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

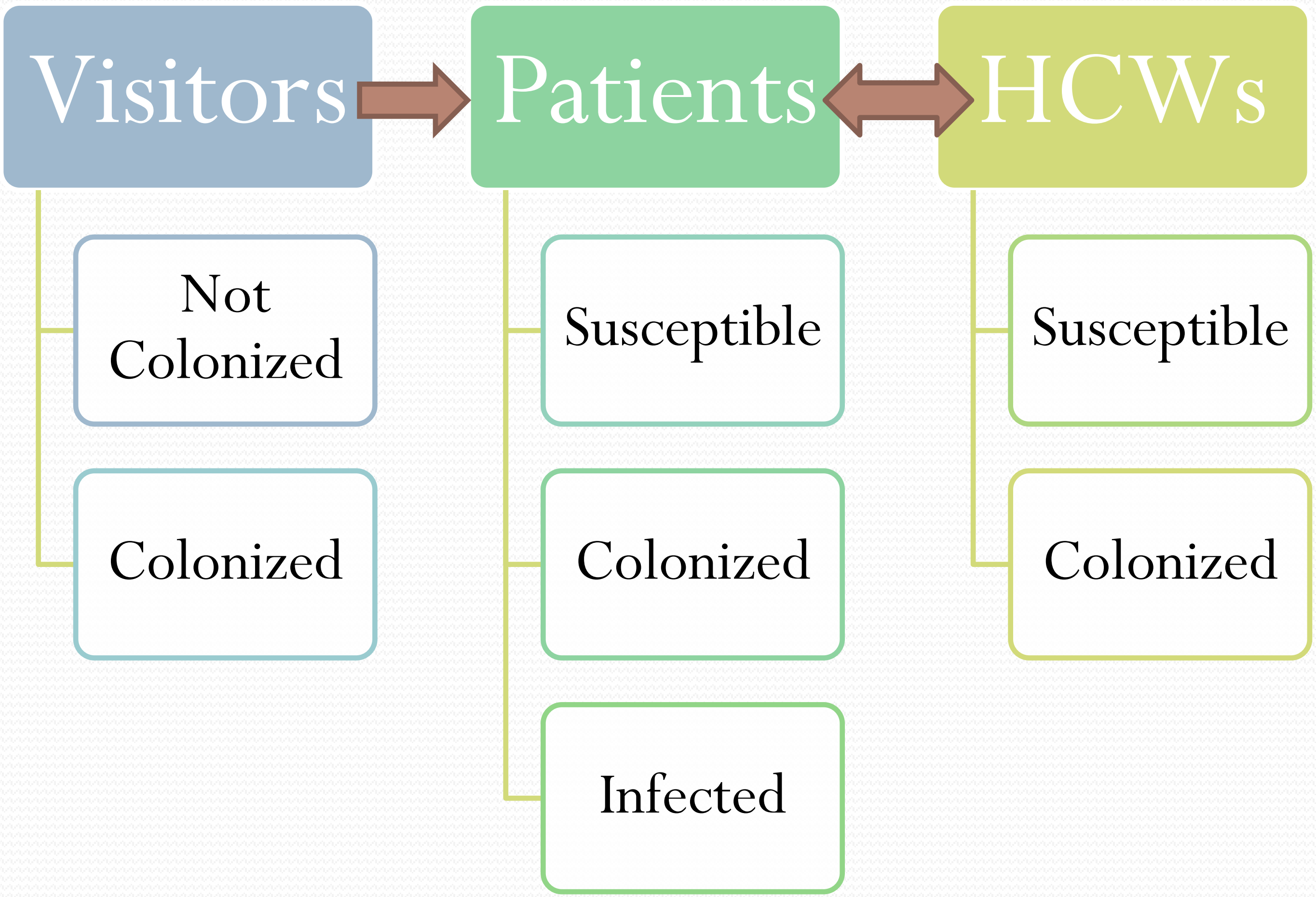
Methodology

- 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



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

Performance

- 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

External

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 I

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

N	Job Time Sum (s)	Run Times (s)	Speedup
1	747	747	-
2	752	377	1.98
4	746	188	3.97
8	752	96	7.78
16	761	50	14.94
32	941	33	22.64

