Modeling mitigation scenarios and the role of behavior on the shape of the epidemic curve.

Jorge X. Velasco-Hernandez
Instituto de Matematicas UNAM
Unidad Juriquilla

November 25, 2020

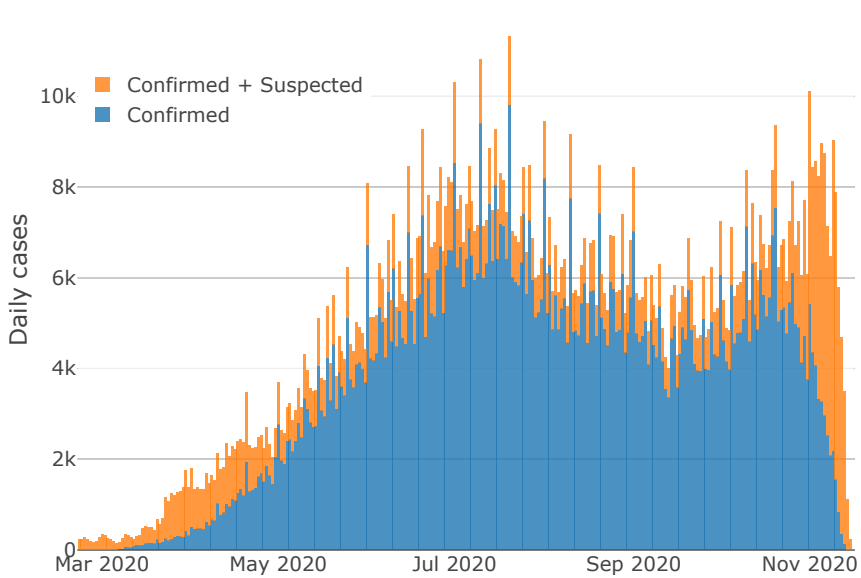
COVID-19 in Mexico

- Mexico confirmed its first case of the novel coronavirus pandemic (COVID-19) on February 28^{th}, 2020.
- On March 23^{rd} and March 30^{th}, 2020, the Mexican Federal government implemented social distancing measures to mitigate the COVID-19 epidemic.
- On June 1^{st}, 2020, the government partially lifted mitigation restrictions in some Mexican states.

The data

COVID-19 data available for Mexico can be found in [1].

- Number of cases
- Number of deaths
- Characteristics of patients: sex, age, job, etc.
- Symptoms
- Comorbidity



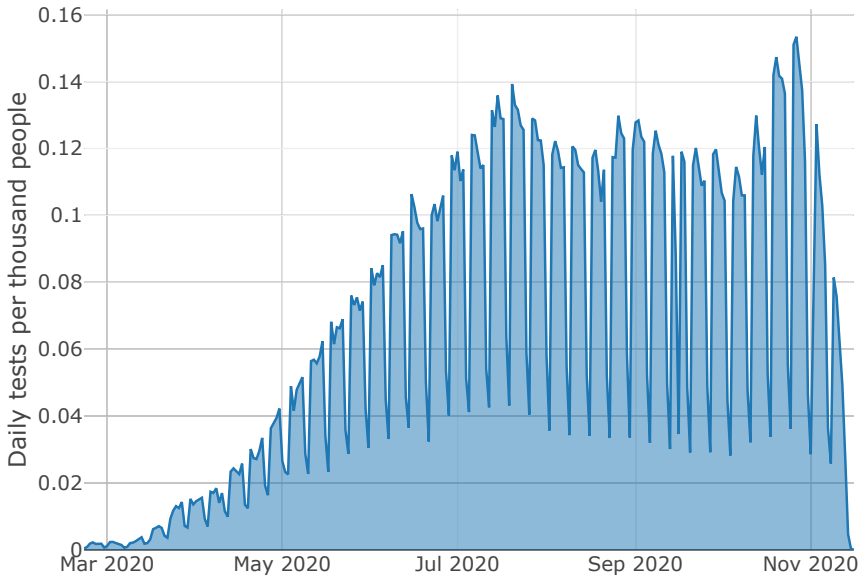
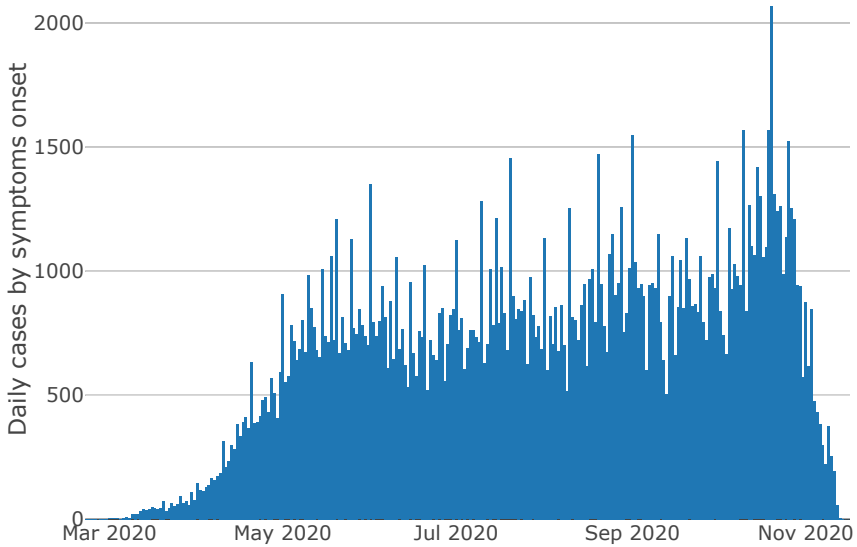


Figure: Total COVID-19 a) reported cases and b) tests per thousand people in Mexico from February 22, 2020 to November 16, 2020.



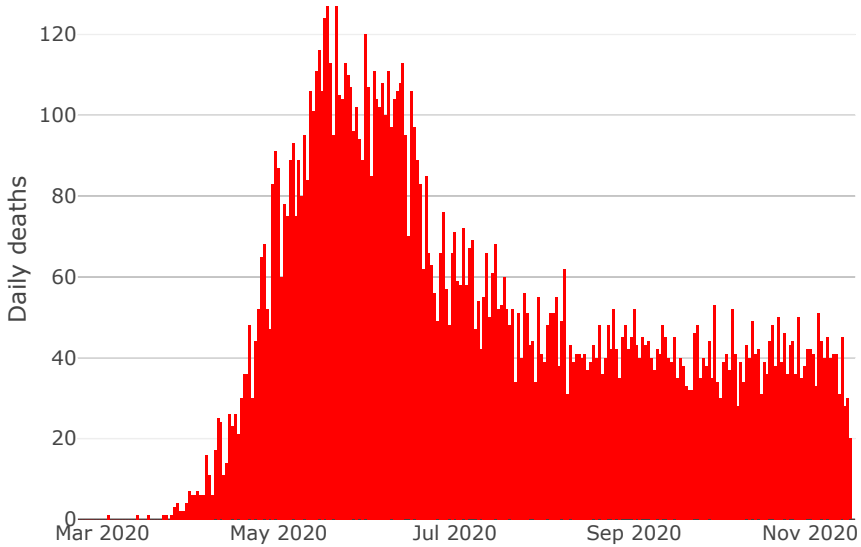


Figure: Daily cases by symptoms onset (blue bars) and daily deaths (red bars) in Mexico City from February 22 to September 5, 2020. Observe in both graphs the marked tendency to remain in a plateau. In the case of the incidence, this behavior is observed right after lockdown termination; in the case of deaths, the plateau occurs until early August after several weeks since the start of the partial reopening of the economy.

R_0 estimates

	Symptoms onset			Hospital registration			Official confirmation		
Method	Lower	Mean	Upper	Lower	Mean	Upper	Lower	Mean	Upper
Exponential growth	1.82	1.88	1.95	2.06	2.17	2.29	2.54	2.80	3.10
Maximum likelihood	1.59	1.70	1.82	1.61	1.77	1.93	2.02	2.35	2.71

Table: Estimates of the basic reproduction number for Mexico (country) using data from February 29 to March 23, 2020. Mean estimate and 95% confidence intervals are reported for three different time series: daily cases by symptoms onset, daily cases by date of hospital registration and daily cases by official confirmation. Estimates were obtained using the "R0" package [2].

