COVID-19 optimal vaccination policies:

A modeling study on efficacy, natural and vaccine-induced immunity responses,

June 15, 2022

CONACYT-UNISON-ITSON Mathematical biology group

Toy example and classic vaccination OC

To fix ideas:

$$
\begin{aligned}
S'(t) &= -\beta IS \\
I'(t) &= \beta IS - \gamma I \\
R'(t) &= \gamma I \\
&\quad S(0) = S_0, I(0) = I_0, R(0) = 0 \\
&\quad S(t) + I(t) + R(t) = 1
\end{aligned}
$$

“Classic” Vaccination

Toy example and classic vaccination OC

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$$S(t) + I(t) + R(t) = 1$$

“Classic” Vaccination

With vaccination

$$
\begin{aligned}
S'(t) &= -\beta IS - \lambda_V(t) \\
I'(t) &= \beta IS - \gamma I \\
R'(t) &= \gamma I \\
V'(t) &= \lambda_V(t)
\end{aligned}
$$

$$S(0) = S_0, I(0) = I_0,$$

$$R(0) = 0, V(0) = 0$$

$$S(t) + I(t) + R(t) + V(t) = 1$$

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\end{aligned}
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“Classic” Vaccination

$$
\begin{aligned}
S'(t) &= -\beta IS - \lambda_V(x,t) \\
I'(t) &= \beta IS - \gamma I \\
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&x^\top = (S, I, R, V)
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“Classic” Vaccination

Gumel,

Toy example and classic vaccination OC

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$$

$$
\begin{aligned}
S'(t) &= -\beta IS - \color{red}{\lambda_V(x,t)} \\
I'(t) &= \beta IS - \gamma I \\
R'(t) &= \gamma I \\
V'(t) &= \color{red}{\lambda_V(x,t)} \\
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"Classic" Vaccination

Gumel,

$$\lambda_V := \underbrace{\xi}_{cte.} \cdot S(t)$$

Alexander, M. E., Bowman, C., Moghadas, S. M., Summers, R., Gumel, A. B., and Sahai, B. M. (2004). **A vaccination model for transmission dynamics of influenza.** *SIAM Journal on Applied Dynamical Systems*, 3(4):503–524.

Iboi, E. A., Ngonghala, C. N., and Gumel, A. B. (2020). **Will an imperfect vaccine curtail the COVID-19 pandemic in the U.S.?** *Infectiuos disease modelling*, 5:510–524.

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“Classic” Vaccination

Gumel,

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Optimal Controlled:

Hethcote, H. W. and Waltman, P. (1973).
Optimal vaccination schedules in a deterministic epidemic model.
Mathematical Biosciences, 18(3-4):365–381.

Wickwire, K. (1977).
Mathematical models for the control of pests and infectious diseases: A survey.
Theoretical Population Biology, 11(2):182–238.

Hypothesis

Cost	The **effort** expended in "**preventing-mitigating** an epidemic" by vaccination is **proportional** to the vaccination rate λ_V.

The Basic Optimization Question

Hypothesis

Cost The **effort** expended in "**preventing-mitigating** an epidemic" by vaccination is **proportional** to the vaccination rate λ_V.

Jabs Counter If $S(0) \approx 1$, $X(\cdot)$: counts vaccine doses, then

$$X(t) = 1 - \exp(-\lambda_V t),$$

estimates the fraction of vaccinated individuals. Thus, for time horizon T and vaccination coverage

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$$\begin{aligned} X_{cov} &= X(T) \\ &\approx 1 - \exp(-\lambda_V T). \end{aligned}$$

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$$\begin{aligned} X_{cov} &= X(T) \\ &\approx 1 - \exp(-\lambda_V T). \end{aligned}$$

Given X_{cov}, T

$$\lambda_V = -\frac{1}{T} \ln(1 - X_{cov})$$

estimates the constant vaccination rate s.t., afther time T, we reach X_{cov}.

The Basic Optimization Question

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X_{COV} : 70%, T: **one** year

$\lambda_V \approx 0.00329$

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X_{COV} : 70%, T: **one** year

$\lambda_V \approx 0.003\,29$

If $S(0)N$ corresponds to HMS ($812\,229$ inhabitants) $\approx 2668\,\mathrm{jabs/day}$.

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Given X_{cov}, T

$$\lambda_V = -\frac{1}{T}\ln(1 - X_{cov})$$

estimates the constant vaccination rate s.t., after time T, we reach X_{cov}.

X_{COV} : 70%, T: one year

$\lambda_V \approx 0.00329$

How to optimize vaccination?

Hypothesis

Cost The **effort** expended in "**preventing-mitigating** an epidemic" by vaccination is **proportional** to the vaccination rate λ_V.

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Common Objectives

Given X_{cov}, T

$$\lambda_V = -\frac{1}{T} \ln(1 - X_{cov})$$

estimates the constant vaccination rate s.t., afther time T, we reach X_{cov}.

