A Tale of Two Doses:
Model Identification and Vaccination for COVID-19

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60th IEEE Conference on Decision and Control

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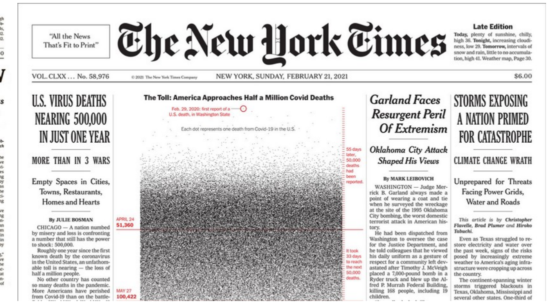
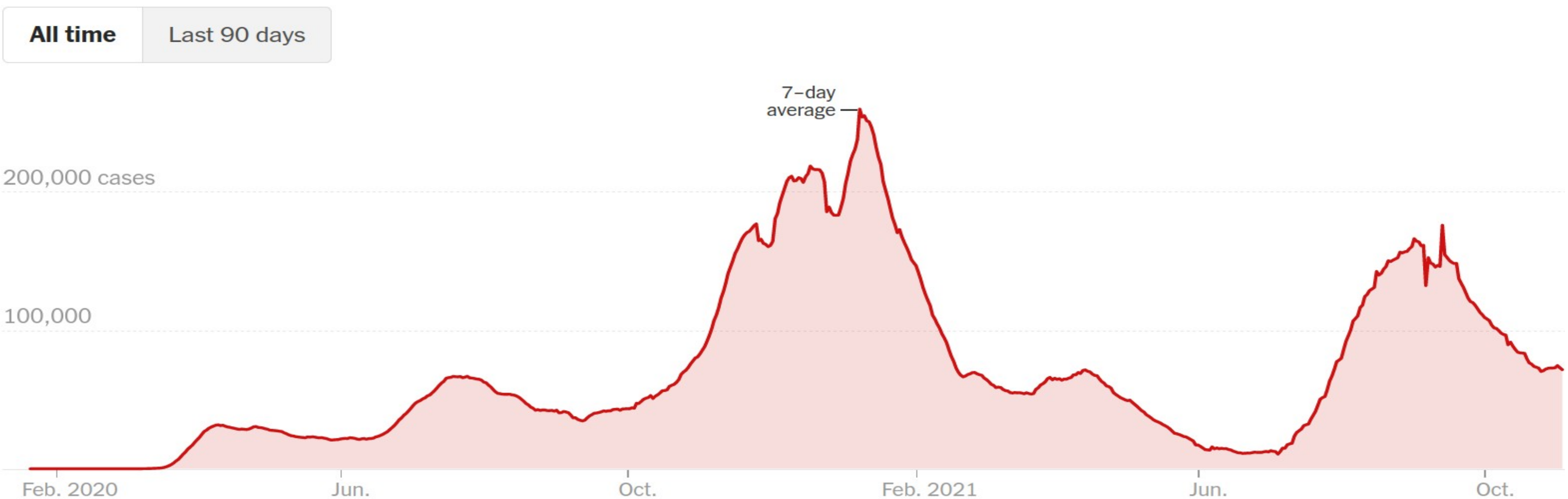
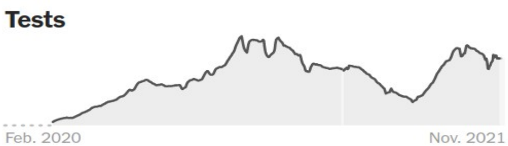
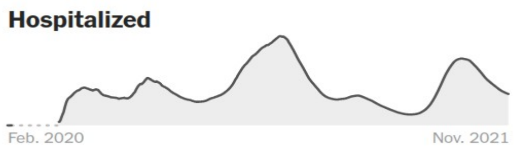
COVID-19 needs no introduction