R_t estimates

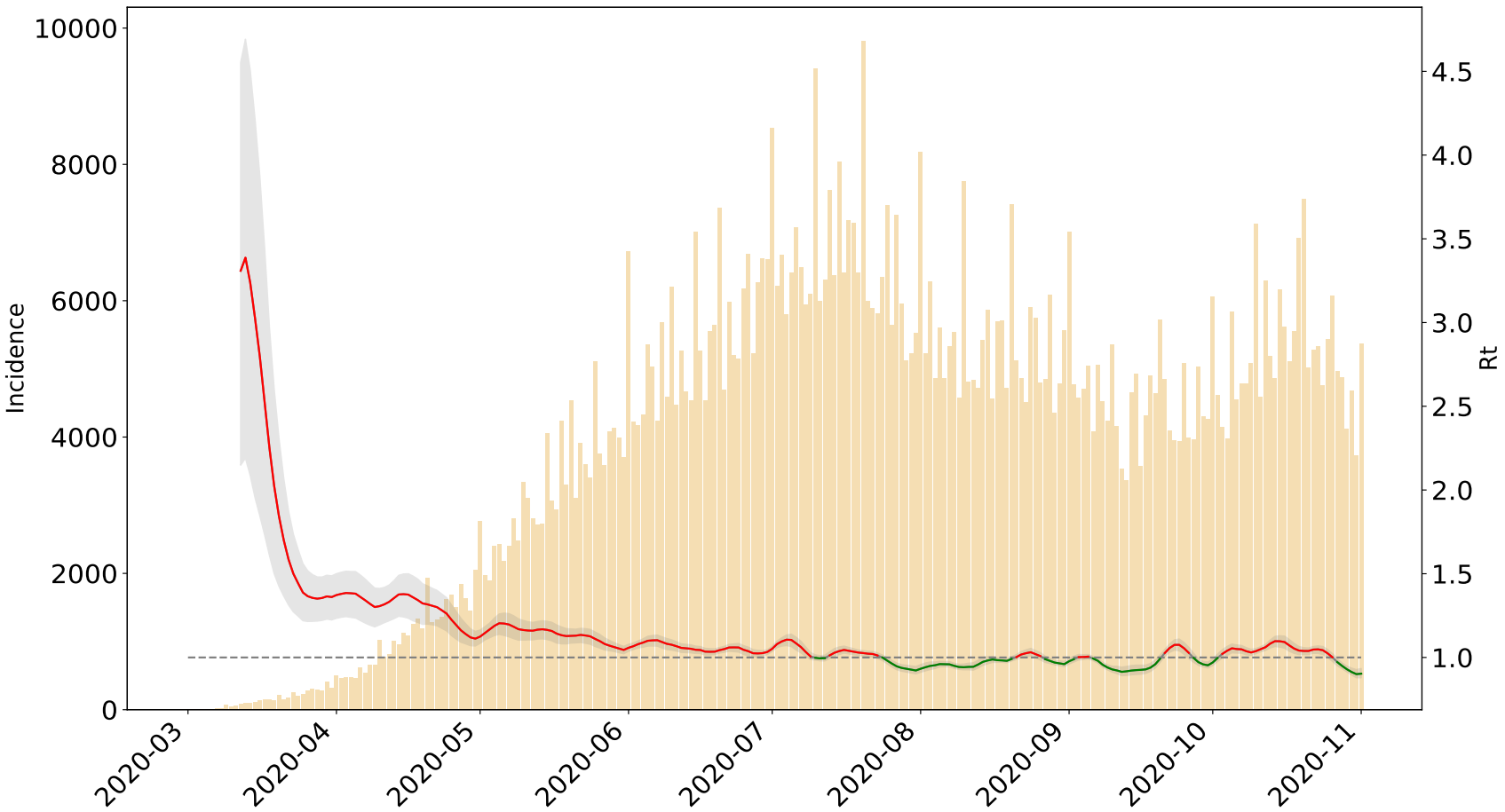


Figure: Instantaneous reproduction number R_t for Mexico from March 13th, 2020 to November 1st, 2020. A median serial interval of 4.7 days was used following the study presented in [3].

Measuring the effect of mitigation measures

We fit data from Mexico City using Richards model for two different periods:

- from February 29 to March 22, 2020;
- from March 23 to April 30, 2020.

This will provide a rough estimation of the mitigation measures effectiveness.

Measuring the effect of mitigation measures

	February 29 - March 22			March 23 - April 30		
	Lower	Median	Upper	Lower	Median	Upper
a	0.017	0.103	1.757	0.012	0.324	1.125
r	0.193	0.455	1.889	0.092	0.127	1.458
K	934	57062	420711	21214	65782	404054

Table: Richards model parameter median estimates and 95% posterior probability intervals before and after March 23, 2020 for Mexico City. Here, r is the growth rate, K is the final size of the outbreak.

Parameter inference

- A Bayesian approach was used to estimate the parameters of the growth models previously discussed.
- The idea is to find all the sets of parameters that create models *close enough* to the data.
- The distance between the model and the data is measured with a probability distribution.

Posterior distribution

Inference is done by exploring the posterior distribution of the parameters of interest.

$$\pi(\boldsymbol{\theta}|y_1, \ldots, y_n) \propto \pi(y_1, \ldots, y_n|\boldsymbol{\theta})\pi(\boldsymbol{\theta}),$$

The likelihood function tell us how plausible is to observe the current data for a given set of parameters. We use a Negative Binomial model with dispersion parameter s.

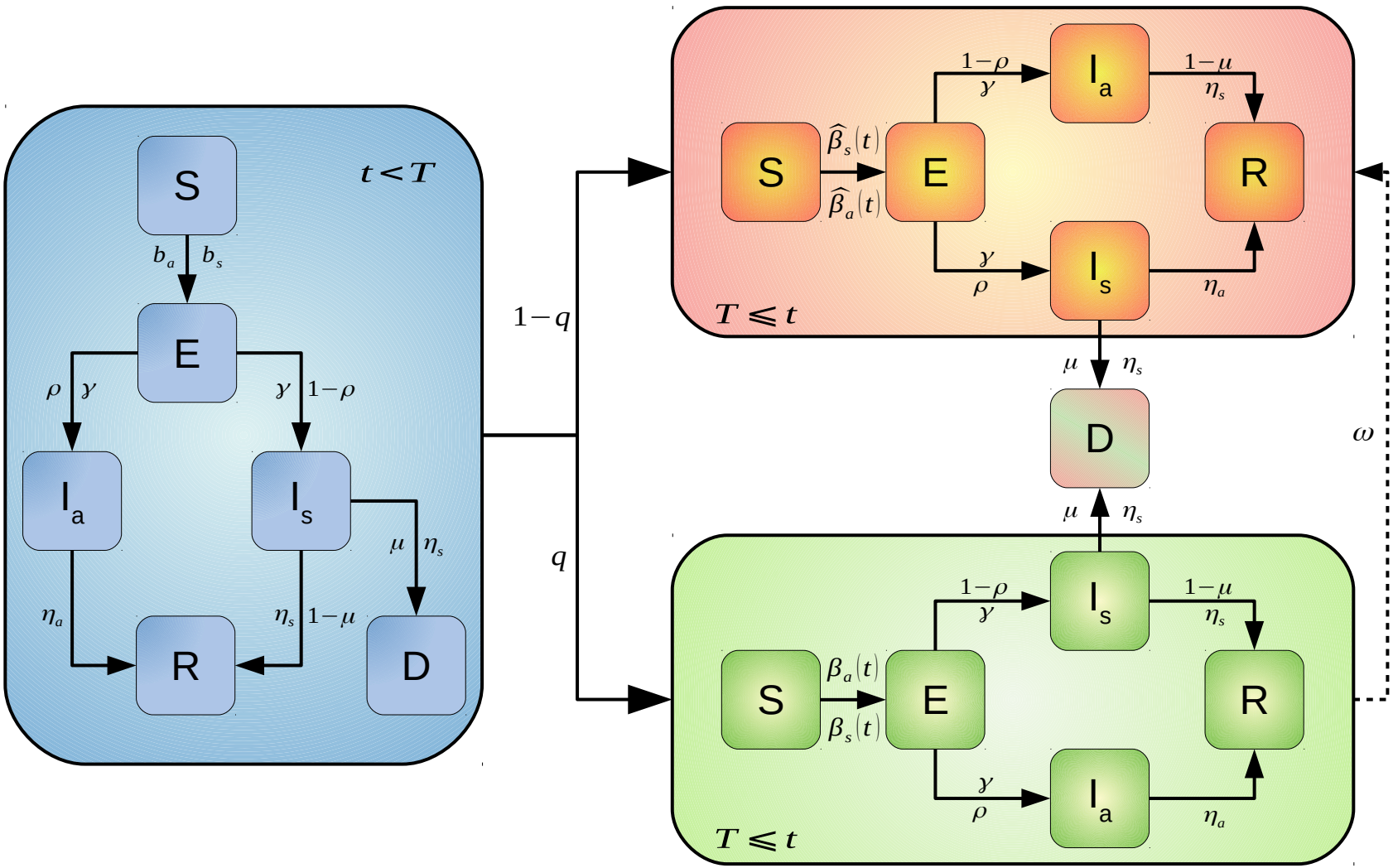
$$\pi(y_1, \ldots, y_n|\boldsymbol{\theta}) = \prod_{j=1}^{n} \frac{\Gamma(y_j + s)}{\Gamma(y_j + 1)\Gamma(s)} \left(\frac{s}{s + \mu_j}\right)^s \left(\frac{\mu_j}{s + \mu_j}\right)^{y_j}. \quad (1)$$

Here, μ_j is the solution of the model (GLM, Richards, Tsallis), which depends on $\boldsymbol{\theta}$.
The joint prior distribution $\pi(\boldsymbol{\theta})$ contains all the information that we have regarding the parameters.