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estimates the fraction of vaccinated individuals. Thus, for time horizon T and vaccination coverage

Common Objectives

Who to vaccine first? (Allocation)

Given X_{cov}, T

$$\lambda_V = -\frac{1}{T} \ln(1 - X_{cov})$$

estimates the constant vaccination rate s.t., afther time T, we reach X_{cov}.

X_{COV} : 70%, T: one year

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How to optimize vaccination?

The Basic Optimization Question

Hypothesis

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estimates the fraction of vaccinated individuals. Thus, for time horizon T and vaccination coverage

Common Objectives

Who to vaccine first? (Allocation)

How and when? (Administration)

Given X_{cov}, T

$$\lambda_V = -\frac{1}{T}\ln(1 - X_{cov})$$

estimates the constant vaccination rate s.t., afther time T, we reach X_{cov}.

X_{COV} : 70%, T: one year

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How to optimize vaccination?

Vaccine optimiztion for COVID-19

Common Objectives

⋆ Who to vaccine first? (Allocation)

Vaccine optimiztion for COVID-19

Common Objectives

- ⋆ Who to vaccine first? (Allocation)
- ⋆ How and when? (Administration)

Cost

Common Objectives

- ⋆ Who to vaccine first? (Allocation)
- ⋆ How and when? (Administration)

Cost

$$J(u) := \varphi(x(T)) + \int_0^T f(t, x(t), u(t))$$

Vaccine optimiztion for COVID-19

Common Objectives

- ⋆ Who to vaccine first? (Allocation)
- ⋆ How and when? (Administration)

Optimal Control Problem

$$
\begin{aligned}
\min_{\mathbf{u}\in\mathscr{U}} J(u) =& \varphi(x(T)) + \int_0^T f(t, x(t), u(t)) \\
\dot{x}(t) =& b(t, u(t), x(t)), \qquad \text{a.e. } t \in [0, T], \\
x(0) =& x_0
\end{aligned}
$$

Vaccine optimiztion for COVID-19

siam Mexico Section

Common Objectives

- ⋆ Who to vaccine first? (Allocation)
- ⋆ How and when? (Administration)

Optimal Control Problem

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\min_{\mathbf{u}\in\mathscr{U}} J(u) =& \varphi(x(T)) + \int_0^T f(t, x(t), u(t)) \\
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Bubar, K. M., Reinholt, K., Kissler, S. M., Lipsitch, M., Cobey, S., Grad, Y. H., and Larremore, D. B. (2021).
Model-informed covid-19 vaccine prioritization strategies by age and serostatus.
Science, 371(6532):916–921.

Buckner, J. H., Chowell, G., and Springborn, M. R. (2021).
Dynamic prioritization of covid-19 vaccines when social distancing is limited for essential workers.
Proceedings of the National Academy of Sciences, 118(16).

Matrajt, L., Eaton, J., Leung, T., and Brown, E. R. (2020).
Vaccine optimization for covid-19: Who to vaccinate first?
Science Advances, 7(6).

Vaccine optimiztion for COVID-19

SIAM Mexico Section

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Mathematical Biosciences, 337:108614.

Salcedo-Varela, G. A., Peñuñuri, F., González-Sánchez, D., and Díaz-Infante, S. (2021).
Optimal piecewise constant vaccination and lockdown policies for covid-19.
medRxiv.

Vaccine optimiztion for COVID-19

siam Mexico Section

Common Objectives

- ⋆ Who to vaccine first? (Allocation)
- ⋆ How and when? **(Administration)**

Optimal Control Problem

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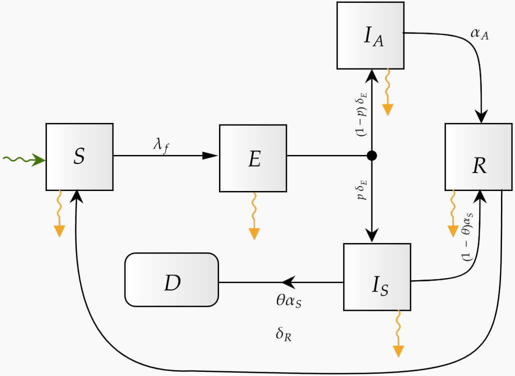
\end{aligned}
$$

Aim of this talk

To illustrate the formulation of optimal vaccination policies based in vaccination rate.

