Spatiotemporal optimization of seasonal vaccination using a metapopulation model of influenza

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Introduction

- Infectious diseases – 13 million deaths per year worldwide
- Seasonal influenza in the United States
  - About 310,000 hospitalizations in 2015/16 season[1]
  - Estimated 61 million cases during 2009/10 pandemic influenza[2]
  - Annual economic burden ~ $87.1 billion

- Human mobility plays a key role in the spread of influenza
- Prophylactic vaccines and antivirals help minimize the impact
- Limited supply, high cost of logistics

[1]*https://www.cdc.gov/flu/about/qa/hospital.htm*
[2]*https://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm*

Questions

Can we optimize the allocation of vaccines to minimize the epidemic impact?

↓

Can we model the spatio-temporal spread of the epidemic?

↓

Can we capture human mobility at the national scale?

Possible solution

Greedy optimization for state level weekly vaccine allocation

↑

Metapopulation (patch) SEIR model for Flu simulation

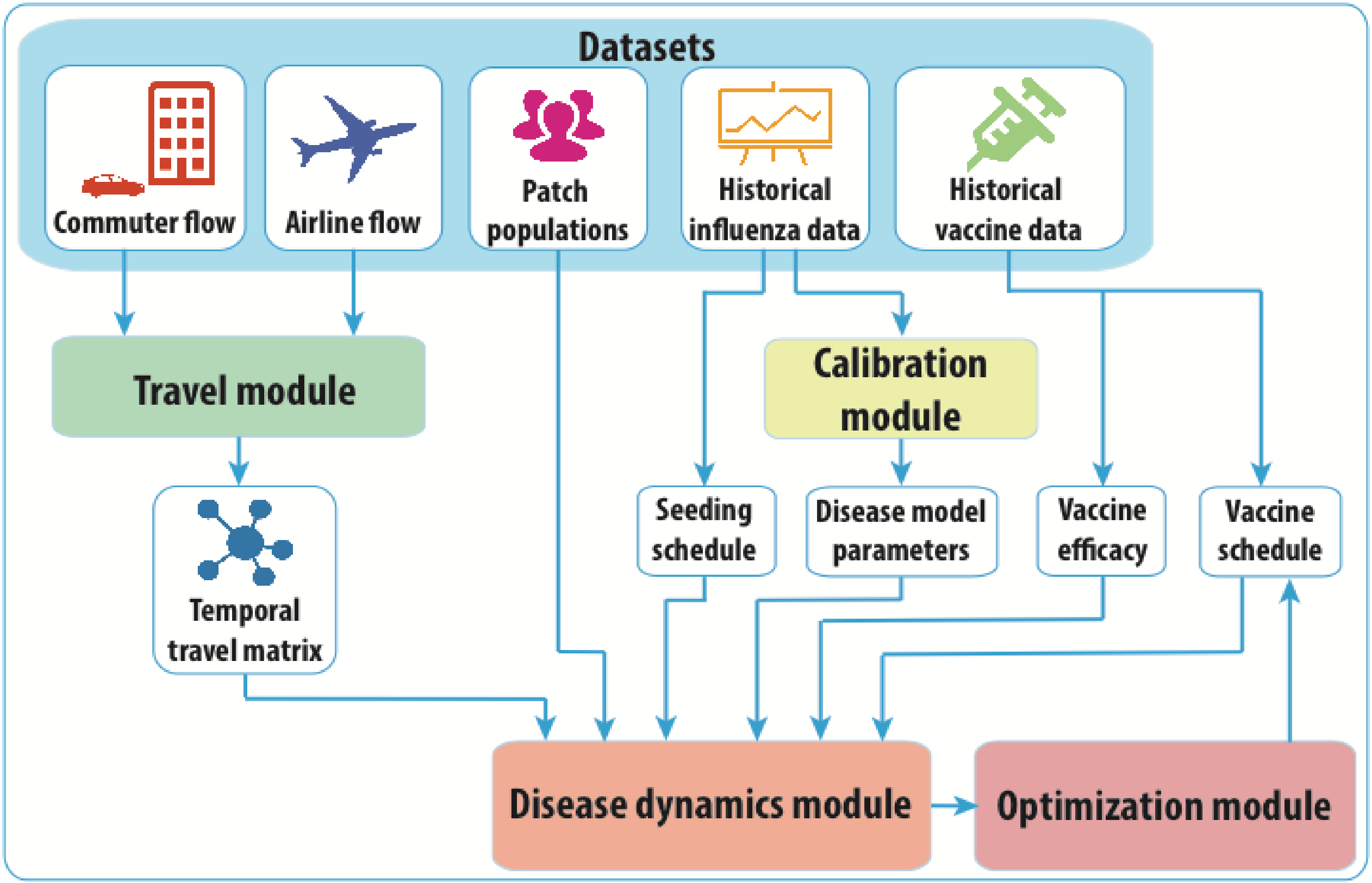
↑

Temporal travel matrix between US counties

Related work

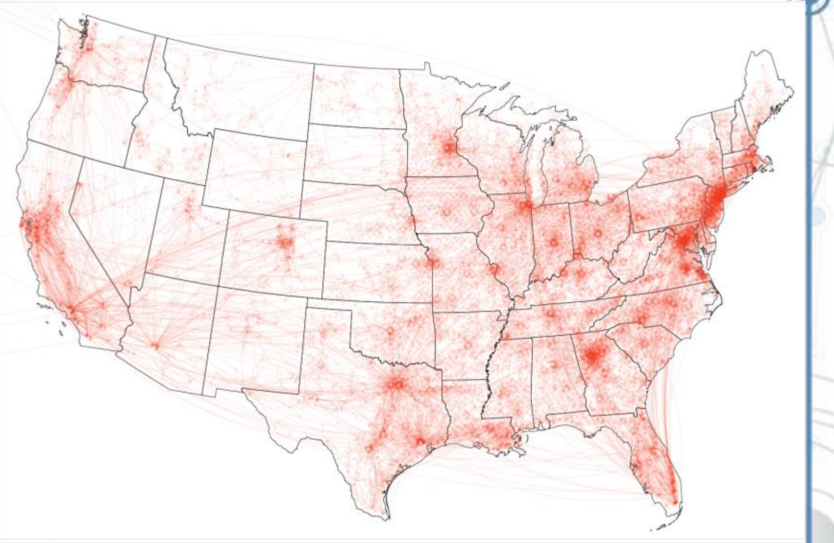
- Jan Medlock and Alison P. Galvani, "*Optimizing Influenza Vaccine Distribution*", Science 2009
  - Analyzed an age-based compartmental model to identify optimal vaccine allocation
- Cecile Viboud et al., "*Synchrony, Waves, and Spatial Hierarchies in the Spread of Influenza*", Science 2006
  - Analyzed the impact of long-range and short-range mobility on the spatial spread patterns of seasonal influenza
- Marcelo Gomes et al., "*Assessing the International Spreading Risk Associated with the 2014 West African Ebola Outbreak*", PLOS Currents 2014.
  - Used a metapopulation model (GLEaM) that combines population and airline mobility data to assess spreading risk of Ebola in 2014.

