Automated and Early Detection of Disease Outbreaks

Kasper Schou Telkamp

Section for Dynamical Systems

DTU Compute
Department of Applied Mathematics and Computer Science

Outline

- Shiga- and verotoxin producing E. coli.
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- State-of-the-art methods
  - Farrington
  - Noufaily
- Novel methods based on general mixed effect models
  - Hierachical Poisson-Normal model
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- Comparison of methods
- References
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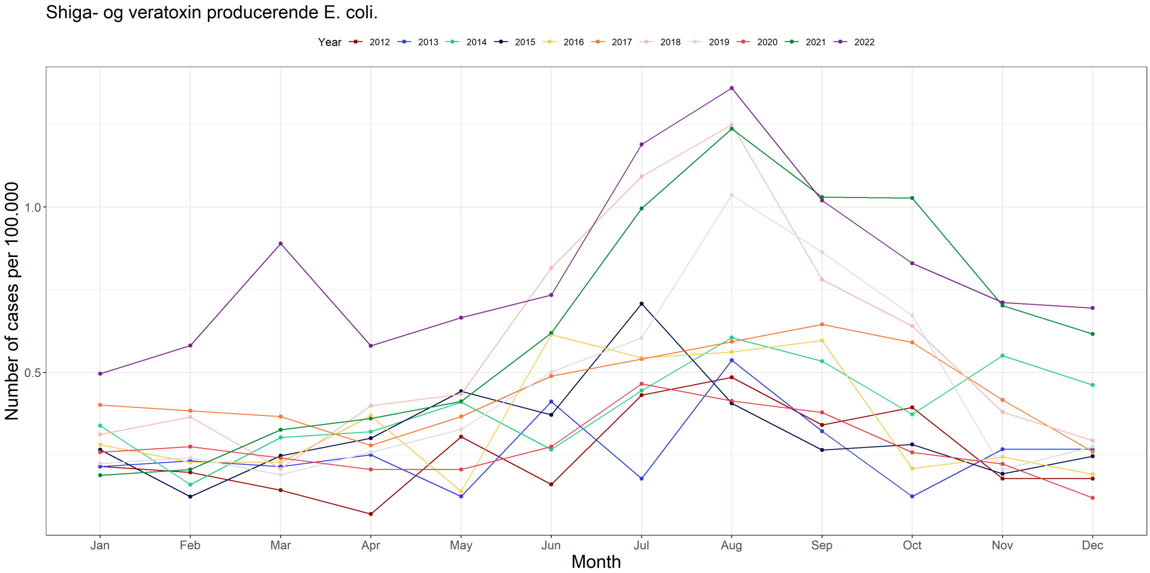
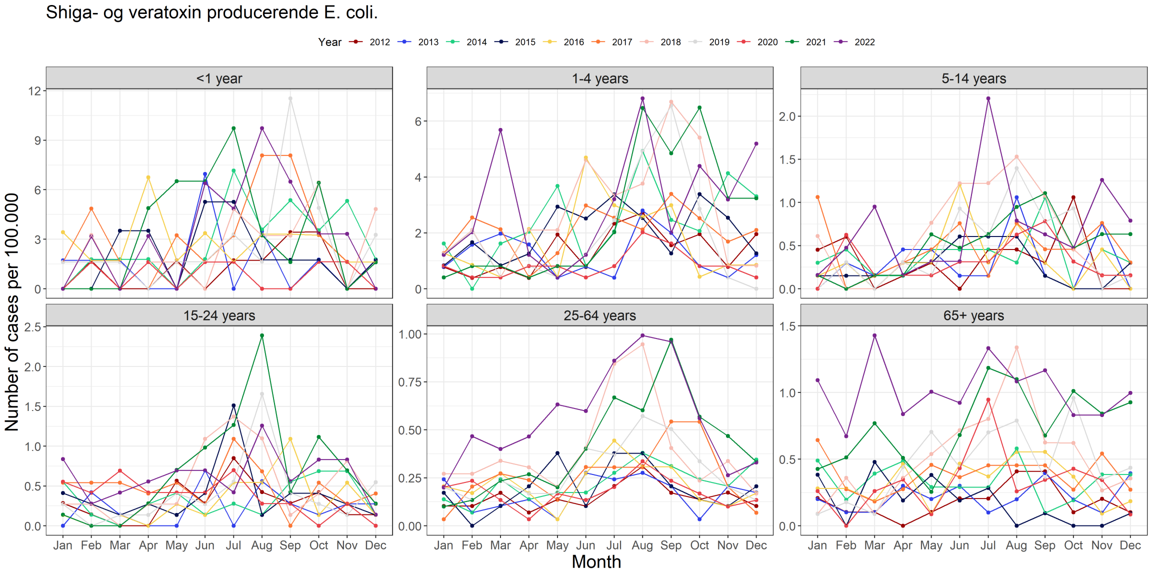
Data exploration

