

# State estimation of Covid-19 disease in Denmark

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## Contents

<b>Introduction</b>	<b>2</b>
<b>Materials and method</b>	<b>2</b>
Data . . . . .	2
Model formulation . . . . .	3
Laplace approximation . . . . .	4
Importance sampling . . . . .	4
Implementations . . . . .	4
<b>Results</b>	<b>5</b>
Parameters . . . . .	5
Estimating the total number of new hospital admissions in Denmark . . . . .	5
Estimating the number of new hospital admissions in Denmark grouped by region . . . . .	6
<b>Discussion</b>	<b>7</b>
<b>References</b>	<b>8</b>

# Introduction

Early detection of outbreaks with communicable diseases are of great importance in order to initiate timely interventions and help prevent disease spread. In this report non-normal mixed effects models will be evaluated on their ability to identify outbreaks of Covid-19 disease using data over new hospital admissions with Covid-19 in Denmark.

## Materials and method

### Data

In this project, the daily record of new hospital admissions with Covid-19 in Denmark grouped by region of residence and totals are used. The data is publicly available and were obtained from Statens Serum Institut (SSI) website<sup>1</sup>. SSI collects the data from the National Patient Registry (NPR), which contains information about outpatient contacts from Danish public as well as private hospitals. The data from NPR has some delay. Therefore, the inventory is updated daily with real-time data from the regions. The regions provide snapshot-data twice to SSI daily at 7am and 3pm. A hospital admission related to Covid-19 is defined as an admission, where a patient is admitted within 14 days after a positive SARS-CoV-2 test. Patients that are tested positive for SARS-CoV-2 during an admission is also registered as a Covid-19 related admission. Furthermore, admissions with Covid-19 are only registered for patients that are present in at least one snapshot, or if the patient have been admitted for more than 12 hours according to NPR.

In Figure 1 the total number of new admissions to the hospital are visualized.

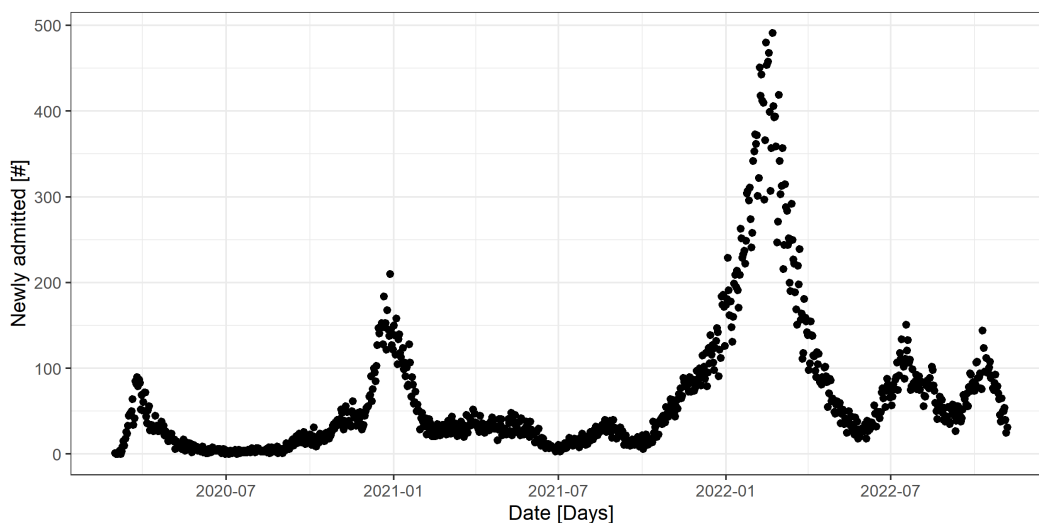


Figure 1: Daily number of new hospital admissions in Denmark.