Our approach

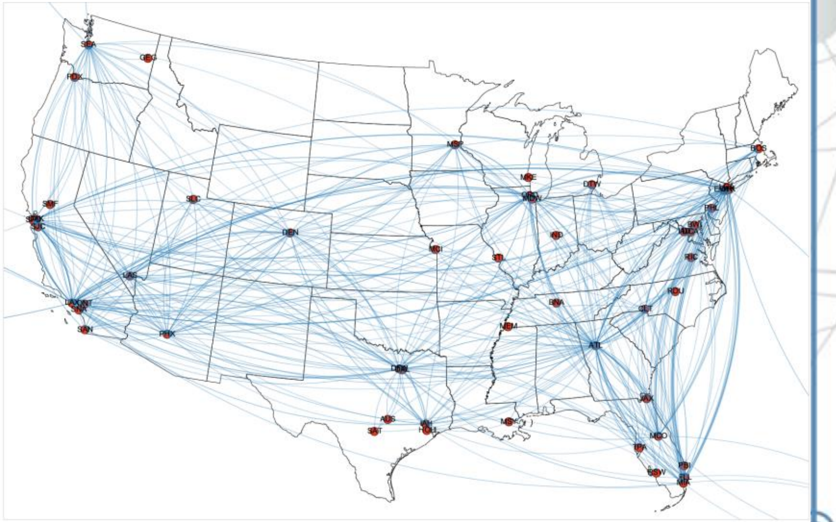


Travel module - Datasets

- Commuter dataset (short-range, regular)
  - Source: American Community Survey[1]
  - Number of commuters between a pair of counties on a typical day



- Domestic airline dataset (long-range, rare)
  - Source: Bureau of Transportation Statistics[2]
  - Number of passengers between two airports each month



[1] *https://www.census.gov/programs-surveys/acs/*
[2] *https://www.rita.dot.gov/bts/data_and_statistics/*

Travel module - Challenges

- Spatial mismatch
  - Need to disaggregate airline flows to county level
  - Define catchment area (120 miles) around the airport
  - Assign flows proportional to county area intersectio
- Temporal mismatch
  - Airline travelers stay longer the commuters
  - Scale the travelers by average stay duration
- Combine and normalize

$$O_{ij}^{m} = C_{ij} + \Delta * A_{ij}^{m}$$

$$\Theta_{ij}^{m} = \begin{cases} \dfrac{O_{ii}^{m} + (P_i - \sum_j O_{ij}^{m})}{P_i} & \text{if } i = j \\ \dfrac{O_{ij}^{m}}{P_i} & \text{otherwise} \end{cases}$$

- Fraction of population of county i, in county j, on a typical day of month m

Disease dynamics module

- Evolution within a county using the traditional SEIR (Susceptible -> Exposed -> Infected -> Recovered) ODE model

$$S \longrightarrow E \longrightarrow I \longrightarrow R$$

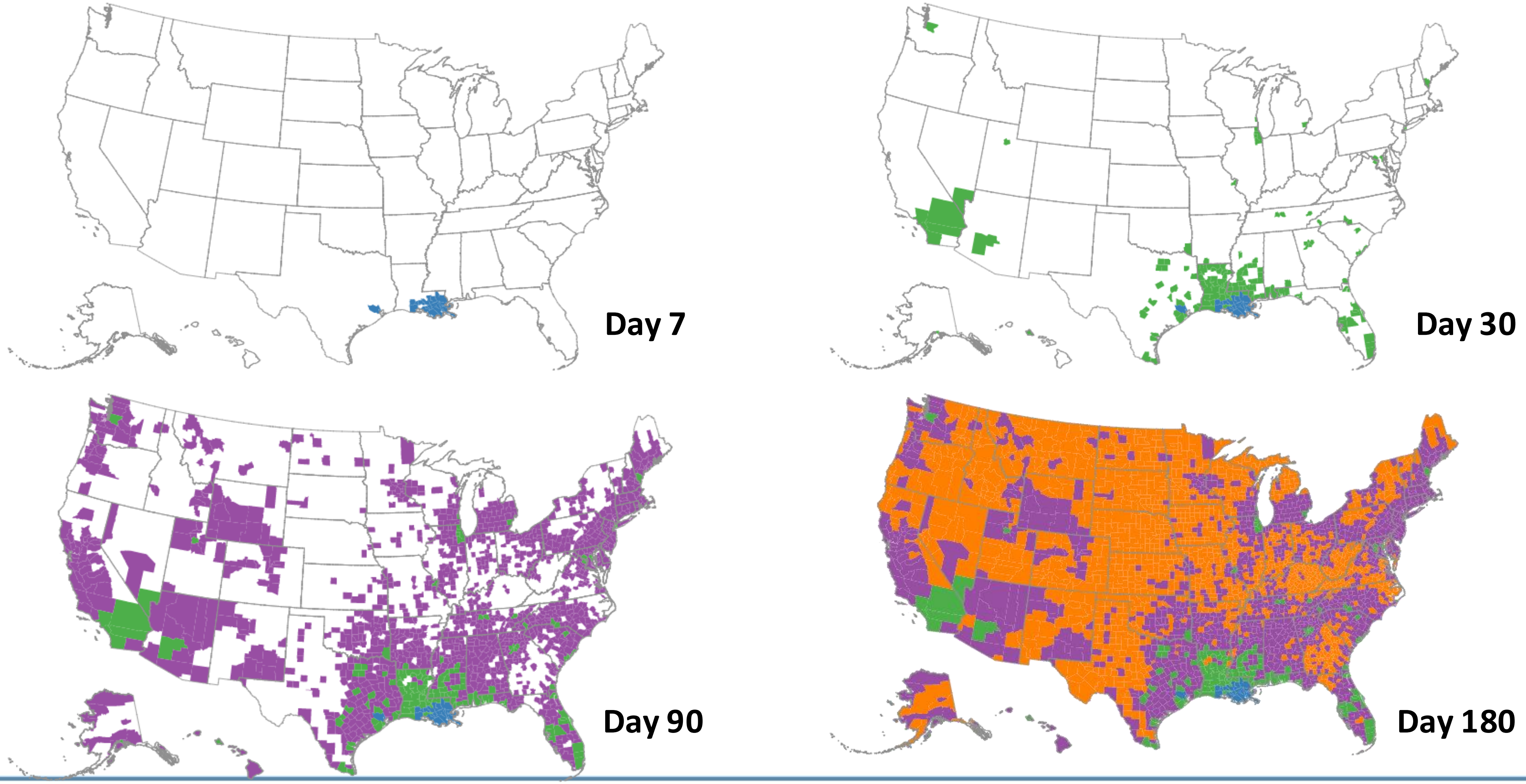
- Travel matrix for force of infection between patches

$$I_j^{\mathtt{eff}} = \sum_i \Theta_{ij} I_i; \;\; N_j^{\mathtt{eff}} = \sum_i \Theta_{ij} N_i$$

- Include vaccination state (S -> V)

$$\begin{aligned}
\frac{dS_i}{dt} &= = -\beta S_i(t)\frac{I_i(t)}{N_i} \\
\frac{dE_i}{dt} &= \beta S_i(t)\frac{I_i(t)}{N_i} - \alpha E_i(t) \\
\frac{dI_i}{dt} &= \alpha E_i(t) - \gamma I_i(t) \\
\frac{dR_i}{dt} &= \gamma I_i(t)
\end{aligned}$$

Spatio-temporal spread



Optimization module

- Spatiotemporal allocation of vaccines
  - Space – State level (proportional distribution to counties)
  - Time – Weekly
- Temporal budget constraint
  - Number of vaccine doses available each week
  - Historical data source: FluVaxView[1]

$$\begin{aligned} \underset{X}{\text{minimize}} \quad & f(X) \\ \text{subject to} \quad & \sum_i X_{i,t} \leq B_t, \quad \text{for all } t, \end{aligned}$$

- In our study, objective is to minimize national attack size (total number of infections)

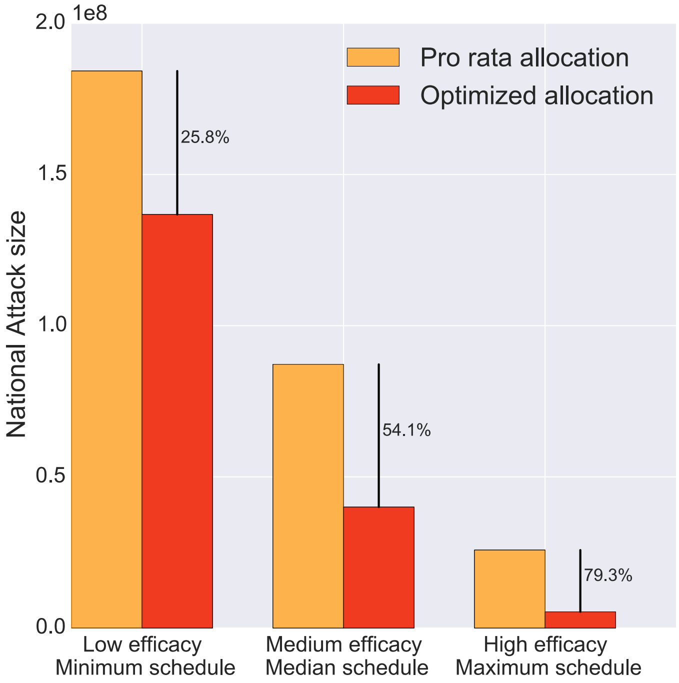
[1] https://www.cdc.gov/flu/fluvaxview/interactive.htm

