How to Coordinate Countermeasures against COVID-19

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Federal Ministry of Education and Research

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KON SENS

ECMI, 14 April 2021

Outline

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Basic compartmental model: SIR

3 compartments

- susceptible S
- infectious I
- removed R (recovered/deceased)

Basic compartmental model: SIR

$$\beta : \frac{\text{average number of contacts}}{\text{person} \times \text{time}} \cdot \mathrm{Prob}(\text{transmission})$$

3 compartments

- susceptible S
- infectious I
- removed R (recovered/deceased)

$$\frac{\mathrm{d}}{\mathrm{d}t} S(t) = -\beta S(t) I(t)$$
$$\frac{\mathrm{d}}{\mathrm{d}t} I(t) = \beta S(t) I(t)$$

Basic compartmental model: SIR

η^{-1} : average recovery time

3 compartments

- susceptible S
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$$
\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}S(t) &= -\beta S(t)I(t) \\
\frac{\mathrm{d}}{\mathrm{d}t}I(t) &= \quad \beta S(t)I(t) - \eta I(t) \\
\frac{\mathrm{d}}{\mathrm{d}t}R(t) &= \quad \eta I(t)
\end{aligned}
$$

Basic compartmental model: SEIR

γ^{-1} : average incubation time

$$S \xrightarrow{\beta I} E \xrightarrow{\gamma} I \xrightarrow{\eta} R$$

4 compartments

- susceptible S
- exposed E
- infectious I
- removed R (recovered/deceased)

$$
\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}S(t) &= -\beta S(t)I(t)\\
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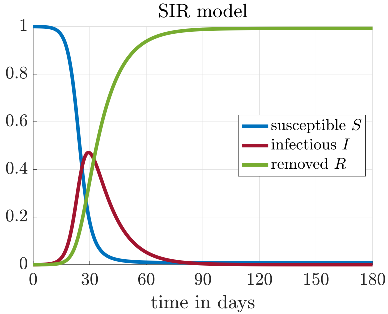
\frac{\mathrm{d}}{\mathrm{d}t}R(t) &= \quad \eta I(t)
\end{aligned}
$$

Basic compartmental model: SEIR



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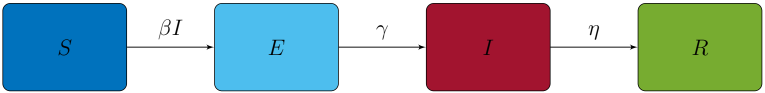

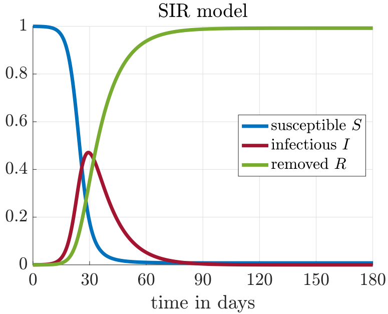

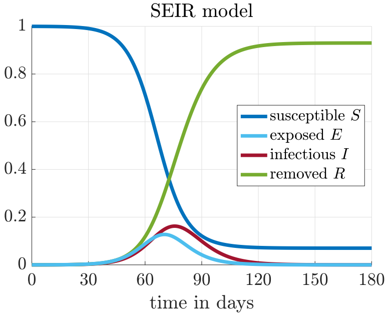

Drawbacks of the SEIR model

Model does not account for

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- symptom severity (ICU occupancy)

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- demographic influences
  - on contacts
  - symptom severity

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- demographic influences
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- counter measures
  - social distancing/quarantine
  - vaccination
  - mass testing

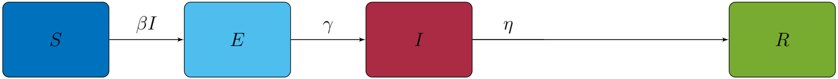
Drawbacks of the SEIR model

Model does not account for

- symptom severity (ICU occupancy)
- demographic influences
  - on contacts
  - symptom severity
- counter measures
  - social distancing/quarantine
  - vaccination
  - mass testing
- births and (natural) deaths
- re-infections

Extension: SEIPHR model

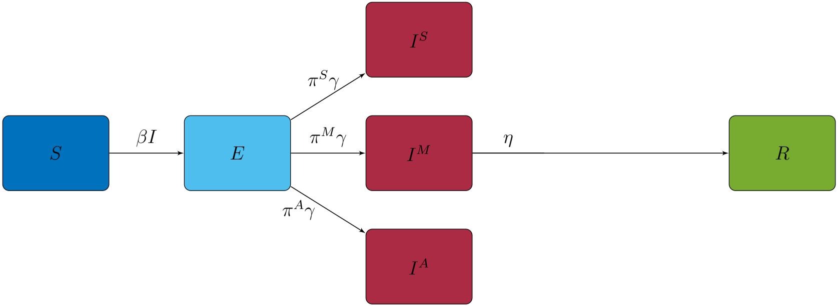
SEIR model



Extension: SEIPHR model

Symptom severity

transmission probabilities $\pi^S + \pi^M + \pi^A = 1$



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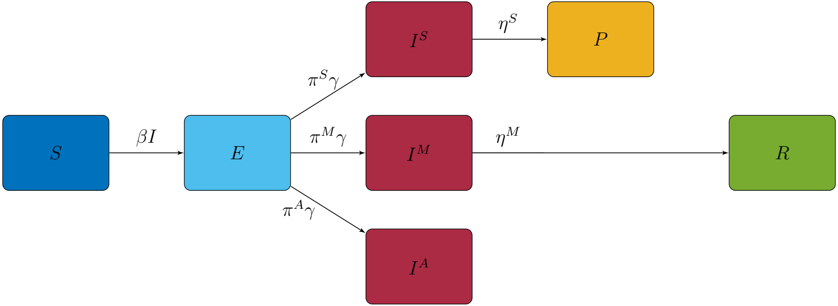
Extension: SEIPHR model

Pre-ICU compartment

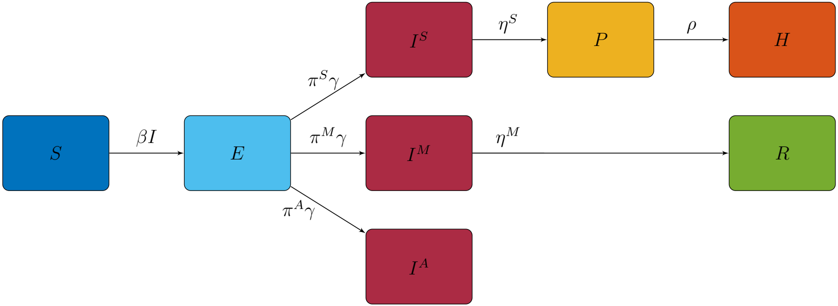
quarantine



Extension: SEIPHR model

ICU compartment

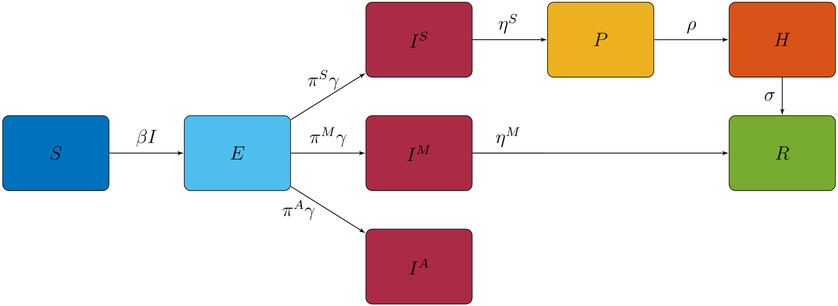
ρ: ICU admittance rate



Extension: SEIPHR model

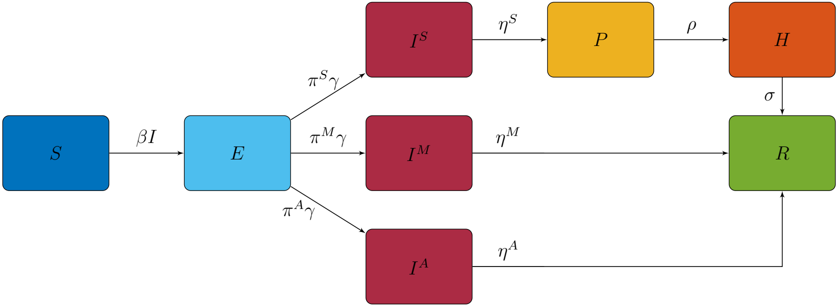
ICU compartment

σ: ICU discharge rate



Extension: SEIPHR model

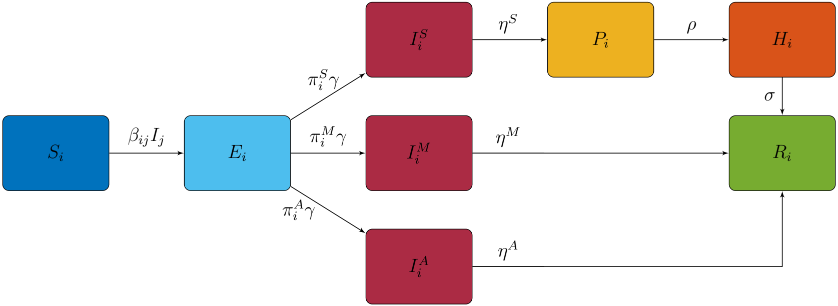
Undetected recovery



Extension: SEIPHR model

Distinguish age groups

$i \in \{1, 2, \ldots, n_\mathrm{g}\}$ (in particular β_{ij} and π_i)

