benefit of implementing prevention strategies across healthcare facilities, including whether a focus on particular facility types (e.g., LTACHs, vSNFs, or STACHs) is likely to be more effective or efficient.
  - Design and implement a multicenter intervention study to prevent CRE transmission in Chicagoland based upon findings of the mathematical modeling.
    - Intervention bundles to be modeled: admission screening, geographic separation, CHG bathing, nasal decolonization (facility-wide or targeted)
  - Measure the impact of the multicenter intervention on regional transmission, Will make use of XDRO registry capabilities, mathematical modeling to design on or more interventions, and economic data

Overview of Social Network Analysis

- Framework in which to describe the relationships among entities in a system (e.g., relationships among individual people)
- Quantifies the connections among entities (i.e., nodes) using mathematical language to describe connections
- Used in many fields including physics, ecology, neurology, computer science, etc.
- Used in public health for understanding transmission of sexually transmitted infections

Use of Social Network Analysis to Support Outbreak Investigations

- Social network analysis may help identify healthcare facilities that are closely connected to facilities with known cases
  - Using historic data, describe regional patient movement from Medicare fee-for-service beneficiary claims
- Has the potential to identify targets for admission screening and/or point prevalence surveys
  - Downstream facilities which may be at increased risk of importation
  - Upstream facilities where previous undetected transmission events may have occurred

Generating Social Networks Using Administrative Data

- Administrative claims are filed for reimbursement each time an individual seeks healthcare
  - Payers (i.e., Medicare, private insurance companies, etc.) compile claims in databases
  - Individuals are given a unique person-level identifier which enables longitudinal analyses of healthcare utilization
- Leveraging these existing data, we can quantify the relationships among healthcare facilities through patient sharing
  - Generate a matrix of interfacility patient sharing

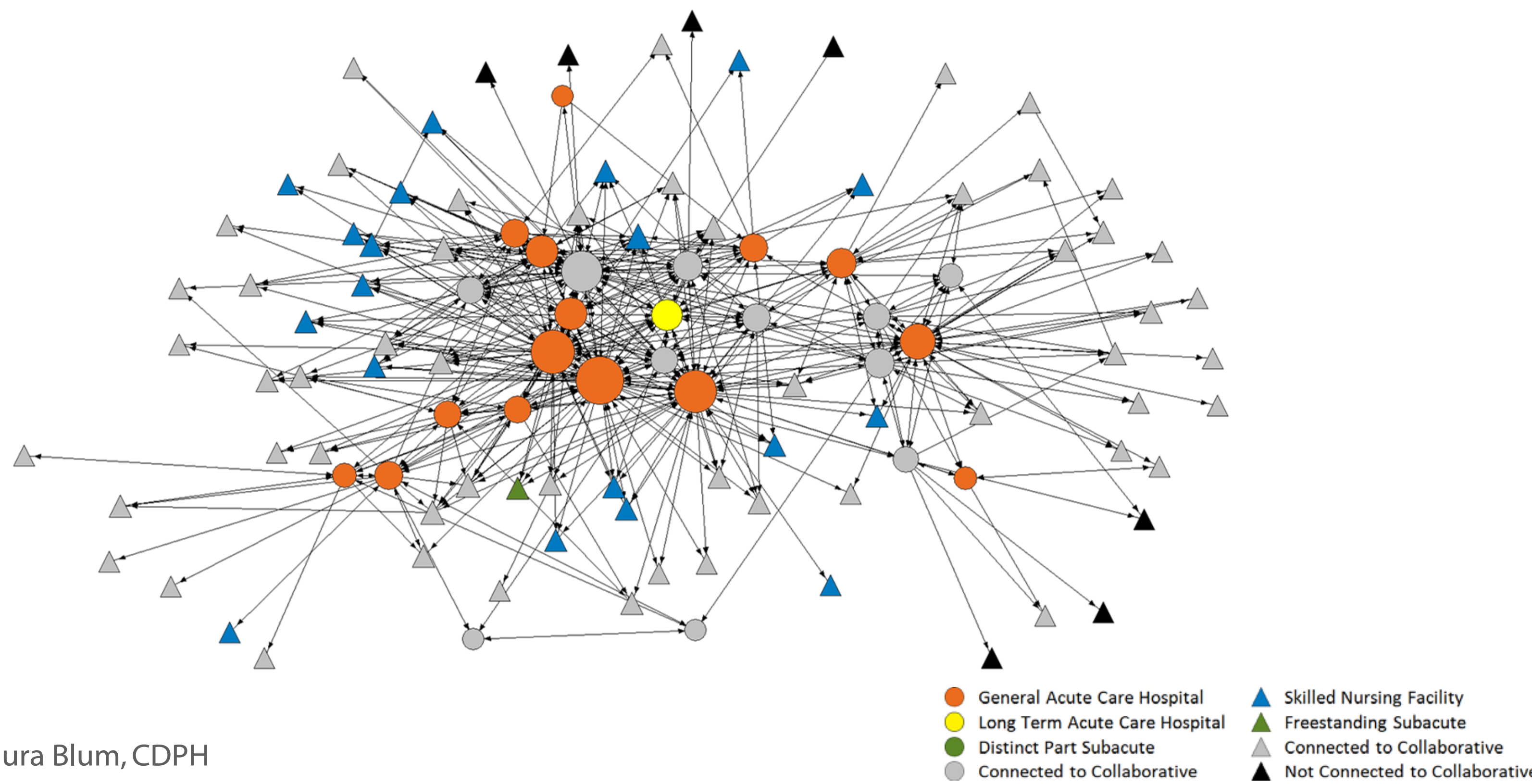
Network Direct and Indirect Effects

- Public health interventions in a network can affect participating facilities (direct effects) *and* facilities in close geographic or social proximity (indirect effects)
- *Example:* Sacramento Metropolitan Area *C. difficile* Infection Prevention Collaborative
  - Prioritized enrollment of highly connected facilities
  - Recruited 36 of 107 facilities in catchment area

Smith D, Nat Acad Sci, 2005
Benjamin-Chung J, Int Init Impact Evaluation, 2015

Slide courtesy of Laura Blum, CDPH

Sacramento Metropolitan Area *Clostridium difficile* Infection Prevention Collaborative



Slide courtesy of Laura Blum, CDPH