A Bayesian hierarchical approach to assess the impact of non-pharmaceutical interventions and to monitor the propagation of COVID-19 in Bavaria

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Aim: Implement a monitoring tool to estimate the impact of non-pharmaceutical interventions and to predict the propagation of COVID-19 in Germany

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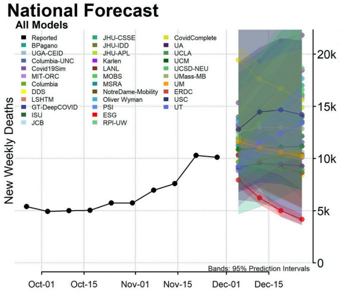
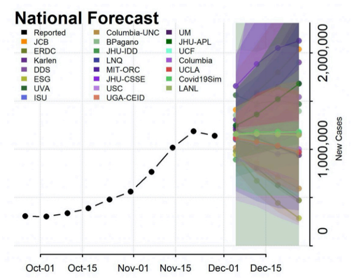
- Estimate the effect of non-pharmaceutical interventions on the reproduction number
- Predict the number of daily new infections and derive the number of cases needing hospitalization and ICU treatment in Germany under different non-pharmaceutical interventions

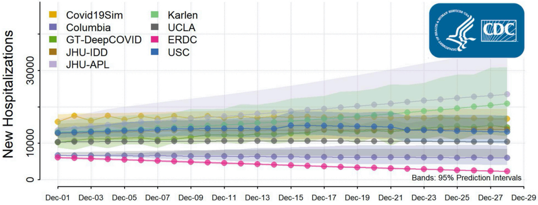
Overview

1. Sources of uncertainty in the modelling of COVID-19
2. A Bayesian hierarchical approach to monitor disease propagation of COVID-19 in Bavaria
3. Simulation study
4. Results for Bavaria
5. Outlook

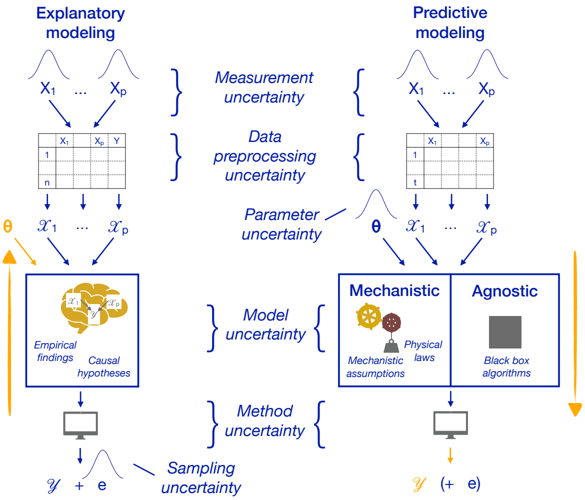
COVID-19 Forecasts from the CDC for the US







Sources of uncertainty in the modelling of COVID-19



Source: "The multiplicity of analysis strategies jeopardizes replicability: Lessons learned across disciplines" by S. Hoffmann, F. Schönbrodt, R. Elsas, R. Wilson, U. Strasser and A. Boulesteix, available on Meta-Arxiv, preprint DOI: `10.31222/osf.io/afb9p`

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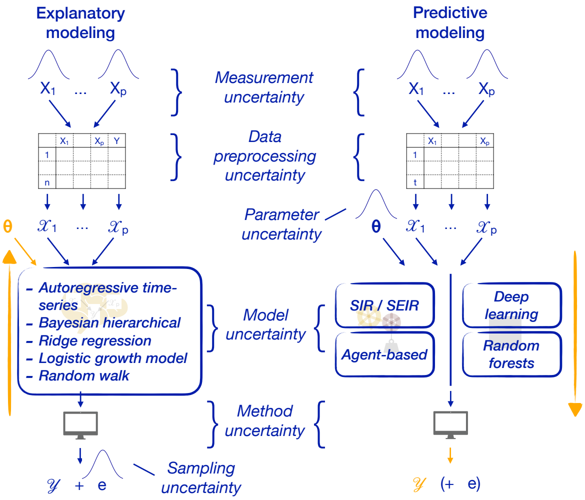

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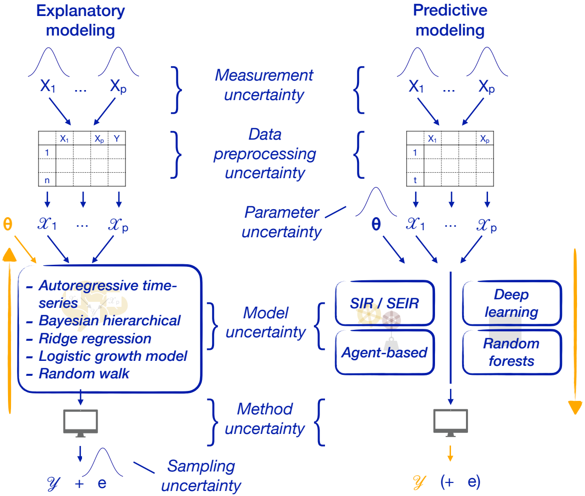
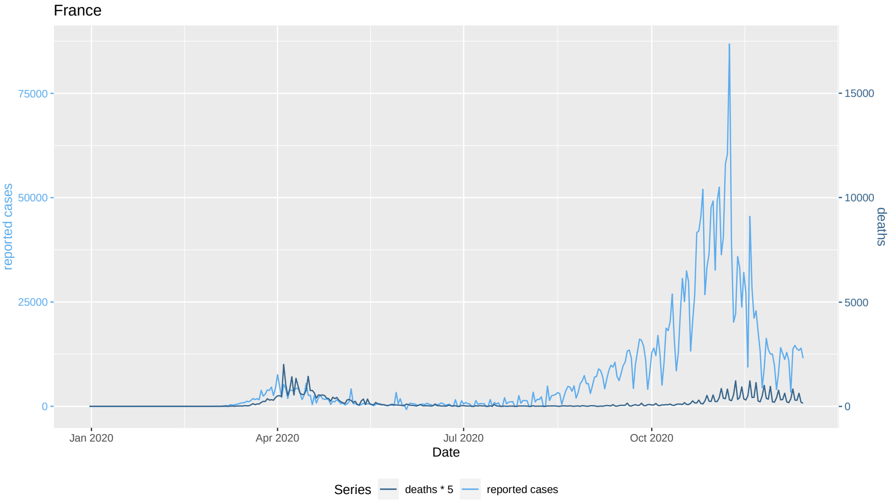


- Generation time
- Incubation time
- Infection fatality rate
- R_0

Measurement uncertainty in COVID-19 modelling



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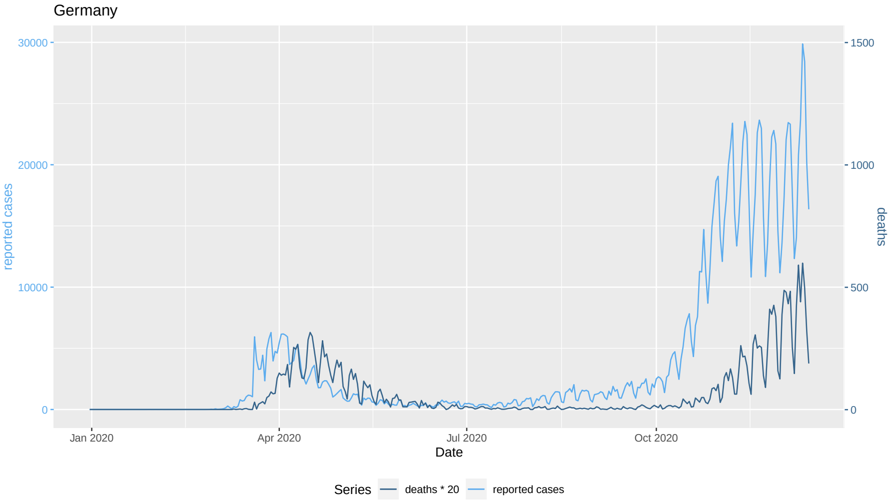

