

# Uncertainty quantification of vaccination policies:

a model for stock management with random fluctuations.

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**YHG, SDIV, AMS**

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UNACH, CONACYT-Universidad de Sonora, Universidad de Sonora

# Introduction

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## Motivation

# Problem

## CALENDARIO DE ENTREGAS (miles de personas inmunizadas):

Laboratorio	2021												
	DIC-20	ENE	FEB	MAR	ABR	MAY	JUN	JUL	AGO	SEP	OCT	NOV	DIC
1. Pfizer	125	969	969	969	969	1,875	1,875	1,875	1,875	1,425	1,425	1,425	1,425
2. CanSino	2,500	2,500	2,500	2,500	2,667	2,667	2,667	5,667	5,667	5,667			
3. COVAX(*)				2,579	2,579	2,579	2,579	2,579	2,579	2,579	2,579	2,579	2,579
4. AstraZeneca				5,000	7,870	7,870	6,270	6,450	5,240				
TOTAL	2,625	3,469	3,469	11,048	14,085	14,991	13,391	16,571	15,361	9,671	4,004	4,004	4,004

**Los contratos establecidos hasta hoy permitirían la inmunización de hasta 116.69 millones de personas al término de 2021.**

# Argument

We argue that sufficiently large random fluctuations in deliveries—due to lags or the number of vaccine doses—convey significant effects on the mitigation of symptomatic cases.

## Aims

We pursue quantifying the uncertainty due to time lags or amount delivery, and evaluates its implications.

# Introduction

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## Methodology



Given a shipment of vaccines calendar describe the stock management with backup protocol and quantify random fluctuations due to schedule or quantity. Then plug this dynamic with a ODE systeme to describe a disease and evalute its response accordingly.

# Vaccine Shipment Program

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Motivation

Methodology

## Model Formulation on continuous time

Non standar discrete approximation

Numeric Results



## Toy example and classic vaccination OC

To fix ideas:

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

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

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

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

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

• **“Classic”  
Vaccination**

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**“Classic”  
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With vaccination

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

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

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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.



Iboi, E. A., Ngonghala, C. N., and Gumel, A. B. (2020).

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Optimal  
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Wickwire, K. (1977).

### Mathematical models for the control of pests and infectious diseases: A survey.

*Theoretical Population Biology*, 11(2):182–238.

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**Cost:** The **effort** expended in “**preventing-mitigating** an epidemic” by vaccination is **proportional** to the vaccination rate  $\lambda_V$ .



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$$\lambda_V \approx 0.00329$$

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

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Given  $X_{COV}$ ,  $T$

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### Common Objectives

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

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# Vaccine optimization for COVID-19

## Common Objectives

- Who to vaccine first?  
(Allocation)

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## Cost

# Vaccine optimization for COVID-19

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- Who to vaccine first?  
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- How and when?  
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## Cost

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

# Vaccine optimization for COVID-19

## Common Objectives

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

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

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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.**

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Matrajt, L., Eaton, J., Leung, T., and Brown, E. R. (2020).

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*Science Advances*, 7(6).