Scenario & Experiment design

- Seasonal influenza scenario categorized by:
  - Seeding, Attack size, Vaccine efficacy, Vaccine schedule
- Seeding: 2009/10 (Louisiana), 2005/06 (Arizona), 2006/07 (Florida)
- Attack size (mitigated under standard vaccination):
  86 million (high AR), 73 million (mid AR), 41 million (low AR)
- Vaccine efficacy: 20%, 40%, 60%
- Vaccine schedule: 2009/10 (low), 2012/13 (medium), 2014/15 (high)
- Other parameters:
  - α = 0.67 (latent period = 1.5 days), γ = 0.4 (infection period = 2.5 days)
  - Vaccine delay = 21 days

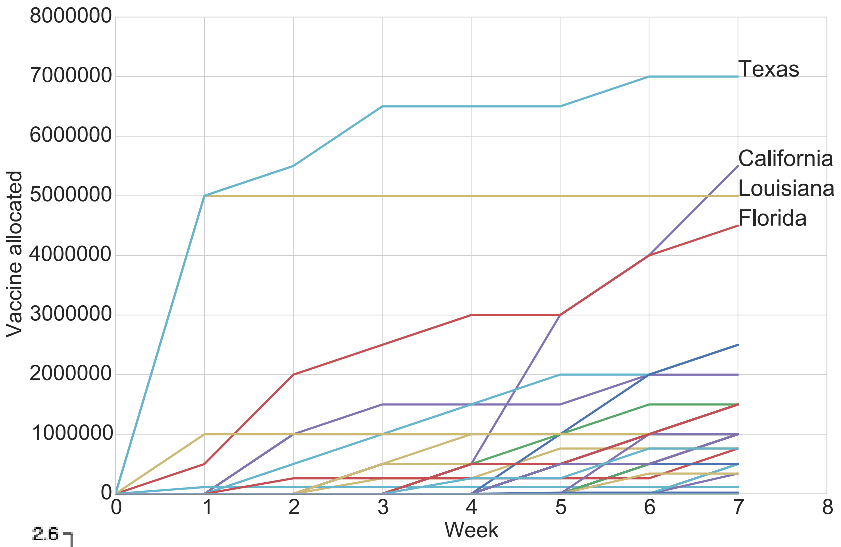
Results

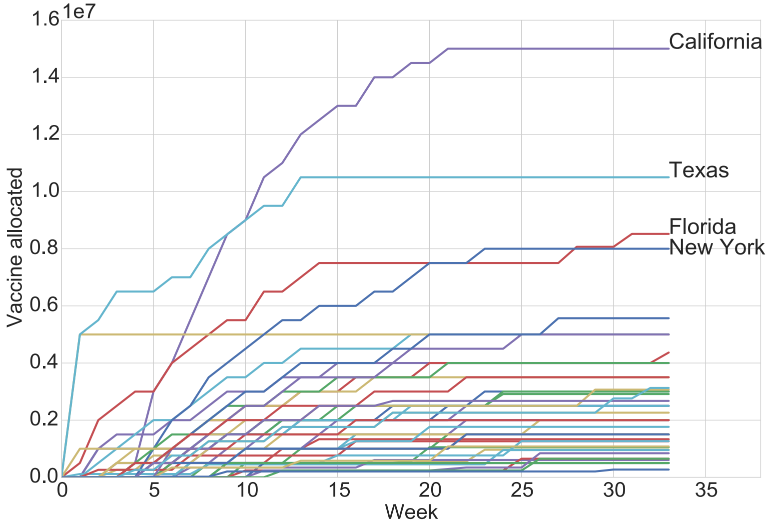
Effect of vaccine efficacy

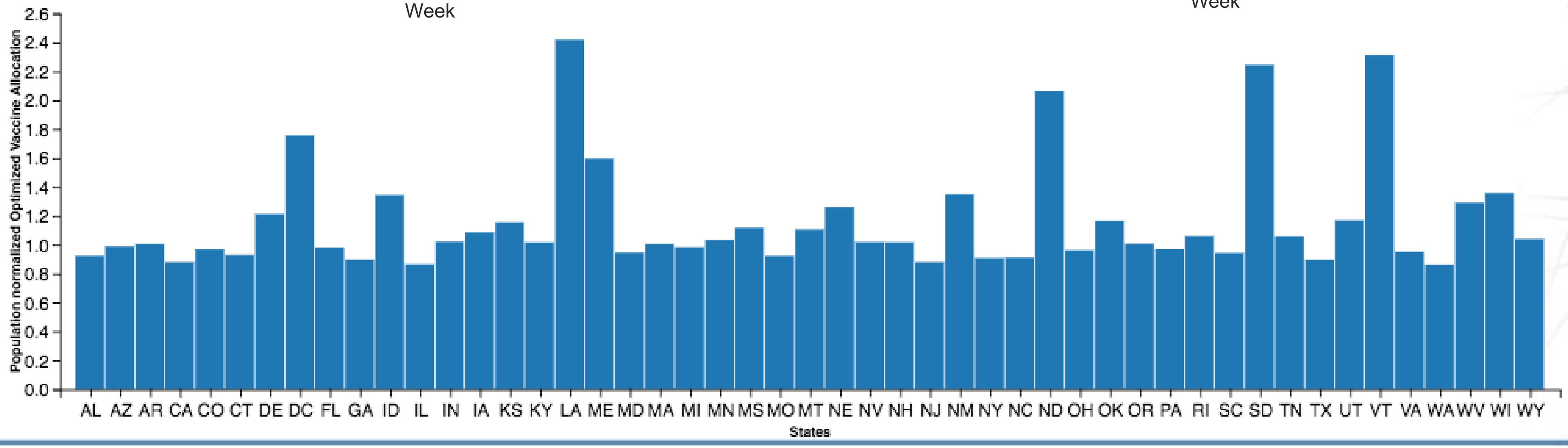


Sample scenario:
2009/10 season, 86M cases

Statewise allocation over time







Limitations & Future work

- More realistic travel model
  - Account for weekends, major holidays, events, vacations, etc.
- Incorporate age distribution into the disease model
- Better spatial calibration of historical influenza seasons
- Incorporate compliance behavior for vaccine adoption
- Other objective functions, optimization methods

- Study related optimization problems of delivery logistics, stockpile rightsizing and placement

Conclusions

- We have developed a simulation based approach to optimize vaccine allocation for seasonal influenza
- The simulation model accounts for both short-range and long-range mobility across United States
- Results of optimization reveal the importance of spatiotemporal allocation
- Improved models with historical calibration can lead to playbook style approach for vaccine allocation in the future

Acknowledgments

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  DTRA CNIMS Contract HDTRA1-11-D-0016-0001,
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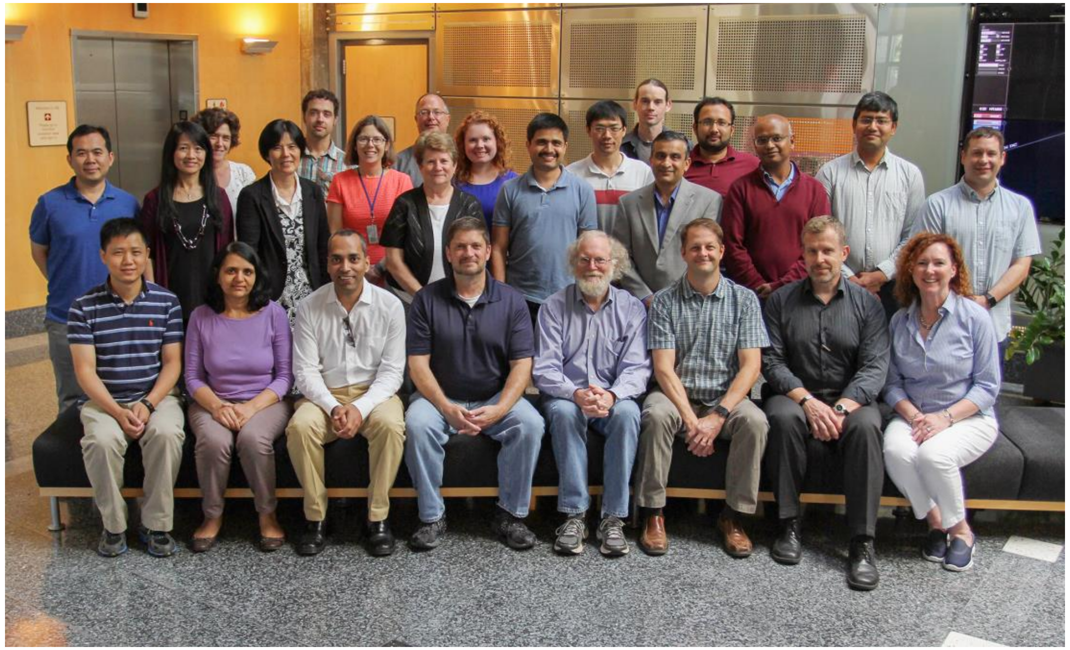

Questions?