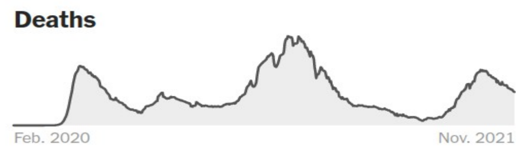


New reported cases



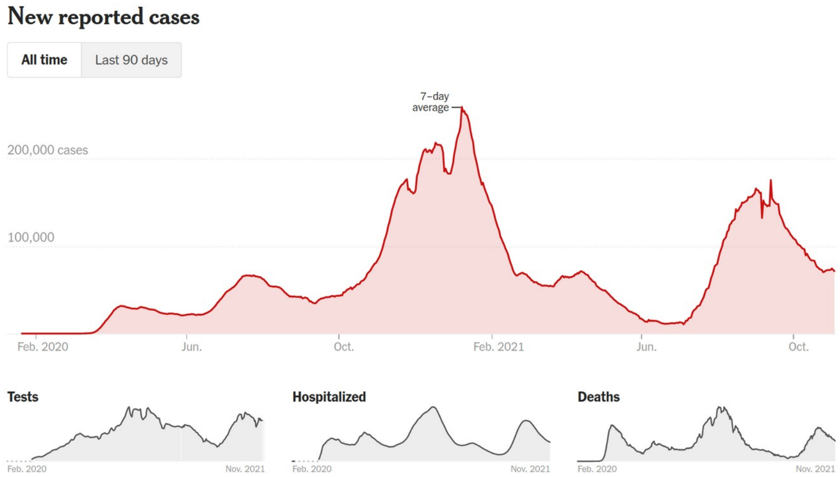






Credits: The New York Times - accessed Nov 2021 https://www.nytimes.com/interactive/2021/us/covid-cases.html

Our work needs introduction



Limits of this graph:

- Reported data only
  - noise? confidence intervals?
  - asymptomatic cases? uncounted deaths?
- No forecasting
  - Policy makers need information on the future not the past
  - How to design vaccination policies?

Reason: does not rely on a model

Our work needs introduction

Limits of this graph:

Our Goal

- Expand on the SIR model
- Estimate the number of infected and recovered people
- Use this knowledge to design optimal vaccination strategies

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Model for COVID-19

We start with an SIR model

Dynamics

$$S(t+1) = S(t) - \frac{\beta \quad I(t)S(t)}{N_0}$$

Susceptible

$$I(t+1) = I(t) + \frac{\beta \quad I(t)S(t)}{N_0} - \gamma I(t)$$

Infected

$$R(t+1) = R(t) + \gamma I(t)$$

Removed

Observations

$$y_C(t) = \frac{\beta \quad I(t)S(t)}{N_0}$$

#cases

$$y_D(t) = \omega I(t)$$

#deaths

Modified Model

Dynamics

$$S(t+1) = S(t) - \frac{\beta \quad I(t)S(t)}{N_0} - \Psi(t)$$

$$I(t+1) = I(t) + \frac{\beta \quad I(t)S(t)}{N_0} - \gamma I(t)$$

$$R(t+1) = R(t) + \gamma I(t) + \Psi(t)$$

Observations

$$y_C(t) = \frac{\beta \quad I(t)S(t)}{N_0}$$

$$y_D(t) = \omega I(t)$$

$$y_\Psi(t) = \Psi(t)$$

#cases

#deaths

#vaccines

1) Include vaccines

efficiency

$$\Psi(t) = \sum_{i=1}^{M} \sum_{j=1}^{m_i} \theta_{ij} \psi_{ij}(t)$$

# of people who got the j^{th} dose of vaccine i^{th} on day t

Modified Model

Dynamics

$$S(t+1) = S(t) - \frac{\beta \quad I(t)S(t)}{N_0} - \Psi(t) + d_\nu(t)$$

$$I(t+1) = I(t) + \frac{\beta \quad I(t)S(t)}{N_0} - \gamma I(t) - d_\nu(t) + d_\rho(t)$$

$$R(t+1) = R(t) + \gamma I(t) + \Psi(t) - d_\rho(t)$$

Observations

$$y_C(t) = \frac{\beta \quad I(t)S(t)}{N_0} + w_C(t)$$

$$y_D(t) = \omega I(t) + w_D(t)$$

$$y_\Psi(t) = \Psi(t)$$

#cases

#deaths

#vaccines

1) Include vaccines

efficiency

$$\Psi(t) = \sum_{i=1}^{M} \sum_{j=1}^{m_i} \theta_{ij} \psi_{ij}(t)$$

# of people who got the j^{th} dose of vaccine i^{th} on day t

2) Stochastic

Process and measurement noise
zero mean independent Gaussian RV

Modified Model

Dynamics

$$S(t+1) = S(t) - \frac{\beta(t) I(t) S(t)}{N_0} - \Psi(t) + d_\nu(t)$$

$$I(t+1) = I(t) + \frac{\beta(t) I(t) S(t)}{N_0} - \gamma I(t) - d_\nu(t) + d_\rho(t)$$