Date	ageGroup	y_{it}	x_{it}
2008-01-01	$<$1 year	2	64137
2008-01-01	1-4 years	2	259910
2008-01-01	5-14 years	2	680529
2008-01-01	15-24 years	1	635838
...	...	...	...
2022-12-01	5-14 years	5	634139
2022-12-01	15-24 years	1	721286
2022-12-01	25-64 years	10	3031374
2022-12-01	65$+$ years	12	1204892

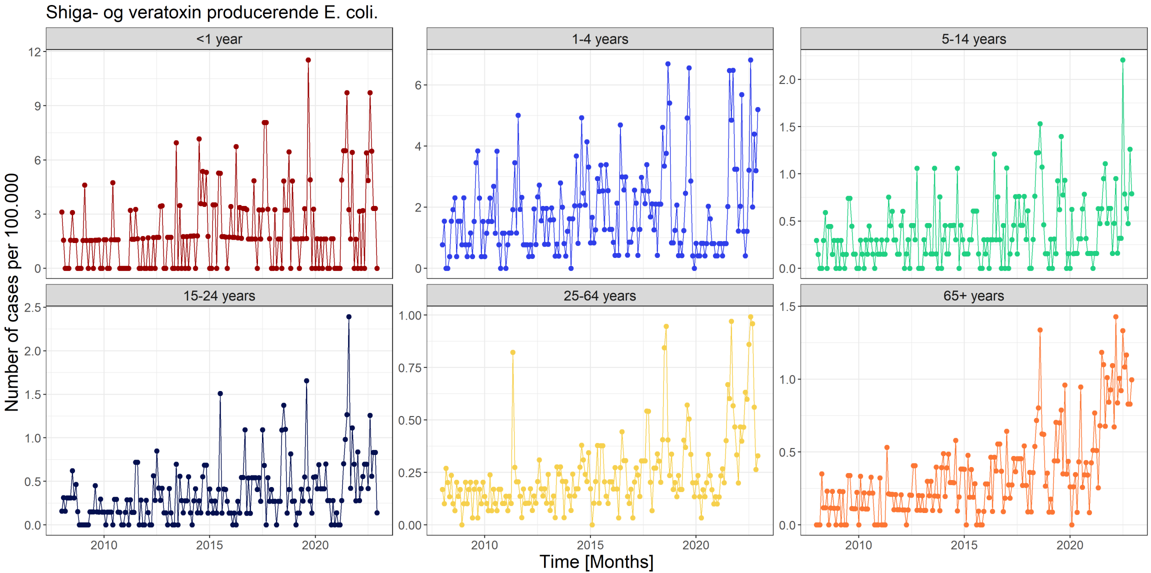
Data exploration



Data exploration



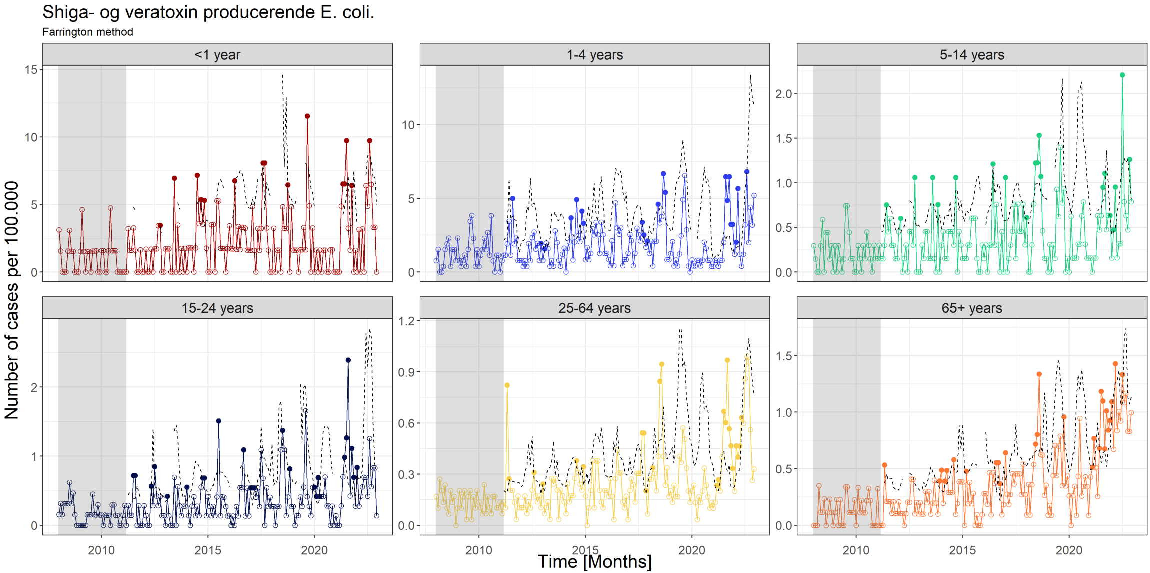
