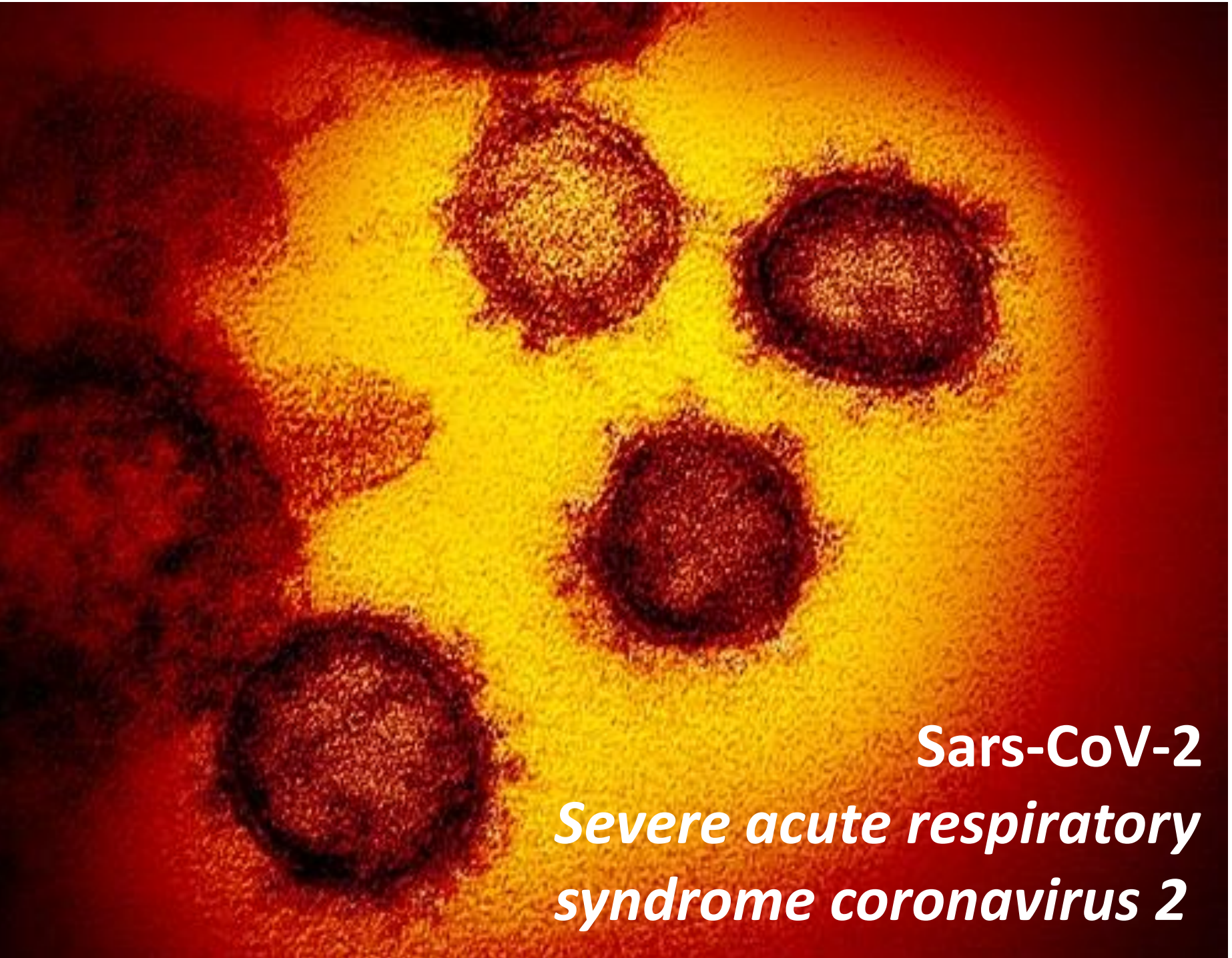

Mathematical modelling of the Sars-CoV-2 pandemic in Norway

Arnoldo Frigessi

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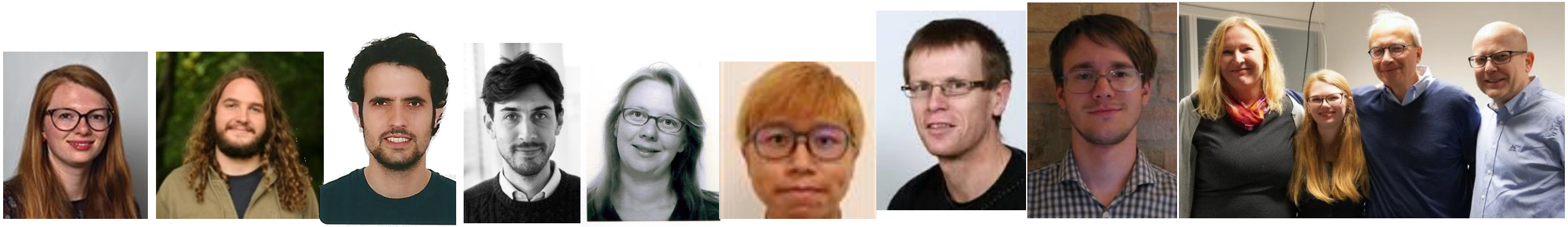
27th Norwegian Conference on Epidemiology Bergen 2021

NIPH COVID-19 modelling team

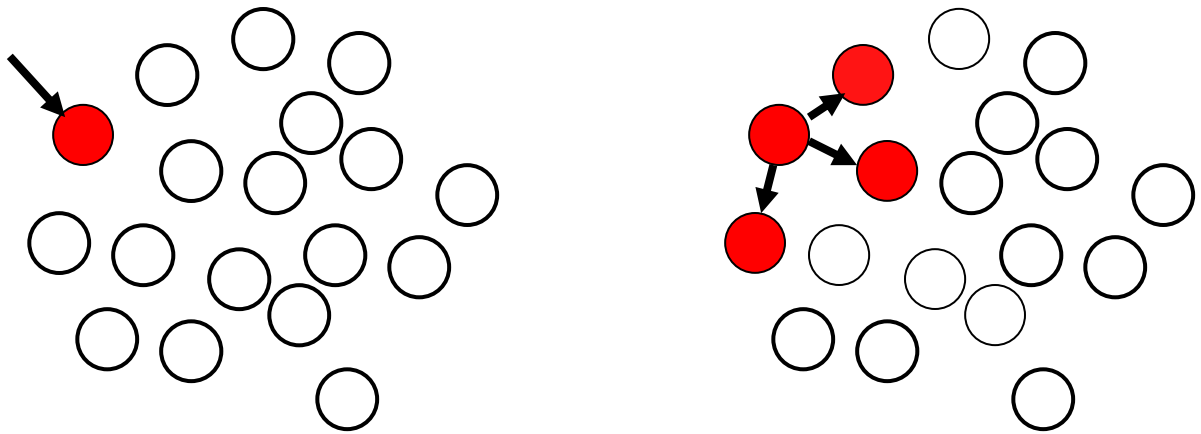


Birgitte Freiesleben de Blasio, Gunnar Øyvind Isaksson Rø, Alfonso Diz-Lois Palomares, Anja Brathen Kristoffersen , Francesco Di Ruscio, Solveig Engebretsen, Geir Storvik, Kenth Engø-Monsen.

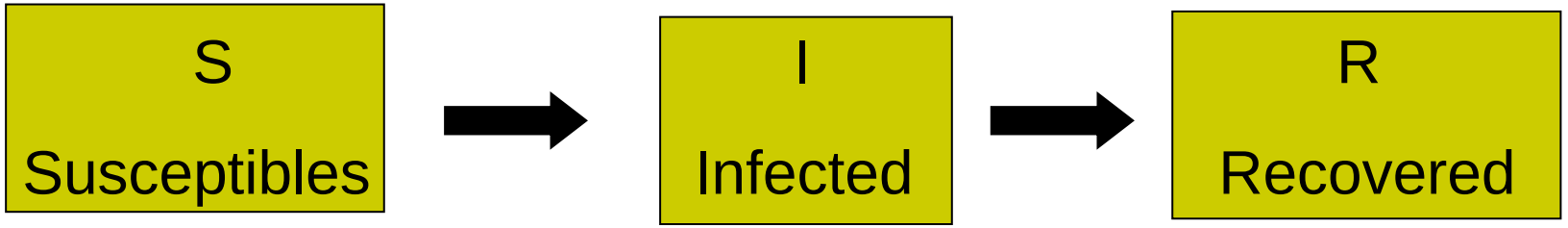
- Mathemtical models for epidemics
- Data and inference
- Results
- Communication

Infectious diseases: dependencies between cases

- A case as a risk factor

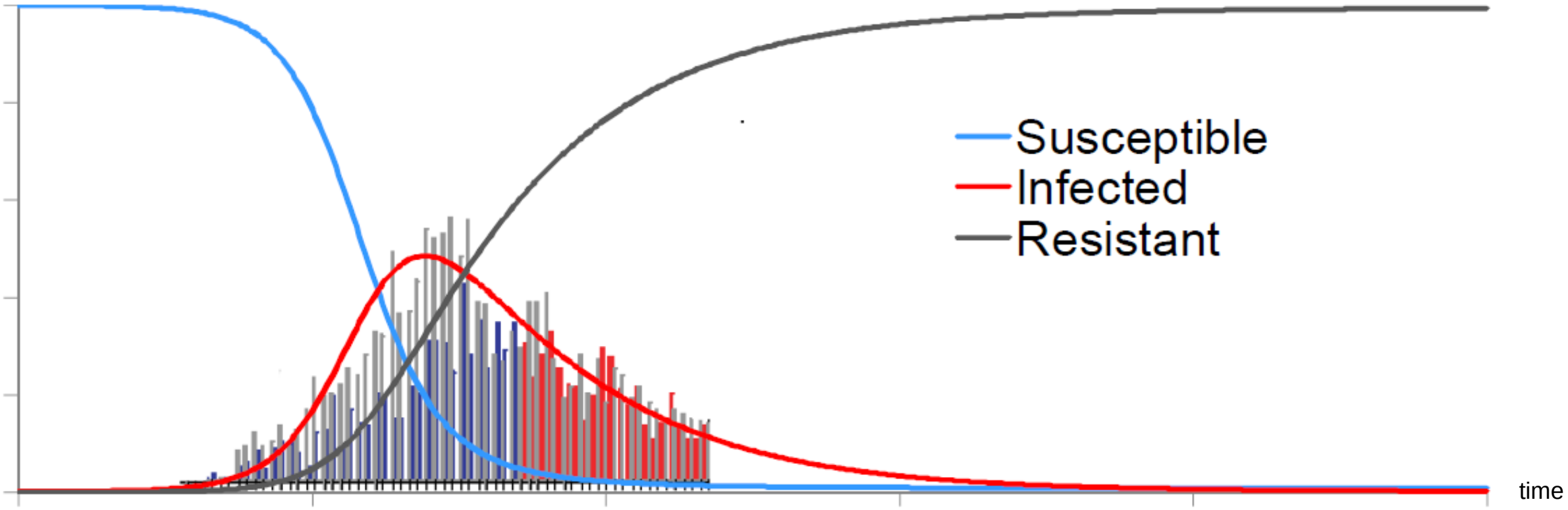


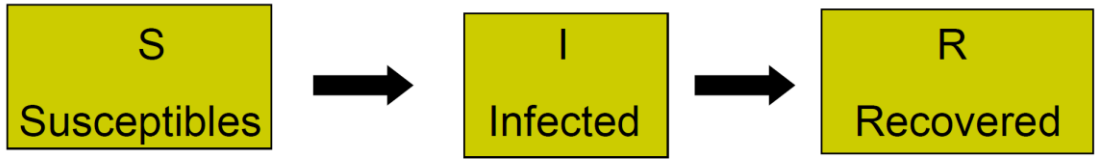
The toolbox of mathematial models: SIR model



- Compartmental model: compartments containing a certain number of individuals at any time (prevalence).
- The arrows indicate possible transitions. To each arrow corresponds a transition intensity, measured in (number of events/time unit).

SIR model -- an epidemic

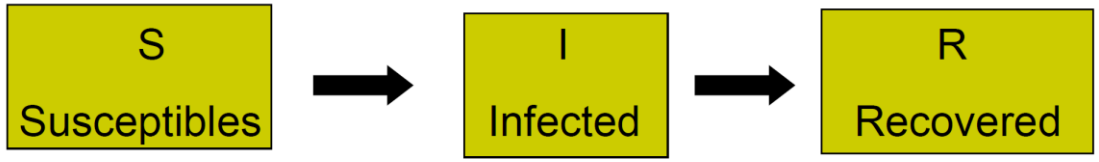




- Basic equation describing change in time of the numbers in each compartment
- Change in number in a compartment = new arrivals – departures
- Number of susceptibles tomorrow evening =
  Number of susceptibles today evening
  - number becoming infected today
  - those who will die
  + those that immigrate

$$S(t+1) = S(t) - \lambda(t)S(t) - D(t) + B(t)$$

where $\lambda(t)$ is the force of infection.



$$S(t+1) = S(t) - \lambda(t)S(t) - \mu(t)S(t) + B(t)$$

$$S'(t) = - \lambda(t)S(t) - \mu(t)S(t) + B(t)$$

- Ordinary differential equations
- Parametrisation:

$\lambda(t) = \beta$ **I(t) / N** -- proportional to the **percent of infectious individuals (cases)**

β number of new infections produced by one infectious individual per unit time

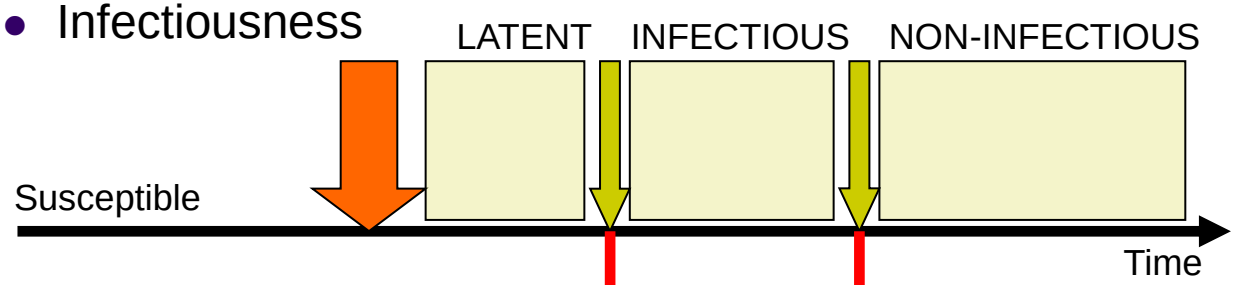
β **I(t)** total number of new cases produced by all infectious individuals per unit time

β **I(t) / N** percentage of total new cases per unit time, probability that a susceptible becomes a case