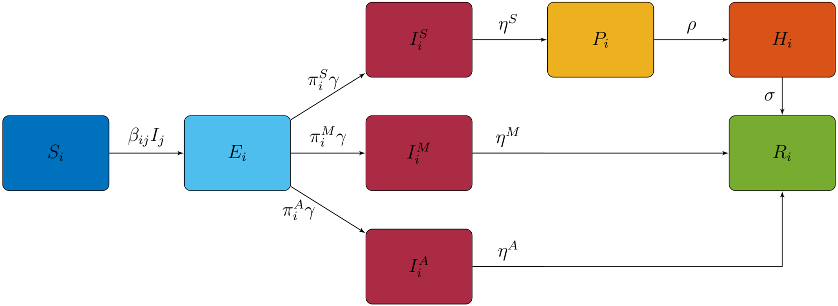


Extension: SEIPHR model

Distinguish age groups

$i \in \{1, 2, \ldots, n_\mathrm{g}\}$ (in particular β_{ij} and π_i)

$n_\mathrm{g} = 3$: children, adults (most contacts), elderly (high-risk)



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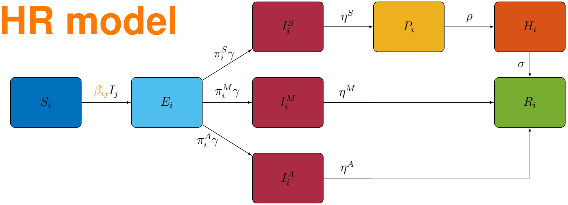


System dynamics

$$\frac{\mathrm{d}}{\mathrm{d}t} S_i(t) = -\sum_{j=1}^{n_g} \beta_{ij} S_i(t) I_j(t) \qquad (I_i = I_i^S + I_i^M + I_i^A)$$

$$\frac{\mathrm{d}}{\mathrm{d}t} E_i(t) = \sum_{j=1}^{n_g} \beta_{ij} S_i(t) I_j(t) - \gamma E_i(t)$$

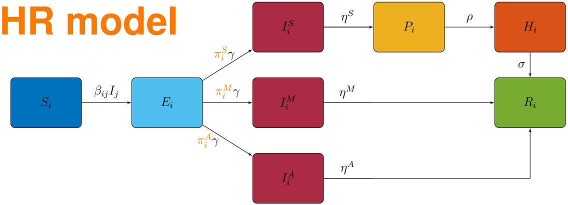
$$\frac{\mathrm{d}}{\mathrm{d}t} I_i^{\#}(t) = \pi_i^{\#} \gamma E_i(t) - \eta^{\#} I_i^{\#}(t) \qquad \# \in \{S, M, A\}$$

$$\frac{\mathrm{d}}{\mathrm{d}t} P_i(t) = \eta^S I_i^S(t) - \rho P_i(t)$$

$$\frac{\mathrm{d}}{\mathrm{d}t} H_i(t) = \rho P_i(t) - \sigma H_i(t)$$

$$\frac{\mathrm{d}}{\mathrm{d}t} R_i(t) = \eta^M I_i^M(t) + \eta^A I_i^A(t)$$

Extension: SEIPHR model



System dynamics

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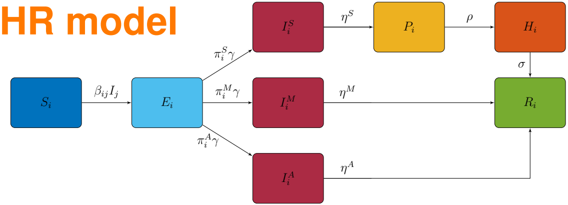
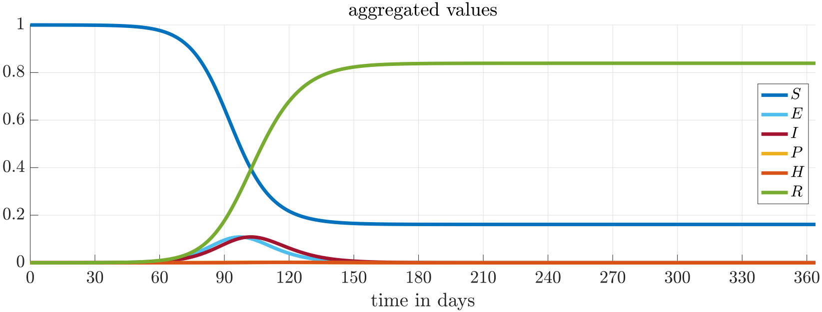
\frac{\mathrm{d}}{\mathrm{d}t} H_i(t) &= \rho P_i(t) - \sigma H_i(t) \\
\frac{\mathrm{d}}{\mathrm{d}t} R_i(t) &= \eta^M I_i^M(t) + \eta^A I_i^A(t)
\end{aligned}
$$

Extension: SEIPHR model



Simulation results



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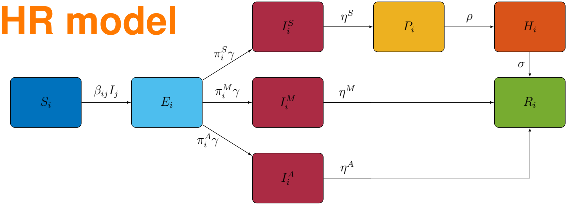

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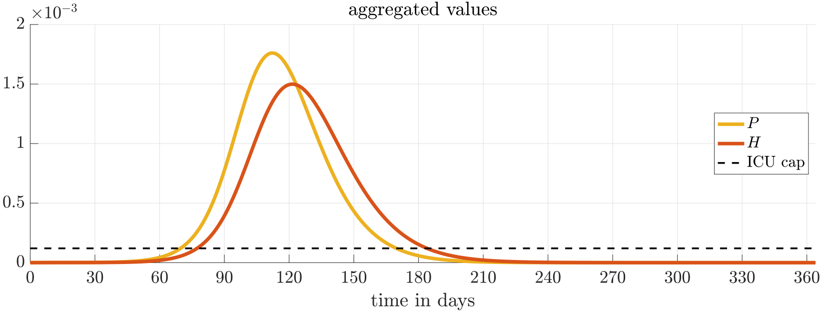
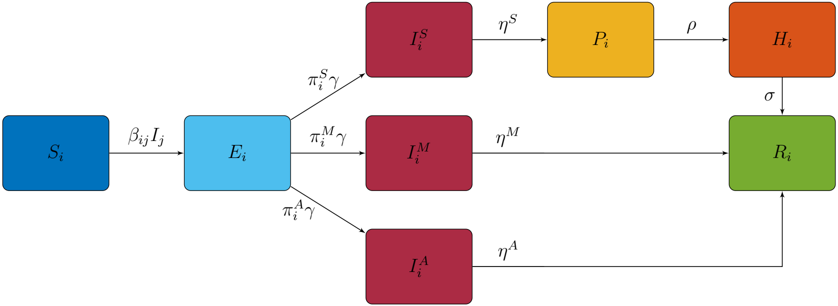