Model Scheme

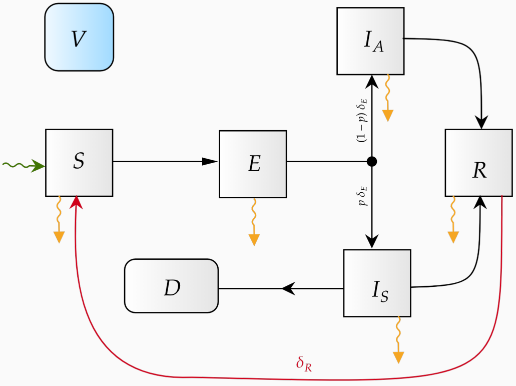


$$\lambda_f := \frac{\beta_A I_A + \beta_S I_S}{N^*}$$

$$N^* := N - D$$


natality

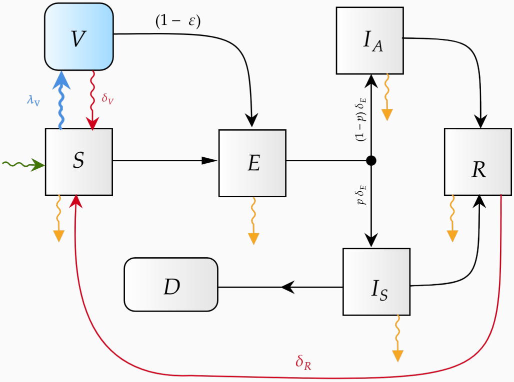

natural death



Vaccine Hypotheses

- Imperfect preventive
- One dose
- Symptomatic exception
- Action over susceptible

Model Scheme



λ_V : vaccination rate

immunity periods

$\frac{1}{\delta_V}$: vaccine-induced

$\frac{1}{\delta_R}$: natural

Vaccine Hypotheses

- Imperfect preventive
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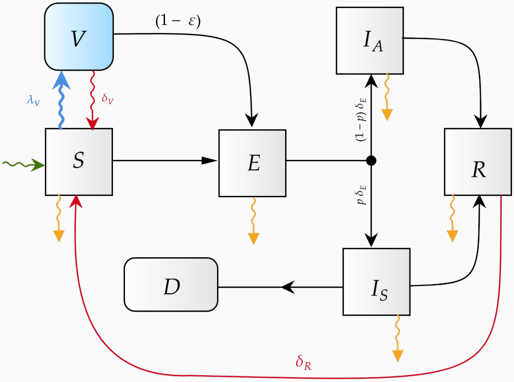
Model Scheme



λ_V : vaccination rate

immunity periods

$\dfrac{1}{\delta_V}$: vaccine-induced

$\dfrac{1}{\delta_R}$: natural

Notation

ε vaccine efficacy

p Generation of symptoms probability

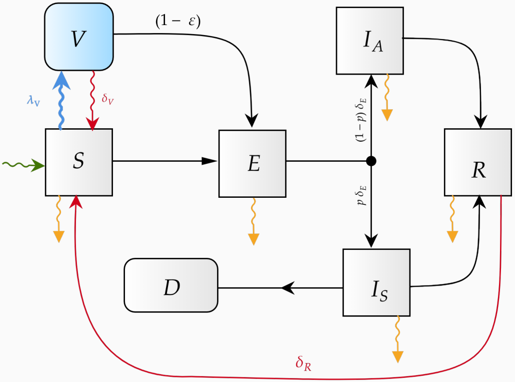
Vaccine Hypotheses

Imperfect preventive

One dose

Symptomatic exception

Action over susceptible



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Notation

ε vaccine efficacy

p Generation of symptoms probability

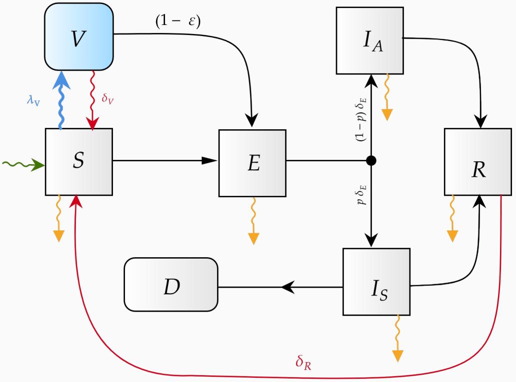
SAGE objectives

Vaccine profile (Efficacy, immunity)

Coverage

Time Horizon

Model Scheme



λ_V : vaccination rate

immunity periods

$\frac{1}{\delta_V}$: vaccine-induced

$\frac{1}{\delta_R}$: natural

Notation

ε	vaccine efficacy
p	Generation of symptoms probability

SAGE objectives

Vaccine profile
(Efficacy, immunity)

Coverage

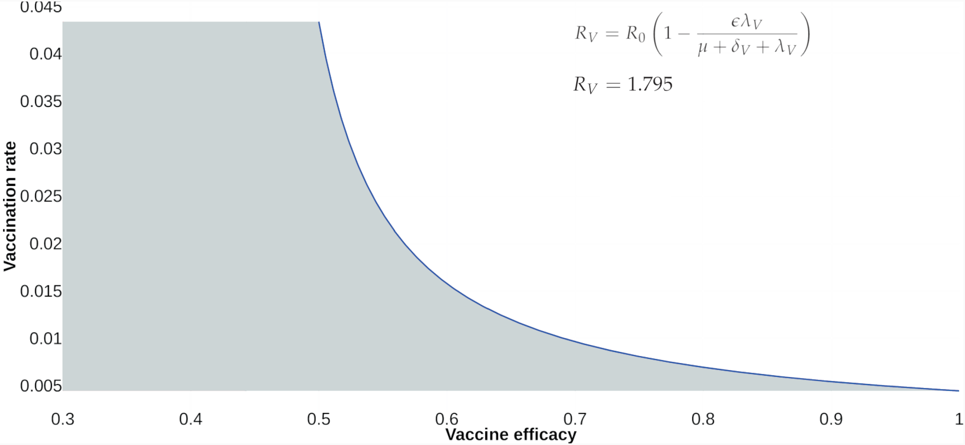
Time Horizon

Immunity:

natural (reinfection)

