

Optimal piecewise constant vaccination and lockdown policies for COVID-19,

May 25, 2021

Toy example and classic vaccination OC

To fix ideas:

$$S'(t) = -\beta IS$$

$$I'(t) = \beta IS - \gamma I$$

$$R'(t) = \gamma I$$

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

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With vaccination

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“Classic”
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 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.

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 Hethcote, H. W. and Waltman, P. (1973).
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 Wickwire, K. (1977).
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The Basic Optimization Question

Hypothesis

Cost

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

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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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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} .

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

$$\lambda_V \approx 0.00329$$

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If $S(0)N$ corresponds to HMS (812229 inhabitants)
 ≈ 2668 jabs/day.

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Who to vaccine first? (Allocation)

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Common Objectives

Who to vaccine first? (Allocation)

How and when? (Administration)

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

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- * Who to vaccine first? (Allocation)

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Common Objectives

- * Who to vaccine first? (Allocation)
- * How and when? (Administration)
- * Vaccination jointly with NPIs (Administration)

Cost

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

Common Objectives

- * Who to vaccine first? (Allocation)
- * How and when? (Administration)
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Optimal Control Problem

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

Vaccine optimization for COVID-19

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- * Who to vaccine first? (Allocation)
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-  Bubar, K. M., Reinholt, K., Kissler, S. M., Lipsitch, M., Cobey, S., Grad, Y. H., and Larremore, D. B. (2020).
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-  Buckner, J. H., Chowell, G., and Springborn, M. R. (2020).
Optimal Dynamic Prioritization of Scarce COVID-19 Vaccines.
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-  Matrajt, L., Eatontra, J., Leung, T., and Brown, E. R. (2020).
Vaccine optimization for COVID-19, who to vaccinate first?
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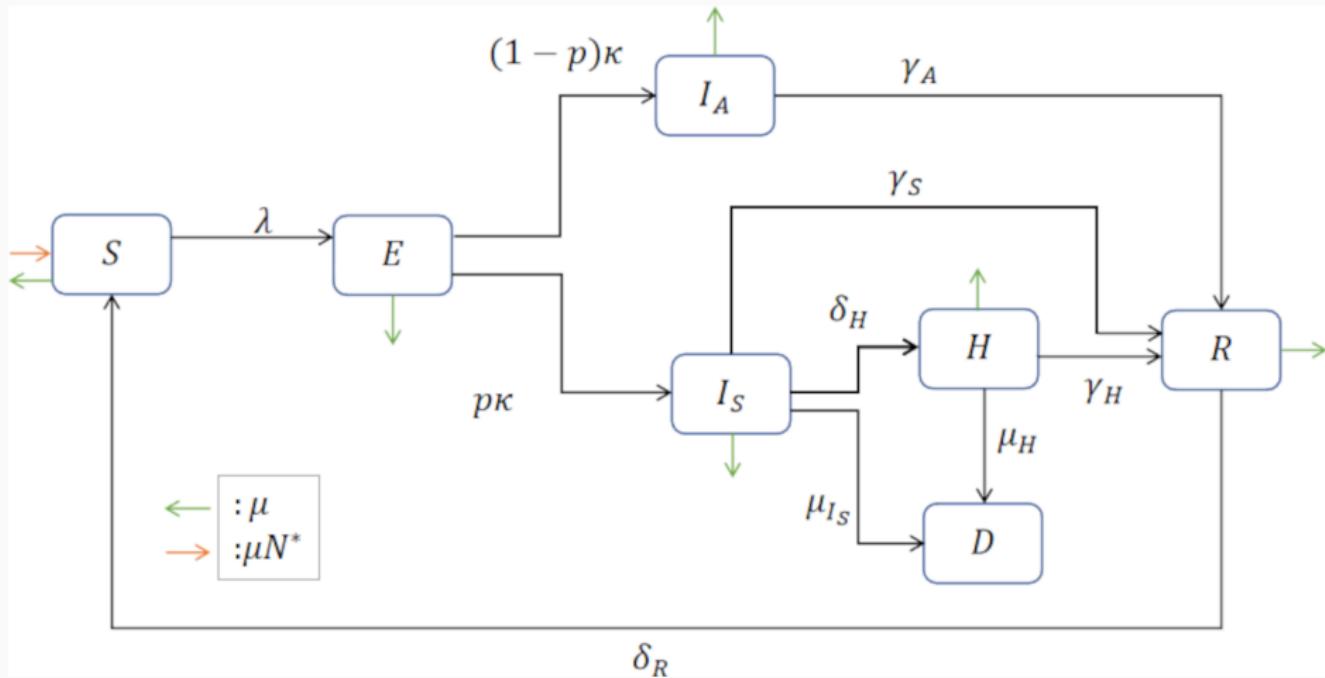
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Aim of this talk

To illustrate the formulation of optimal Lockdown-vaccination policies based in piecewise constant policies.

The Model Without Vaccination



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

$$N^*(t) = L + S + E + I_S + I_A + H + R.$$

Model Scheme

$$\begin{aligned}
 L' &= \theta\mu N^* - (\varepsilon\lambda + \delta_L + \lambda_V + \mu)L \\
 S' &= (1-\theta)\mu N^* + \delta_L L + \delta_V V + \delta_R R \\
 &\quad - (\lambda + \lambda_V + \mu)S \\
 E' &= \lambda(\varepsilon L + (1-\varepsilon)V + S) - (\kappa + \mu)E \\
 I'_S &= p\kappa E - (\delta_H + \gamma_S + \mu_{I_S} + \mu)I_S \\
 I'_A &= (1-p)\kappa E - (\gamma_A + \mu)I_A \\
 H' &= \delta_H I_S - (\gamma_H + \mu_H + \mu)H \\
 R' &= \gamma_S I_S + \gamma_A I_A + \gamma_H H - (\delta_R + \mu)R \\
 D' &= \mu_{I_S} I_S + \mu_H H \\
 V' &= \lambda_V(S + L) - [(1-\varepsilon)\lambda + \delta_V + \mu]V \\
 \lambda &:= \frac{\beta_A I_A + \beta_S I_S}{N^*} \\
 N^*(t) &= L + S + E + I_S + I_A + H + R + V.
 \end{aligned}$$

$$\begin{aligned}
 \frac{dX_{vac}}{dt} &= \lambda_V [L + S + E + I_A + R] \\
 \frac{dY_{I_S}}{dt} &= p\kappa E \\
 L(0) &= L_0, \quad S(0) = S_0, \quad E(0) = E_0, \\
 I_S(0) &= I_{S_0}, \quad I_A(0) = I_{A_0}, \quad H(0) = H_0, \\
 R(0) &= R_0, \quad D(0) = D_0, \quad V(0) = 0, \\
 X_{vac}(0) &= 0, \quad X_{vac}(T) = x_{coverage},
 \end{aligned}$$

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$$\frac{dX_{vac}}{dt} = \lambda_V [L + S + E + I_A + R]$$