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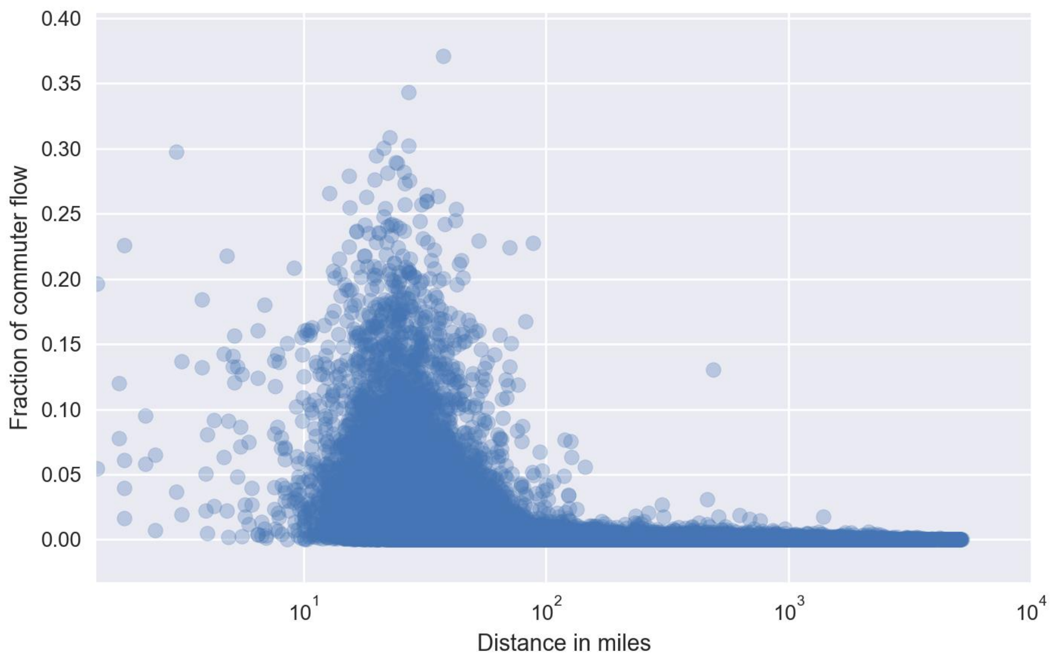
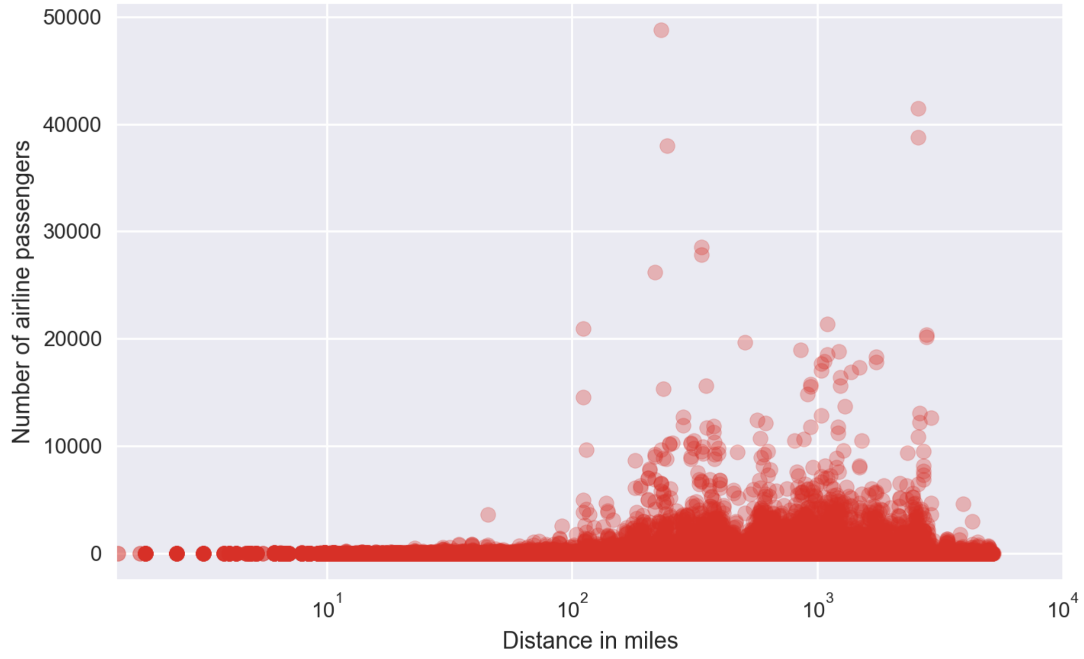
Backup slides