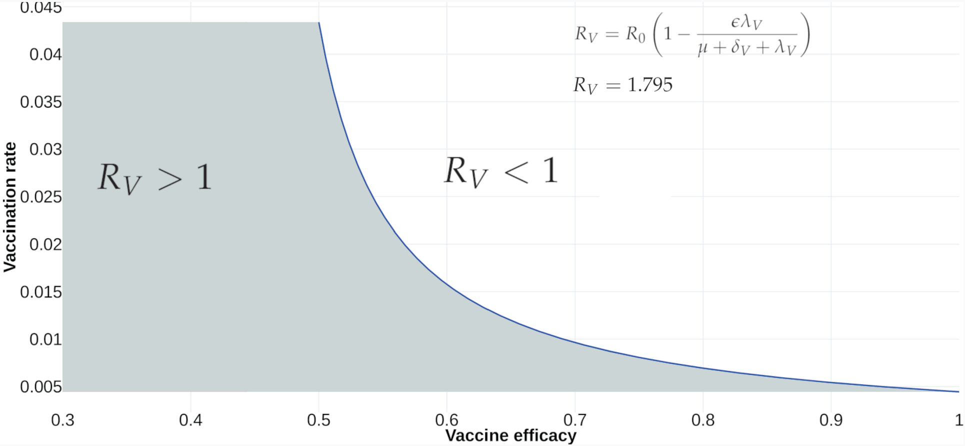
vaccine-induced

Reproductive number



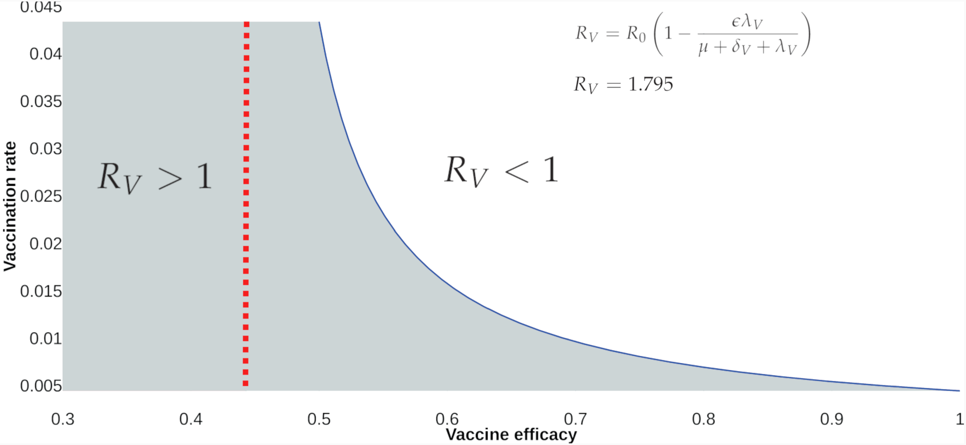
$$R_V = R_0\left(1 - \frac{\epsilon\lambda_V}{\mu + \delta_V + \lambda_V}\right)$$

$$R_V = 1.795$$

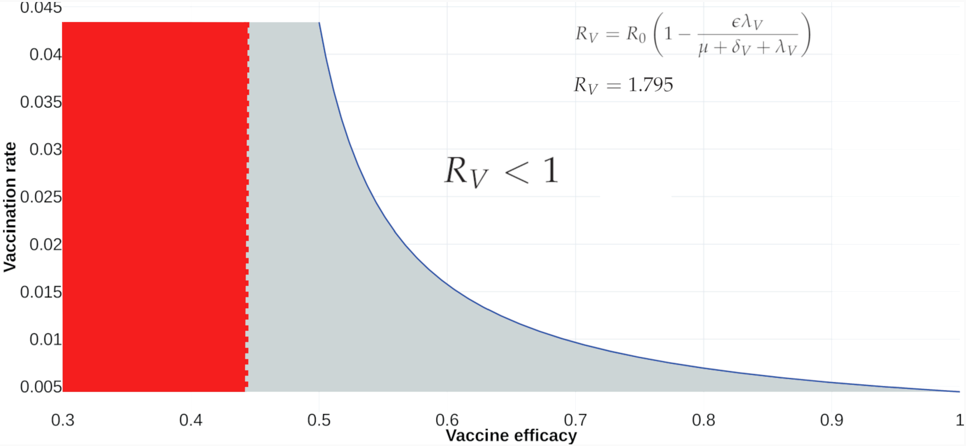


$R_V = R_0 \left(1 - \frac{\epsilon \lambda_V}{\mu + \delta_V + \lambda_V}\right)$
$R_V = 1.795$
$R_V > 1$
$R_V < 1$
Vaccination rate
Vaccine efficacy
0.045
0.04
0.035
0.03
0.025
0.02
0.015
0.01
0.005
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