Data exploration



State-of-the-art methods

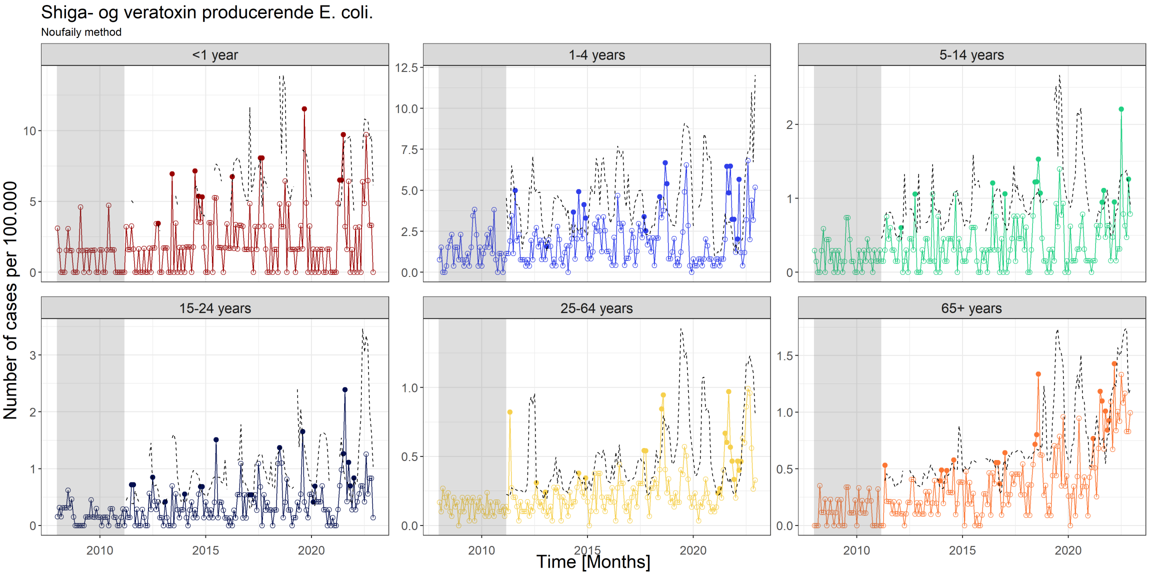
State-of-the-art methods for aberration detection is presented in Salmon, Schumacher, and Höhle 2016 and implemented in the R package **surveillance**. The R package includes methods such as the Farrington method introduced by Farrington et al. 1996 together with the improvements proposed by Noufaily et al. 2013.