Travel data statistics

Commuting data



Domestic airline data



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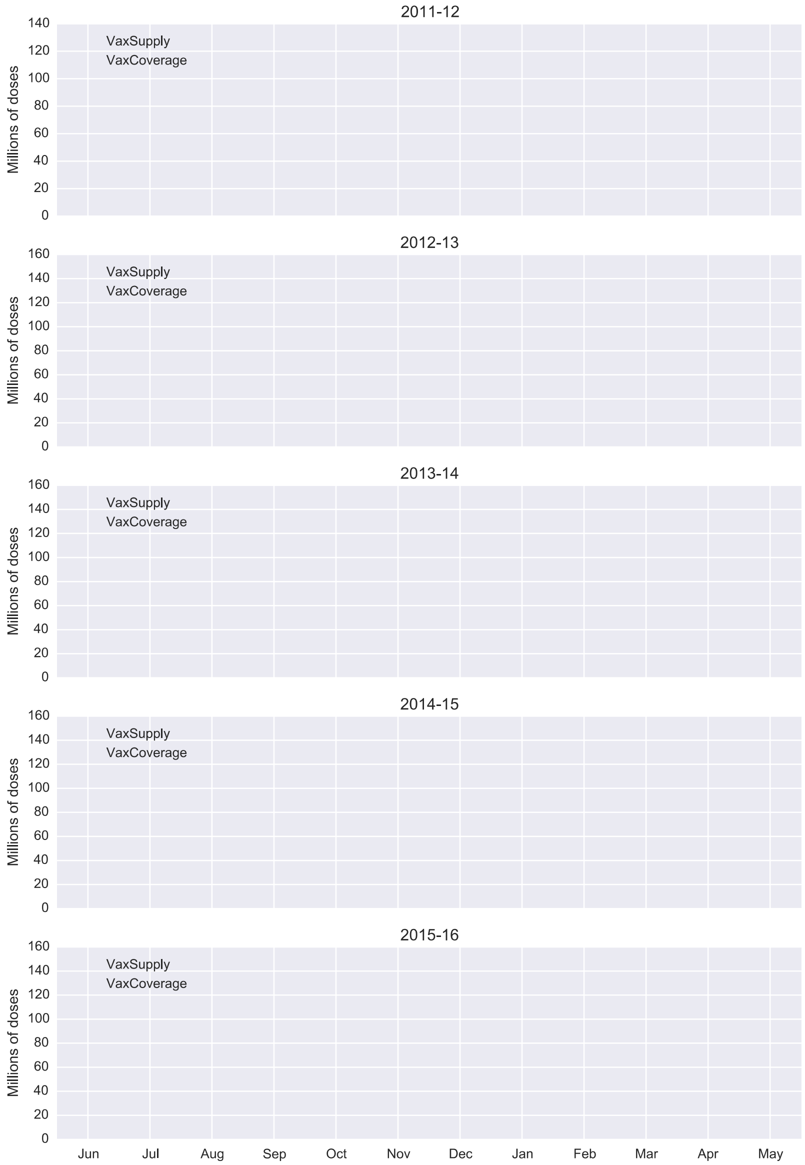
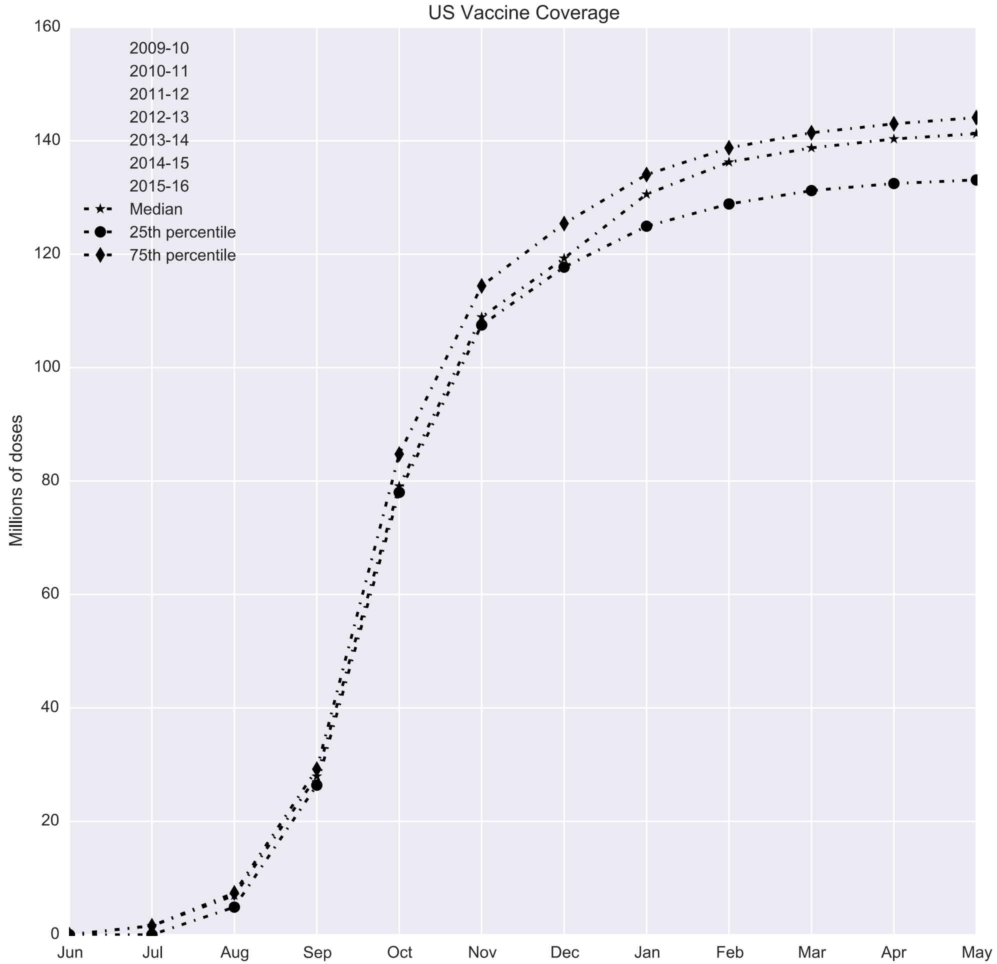
Vaccine schedule





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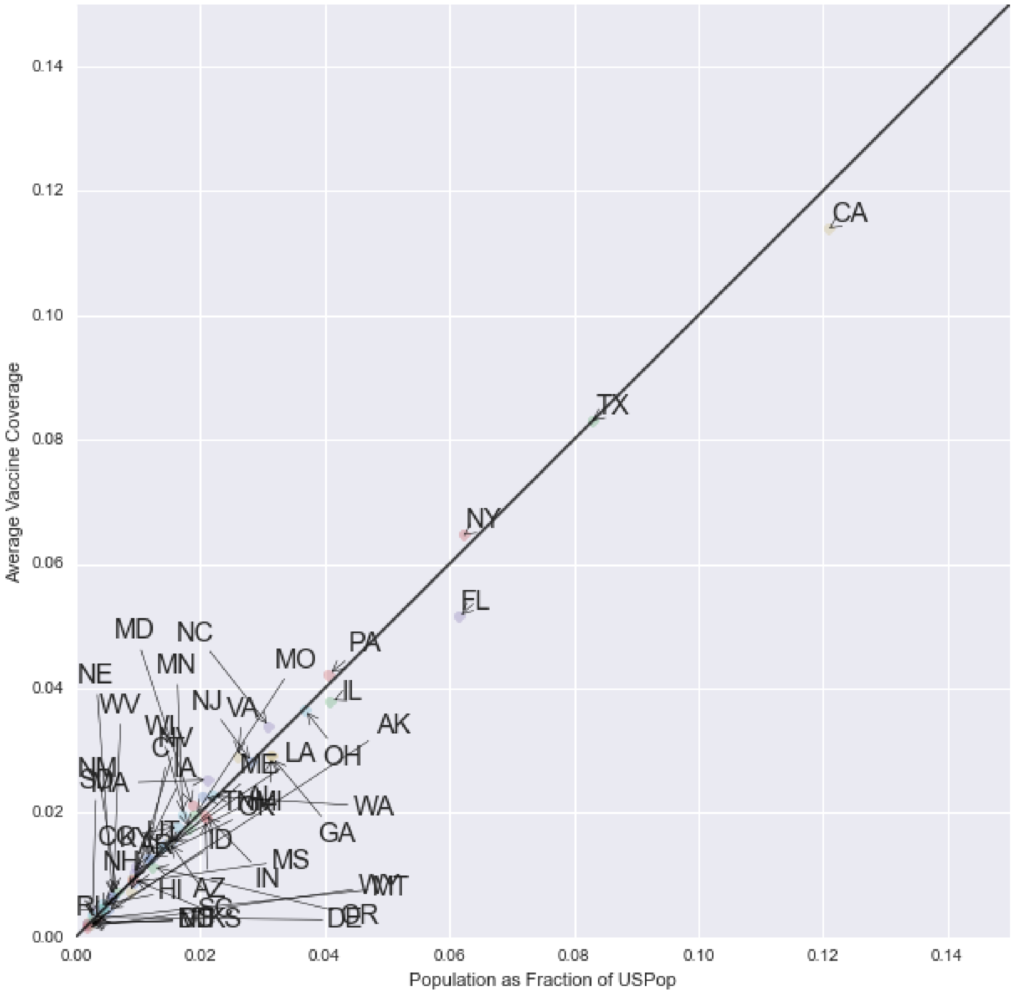
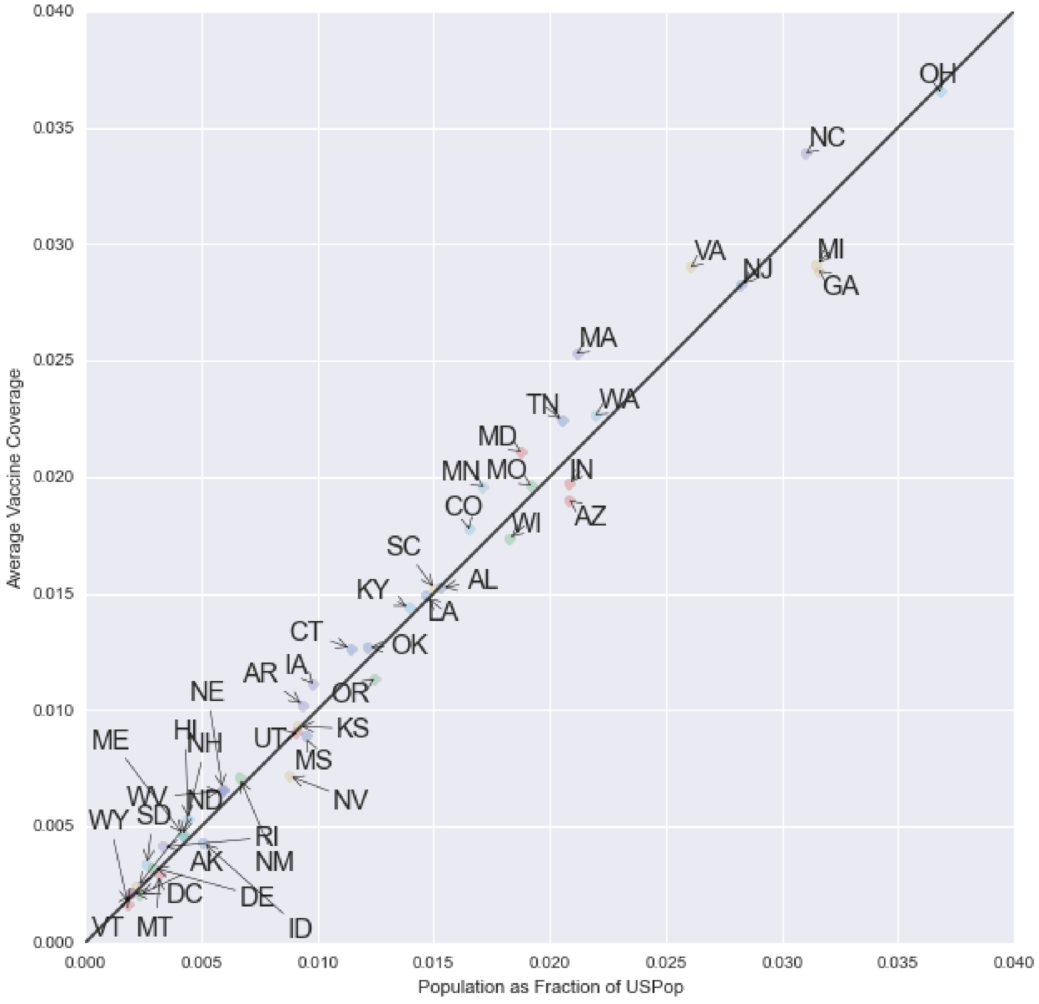
Historical vaccine allocation