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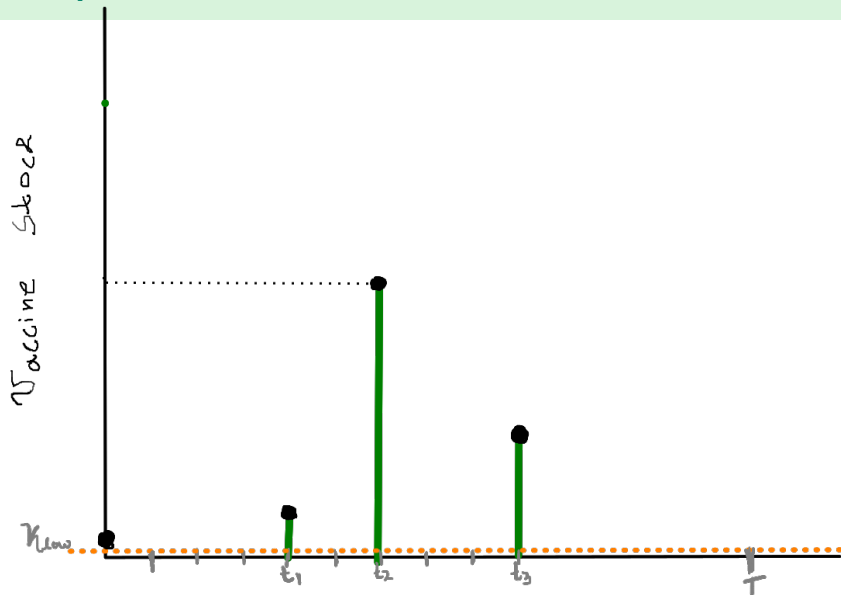
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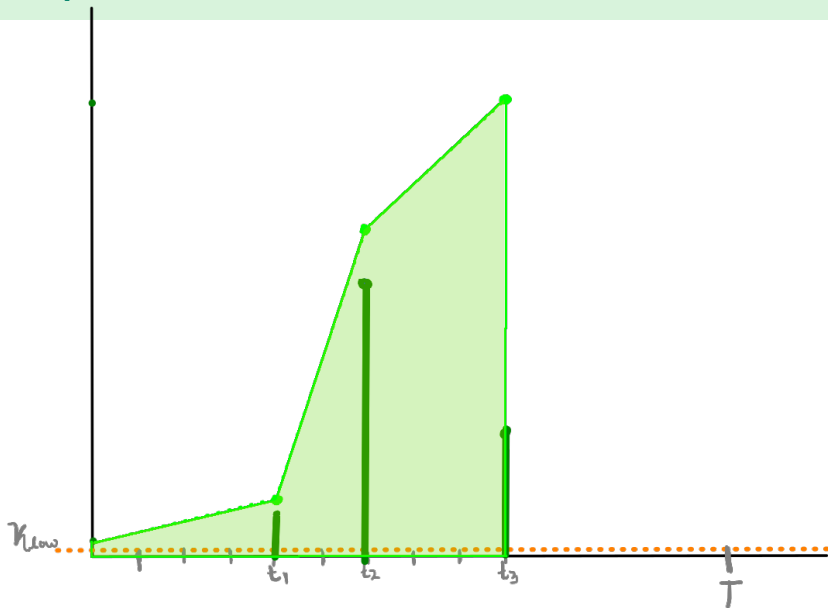
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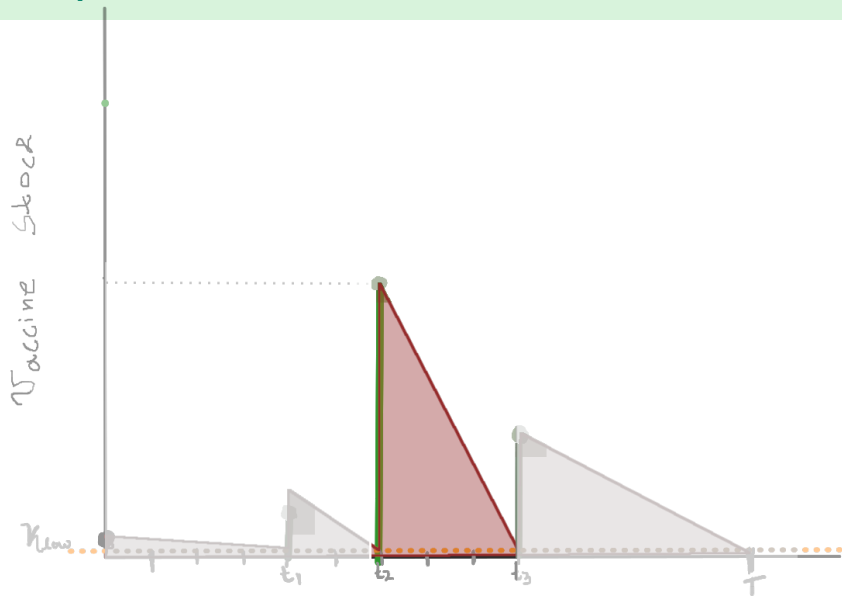
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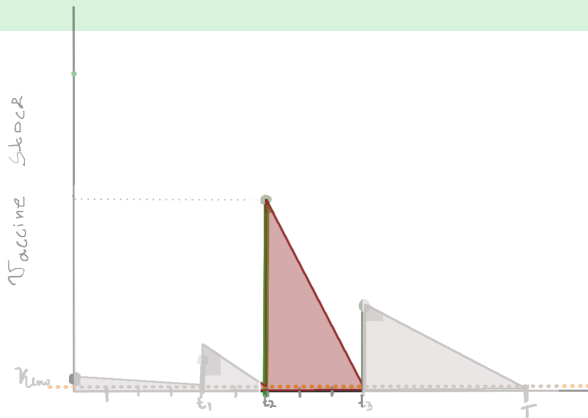
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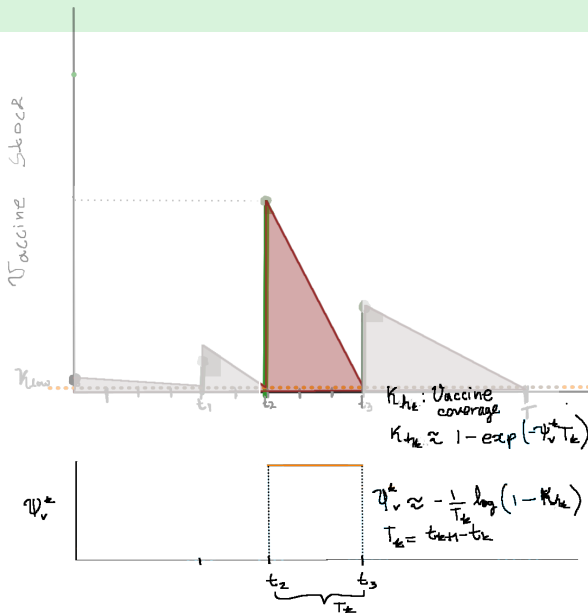