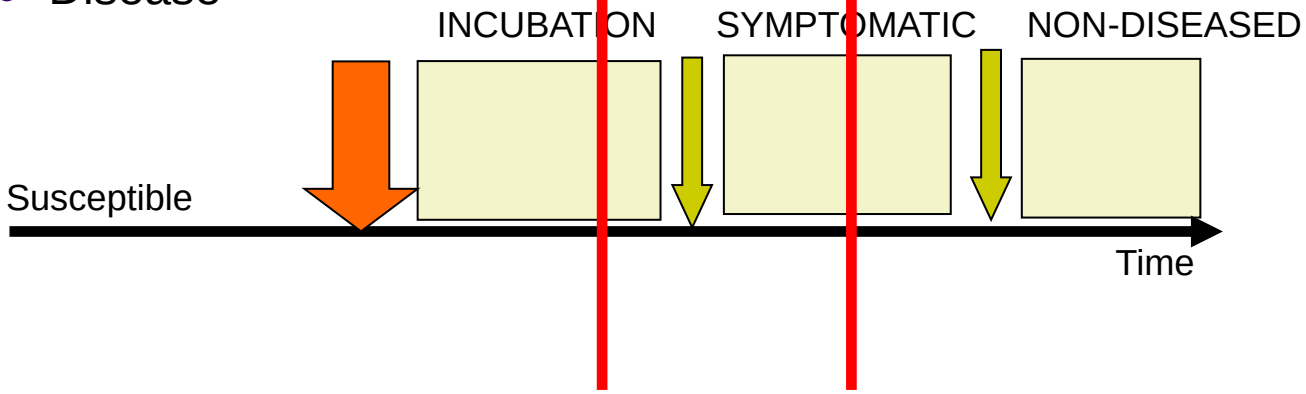
$- \lambda(t)S(t)$ is the number of susceptibles that leave the S compartment at time t

Timeline of an infection

- Infectiousness

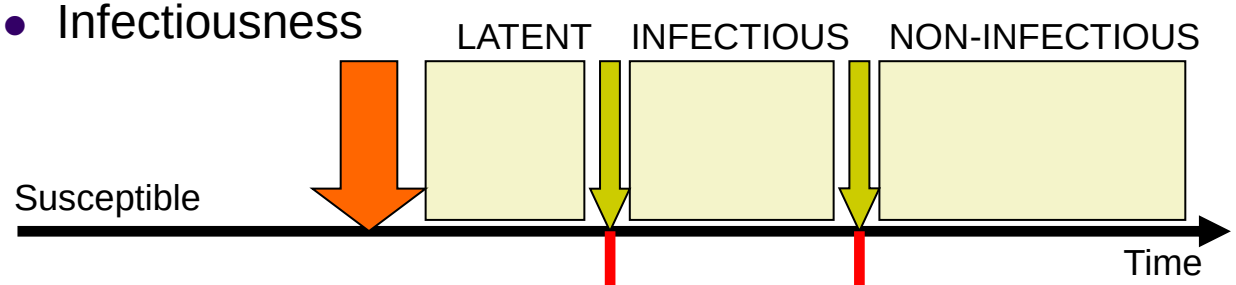


- Disease

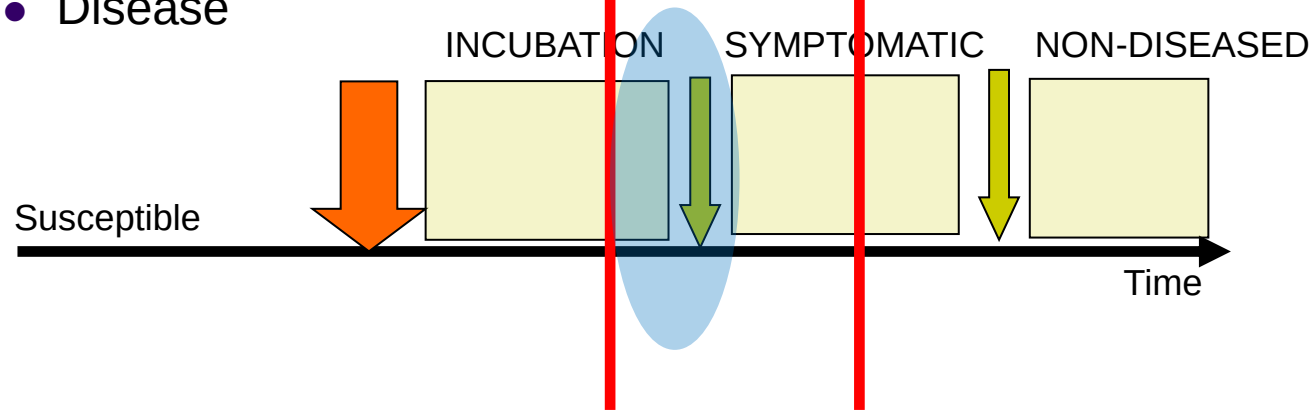


Timeline of an infection

- Infectiousness

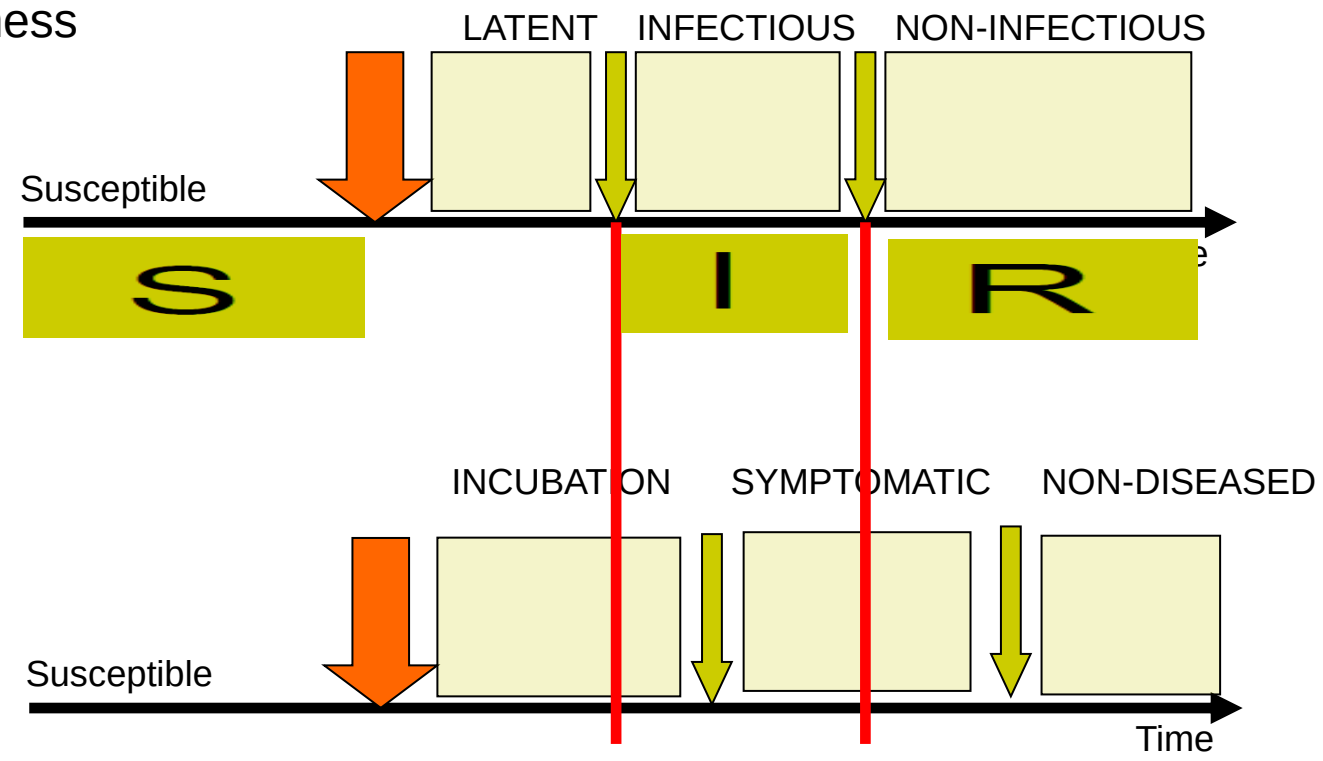


- Disease



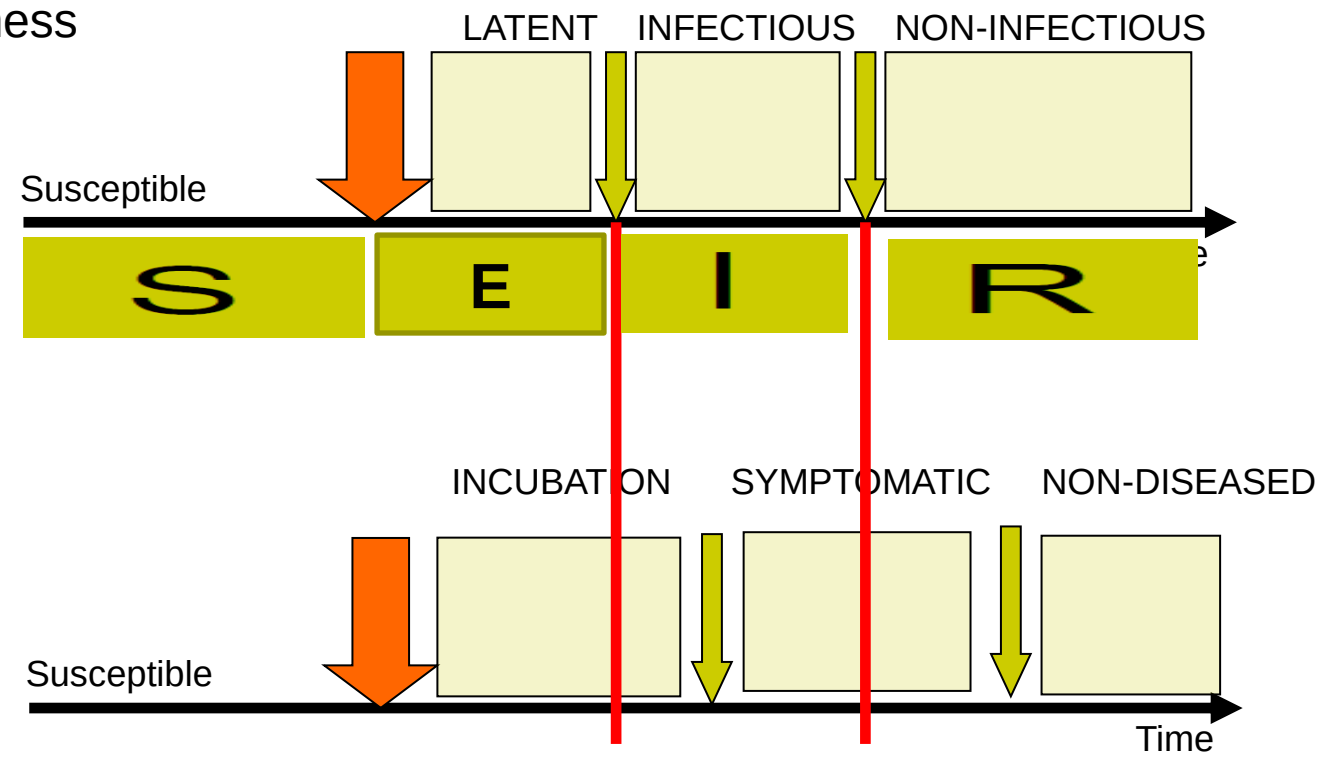
Timeline of an infection

- Infectiousness
- Disease



Timeline of an infection

- Infectiousness
- Disease



- A complete set of equations for a SEIR model

$$S'(t) = B - \beta I(t)S(t)/N - \mu S(t) + B(t)$$

$$E'(t) = \beta I(t)S(t)/N - \alpha E(t) - \mu E(t)$$

$$I'(t) = \alpha E(t) - \gamma I(t) - \mu I(t) + \text{Imported cases } (t)$$

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

- $1/\gamma$ is the mean infectious period

Basic reproductive number R_0

- Mean number of new cases produced by an infected *individual when all individuals (= contacts) are susceptible* (at the beginning of epidemic)

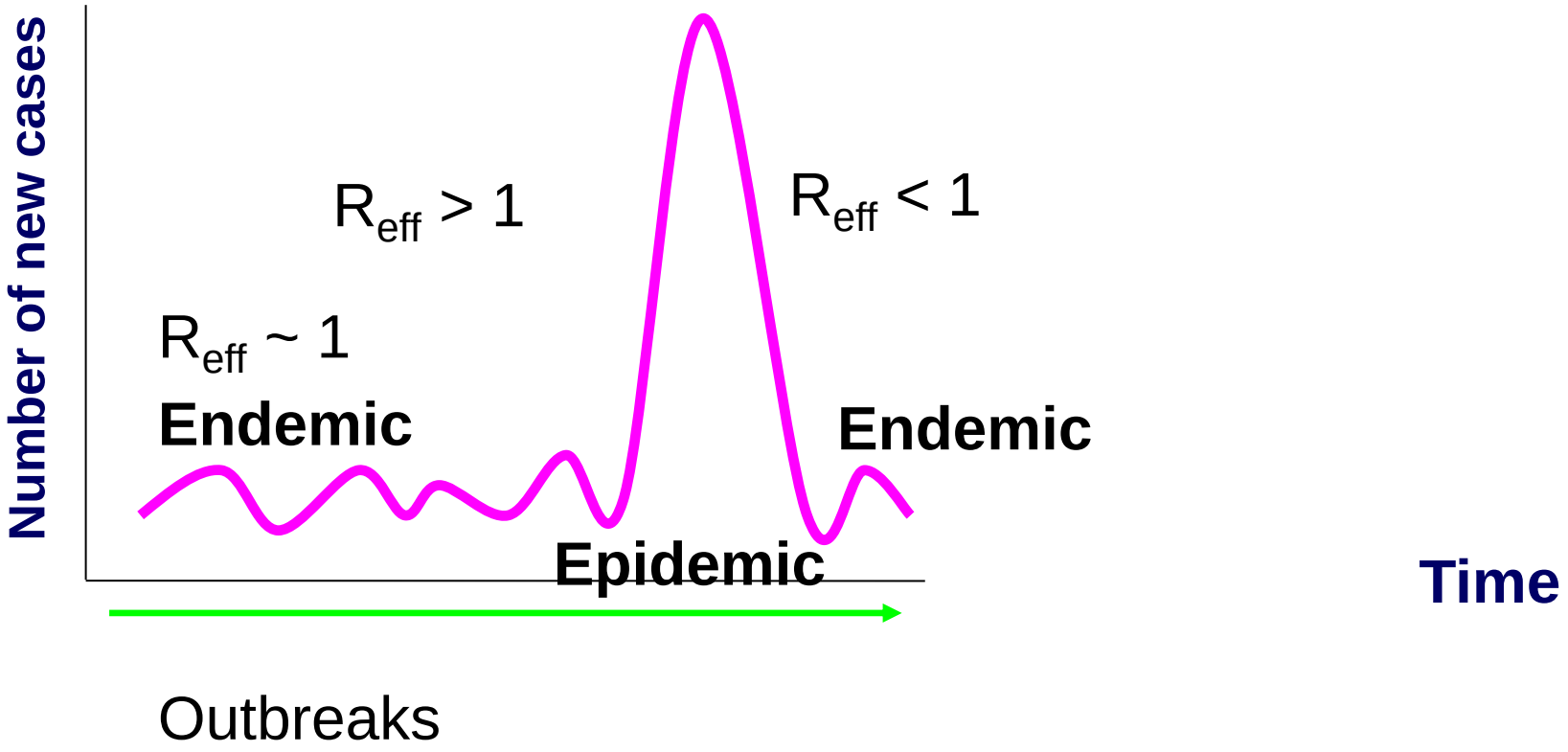
$$R_0 = \beta/\gamma$$

β is the number of new infected made by one infectious person per **unit time**

$1/\gamma$ is the **mean infectious period**

What about the repruduction number when there are recovered?

$$R_{eff} = R_0 \bullet (S/N)$$



Control?