$$R(t+1) = R(t) + \gamma I(t) + \Psi(t) - d_\rho(t)$$

Observations

case report rate

$$y_C(t) = \phi(t) \frac{\beta(t) I(t) S(t)}{N_0} + w_C(t)$$

#cases

$$y_D(t) = \omega I(t) + w_D(t)$$

#deaths

$$y_\Psi(t) = \Psi(t)$$

#vaccines

Parameter drift

$$\beta(t+1) = \beta(t) + d_\beta(t)$$

$$\phi(t+1) = \phi(t) + d_\phi(t)$$

1) Include vaccines

efficiency

$$\Psi(t) = \sum_{i=1}^{M} \sum_{j=1}^{m_i} \theta_{ij} \psi_{ij}(t)$$

# of people who got the j^{th} dose of vaccine i^{th} on day t

2) Stochastic

Process and measurement noise
zero mean independent Gaussian RV

3) Time varying parameters

- Can model multiple waves
- Capture change in testing
- In absence of additional information, parameter will most likely not change

Modified Model

Dynamics

$$S(t+1) = S(t) - \frac{\beta(t) I(t) S(t)}{N_0} - \Psi(t) + d_\nu(t)$$

$I(t+1) =$ …

$R(t+1) =$ …

case report rate

$y_C(t) = \phi$ …

$y_D(t) = \omega$ …

$y_\Psi(t) = \Psi$ …

$$\beta(t+1) = \beta(t) + d_\beta(t)$$

$$\phi(t+1) = \phi(t) + d_\phi(t)$$

1) Include vaccines

efficiency

… $\psi_{ij}(t)$

…o got the j^th

…i^th on day t

…ent noise

…aussian RV

- In absence of additional information, parameter will most likely not change

Everything is estimated!

- Number of cases, infection rate, death rate, report rate noise/disturbance variances, etc
- Parameters influenced by non bio factors
  - Are people wearing masks?
  - Are people social distancing?
  - Is the area densely populated?
  - Average population age?

Identification and Estimation

Identifiability

Can we uniquely identify all the parameters? Yes!

Theorem: A tuple of initial states and parameters $(R_1, U_1, \Theta) \in \mathbb{R}^6_{\geq 0}$ is locally identifiable on the interval $\{1, 2, 3\}$ for an input sequence $\Psi : \mathbb{N} \to \mathbb{R}_{\geq 0}$ if

$$\beta, \phi, \omega > 0, S(1), I(t) > 0 \qquad \forall t \in \{1, 2, 3\}$$

$$\Psi(2) \neq \frac{I(2)S(2)}{I(1)S(1)} \Psi(1),$$

where $S(t) = N_0 - U(t)$ and $I(t) = U(t) - R(t)$ are the susceptible and infected state variables at $t \in \mathbb{N}$.

Interpretation: Identifiable if vaccine

Estimation

$$V = (\sigma_\nu, \sigma_\rho, \sigma_C, \sigma_D, \sigma_\beta, \sigma_\phi)$$ variances

$$Y = \big(y_C(1), \dots, y_C(T), y_D(1), \dots, y_D(T)\big)$$ observation

$$Z = \big(S(1), \dots, S(T), I(1), \dots, I(T), R(1), \dots, R(T), \beta(1), \dots, \beta(T), \phi(1), \dots, \phi(T), \omega, \gamma\big)$$ states

Model: Additive *i.i.d.* disturbances = explicit Probability density function $p_{Z,Y}(Z, Y; V)$