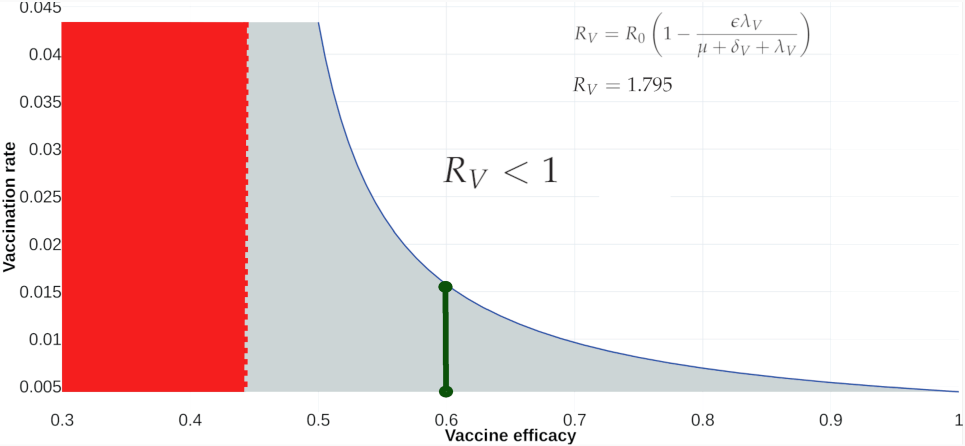
Reproductive number



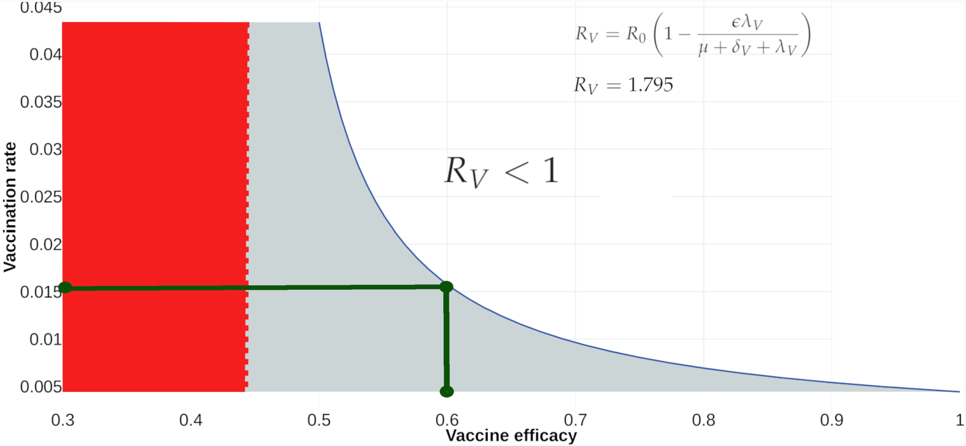
Reproductive number

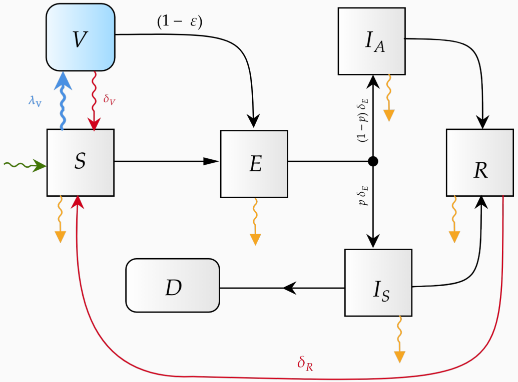


Reproductive number



Reproductive number





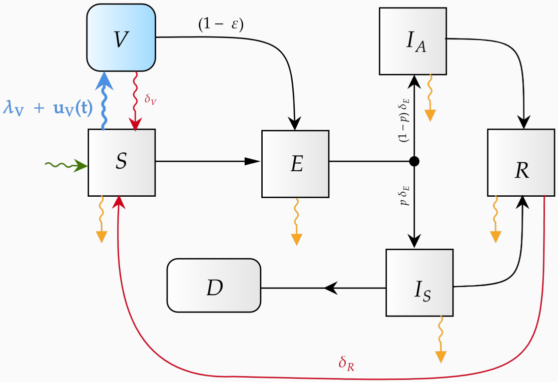
λ_V : vaccination rate

immunity periods

$\frac{1}{\delta_V}$: vaccine-induced

$\frac{1}{\delta_R}$: natural

The Optimal Control Problem

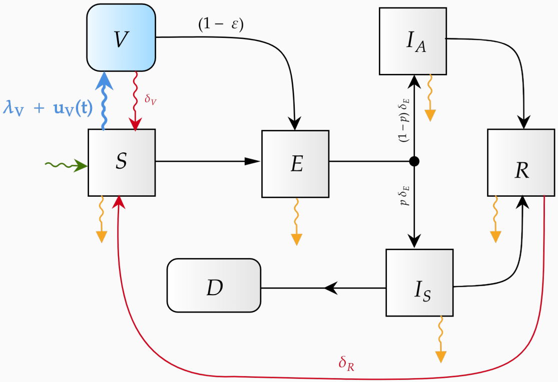


λ_V : vaccination rate

$\mathbf{u}_V(t)$: control signal

$\lambda_V\ +\ \mathbf{u}_V(t)$: modulates the number of administrated vaccine doses per day