- Interventions are intended to force the reproductive number below 1

$$R_{eff} = \beta/\gamma \, (S/N)$$

by:

- Reducing contacts
- Shortening infectious period
  - treatment, (vaccination), isolation
- Decreasing number of susceptibles
  - vaccination

Herd (community) immunity

- When most of a population is immune to the infectious disease, this provides indirect protection—or herd immunity—to those who are not immune to the disease.
- Herd immunity threshold
  - Not all individuals need to be vaccinated in order to get reproduction number below 1

The relationship between R_{eff} and herd immunity

$$R_{eff} = R_0 * (S / N)$$

At the herd immunity threshold

$$R_{eff} = 1 \quad \Leftrightarrow \quad 1 = R_0 * (S/N)$$

Proportion susceptible (S/N) at the threshold

$$(S/N) = 1 / R_0$$

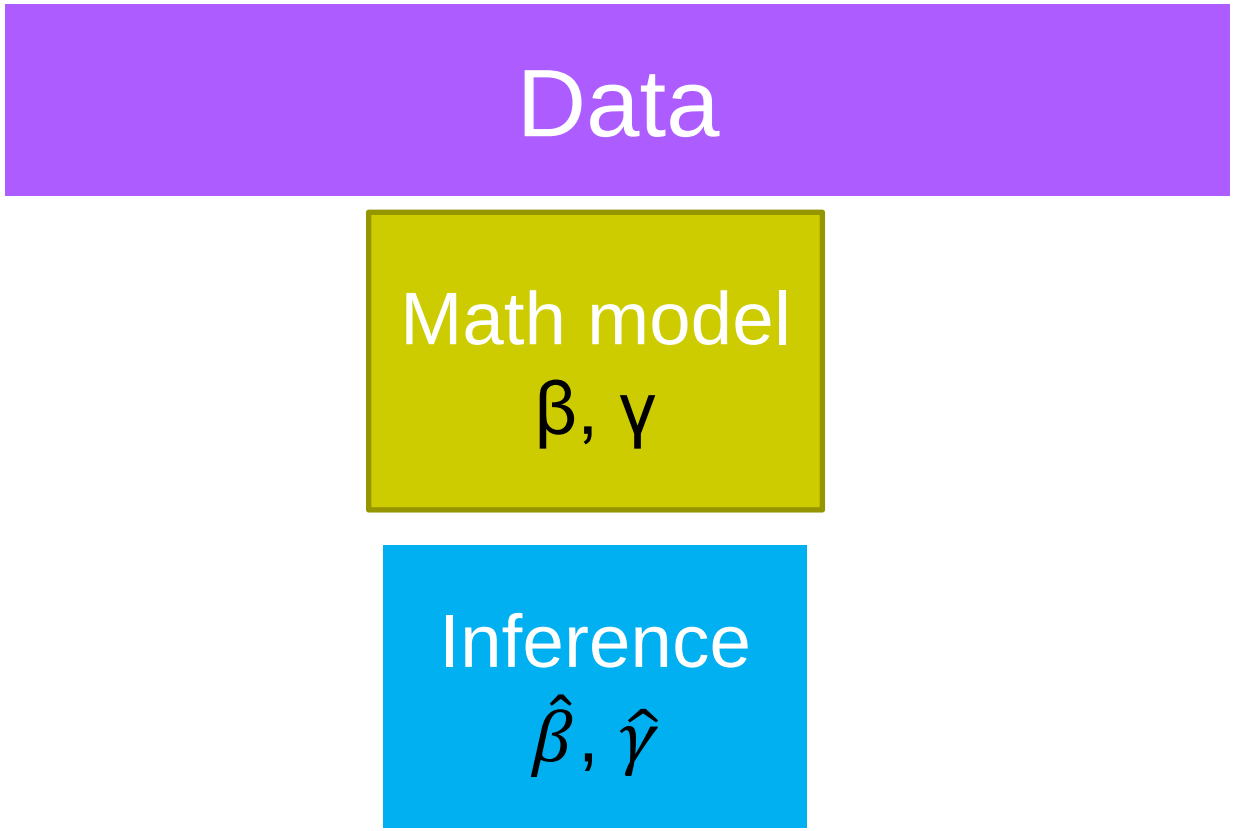
Covid-19

R_{eff}=1.2 then S= 1/1.2 N =5/6 N

R_{eff}=1.5 then S= 2/3 N

How to estimate R0 from data

- Contact tracing
- Intrinsic growth rate
- all sorts of data, using SEIR-type models



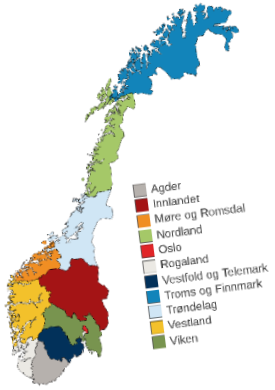
Math model
β, γ

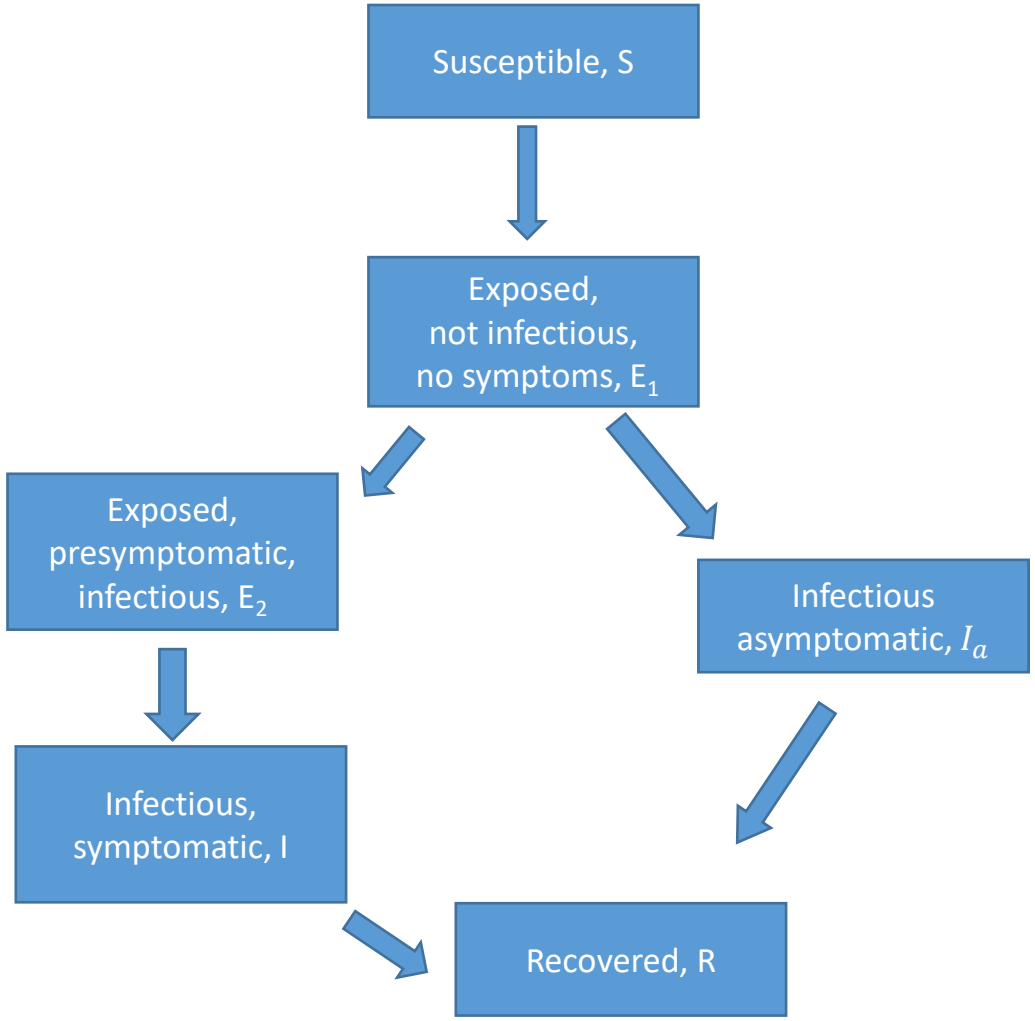
Stochastic $SEII_aR$

- One model per fylke
- Transmission parameter changing in time and fylke

$$\beta_t^f$$

- Other parameters at nation level





Math model
β, γ

Stochastic difference equations

$$S(t+\delta t) = S(t) \boxed{- X_1(t)} - X_2(t) - X_3(t),$$

$$E_1(t+\delta t) = E_1(t) + X_1(t) + X_2(t) + X_3(t) - X_4(t),$$

$$E_2(t+\delta t) = E_2(t) + X_5(t) - X_6(t),$$

$$I(t+\delta t) = I(t) + X_6(t) - X_7(t),$$

$$I_a(t+\delta t) = I_a(t) + X_4(t) - X_5(t) - X_8(t),$$

$$\delta t = \frac{6}{24}$$

$$X_1(t) \sim \text{Binom}(S(t), \beta_t I(t)/N),$$

$$X_2(t) \sim \text{Binom}(S(t), r_{I_a} \beta_t I_a(t)/N),$$

$$X_3(t) \sim \text{Binom}(S(t), r_{E_2} \beta_t E_2(t)/N),$$

$$X_4(t) \sim \text{Binom}(E_1(t), \lambda_1),$$

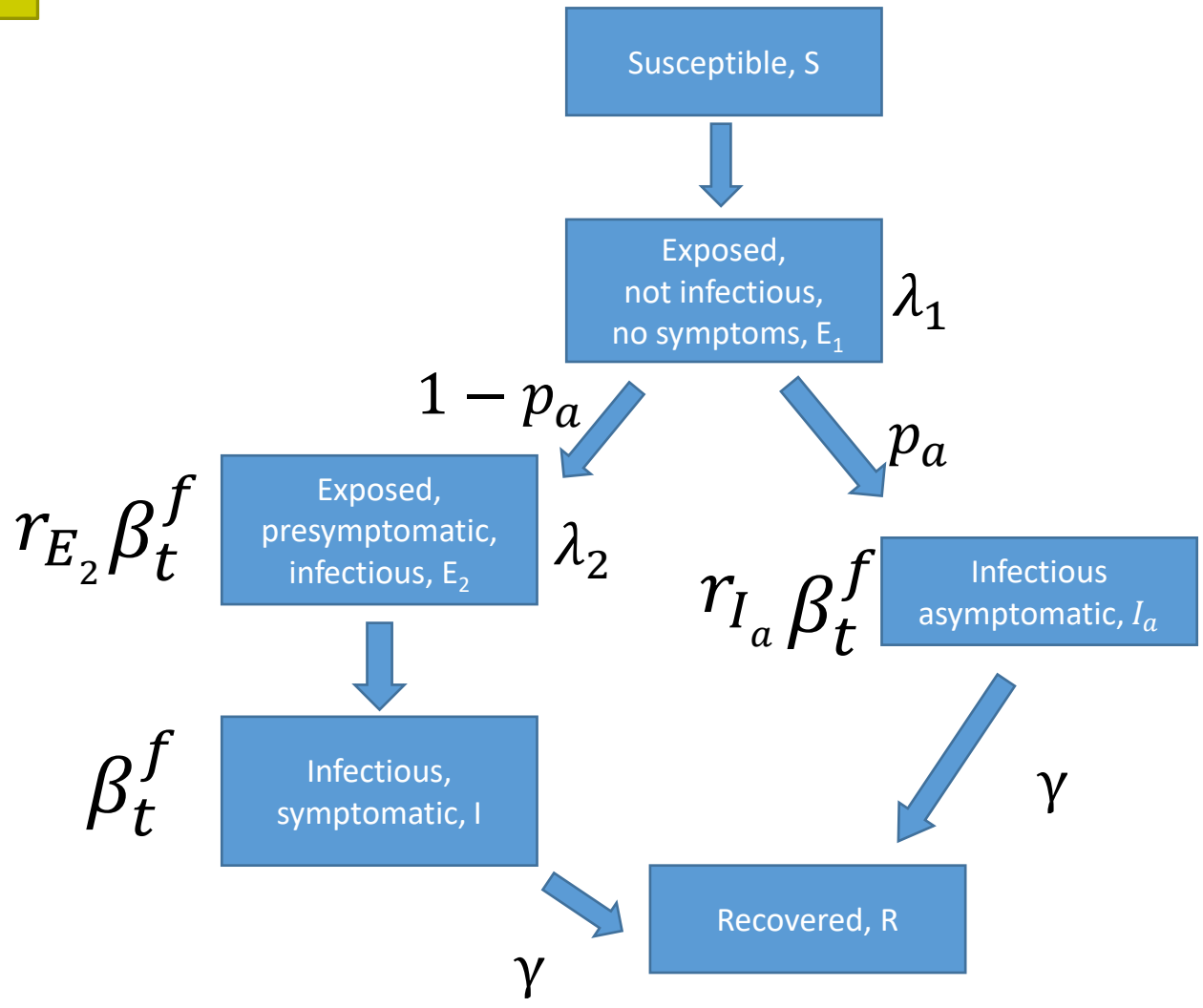
$$X_5(t) \sim \text{Binom}(X_4(t), 1 - p_a),$$

$$X_6(t) \sim \text{Binom}(E_2(t), \lambda_2),$$

$$X_7(t) \sim \text{Binom}(I(t), \gamma),$$

$$X_8(t) \sim \text{Binom}(I_a(t), \gamma).$$

Math model
β, γ



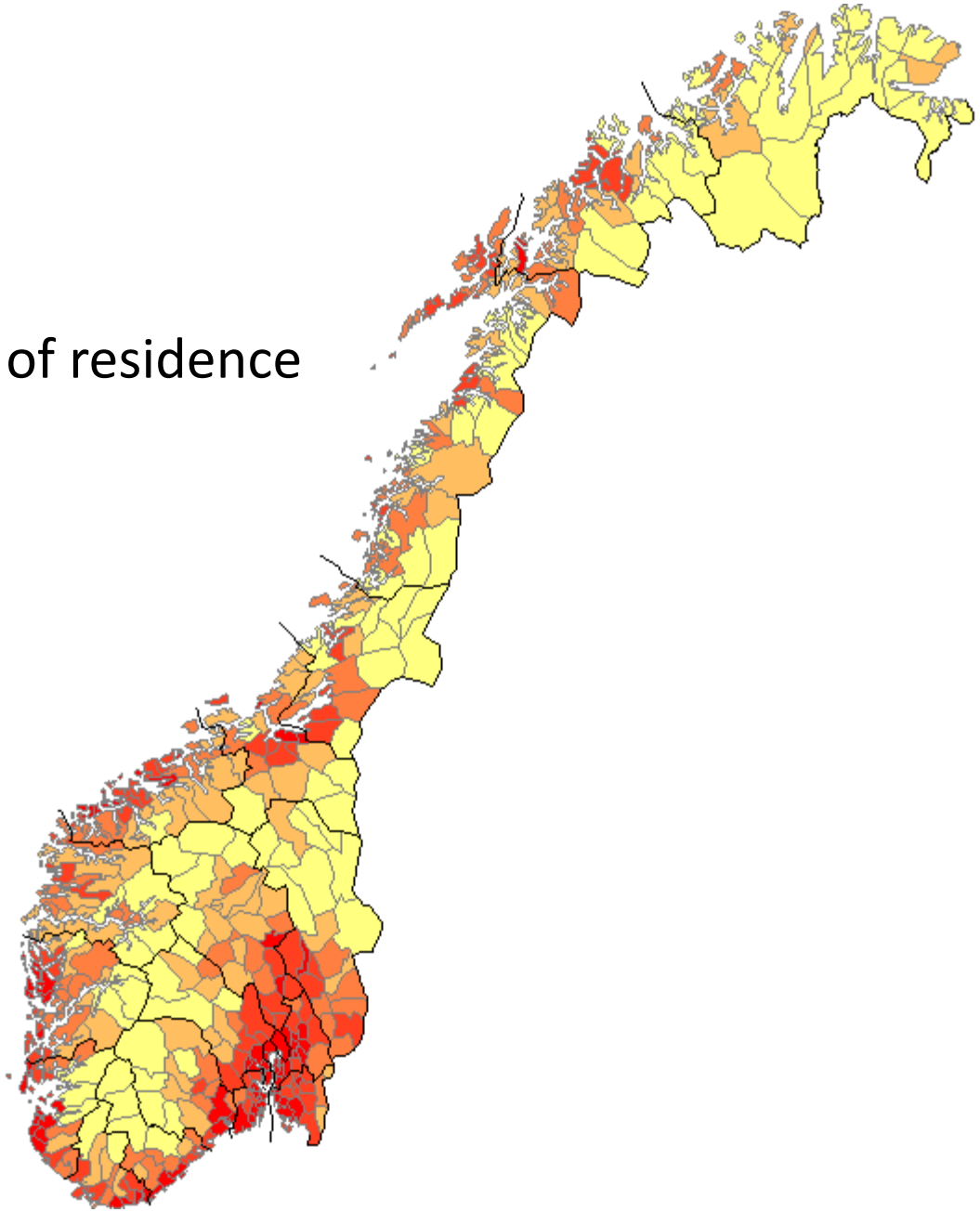
$$\lambda_1 \sim Exp(\,3\ days\,)$$
$$\lambda_2 \sim Exp(\,2\ days\,)$$
$$\gamma \sim Exp(\,5\ days\,)$$
$$p_a = 0.4$$
$$r_{E_2} = 1.25$$
$$r_{I_a} = 0.1$$

Constant population size per fylke

β_t^f probability of transmission upon contact, times contact rate, estimated

Data

5.391.0000 individuals
Placed in the municipality of residence



Data

telenor mobile phone mobility, surrogate for real time mobility patterns

- Total movements between the 356 municipalities.
- Every 6 hours.
- Counts below 20 are censored.
- Every day, since February 24.