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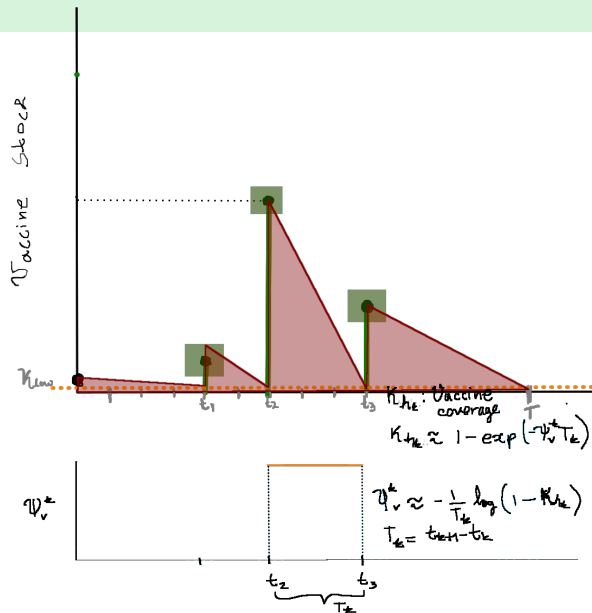
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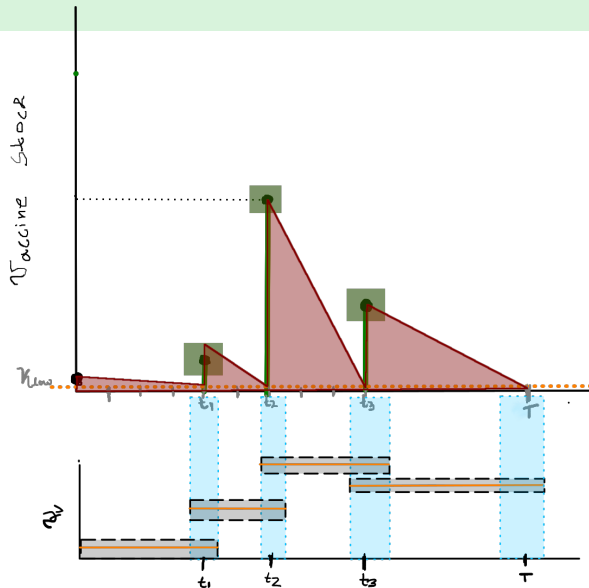
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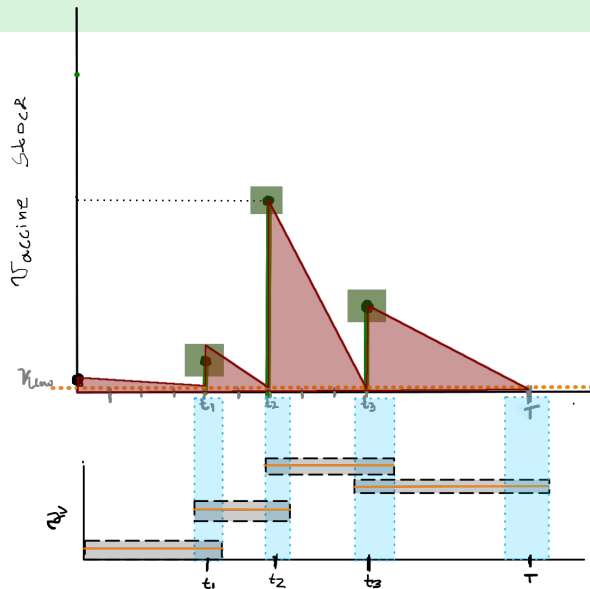
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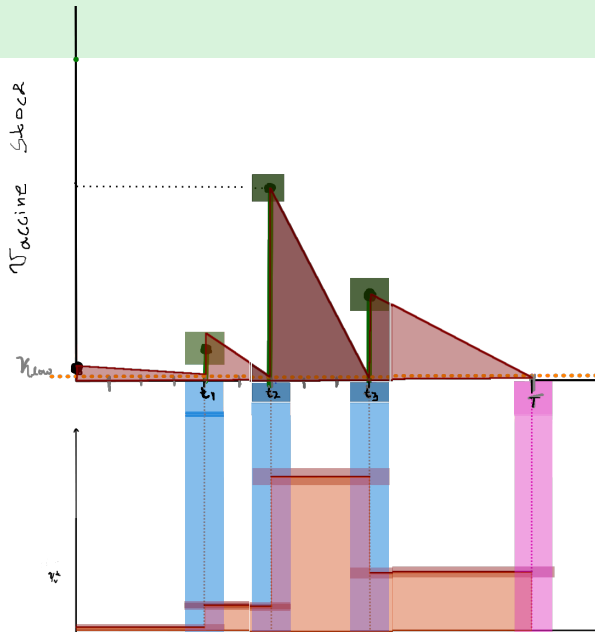


