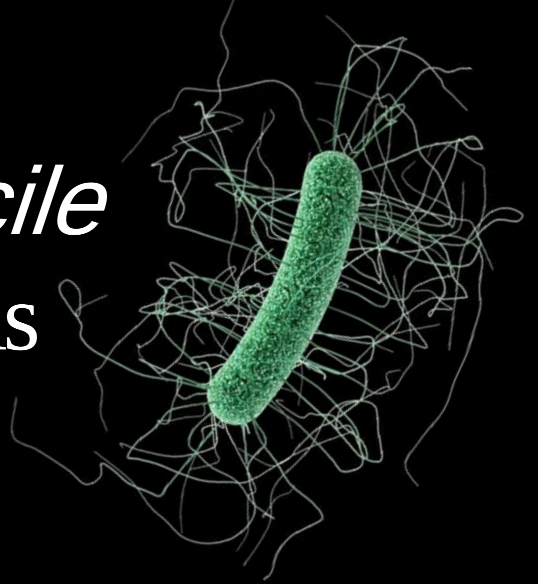
Intervening in *Clostridium difficile* Infections in California Hospitals



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What is *Clostridium difficile*?

- Bacteria
- Common symptoms:
  - Colitis
  - Diarrhea
  - Fever
  - Loss of appetite
  - Nausea
  - Abdominal pain
- How it spreads:
  - Spores passed through feces that have contacted other surfaces
  - Passed through hands of healthcare personnel who have touched contaminated surfaces

Why are *Clostridium difficile* infections a problem?

- Costly
  - $6.3 billion dollars annually
  - Resulted in an estimated 2.4 million days of inpatient stay
- Dangerous
  - The most common microbial cause of healthcare-associated infections in U.S. hospitals
  - 2015 - Infections 500,000 ; Deaths 29,000
  - Increasingly resistant to antibiotic treatments
- Previous clinical trials have failed or had short term effects
  - Cooper et al. 2004
  - Harris et al. 2013
  - Hobson et al. 1996

What causes a *Clostridium difficile* infection?

- Risk Factors
  - Individual
    - Advanced age
    - Extended antibiotic use (broad spectrum)
    - Severe illness
  - Environmental
    - Bathroom sharing with infected patients
    - Patient transfers
    - Seasonal trends
- Treatment
  - Discontinuing current antibiotics
  - Taking antibiotics specifically to treat CDI
  - Fecal transplant

Question of Interest

Can we **effectively** choose hospitals within a region to include in a clinical study with the aim of **maximizing the reduction of CDI** cases for a fixed treatment efficacy rate?

Data

- Healthcare Cost and Utilization Project California State Inpatient Database
- December 2005 through November 2011
- 383 hospitals and their patient transfers
- 23,296,211 total admissions
- 196,912 total CDI cases
- 535,223 total number of transfers

Our Approach

Construct prediction model

Accurately predicts future cases

↓

Determine which hospitals to target

Given an arbitrary cost constraint (10% of total patients)

↓

Simulate interventions

By modifying our model (10% in-house reduction)

↓

Compare interventions

To evaluate intervention effectiveness

Overview of the Predictive Model

The model used was a linear mixed model:

- Predicts based on
  - Covariates (fixed effects)
  - Hospital specific effects (random effects)
- Errors are temporally correlated (AR structure)

	Inclusion Strategy	Motivation
01	Target hospitals with high CDI rates	• Historical incidence
02	Target hospitals with larger patient populations with an age over 65	• Advanced age
03	Target hospitals with high centrality measures	• Patient Transfers