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

N	Job Time Sum (m)	Run Times (m)	Speedup
1	136.9	136.9	-
2	138.4	71.84	1.91
4	136.1	37.91	3.61
8	133.7	21.10	6.49
16	141.3	11.88	11.52
32	182.3	8.96	15.28

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

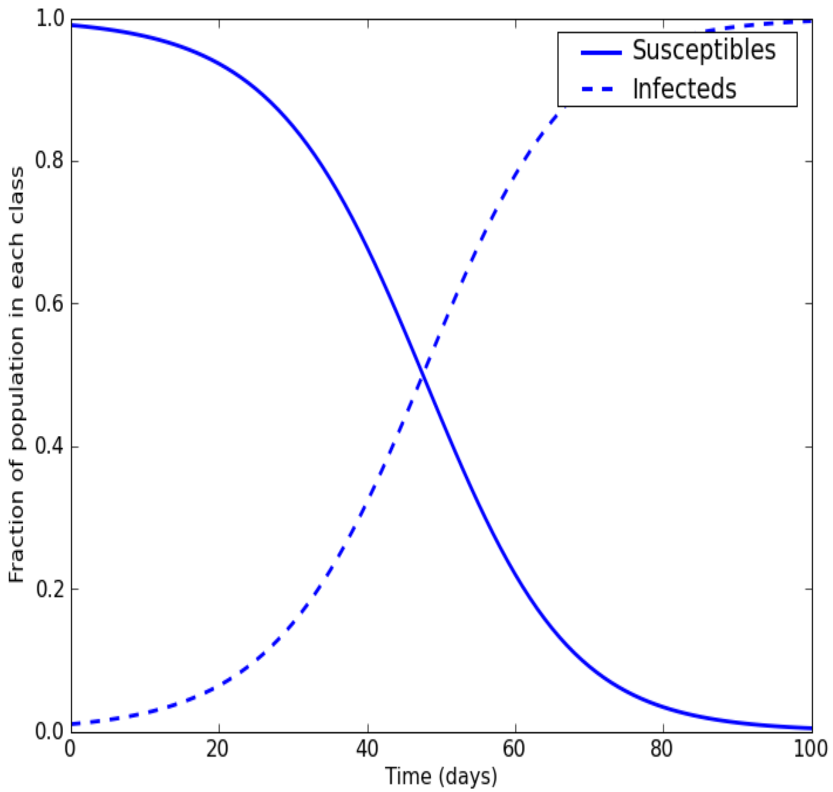
- Population transitions between **S**usceptible, **I**nfected, and **R**ecovered states
- Assumptions:
  - Closed population (i.e. no births, deaths, migration)
  - Homogeneous population, well-mixed
- Model equations:

$$\frac{dS}{dt} = -\beta SI, \ \frac{dI}{dt} = \beta SI - \gamma I, \ \frac{dR}{dt} = \gamma I$$