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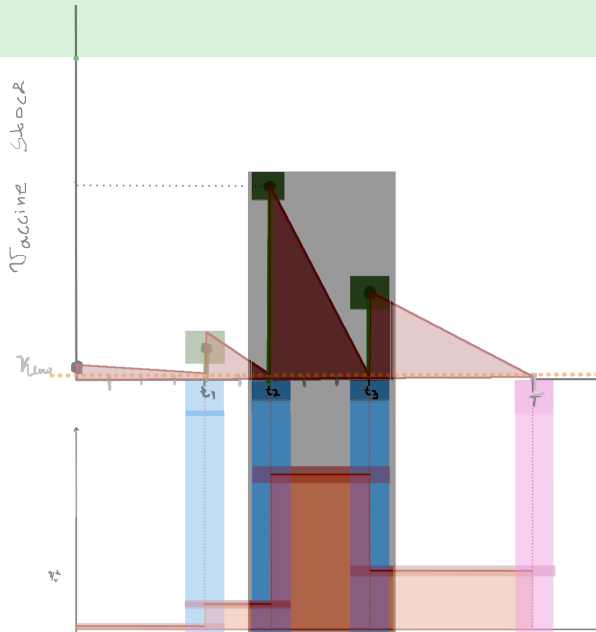




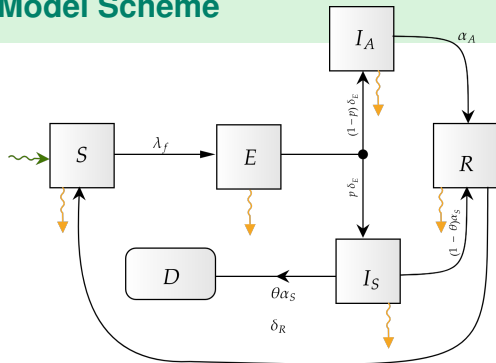
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# Model Scheme