We can estimate parameters using Maximum Likelihood Estimation

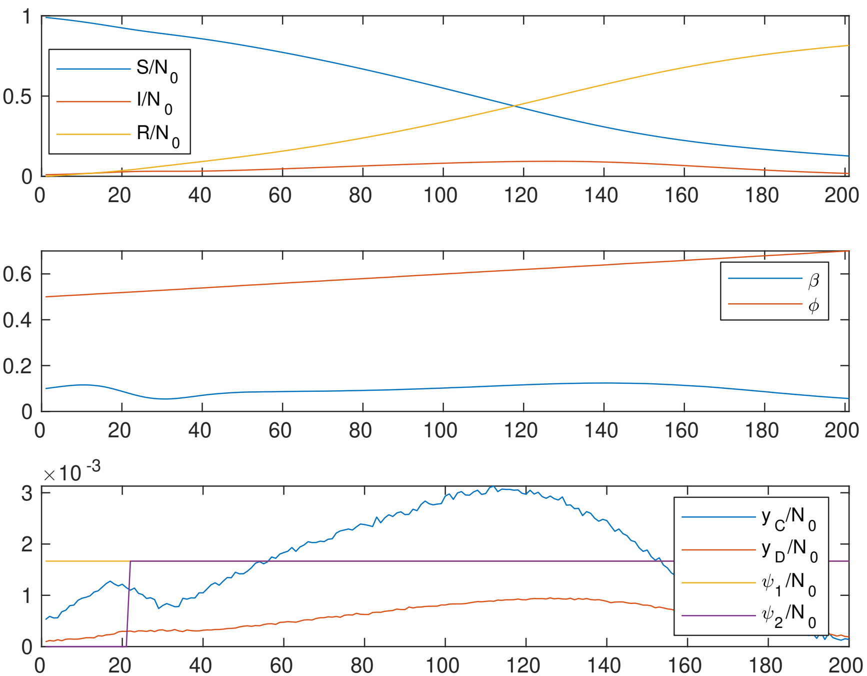
Theorem (simplified): If the conditional distribution $p_{Z|Y}(\cdot)$ is a multivariable Gaussian, then the maximum likelihood estimator for V can be obtained using

$$\hat{V} = \arg\max_{V} \left[-\frac{1}{2} \log\det \left(\frac{d^2 \log p_{Z,Y}(\hat{Z}, Y; V)}{dZ^2} \right) + \max_{Z} \log p_{Z,Y}(Z, Y; V) \right]$$

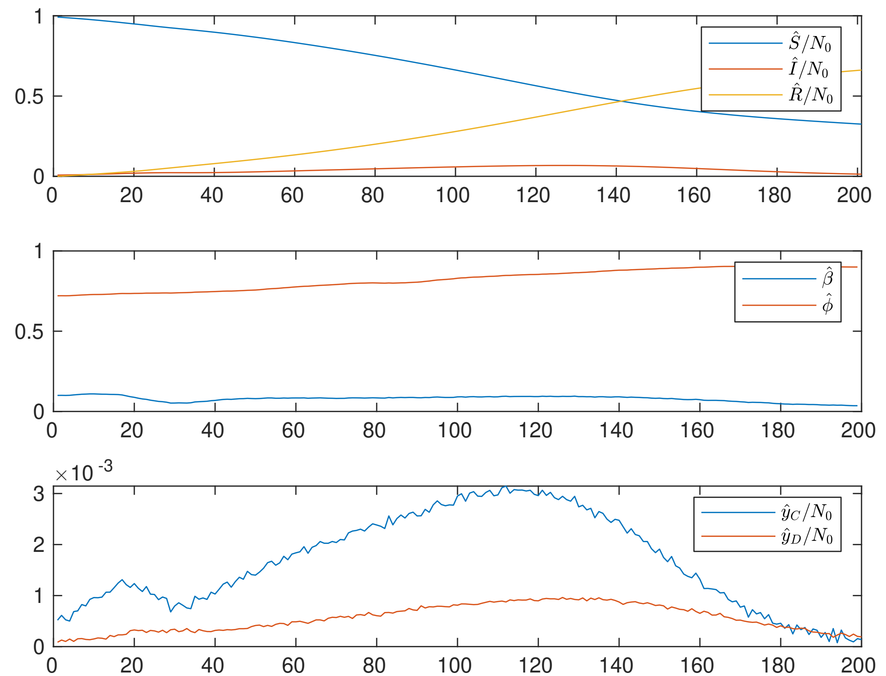
and the associated minimum variance estimator for Z is given by $\hat{Z} = \arg\max_Z \log p_{Z,Y}(Z, Y; \hat{V})$ with covariance