Social distancing

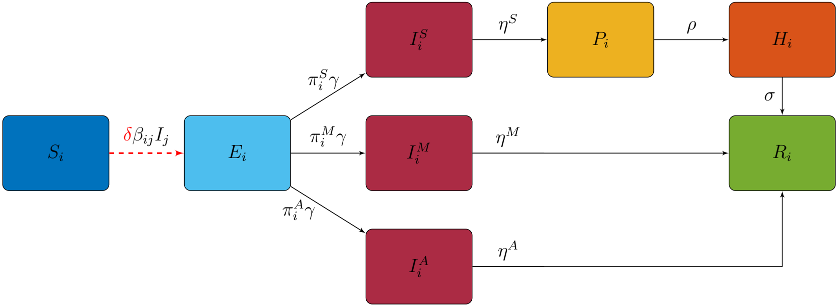
SEIPHR model



Social distancing

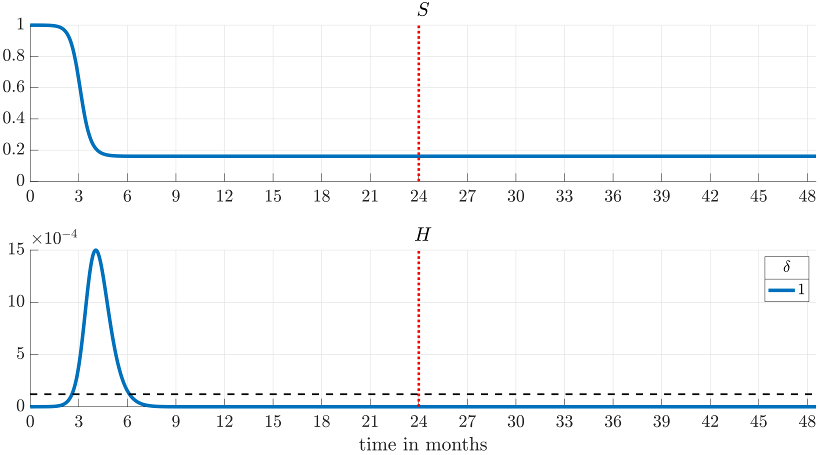
Contact restrictions

control input $\delta : [0, \infty) \to [0, 1]$



Impact of constant restrictions

Simulation results over 4 years with lift of restrictions after 2 years



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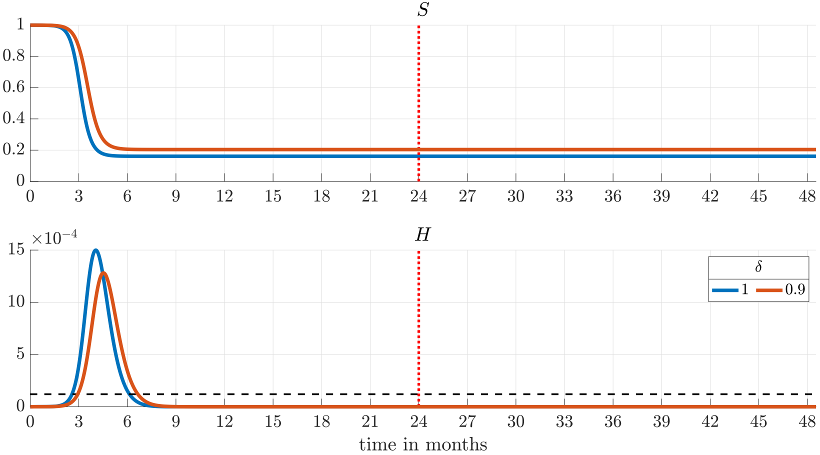

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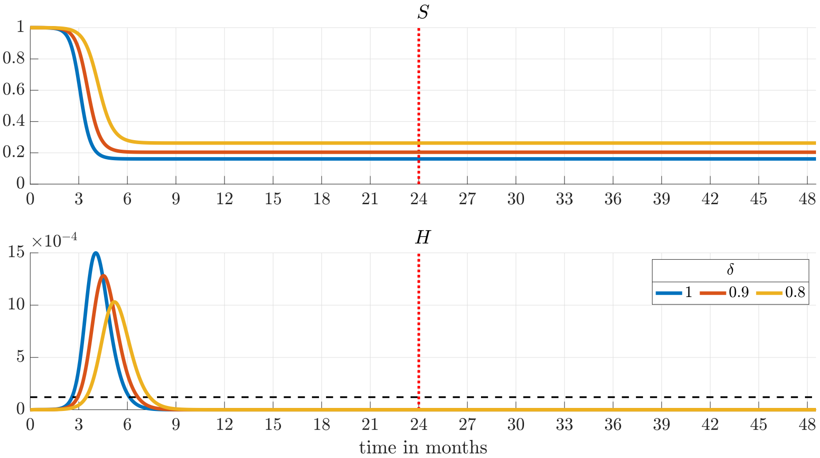

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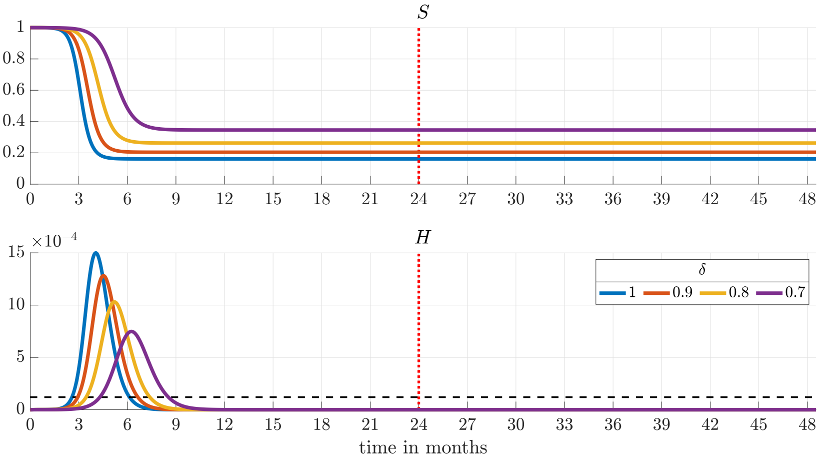

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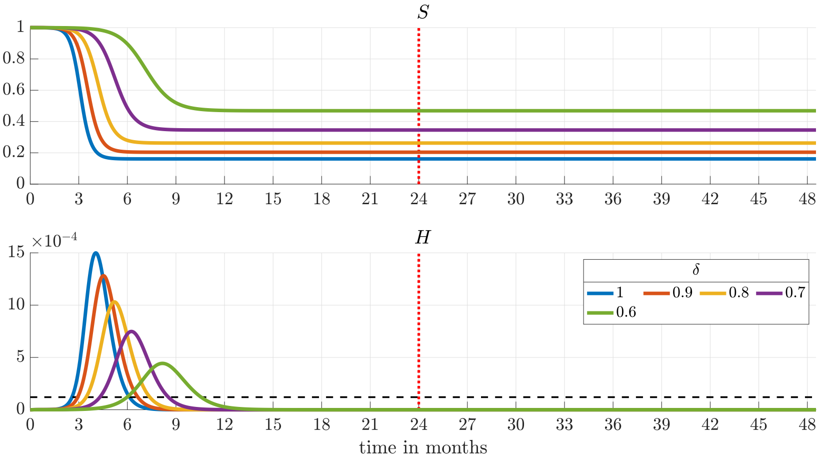
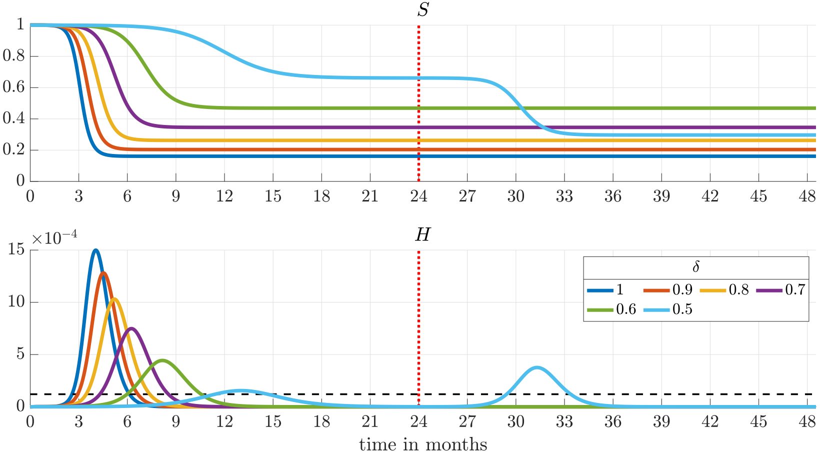