Farrington



Shiga- og veratoxin producerende E. coli.
Farrington method
<1 year
1-4 years
5-14 years
15-24 years
25-64 years
65+ years
Number of cases per 100.000
Time [Months]
0
5
10
15
0.0
0.5
1.0
1.5
2.0
1
2
0.3
0.6
0.9
1.2
2010
2015
2020

Noufaily



Shiga- og veratoxin producerende E. coli.
Noufaily method
<1 year
1-4 years
5-14 years
15-24 years
25-64 years
65+ years
Number of cases per 100.000
Time [Months]
2010
2015
2020
0
5
10
0.0
2.5
5.0
7.5
10.0
12.5
1
2
3
0.5
1.0
1.5

Novel methods based on general mixed effect models

In the following two novel methods, based on theory presented in Madsen and Thyregod 2011, for aberration detection is presented. Namely, a hierachical Poisson-Normal model and a hierachical Poisson-Gamma model.

Hierachical models

It is useful to formulate the model as a hierarchical model containing a *first stage model*

$$f_{Y|u}(\boldsymbol{y}; \boldsymbol{u}, \boldsymbol{\beta}) \tag{1}$$

which is a model for the data given the random effects, and a *second stage model*

$$f_U(\boldsymbol{u}, \boldsymbol{\Psi}) \tag{2}$$

which is a model for the random effects. The total set of parameters is $\boldsymbol{\theta} = (\boldsymbol{\beta}, \boldsymbol{\Psi})$.

Objective

- The objective is to assess the unobserved random effects, $\boldsymbol{u}$, and determine the critical value, C_α, with significance level α.
- If $u_{it} > C_\alpha$, the observation is characterized as an outbreak.

NOTE: For this presentation a default of $\alpha = 0.05$ is used.

Hierachical Poisson-Normal model

The model can be formulated as a two-level hierarchical model

$$\boldsymbol{Y}|\boldsymbol{u} \sim \mathrm{Pois}(\boldsymbol{\lambda} e^{\boldsymbol{u}}) \tag{3a}$$

$$\boldsymbol{u} \sim \mathrm{N}(\boldsymbol{0}, \sigma^2) \tag{3b}$$

Hierachical Poisson-Normal model

- $\boldsymbol{Y}|\boldsymbol{u}$ are assumed to be a Poisson distribution with intensities $\boldsymbol{\lambda}$.
- An offset is included to account for the population size, x_{it}.
- Hence, the model for the fixed effect is