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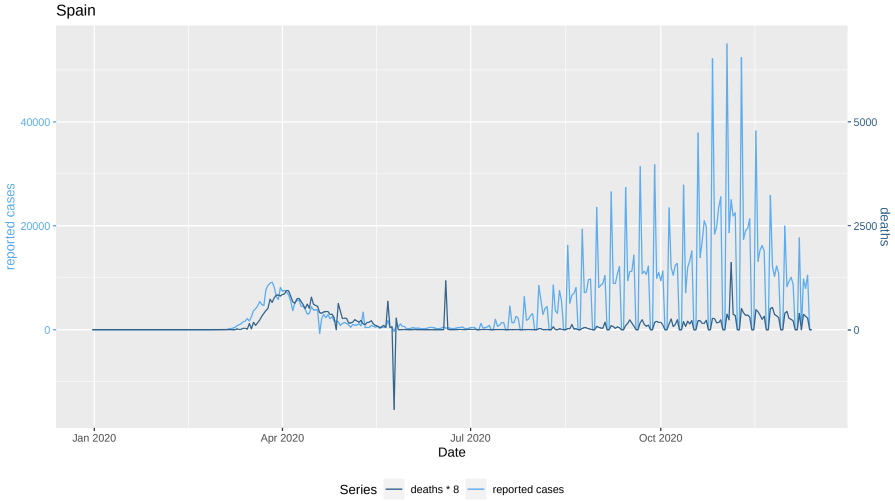

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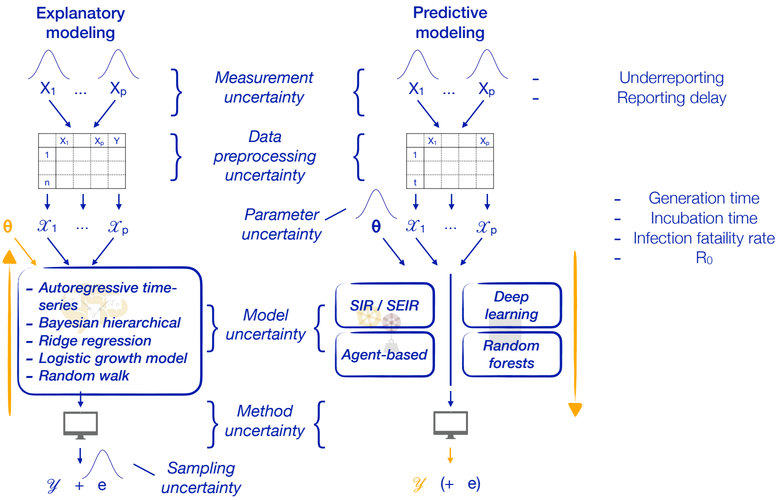

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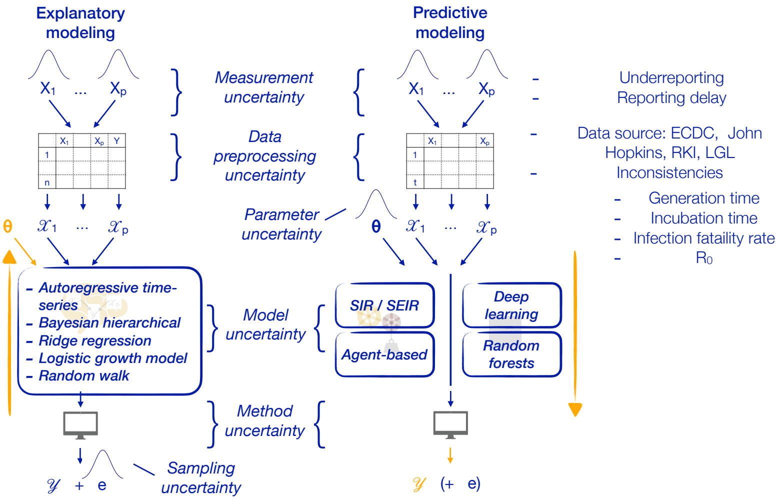

Advantages of a Bayesian hierarchical approach

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- Flexible framework to describe complex phenomena through the combination of submodels
- Account for all sources of uncertainty:
  - Underreporting and reporting delay in the number of cases
  - Parameter uncertainty
- Integrate all available information
  - Use data on the reported number of cases, the number of deaths and the number of hospitalizations in the estimation of new infections
  - Borrow information by integrating data from other countries
  - Information from previous studies

Article

Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe

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Check for updates

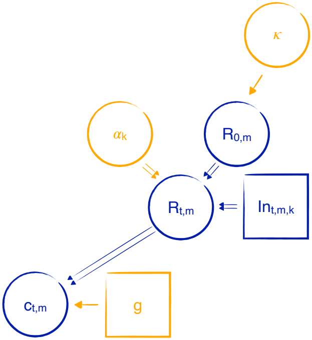
Seth Flaxman[1,7], Swapnil Mishra[2,7], Axel Gandy[1,7], H. Juliette T. Unwin[2], Thomas A. Mellan[2], Helen Coupland[2], Charles Whittaker[2], Harrison Zhu[1], Tresnia Berah[1], Jeffrey W. Eaton[2], Mélodie Monod[1], Imperial College COVID-19 Response Team*, Azra C. Ghani[2], Christl A. Donnelly[2,3], Steven Riley[2], Michaela A. C. Vollmer[2], Neil M. Ferguson[2], Lucy C. Okell[2] & Samir Bhatt[2,7]✉

Following the detection of the new coronavirus[1] severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its spread outside of China, Europe has experienced large epidemics of coronavirus disease 2019 (COVID-19). In response, many European countries have implemented non-pharmaceutical interventions, such as the closure of schools and national lockdowns. Here we study the effect of major interventions across 11 European countries for the period from the start of the COVID-19 epidemics in February 2020 until 4 May 2020, when lockdowns started to be lifted. Our model calculates backwards from observed deaths to estimate transmission that occurred several weeks previously, allowing for the time lag between infection and death. We use partial pooling of information between countries, with both individual and shared effects on the time-varying reproduction number (R_t). Pooling allows for more information to be used, helps to overcome idiosyncrasies in the data and enables more-timely estimates. Our model relies on fixed estimates of some epidemiological parameters (such as the infection fatality rate), does not include importation or subnational variation and assumes that changes in R_t are an immediate response to interventions rather than gradual changes in behaviour. Amidst the ongoing pandemic, we rely on death data that are incomplete, show systematic biases in reporting and are subject to future consolidation. We estimate that—for all of the countries we consider here—current interventions have been sufficient to drive R_t below 1 (probability $R_t < 1.0$ is greater than 99%) and achieve control of the epidemic. We estimate that across all 11 countries combined, between 12 and 15 million individuals were infected with SARS-CoV-2 up to 4 May 2020, representing between 3.2% and 4.0% of the population. Our results show that major non-pharmaceutical interventions—and lockdowns in particular—have had a large effect on reducing transmission. Continued intervention should be considered to keep transmission of SARS-CoV-2 under control.

