Factorial Design Quantifies Effects of Hand Hygiene and Nurse-to-Patient Ratio on MRSA Acquisition

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Motivation

Optimal methods to control the spread of Methicillin-resistant *S. aureus* (MRSA) are still unknown

Two commonly known causes of outbreaks:

- Infrequent hand washing by health care workers
- Understaffing of hospital units

<u>Objectives</u>

I. Quantify the relative effectiveness of hand hygiene and nurse-to-patient ratio as control measures against patient-to-patient transmission of MRSA

II. Evaluate the effectiveness of our methods

Methods: Two-Staged Approach

1. Stochastic, agent-based model of patient-to-patient transmission in a 20-bed intensive care unit

2. Apply full 2^k factorial design to the output of the simulation to quantify the effect of each factor on MRSA transmission

Agent-Based Modeling and Simulation (ABMS)

Contemporary simulation technique that models the *interactions* between individual *agents*

Agents

- Patients
- Health care workers (HCWs)
  - Nurses
  - Physicians

All agents have individual characteristics and states

Interactions

- Patients are admitted to the hospital and are visited by nurses and physicians on a daily basis

Key Simulation Parameters

Parameter	Value
Simulation Period	1 year
Beds	20
Number of physicians	2 (1:10 ratio)
Physician hand hygiene compliance	65%
Hand hygiene efficacy	95%
Proportion of admitted MRSA-positive patients	0.10
Transmission probability from patient to HCW	0.20
Transmission probability from HCW to patient	0.05
Patient length of stay	Mean 3.94 days, median 2 days
Visits per day per patient	48
% of patient visits by nurses (vs. physicians)	90%

Full 2^k Factorial Design

Objective: Calculate the main effect of each factor on the response and characterize the interaction effect between the two factors

- *Main effects represent the average number of MRSA acquisitions prevented by improving each factor*

- *Interaction effects convey the efficiency (or lack thereof) of the changing both factors*

Factorial Design Calculations

Design Point	Factor A	Factor B	Response
1	-	-	R_1
2	-	+	R_2
3	+	-	R_3
4	+	+	R_4

Main Effects

$$e_A = \frac{-R_1 + R_2 - R_3 + R_4}{2}$$

$$e_B = \frac{-R_1 - R_2 + R_3 + R_4}{2}$$

Interaction Effect

$$e_{AB} = \frac{R_1 - R_2 - R_3 + R_4}{2}$$

Special Cases

- No main effect
  - $e_A = 0 \rightarrow R_1 = R_3, R_2 = R_4$
  - $e_B = 0 \rightarrow R_1 = R_2, R_3 = R_4$
- No interaction effect
  - $e_A = 0$ or $e_B = 0$
  - $\left.\begin{array}{l} R_1 - R_3 = R_2 - R_4 \\ R_1 - R_2 = R_3 - R_4 \end{array}\right\}$ Equivalent
- Maximum interaction effect
  - $R_1 \mid R_2 = R_3 = R_4$

Application

Problem: What happens if we want to examine more than two levels for each factor?

Solution: Apply factorial design methods iteratively across entire parameter space:

- Nurse hand hygiene compliance
  - Vary from 0% to 100% in increments of 5%
  - Evaluate changes of 5%, 10%, 15%, 20%, and 25%
- Nurse-to-patient ratio
  - Vary from 1:4 to 1:1
  - Evaluate changes of one and two levels

Interaction Effect Comparison Issues

Typically, we use a single design matrix for k factors:

- Interaction effects are comparable because our parameter space only has two levels in each of the k dimensions

For this design, we only have two factors, but we are computing interaction effects between numerous levels of those factors

How can we compare interaction effects between different cases?

Normalizing Interaction Effects

We can normalize our interaction effects using the maximum theoretical interaction effect for each case:

$$e_{AB} = \frac{R_1 - R_2 - R_3 + R_4}{2}$$

$R_1 \mid R_2 = R_3 = R_4$ for maximum interaction effect

$$e_{AB\ \max} = \frac{R_1 - R_4}{2}$$

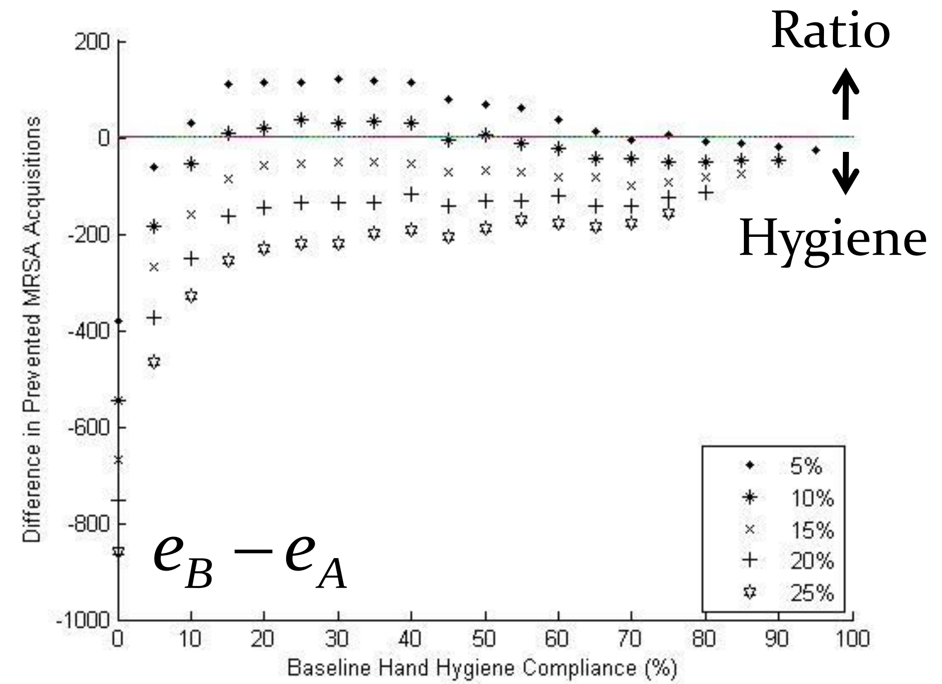
Half the distance between the 1st and 4th design points

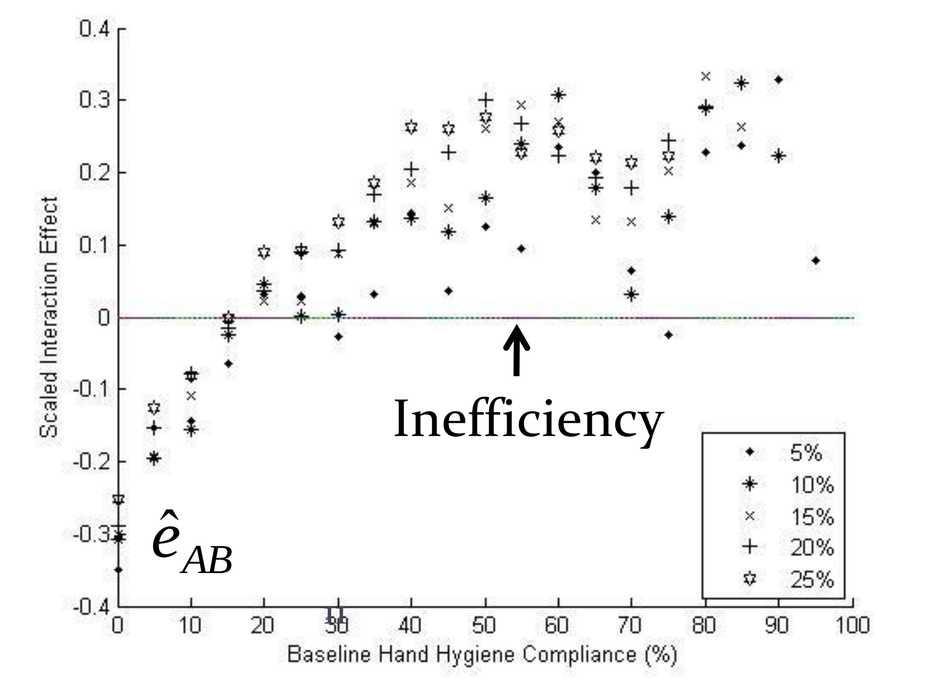
$$\hat{e}_{AB} = \frac{e_{AB}}{e_{AB\ \max}} = \frac{R_1 - R_2 - R_3 + R_4}{R_1 - R_4}$$

Factorial Design Results: 1:4 to 1:3

Nurse-to-patient ratio is better than small improvements in hand hygiene (5%-10%) , except when baseline compliance levels are high