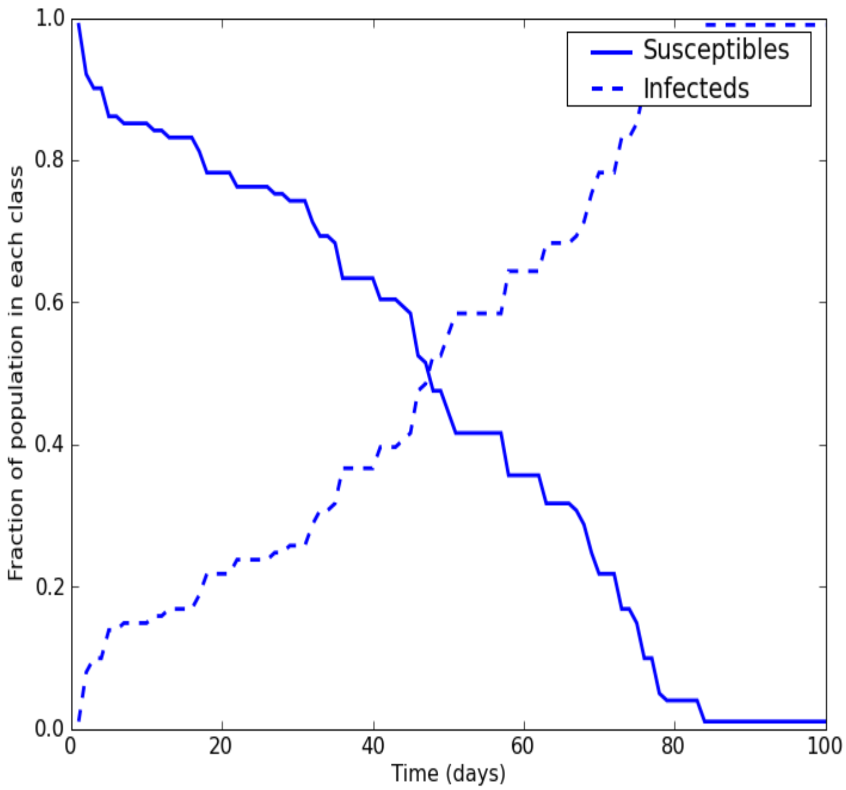
- Used to validate transmission dynamics of ABMS software

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

Mean Statistic	**Baseline**	**Isolation**	**Decolonization**	**Cohorting (1:1/2:1)**	
Patients Colonized	51.46	39.56	45.42	**34.79**	40.65
Colonized Patients Admitted	36.50	34.48	34.76	**33.85**	33.89
No. of Secondary Cases	14.97	5.08	10.66	**0.94**	6.75
Ward Prevalence	82.51%	81.44%	**78.82%**	78.99%	80.57%
Colonized Patient Days	6.49%	5.66%	5.72%	**5.14%**	5.64%
Attack Rate	0.004989	0.001693	0.003553	**0.000313**	0.002251
R_0	0.4098	0.1474	0.3056	**0.0272**	0.1991