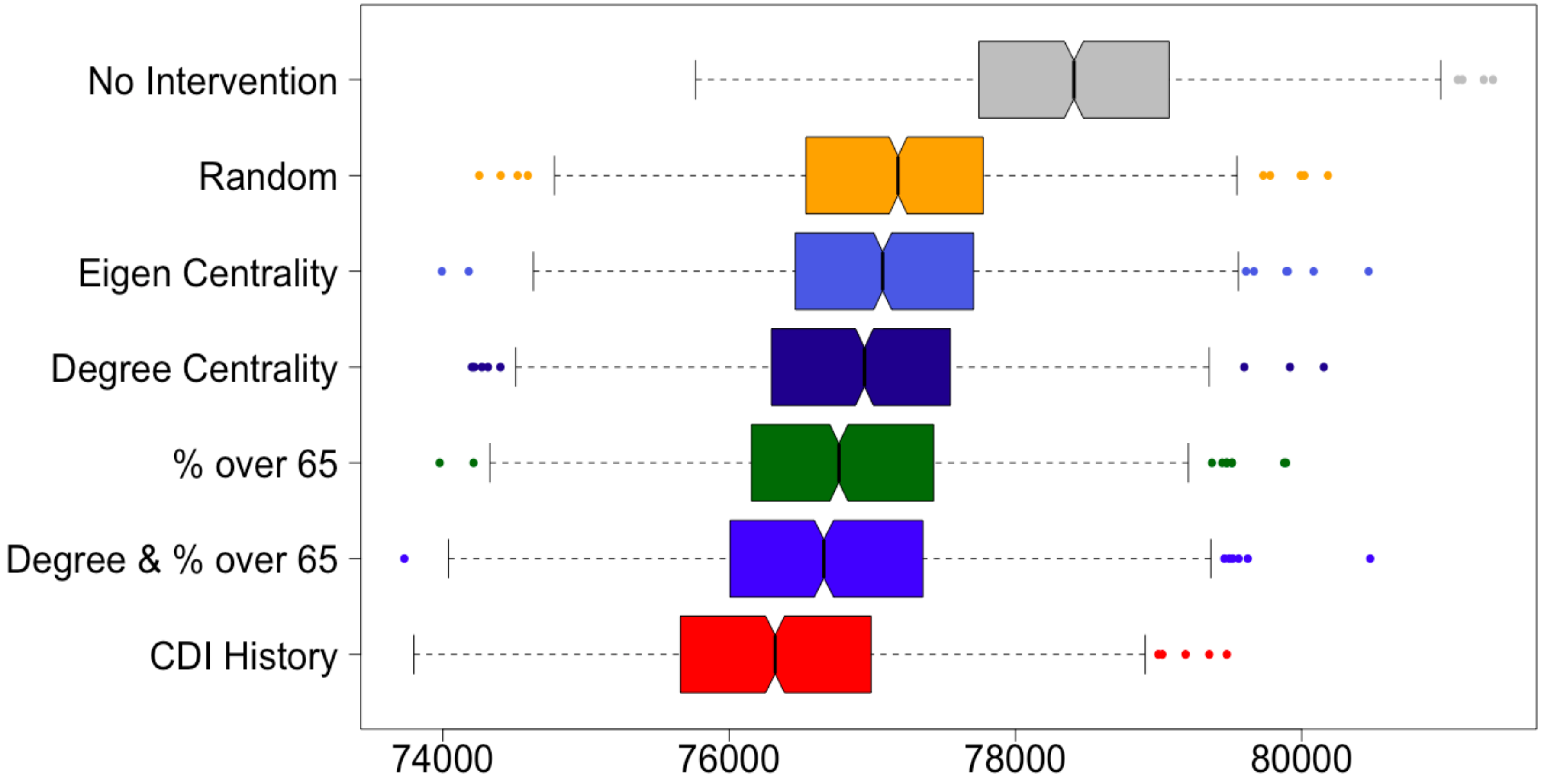
Choosing Hospitals to Include

- Given:
  - Score vector (inclusion criteria), $\boldsymbol{s} \in \mathbb{R}^{\boldsymbol{n}}$
  - Cost vector (total number of admissions), $\boldsymbol{c} \in \mathbb{R}^{n}$
  - Total cost constraint, $\boldsymbol{C} \in \mathbb{R}$
  - Inclusion vector, $\boldsymbol{\tau} \in \{\boldsymbol{0}, \boldsymbol{1}\}^{\boldsymbol{n}}$
- Can we find $\boldsymbol{\tau}$ such that, $\max(\boldsymbol{s}^{\boldsymbol{T}}\boldsymbol{\tau})$ subject to $\boldsymbol{c}^{\boldsymbol{t}}\boldsymbol{\tau} \leq \boldsymbol{C}$?
  - Binary linear programming