Large increases in hand hygiene (above 10%) always do better

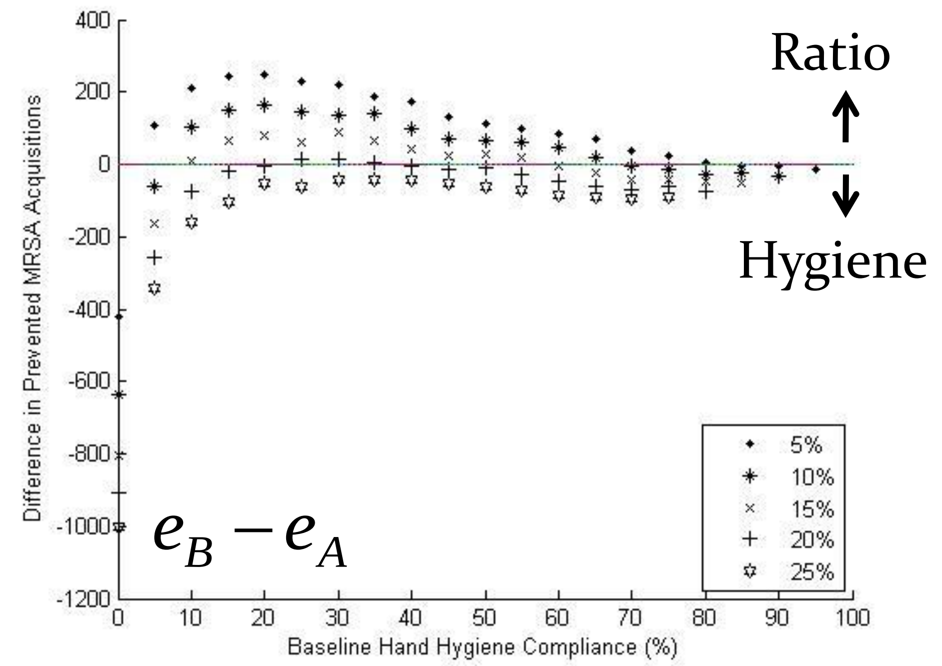


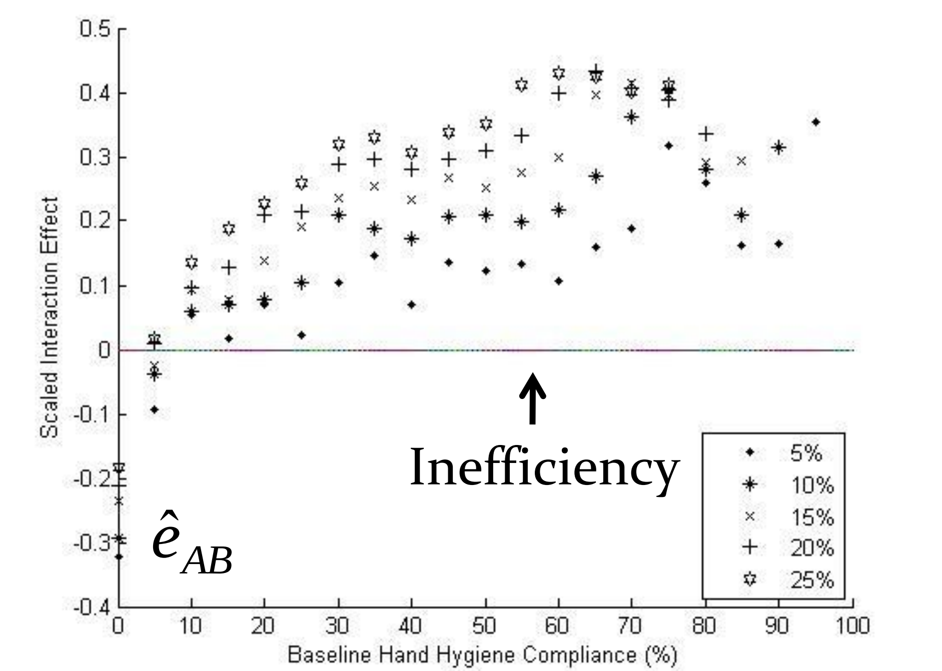


Factorial Design Results: 1:3 to 1:2

Nurse-to-patient ratio performs better than most improvements in hand hygiene, except when baseline compliance levels are high