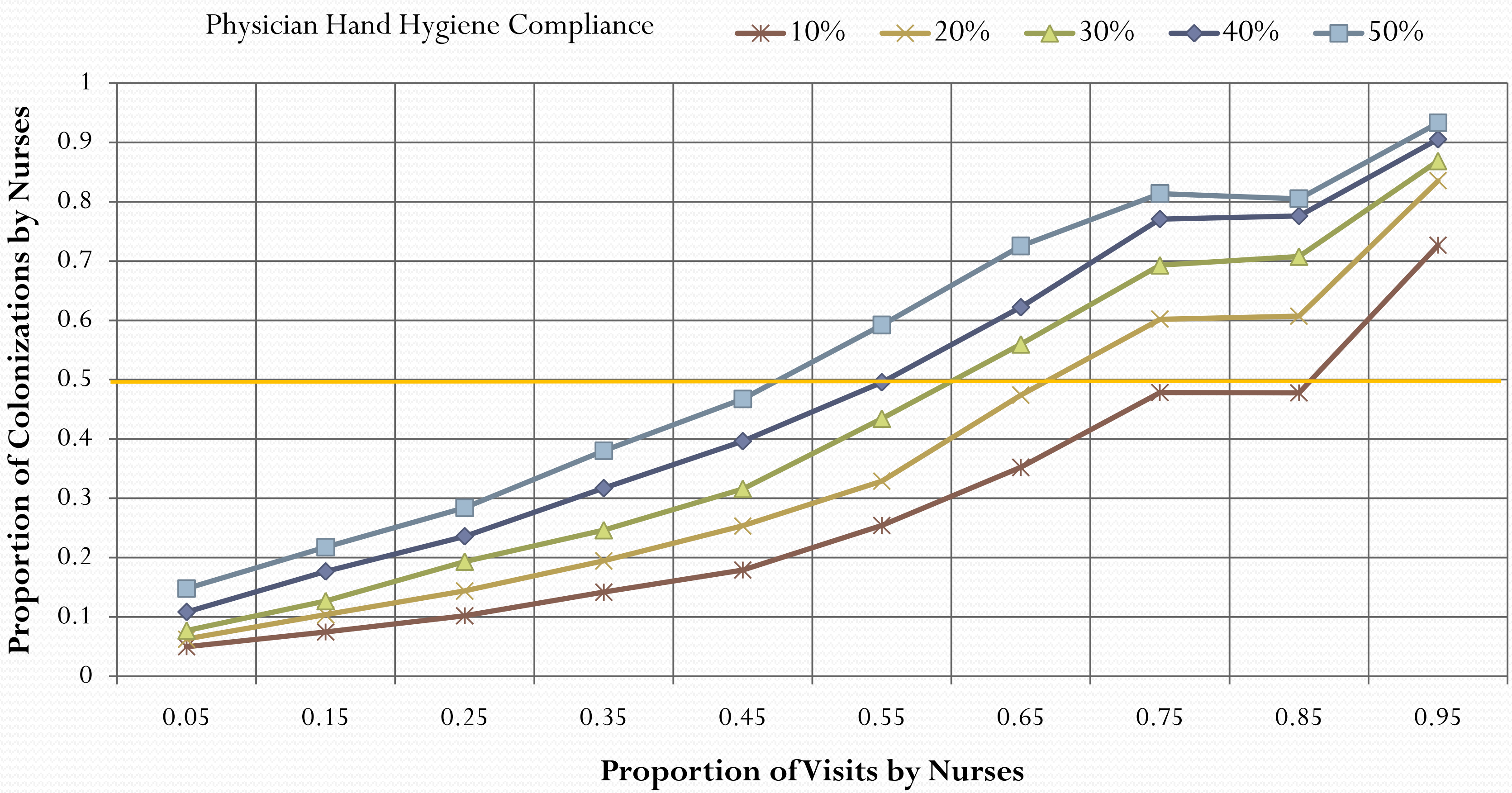
* Best case results shown for each infection control measure