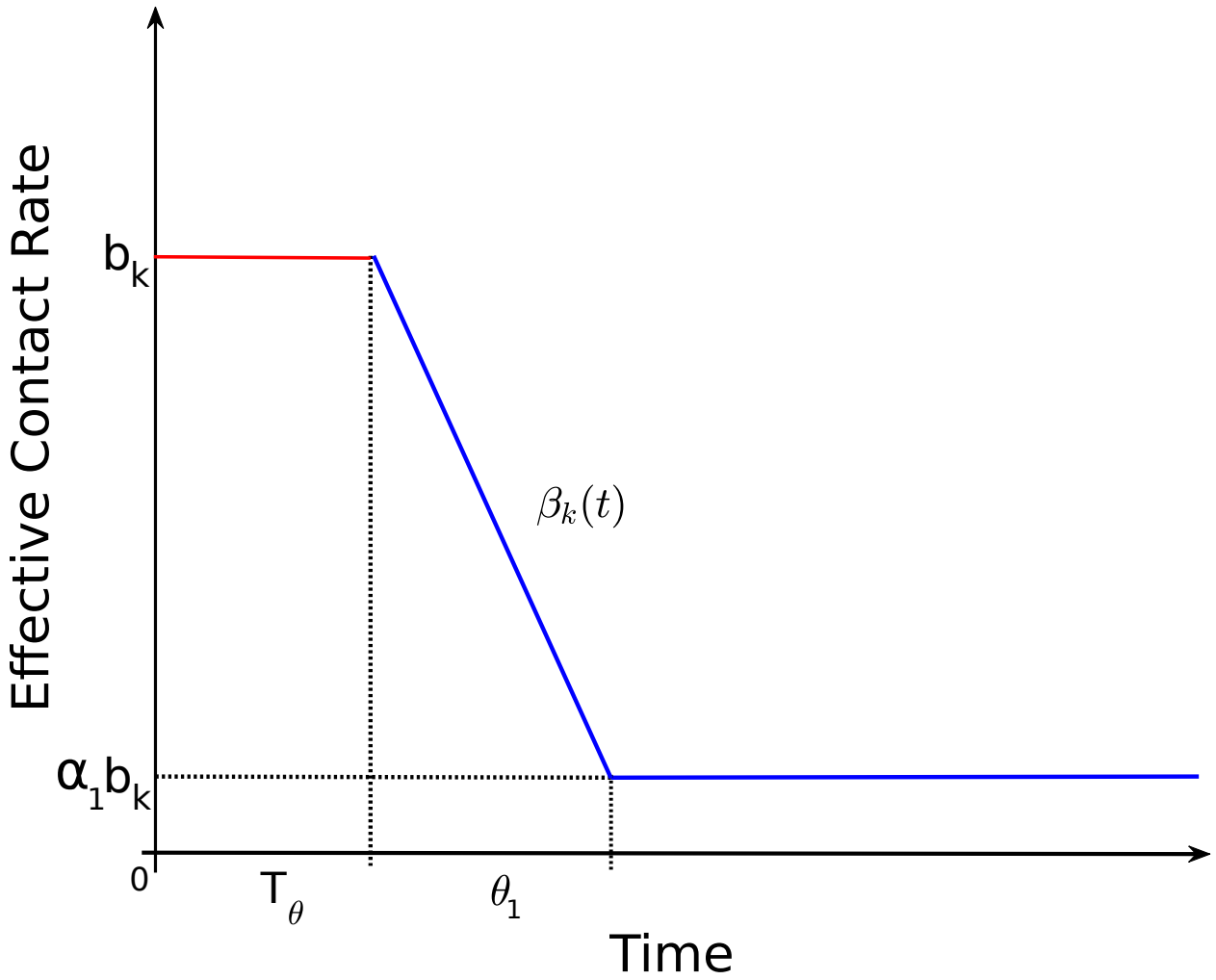
Modeling nonpharmaceutical interventions

- A modification of the Kermack-McKendrick model was used to explore the transmission dynamics under suspension of non-essential activities in Mexico City [5].
- We consider that once the mitigation measures are implemented at day T_θ, certain fraction of the population will adhere to those directives, while another proportion will not.
- We incorporate both symptomatic and asymptomatic carriers, each class with a different and variable contact rate.

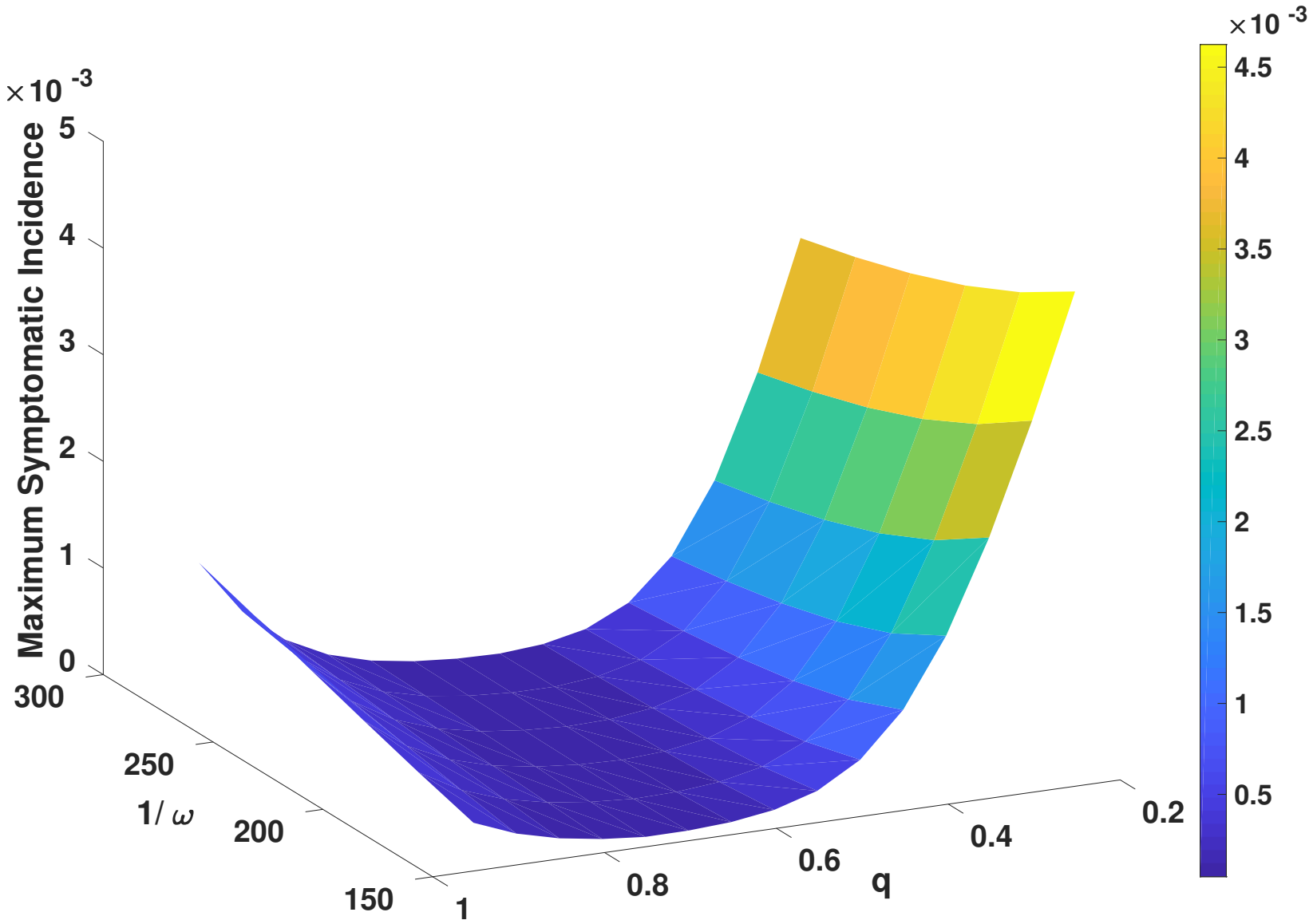
Model 1


S
$t < T$
b_a
b_s
E
ρ
γ
γ
$1-\rho$
I_a
I_s
μ
η_s
η_a
η_s
$1-\mu$
R
D
$1-q$
q
S
$\widehat{\beta}_s(t)$
$\widehat{\beta}_a(t)$
E
$1-\rho$
γ
I_a
$1-\mu$
η_s
R
γ
ρ
I_s
η_a
$T \leqslant t$
μ
η_s
D
ω
μ
η_s
S
$\beta_a(t)$
$\beta_s(t)$
E
$1-\rho$
γ
I_s
$1-\mu$
η_s
R
γ
ρ
I_a
η_a
$T \leqslant t$