Application of Model

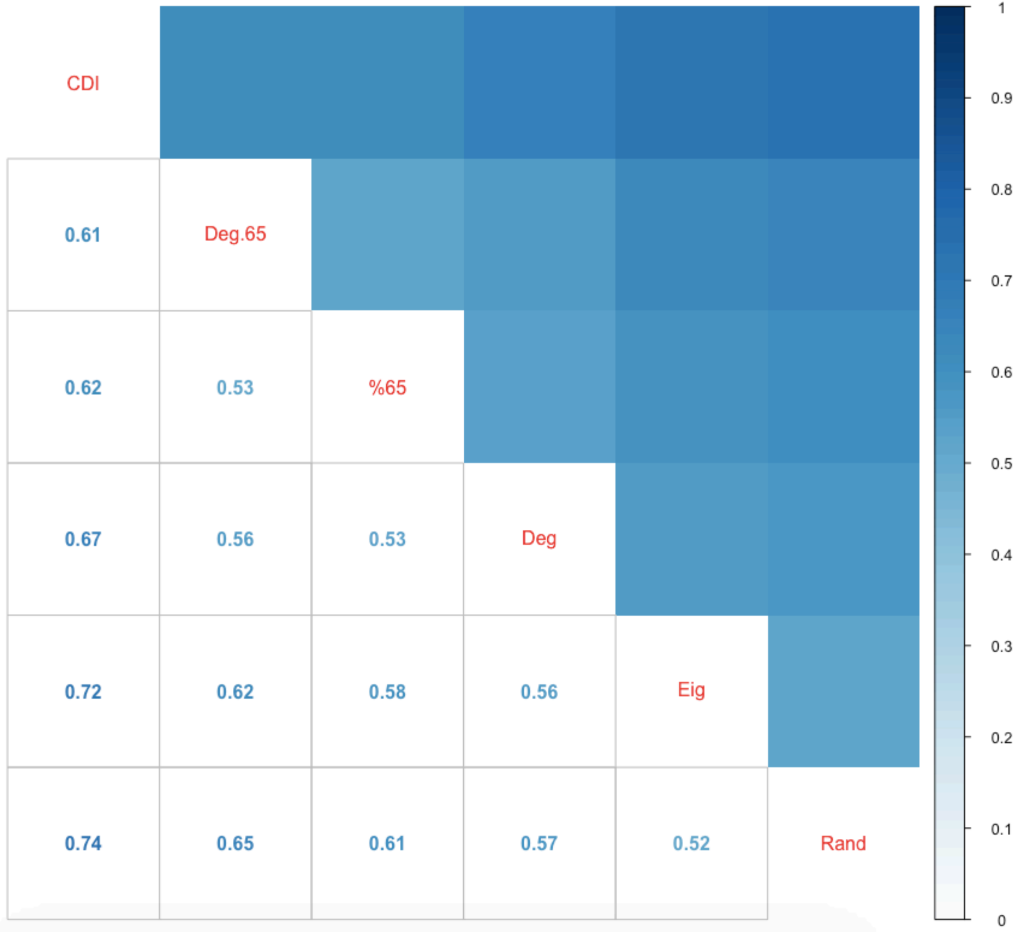
- $\log(Y_{i,t} + c) = X_{i,t}\beta + \alpha_i + \epsilon_{i,t}$
- Simulate an intervention by modifying specific α_i
  - $\alpha_i \leftarrow \alpha_i + \log(1 - \tau_i(reduction)) \Rightarrow y_i \approx e^{X\beta + \alpha_i}(1 - \tau_i(reduction))$
- Compare to a baseline
  - No intervention
  - Random intervention

Number of Predicted CDI Cases over 24 Months



Inclusion Strategy	Treated Hospitals (Proportion)	Spillover Hospitals (Proportion)	Total Reduction (count)
CDI History	0.92	0.08	2095.73
Degree & % over 65	0.85	0.15	1730.05
% over 65	0.87	0.13	1635.52
Degree Centrality	0.86	0.14	1502.21
Eigenvector Centrality	0.81	0.19	1326.31

P(Number of CDI cases of the Row < Number of CDI case of the Column)*



*By the color spectrum

Conclusion

Our results suggest that **targeting certain hospitals** within a network can be **beneficial to decreasing CDI** cases, potentially leading to more powerful studies.