Impact of constant restrictions

Simulation results over 4 years with lift of restrictions after 2 years:

2nd wave (no herd immunity)



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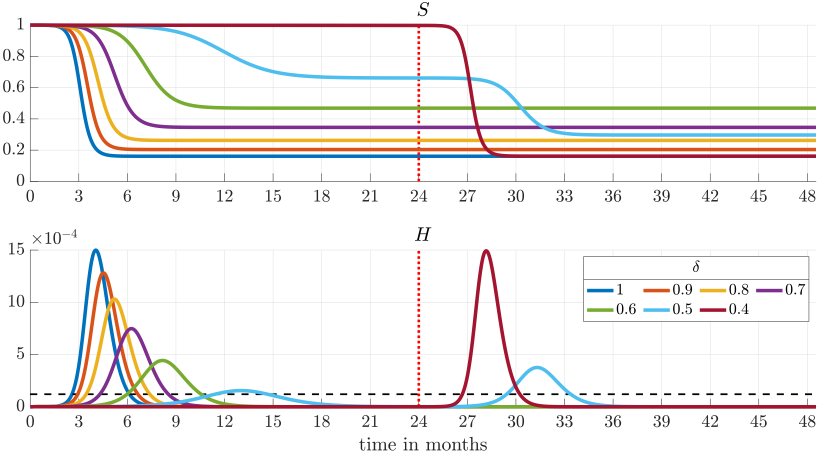

Optimal social distancing

Goal: maintain hard ICU cap with as few contact restrictions as possible

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Optimal control problem

$$\begin{aligned} \min_{\delta} \quad & \int_0^{t_f} (1-\delta(t))^2 \, \mathrm{d}t \\ \text{subject to} \quad & \dot{x}(t) = f(x(t), \delta(t)), \quad x(0) = x^0 \\ & \sum_{i=1}^{n_{\mathrm{g}}} H_i(t) \le H^{\max} \quad \forall\, t \ge 0 \\ & \delta(t) \in [0,1] \quad \forall\, t \ge 0 \end{aligned}$$

Optimal social distancing

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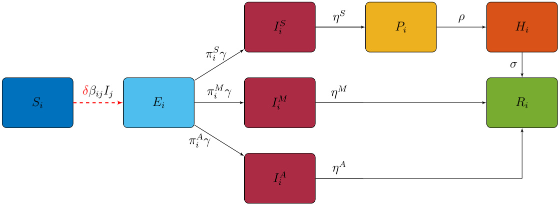
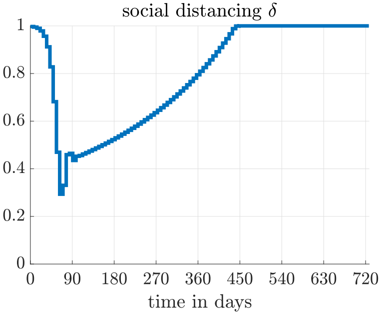
& \delta(t) = \delta(k\Delta t), \quad t \in [k\Delta t, (k+1)\Delta t), \quad k = 0, 1, \ldots
\end{aligned}
$$

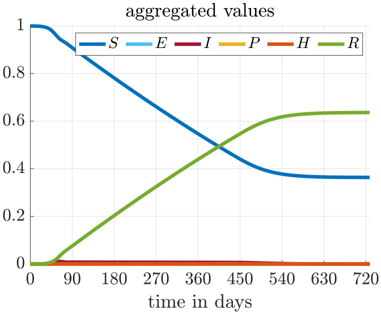
with $\Delta t = 1$ week

Results

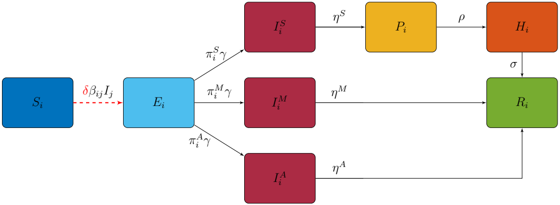


Simulation results

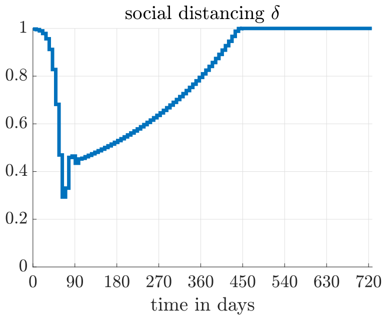


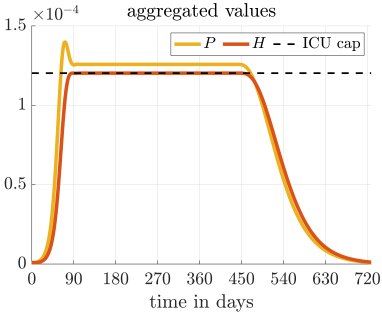


Results



Simulation results

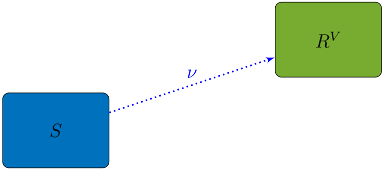




Vaccination

Vaccination of susceptible people

vaccination rate $\nu : [0, \infty) \to \mathbb{R}_{\geq 0}$

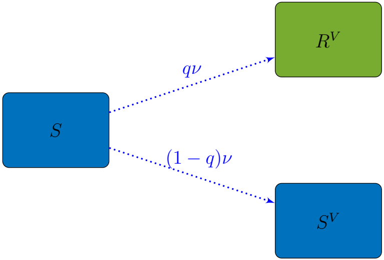


Vaccination

Vaccination of susceptible people

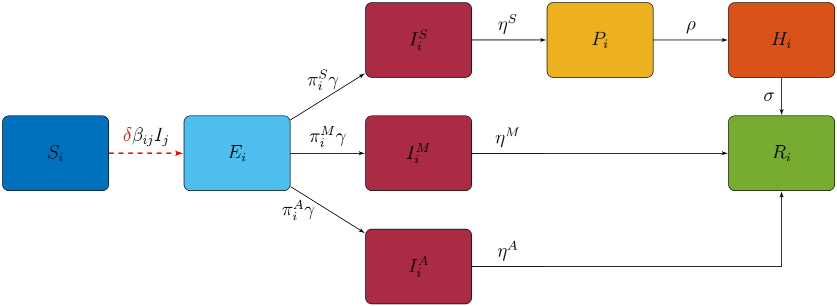
vaccination rate $\nu : [0, \infty) \to \mathbb{R}_{\geq 0}$