Flaxman et al. (2020)

- The number of infections $c_{t,m}$ on day t in country m is given by $c_{t,m} = R_{t,m} \sum_{\tau=0}^{t-1} c_{\tau,m} g_{t-\tau}$ where g_t is a discretized version of the serial interval distribution $g \sim Gamma(6.5, 0.62)$ and $R_{t,m} = R_{0,m} \exp\left(-\sum_{k=1}^{6} \alpha_k, I_{k,t,m}\right)$

Flaxman et al. (2020): DAG



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- Deterministic link between the expected number of deaths $d_{t,m} = E(D_{t,m})$ and the number of infections $c_{t-1,m}, c_{t-2,m}, c_{t-3,m}, \ldots$ occurring in previous days:

$$d_{t,m} = \sum_{\tau=0}^{t-1} c_{\tau,m} \pi_{t-\tau,m}$$

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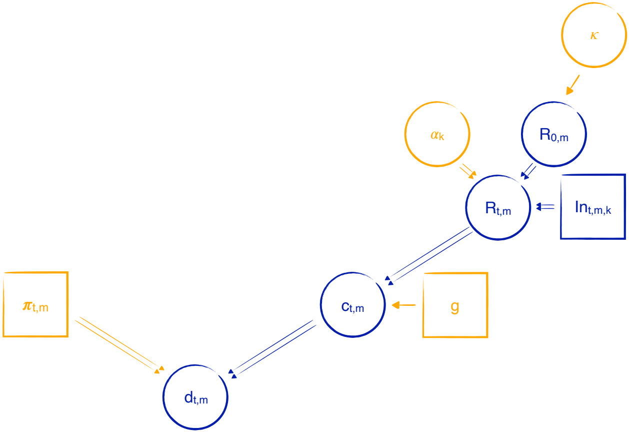

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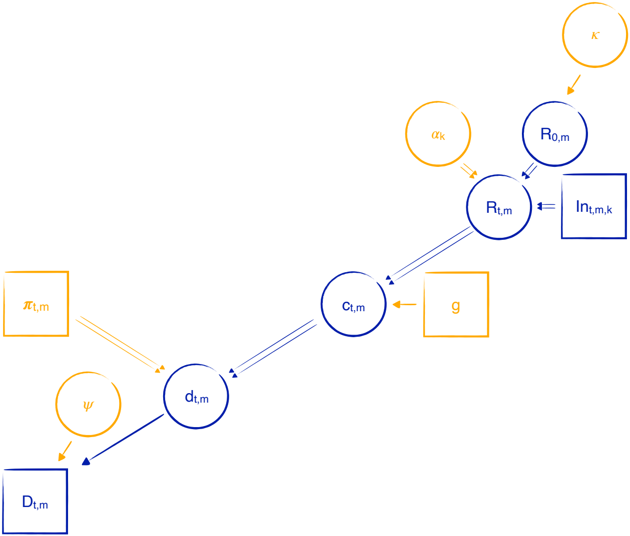
$$d_{t,m} = \sum_{\tau=0}^{t-1} c_{\tau,m} \pi_{t-\tau,m}$$

- Daily deaths $D_{t,m}$ for days $t \in 1, \ldots, n$ and countries $m \in 1, \ldots, p$

$$D_{t,m} \sim NegativeBinomial\left(d_{t,m}, d_{t,m} + \frac{d_{t,m}^2}{\psi}\right)$$

Flaxman et al. (2020): DAG



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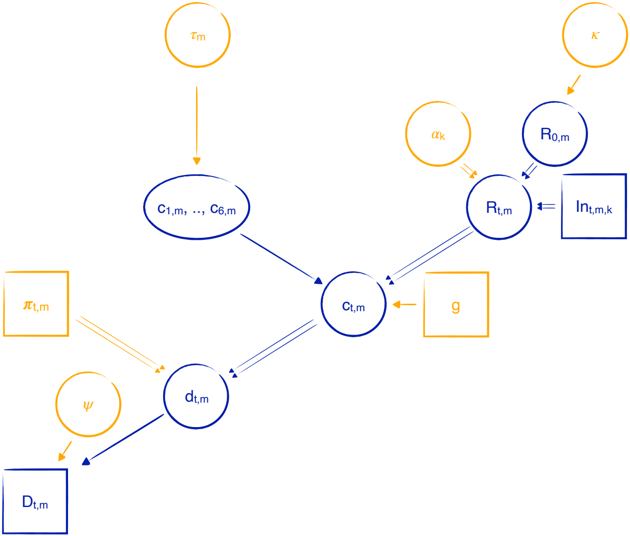

Possible improvements

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⇒ Include information on the number of reported cases $C^R_{t,m}$ while accounting for underreporting and reporting delay

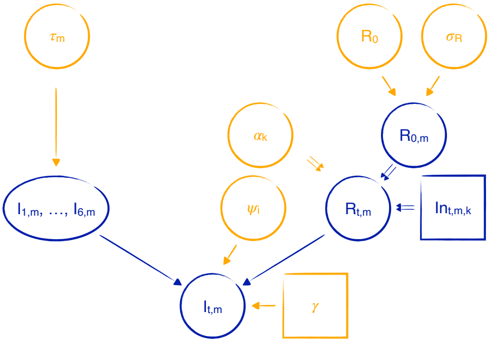
A hierarchical model of COVID-19 propagation

- The renewal model:

$$I_{t,m} \sim NegativeBinomial\left(\tau_m, \phi_i\right) \text{ for t} \leq 6$$

$$I_{t,m} \sim NegativeBinomial\left(R_{t,m} \sum_{u<t} I_{u,m}(F_\gamma(t-u+1) - F_\gamma(t-u)), \phi_i\right)$$

with $R_{t,m} = R_{0,m} \exp\left(-\sum_{k=1}^{K} \alpha_k I_{k,t,m}\right)$


τ_m
R_0
σ_R
α_k
$R_{0,m}$
$I_{1,m}, \ldots, I_{6,m}$
ψ_i
$R_{t,m}$
$In_{t,m,k}$
$I_{t,m}$
γ

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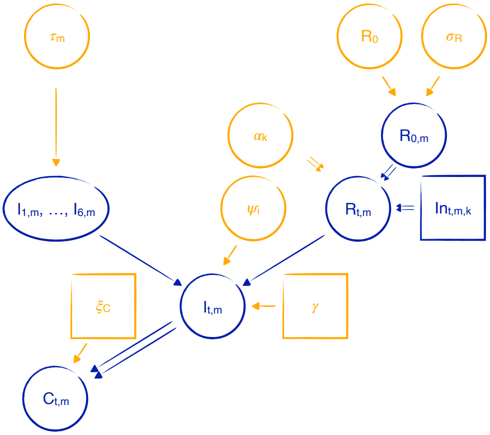
- The disease model:

$$C_{t,m} = \sum_{u<t} I_{u,m}(F_{\xi_C}(t-u+1) - F_{\xi_C}(t-u))$$


τm
R0
σR
αk
R0,m
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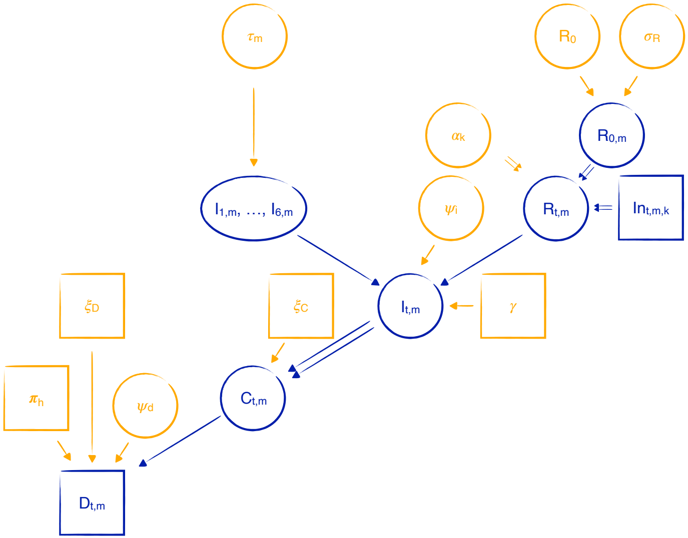
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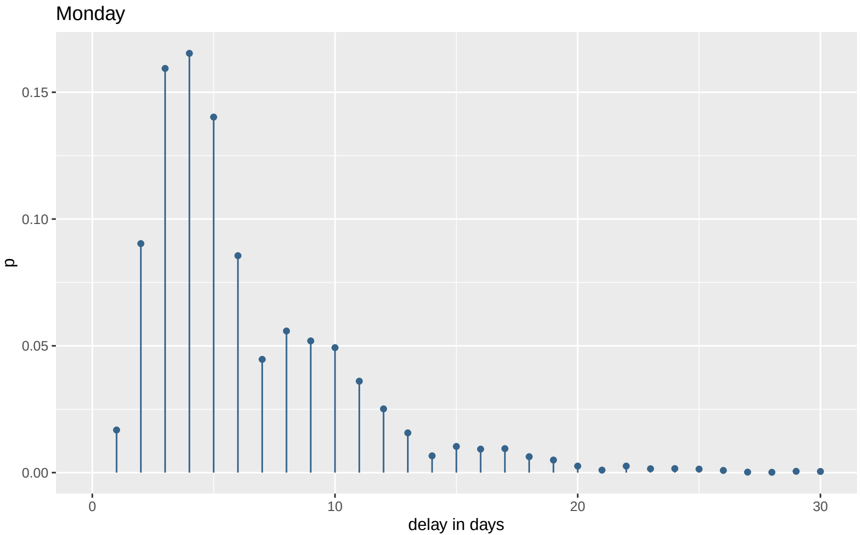
Reporting delay