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Auxiliary Slides (Mostly Plots)

The Prediction Model

$$Z_{i,t} = X_{i,t}\boldsymbol{\beta} + \alpha_i + \epsilon_{i,t}$$

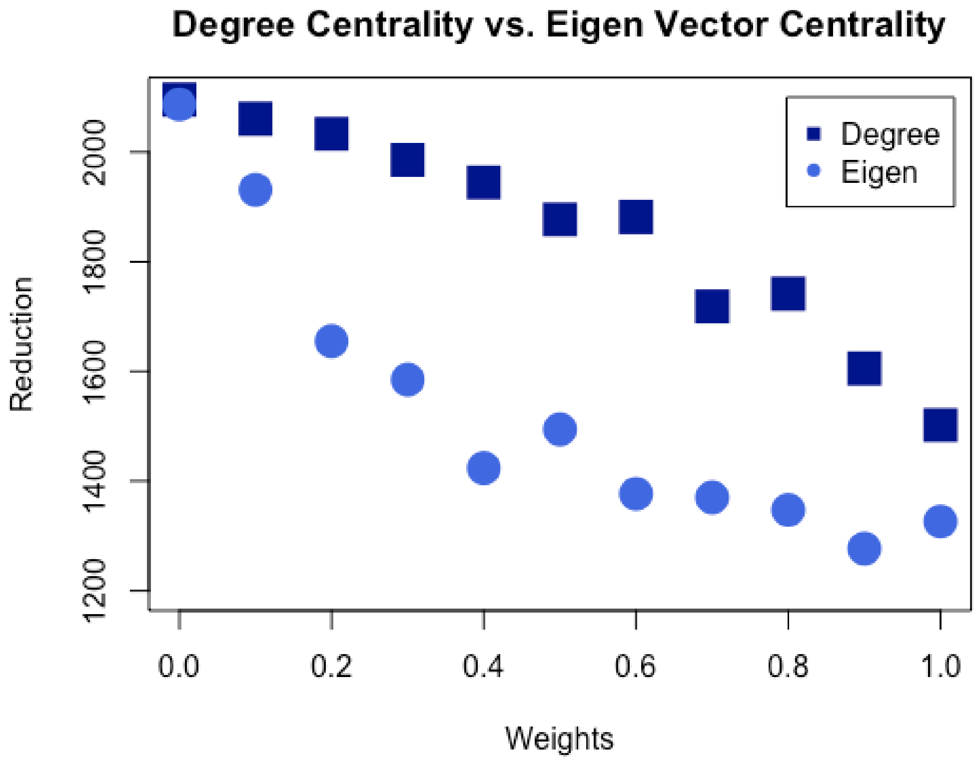
$$Z_{i,t} := \log(Y_{i,t} + c)$$