The Optimal Control Problem



λ_V : vaccination rate

$u_V(t)$: control signal

$\lambda_V + u_V(t)$: modulates the number of administrated vaccine doses per day

$$\min_{\{u_V \in \mathcal{U}\}} J(u_V) = \varphi(x(T)) + \int_0^T f(t, x(t), u_V(t))$$

$s.t.$

$$\dot{x}(t) = b(t, u(t), x(t))$$
$$x(0) = x_0$$

$$DALY(c,s,a,t) = YLL(c,s,a,t) + YLD(c,s,a,t)$$

For given cause c, age a, sex s and year t

YLL : Years of life lost due to premature death.

$$YLL(c,s,a,t) = N(c,s,a,t) \times L(s,a)$$

$N(c,s,a,t)$: is the number of deaths due to the cause c
$L(s,a)$: is a standard loss function specifying years of life lost

YLD : Years of life list due to disability

$$YLD(c,s,a,t) = I(c,s,a,t) \times DW(c,s,a) \times L(c,s,a,t)$$

$I(c,s,a,t)$: number of incident cases for cause c
$DW(c,s,a)$: disability weight for cause c
$L(c,s,a,t)$: average duration of the case until remission or death (years)

$$J(u_V) :=$$

The disability-adjusted life year (DALY)

$DALY(c,s,a,t) = YLL(c,s,a,t) + YLD(c,s,a,t)$

For given cause c, age a, sex s and year t

YLL : Years of life lost due to premature death.

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$$\min_{u_V \in \mathscr{U}[0,T]} J(u_V) :=$$

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Optimal Control Problem

$$\min_{u_V \in \mathscr{U}[0,T]} J(u_V) := \underbrace{a_D(D(T) - D(0))}_{:=YLL} + \underbrace{a_S(Y_{I_S}(T) - Y_{I_S}(0))}_{:=YLD}$$

$$u_V(\cdot) \in [u_{\min}, u^{\max}],$$

$$\kappa I_S(t) \leq B, \quad \forall t \in [0, T],$$

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s.t.

$$f_\lambda := \frac{\beta_S I_S + \beta_A I_A}{\bar{N}}$$

$$\begin{aligned}
S'(t) &= \mu \bar{N} + \delta_V V + \delta_R R \\
&\quad - (f_\lambda + \mu + \lambda_V + u_V(t))S \\
E'(t) &= f_\lambda (S + (1-\varepsilon)V) - (\mu + \delta_E)E \\
I_S'(t) &= p\delta_E E - (\mu + \alpha_S) I_S \\
I_A'(t) &= (1-p)\delta_E E - (\mu + \alpha_A) I_A \\
R'(t) &= (1-\theta)\alpha_S I_S + \alpha_A I_A - (\mu + \delta_R) R \\
D'(t) &= \theta \alpha_S I_S \\
V'(t) &= (\lambda_V + u_V(t))S - ((1-\varepsilon) f_\lambda V + \mu + \delta_V) V \\
X'(t) &= (\lambda_V + u_V(t))(S + E + I_A + R)
\end{aligned}$$

$$\begin{aligned}
&S(0) = S_0, \ E(0) = E_0, \ I_S(0) = I_{S_0}, \\
&I_A(0) = I_{A_0}, \ R(0) = R_0, \ D(0) = D_0, \\
&V(0) = 0, \ X(0) = 0, \ X(T) = x_{coverage}, \\
&u_V(\cdot) \in [u_{\min}, u^{\max}], \\
&\kappa I_S(t) \leq B, \quad \forall t \in [0, T], \\
&\bar{N}(t) = S + E + I_S + I_A + R + V.
\end{aligned}$$