In Figure 2 the daily number of new hospital admissions grouped by region of residence

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<sup>1</sup><https://covid19.ssi.dk/overvagningsdata/download-fil-med-overvaagningdata>

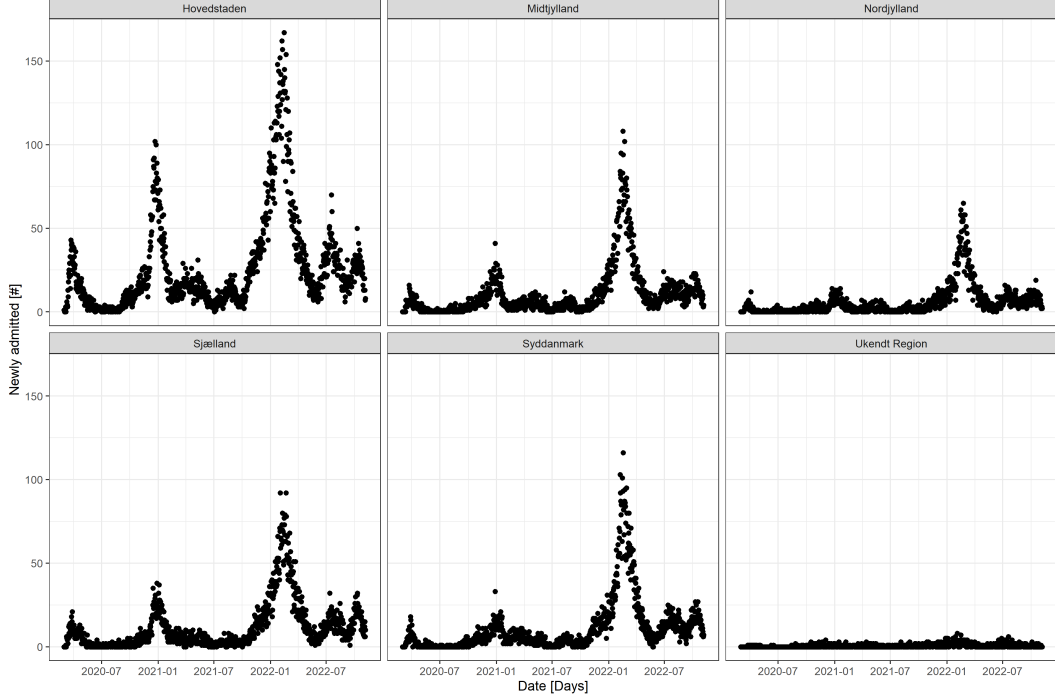


Figure 2: Total number of new hospital admissions in Denmark.

## Model formulation

In order to analyze the data a simple state space model is proposed. The count observations  $h_t$  of new hospital admissions is assumed to follow a Poisson distribution  $h_t \sim P(\lambda_t)$  with intensities given by

$$\log(\lambda_t) = \beta + u_t \quad (1)$$

Here  $\beta$  is a fixed parameter, that represents the average intensity and  $u_t$  is a random effect that is assumed to follow a first order autoregressive process

$$u_t = au_{t-1} + \epsilon_t \quad (2)$$

where  $\epsilon \sim N(0, \sigma^2)$ ,  $t > 1$  is a white noise process, and  $a$  and  $\sigma$  are model parameters. Using the results from Madsen (2007), it is assumed that  $u_1$  follow the stationary distribution of the first order autoregressive process  $u_1 \sim N(0, \sigma^2/(1 - a^2))$ .

The joint likelihood becomes

$$L(a, \beta, \sigma; \mathbf{u}, \mathbf{y}) = \phi_{0, \frac{\sigma^2}{1-a^2}}(u_1) \prod_{t=2}^n (\phi_{0, \sigma^2}(u_t - au_{t-1})) \prod_{t=1}^n (p_{\lambda_t}(h_t)) \quad (3)$$

where  $\phi_{\mu, \sigma^2}$  is the probability density function (pdf) of the normal distribution with mean  $\mu$  and variance  $\sigma^2$ , and  $p_{\lambda}$  is the pdf of the Poisson distribution with mean  $\lambda$ .