$$\alpha_i \overset{iid}{\sim} N(0, \tau^2)$$

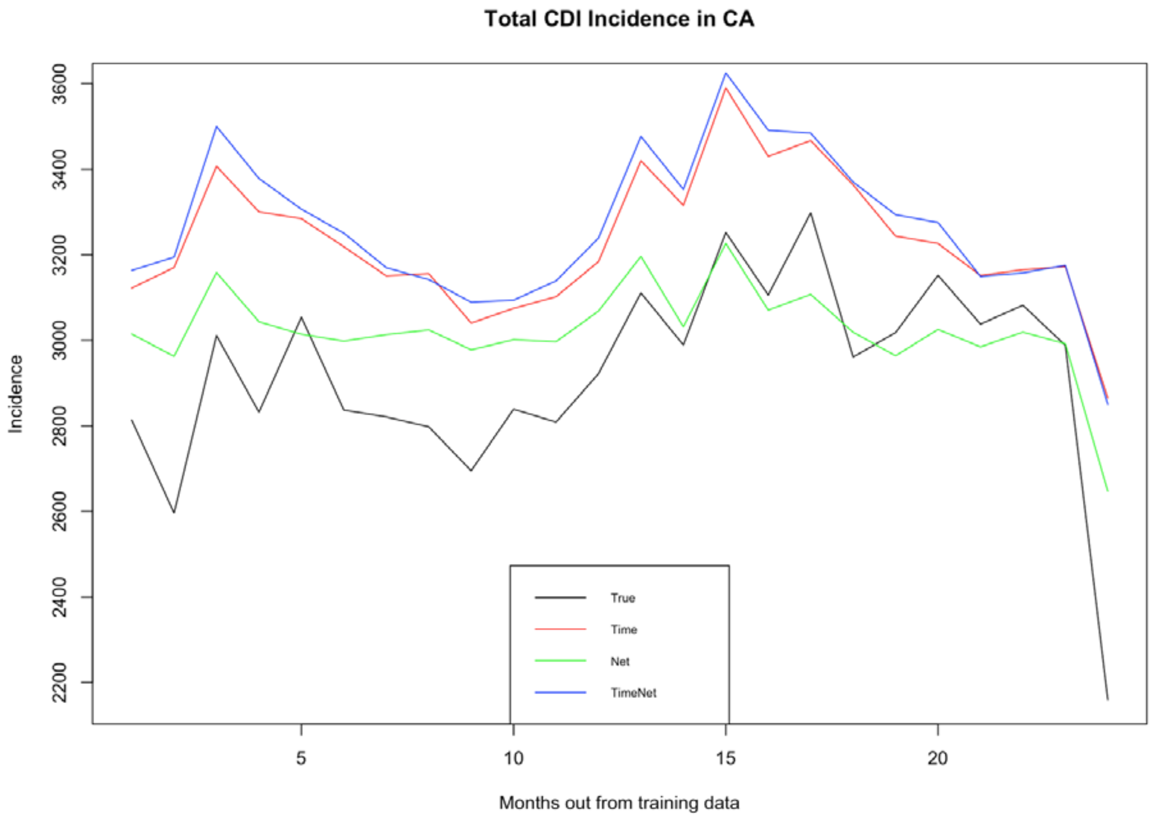
$$\epsilon_{i,t} \sim N(0, \sigma^2)$$

$$\mathrm{Cor}(\epsilon_{i,t}, \epsilon_{i',s}) = \begin{cases} \phi^{|t-s|} & \text{if } i = i' \\ 0 & \text{otherwise} \end{cases}$$