Testing

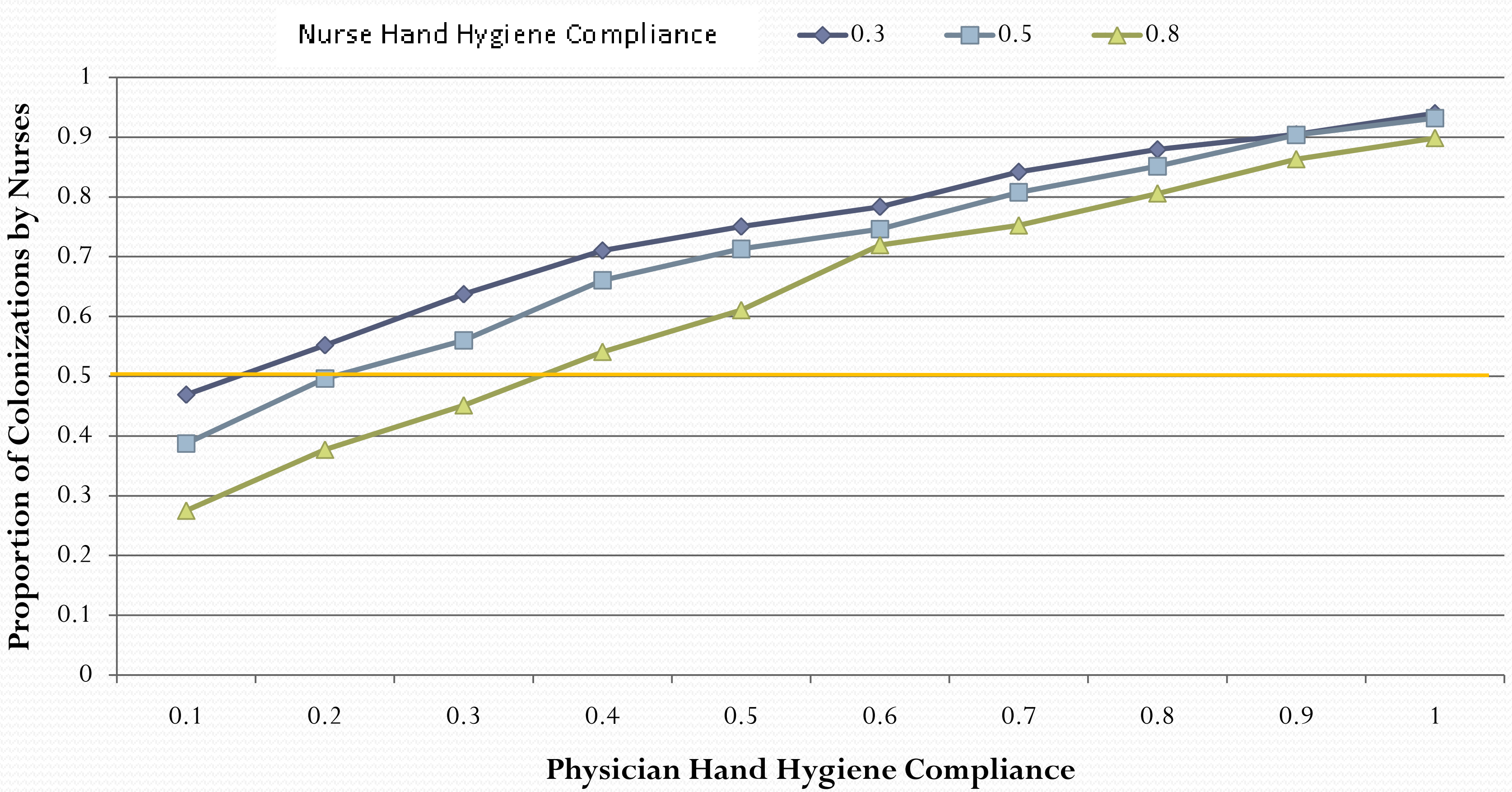
- A verified and validated AMBS software package allows us to perform a wide variety of *simulation experiments* to answer relevant questions