Contact rate



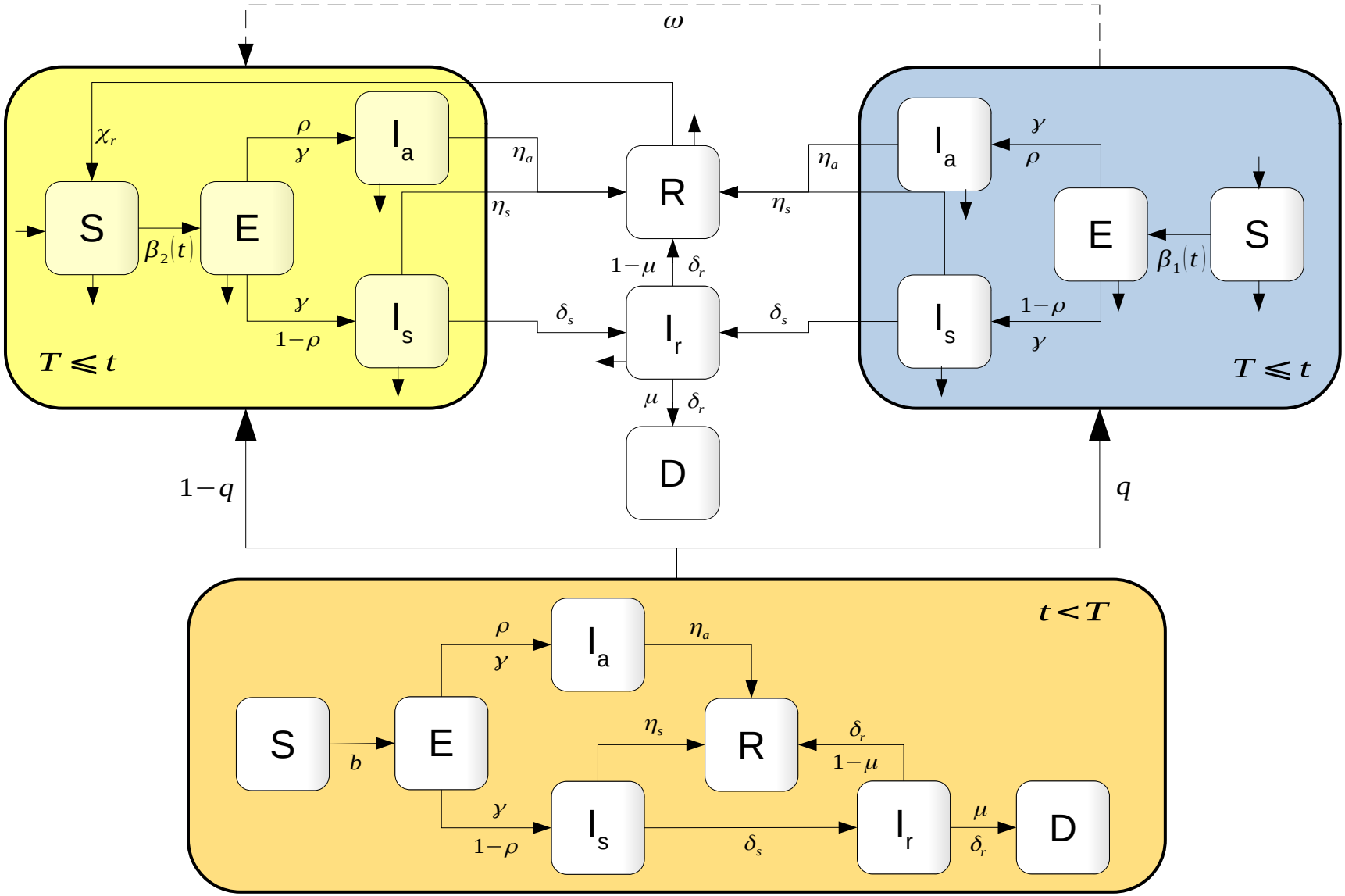
Trade off between lockdown and compliance



Short duration superspreading events

- Now we analyze the effect of short term superspreading events that occur during the confinement period [6].
- It is expected that an increase in population mobility during a few days weakens the strength of the NPIs.

Model 2



Model 2 before mitigation measures

$$
\begin{aligned}
S' &= -b\left(I_s + I_a\right)\frac{S}{N^*} \\
E' &= b\left(I_s + I_a\right)\frac{S}{N^*} - \gamma E \\
{I_a}' &= \rho\gamma E - \eta_a I_a \\
{I_s}' &= (1-\rho)\gamma E - \left(\eta_s + \delta_s\right) I_s \\
{I_r}' &= \delta_s I_s - \delta_r I_r, \\
R' &= \eta_a I_a + \eta_s I_s + (1-\mu)\,\delta_r I_r \\
D' &= \mu\delta_r I_r
\end{aligned}
\tag{2}
$$

Model 2 after mitigation measures

$$
\begin{aligned}
S_i' &= \mu_h \left(S_i + E_i + I_{ai} + I_{si}\right) + \left[(2-i)\, q + (i-1)\,(1-q)\right] \mu_h \left(I_r + R\right) \\
&\quad - \beta_i(t) \left(I_{si} + I_{ai}\right) \frac{S_i}{N^*} + (-1)^i \omega(t) S_1 - \mu_h S_i + (1-i)^i \, \chi_r R \\
E_i' &= \beta_i(t) \left(I_{si} + I_{ai}\right) \frac{S_i}{N^*} - \gamma E_i + (-1)^i \omega(t) E_1 - \mu_h E_i \\
{I_{ai}}' &= \rho\gamma E_i - \eta_a I_{ai} + (-1)^i \omega(t) I_{a1} - \mu_h I_{ai} \\
{I_{si}}' &= (1-\rho)\gamma E_i - \left(\eta_s + \delta_s\right) I_{si} + (-1)^i \omega(t) I_{s1} - \mu_h I_{si} \\
{I_r}' &= \delta_s \left(I_{s1} + I_{s2}\right) - \delta_r I_r - \mu_h I_r \\
R' &= \eta_a \left(I_{a1} + I_{a2}\right) + \eta_s \left(I_{s1} + I_{s2}\right) + (1-\mu)\, \delta_r I_r - \mu_h R - \chi_r R \\
D' &= \mu \delta_r I_r
\end{aligned}
\tag{3}
$$

Model parameters

Parameters	Definition
b	Effective contact rate
γ^{-1}	Incubation period
ρ	Proportion of individuals that become asymptomatic
η_a^{-1}	Average recovery time for asymptomatic
η_s^{-1}	Average recovery time for symptomatic
δ_s^{-1}	Average time until medical attention
δ_r^{-1}	Average time until recovery or death for a reported case
μ	Proportion of reported individuals that die

Table: Parameters for system (2).

Modeling short duration superspreading events

Atypical increases in mobility are modeled as follows:

- it is assumed that the increase in mobility lasts only for a period of τ days;
- the change in mobility on these days is reflected by increasing the compliance-failure rate ω_0 by a factor k;
- contact rates remain as in Model 1

$$\beta_i(t) = \begin{cases} b - \frac{(1-q_i)}{\theta} b\,(t - T)\,, & T \leq t < T + \theta, \\ q_i b, & t \geq T + \theta. \end{cases} \tag{4}$$