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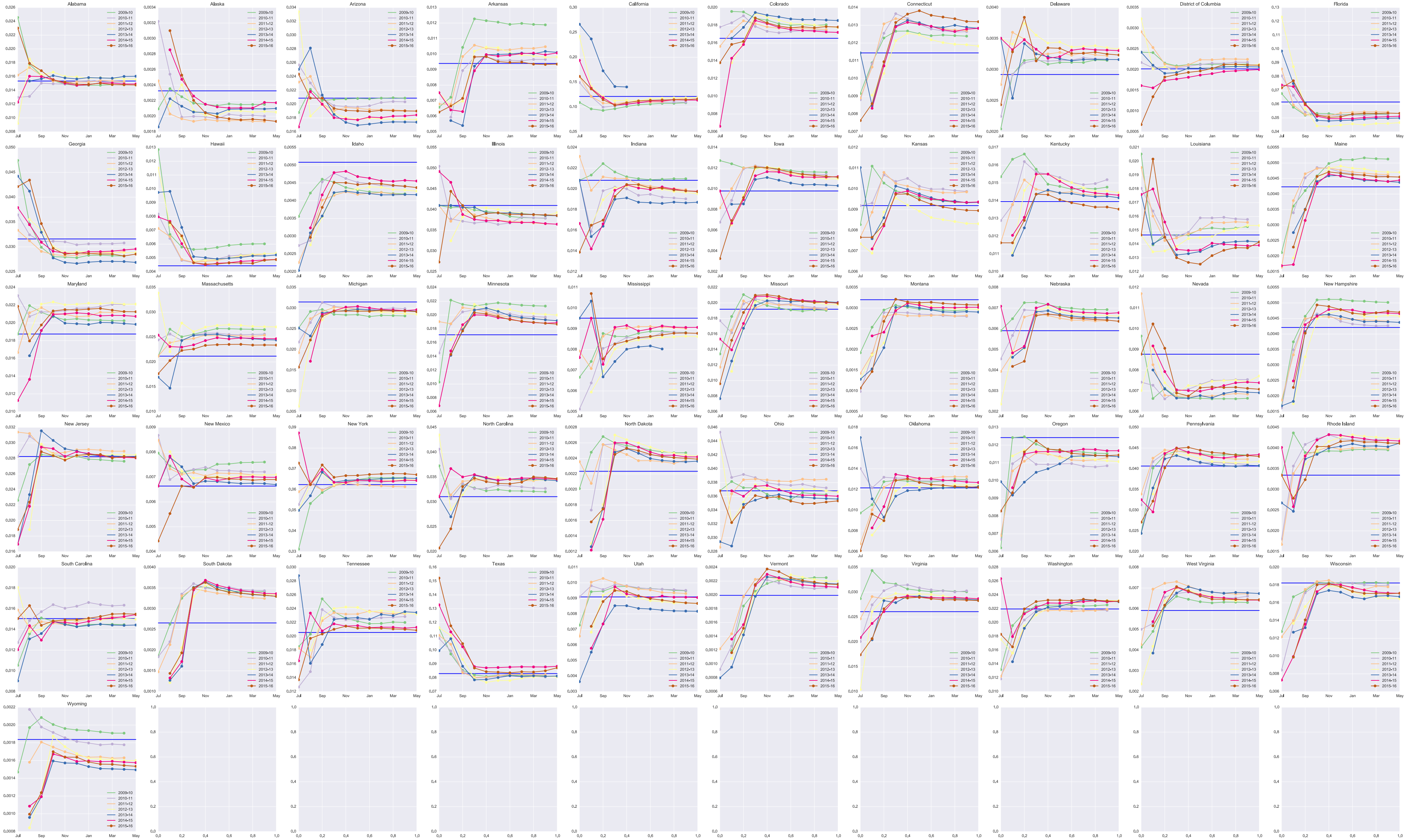
Historical temporal allocation