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$$L(0) = L_0, S(0) = S_0, E(0) = E_0,$$

$$I_S(0) = I_{S_0}, I_A(0) = I_{A_0}, H(0) = H_0,$$

$$R(0) = R_0, D(0) = D_0, V(0) = 0,$$

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Vaccine Hypotheses

Imperfect preventive

One dose

Symptomatic exception

Action over susceptible

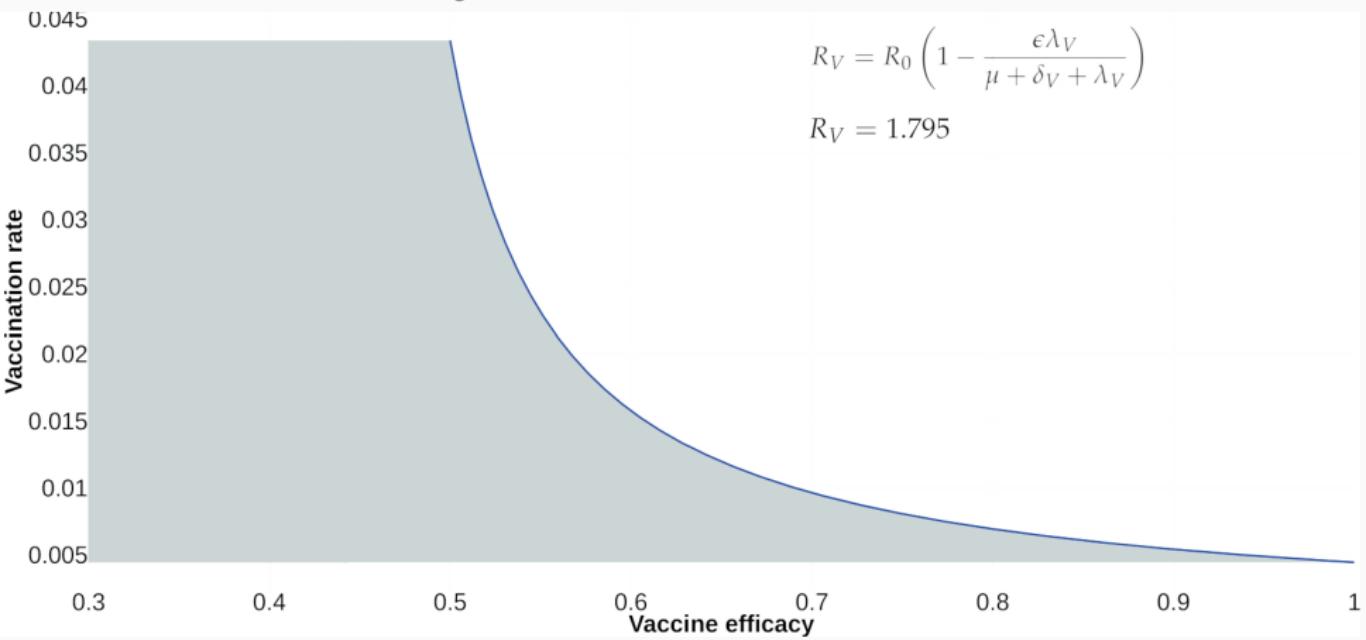
LOCKDOWN: Reduced infection and bidirectional migration to Susceptible class.

Reproductive number

$$R_0^{L,V} := \left[1 - \frac{\varepsilon \lambda_V}{\mu + \lambda_V + \delta_V} - \frac{\theta \mu (1 - \varepsilon)}{\mu + \delta_L + \lambda_V} \right] (\mu R_1 + \delta_L) R_0,$$

$$R_1 = 1 - \theta(1 - \varepsilon),$$

$$R_2 = \mu + \delta_H + \gamma_S + \mu_{I_S}.$$

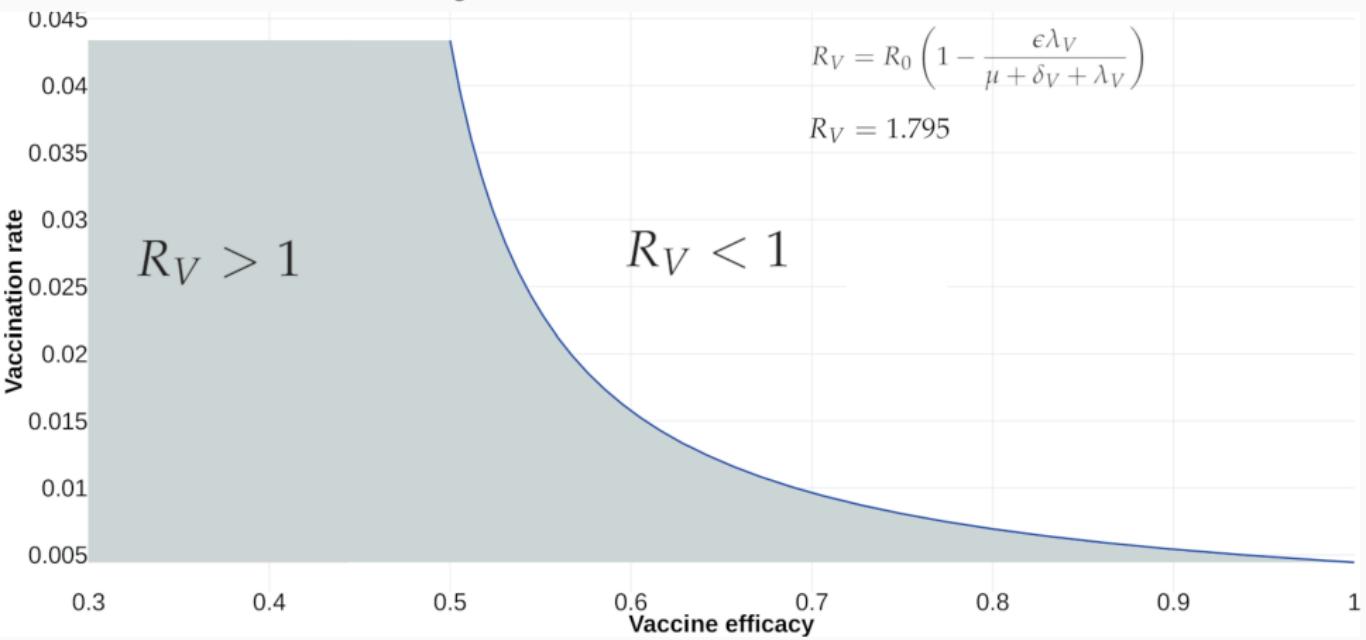


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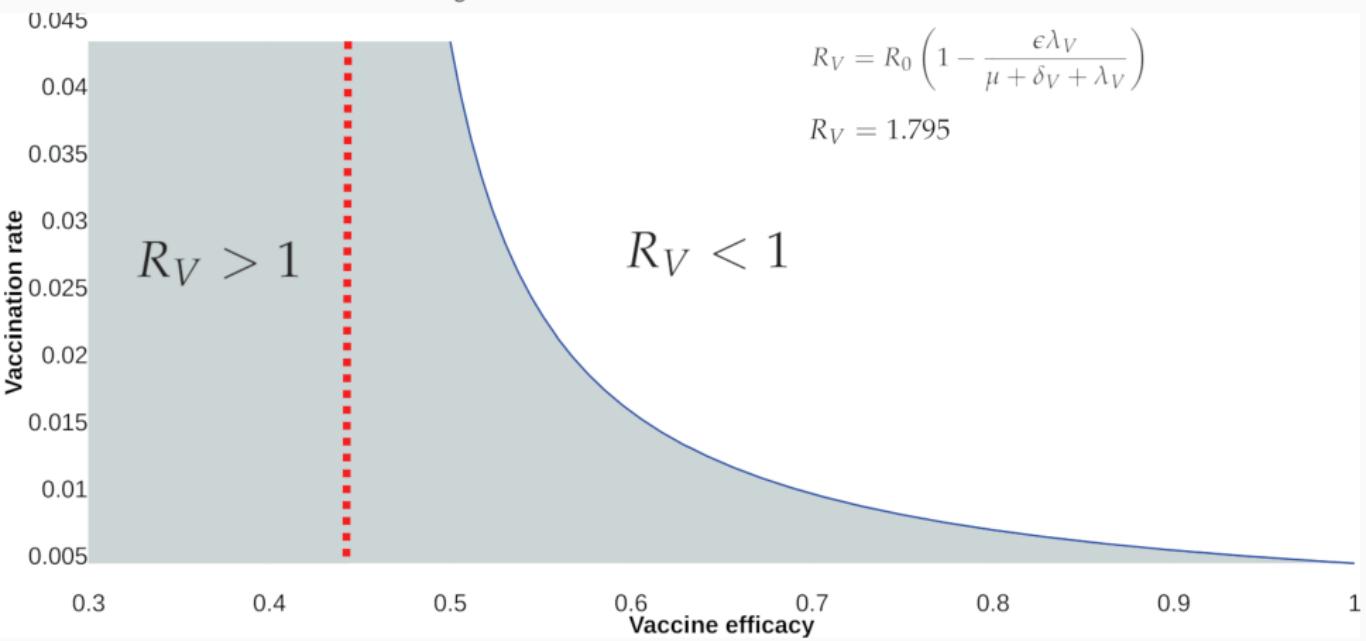