success rate $q \in [0, 1]$



Vaccination

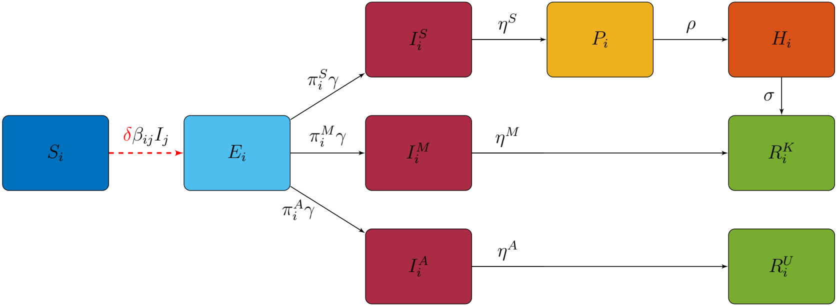
SEIPHR model



Vaccination

SEIPHR model

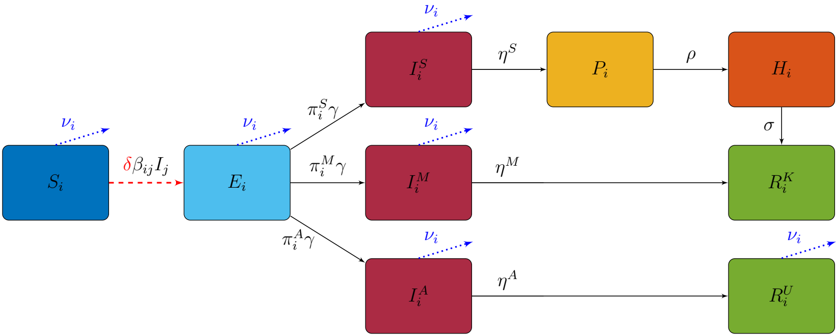
separate undetected recovery



Vaccination

Non-vaccinated part of population

vaccination rate $\nu_i : [0, \infty) \to \mathbb{R}_{\geq 0}$



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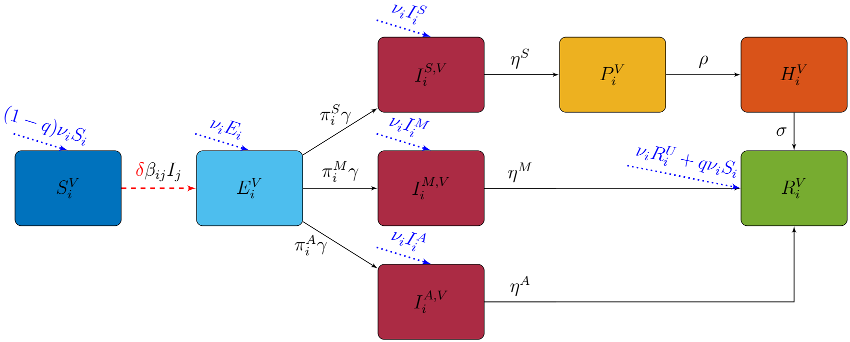
Vaccination

Vaccinated part of population

vaccination rate $\nu_i : [0, \infty) \to \mathbb{R}_{\geq 0}$



Coordination of social distancing & vaccination

Goal: reduce social distancing

Optimal control problem

$$\min_{\delta} \quad \int_0^{t_f} (1-\delta(t))^2 \, \mathrm{d}t$$

$$\text{subject to} \quad \dot{x}(t) = f(x(t), \delta(t) \qquad), \quad x(0) = x^0$$

$$\sum_{i=1}^{n_\mathrm{g}} H_i(t) \qquad \leq H^{\max} \quad \forall\, t \geq 0$$

$$\delta(t) \in [0,1] \quad \forall\, t \geq 0$$

$$\delta(t) = \delta(k\Delta t), \quad t \in [k\Delta t, (k+1)\Delta t), \quad k = 0, 1, \dots$$

Coordination of social distancing & vaccination

Goal: reduce social distancing

Optimal control problem

$$\min_{\delta,\nu} \quad \int_0^{t_f} (1-\delta(t))^2 \,\mathrm{d}t + \kappa \|\nu\|_2^2$$

$$\text{subject to} \quad \dot{x}(t) = f(x(t), \delta(t), \nu(t)), \quad x(0) = x^0$$

$$\sum_{i=1}^{n_\mathrm{g}} H_i(t) + H_i^V(t) \le H^{\max} \quad \forall\, t \ge 0$$

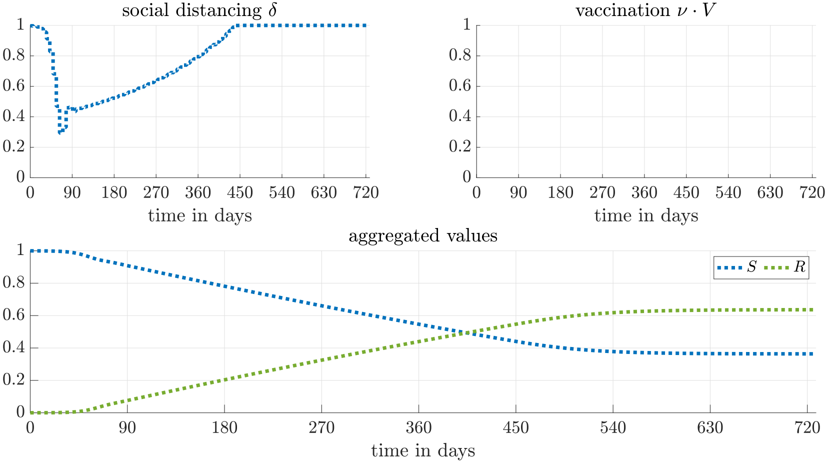
$$\delta(t) \in [0,1] \quad \forall\, t \ge 0$$

$$\delta(t) = \delta(k\Delta t), \quad t \in [k\Delta t, (k+1)\Delta t), \quad k = 0, 1, \ldots$$

$$\int_0^t \sum_{i=1}^{n_\mathrm{g}} \nu_i(s) V_i(s) \,\mathrm{d}s \le V^{\max} \cdot t \quad \forall\, t \ge 0$$

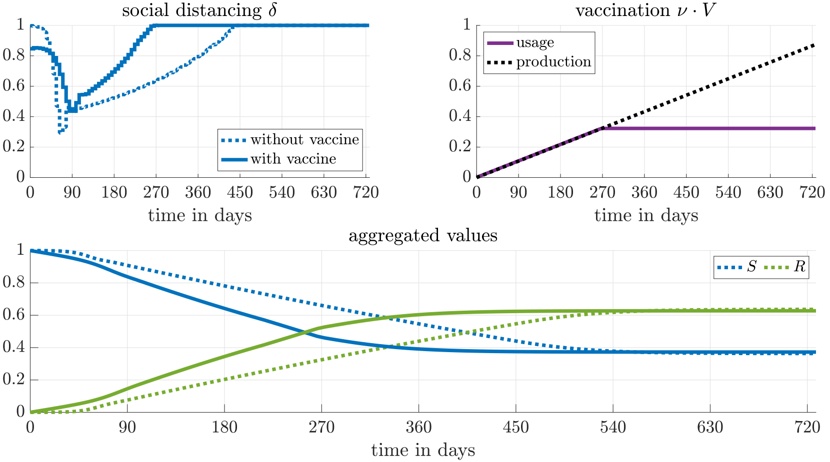
$$\nu(t) = \nu(k\Delta t), \quad t \in [k\Delta t, (k+1)\Delta t), \quad k = 0, 1, \ldots$$

Results

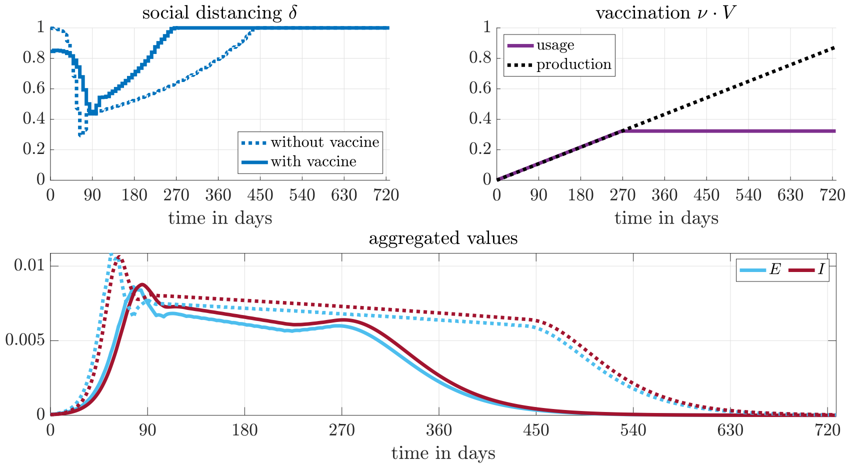


social distancing δ
1
0.8
0.6
0.4
0.2
0
0 90 180 270 360 450 540 630 720
time in days
vaccination $\nu \cdot V$
1
0.8
0.6
0.4
0.2
0
0 90 180 270 360 450 540 630 720
time in days
aggregated values
S R
1
0.8
0.6
0.4
0.2
0
0 90 180 270 360 450 540 630 720
time in days

Results


social distancing δ
without vaccine
with vaccine
time in days
vaccination $\nu \cdot V$
usage
production
time in days
aggregated values
S
R
time in days
0
0.2
0.4
0.6
0.8
1
0
90
180
270
360
450
540
630
720