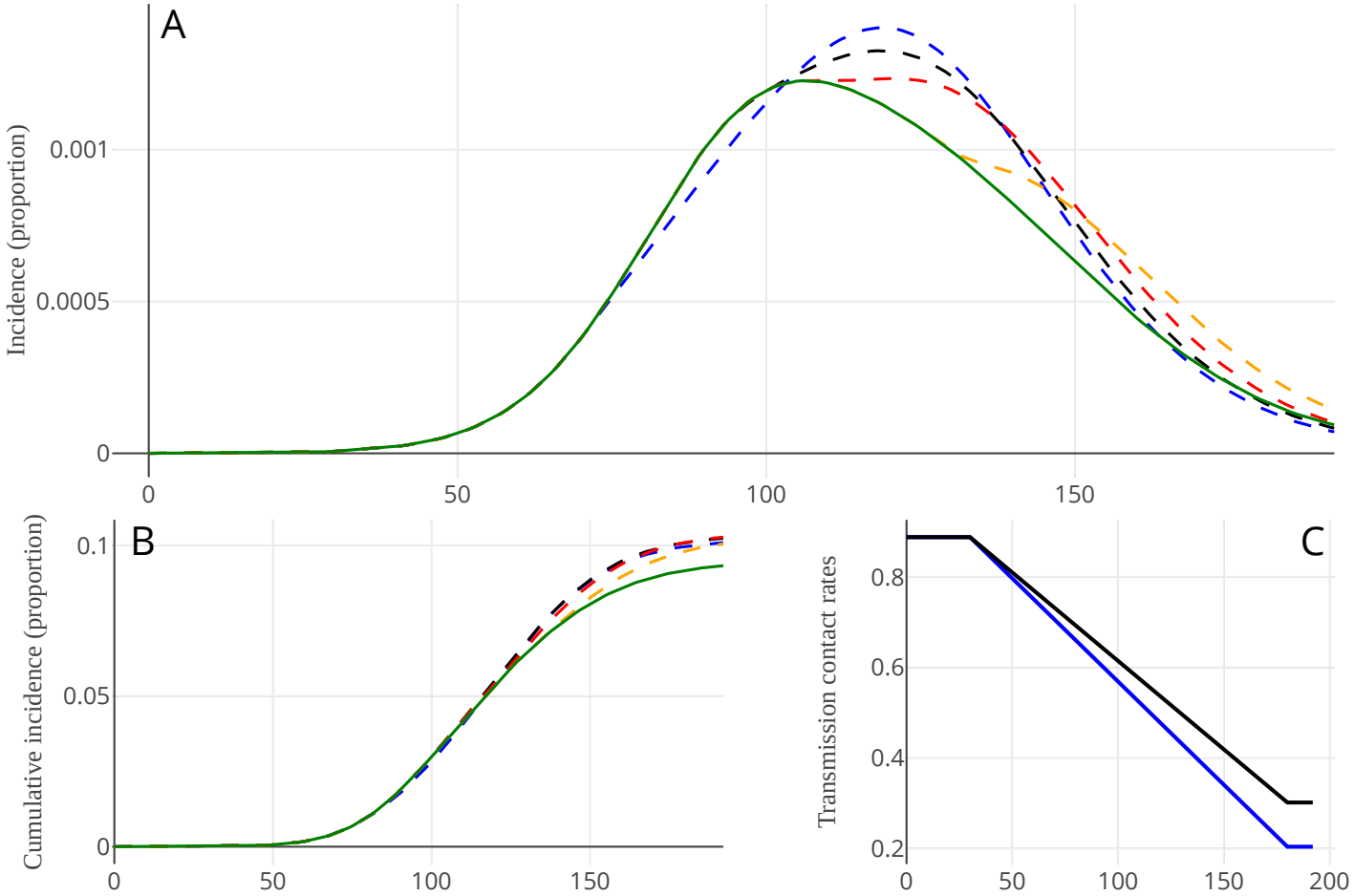


Figure: The increase in mobility is given by $10\omega_0$ ($\omega_0 = 0.005$). The green line is the baseline epidemic curve. Blue, black, red, and yellow discontinuous lines illustrate the scenarios when the mobility event starts four weeks before, a week before, a week after, and four weeks after peak incidence, respectively.

Atypical superspreading events in Mexico City

- There are two important holidays (in terms of population mobility) within the period of confinement: April 30^{th} (children's day), and May 10^{th} (mother's day).
- We use one period of increased mobility: April 29^{th} - May 10^{th}.
- We consider scenarios where mobility increases 1.5, 3, 4.5, and 6 times with ($\omega_0 = 0.005$).

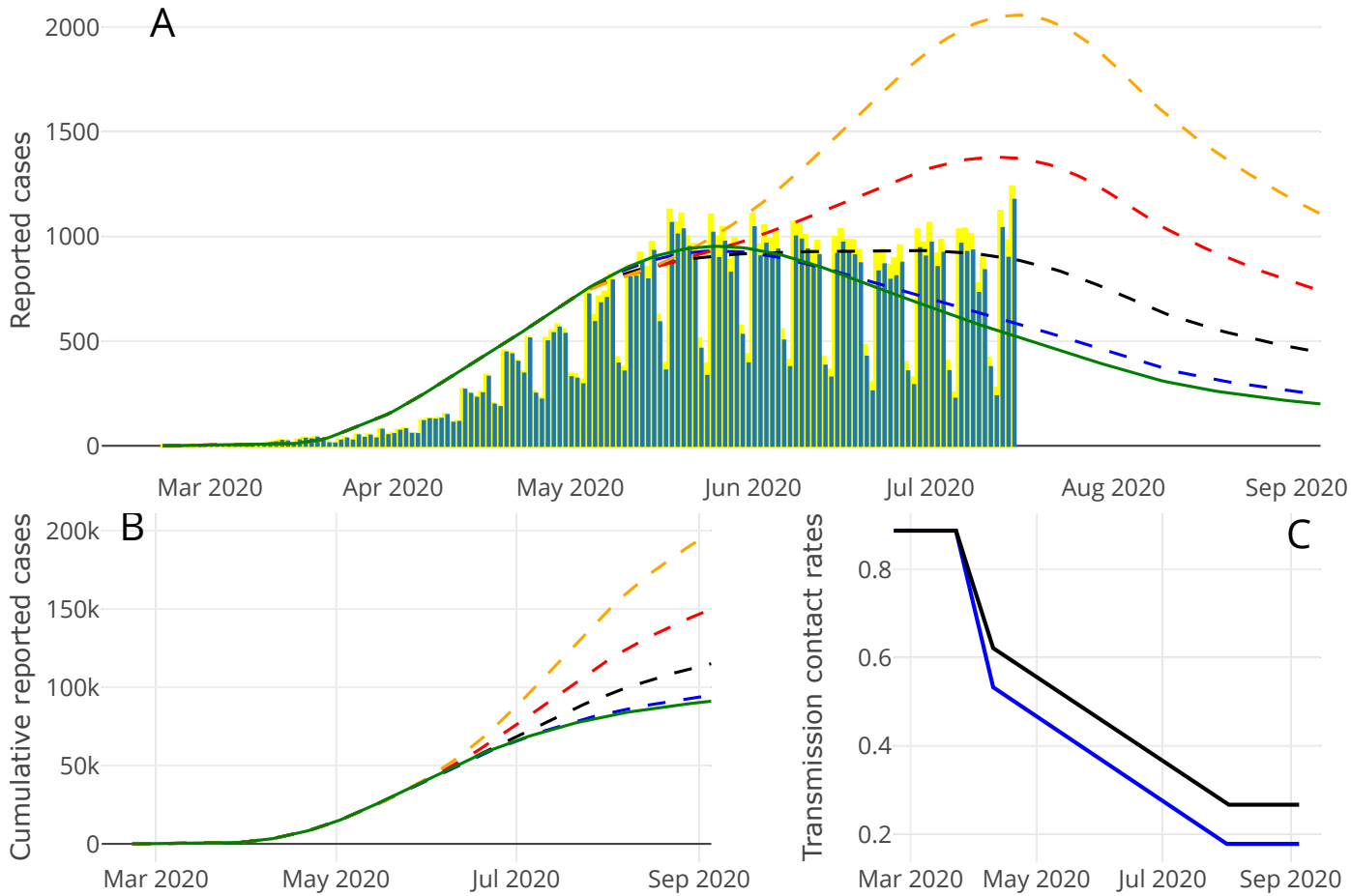


Figure: Impact of different increases in mobility on the epidemic curve of Mexico City. Blue bars shows daily confirmed cases by hospital registration while yellow bars show suspected cases from February 22, 2020 to July 15, 2020.

Constant changes in transmission dynamics

- Due to the interventions of the government and the behavioral of the population, the transmission dynamics of COVID-19 are constantly changing.
- In order to correctly describe and predict the epidemic curve dynamics, those changes must be considered.