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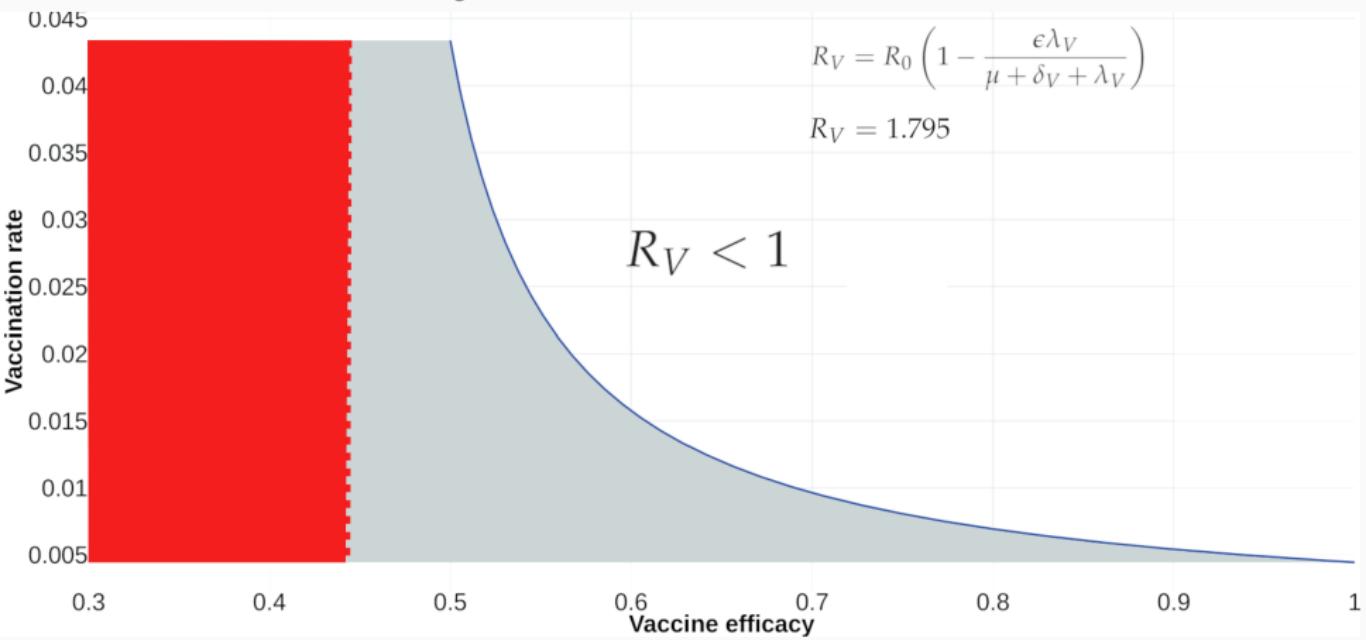


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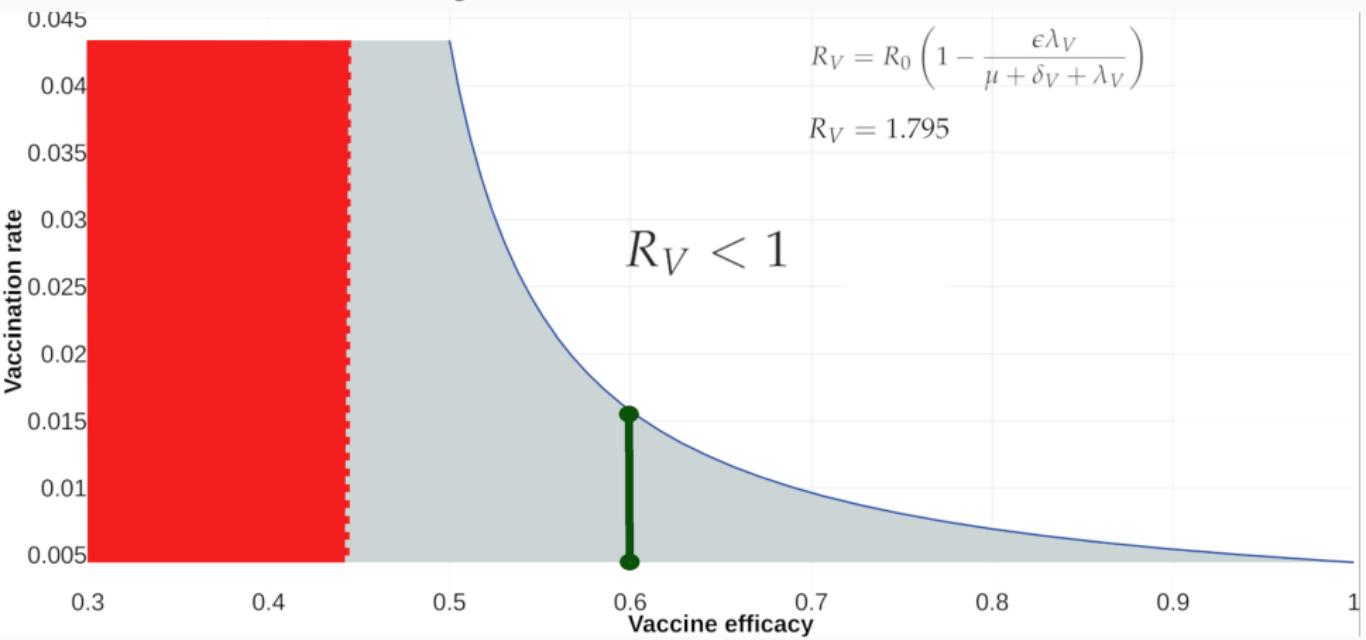