- Telenor has ca. 47.5% market share – we scale up.

Date,	Time,	From,	To,	Count
20200224,	12,	1101,	1101,	8960
20200224,	12,	1101,	1103,	239
20200224,	12,	1101,	1108,	194
20200224,	12,	1101,	1111,	91

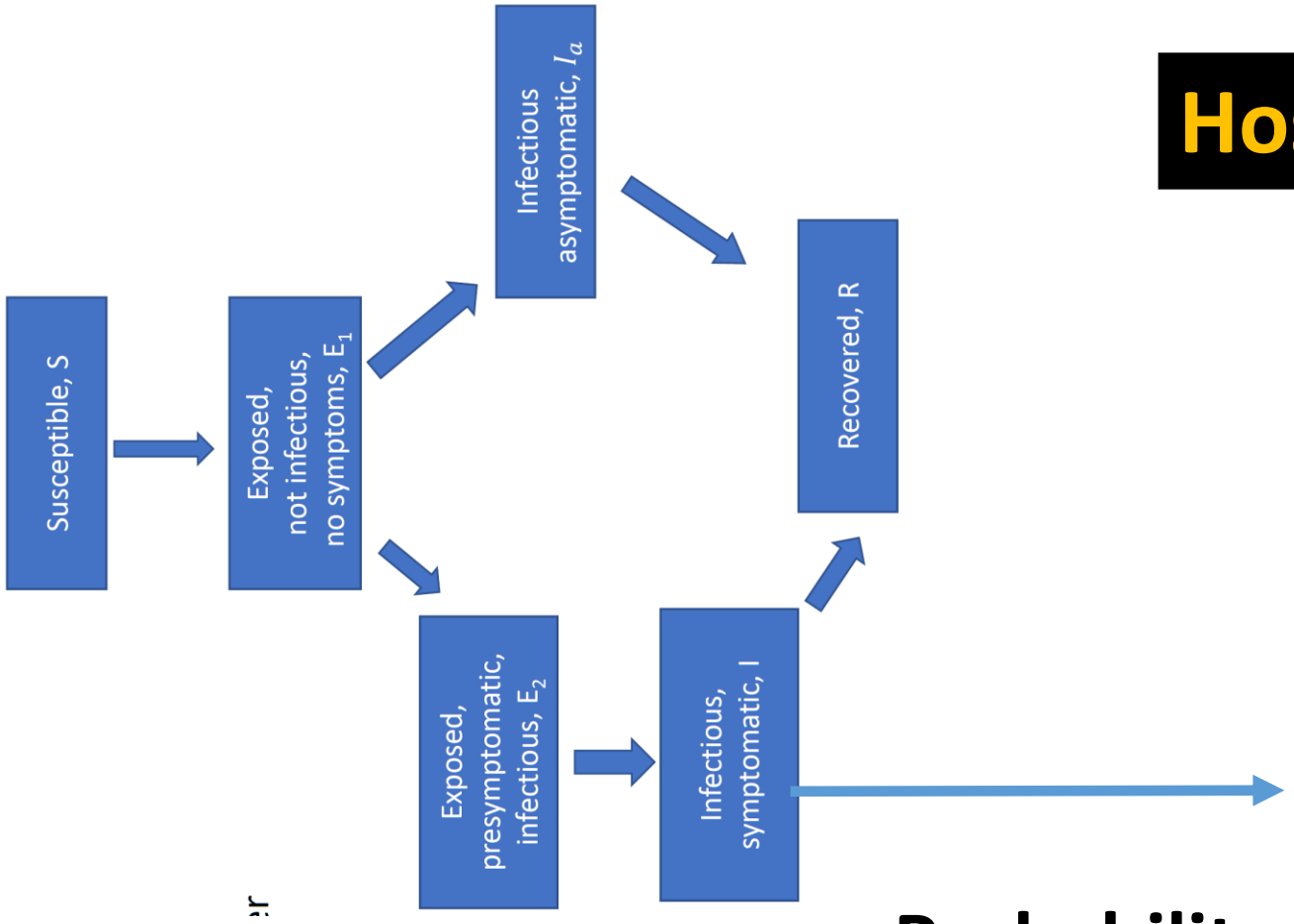
Data

- Number tested
- Number positive
- Number imported cases
- Number in hospital
- Number in ICU
- Number new admitted to hospital
- Number of deaths

Daily at fylke level.

Inference
$\hat{\beta}, \hat{\gamma}$

Hospitalisation



Hospital

Probability

Time gap

Science

CORONAVIRUS

Estimating the burden of SARS-CoV-2 in France

Henrik Salje[1,2,3]*, Cécile Tran Kiem[1,4]*, Noémie Lefrancq[1], Noémie Courtejoie[5], Paolo Bosetti[1], Juliette Paireau[1,6], Alessio Andronico[1], Nathanaël Hozé[1], Jehanne Richet[5], Claire-Lise Dubost[5], Yann Le Strat[6], Justin Lessler[3], Daniel Levy-Bruhl[6], Arnaud Fontanet[7,8], Lulla Opatowski[9,10], Pierre-Yves Boelle[11], Simon Cauchemez[1]†

8 July 2020

Probability of hospitalization per age group

Table S1

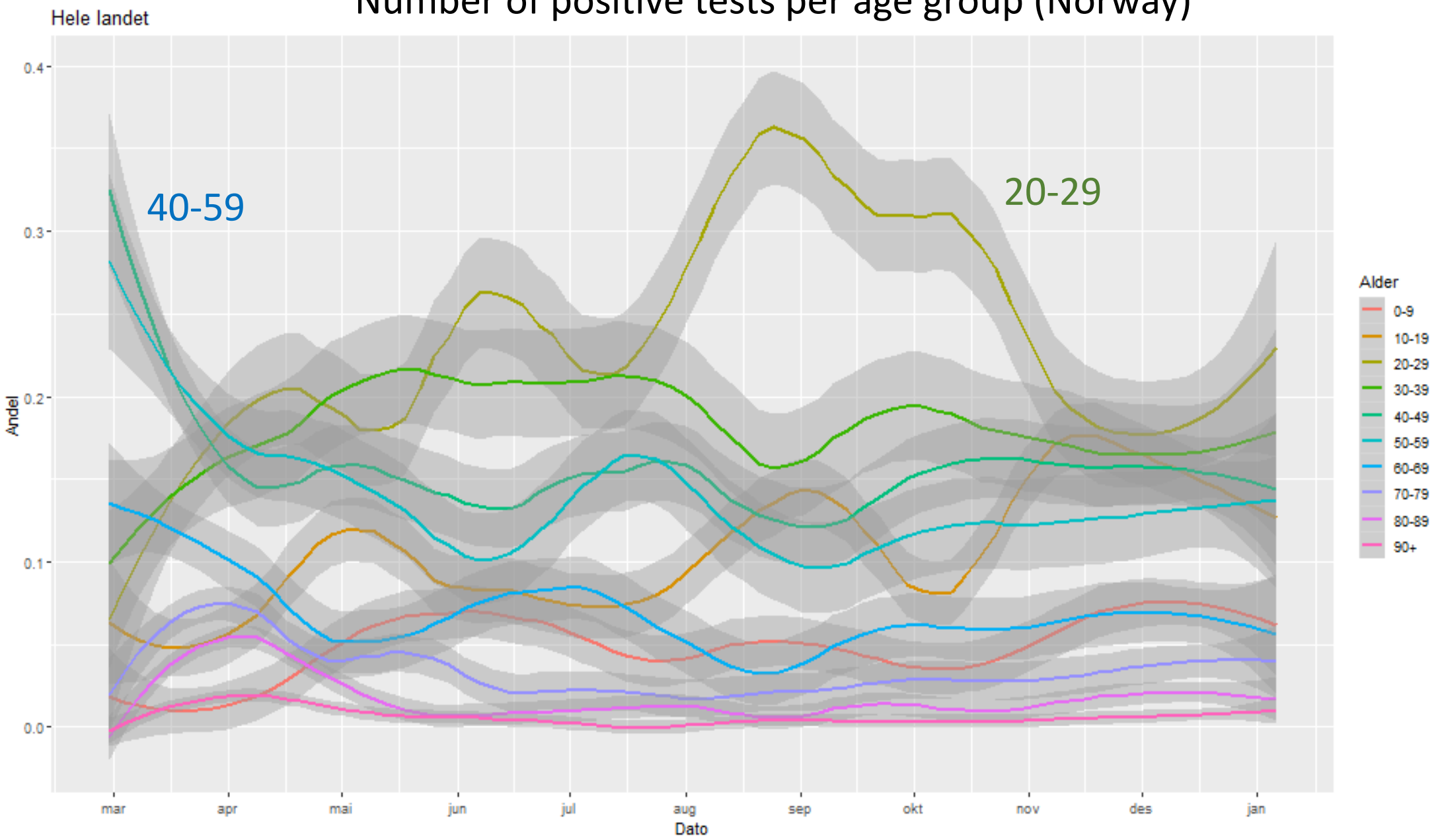
Age group	Percent infections hospitalized			Percent of hospitalized cases that go to ICU		
	Male	Female	Mean	Male	Female	Mean
<20	0.2 (0.08-0.2)	0.1 (0.07-0.2)	0.1 (0.08-0.2)	26.9 (23.1-31.1)	16.7 (14.3-19.3)	22.2 (19.1-25.7)
20-29	0.6 (0.3- 0.9)	0.5 (0.3-0.8)	0.5 (0.3-0.8)	14.0 (12.2-16.0)	8.7 (7.5-9.9)	11.6 (10.1-13.2)
30-39	1.2 (0.7-1.9)	0.9 (0.5-1.5)	1.1 (0.6-1.7)	19.2 (17.6-20.9)	11.9 (10.9-13.0)	15.9 (14.5-17.3)
40-49	1.6 (0.9-2.6)	1.3 (0.7-2.1)	1.4 (0.8-2.3)	26.9 (25.4-28.4)	16.6 (15.6-17.7)	22.2 (21.0-23.5)
50-59	3.2 (1.8-5.2)	2.6 (1.5-4.2)	2.9 (1.6-4.7)	33.4 (32.0-34.8)	20.7 (19.8-21.6)	27.6 (26.5-28.7)
60-69	6.7 (3.7-10.9)	5.1 (2.9-8.3)	5.8 (3.3-9.5)	37.3 (36.0-38.6)	23.1 (22.2-24.0)	30.8 (29.8-31.8)
70-79	11.0 (6.2-17.9)	7.8 (4.4-12.8)	9.3 (5.2-15.1)	30.2 (29.1-31.3)	18.7 (18.0-19.5)	24.9 (24.1-25.8)
80+	37.6 (21.1-61.3)	19.3 (10.9-31.6)	26.2 (14.8-42.7)	6.8 (6.5-7.2)	4.2 (4.0-4.5)	5.6 (5.3-5.9)
Mean	3.3 (1.8-5.3)	2.6 (1.5-4.3)	2.9 (1.7-4.8)	23.1 (22.6-23.6)	14.3 (13.9-14.7)	19.0 (18.7-19.44)

Table S1: Percent of infections that are hospitalized and end up in ICU by age and sex. Percentage of infections that are hospitalized and the percentage that end up in ICU, conditional on being hospitalized.

- Scaled to the **demography of each municipality** in Norway and corrected for percentage of elderly living in elderly homes.
- Assumes diseases burden follows demography

0-9 years	0.2%
10 - 19 years	0.2%
20 - 29 years	0.6%
30 - 39 years	1.3%
40 - 49 years	1.7%
50 - 59 years	3.5%
60 - 69 years	7.1%
70 - 79 years	11.3%
80+ years	27%

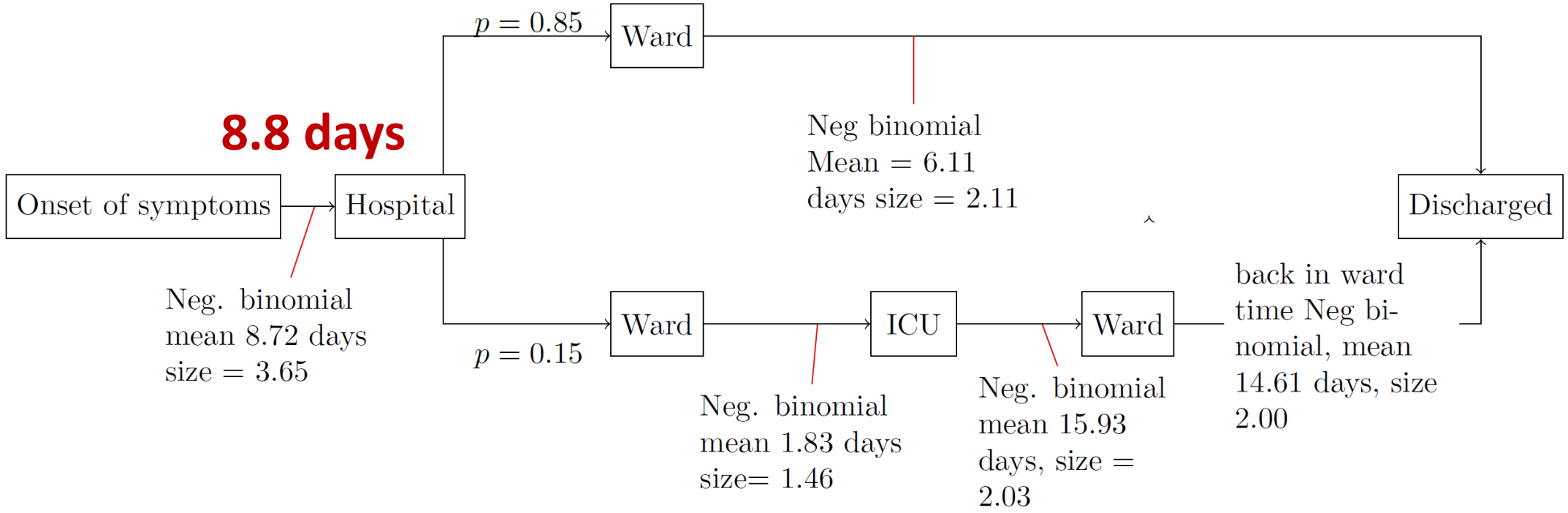
Number of positive tests per age group (Norway)



Inference
$\hat{\beta}, \hat{\gamma}$

Hospitalisation lengths

Estimates from Norwegian registry data.