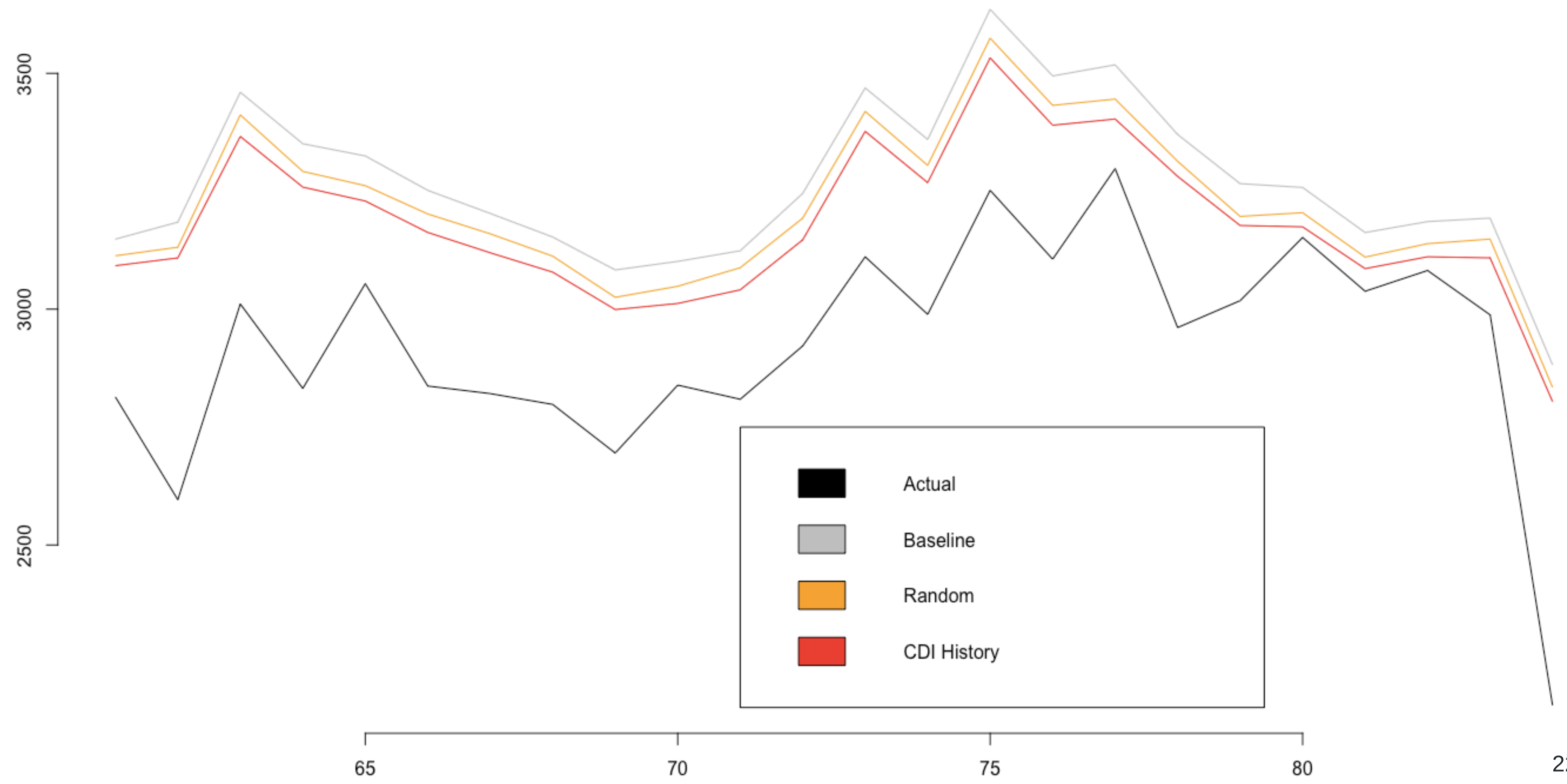
Assessing the Network Effect



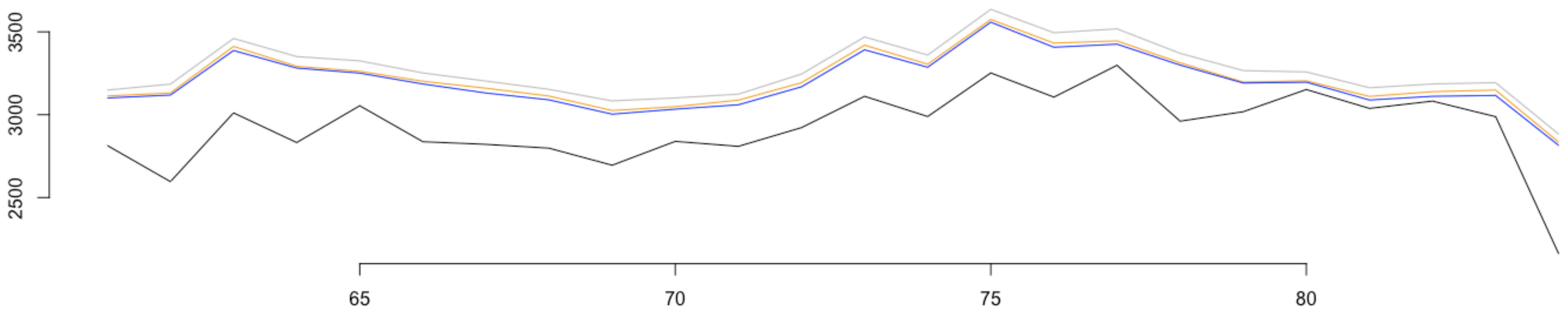
Model Outputs on Testing Data



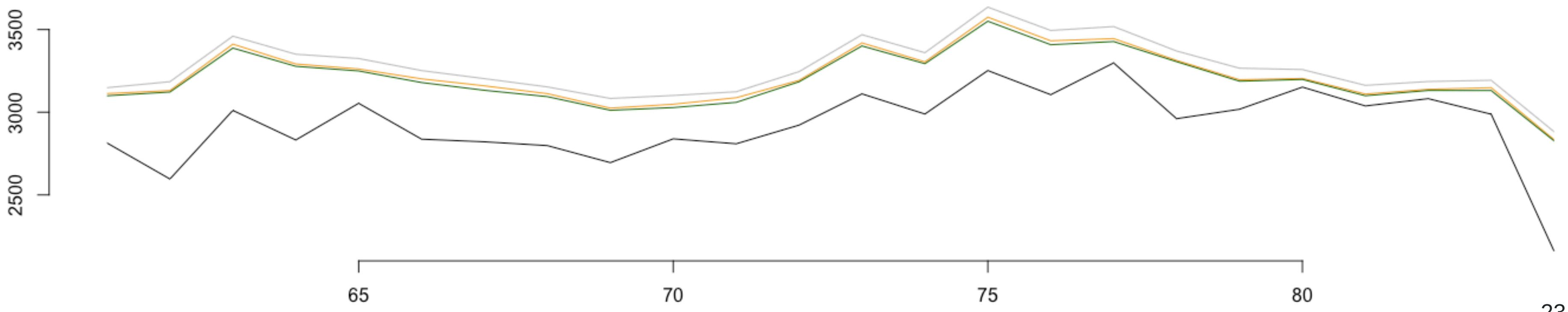
Predicted CDI Cases over 24 months given CDI History