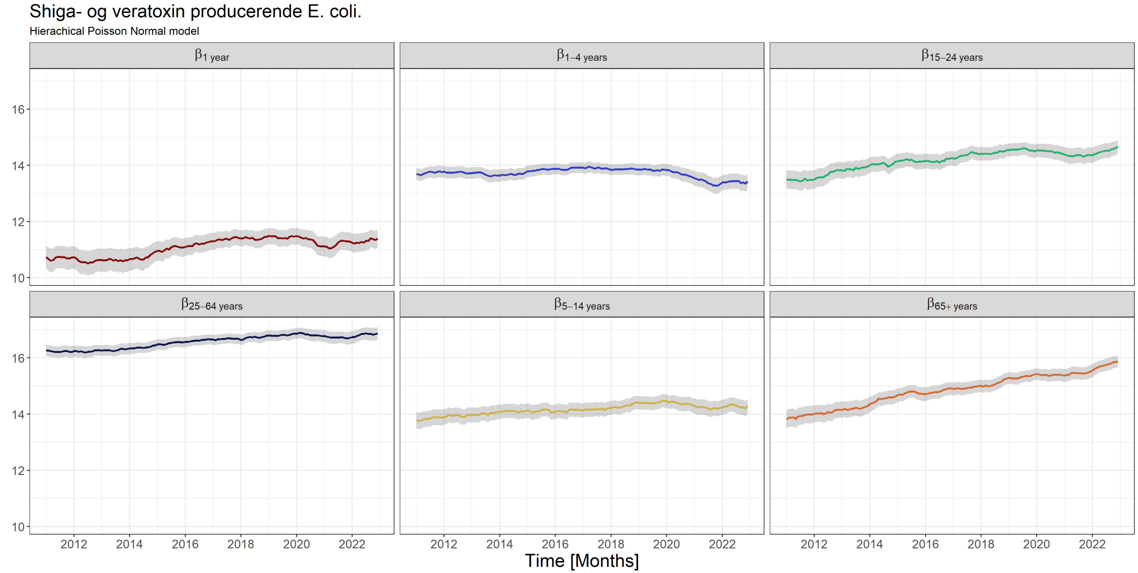
$$\log(\lambda_i) = \boldsymbol{X}_i^T \boldsymbol{\beta} + \log(x_{it}) \tag{4}$$

- Here $\boldsymbol{X}_i$ is a p-dimensional vector of covariates, and $\boldsymbol{\beta}$ contains the corresponding fixed effect parameters.
- The random effects $\boldsymbol{u}$ are assumed to be Gaussian.

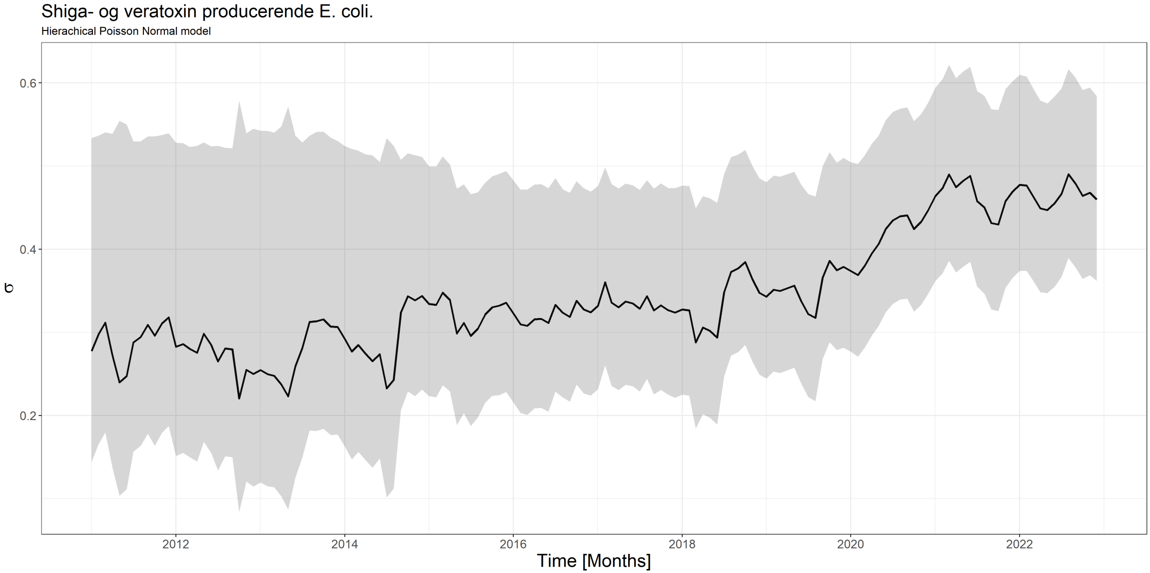
$$u_{it} = \epsilon_{it} \tag{5}$$

- Here $\epsilon_{it} \sim \mathrm{N}(\mathbf{0}, \sigma^2)$ is a white noise process, and σ is a model parameter.
- The model parameters are estimated in a rolling window of length k.