In order to obtain the likelihood for the model parameters  $(a, \beta, \sigma)$  the observed random effects are integrated out. Hence, the marginal likelihood is obtained

$$L_M = (a, \beta, \sigma; \mathbf{y}) = \int_{\mathbb{R}^q} L(a, \beta, \sigma; \mathbf{u}, \mathbf{y}) d\mathbf{u} \quad (4)$$

where  $q$  is the number of random effects and  $a$ ,  $\beta$ , and  $\sigma$  are the parameters to be estimated.

## Laplace approximation

In order to make computation of the joint likelihood function in (4) feasible, the estimation is carried out using the multivariate Laplace approximation.

The joint log-likelihood  $l(a, \beta, \sigma; \mathbf{y}) = \log(L(a, \beta, \sigma; \mathbf{y}))$  is approximated by a second order Taylor approximation around the optimum  $\tilde{u} = \hat{u}_\theta$  of the log-likelihood function w.r.t. the unobserved random variables  $u$ , i.e.,

$$l(\theta, \mathbf{u}, \mathbf{y}) \approx l(\theta, \tilde{\mathbf{u}}, \mathbf{y}) - \frac{1}{2}(\mathbf{u} - \tilde{\mathbf{u}})^T H(\tilde{\mathbf{u}})(\mathbf{u} - \tilde{\mathbf{u}})$$

where the first-order term of the Taylor expansion disappears since the expansion is done around the optimum  $\tilde{\mathbf{u}}$  and  $H(\tilde{\mathbf{u}}) = -l''_{uu}(\theta, \mathbf{u}, \mathbf{y})|_{\mathbf{u}=\tilde{\mathbf{u}}}$  is the negative Hessian of the joint log-likelihood evaluated at  $\tilde{\mathbf{u}}$ .

## Importance sampling

Importance sampling is a re-weighting technique for approximating integrals w.r.t. a density  $f$  by simulation in cases where it is not feasible to simulate from the distribution with density  $f$ . Instead it uses samples from a different distribution with density  $g$ , where the support of  $g$  includes the support of  $f$ .

## Implementations

In this section two different R packages, **glmmTMB** and **KFAS** available at Comprehensive R Archive Network (CRAN) are presented.

### glmmTMB

This section describes the R package **glmmTMB** by Brooks et al. (2017) for linear and generalized linear mixed models (GLMMs) using Template Model Builder (TMB). The models are estimated using maximum likelihood estimation via TMB. Random effects are assumed to be Gaussian on the scale of the linear predictor and are integrated out using Laplace approximation. Additionally, gradients are calculated using automatic differentiation.

### KFAS

This section goes into detail with the R package **KFAS** by Helske (2017) for state space modelling with observations from the exponential family.

In **KFAS** the Poisson distribution with intensity  $\lambda_t$  together with the log-link is supported.

In order to make inferences of the Poisson model, a Gaussian model which has the same conditional posterior mode as  $p(\theta|y)$  has to be found

The **KFAS** package can perform Kalman filtering and smoothing with exact diffuse initialization using an univariate approach.

# Results

## Parameters

	Estimate	Std. Error	z value	Pr(> z )
(Intercept)	3.175176	0.7257113	4.375261	1.21e-05

## Estimating the total number of new hospital admissions in Denmark

In Figure 3 the total number of new hospitals admissions in Denmark is visualized together with the smoothed estimates from `glmmTMB` and `KFAS`.