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

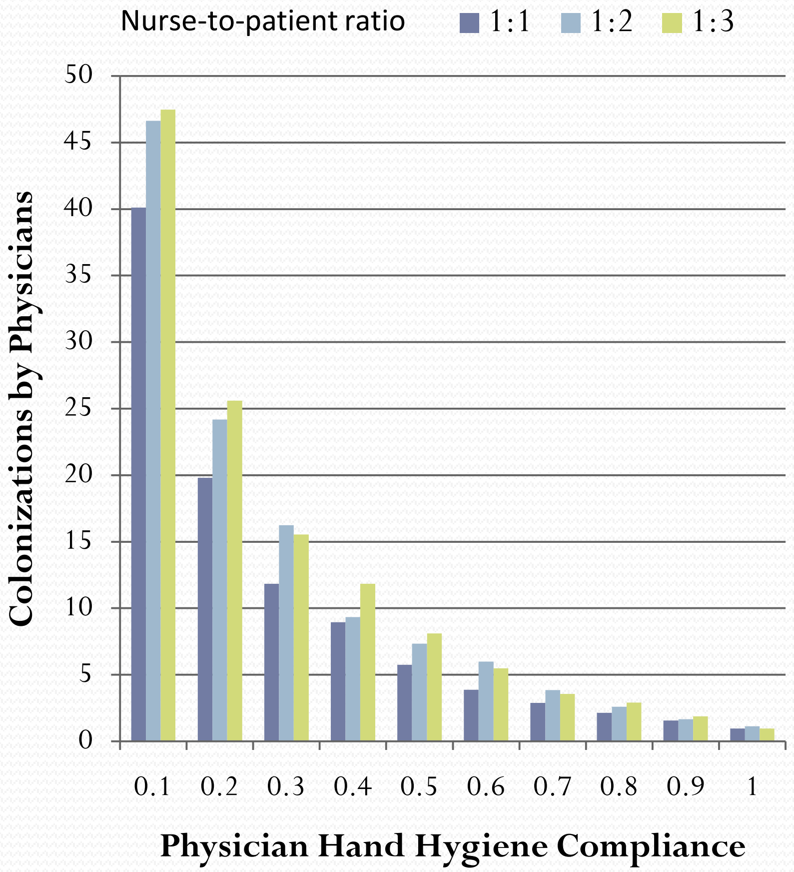
Physician Compliance – General Ward

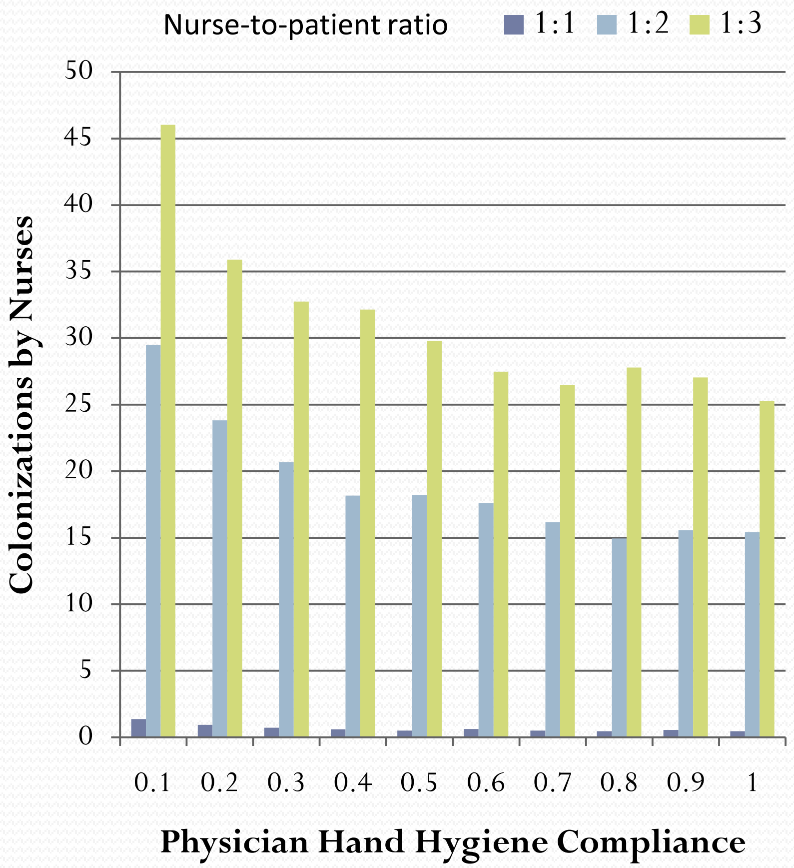