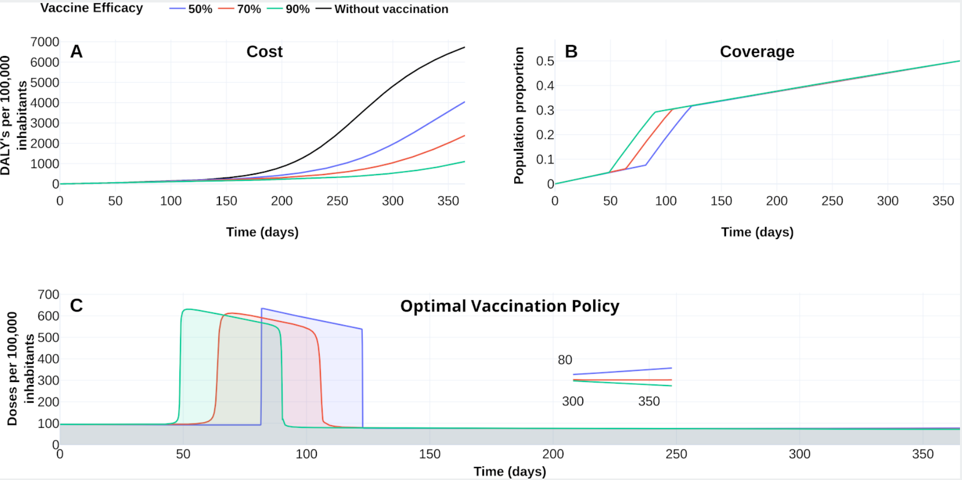
Vaccine efficacy

Developer	Vaccine Name	Efficacy %, (95% CI)	Reference
Pfizer-BioNTech	BNT162b2	95 (90.3–97.6)	[?]
Gamaleya Institute	Sputnik V	91.6 (85.6–95.2)	[?]
Oxford University-AztraZeneca	AZD1222	74.6 (41.6-88.9)	[?]
Johnson & Johnson*	Ad26.COV2.S	57 %, 66 % or 72 %	[?]
Sinovac Biotech*	CoronaVac	50.4 %	[?]

Table: Vaccine efficacy of some of the approved developments for emergency use. (*) No available information about the confidence intervals.

The response of COVID-19 burden due to vaccine efficacy

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: [50 %, 365 days, $\star$, 730 days, 365 days]



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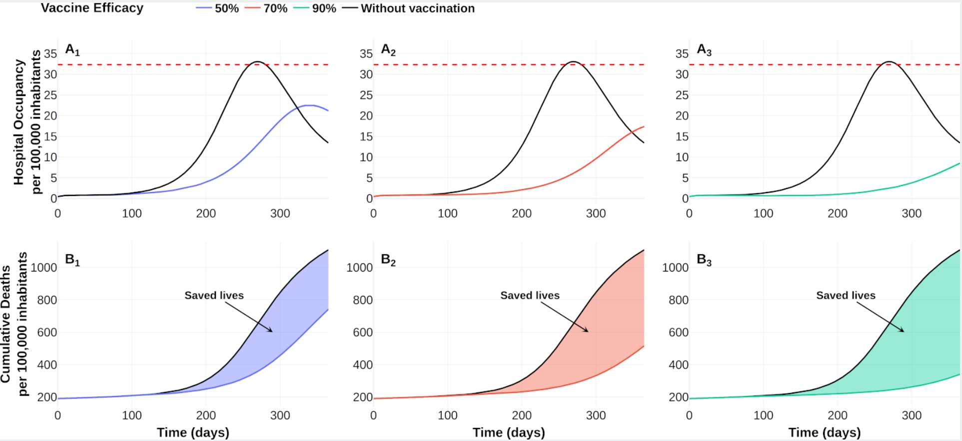
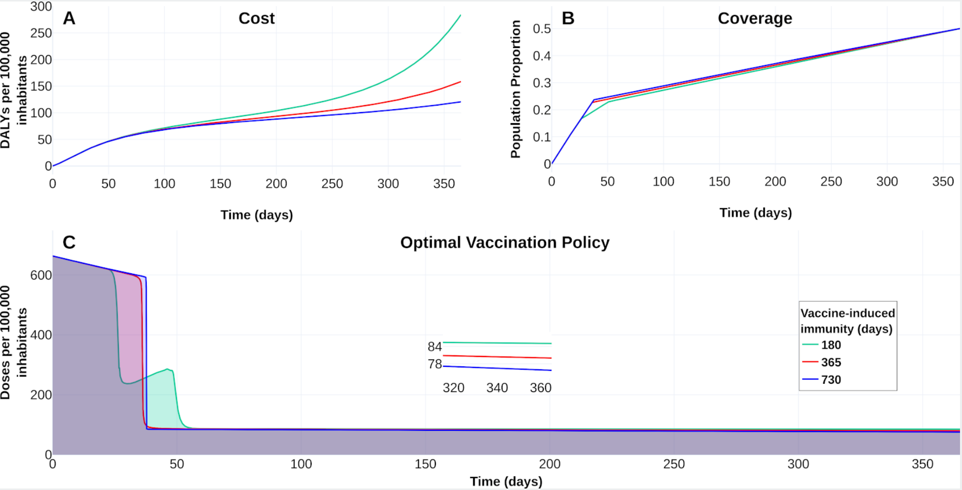