Up to 31 May 2020

Based on > 1500 hospitalisation cases, taking censoring into account.

Inference
$\hat{\beta}, \hat{\gamma}$

Oslo

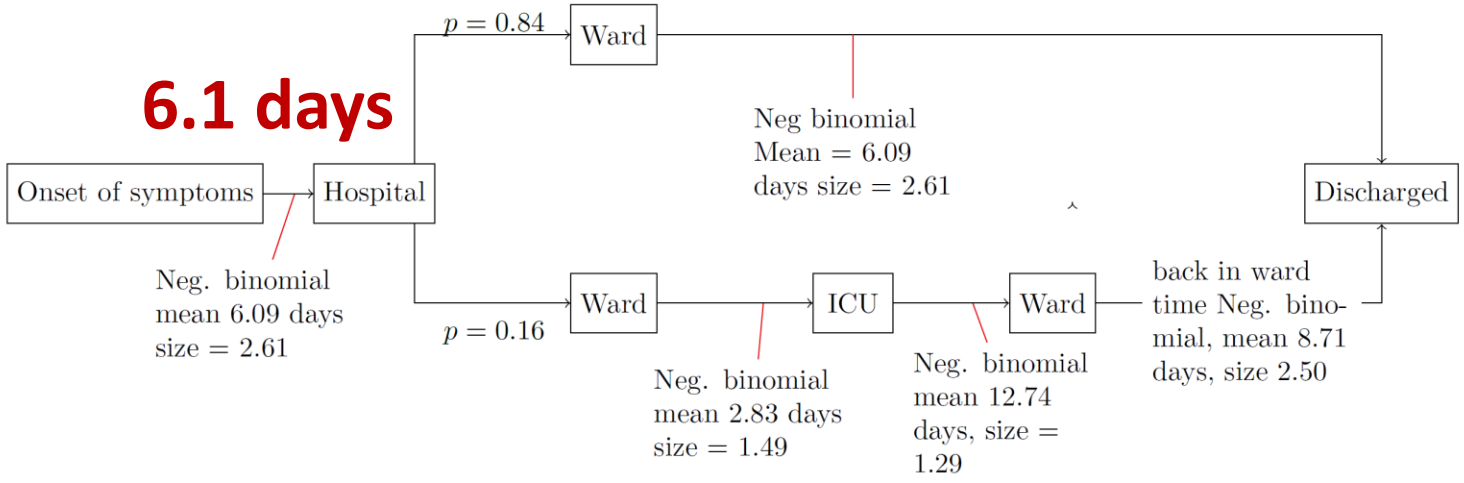


Figure 33: Hospital assumptions and parameters used between 1 January 2021 and 1 March 2021 for those living in Oslo

not Oslo

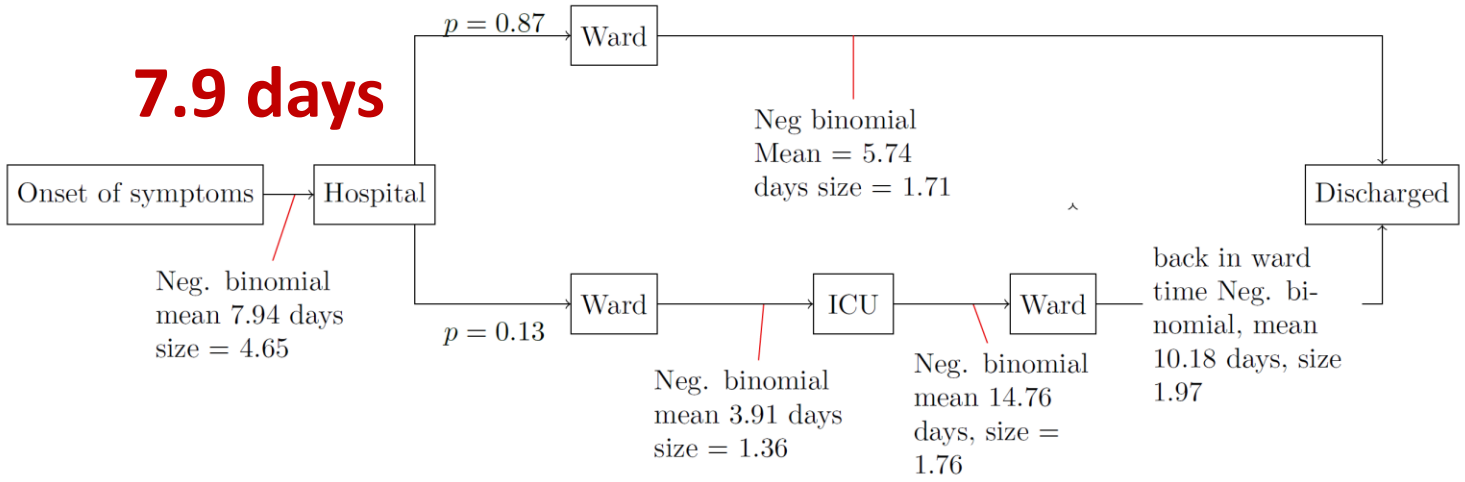
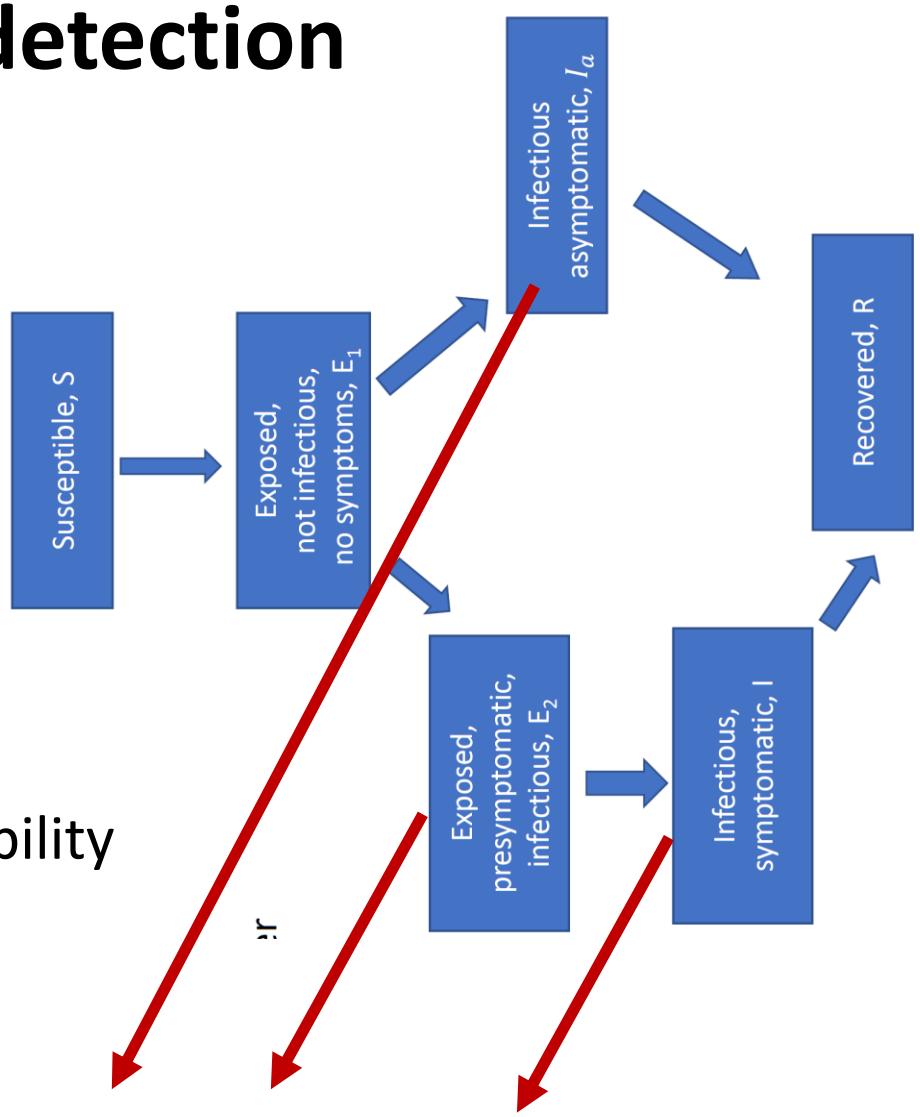


Figure 34: Hospital assumptions and parameters used between 1 January 2021 and 1 March 2021 for those not living in Oslo

From 1 Jan 2021

Inference
$\hat{\beta}, \hat{\gamma}$

Case detection



Probability

Tested and detected

Inference
$\hat{\beta}, \hat{\gamma}$

Probability to detect a case π_t

$$\text{logit}(\pi_t) = \alpha + \beta \cdot k_t$$

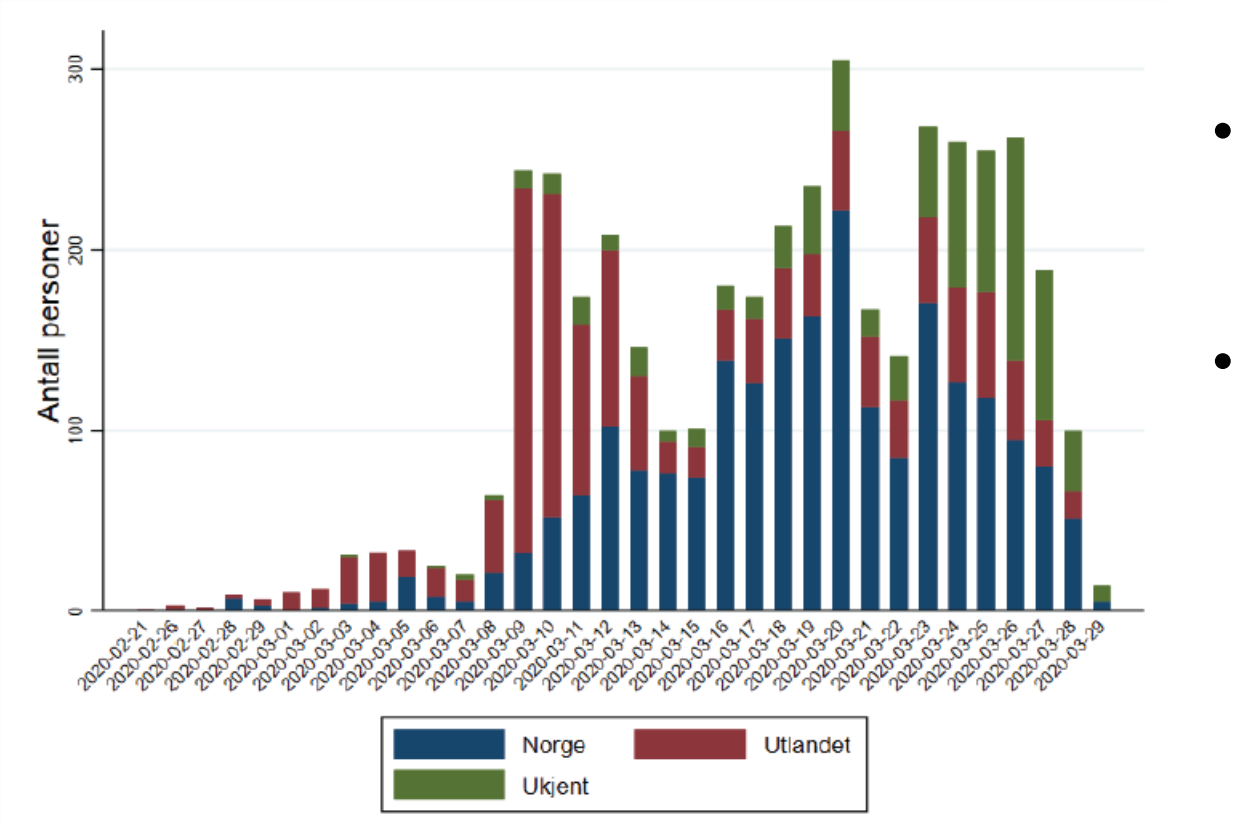
k_t is the number of tests actually performed on day t

α, β are estimated

Limitation: we only take into account the changes in the test criteria that are captured by the total number of tests performed.

Inference
$\hat{\beta}, \hat{\gamma}$

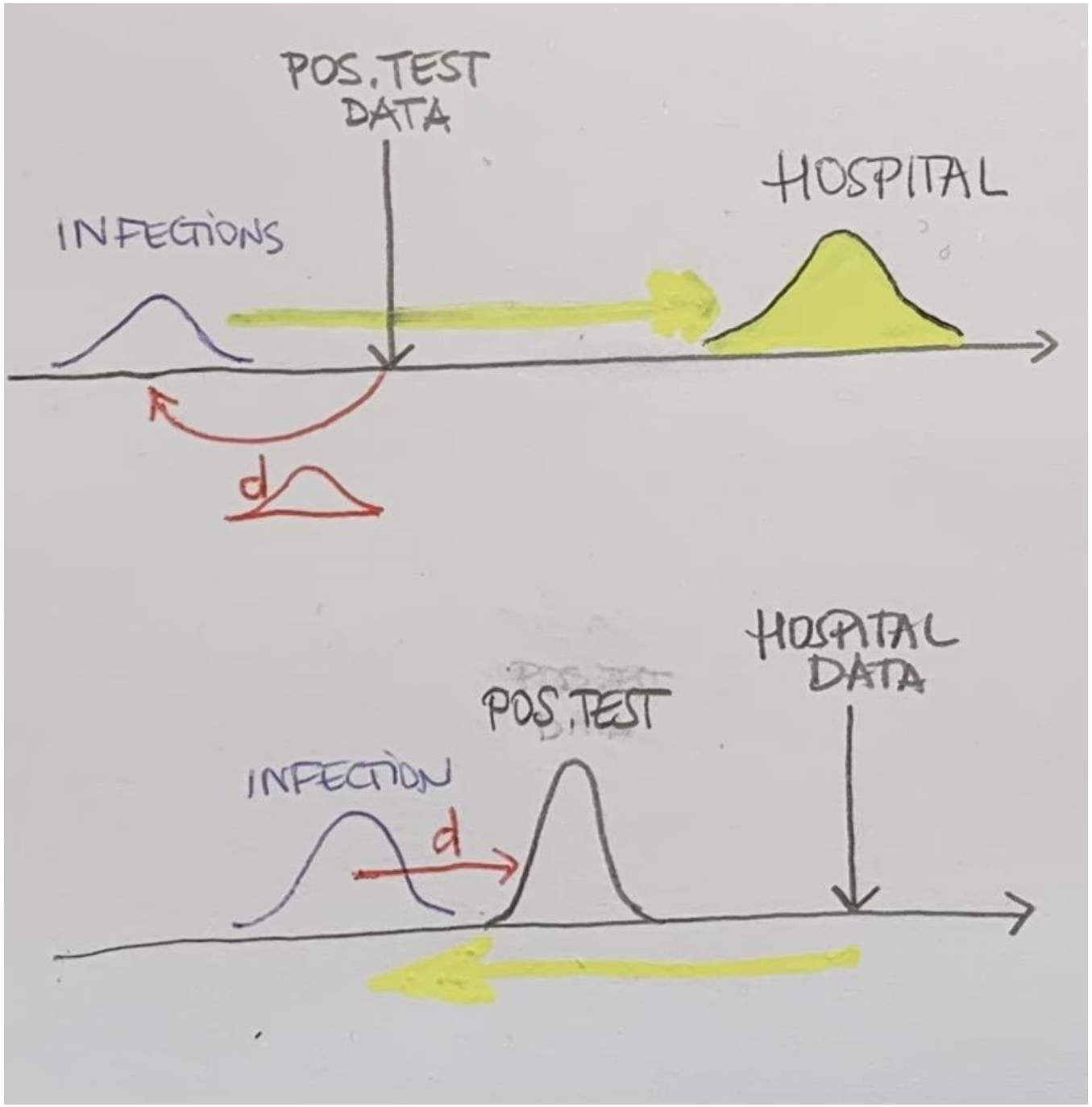
Seeding



- Imported cases set in municipality of residence, or at testing place
- **Amplification factor**, representing undetected cases per detected case. Poisson distributed with estimated mean.