Physician Compliance - ICU

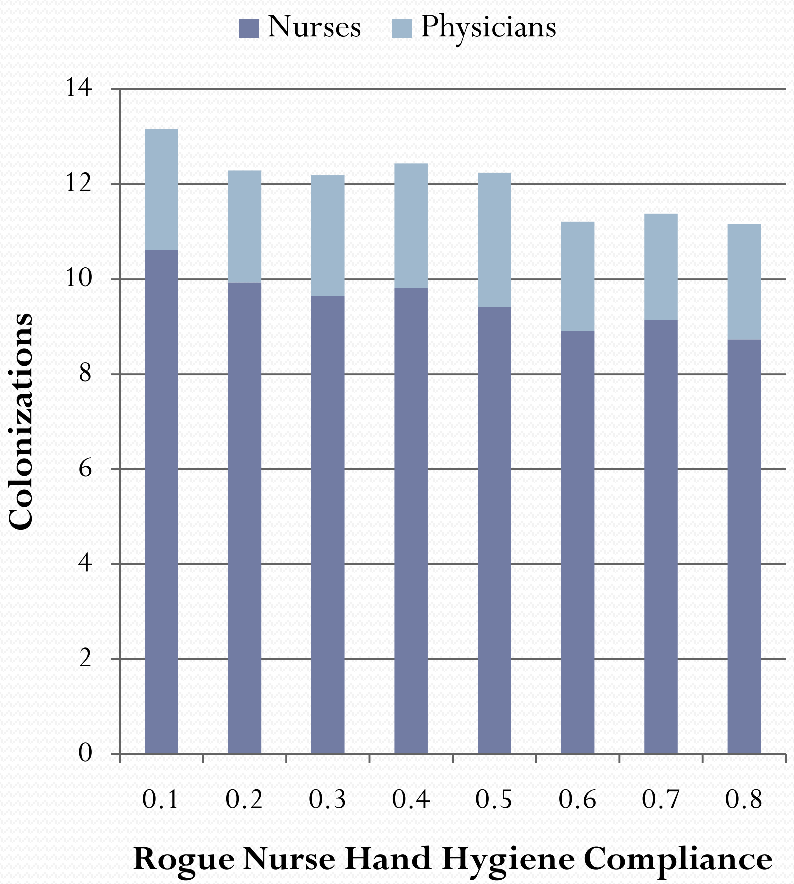


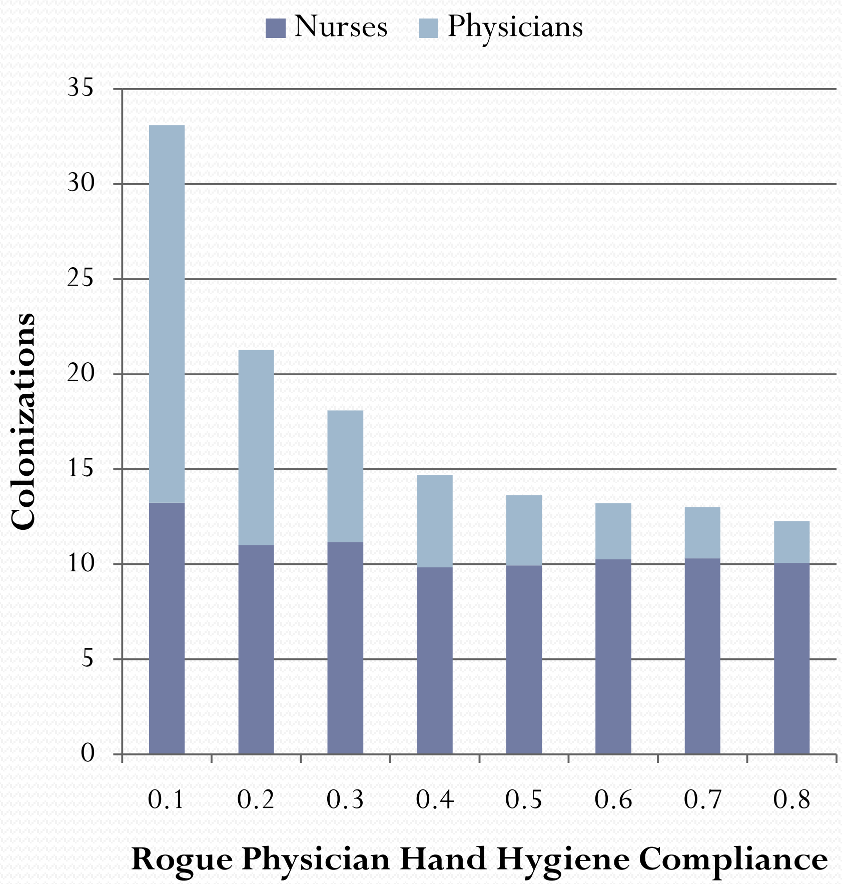
HCW Comparison



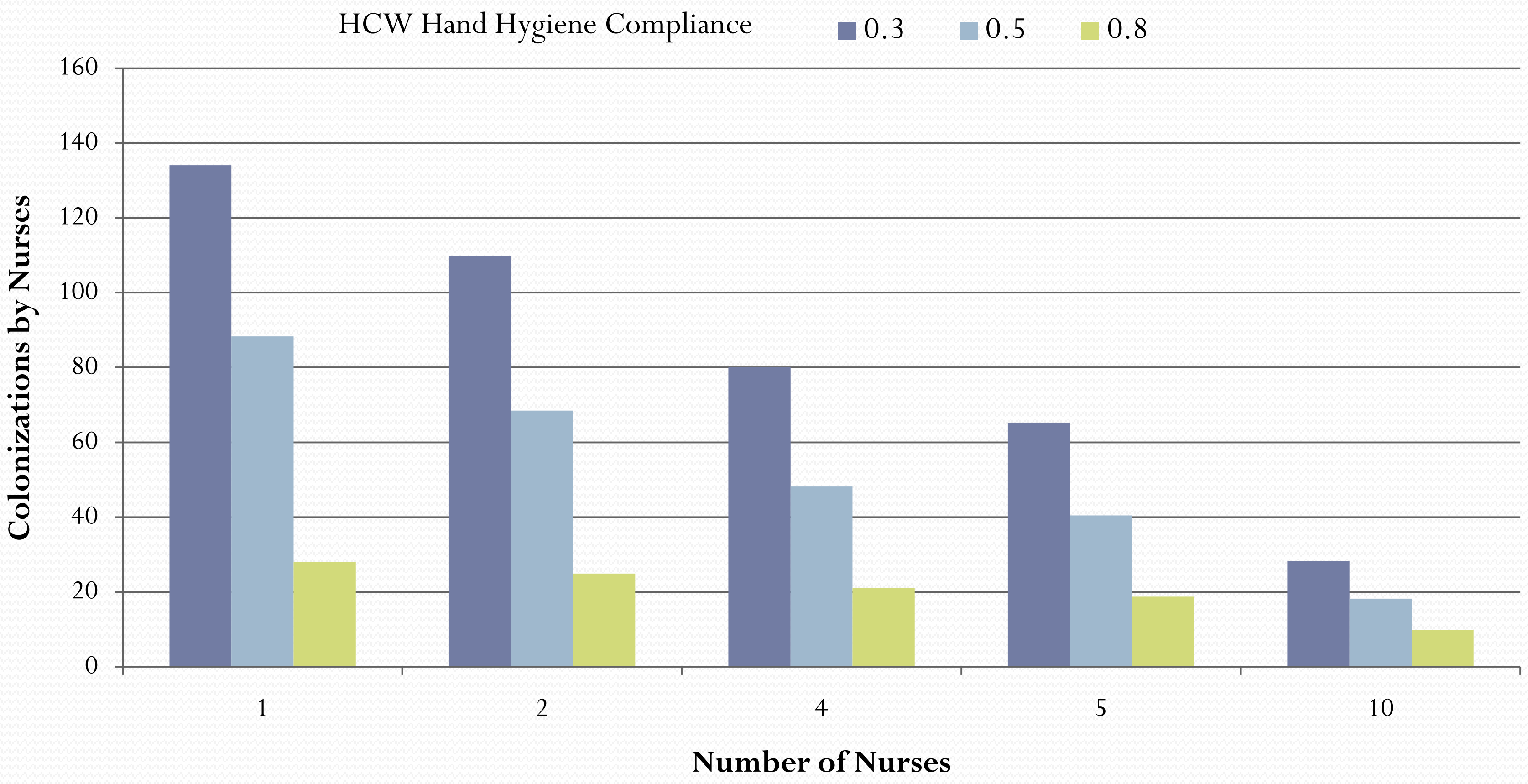


Rogue Behavior





Compliance vs. Nurse-to-Patient Ratios



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

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