$$\left(\frac{d^2 \log p_{Z,Y}(\hat{Z}, Y; V)}{dZ^2} \right)^{-1}$$

Example with simulated data



Simulation



Estimation

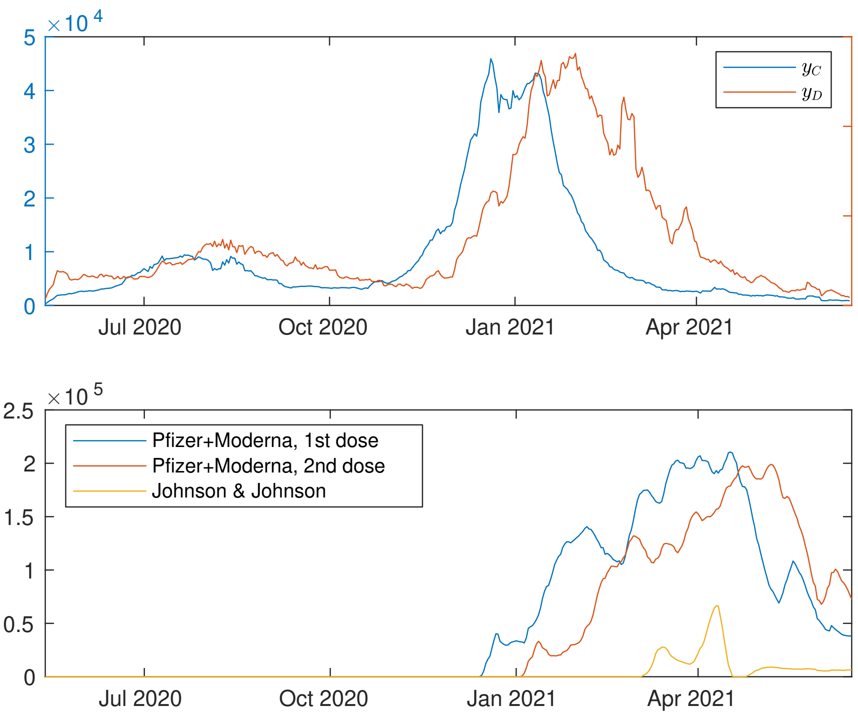
<u>Legend:</u>

S = Susceptible
I = Infected
R = Removed
N_0= population

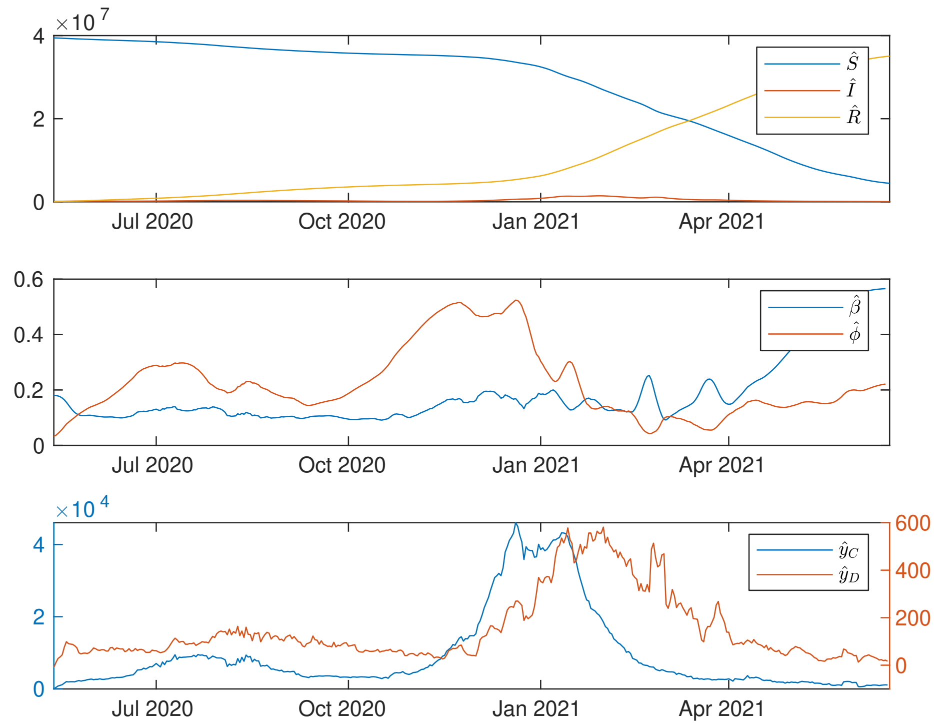
β= infection rate
ϕ= new cases report rate
ψ= vaccine

y_C= number of cases
y_D= number of deaths

Example with data from California



Data



Estimation

Legend:

S = Susceptible
I = Infected
R = Removed
N_0= population

β= infection rate
ϕ= new cases report rate
ψ= vaccine

y_C= number of cases
y_D= number of deaths

Vaccination strategies

Optimal vaccination

If we can estimate current state we can design optimal vaccination strategies!
We model this as an optimization problem with constraints

Cost function: $J = \sum_{t=1}^{P} I(t)$ → Possible interpretations:
-Minimize total number of simultaneous infected people.
-Equivalent to minimize ωJ i.e. total # deaths
-Minimize economic impact of infected not working

Constraints:

Vaccine supply constraint

$$\sum_{s=1}^{t} \sum_{j=1}^{m_i} \psi_{ij}(s) \leq \sum_{s=1}^{t} A_i(s), \quad \forall i \in \{1, \ldots, M\}$$

#newly available doses on day s

M different vaccines m_i doses each

Healthcare sys. capacity

$$\sum_{i=1}^{M} \sum_{j=1}^{m_i} \psi_{ij}(t) \leq B(t)$$

#doses nurses, doctors,..., can administer every day

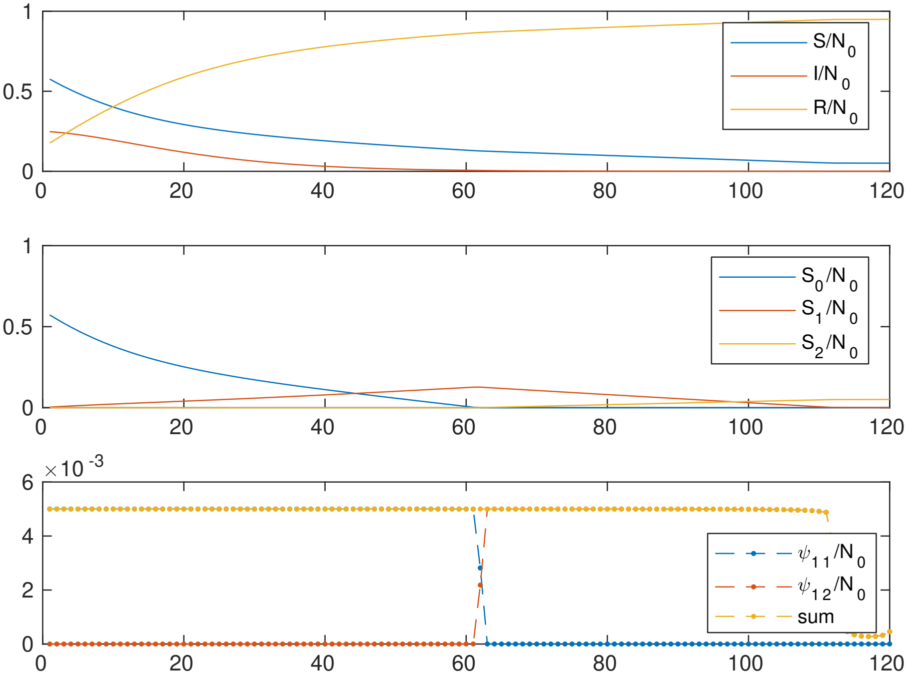
Interval between doses

$$\sum_{s=1}^{t} \psi_{i(j+1)}(s) \leq \sum_{s=1}^{t-\tau_{ij}} \psi_{ij}(s),$$

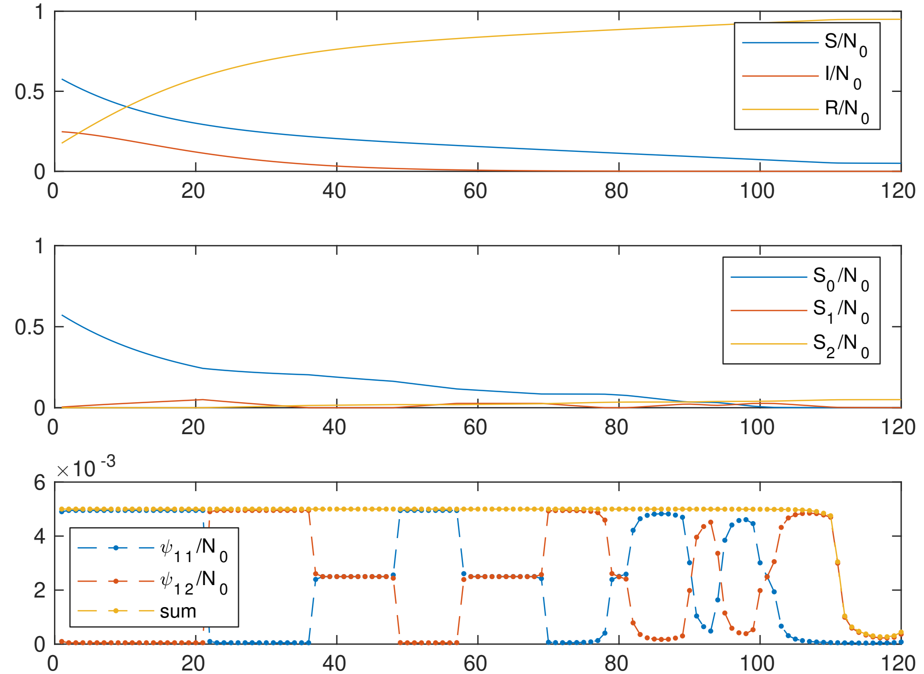
$$\forall i \in \{1, \ldots, M\}, j \in \{1, \ldots, m_i - 1\}$$

#days between doses

When to give the second dose?



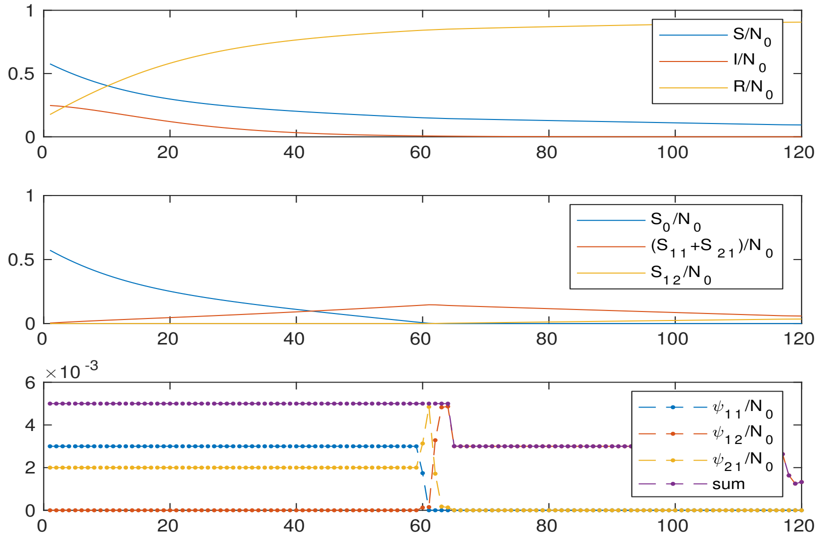
$\theta_{11} = 0.5,\ \theta_{12} = 0.3$



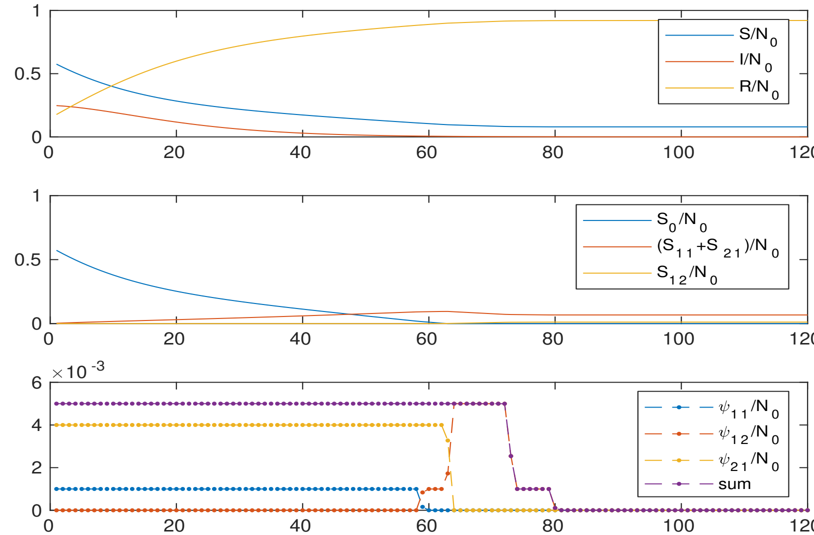
$\theta_{11} = 0.39,\ \theta_{12} = 0.41$