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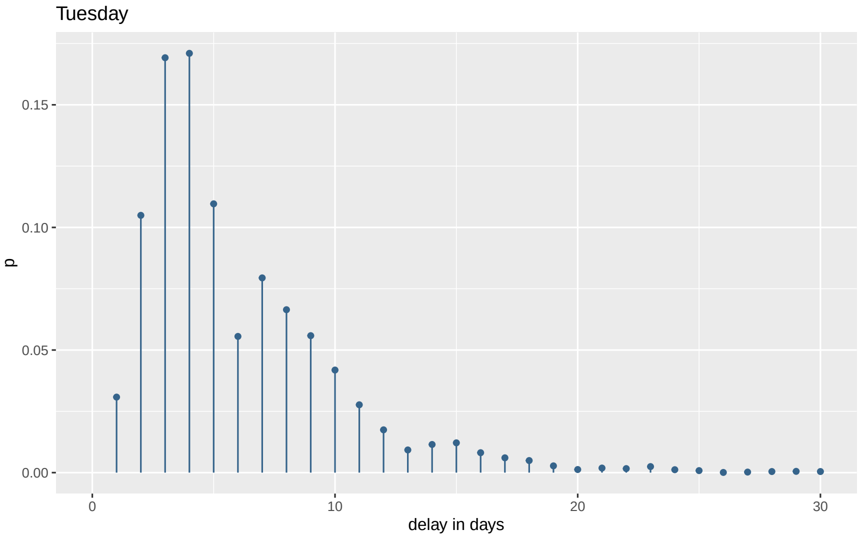

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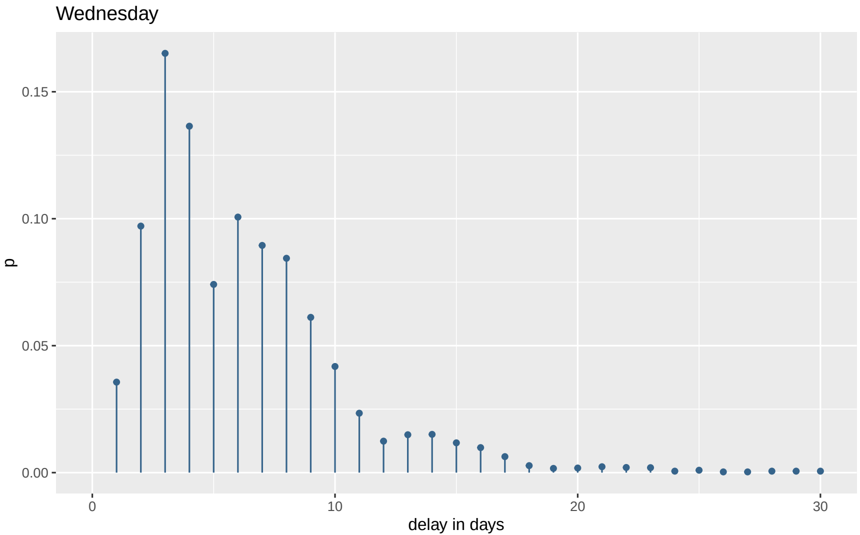

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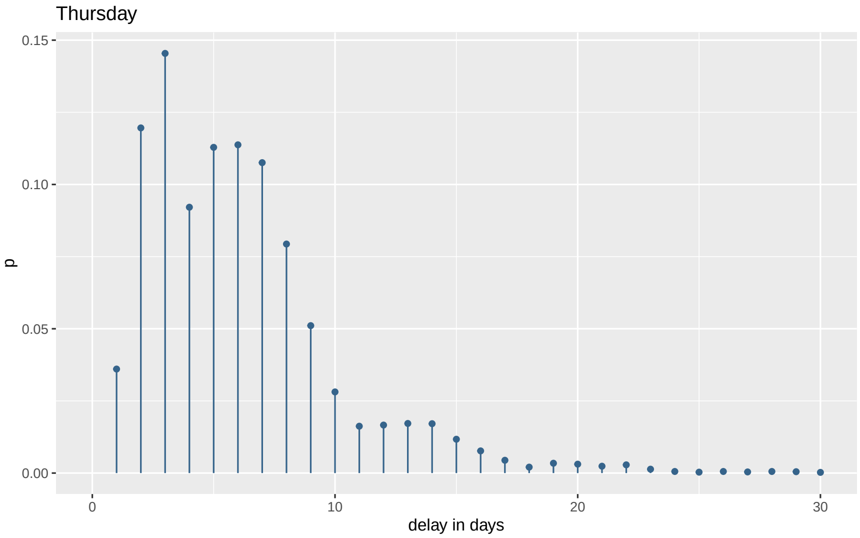

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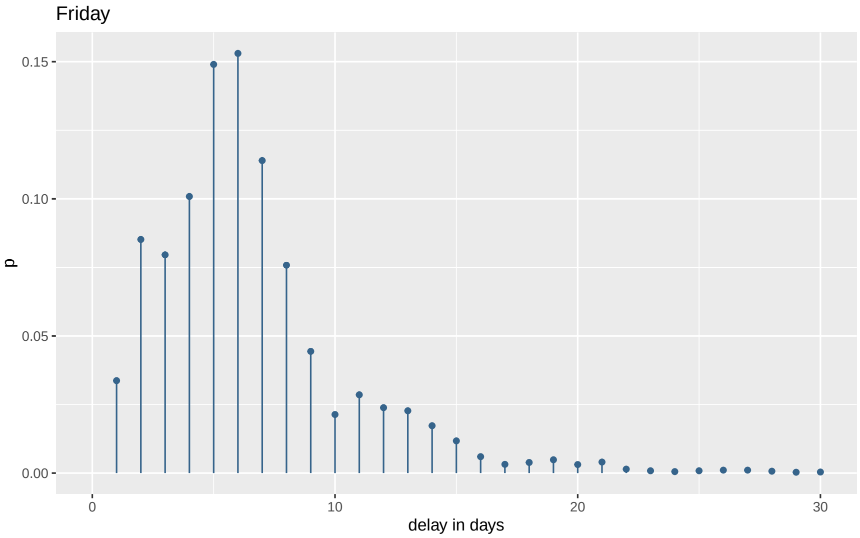

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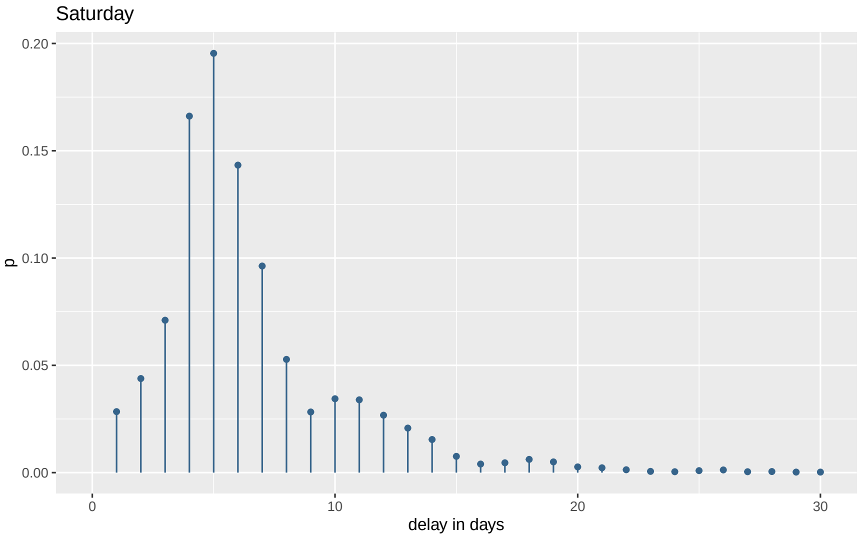