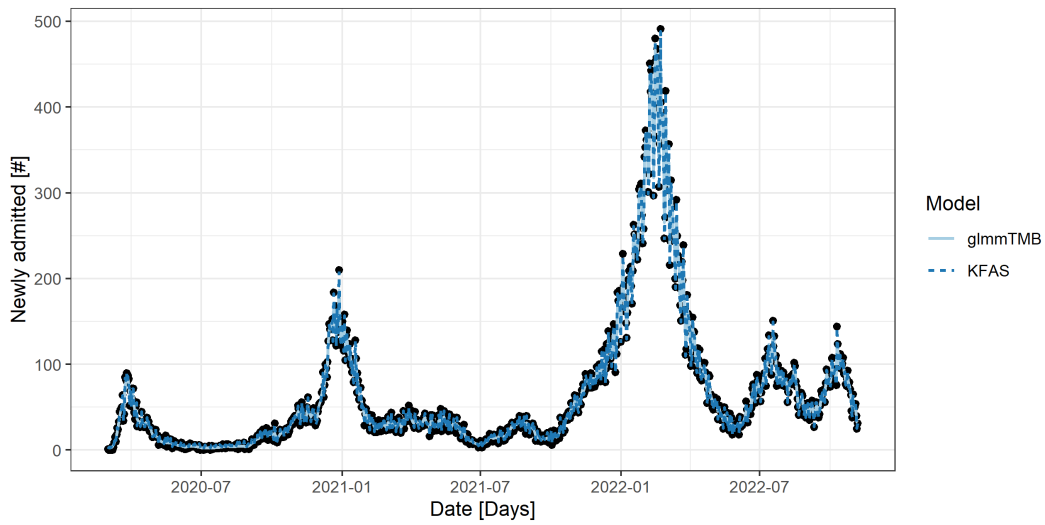


Figure 3: Total number of new hospital admissions in Denmark with smoothed estimates from `glmmTMB` and `KFAS`.

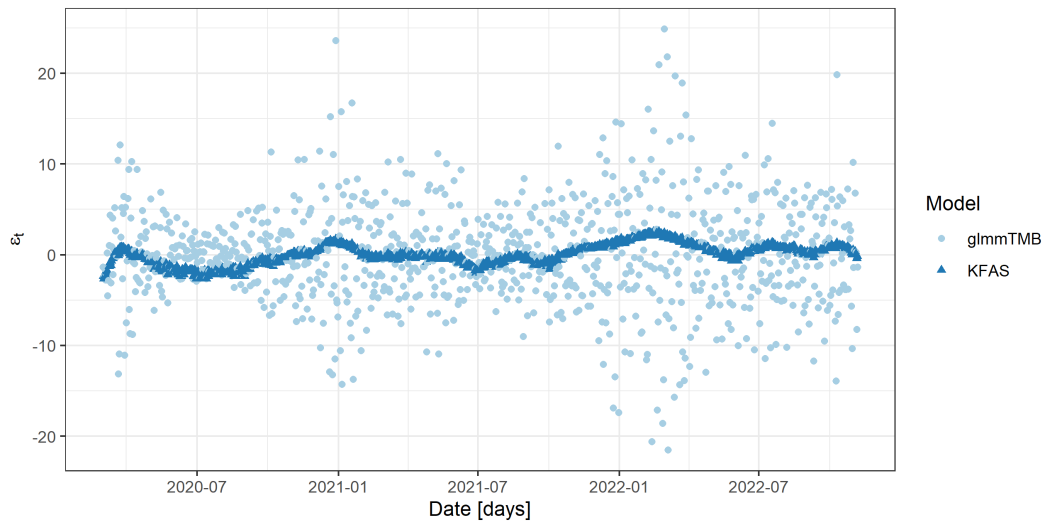


Figure 4: Model residuals from `glmmTMB` and `KFAS`.

The smoothed estimate of the latent state estimated from `glmmTMB` and `KFAS` is visualized in Figure 5.