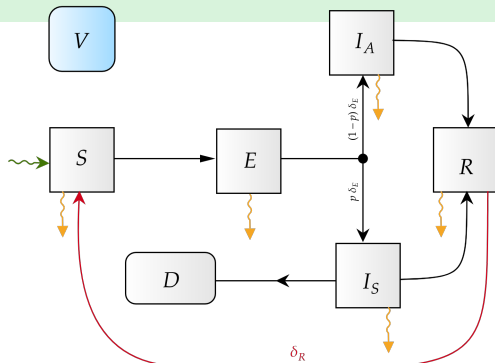


$$\lambda_f := \frac{\beta_A I_A + \beta_S I_S}{N^*}$$

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

Wavy green arrow: natality  
Wavy orange arrow: natural death

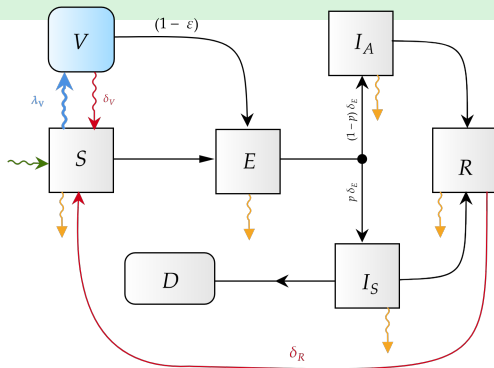
# Model Scheme



## Vaccine Hypotheses

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

# Model Scheme



$\lambda_V$ : vaccination rate

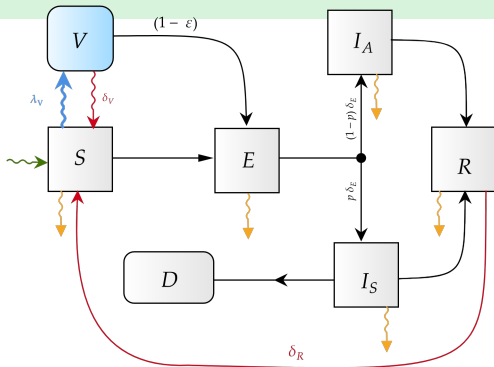
immunity periods

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

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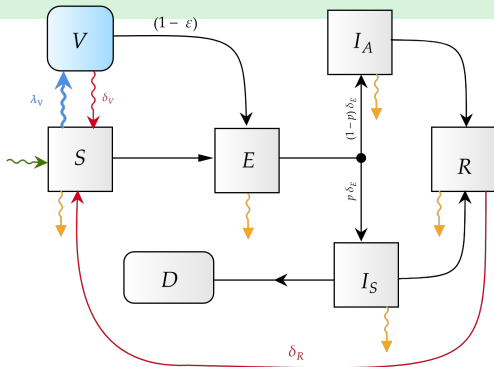
### Notation