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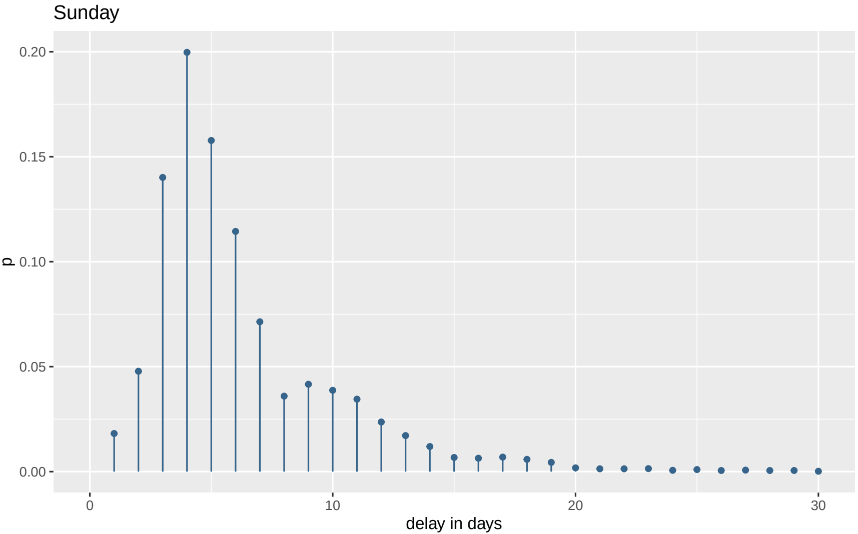


Nowcasting

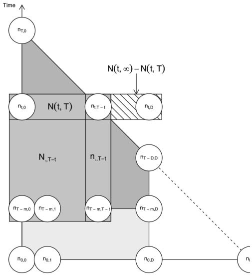
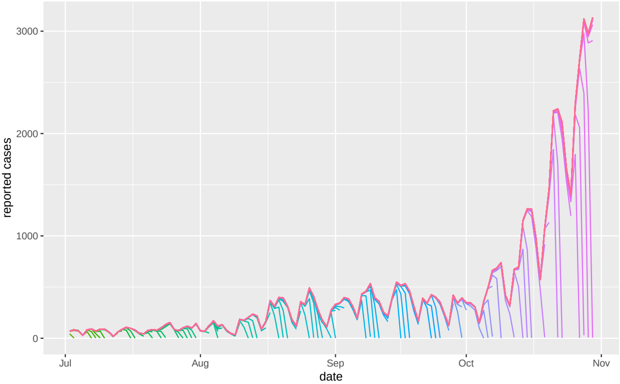


Figure 2. Reporting triangle at time T. The right trapezoid spanned by $n_{0,0}, n_{T,0}, n_{T-D,D}$, and $n_{0,D}$ defi available observations. Delays larger than D are not ered. The shaded box $N(t,\infty) - N(t,T)$ indicates the vations, which at time t are not yet available.



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- The reporting model:
  $C^R_{t,m} \sim$
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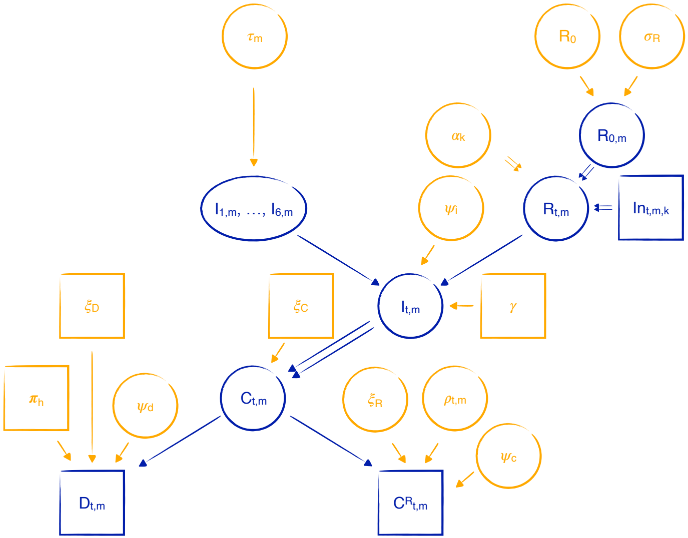
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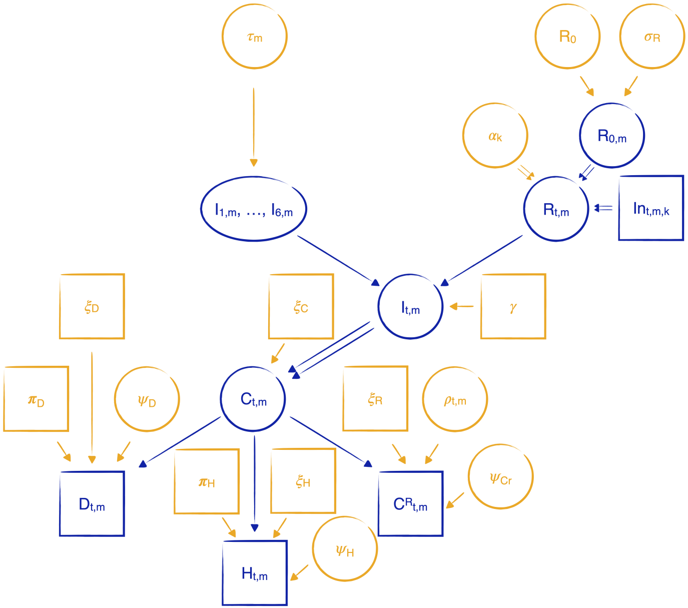
- The hospitalization model:
  $H_{t,m} \sim$
  $NegativeBinomial\left(\pi_h \sum_{u<t} C_{u,m}(F_{\xi_H}(t-u+1)-F_{\xi_H}(t-u)), \phi_h\right)$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ρt,m
πH
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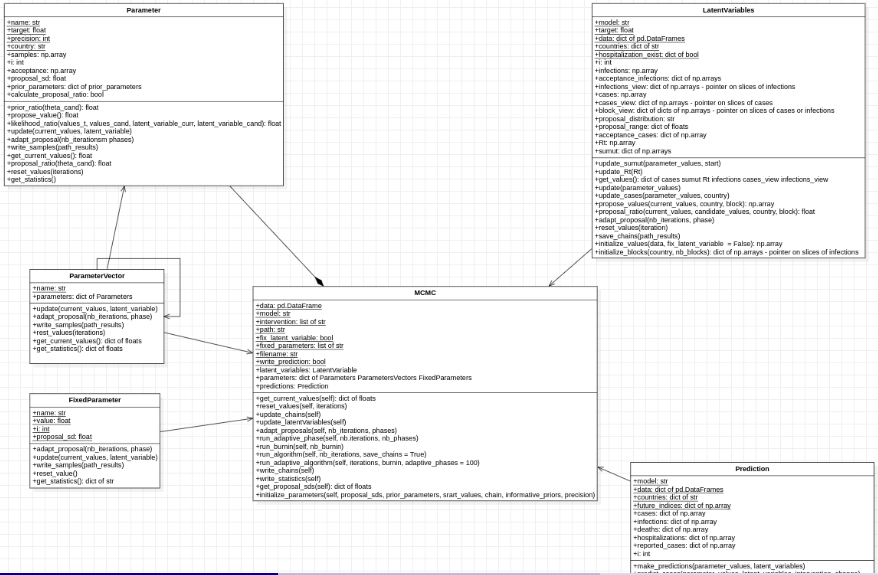
Dt,m
CRt,m
ψCr
ψH
Ht,m

