# Hospitals as Reservoirs for Clostridioides difficile in the Community

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# What is C. difficile?

- A bacterium that causes infection in the large intestine.
- One of the most common healthcare facilityacquired infections.
- Symptoms: diarrhea to life-threatening colitis.
- Transmission occurs by the fecal-oral route.
- Spores could persist in the environment for a long time.
- Asymptomatic patients could still spread the infection.



https://www.health.harvard.edu/blog/stooltransplants-are-now-standard-of-care-forrecurrent-c-difficile-infections-2019050916576

# What is C. difficile?

- Risk factors:
  - Presence of other CDI patients in the hospital
  - Use of antibiotics
  - Old age
  - Longer hospital stays
  - Comorbidities
  - Exposure to agents that reduce levels of gastric acid





# **OBJECTIVE**

 To determine if individuals that experience healthcare facility-onset C. difficile infections (HCFO-CDIs) are contributing to the spread of community-onset C. difficile infections (CO-CDIs).



### **STUDY DESIGN**





Create a real-world emulator to predict CO-CDI **CQSeS** 

Create a simulation that predicts state counties and their neighboring counties' CO-CDI cases based on previous months



# INTERVENTION

- Made a counterfactual scenario of negating the effect of HCFO-CDIs on community spread.
- Manage to predict the CO-CDI cases if the detrimental effect of HCFO-CDIs was eliminated.



# INTERVENTION

### REAL-WORLD EMULATOR









https://www.nationsonline.org/oneworld/us\_states\_ maps.htm

# DATA

 State Inpatient Database from the Healthcare Cost and Utilization Project (HCUP SID) • Over 20 million hospital inpatient visits from six U.S. states (VT, NC, AZ, AR, UT, IA) from 2003 to 2015 Census data County adjacency spatial data to predict local spread



#### HCFO-CDI = 16407 cases CO-CDI = 14679 cases

hospital stay is longer

**HCFO-CDI** 

# Temporal

#### PAST



#### PRESENT



https://geology.com/state-map/iowa.shtml

#### FUTURE



#### AUGUST



# Temporal

#### PAST

#### PRESENT



https://geology.com/state-map/iowa.shtml

#### **FUTURE**





PAST



JUNE

https://geology.com/state-map/iowa.shtml

#### PRESENT







PAST



JUNE

https://geology.com/state-map/iowa.shtml

#### PRESENT

JULY



### SIMULATION VISION

#### PRESENT















#### FUTURE

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### AUGUST NO HCFO-CDIS CO-CDIs start decreasing

### **SIMULATION VISION**

#### PRESENT















#### **FUTURE**

### AUGUST NO HCFO-CDIS CO-CDIs start decreasing

### **METHOD: RANDOM FOREST**

- Modification of bagging
- Builds numerous decorrelated regression trees to predict an outcome
- Split data set into "train" (80%) and "test" (20%)
- Use the training data to build the random forest and predict the test data



https://www.tibco.com/reference-center/what-is-a-random-forest

# **RANDOM FOREST**

- Predictor variables:
  - Year
  - State
  - Seasonality
  - Population 65 and older
  - Population under 65
  - HCFO-CDIs
  - HCFO-CDIs from the month prior
  - HCFO-CDIs in neighboring counties
  - CO-CDIs from the month prior
  - CO-CDIs in neighboring counties

• CO-CDIs





# • Response variable:



## RANDOM FOREST

- Tried several combinations of random forest tuning parameters
- Calculated the lower mean squared error (MSE) value.
- Use result for final fit:
  - Mean of squared residuals: 2.214183
  - %Var explained: 92.88

|      | Nodesize |          |          |  |  |  |
|------|----------|----------|----------|--|--|--|
| Mtry | 5        | 10       | 15       |  |  |  |
| 2    | 2.364351 | 2.412077 | 2.424765 |  |  |  |
| 3    | 2.136656 | 2.137867 | 2.200545 |  |  |  |
| 4    | 2.113935 | 2.097265 | 2.129924 |  |  |  |
| 5    | 2.117038 | 2.104251 | 2.084148 |  |  |  |

- 2.310533

| Random Forest MSE V |
|---------------------|
|---------------------|

• Implementing Random Forest without HCFO variables: • Mean of squared residuals: % Var explained: 92.57

### Important Variables for Validation Predictions

## RESULTS: ASSESSING CO-CDI PREDICTORS

year statenc stateia HCFO\_count HCFO\_t\_minus\_1 CO\_t\_minus\_1 co\_nb greater64 under65 hcfo\_nb stateut statevt statear stateaz seasonality\_cos seasonality\_sin

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|   | 0         | 5 | 10                                    | 15 | 20 | 25               |  |  |
|   | %INCIVISE |   |                                       |    |    |                  |  |  |

# SIMULATIONS

- Using the final fit from the
- We took into consideration the fips region, county adjacency, and the present and future month and year variables.

random forest, we predict the CO-CDI cases in future months.