Results


social distancing δ
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0
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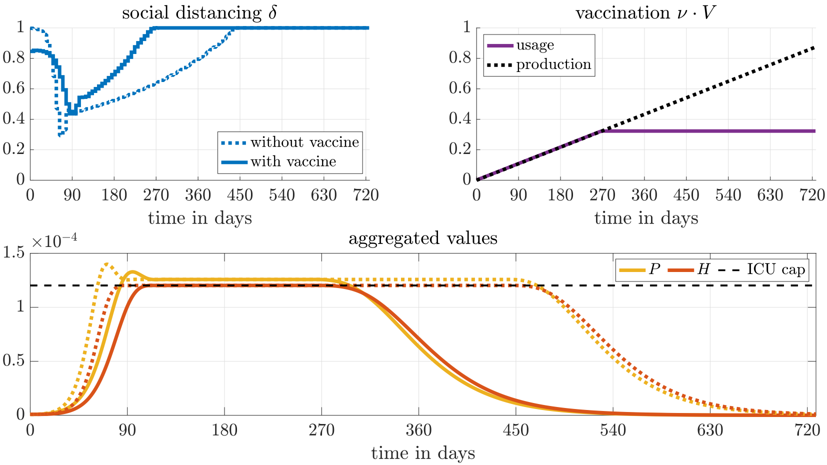
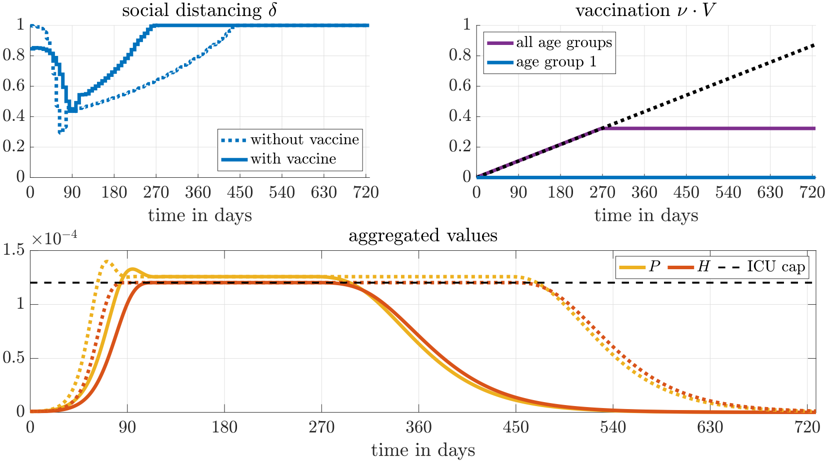
time in days
usage
production
aggregated values
0.01
0.005
0
0 90 180 270 360 450 540 630 720
time in days
E
I

Results

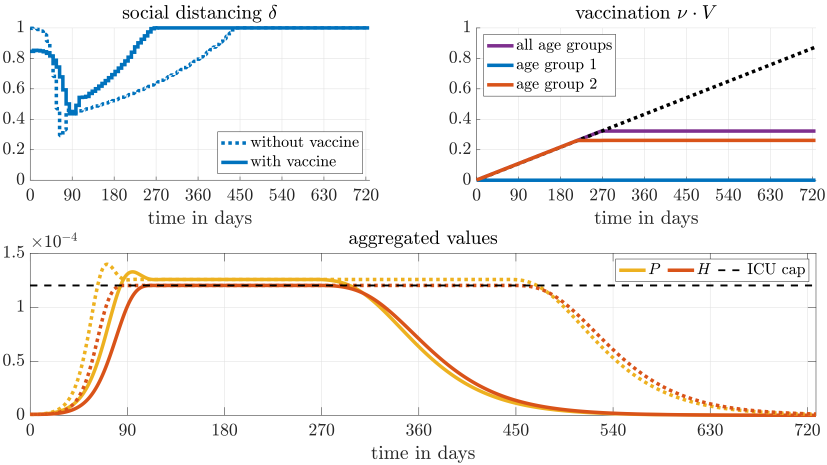

social distancing δ
without vaccine
with vaccine
time in days
vaccination $\nu \cdot V$
usage
production
time in days
aggregated values
$\times 10^{-4}$
P
H
ICU cap
time in days

Results



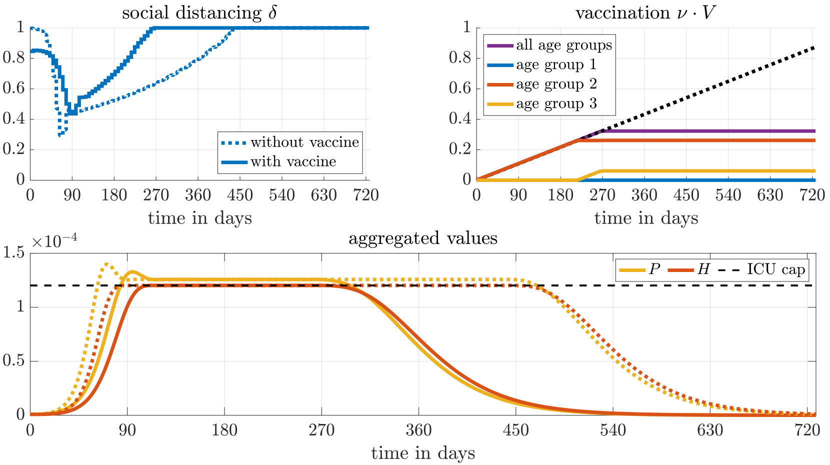
social distancing δ
without vaccine
with vaccine
time in days
vaccination $\nu \cdot V$
all age groups
age group 1
time in days
aggregated values
$\times 10^{-4}$
P
H
ICU cap
time in days

Results



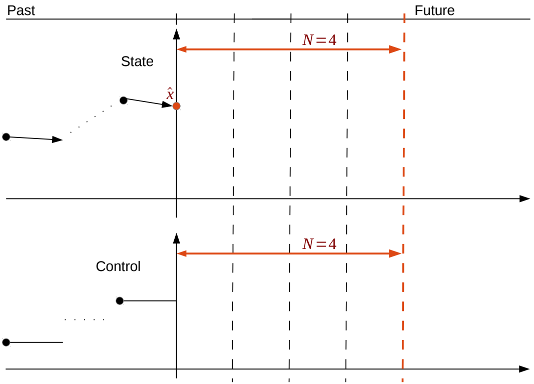
social distancing δ
1
0.8
0.6
0.4
0.2
0
0 90 180 270 360 450 540 630 720
time in days
without vaccine
with vaccine
vaccination $\nu \cdot V$
all age groups
age group 1
age group 2
aggregated values
$\times 10^{-4}$
1.5
0.5
P
H
ICU cap

Results



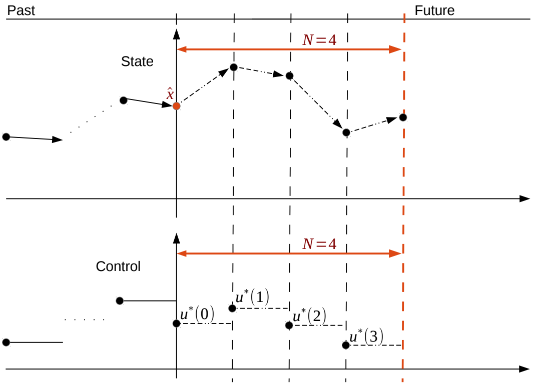
social distancing δ
without vaccine
with vaccine
time in days
vaccination $\nu \cdot V$
all age groups
age group 1
age group 2
age group 3
time in days
aggregated values
$\times 10^{-4}$
P
H
ICU cap
time in days

Model Predictive Control



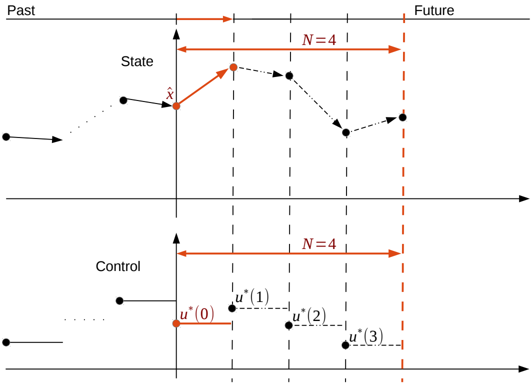
1. Measure/Estimate current state and update parameters.

Model Predictive Control



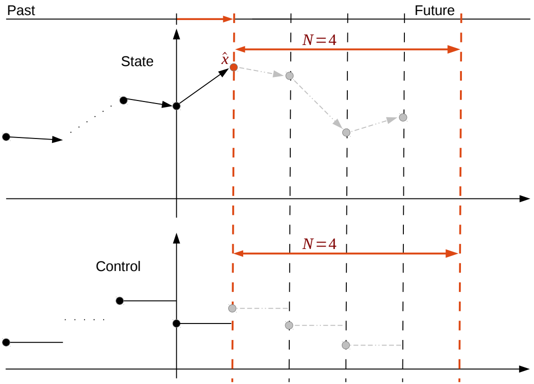
1. Measure/Estimate current state and update parameters.
2. Solve optimal control problem *on small time window*.