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$$R_0^{L,V} := \left[1 - \frac{\varepsilon \lambda_V}{\mu + \lambda_V + \delta_V} - \frac{\theta \mu (1 - \varepsilon)}{\mu + \delta_L + \lambda_V} \right] (\mu R_1 + \delta_L) R_0,$$

$$R_1 = 1 - \theta(1 - \varepsilon),$$

$$R_2 = \mu + \delta_H + \gamma_S + \mu_{I_S}.$$

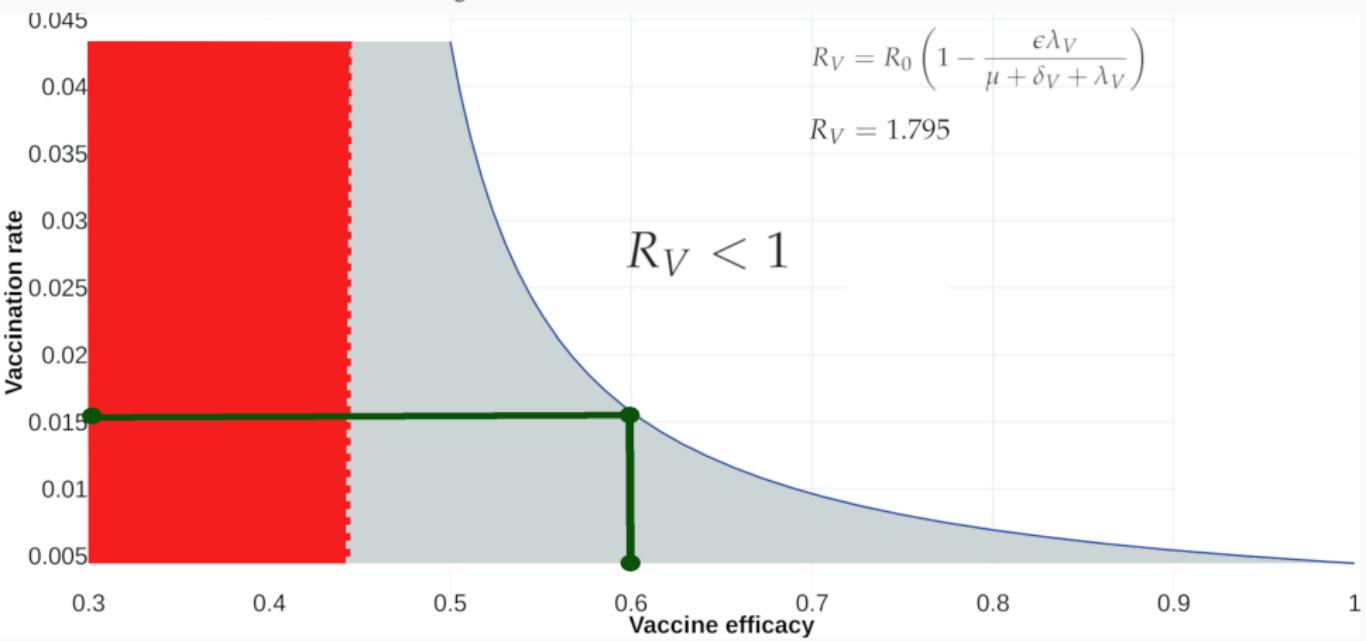


Reproductive number

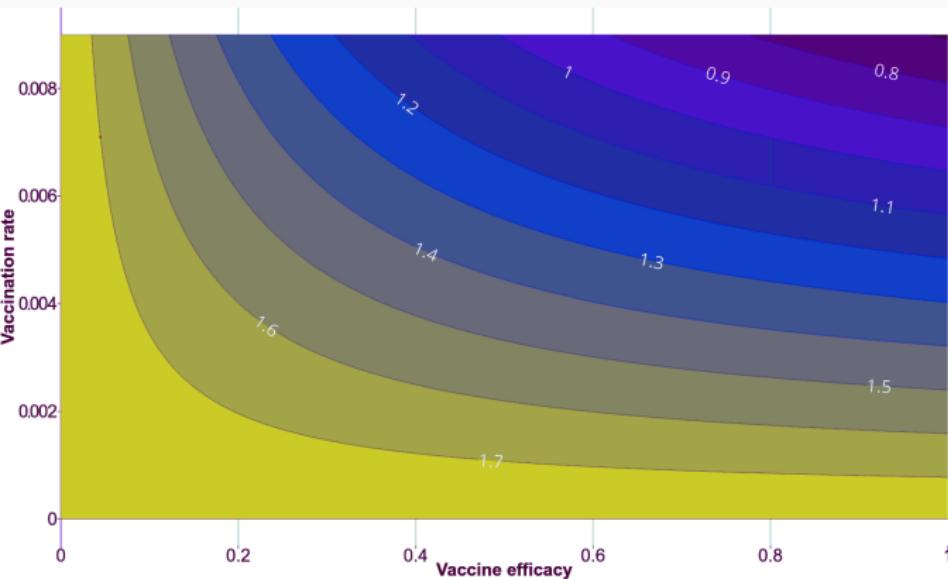
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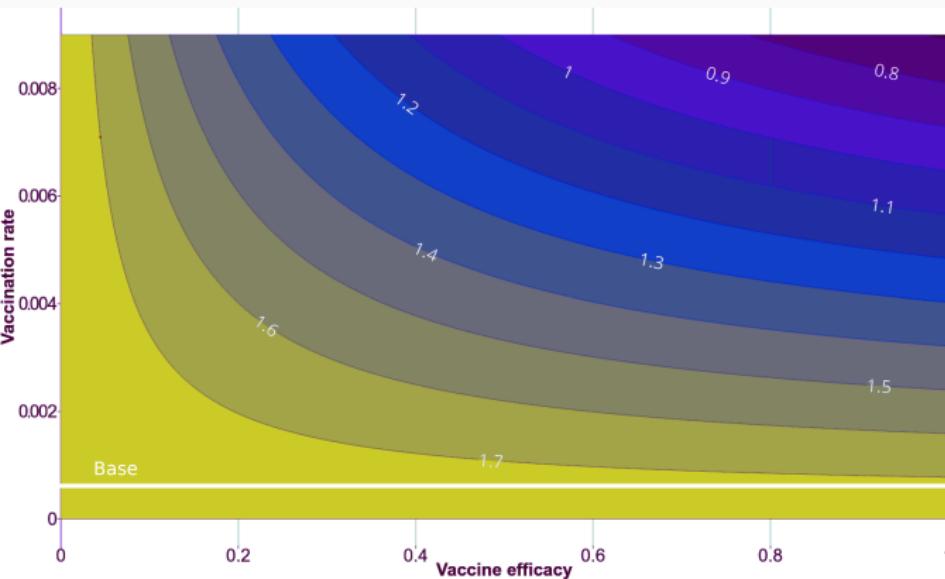
$$R_2 = \mu + \delta_H + \gamma_S + \mu_{I_S}.$$