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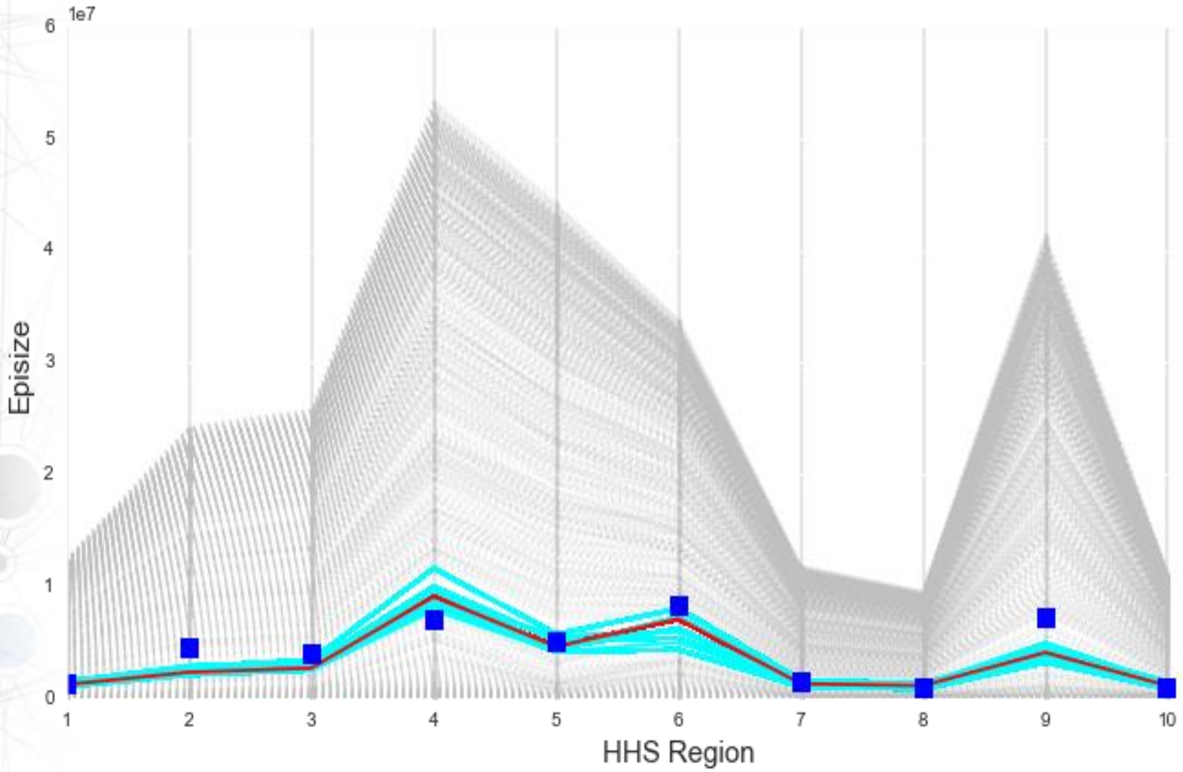
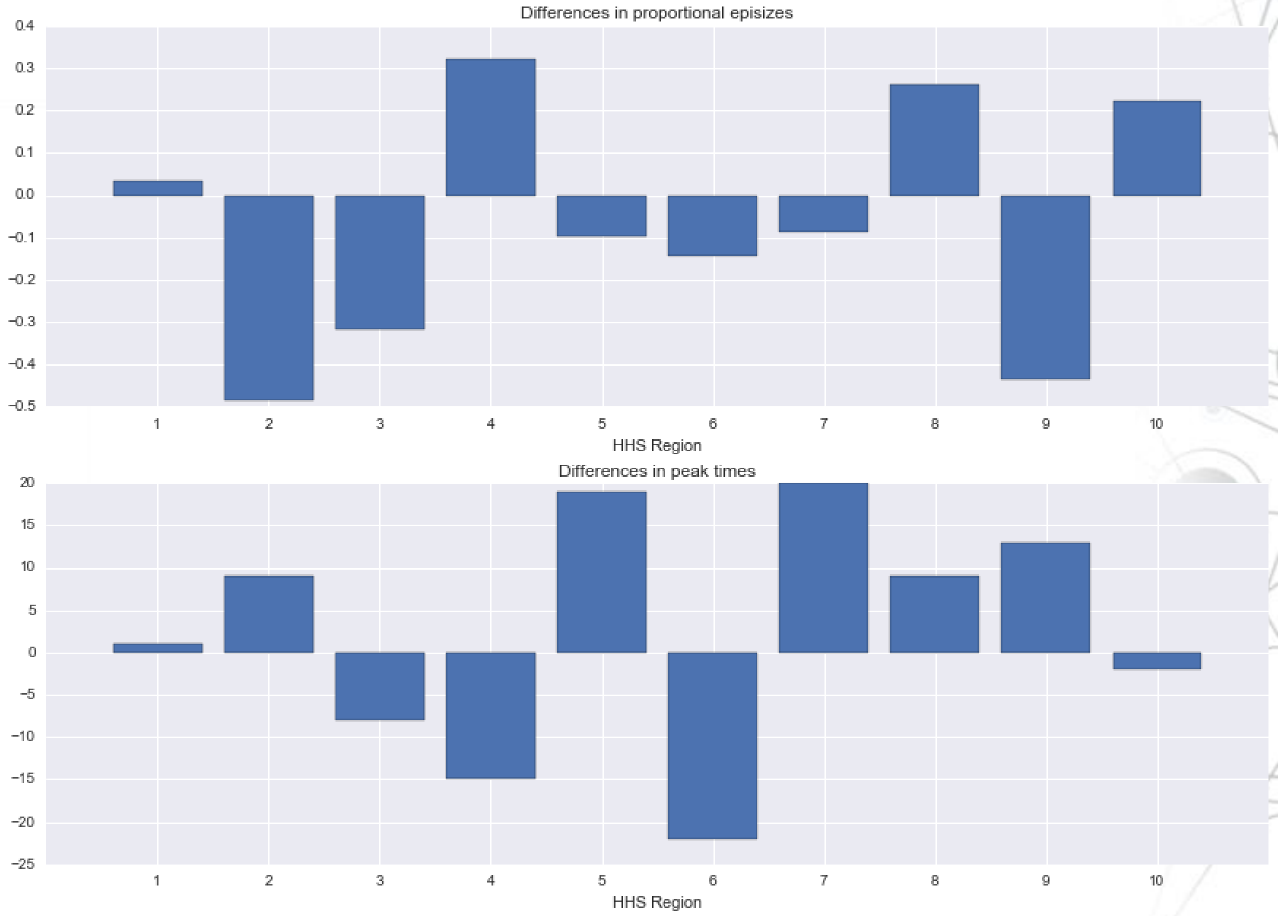
Spatial calibration





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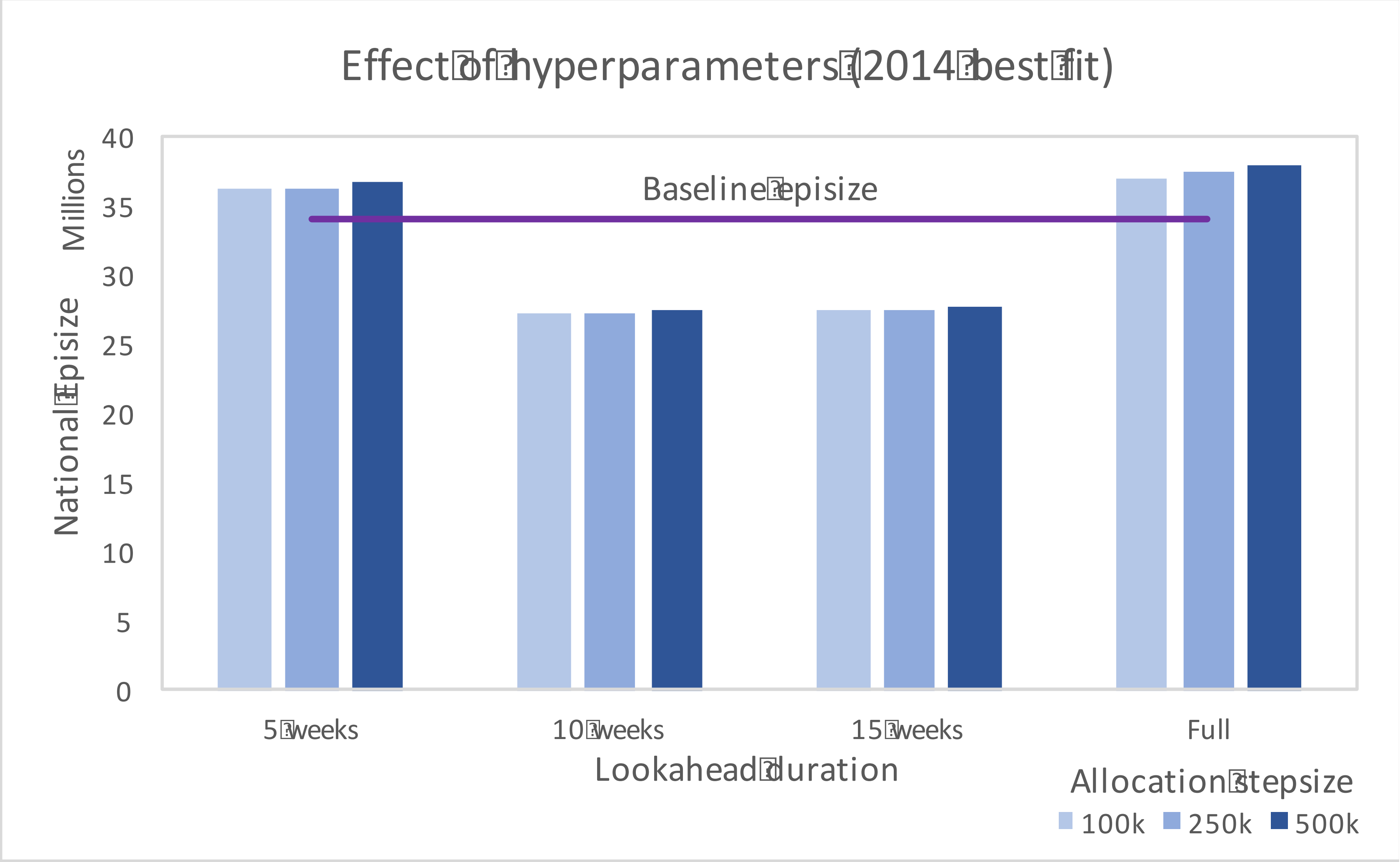
Hyperparameters