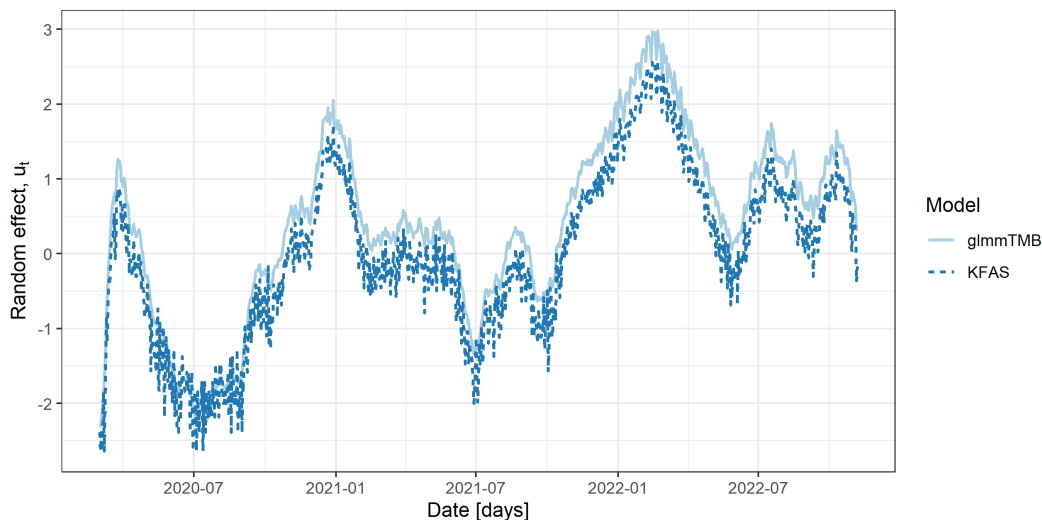


Figure 5: Smoothed estimates of the latent states from `glmmTMB` and `KFAS`.

## Estimating the number of new hospital admissions in Denmark grouped by region

In Figure 6 the total number of new hospitals admissions in Denmark grouped by region is visualized together with the smoothed estimates from `glmmTMB` and `KFAS`.

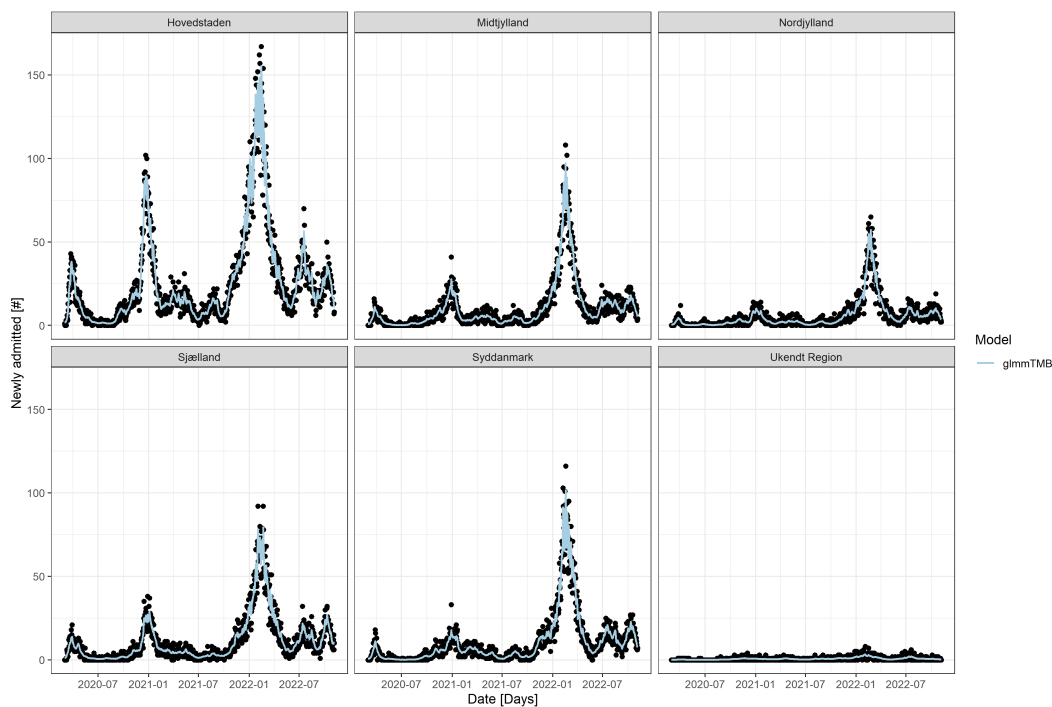


Figure 6: Total number of new hospital admissions in Denmark grouped by region with smoothed estimates from `glmmTMB` and `KFAS`.

## Discussion

Write it later

## References

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