- $\varepsilon$  vaccine efficacy
- $p$  Generation of symptoms probability

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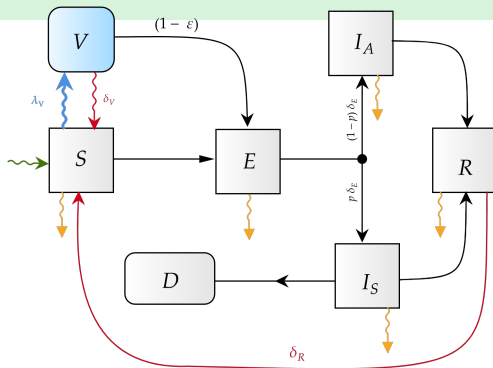
### SAGE objectives

- Vaccine profile (Efficacy, immunity)
- Coverage
- Time Horizon

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Immunity:

- natural (reinfection)
- vaccine-induced



$$\frac{dS}{dt} = \mu \hat{N} - (\lambda_f + \mu + \psi_V)S + \omega_V V + \delta_R R$$

$$\frac{dE}{dt} = \lambda_f S + (1 - \varepsilon)V - (\mu + \delta_E)E$$

$$\frac{dI_S}{dt} = p\delta_E E - (\mu + \alpha_S)I_S$$

$$\frac{dI_A}{dt} = (1 - p)\delta_E E - (\mu + \alpha_A)I_A$$

$$\frac{dR}{dt} = (1 - \theta)\alpha_S I_S + \alpha_A I_A - (\mu + \delta_R)R$$

$$\frac{dD}{dt} = \theta\alpha_S I_S$$

$$\frac{dV}{dt} = \psi_V S - [(1 - \varepsilon)\lambda_f + \mu + \omega_V] V$$

$$X'_{vac} = \psi_V (S + E + I_A + R)$$

$$\hat{N} = S + E + I_A + I_S + R, \quad \hat{N} + D = 1$$

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



Motivation

Methodology

Model Formulation on continuous time

Non standar discrete approximation

Numeric Results

## Nonstandard Finite Differences: Dynamic consistency

We study the evolution of SEIR - mitigation model between deliveries.

Consider for each time sub-interval  $k$  a grid time  $N_k$  partition of sub interval  $[t_*^{(k)}, t^{*(k)}]$ .

$$h_k := \frac{t^{*(k)} - t_*^{(k)}}{N_k}.$$

If  $t_n^{(k)}$  denotes the time of the  $n$  step SEIR model for the  $k$  sub interval, then

$$t_n^{(k)} = nh_k \in [t_*^{(k)}, t^{*(k)}], \quad k = 1, \dots, K.$$

Also, we use an adaptive functional discretization

$$\begin{aligned} \varphi(h) &:= h + \mathcal{O}(h^2) \\ \varphi(h) &= \frac{1 - \exp(-h)}{h} \end{aligned}$$

$$\frac{S^{n+1} - S^n}{\varphi(h)} = \mu \hat{N}^n - (\lambda_f + \varphi_V^{(k)}) S^{n+1} - \mu S^n + \omega_V V^n + \delta_R R^n$$

$$S^{n+1} = \varphi(h) [\mu \hat{N}^n - (\lambda_f + \varphi_V^{(k)}) S^{n+1} - \mu S^n + \omega_V V^n + \delta_R R^n] + S^n$$

$$S^{n+1} = \frac{(1 - \varphi(h)\mu) S^n + \varphi(h)\mu \hat{N}^n + \varphi(h)[\omega_V V^n + \delta_R R^n]}{(1 + \varphi(h))(\lambda_f + \varphi_V^{(k)})}$$

# Discrete Model

$$S^{n+1} = \frac{(1 - \varphi(h)\mu)S^n + \varphi(h)\mu\hat{N}^n + \varphi(h)[\omega_V V^n + \delta_R R^n]}{(1 + \varphi(h))(\lambda_f + \psi_V^{(k)})}$$

$$E^{n+1} = \frac{(1 - \mu\varphi(h))E^n + \varphi(h)\lambda_f[S^{n+1} + (1 - \varepsilon)V^n]}{(1 + \varphi(h)\delta_E)}$$

$$I_S^{n+1} = \frac{(1 - \varphi(h)\mu)I_S^n + \varphi(h)p\delta_E E^{n+1}}{1 + \varphi(h)\alpha_S}$$

$$\vdots$$

$$V^{n+1} = V^n(1 - \varphi(h)[(1 - \varepsilon)\lambda_f + \mu + \omega_V]) + \varphi(h)(\psi_V^{(k)})S^{n+1}$$

$$X_{vac}^{n+1} = \varphi(h)\psi_V^{(k)}(S^n + E^n + I_A^n + R^n) + X_{vac}^n$$

$$K^{n+1} = \max\{0, K^n - (X_{vac}^{n+1} - X_k^0 - L)\}$$

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

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 lost 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