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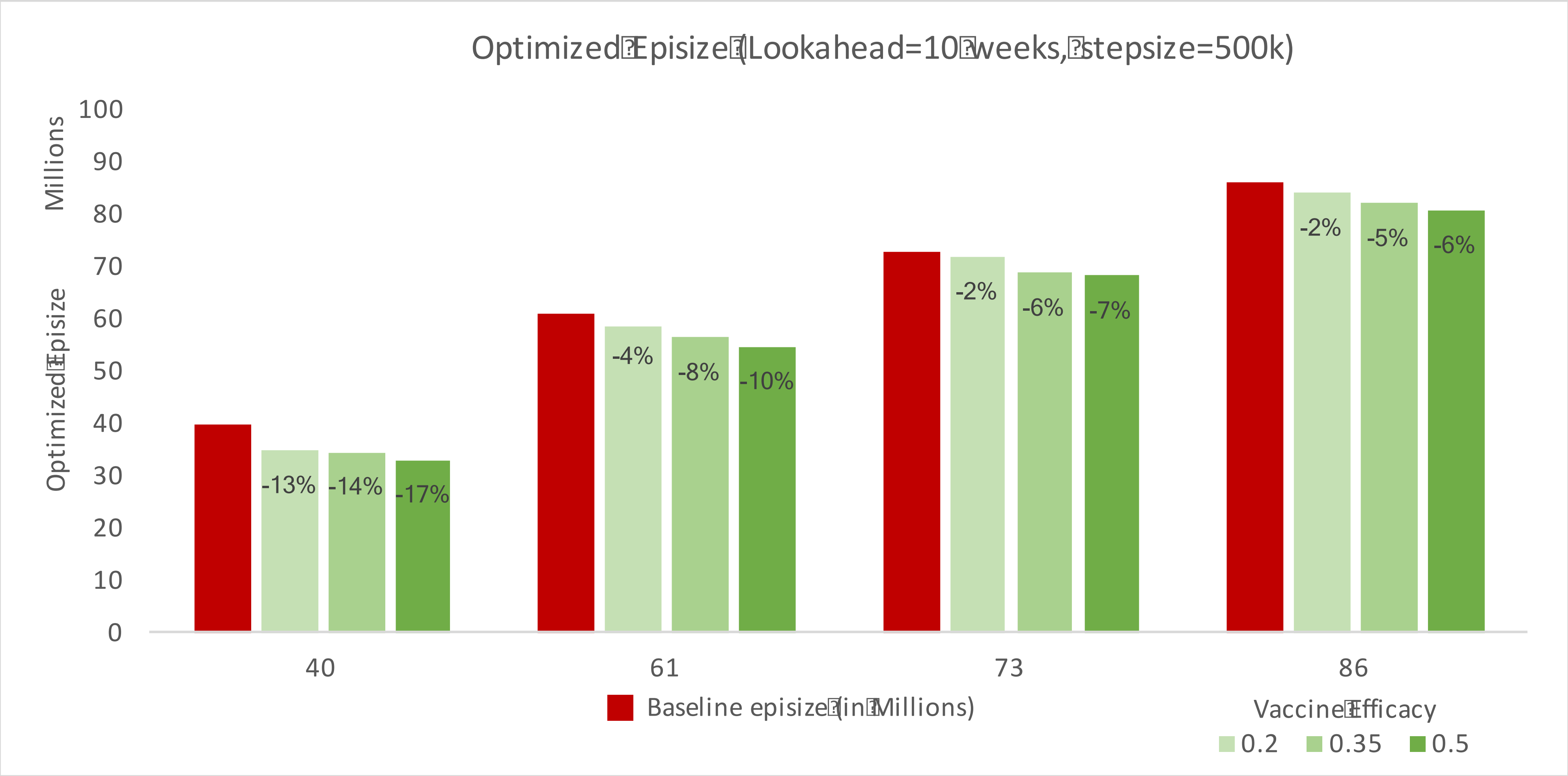
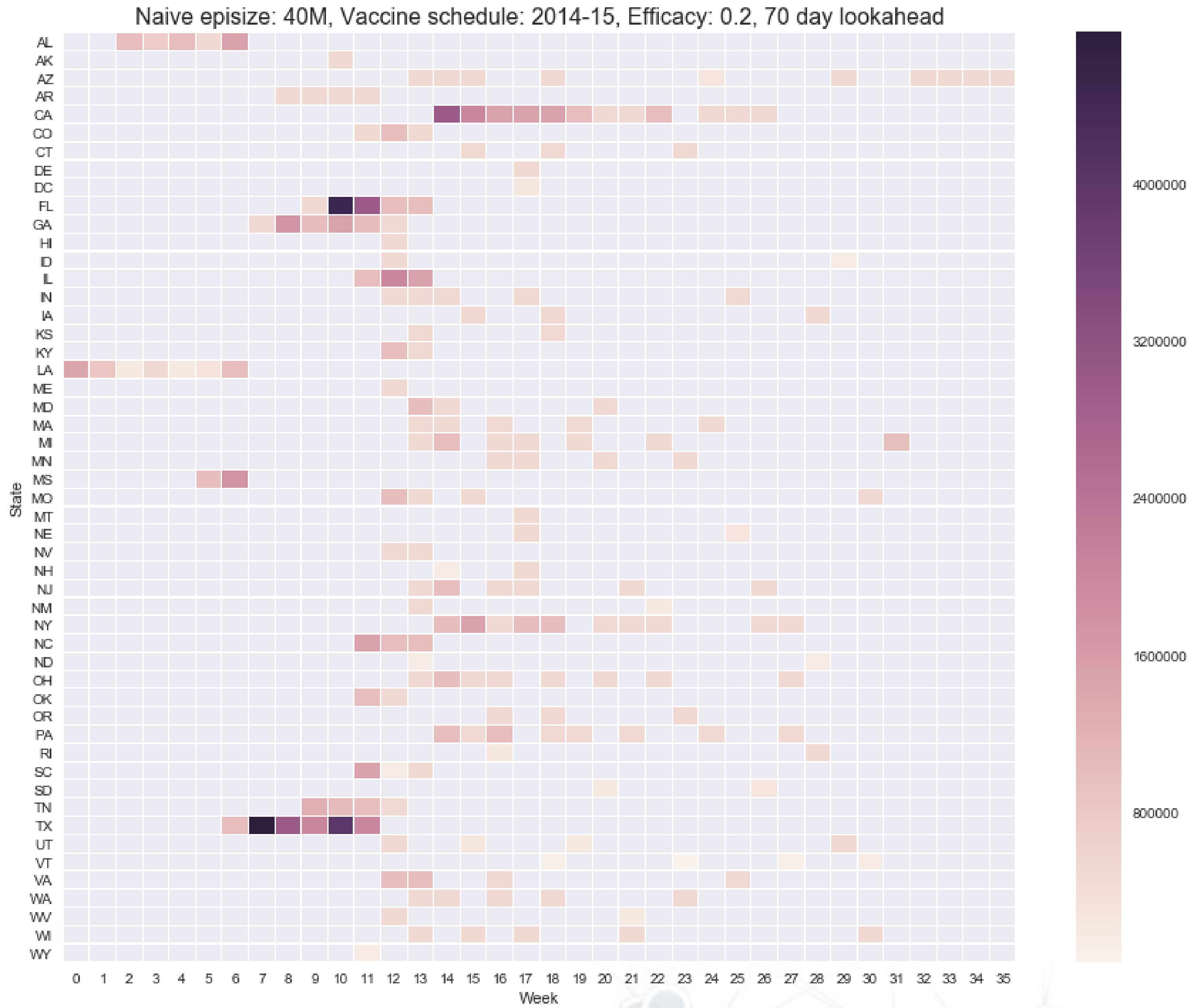
Updated results



Spatio-temporal heatmap



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