Reproductive number



Reproductive number

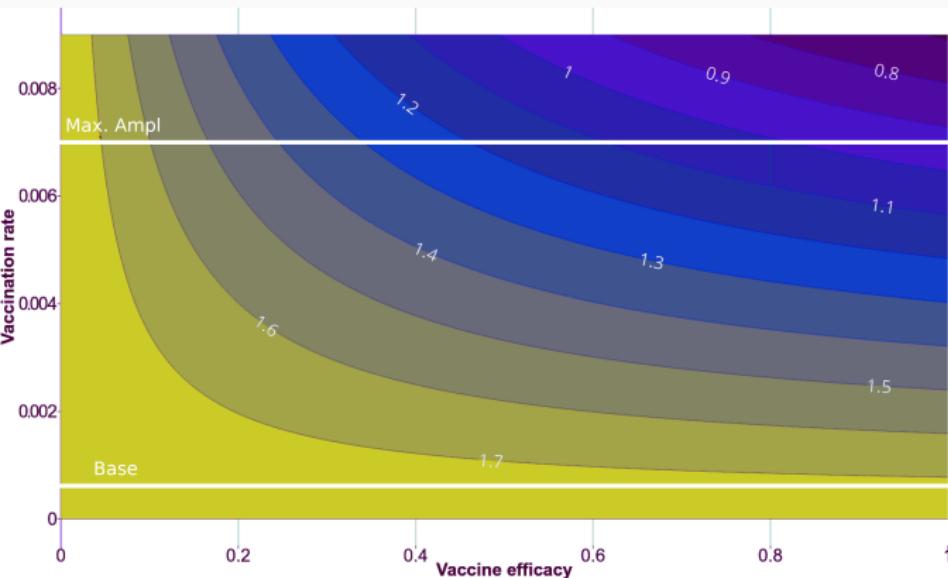


λ_V estimation

Given a fixed coverage X_{cov} and time horizon T

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

Reproductive number



$X_{COV} : 20\%$
 $T : 1 \text{ year}$

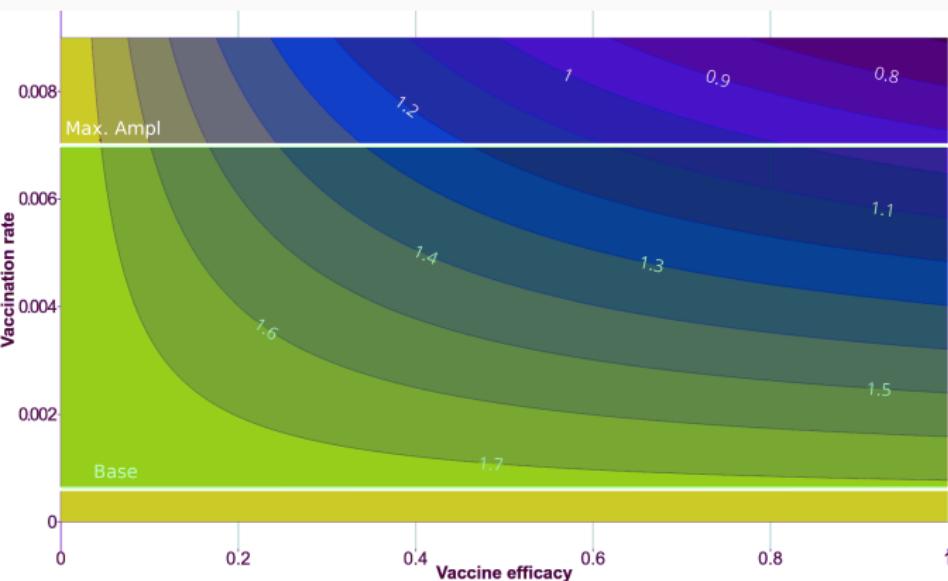
$$\lambda_V \approx 0.000611352$$

λ_V estimation

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

Reproductive number



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 $T : 1 \text{ year}$

$$\lambda_V \approx 0.000611352$$

To decrease $R_V \leq 1$, we require

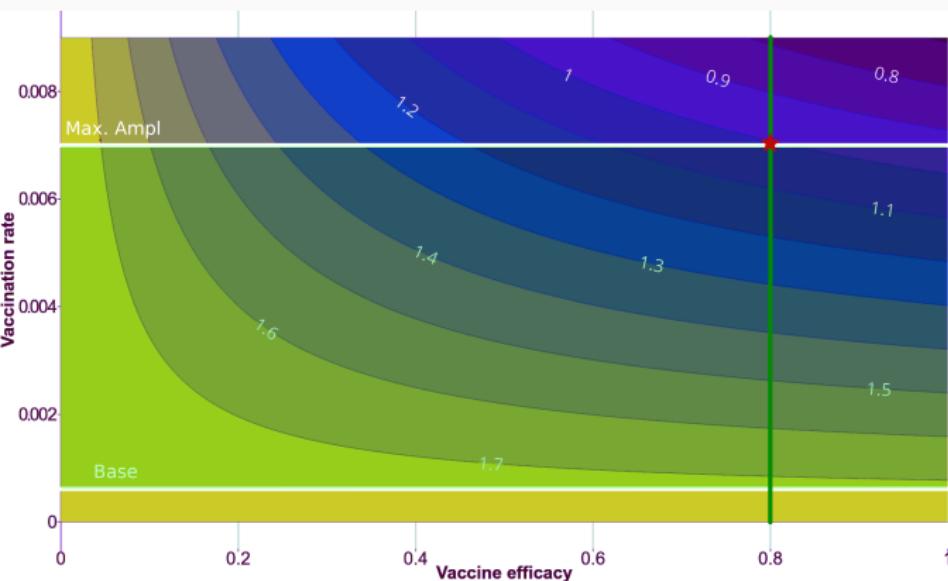
$$\varepsilon \geq 0.8, \quad \lambda_V \geq 0.007$$