Adding more atypical events

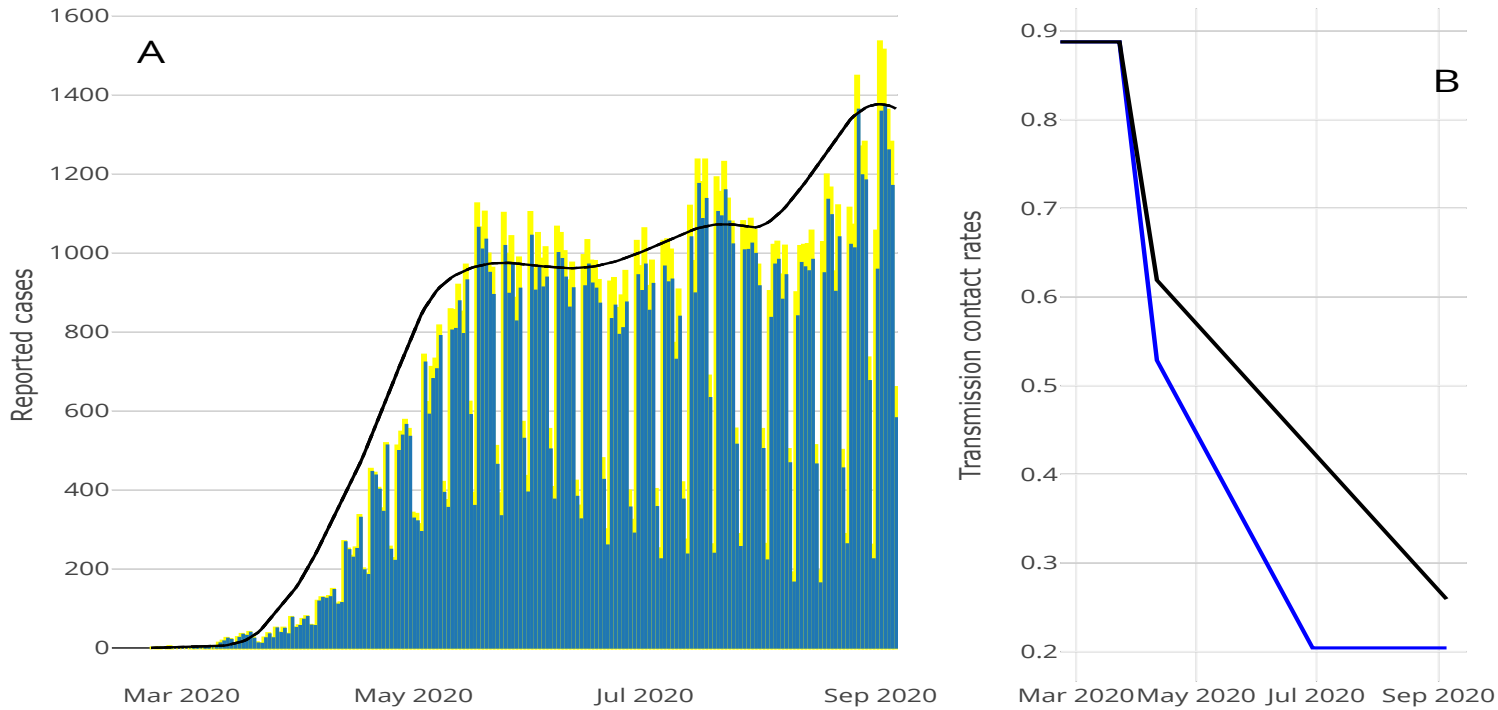


Figure: Mexico City data and model projected trajectory from February 22, 2020 to September 5, 2020. Two periods of high mobility are considered: i) from April 29, 2020, to May 10, 2020 with a failure rate of $(6.5\omega_0)$, and ii) from July 26, 2020, to August 19, 2020 with a failure rate of $(11\omega_0)$.

We need to anticipate...

In order to create better predictions we need to anticipate the changes on the COIVD-19 trnsmission dynamics.

Long-term scenarios with one year immunity

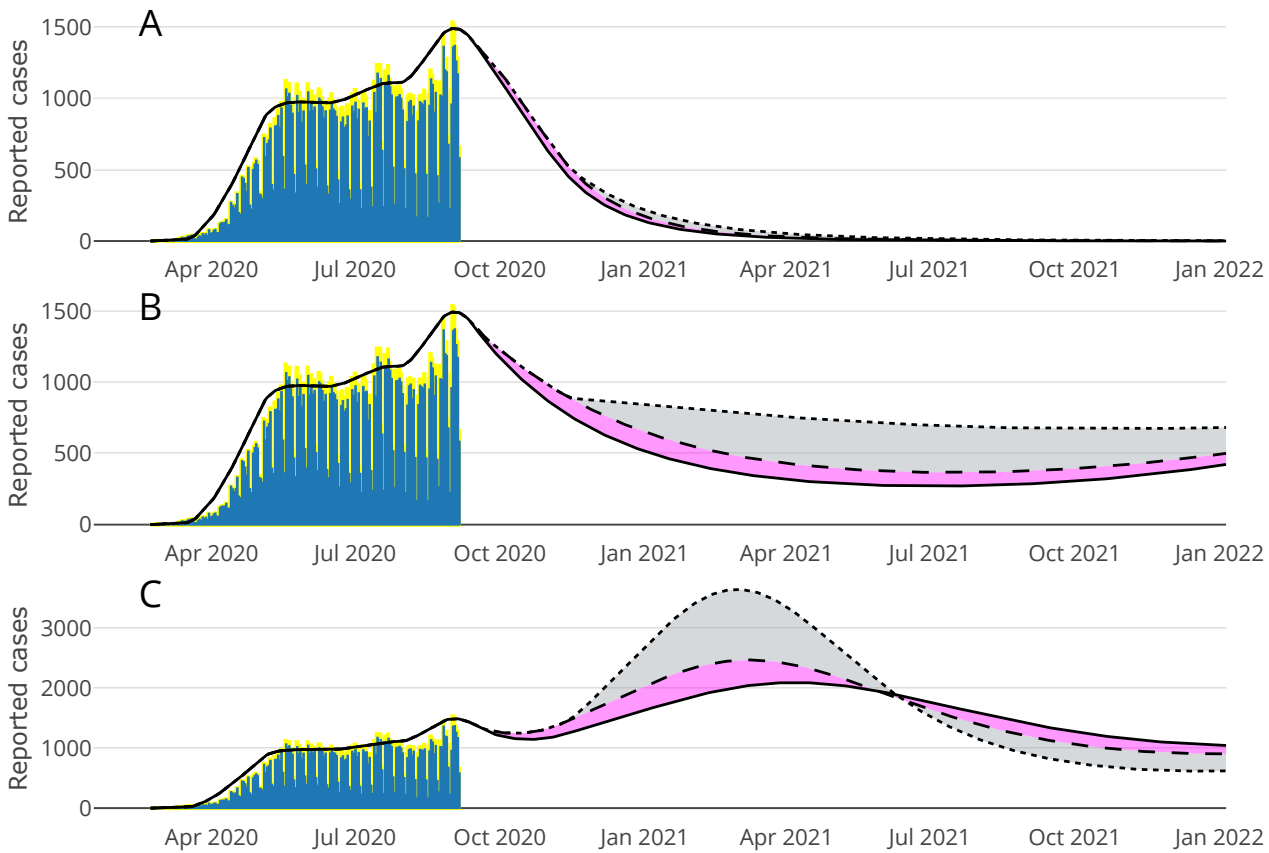


Figure: Daily reported cases when considering temporal immunity equal to twelve months. Effective transmission contact rates are: A) decreased 5%, B) held constant, C) increased 5%.

Long-term scenarios with six months immunity

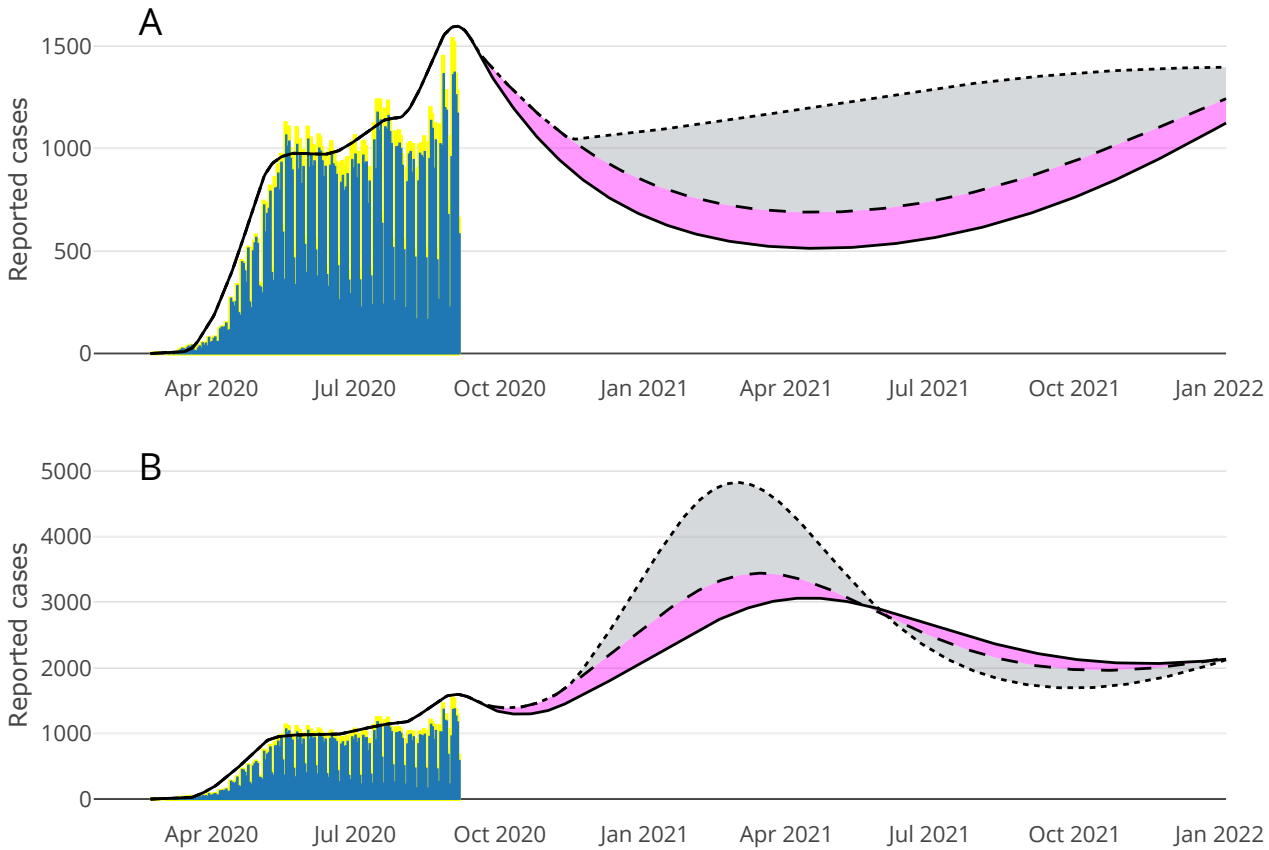


Figure: Daily reported cases when considering temporal immunity equal to six months. Effective transmission contact rates are: A) held constant, B) increased 5%.