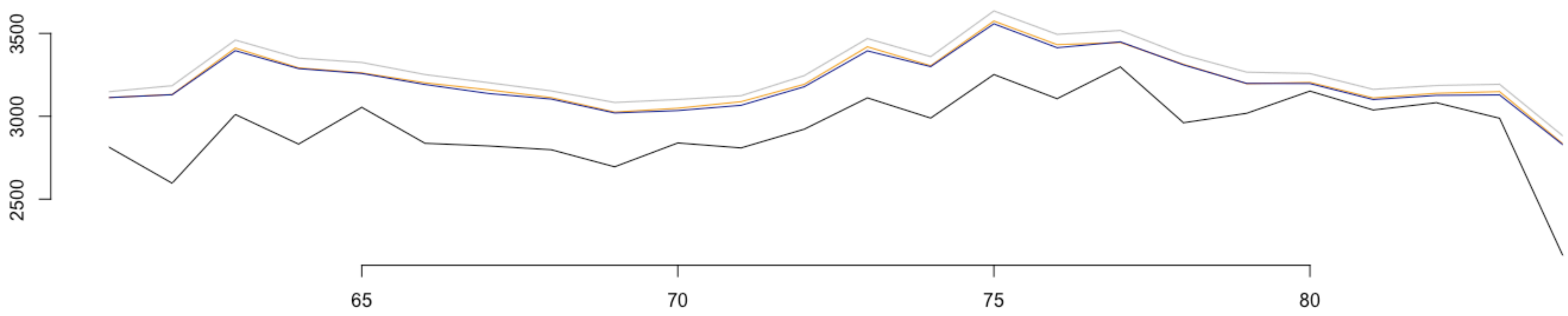
Predicted CDI Cases over 24 months given Degree and % 65



Predicted CDI Cases over 24 months given % 65



Predicted CDI Cases over 24 months given Degree



Predicted CDI Cases over 24 months given Eigen