Inference
$\hat{\beta}, \hat{\gamma}$

Lack of coherence between test and hospital data

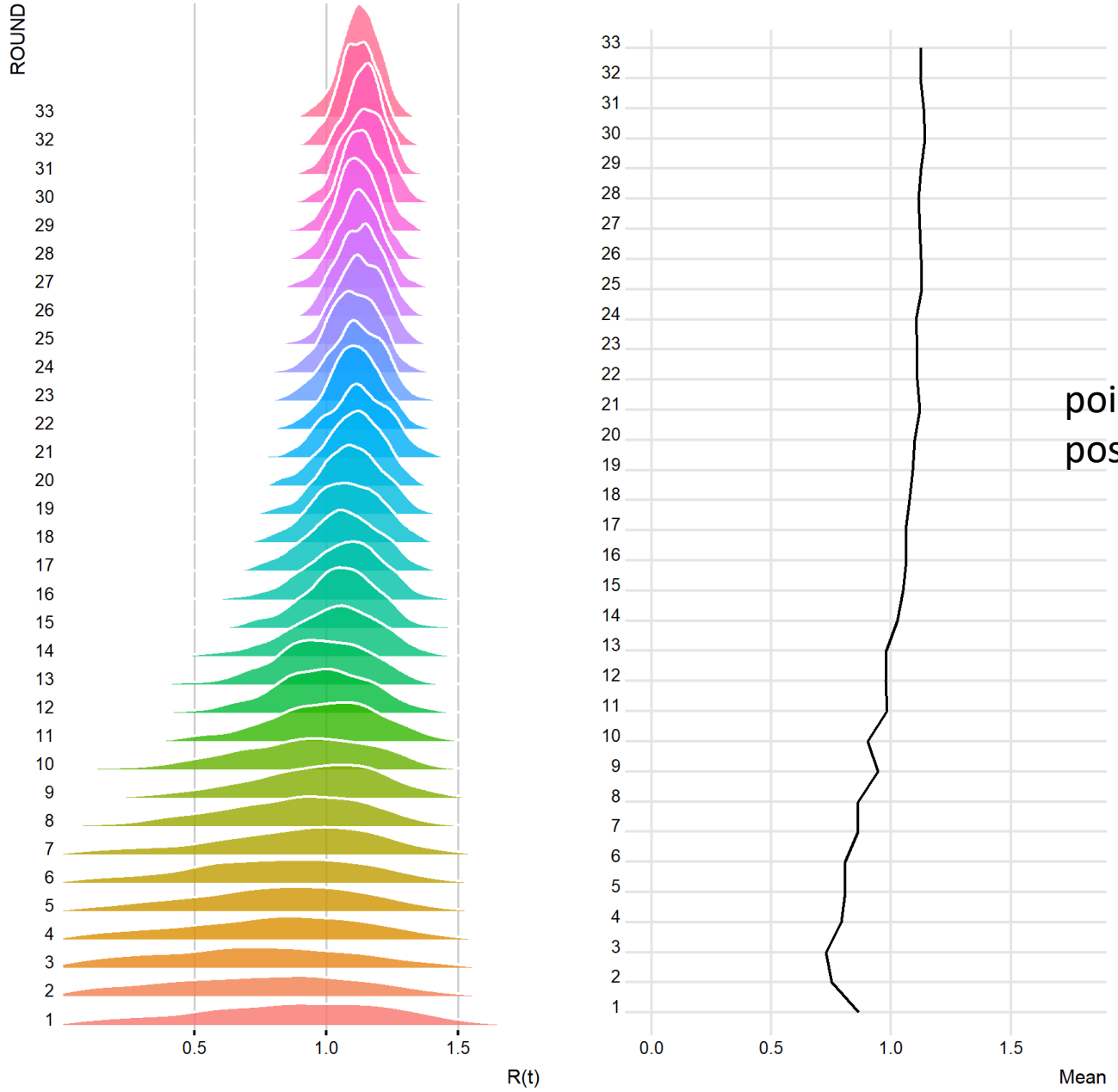


Inference
$\hat{\beta}, \hat{\gamma}$

Sequential Approximate Bayesian Computation, combines particle filters with ABC.
Good parameters found in subsequent rounds, improving each time

Iterative algorithm:
ca. 2 days
on 2000 cores

effective reproduction number, now, Oslo

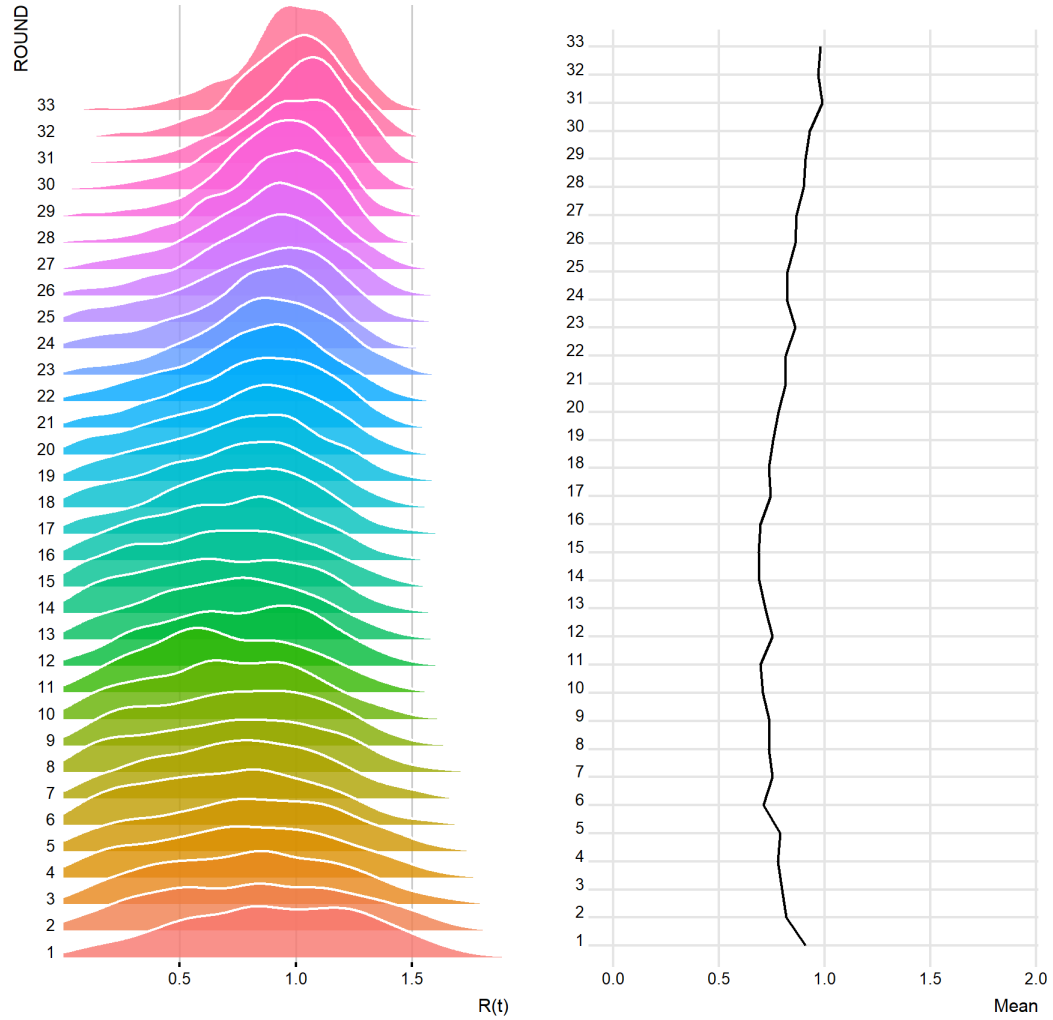


point estimate,
posterior mean

Inference
$\hat{\beta}, \hat{\gamma}$

effective reproduction number, Rogaland

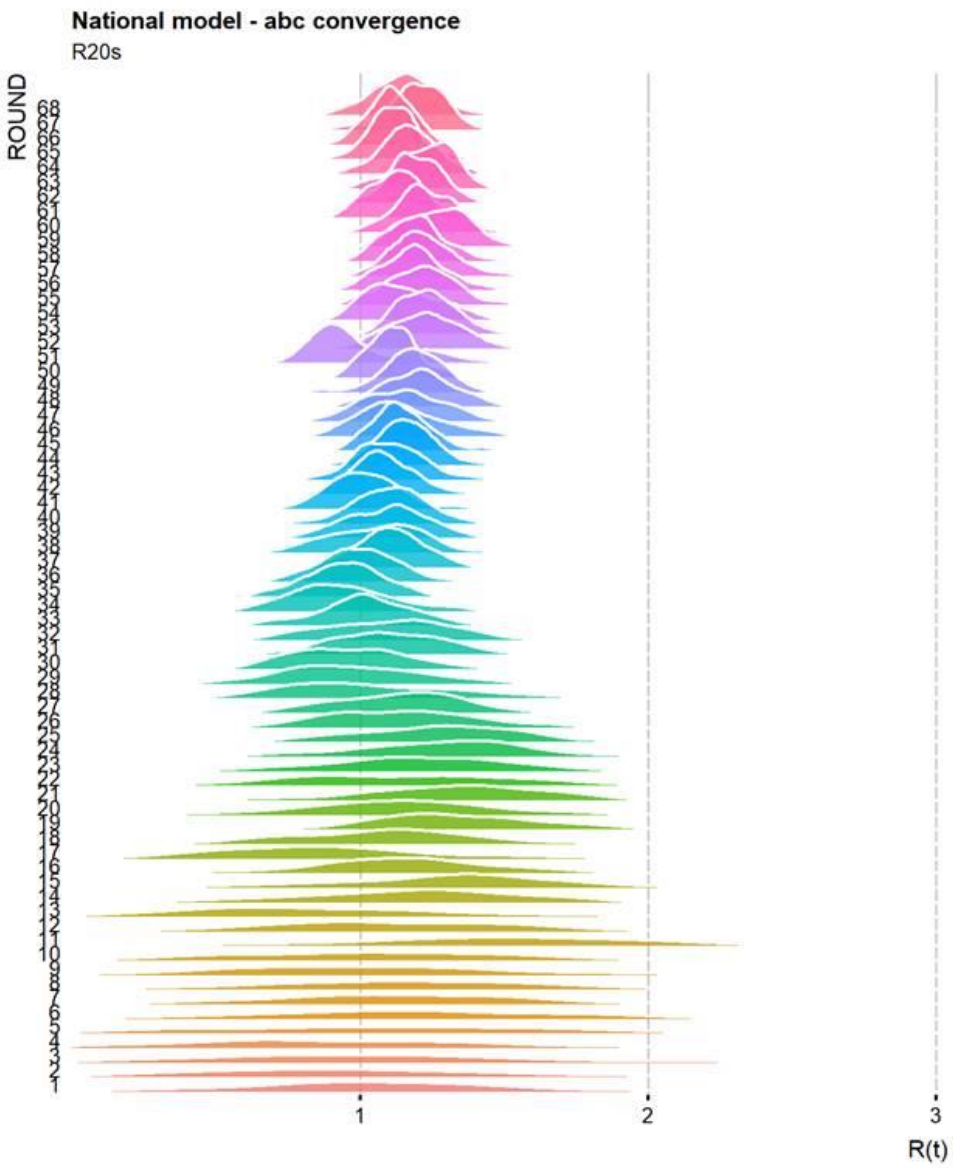
Some counties with
very uncertain estimates.



0 1.5

Inference

$\hat{\beta}, \hat{\gamma}$



Inference
$\hat{\beta}, \hat{\gamma}$

- Start sampling the prior, compute mean squared distance between predicted number in hospital and case data, accept the best 1000 parameters out of 10000.

For all subsequent rounds:

- Sample set of parameters θ from the previous round using importance weights.
- Propose a new set of parameters θ’ by sampling from a multivariate Gaussian centered in θ and with empirical covariance matrix estimated from accepted parameter sets at previous round.
- Keep those θ’ with mean squared distance below the 0.80-quantile of the error in the previous round (20% improve each round).

Inference
$\hat{\beta}, \hat{\gamma}$

- importance weights.