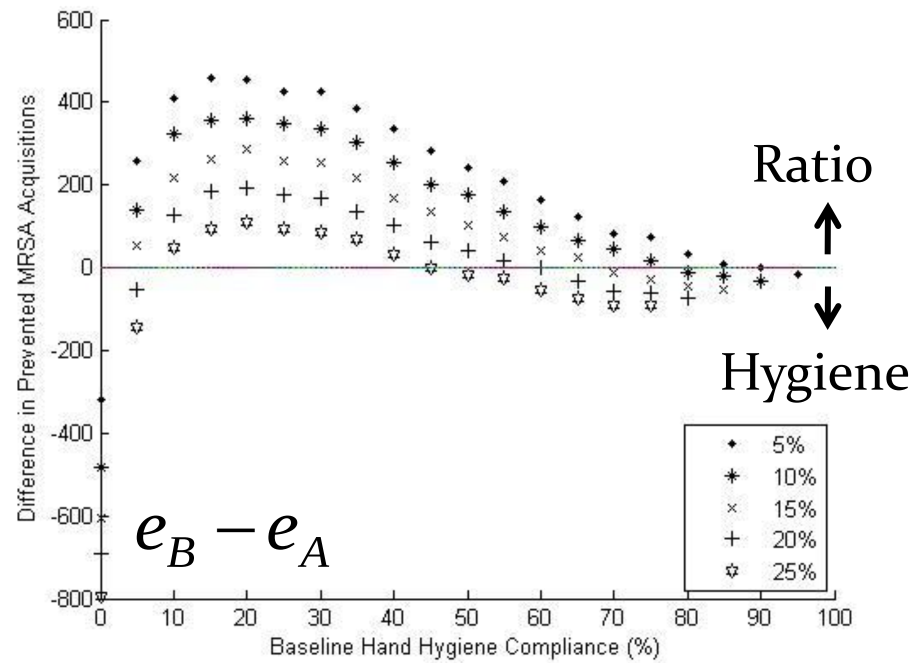
Large increases in hand hygiene (above 20%) are required to do better