Prior assumptions

- $\alpha \sim \mathcal{N}(0, 0.2)$
- $R_0 \sim \mathcal{N}(2.4, 4)$
- $\rho \sim \mathcal{B}eta(1, 1)$
- $\pi_h \sim \mathcal{B}eta(1, 1)$
- $\tau \sim \mathcal{G}amma(20/5, 5)$
- $\sigma_R \sim \mathcal{IG}amma(0.1, 0.1)$
- $\phi_i = \left(\frac{1}{\xi_i}\right)^2$ where $\xi_i \sim \mathcal{N}(0, 0.1)$
- $\phi_d = \left(\frac{1}{\xi_d}\right)^2$ where $\xi_d \sim \mathcal{N}(0, 0.1)$
- $\phi_c = \left(\frac{1}{\xi_c}\right)^2$ where $\xi_c \sim \mathcal{N}(0, 0.1)$
- $\phi_h = \left(\frac{1}{\xi_h}\right)^2$ where $\xi_h \sim \mathcal{N}(0, 0.1)$

Adaptive Metropolis-within-Gibbs algorithm

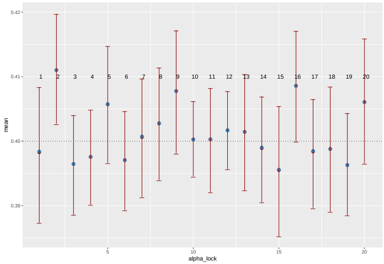


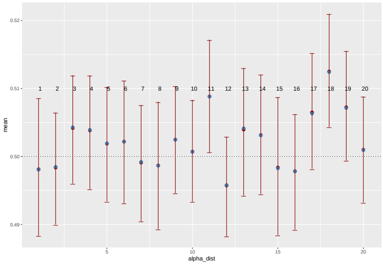
Results on simulated data

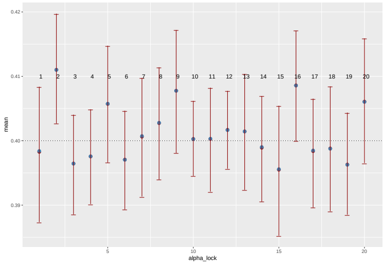
Internal validation

- Generate data according to the model with known parameter values
- Apply the algorithm to the simulated data sets to assess bias and coverage rates

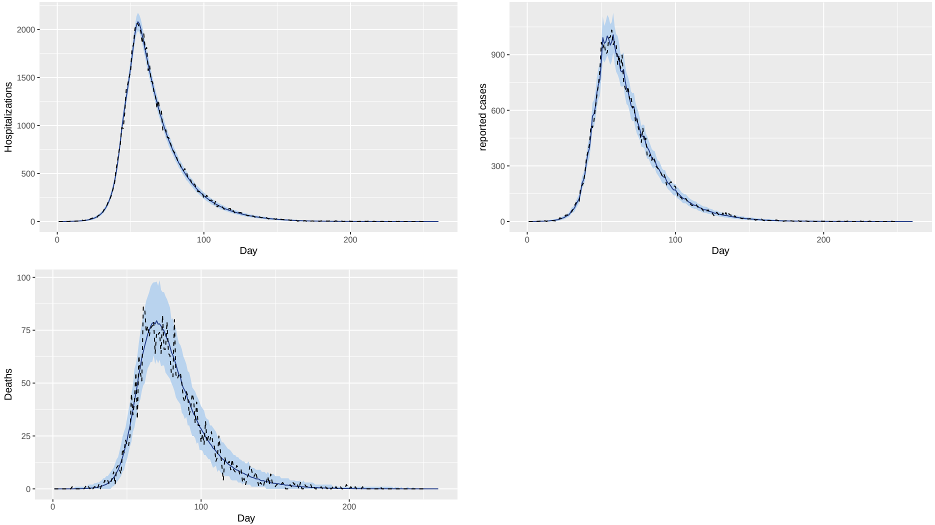
Internal validation: Coverage rates





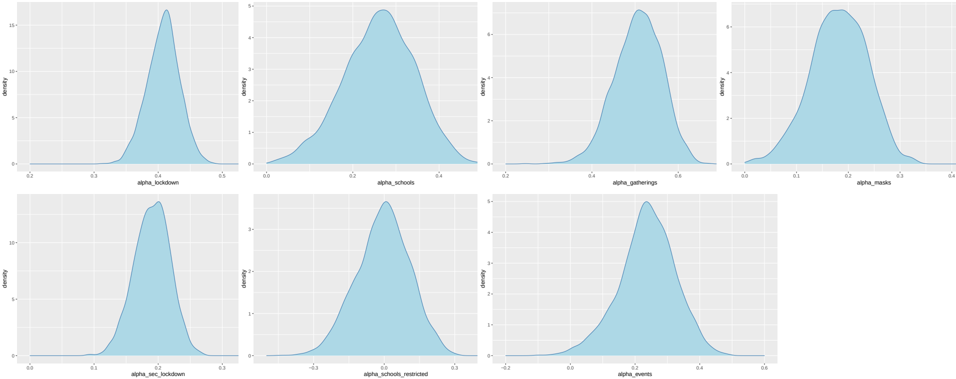


Internal validation: Posterior predictive checks

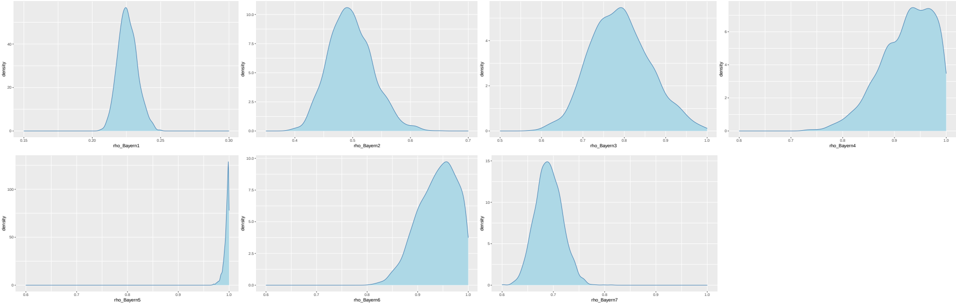


Results for Bavaria

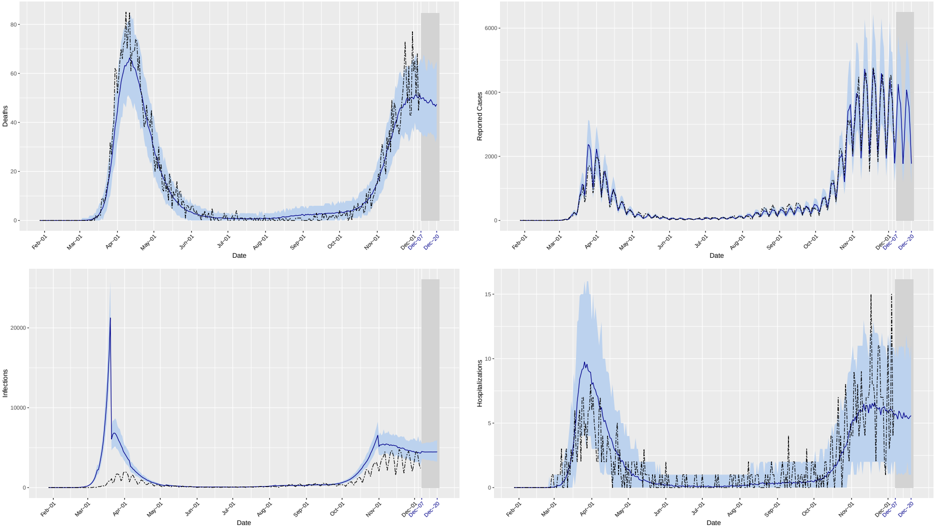
Estimated effectiveness of interventions