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$$\begin{aligned} \min_{a_V \in \mathcal{U}[0, T]} J(a_t) := \\ a_t := p_k \psi^k, \\ \text{s.t. } \{\text{Stock constrains}\} \end{aligned}$$

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

$$a_t := p_k \Psi^k,$$

s.t. {Stock constrains}



Motivation

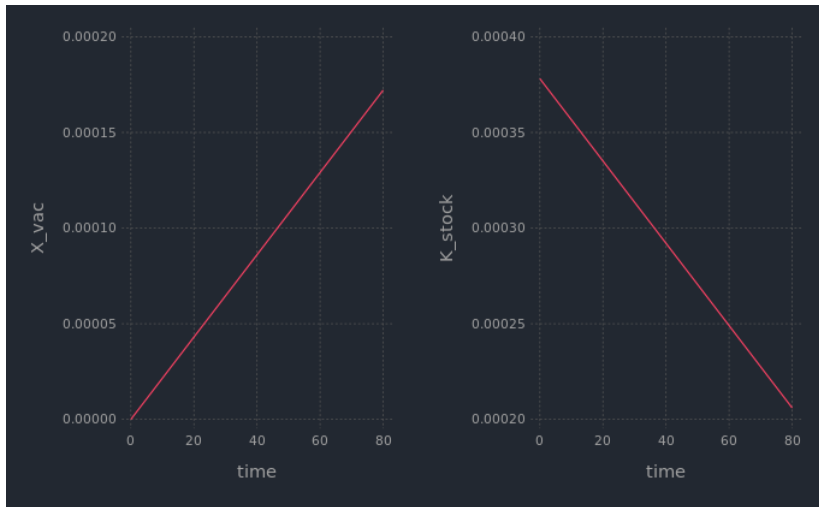
Methodology

Model Formulation on continuous time

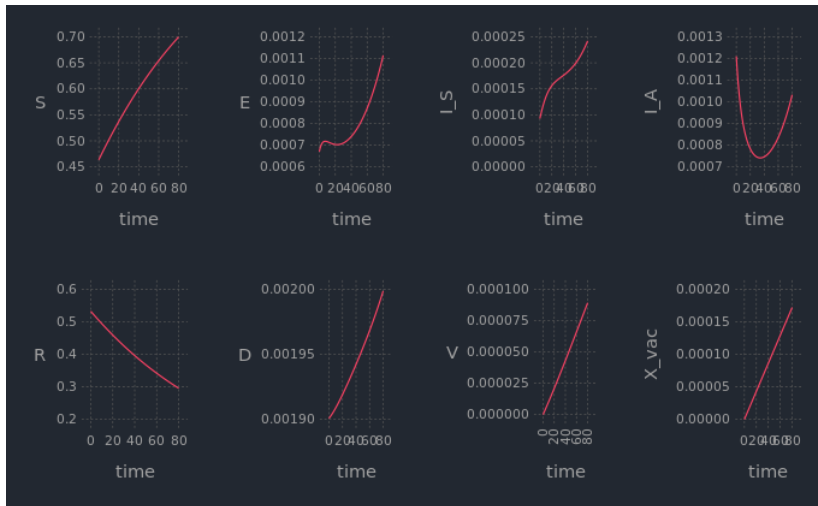
Non standar discrete approximation

Numeric Results

# Results



# Results



# Results

Git Hub



# Outline

Motivation

Methodology

1. Model Formulation on continuous time

2. Non standar discrete approximation

3. Numeric Results