The response of COVID-19 burden due to vaccine-immunity

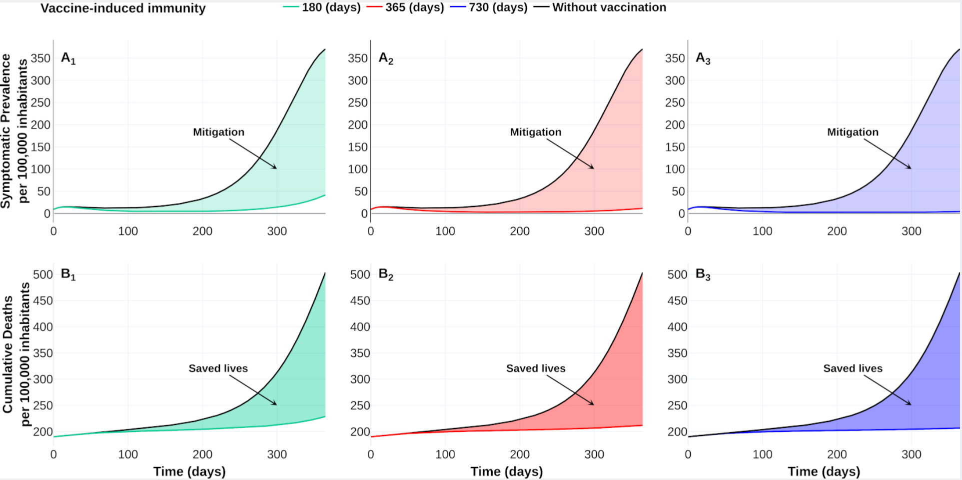
$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: [50 %, 365 days, 90 %, $\star$, 365 days,]



The response of COVID-19 burden due to vaccine-immunity

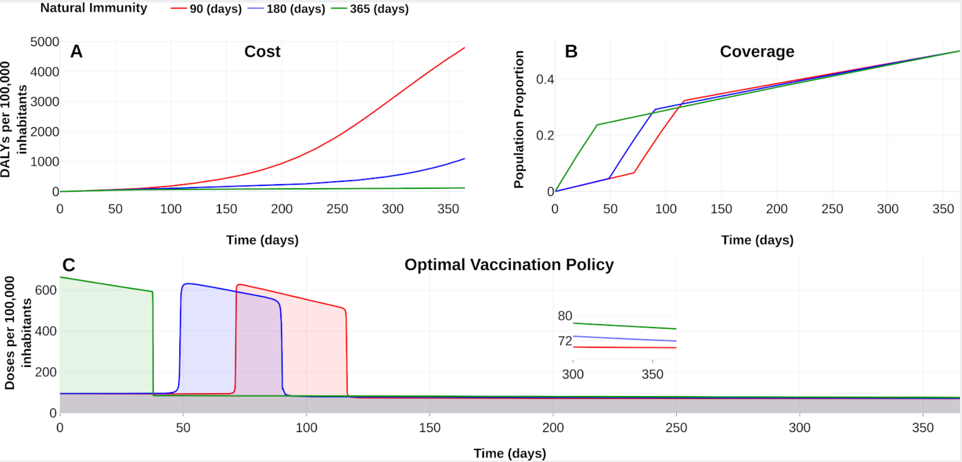
Mexico Section

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1}):$ [50 %, 365 days, 90 %, $\star$, 365 days,]



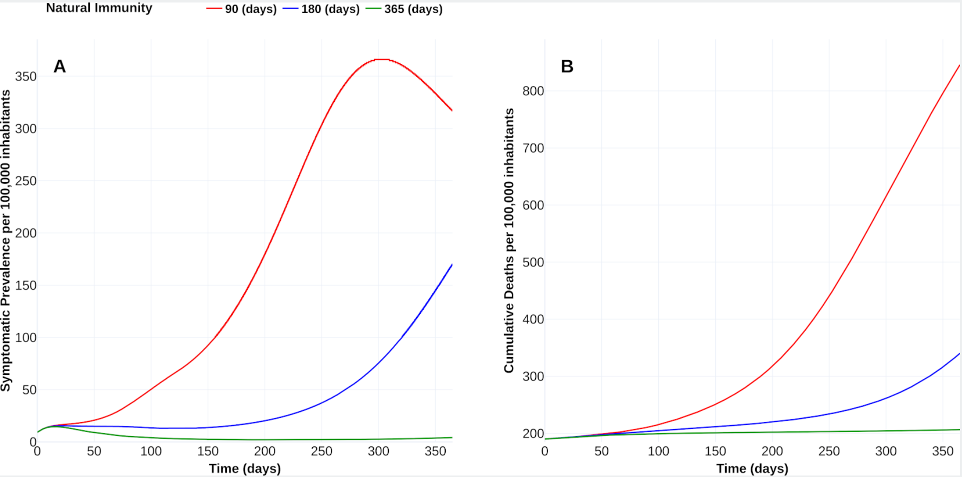
The response of COVID-19 burden due to natural-immunity

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: [50 %, 365 days, 90 %, 730 days, $\star$]



The response of COVID-19 burden due to natural-immunity

$(x_{coverage}, T, \varepsilon, \delta_V^{-1}, \delta_R^{-1})$: $[\,50\,\%, 365\,\text{days}, 90\,\%, 730\,\text{days}, \star]$



Important questions

(⋆) Optimal vaccination strategies in terms of target groups and under different possible supply scenarios

- Two or more vaccine platforms
- Multi-doses

(⋆) Potential reduction in infectiousness of breakthrough infections among vaccinated individuals

(⋆) Potential differences in vaccine efficacy against mild or severe/fatal COVID-19 disease

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Thanks a lot

GitHub

References I