Total efficacy of first + second dose: $\theta_{11} + \theta_{12} = 0.8$

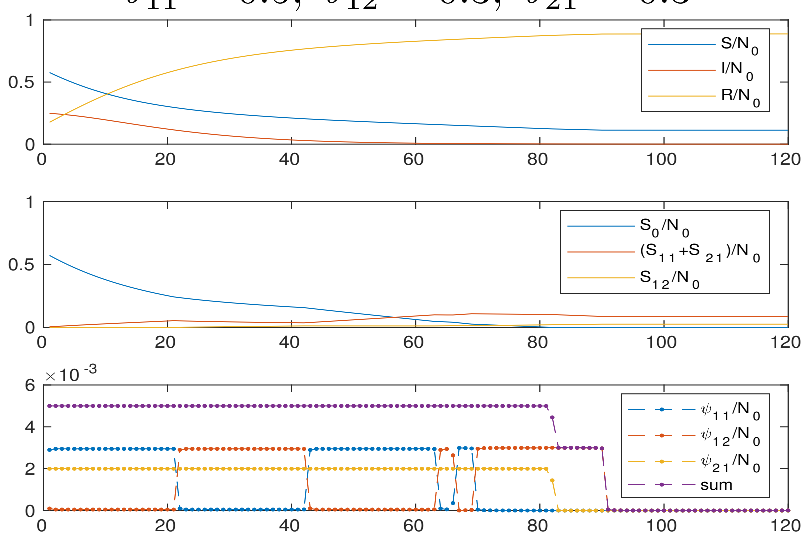
Balancing between availability and efficacy



$$\theta_{11} = 0.5,\ \theta_{12} = 0.3,\ \theta_{21} = 0.3$$



$$\theta_{11} = 0.5,\ \theta_{12} = 0.3,\ \theta_{21} = 0.65$$



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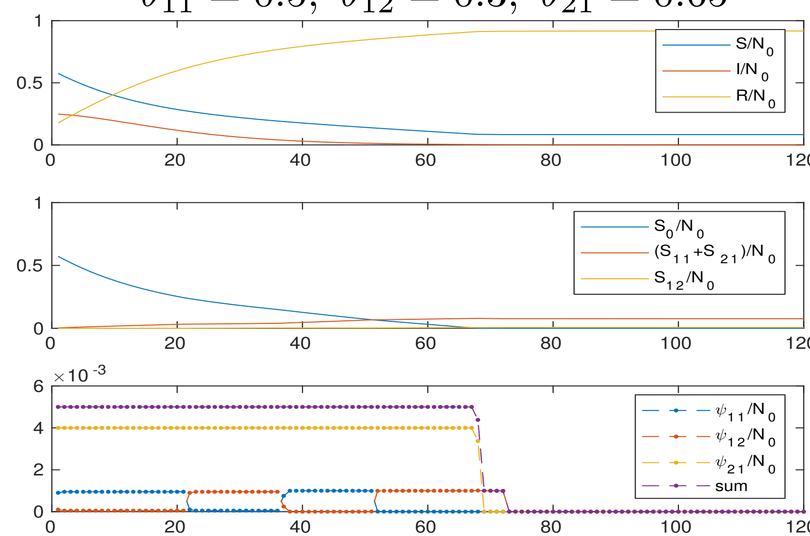

$$\theta_{11} = 0.39,\ \theta_{12} = 0.41,\ \theta_{21} = 0.65$$

Conclusion

Conclusion

- Expanded on SIR to construct model with vaccination, stochastic disturbances and time varying parameters
- Including vaccination renders the model identifiable
- Results applied in California seems to indicate much larger infection numbers than reported
- Model can be used to design vaccination strategies
- Optimal vaccination policies depend on proportion between efficacy

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Ending of A Tale of Two Cities by Charles Dickens:
I see a beautiful city and a brilliant people rising from this abyss, and, in their struggles to be truly free, in their triumphs and defeats, through long years to come, I see the evil of this time and of the previous time of which this is the natural birth, gradually making expiation for itself and wearing out.