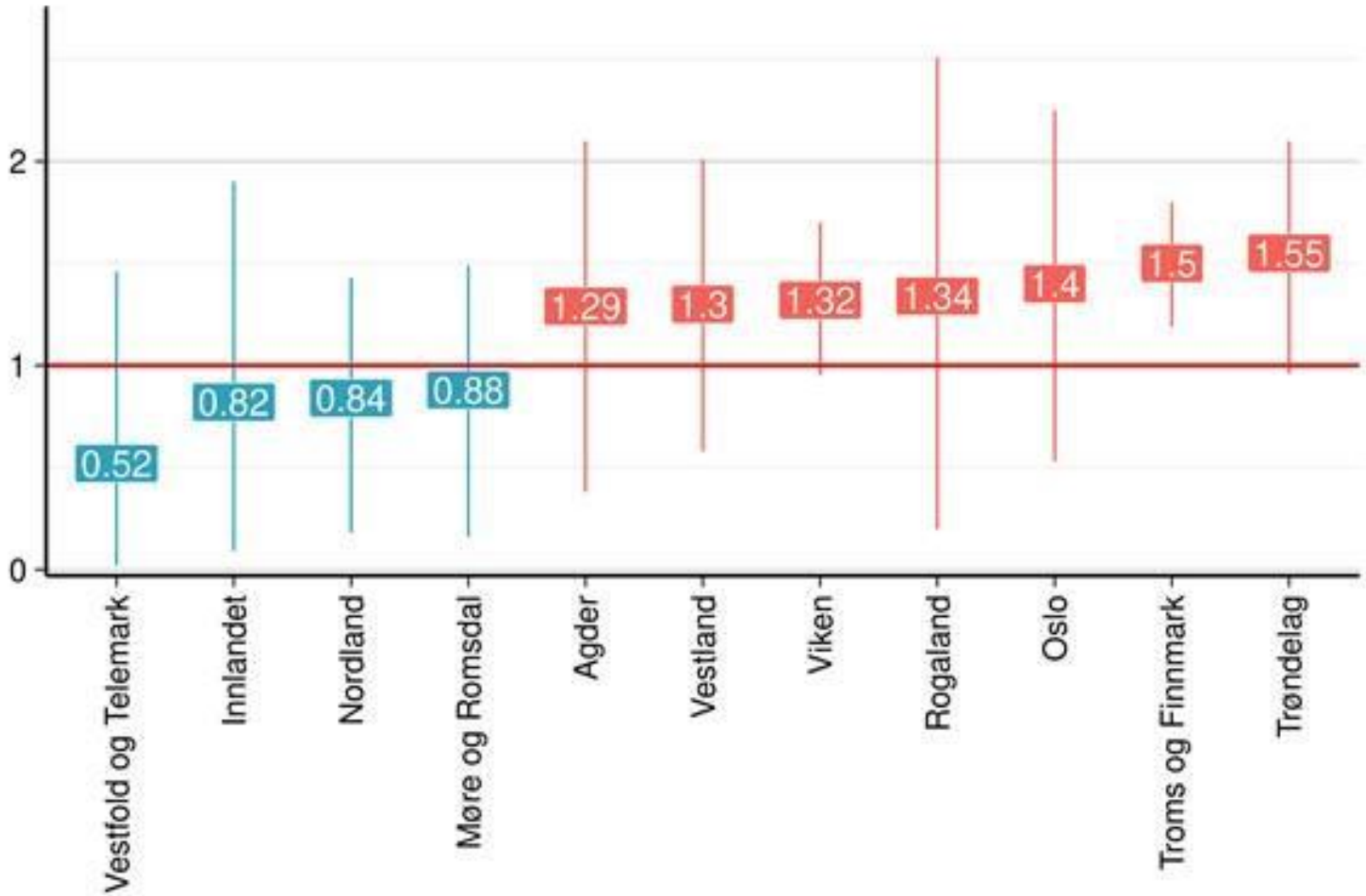
$$w_i^r = \frac{\pi(i)}{\sum_{j=1}^{n} w_j^{r-1} K(i_r | j_{r-1})}$$

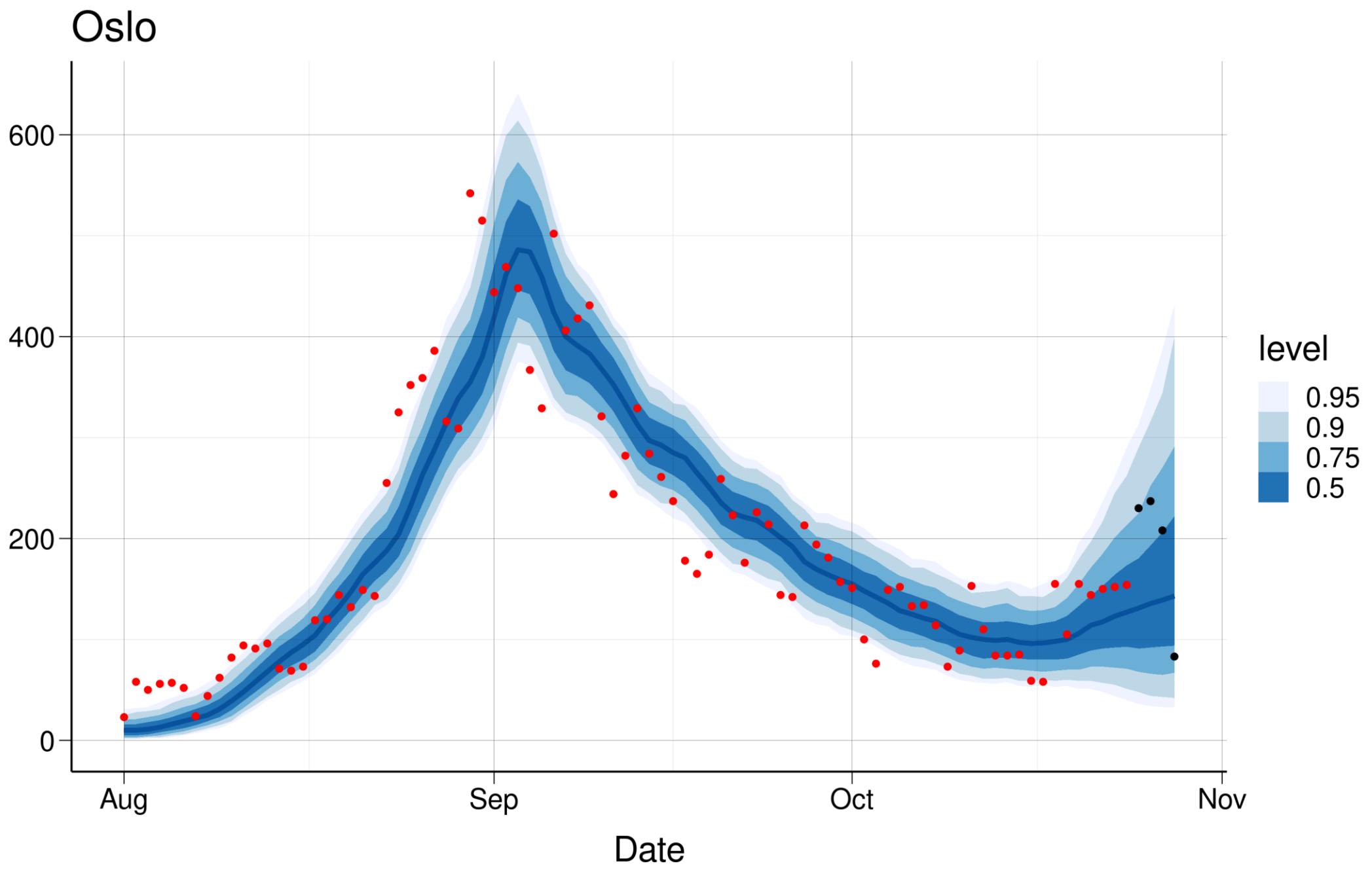
- Continue until we obtain 1000 parameters in each round.

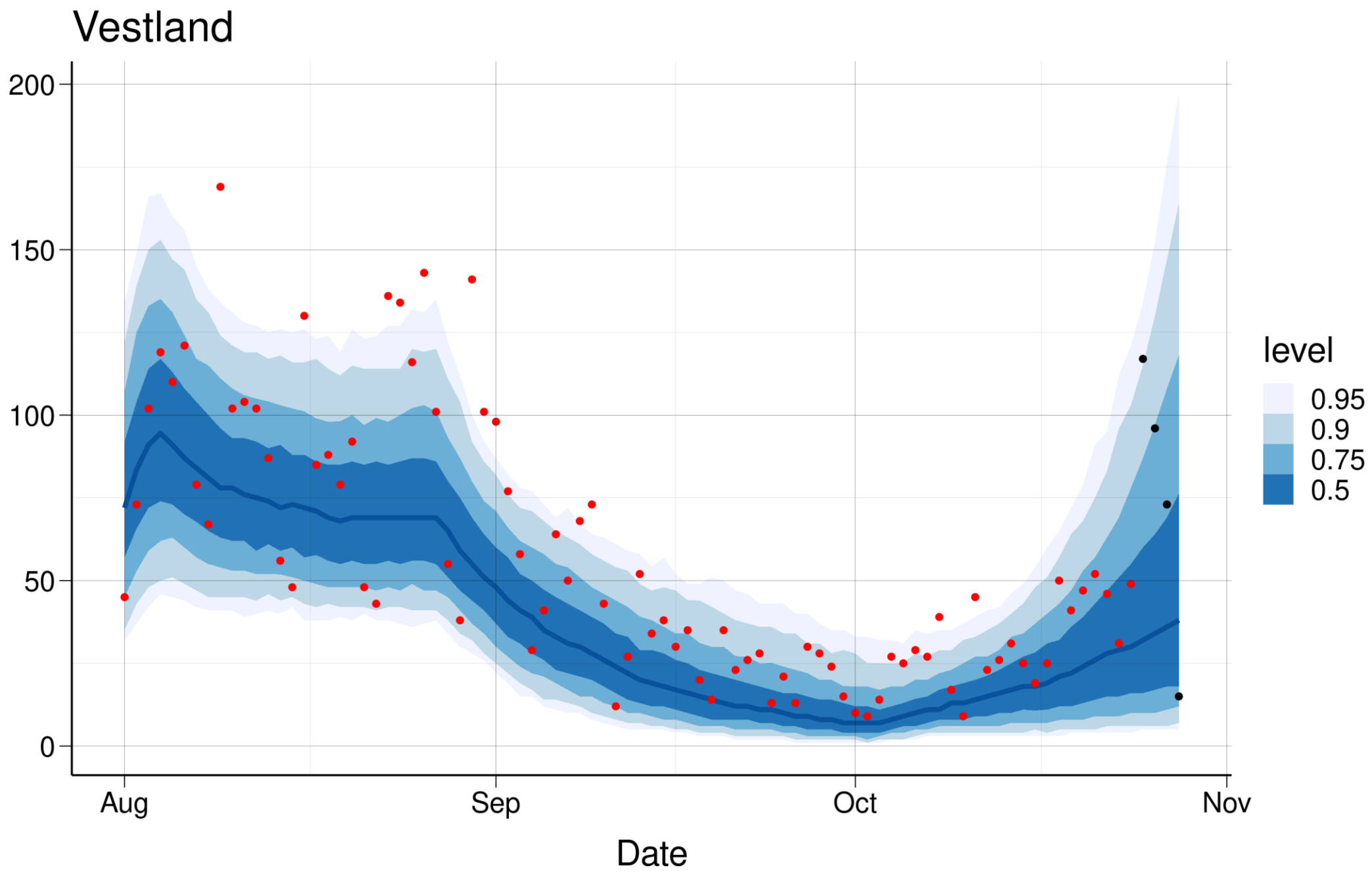
- 1000 parameters at the end, used to compute point estimates and credibility bounds and for predictions.

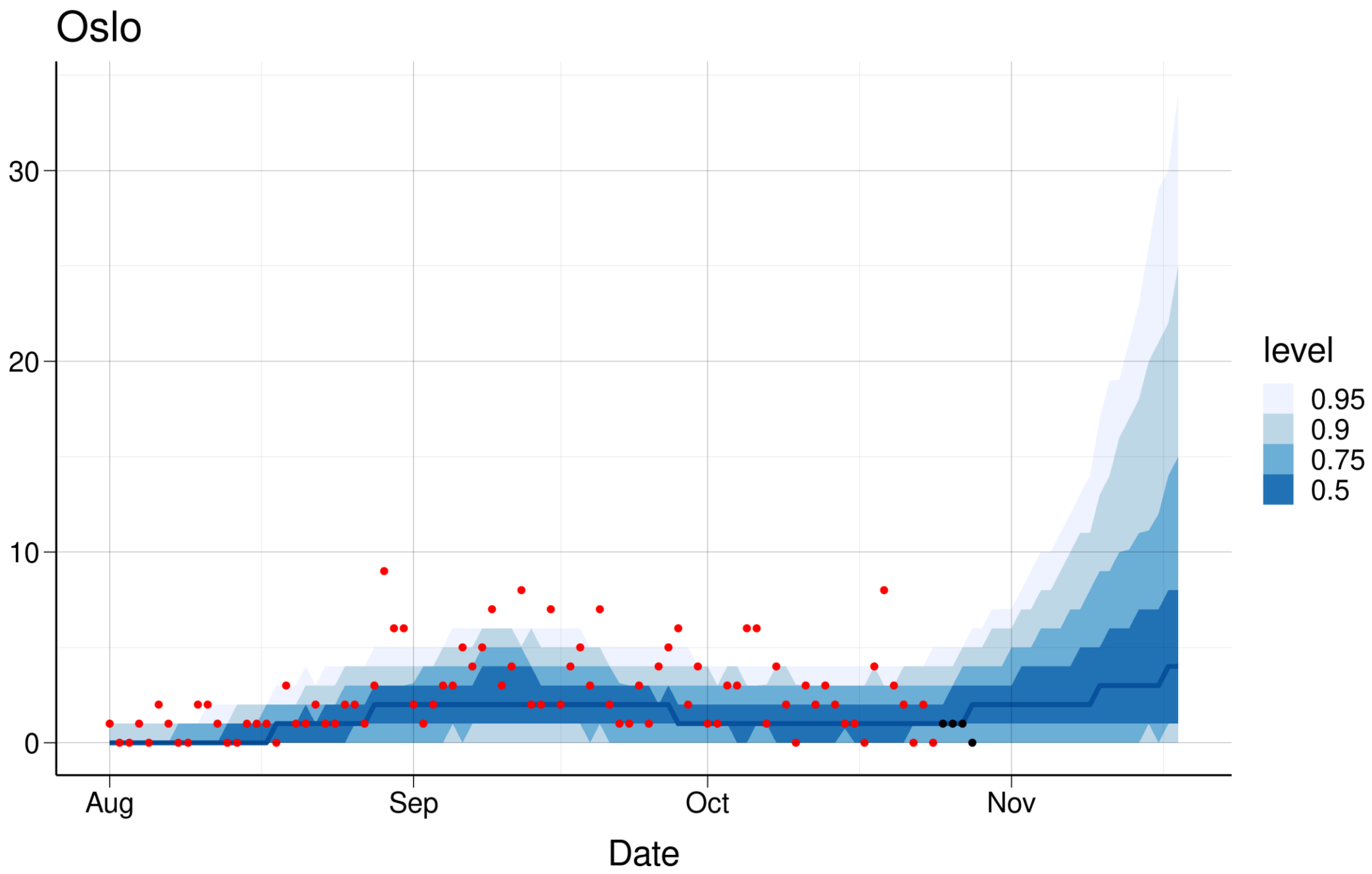
β_t^f piecewise constant, from 1.8.21 to 1.9.21
from 2.9.21 60 14.10.21
from 15.10.21,