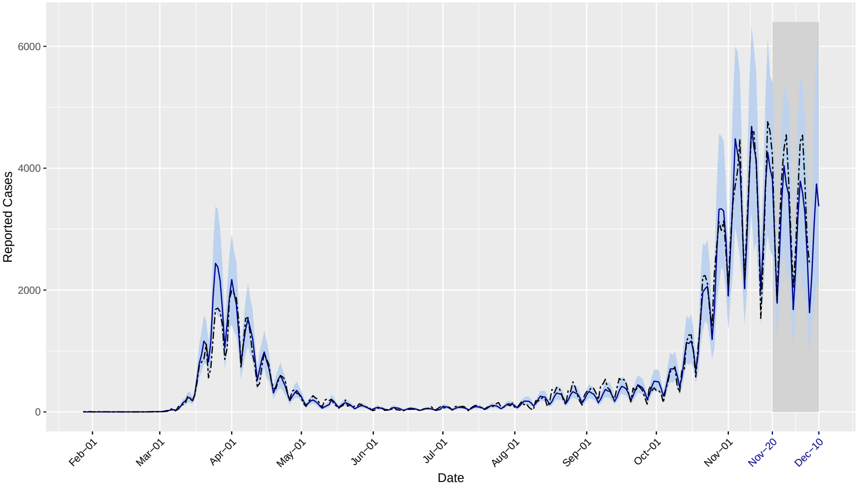
Estimated underreporting



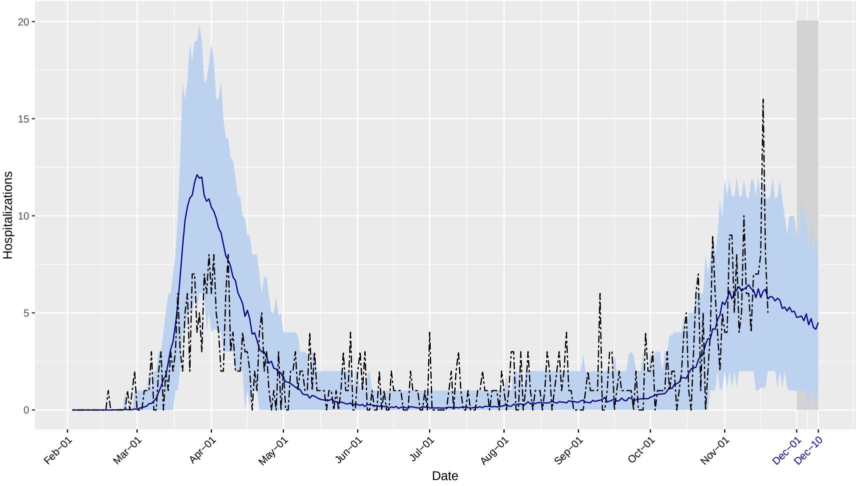
Posterior predictive checks



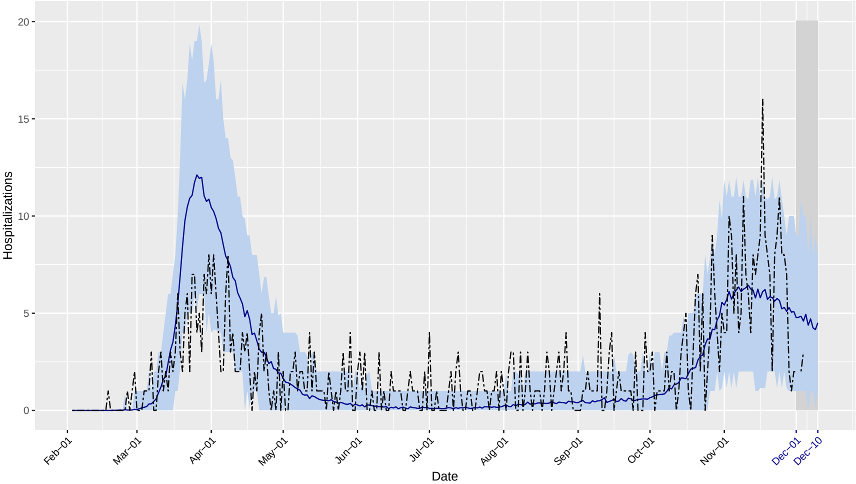
Assessing out of sample performance



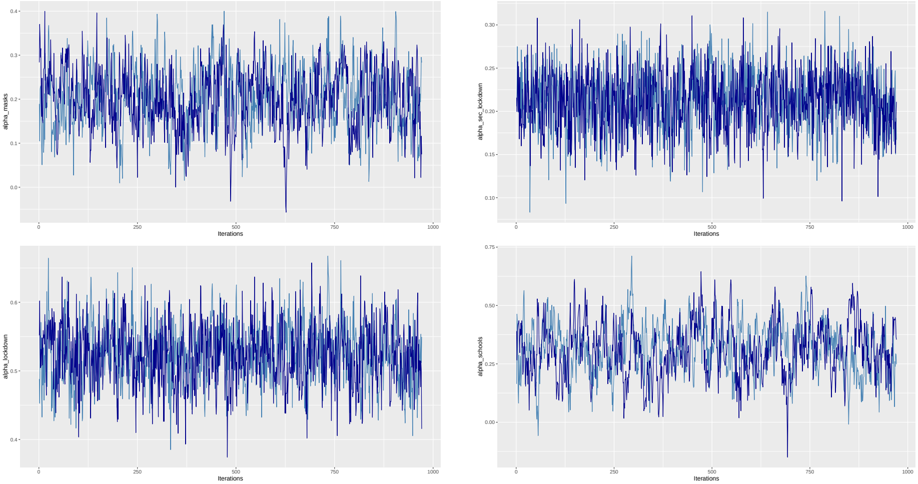
Assessing out of sample performance for hospitalizations



Assessing out of sample performance for hospitalizations

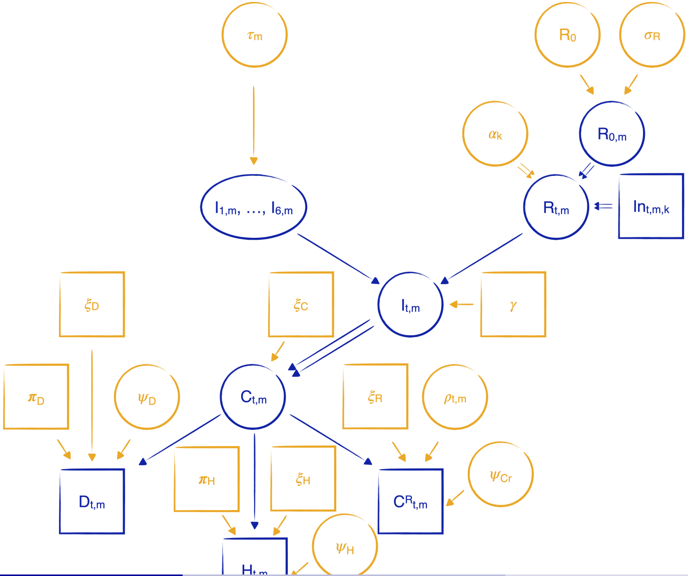


Traceplots


alpha_masks
0.4
0.3
0.2
0.1
0.0
0
250
500
750
1000
Iterations
alpha_sec_lockdown
0.30
0.25
0.20
0.15
0.10
0
250
500
750
1000
Iterations
alpha_lockdown
0.6
0.5
0.4
0
250
500
750
1000
Iterations
alpha_schools
0.75
0.50
0.25
0.00
0
250
500
750
1000
Iterations

