Methicillin-Resistant *Staphylococcus aureus* Transmission Reduction using Agent-Based Modeling and Simulation

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Agenda

- Motivation
- Methodology
- Implementation
- Verification and Validation
- Testing
- Conclusions
Motivation

- The spread of infection is a dangerous problem, particularly in hospitals and communities around the country.
- One of the most prevalent types of infection is Methicillin resistant Staphylococcus aureus (MRSA), the cause of close to 300,000 hospital-acquired infections and 20,000 deaths per year in the US.

Project Goals:

1. Model the transmission dynamics of MRSA within a hospital.
2. Test the effectiveness of various infection control measures on preventing the spread of MRSA.
3. Use the software to answer novel questions about transmission dynamics in a hospital.
Methodology

- The majority of modeling efforts on this problem have relied heavily upon equation based methods.
- The tractability of these methods depends on limiting assumptions that make it difficult to examine complex scenarios.
- **Agent-based modeling and simulation (ABMS)** allows us to model explicitly the *interactions* between patients, health care workers, and visitors.
ABMS

- Seeks to generate unexpected (emergent) macroscopic behavior from modeling microscopic interactions
- Easily allows for heterogeneity within the population
- Requires:
  - Definition of agents and their behaviors
  - Scope of interactions between agents
  - Optional: Explicit representation of the environment
- Agents:
  - Patients
  - Health care workers (HCWs, i.e., nurses and physicians)
  - Visitors
- The hospital serves as the environment in which agents interact
Agent States and Interactions

Visitors
- Not Colonized
- Colonized

Patients
- Susceptible
- Colonized
- Infected

HCWs
- Susceptible
- Colonized

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Implementation

- Stochastic agent-based simulation package developed in **Python** using various modules, most prevalently **SimPy** and **Parallel Python**
- SimPy: Discrete event simulation package which provides built-in functionality for simulating the interactions between agents and generating useful data
- Parallel Python: Multi-core parallel processing package which allowed for simultaneous execution of Monte Carlo simulation replications
- Agents were developed as object-oriented classes, with process execution methods defined for SimPy
Transmission Factors

- Hand hygiene compliance
- Hand hygiene efficacy
- HCW to patient ratios
- Transmissibility
  - Patient to HCW
  - HCW to Patient
  - Visitor to Patient
- Length of stay
- Number of daily contacts
- Proportion of colonized patients admitted
- Number of visitors

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Infection Control Measures

- Active surveillance/Patient screening
  - On admission (with some probability)
  - With some frequency during patient stay
- Patient isolation
  - Once patient has been positively identified as a MRSA carrier, they can be isolated in a single room if there is one available
  - Cannot transmit MRSA to other patients by way of HCWs
- Decolonization
  - Once patient has been positively identified as a MRSA carrier, they can begin the decolonization process
  - When the treatment process is completed, patient returns to susceptible state
Infection Metrics

- **Basic reproduction number, \( R_0 \):** Mean number of secondary cases directly attributable to a single primary case
- **Successful introduction rate:** No. of secondary cases
- **Attack rate:** Ratio of transmissions to uncolonized patient days
- **Colonized patient days:** Percentage of total days spent as a colonized or infected patient
- **Ward prevalence:** Percentage of days on which at least one colonized patient was present
Computing 1

Small Case

- 100 days, 250 replications
- 10 single/10 double rooms
- 10 nurses/5 physicians
- 10 day length of stay
- 5 daily contacts
- No infection control measures

All testing was performed on
Genome cluster machine: 32 processors/128 GB RAM

Results

<table>
<thead>
<tr>
<th>N</th>
<th>Job Time Sum (s)</th>
<th>Run Times (s)</th>
<th>Speedup</th>
</tr>
</thead>
<tbody>
<tr>
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<td>747</td>
<td>747</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>752</td>
<td>377</td>
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<td>752</td>
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<td>16</td>
<td>761</td>
<td>50</td>
<td>14.94</td>
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<tr>
<td>32</td>
<td>941</td>
<td>33</td>
<td>22.64</td>
</tr>
</tbody>
</table>

Degradation in speedup due to extraction of results from larger number of processors
Computing II

Large Case

- 500 days, 25 replications
- 50 single/150 double rooms
- 50 nurses/20 physicians
- 10 day length of stay
- 5 daily contacts
- All infection control measures

All testing was performed on Genome cluster machine: 32 processors/128 GB RAM

Results

<table>
<thead>
<tr>
<th>N</th>
<th>JobTime Sum (m)</th>
<th>Run Times (m)</th>
<th>Speedup</th>
</tr>
</thead>
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<td>136.9</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>138.4</td>
<td>71.84</td>
<td>1.91</td>
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<tr>
<td>4</td>
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<td>37.91</td>
<td>3.61</td>
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<tr>
<td>8</td>
<td>133.7</td>
<td>21.10</td>
<td>6.49</td>
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<tr>
<td>16</td>
<td>141.3</td>
<td>11.88</td>
<td>11.52</td>
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<tr>
<td>32</td>
<td>182.3</td>
<td>8.96</td>
<td>15.28</td>
</tr>
</tbody>
</table>

Degradation in speedup due to extraction of results from larger number of processors
Verification and Validation