λ_V estimation

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

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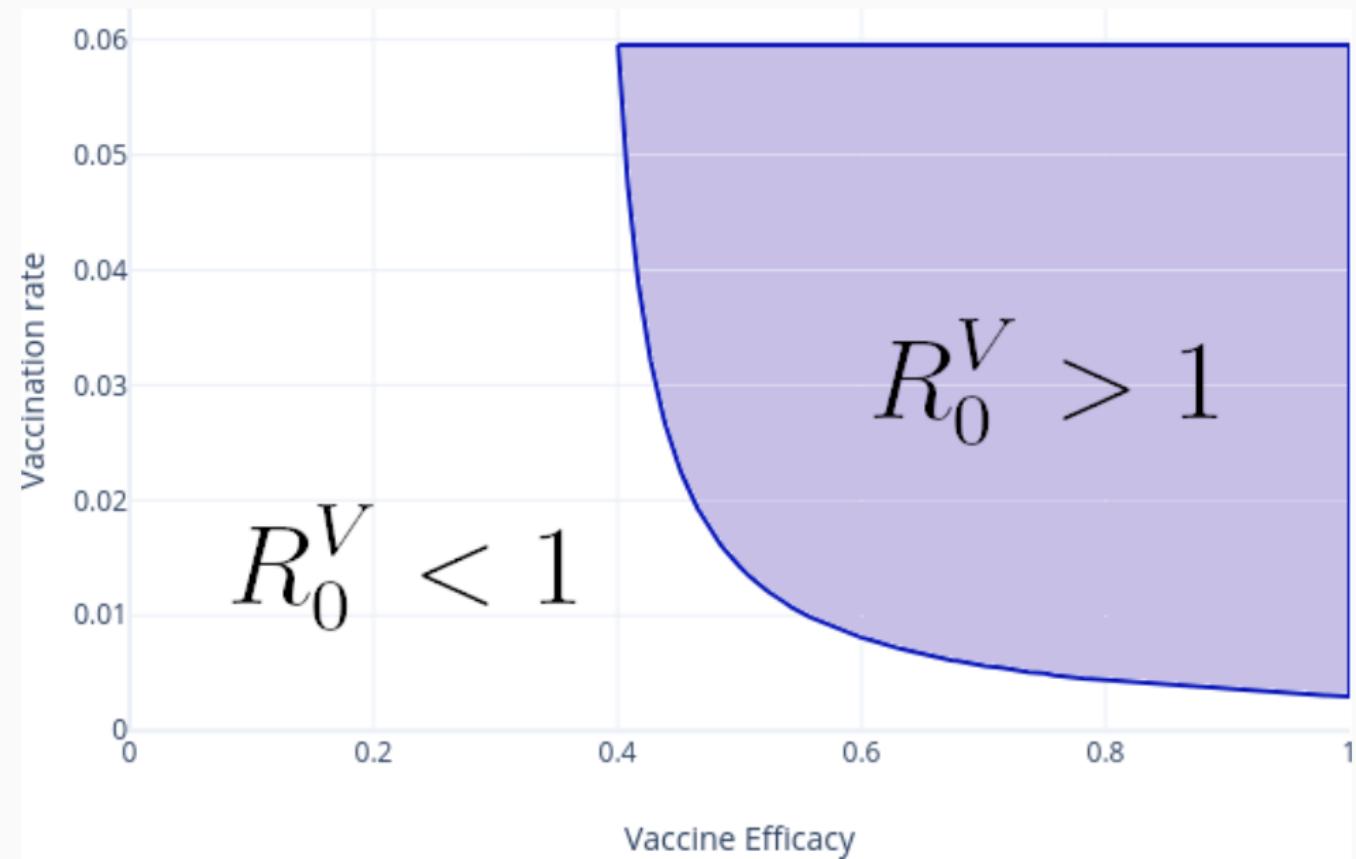
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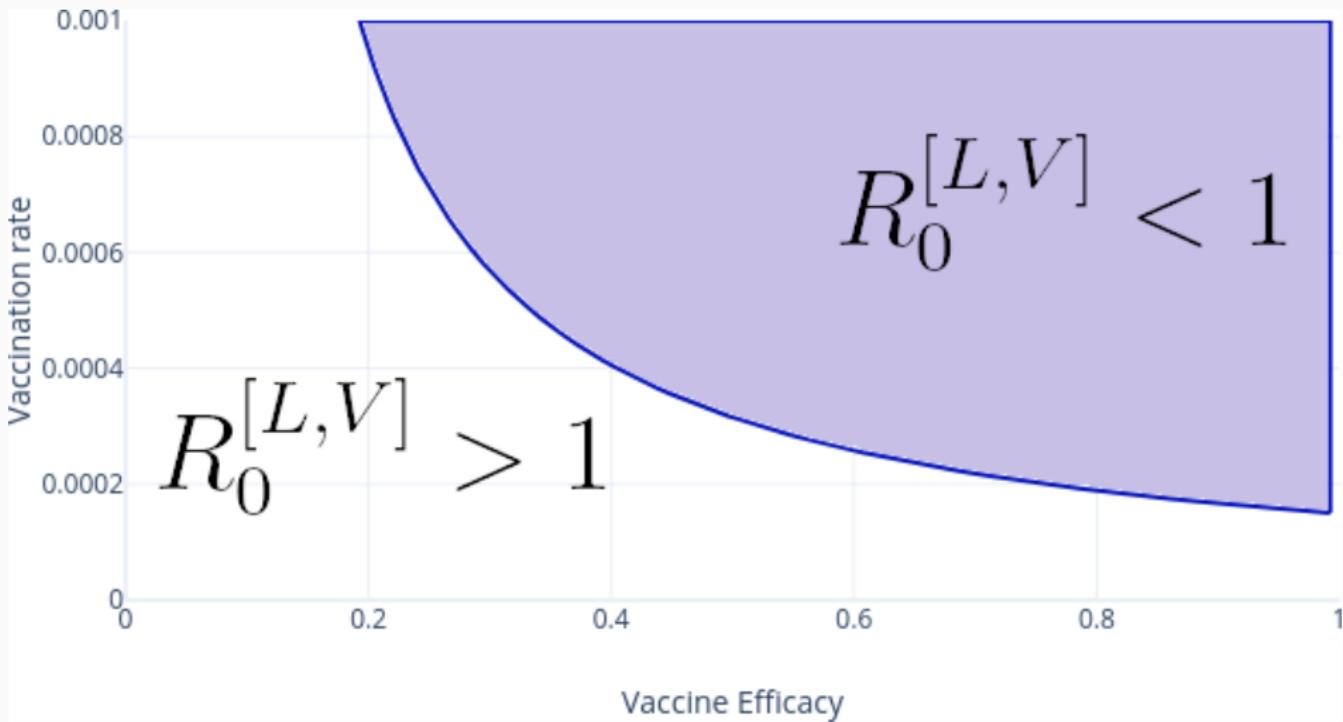
Given a fixed coverage X_{cov} and time horizon T

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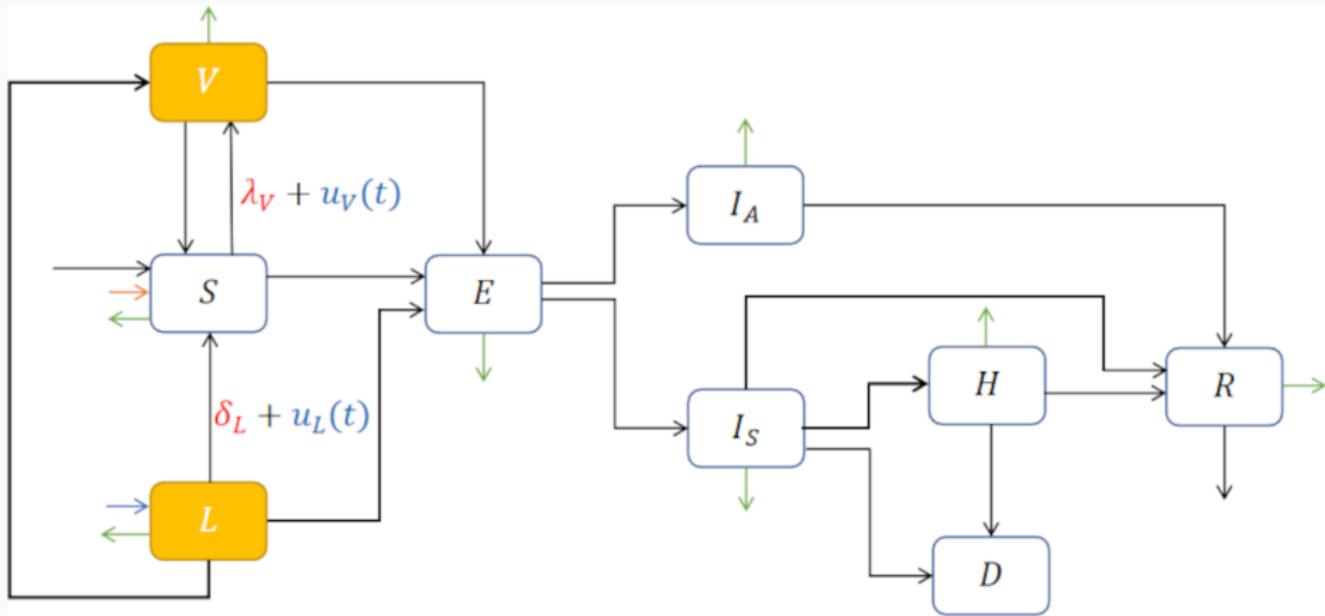
Lockdown-Vaccination Policy



Lockdown-Vaccination Policy



The Optimal Control Problem



$$\min_{u \in \mathcal{U}} J(u_L, u_V)$$

$$X_{vacc}(T) = x_{coverage}$$

$$\Phi(x, t) := \kappa I_S(t) \leq B, \forall t \in [0, T]$$

The disability-adjusted life year (DALY)

$$\text{DALY}(c, s, a, t) = \text{YLL}(c, s, a, t) + \text{YLD}(c, s, a, t)$$

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

YLL : Years of life lost due to premature death.