Outlook

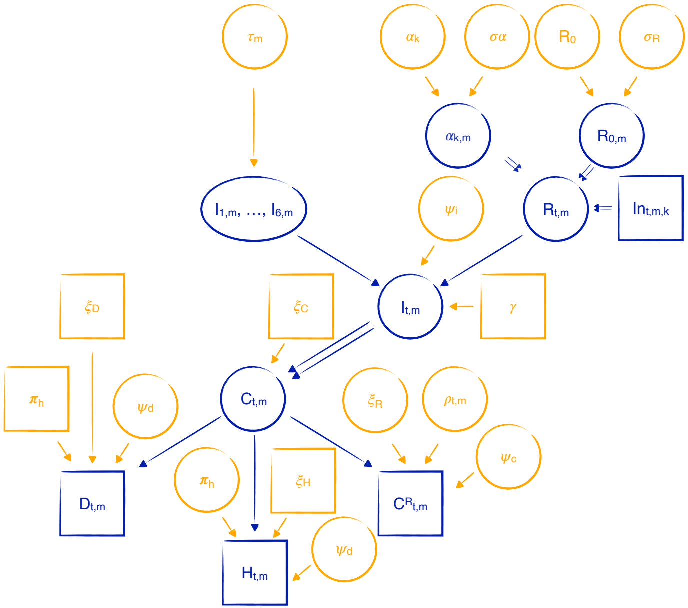
Outlook



τm
R0
σR
αk
R0,m
I1,m, ..., I6,m
Rt,m
Int,m,k
ξD
ξC
It,m
γ
πD
ψD
Ct,m
ξR
ρt,m
Dt,m
πH
ξH
CRt,m
ψCr
ψH

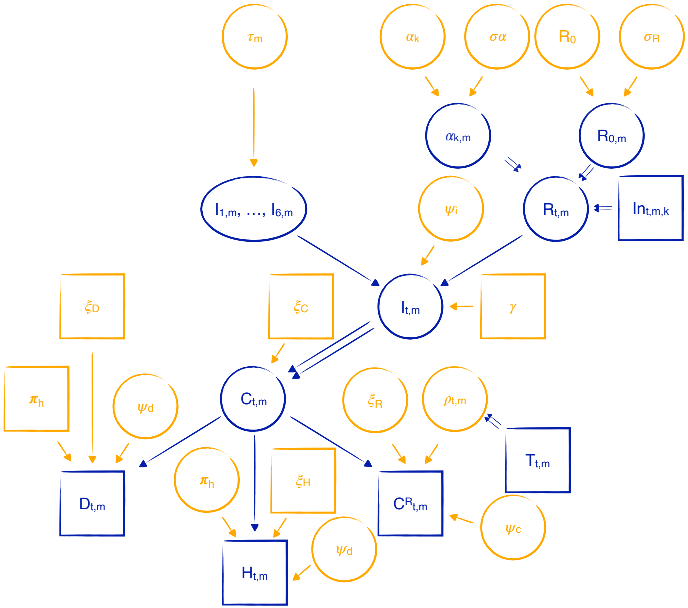
Outlook

- Estimate effectiveness of interventions in different countries in a hierarchical model and/or pre- and post lockdown


τm
αk
σα
R0
σR
αk,m
R0,m
I1,m, …, I6,m
ψi
Rt,m
Int,m,k
ξD
ξC
It,m
γ
πh
ψd
Ct,m
ξR
ρt,m
ψc
Dt,m
πh
ξH
CRt,m
ψd
Ht,m

Outlook

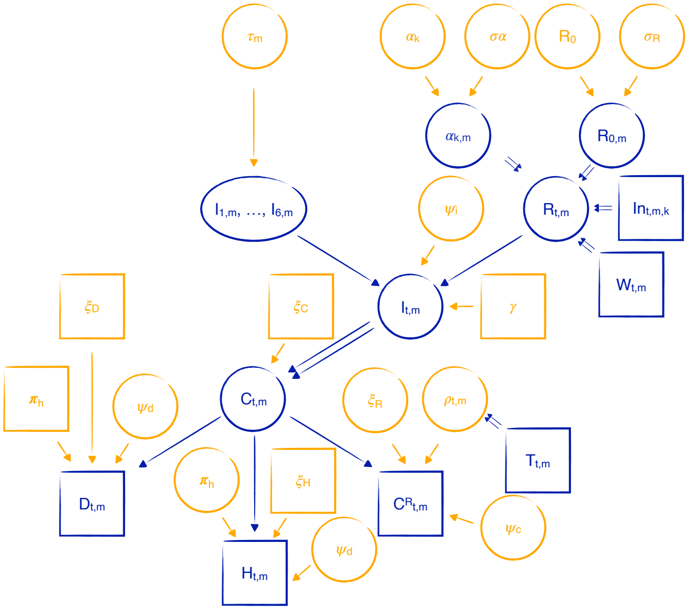
- Estimate effectiveness of interventions in different countries in a hierarchical model and/or pre- and post lockdown
- Model the reporting rate $\rho_{t,m}$ as a function of $T_{t,m}$ the number of tests per capita and/or the percentage of positive tests



τ_m
α_k
$\sigma\alpha$
R_0
σ_R
$\alpha_{k,m}$
$R_{0,m}$
$I_{1,m}, \ldots, I_{6,m}$
ψ_i
$R_{t,m}$
$In_{t,m,k}$
ξ_D
ξ_C
$I_{t,m}$
γ
π_h
ψ_d
$C_{t,m}$
ξ_R
$\rho_{t,m}$
$T_{t,m}$
$D_{t,m}$
π_h
ξ_H
$CR_{t,m}$
ψ_c
ψ_d
$H_{t,m}$

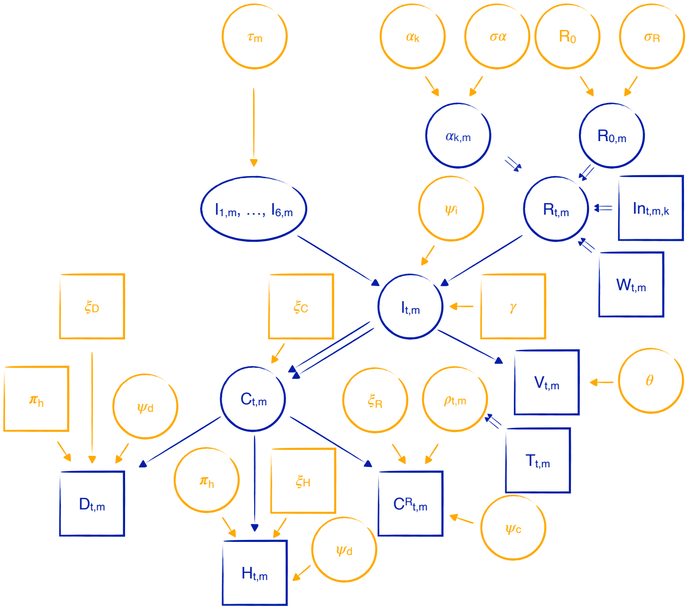
Outlook

- Estimate effectiveness of interventions in different countries in a hierarchical model and/or pre- and post lockdown
- Model the reporting rate $\rho_{t,m}$ as a function of $T_{t,m}$ the number of tests per capita and/or the percentage of positive tests
- Model the reproduction number as a function of weather conditions by integrating publicly available data


τm
αk
σα
R0
σR
αk,m
R0,m
I1,m, …, I6,m
ψi
Rt,m
Int,m,k
Wt,m
ξD
ξC
It,m
γ
πh
ψd
Ct,m
ξR
ρt,m
Tt,m
Dt,m
πh
ξH
CRt,m
ψc
Ht,m
ψd

Outlook

- Estimate effectiveness of interventions in different countries in a hierarchical model and/or pre- and post lockdown
- Model the reporting rate $\rho_{t,m}$ as a function of $T_{t,m}$ the number of tests per capita and/or the percentage of positive tests
- Model the reproduction number as a function of weather conditions by integrating publicly available data
- Integrate data on virus concentration in wastewater


τm
αk
σα
R0
σR
αk,m
R0,m
I1,m, …, I6,m
ψi
Rt,m
Int,m,k
Wt,m
ξD
ξC
It,m
γ
πh
ψd
Ct,m
ξR
ρt,m
Vt,m
θ
Tt,m
Dt,m
πh
ξH
CRt,m
ψc
ψd
Ht,m

Thank you for your attention