Long-term scenarios with 24 months immunity

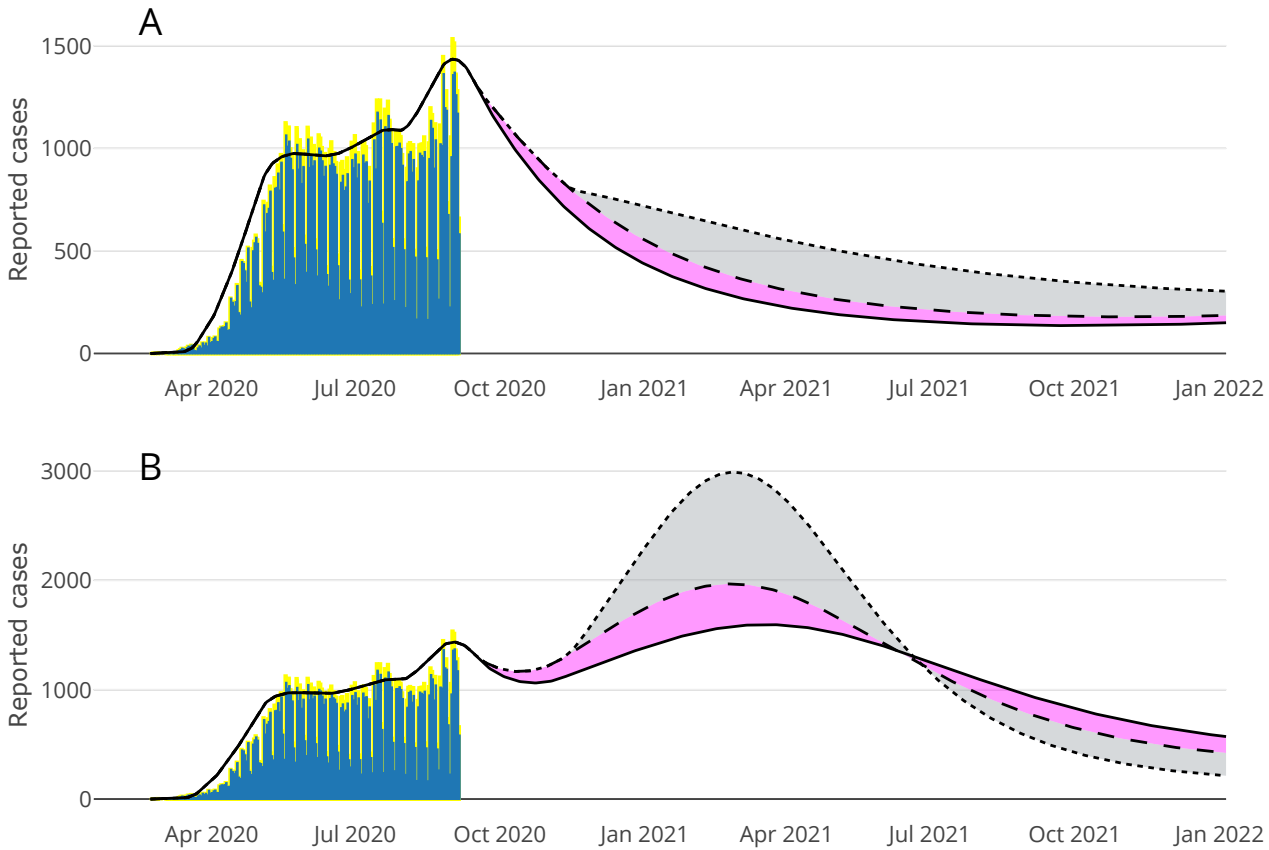


Figure: Daily reported cases when considering temporal immunity equal to 24 months. Effective transmission contact rates are: A) held constant, B) increased 5%.

Best projection

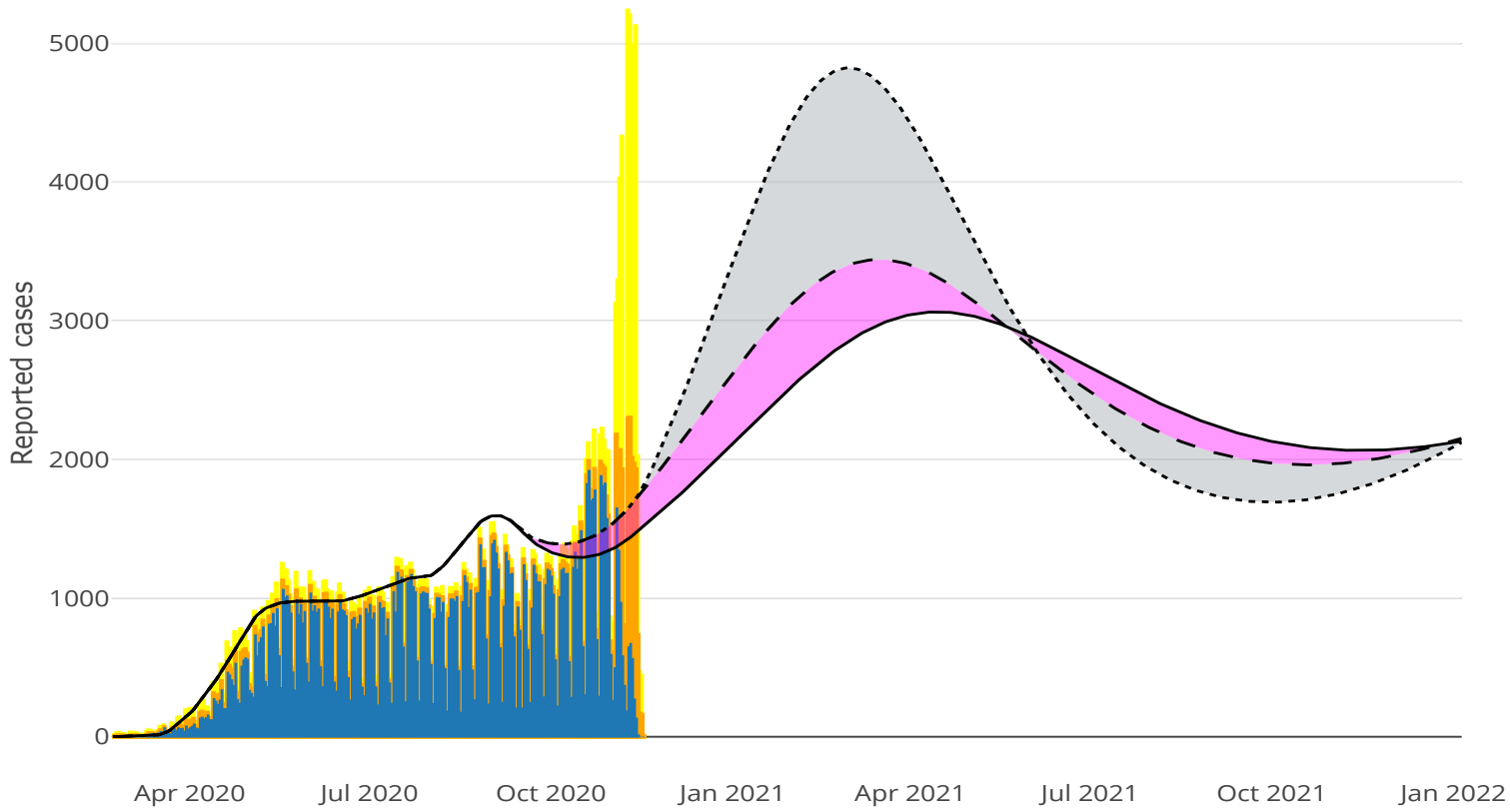


Figure: Daily reported cases when considering temporal immunity equal to six months. Effective transmission contact rates are: A) held constant, B) increased 5%.