# INTERVENTION

- Made a counterfactual scenario of negating the effect of HCFO-CDIs on community spread.
- Manage to predict the CO-CDI cases if the detrimental effect of HCFO-CDIs was eliminated.



# INTERVENTION

### REAL-WORLD EMULATOR

DATA



# **RESULTS: ASSESSING THE PREDICTION OF CO-CDIS**





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#### **Counterfactual Predictions**



# GRAPH: TOTAL ANNUAL PREDICTIONS



Annual True, Validation Predicted, and Counterfactual Predicted CO-CDI Counts



Comparison between true counts and simulations with and without intervention

- True CO-CDIs
- Validation Predicted CO-CDIs
  - Predicted CO-CDIs w/o HCFO-CDIs

# CONCLUSION

- More error in predictions omitting the HCFO variables.
- The year, number of CO-CDIs in surrounding counties, number of CDIs from the previous month, patient's age, and HCFO count are the most significant predictors of the number of CO-CDIs
- Without HCFO-CDIs, there would be a decrease in the CO-CDI cases



## LIMITATIONS

- The database was composed of only 6 states.
- CDI cases that don't lead to hospitalization are not captured in the data.
- With claims data, we do not know the diagnostic errors involved in diagnosing CDI.





### LIMITATIONS



- Could only compute the number of positive CDI tests. Obtained a point, rather than an interval, estimate. Took into consideration patients who were admitted to hospitals in the state in which they reside.



# What's next?

- Get interval estimates from our point estimate predictions
- Implement the use of a *Poisson* distribution
- Determine another way to analyze the data
- Expand the investigation to other states and years
- Investigate CO-CDIs and socioeconomic status based on FIPS region







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# REFERENCES

- Czepiel, J., Dróżdż, M., Pituch, H. et al. Clostridium difficile infection: review. Eur J Clin Microbiol Infect Dis 38, 1211-1221 (2019). https://doi.org/10.1007/s10096-019-03539-6
- Mayo Foundation for Medical Education and Research. (2021, August 27). C. difficile infection. Mayo Clinic. Retrieved July 19, 2022, from https://www.mayoclinic.org/diseases-conditions/c-difficile/symptoms-causes/syc-20351691
- Miller, A. C., Arakkal, A. T., Sewell, D. K., Segre, A. M., Pemmaraju, S. V., & Polgreen, P. M. (2022). Risk for Asymptomatic Household Transmission of Clostridioides difficile Infection Associated with Recently Hospitalized Family Members. Emerging Infectious Diseases, 28(5), 932–939. https://doi.org/10.3201/eid2805.212023
- Miller, A. C., Segre, A. M., Pemmeraju, S. V., Sewell, D. K., & Polgreen, P. M. (2020). Association of Household Exposure to Primary Clostridioides difficile Infection with Secondary Infection in Family Members. JAMA Health Forum, 3(6), e208925–e208925. https://doi.org/10.1001/jamanetworkopen.2020.8925
- Random forests. Random Forests · UC Business Analytics R Programming Guide. (n.d.). Retrieved July 19, 2022, from https://uc-r.github.io/random\_forests
- *Regression trees.* Regression Trees · UC Business Analytics R Programming Guide. (n.d.). Retrieved July 19, 2022, from https://uc-r.github.io/regression\_trees
- Sewell, D. K., Simmering, J. E., Justice, S., Pemmaraju, S. V., Segre, A. M., & Polgreen, P. M. (2019). Estimating the Attributable Disease Burden and Effects of Interhospital Patient Sharing on Clostridium difficile Infections. Infection Control and Hospital Epidemiology, 40(6), 656–661. https://doi.org/10.1017/ice.2019.73