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

$N(c, s, a, t)$: 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

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

$I(c, s, a, t)$: 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)

$$J(u_V) :=$$

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Optimal Control Problem

$$\min_{u_V \in \mathcal{U}[0, T]} J(u_V) := \int_0^T \underbrace{a_S p \kappa E(r) + a_H \delta_H I_S(r)}_{:= YLL} + \underbrace{a_D [\mu_{I_S} I_S(r) + \mu_H H(r)]}_{:= YLD} dr + \\ \int_0^T \frac{1}{2} [c_L u_L^2(r) + c_V u_V^2(r)] dr$$

$$u_V(\cdot) \in [u_{\min}, u^{\max}], \\ \kappa I_S(t) \leq B, \quad \forall t \in [0, T],$$

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s.t.

$$L' = \theta \mu N^* - \varepsilon \lambda L - (u_L(t) + \delta_L)L - \mu L \quad \frac{dX_{vac}}{dt} = (u_V(t) + \lambda_V)[L + S + E + I_A + R]$$

$$S' = (1 - \theta)\mu N^* + (u_L(t) + \delta_L)L + \delta_V V + \delta_R R - [\lambda + (\lambda_V + u_V(t)) + \mu] S \quad \frac{dY_{I_S}}{dt} = p \kappa E$$

$$E' = \lambda(\varepsilon L + (1 - \varepsilon)V + S) - (\kappa + \mu)E \quad \lambda := \frac{\beta_A I_A + \beta_S I_S}{N^*}$$

$$I'_S = p \kappa E - (\gamma_S + \mu_{I_S} + \delta_H + \mu) I_S$$

$$I'_A = (1 - p) \kappa E - (\gamma_A + \mu) I_A$$

$$H' = \delta_H I_S - (\gamma_H + \mu_H + \mu) H$$

$$R' = \gamma_S I_S + \gamma_A I_A + \gamma_H H - (\delta_R + \mu) R$$

$$D' = \mu_{I_S} I_S + \mu_H H$$

$$V' = (\lambda_V + u_V(t)) V$$

$$- [(1 - \varepsilon)\lambda + \delta_V + \mu] V$$

$$L(0) = L_0, \quad S(0) = S_0, \quad E(0) = E_0, \quad I_S(0) = I_{S_0},$$

$$I_A(0) = I_{A_0}, \quad H(0) = H_0, \quad R(0) = R_0, \quad D(0) = D_0,$$

$$V(0) = 0, \quad X_{vac}(0) = 0, \quad u_V(\cdot) \in [u_{\min}, u^{\max}],$$

$$X_{vac}(T) = x_{coverage}, \quad \kappa I_S(t) \leq B, \quad \forall t \in [0, T],$$

$$N^*(t) = L + S + E + I_S + I_A + H + R + V$$

Vaccine efficacy

Developer	Vaccine Name	Efficacy %, (95% CI)	Reference
Pfizer-BioNTech	BNT162b2	95 (90.3–97.6)	[1]
Gamaleya Institute	Sputnik V	91.6 (85.6–95.2)	[4]
Oxford University-AztraZeneca	AZD1222	74.6 (41.6-88.9)	[2]
Johnson & Johnson*	Ad26.COV2.S	57 %, 66 % or 72 %	[3]
Sinovac Biotech*	CoronaVac	50.4 %	[5]

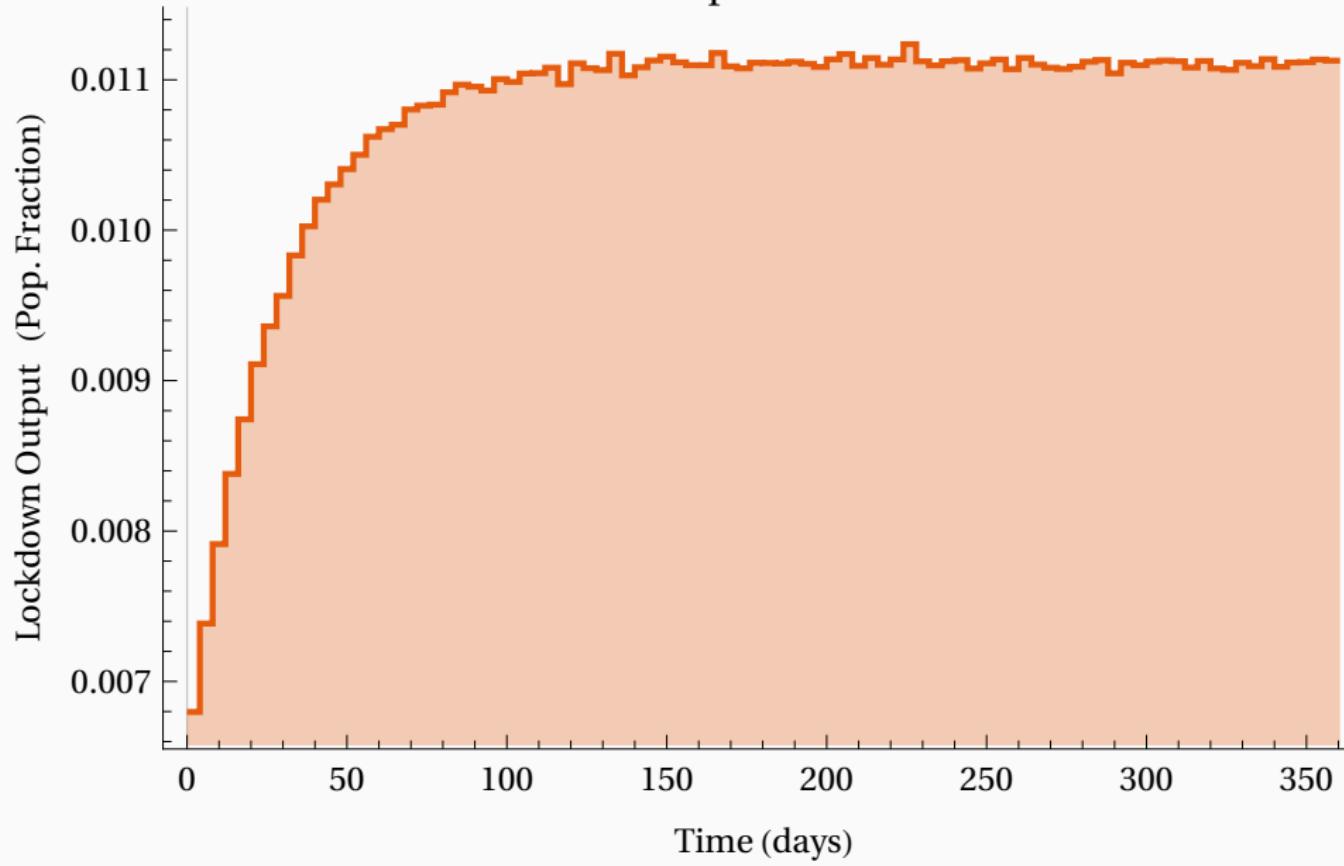
Table: Vaccine efficacy of some of the approved developments for emergency use. (*) No available information about the confidence intervals.