Concluding remarks

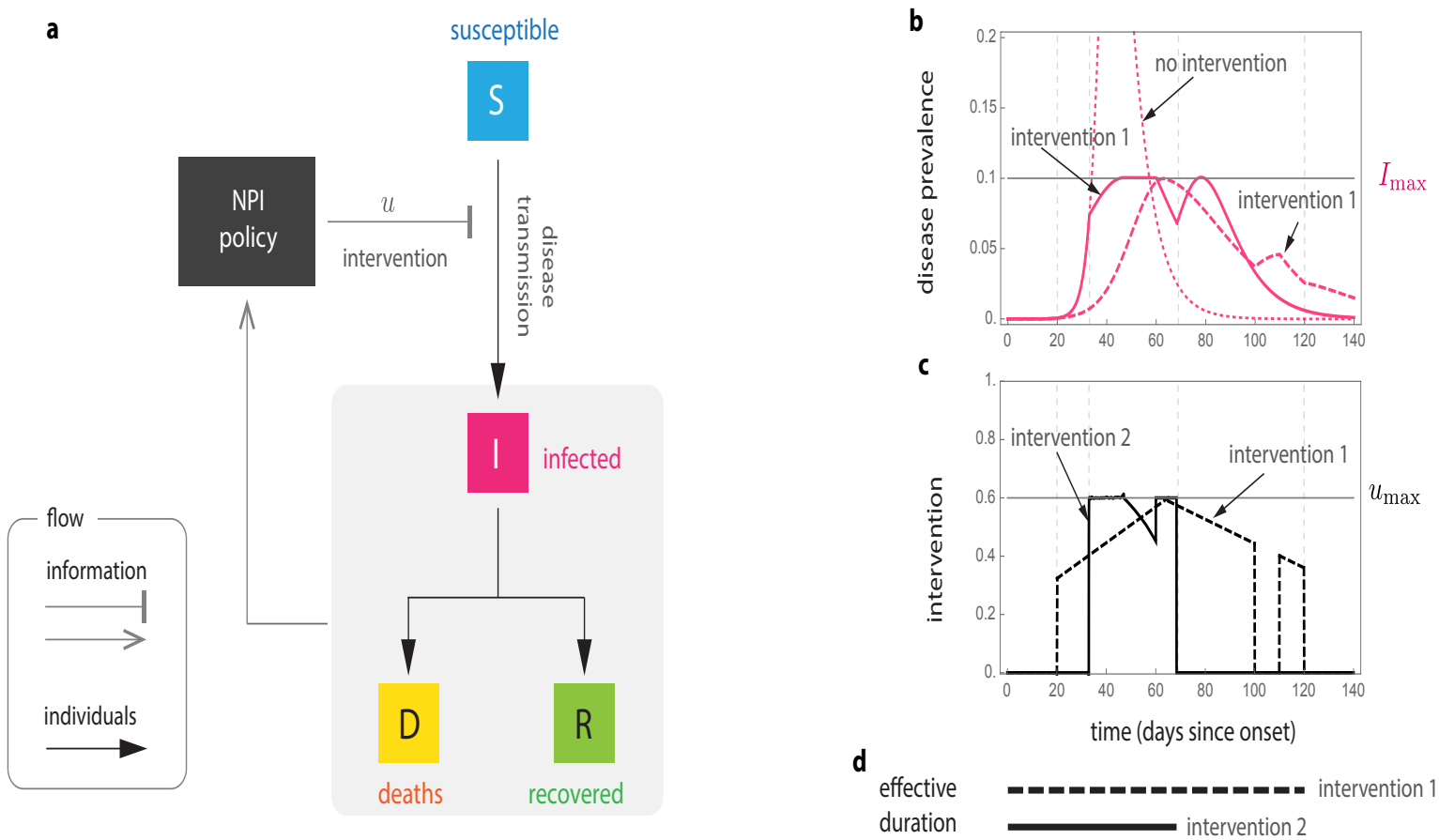


Figure: Optimal design of mitigation strategies: lockdown duration.

BOX 1. Optimal NPIs for the Susceptible-Infected-Removed (SIR) model.

The SIR model with interventions $u(t) \in [0, u_{\max}]$ reducing disease transmission takes the form

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -(1-u)\beta\, SI, \quad \frac{\mathrm{d}I}{\mathrm{d}t} = (1-u)\beta\, SI - \gamma I.$$

Here, $S(t)$ and $I(t)$ are the proportion of the population that is susceptible or infected at time $t \geq 0$, respectively. We denote by (S_0, I_0) the initial state at $t = 0$. The parameters of the SIR model are the (effective) *contact rate* $\beta \geq 0$, and the mean *residence time* of infected individuals $\gamma \geq 0$ (in units of day^{-1}). By assuming $S_0 \approx 1$, these two parameters yield the *basic reproduction number* $R_0 = \beta/\gamma$.
We are interested in reaching the *safe zone*

$$\mathcal{S} = \{(S, I) \mid I \leq \Phi_{R_0}(S)\} \ ,$$

where

$$\Phi_R(S) = \begin{cases} I_{\max} & \text{if } S \leq R^{-1}, \\ I_{\max} + R^{-1}\big[\log(RS) + 1 - RS\big] & \text{otherwise.} \end{cases} \tag{2}$$

The safe zone is the largest set with the following property: If, for any given time t_1, the state (S_1, I_1) belongs to $\mathcal{S}$, we can set $u = 0$ henceforth and still have $I(t) \leq I_{\max}$ for all $t \geq t_1$. That is, when $\mathcal{S}$ is reached, we can terminate the intervention with the assurance that a possible rebound in the disease prevalence will not exceed $I_{\max}$.
Our goal is to steer an arbitrary initial state (S_0, I_0) to the safe zone $\mathcal{S}$ in minimal time without violating the constraint $I(t) \leq I_{\max}$. We say that an intervention achieving this goal is an *optimal intervention*.
In Supplementary Note S1, we prove that the existence of an optimal intervention is characterized by the *separating curve* Φ_{R_c} as follows:

(1) An optimal intervention exists if and only if the initial state (S_0, I_0) lies below this separating curve (i.e., $I_0 \leq \Phi_{R_c}(S_0)$).

Above, $R_c := (1 - u_{\max})R_0$ is the *controlled reproduction number*. Moreover:

(2) If it exists, the optimal intervention u^* at the state (S, I) is

$$u^*(S, I) = \begin{cases} 0 & \text{if } (S, I) \in \mathcal{S} \cup \mathcal{W} \\ 1 - 1/(R_c S) & \text{if } I = \Phi_{R_c}(S) \text{ and } S^* < S < R_c^{-1} \\ u_{\max} & \text{otherwise} \end{cases} \tag{3}$$

with

$$\mathcal{W} = \{(S, I) \mid I < \Phi_{R_c}(S),\ S > \Psi(I)\} \ .$$

Above, the curve $S = \Psi(I)$ is defined in Supplementary Note S1, while S^* denotes the intersection of $S = \Psi(I)$ and $I = \Phi_{R_c}(S)$.

Figure: Basic criteria for the existence of an optimal strategy.

What is next?

- Analysis of R_t estimation
- Superinfection models (COVID-19 and flu)
- Vaccination models

Join work with:

- Manuel A. Acuña-Zegarra
  Departamento de Matematicas, Universidad de Sonora
- Mario Santana-Cibiran
  CONACyT-Instituto de Matematicas UNAM
- Marco Tulio Angulo
  CONACyT-Instituto de Matematicas UNAM
- Ruth Corona-Moreno
  Posgrado UNAM
- Nancy Gonzalez-Morales
  Posgrado UNAM

Thank you

- Gobierno de la Ciudad de México, "Datos abiertos.." `https://datos.cdmx.gob.mx/explore/dataset/base-covid-sinave/table/`, 2020.
- T. Obadia, R. Haneef, and P. Boëlle, "The R0 package: a toolbox to estimate reproduction numbers for epidemic outbreaks," *BMC Medical Informatics and Decision Making*, vol. 12, p. 147, 2012.
- H. Nishiura, N. M. Linton, and A. R. Akhmetzhanov, "Serial interval of novel coronavirus (COVID-19) infections," *International Journal of Infectious Diseases*, vol. 93, pp. 284–286, apr 2020.
- C. Tsallis and U. Tirnakli, "Predicting COVID-19 Peaks Around the World," *Frontiers in Physics*, vol. 8, p. 217, 2020.
- M. A. Acuña-Zegarra, M. Santana-Cibrian, and J. X. Velasco-Hernandez, "Modeling behavioral change and COVID-19 containment in Mexico: A trade-off between lockdown and compliance," *Mathematical biosciences*, vol. 325, p. 108370, 2020.


M. Santana-Cibrian, M. A. Acuña-Zegarra, and J. X. Velasco-Hernandez, "Lifting mobility restrictions and the effect of superspreading events on the short-term dynamics of COVID-19," *Mathematical Biosciences and Engineering*, vol. 17, no. 5, pp. 6240–6258, 2020.