Last, R_{eff} from 15.10.21




Oslo
600
400
200
0
Aug
Sep
Oct
Nov
Date
level
0.95
0.9
0.75
0.5


Vestland
200
150
100
50
0
Aug
Sep
Oct
Nov
Date
level
0.95
0.9
0.75
0.5


Oslo
30
20
10
0
Aug
Sep
Oct
Nov
Date
level
0.95
0.9
0.75
0.5

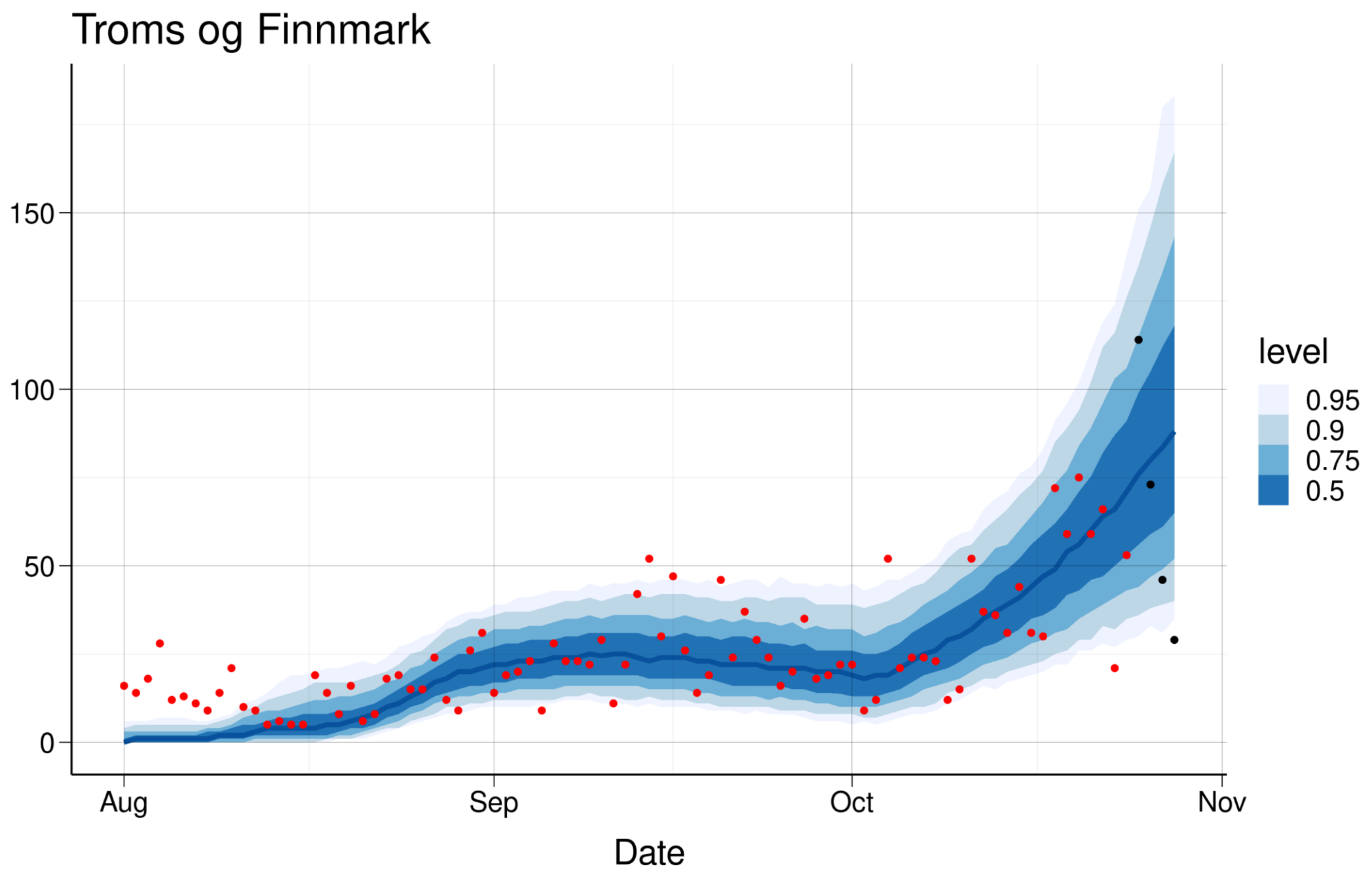
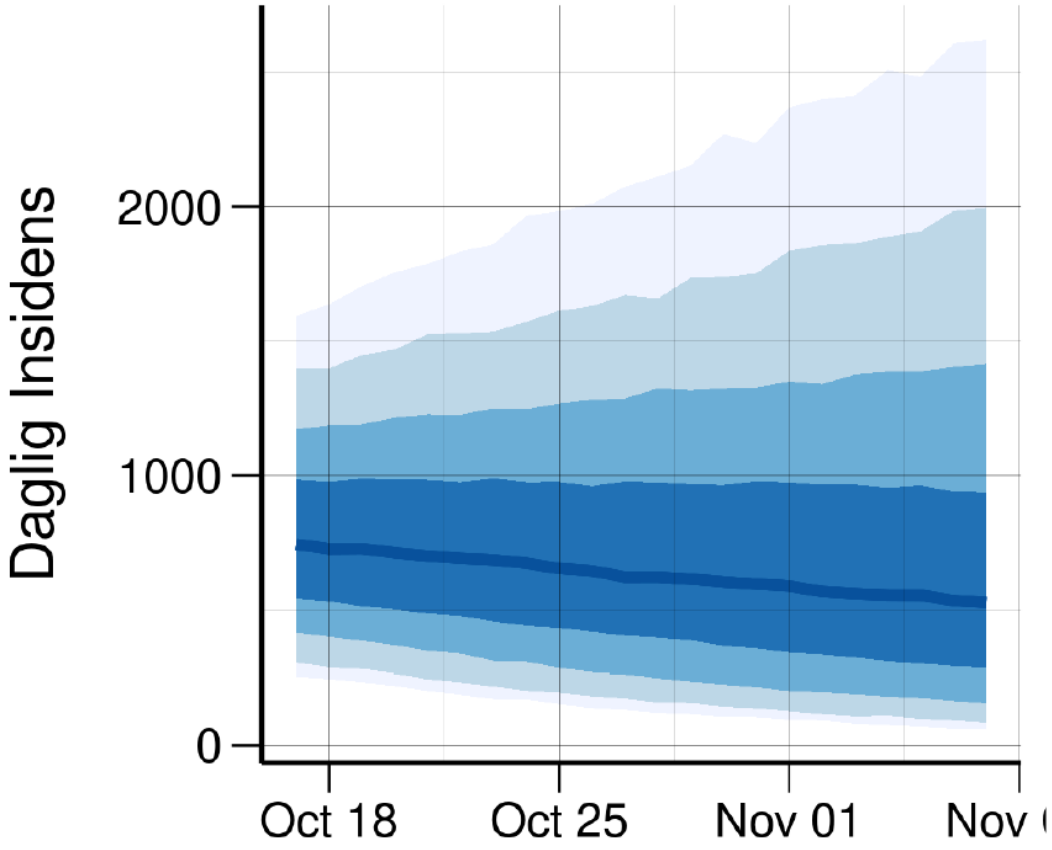

Troms og Finnmark
150
100
50
0
Aug
Sep
Oct
Nov
Date
level
0.95
0.9
0.75
0.5

Table 7: Predicted incidence per day: Median/Mean (CI)

Region	1 week prediction (24 Oct)	2 weeks prediction (31 Oct)	3 weeks prediction (07 Nov)
Agder	8/14 (0-74)	7/17 (0-112)	9/23 (0-147)
Innlandet	4/11 (0-71)	3/10 (0-83)	2/11 (0-88)
Møre og Romsdal	1/5 (0-25)	1/6 (0-37)	1/9 (0-60)
Nordland	7/15 (0-87)	8/22 (0-127)	12/36 (0-207)
Oslo	34/44 (6-151)	26/37 (5-136)	25/38 (4-146)
Rogaland	8/19 (0-113)	9/29 (0-204)	10/44 (0-323)
Troms og Finnmark	77/106 (8-376)	105/177 (6-753)	145/292 (7-1503)
Trøndelag	15/51 (0-353)	12/84 (0-676)	11/148 (0-1262)
Vestfold og Telemark	26/40 (3-164)	25/52 (1-274)	25/69 (1-425)
Vestland	3/10 (0-64)	3/15 (0-89)	4/23 (0-128)
Viken	26/58 (5-323)	18/53 (3-355)	18/56 (3-403)

Table 9: Number of hospitalisation beds occupied by Covid-19 patients: Median/Mean (CI)

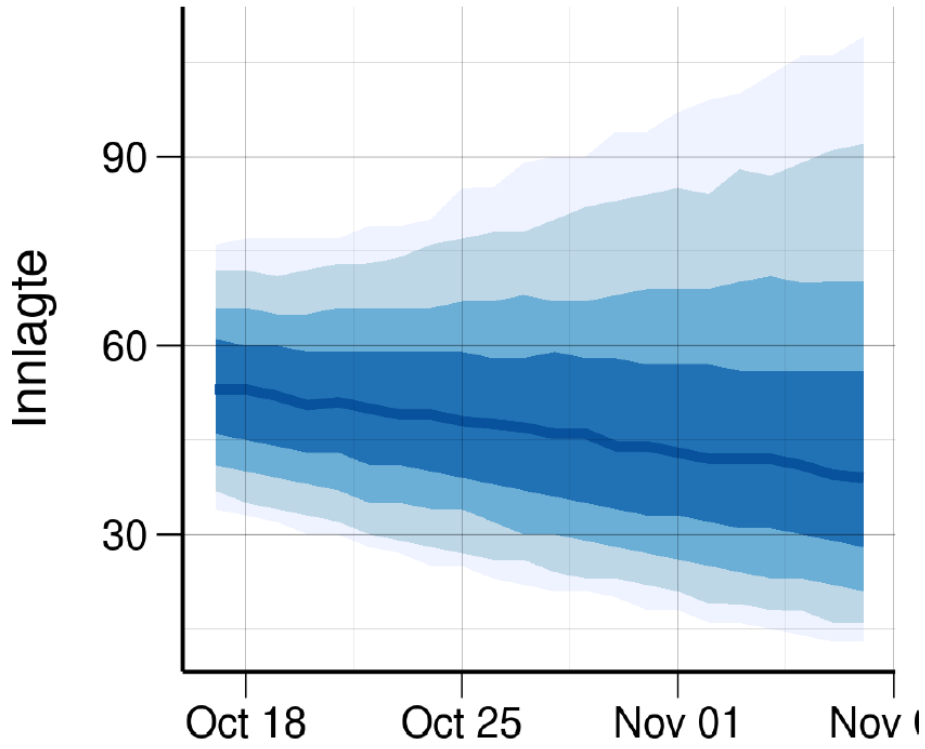
Region	1 week prediction (24 Oct)	2 weeks prediction (31 Oct)	3 weeks prediction (07 Nov)
Agder	0/1 (0-4)	0/1 (0-5)	0/1 (0-6)
Innlandet	1/1 (0-6)	0/1 (0-5)	0/1 (0-5)
Møre og Romsdal	0/0 (0-3)	0/0 (0-3)	0/0 (0-4)
Nordland	1/1 (0-7)	1/2 (0-10)	1/2 (0-14)
Oslo	4/5 (0-12)	4/4 (0-11)	2/3 (0-11)
Rogaland	0/1 (0-5)	0/1 (0-7)	0/2 (0-10)
Troms og Finnmark	3/4 (0-13)	4/7 (0-23)	7/11 (0-46)
Trøndelag	1/2 (0-10)	1/2 (0-13)	1/3 (0-24)
Vestfold og Telemark	3/4 (0-12)	3/5 (0-18)	4/7 (0-30)
Vestland	0/1 (0-4)	0/1 (0-4)	0/1 (0-5)
Viken	5/6 (0-20)	4/6 (0-23)	2/5 (0-27)



Predicting number of infected, next three weeks:

Stable, going slowly down
Uncertainty grows (of course)

Today ca. 400 cases are test-confirmed. We estimate this number to be ~ 750. 55% cases are detected by testing (and isolated), the others are not.



Hospital admission

3-weeks predictions of hospital prevalence

- Under the assumption that nothing changes compared to today
- Whenever interventions, people's behaviour and mobility change, the predictions are ***wrong***
- Typically when we estimate a high R and therefore the 3-weeks-ahead predictions were bad, interventions and self-regulation led to better outcomes: we are accused of being ***pessimistic***.

4 Nyheter Koronaviruset

Aftenposten
Tirsdag 15. juni 2021

Skrekkscenarioene slo ikke til. De var feil gang på gang.

Per Anders Johansen og Olav Olsen (foto)

Aftenposten

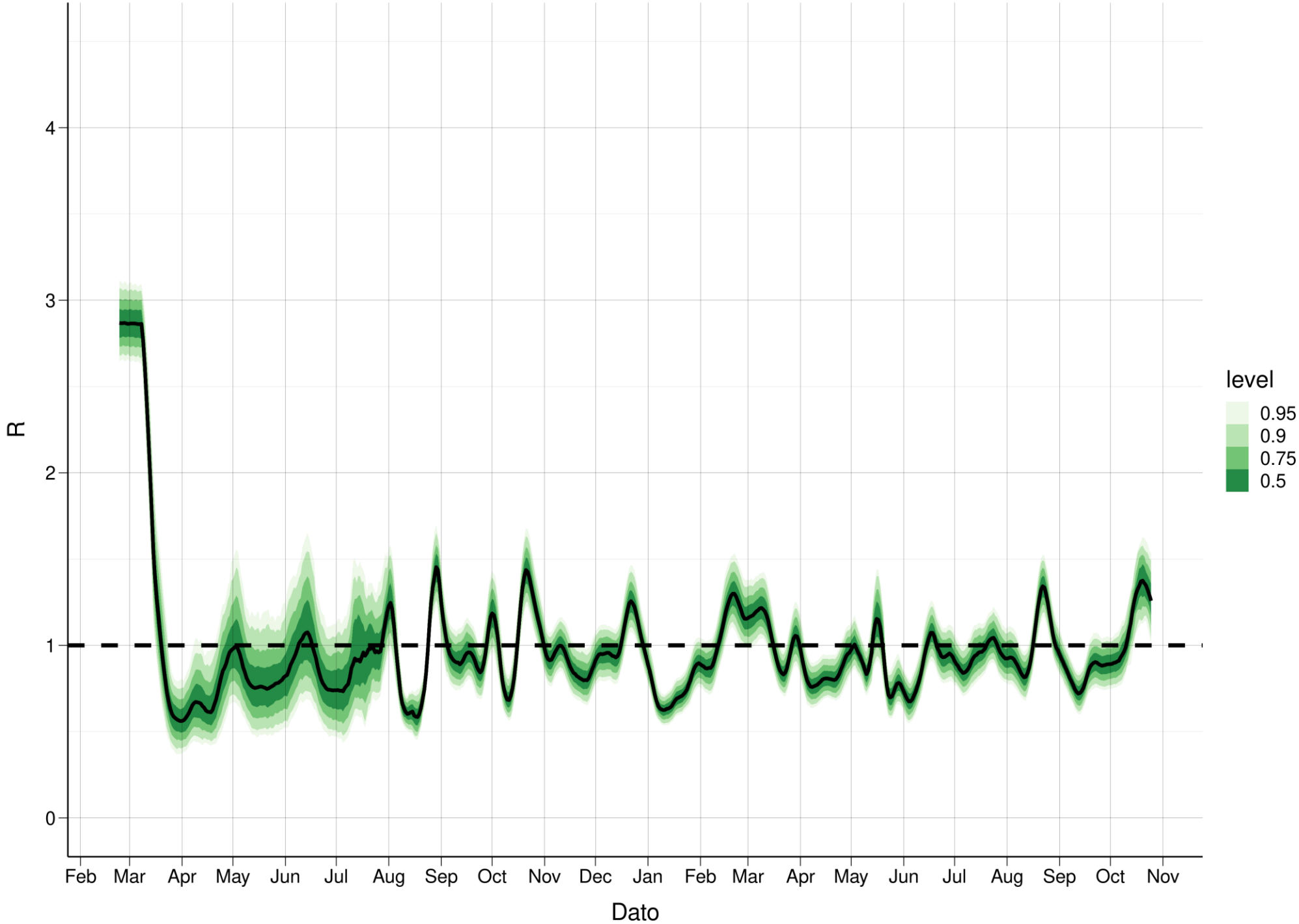
Kronikk | Koronaviruset

Aftenposten bommer om prognoser. Igjen og igjen.

Camilla Stoltenberg *Direktør, Folkehelseinstituttet*
Preben Aavitsland *Overlege, Folkehelseinstituttet*
Gunnar Rø *Forsker, Folkehelseinstituttet*
Birgitte Freiesleben de Blasio *Avdelingsdirektør, Folkehelseinstituttet*
Arnoldo Frigessi *Professor*
Solveig Engebretsen *Forsker, Norsk regnesentral*

- Keep control of the spread of the virus.
- Control means that the number of patients is manageable for the health system, …
- even though the number of patients may periodically increase and vary between regions.

Modelling group


R
4
3
2
1
0
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dec
Jan
Feb
Mar
Apr
May
Jun
Jul
Aug
Sep
Oct
Nov
Dato
level
0.95
0.9
0.75
0.5