Model Predictive Control



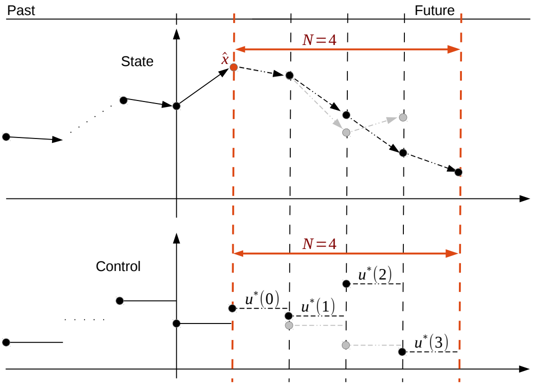
1. Measure/Estimate current state and update parameters.
2. Solve optimal control problem *on small time window*.
3. Implement first control instance.

Model Predictive Control



1. Shift time step, measure/estimate current state, and update parameters.
2. Solve optimal control problem *on small time window*.
3. Implement first control instance.

Model Predictive Control



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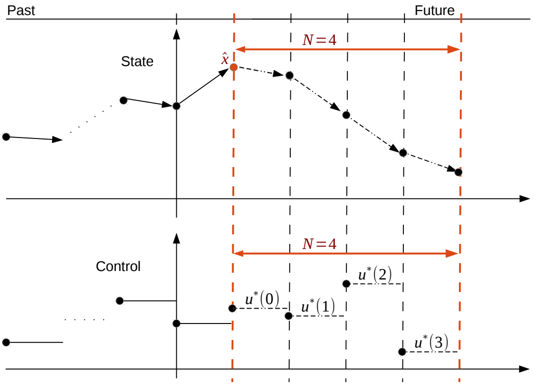

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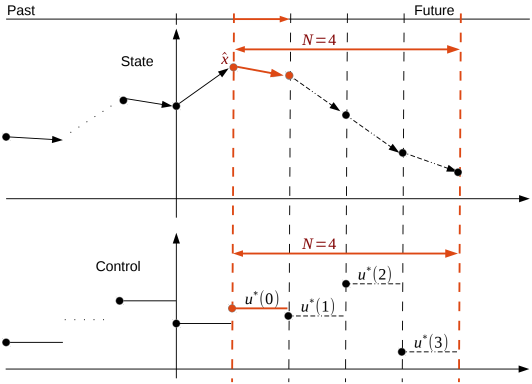

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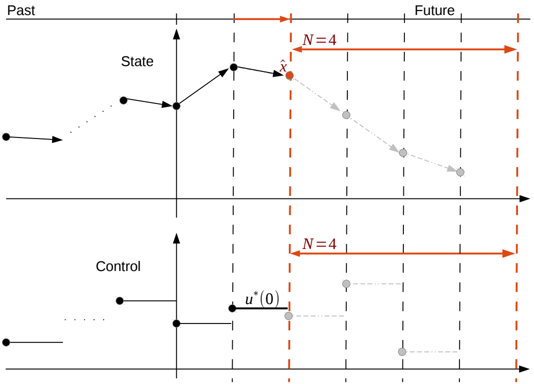

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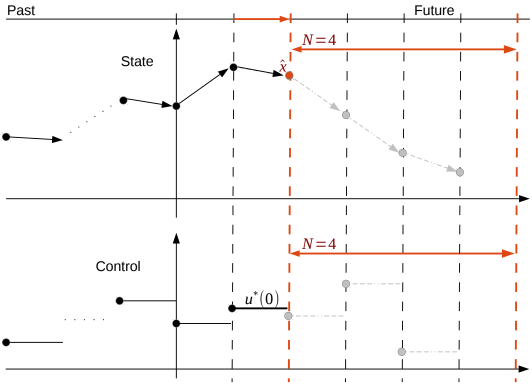

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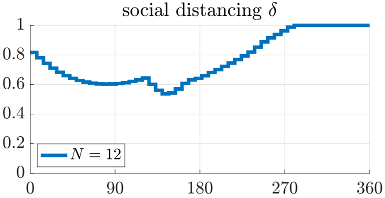
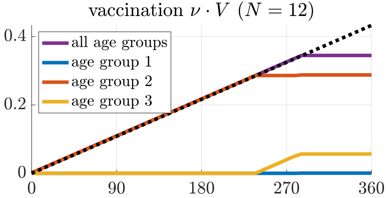
Closed-loop simulations

Impact of prediction horizon N (in weeks) on controls





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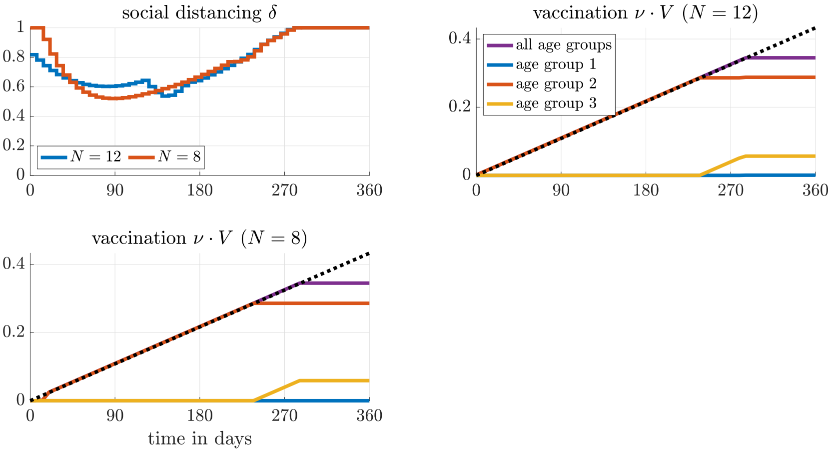

Philipp Sauerteig
Institute for Mathematics

Closed-loop simulations

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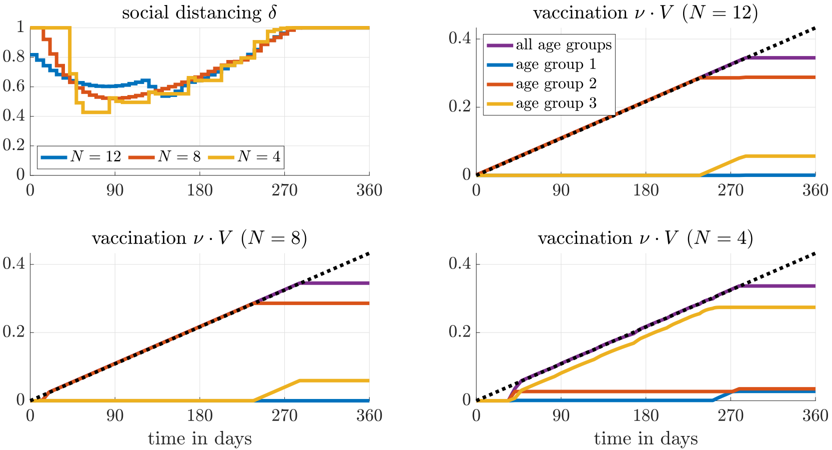

Philipp Sauerteig
Institute for Mathematics

Conclusions & outlook

Recap

- extension of the SEIR model to account for age-dependent symptom severity and countermeasures

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Further extensions and future work

- minimizing fatalities

Conclusions & outlook

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- uncertainty quantification of parameters

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- mass testing, age-differentiated contact restrictions
- re-infections
- uncertainty quantification of parameters
- breakpoints/bifurcation

References

The presented results are based on

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How much testing and social distancing is required to control COVID-19? Some insight based on an age-differentiated compartmental model
Submitted. (Preprint available at https://arxiv.org/abs/2011.01282)

[2] S. Grundel, S. Heyder, T. Hotz, T. K. S. Ritschel, P. Sauerteig, K. Worthmann
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Vorläufige Bewertung der Krankheitsschwere von COVID-19 in Deutschland basierend auf übermittelten Fällen gemäß Infektionsschutzgesetz

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Clinical presentation and virological assessment of hospitalized cases of coronavirus disease 2019 in a travel-associated transmission cluster