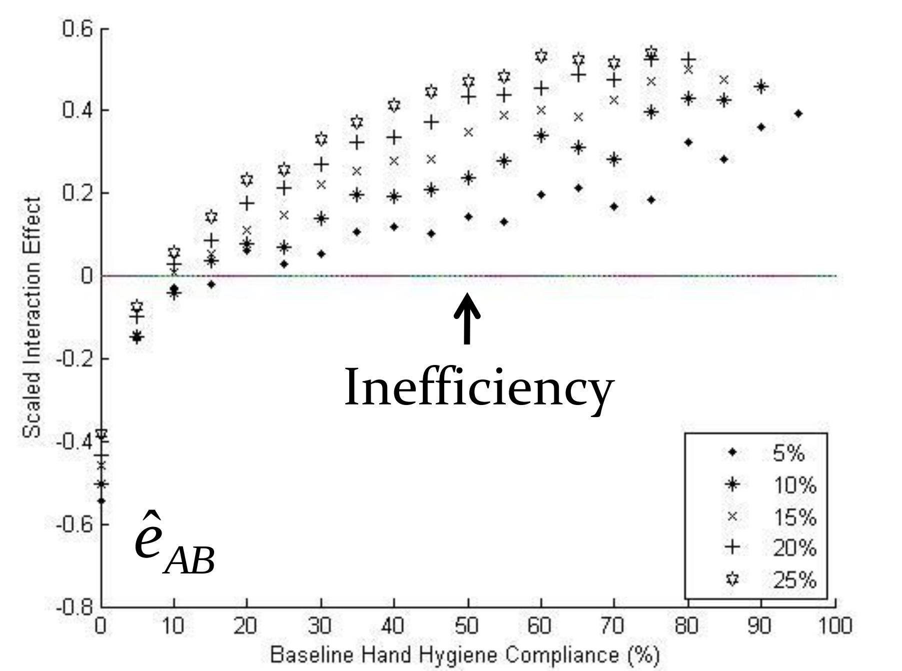




Factorial Design Results: 1:4 to 1:2

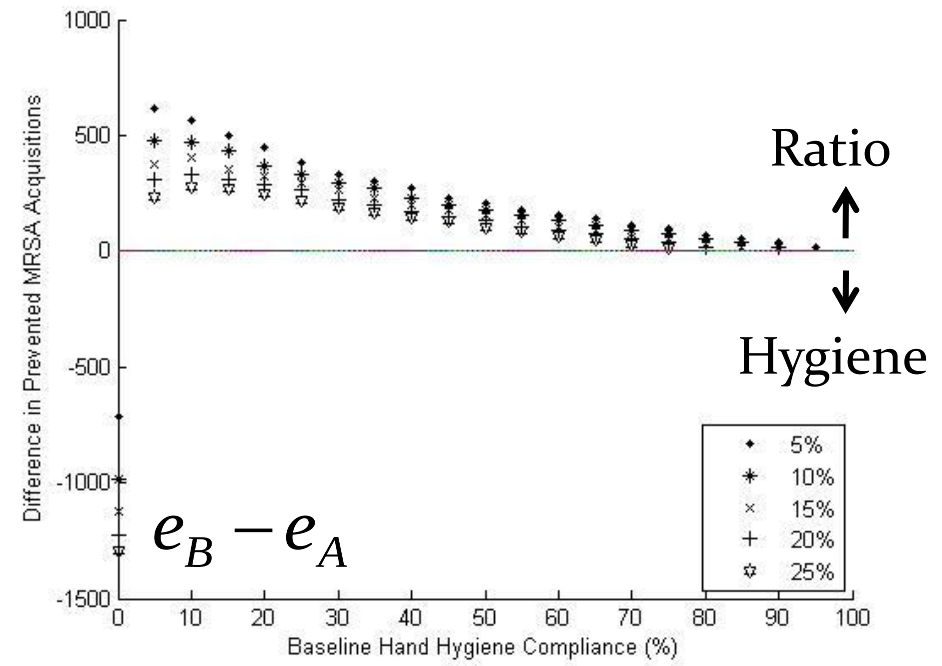
Nurse-to-patient ratio is better than all reasonable improvements in hand hygiene, except when baseline compliance levels are high (above ~60%)

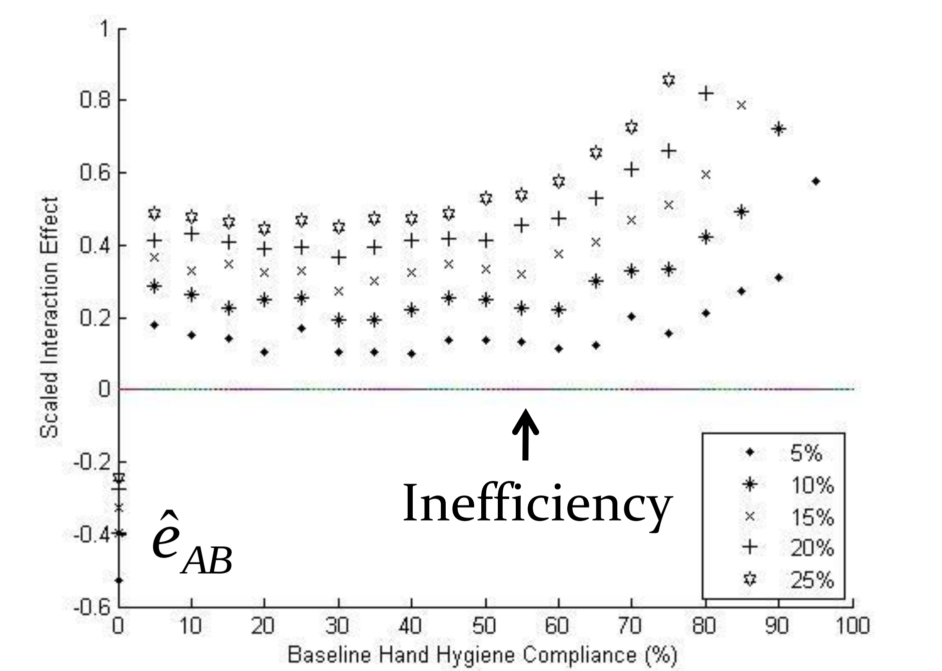




Factorial Design Results: 1:2 to 1:1

Increasing to a 1:1 ratio dominates any reasonable improvement in hand hygiene, even when baseline compliance levels are high





Summary of Results – Main Effects

Nurse-to-patient ratio typically performs better than hand hygiene in the 10%-60% range and **presents a viable option while efforts to improve hand hygiene are ongoing**

- **Nurse-to-patient ratios of 1:1 always do better**

Hand hygiene performs better at higher baseline levels, suggesting that **hospitals that have been successful at increasing compliance should continue to focus on improving hygiene further**

Summary of Results – Interaction Effects

Interaction effects are typically small at low compliance levels (under 30%) and grow significantly with increasing compliance

- Smaller increases in compliance can be combined more *efficiently* with increases in nurse-to-patient ratio, although larger increases are more *effective*

Increasing to a 1:1 ratio is highly inefficient when combined with increases in compliance

Conclusions

Both factors have a significant effect on the response (main effects), but the effectiveness of each factor depends on the level of the other (interaction effects)

ABMS combined with factorial design provides a powerful engine for determining the effectiveness of infection control measures