Numerical Results: Differential Evolution

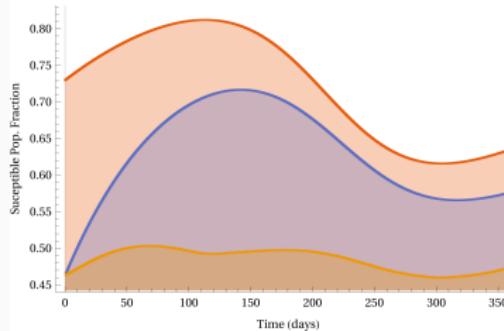
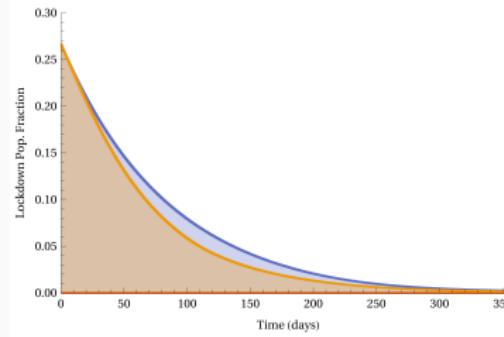
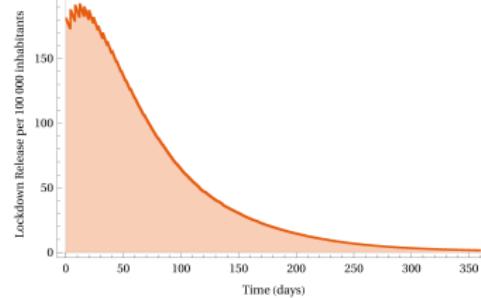
Algorithm 1 Differential Evolution Algorithm

```
 $X \leftarrow \mathbf{X}_0(Np, \mathcal{V})$ 
while (the stopping criterion has not been met) do
     $M \leftarrow \mathbf{M}(X, F, \mathcal{V})$ 
     $C \leftarrow \mathbf{C}(X, M, C_r)$ 
     $X \leftarrow \mathbf{S}(X, C, f_{ob})$ 
end while
 $\mathbf{x}_{best} \leftarrow \mathbf{Best}(X, f_{ob})$ 
```

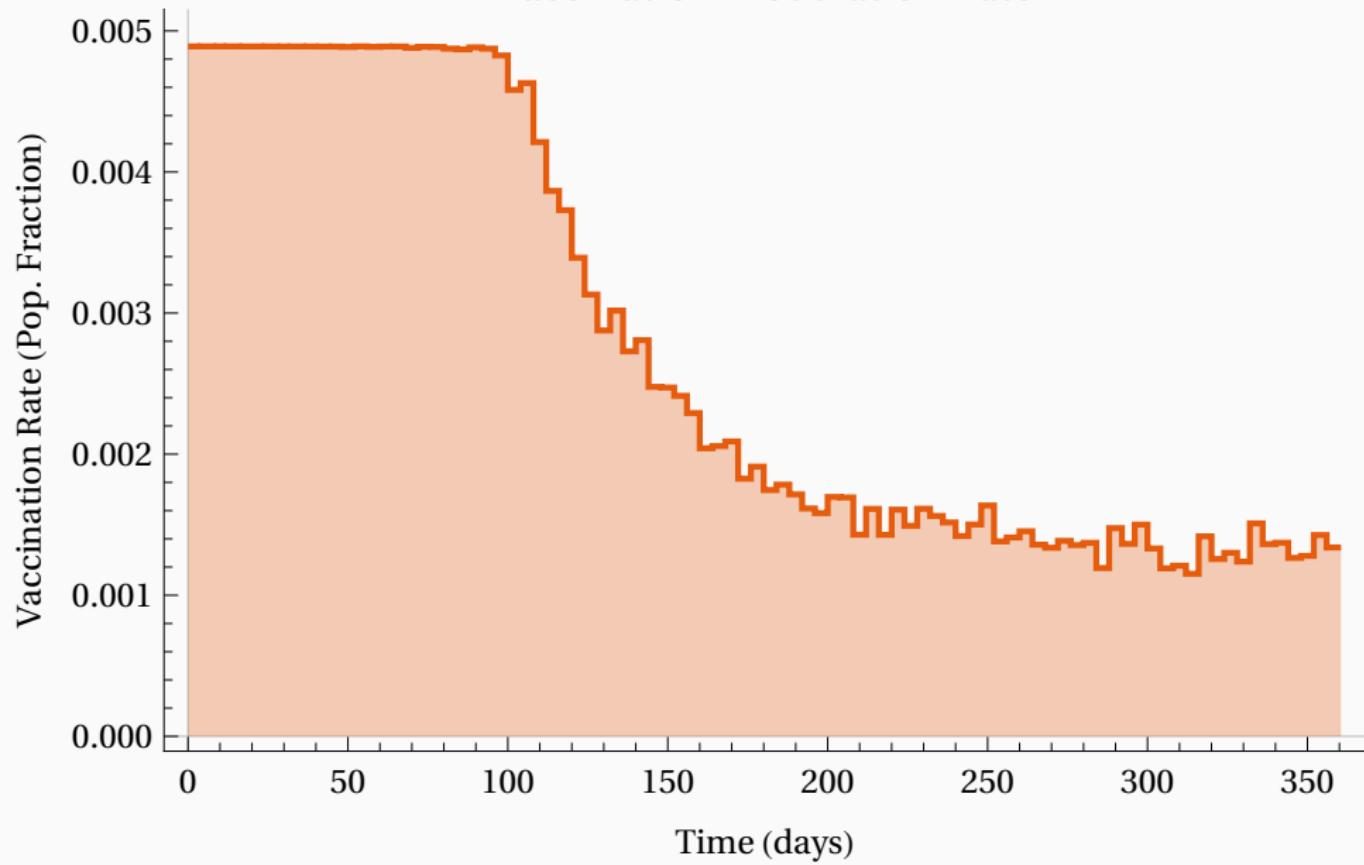
Lockdown Output Modulation Rate

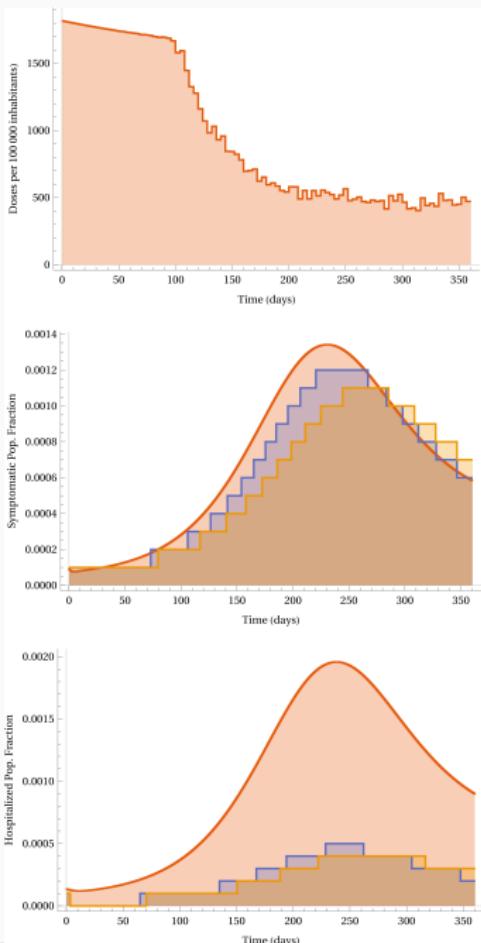


Lockdown Output Modulation Rate



Vaccination Modulation Rate





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