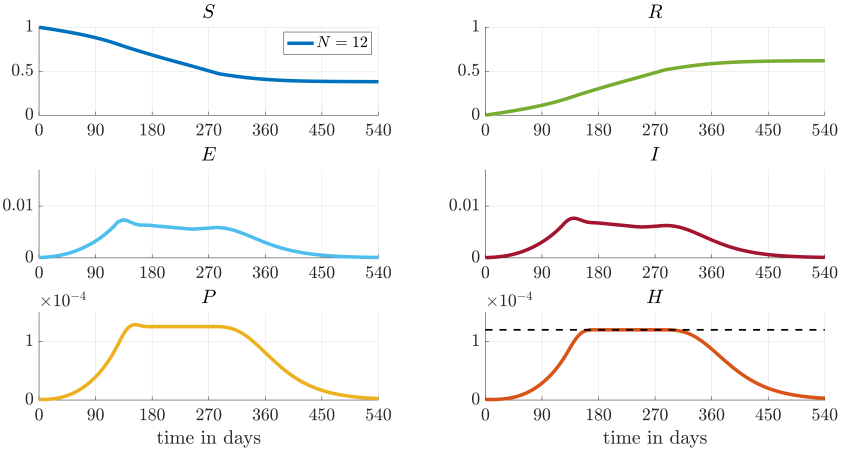
Thank you for your attention!

Parameters

Description	Symbol	Value		
Number of age groups	n_{g}	3		
Regularization parameter	κ	10^{-3}		
Removal rate (severe)	η^S	0.2500		
Removal rate (mild)	η^M	0.2500		
Removal rate (asymptomatic)	η^A	0.1667		
Rate of becoming infectious	γ	0.1923		
ICU admittance rate	ρ	0.0910		
ICU discharge rate	σ	0.0952		
Vaccine production limit	$V^{\max}$	$100,000$		
Success rate	q	0.9		
Age-differentiated parameters				
Age group	i	1	2	3
Age range (in years)	–	< 15	$15 - 59$	> 60
Relative age group size	N_i	0.1370	0.5776	0.2854
Probability of severe symptoms	π_i^S	0.0053	0.0031	0.0302
Probability of mild symptoms	π_i^M	0.1211	0.2201	0.2512
Probability of no symptoms	π_i^A	0.8737	0.7768	0.7186
Transmission rate (age group 1)	β_{1i}	0.4612		
Transmission rate (age group 2)	β_{2i}	0.4819	0.6304	
Transmission rate (age group 3)	β_{3i}	0.1243	0.2944	0.1802

Closed-loop simulations II

Impact of prediction horizon N (in weeks) on states



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Closed-loop simulations II

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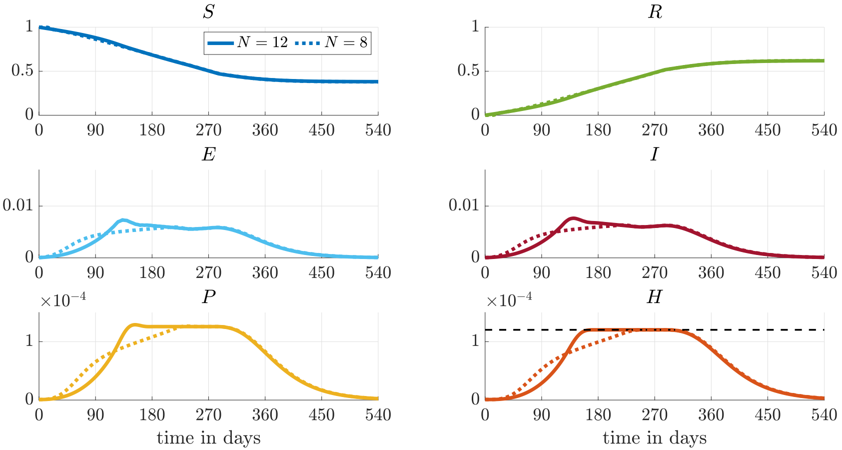

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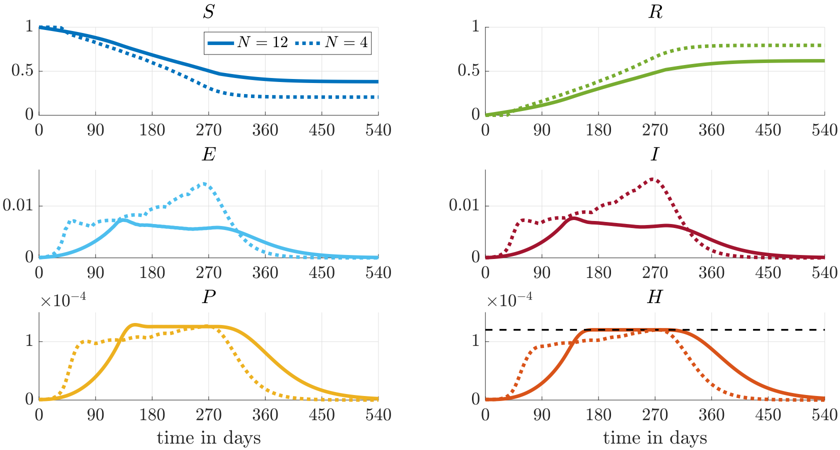


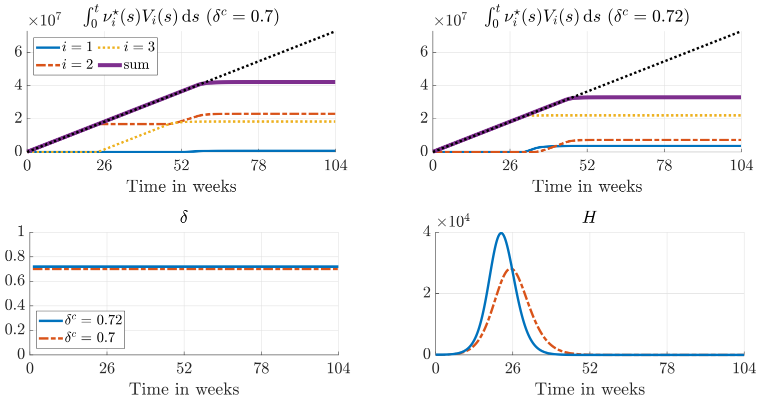
Minimizing fatalities

Assumption: total number of fatalities $\propto$ total number of people treated on ICU

For given $\delta^c \in [0,1]$ solve

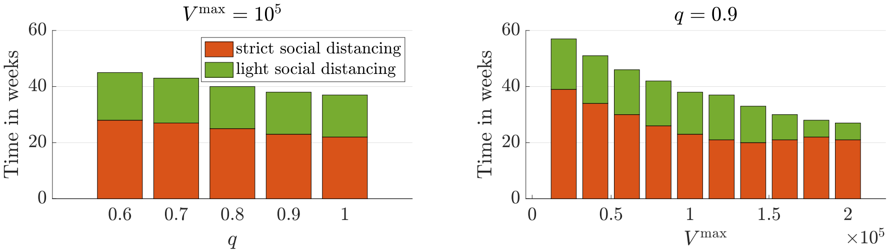
$$
\begin{aligned}
\min_{\nu} \quad & H^C(t_f) + \kappa \|\nu\|_2^2 \\
\text{subject to} \quad & \dot{H}^C(t) = \sum_{i=1}^{n_g} \sigma(H_i(t) + H_i^V(t)), \quad H^C(0) = 0 \\
& \dot{x}(t) = f(x(t), \delta^c, \nu(t)), \quad x(0) = x^0 \\
& \int_0^t \sum_{i=1}^{n_\mathrm{g}} \nu_i(s) V_i(s)\,\mathrm{d}s \le V^{\max} \cdot t \quad \forall t \ge 0 \\
& \nu(t) = \nu(k\Delta t), \quad t \in [k\Delta t, (k+1)\Delta t), \quad k = 0, \dots, N-1
\end{aligned}
$$

Minimizing fatalities



- contact restrictions sufficiently strict $\rightsquigarrow$ vaccinate group with most contacts first
- otherwise $\rightsquigarrow$ vaccinate high-risk group first ("damage control")

Impact of $V^{\max}$ and q



for convenience:

- light contact restrictions: $0.8 \leq \delta$
- strict contact restrictions: $0.6 \leq \delta < 0.8$
- lockdown: $\delta < 0.6$