- **Verification -- Is the model implemented correctly?**
  - Programmatic testing
  - Simple test cases and scenarios (i.e. corner cases, relative value testing)
  - Event logging

- **Validation -- Does the model represent real world behavior?**
  - Matching behavior from the literature
    - SIR Model – Kermack and McKendrick (1927)
    - Beggs, Shepherd, and Kerr (2008)
    - Other models
SIR Model

- Population transitions between Susceptible, Infected, and Recovered states
- Assumptions:
  - Closed population (i.e. no births, deaths, migration)
  - Homogeneous population, well-mixed
- Model equations:
  \[
  \frac{dS}{dt} = -\beta SI, \quad \frac{dI}{dt} = \beta SI - \gamma I, \quad \frac{dR}{dt} = \gamma I
  \]
- Used to validate transmission dynamics of ABMS software
Comparison

SI Model

ABMS
Targeting Zero

- Additional control measures are required to further reduce the incidence of transmission

- Baseline Case:
  - 100 days, 250 replications
  - 30 patients, 5 HCWs
  - 10 single, 10 double rooms
  - 5% of patients admitted are colonized with MRSA
  - 5 daily contacts per patient, U(0,10) day LOS
  - 50% hand hygiene compliance, 80% efficacy
  - No interventions
## Comparison

<table>
<thead>
<tr>
<th>Mean Statistic</th>
<th>Baseline</th>
<th>Isolation</th>
<th>Decolonization</th>
<th>Cohorting (1:1/2:1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Colonized</td>
<td>51.46</td>
<td>39.56</td>
<td>45.42</td>
<td>34.79</td>
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<tr>
<td>Colonized Patients Admitted</td>
<td>36.50</td>
<td>34.48</td>
<td>34.76</td>
<td>33.85</td>
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<tr>
<td>No. of Secondary Cases</td>
<td>14.97</td>
<td>5.08</td>
<td>10.66</td>
<td>0.94</td>
</tr>
<tr>
<td>Ward Prevalence</td>
<td>82.51%</td>
<td>81.44%</td>
<td>78.82%</td>
<td>78.99%</td>
</tr>
<tr>
<td>Colonized Patient Days</td>
<td>6.49%</td>
<td>5.66%</td>
<td>5.72%</td>
<td>5.14%</td>
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<tr>
<td>Attack Rate</td>
<td>0.004989</td>
<td>0.001693</td>
<td>0.003553</td>
<td>0.000313</td>
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<td>R₀</td>
<td>0.4098</td>
<td>0.1474</td>
<td>0.3056</td>
<td>0.0272</td>
</tr>
</tbody>
</table>

* Best case results shown for each infection control measure
Testing

- A verified and validated AMBS software package allows us to perform a wide variety of simulation experiments to answer relevant questions.

- Two Important Questions
  1. Do nurses or physicians spread more to patients?
  2. Could a ‘good’ hospital still be susceptible to an outbreak?
Physician Compliance – General Ward

Physician Hand Hygiene Compliance

Proportion of Colonizations by Nurses

Proportion of Visits by Nurses

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Physician Compliance - ICU

Proportion of Colonizations by Nurses

Physician Hand Hygiene Compliance

Nurse Hand Hygiene Compliance

0.3

0.5

0.8
HCW Comparison

Physician Hand Hygiene Compliance

Colonizations by Physicians

Nurse-to-patient ratio  1:1  1:2  1:3

Physician Hand Hygiene Compliance

Colonizations by Nurses

Nurse-to-patient ratio  1:1  1:2  1:3
Rogue Nurse Hand Hygiene Compliance

- Nurses
- Physicians

Colonizations

Rogue Physician Hand Hygiene Compliance

- Nurses
- Physicians

Colonizations
Compliance vs. Nurse-to-Patient Ratios

HCW Hand Hygiene Compliance

Colonizations by Nurses

Number of Nurses

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Striving For Excellence

- Hospital: 100 patients, 20 nurses, 10 physicians
- Even with 70% hand hygiene compliance, the following cases can lead to $R_0 > 1$:
  - 10 daily contacts or more between HCWs and each patient,
  - 20 day or more average patient length of stay
  - Transmissibility greater than 0.15,
  - Hand hygiene efficacy less than 0.6, or
  - 200 or more visitors per day at 2% transmission rate
- The addition of patient screening on admission, isolation, and decolonization still does not prevent all outbreaks, as the following cases can still lead to $R_0 > 1$:
  - Transmissibility $> 0.28$
  - 200 or more visitors per day (2% transmission rate) – Small world effect

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Conclusions

• ABMS is a powerful technique for exploring complex systems
• Parallel processing provides an indispensable capability for running experiments
• **Key Findings:**
  • Hand hygiene compliance is a critical factor affecting transmission, but it demonstrates diminishing returns, necessitating additional measures
  • Nurses appear to spread more often than physicians due to more frequent contact, but physicians pose a great danger by introducing MRSA into unaffected cohorts
  • Even the best hospitals can still be susceptible to outbreaks
• Best defense:
  1. Decrease the connectivity of the patient network (isolation, low HCW-to-patient ratios) and
  2. Decrease the likelihood of transmission by increasing compliance and efficacy and limiting transmissibility and daily contacts