Results


Shiga- og veratoxin producerende E. coli.
Hierachical Poisson Normal model
β1 year
β1–4 years
β15–24 years
β25–64 years
β5–14 years
β65+ years
10
12
14
16
2012
2014
2016
2018
2020
2022
Time [Months]

Results

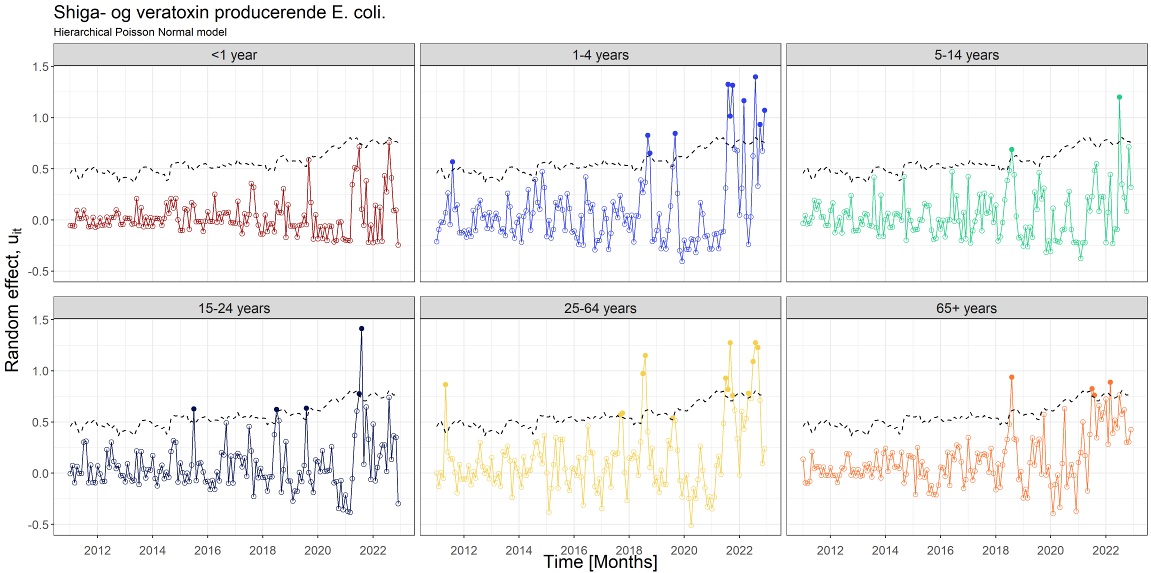

Shiga- og veratoxin producerende E. coli.
Hierachical Poisson Normal model
σ
0.6
0.4
0.2
2012
2014
2016
2018
2020
2022
Time [Months]

Threshold calculation

The critical value, C_α, is computed from the $1-\alpha$-quantile of the Normal distribution with the maximum-likelihood estimate for the variance, $\hat{\sigma}$.

$$C_\alpha = \mathrm{N}(\mathbf{0}, \hat{\sigma}^2)_{1-\alpha} \tag{6}$$

Results - Out-of-sample random effects



Hierachical Poisson-Gamma model

- $\boldsymbol{Y}|\boldsymbol{u}$ are assumed to follow a Poisson distribution.
- The intensities, λ_i, are defined as

$$\log(\lambda_i) = \boldsymbol{X}_i^T \boldsymbol{\beta} + \log(x_{it}) \tag{7}$$

- Here $\boldsymbol{X}_i$ is a p-dimensional vector of covariates, and $\boldsymbol{\beta}$ contains the corresponding fixed effect parameter.
- The random effects $\boldsymbol{u}$ are assumed to follow a reparametrized Gamma distribution with mean $\boldsymbol{1}$.
- The model parameters are estimated in a rolling window of length k.

Hierachical Poisson-Gamma model

Subsequently, the model can be formulated as a two-level hierarchical model

$$\boldsymbol{Y}|\boldsymbol{u} \sim \mathrm{Pois}(\boldsymbol{\lambda}\boldsymbol{u}) \tag{8a}$$

$$\boldsymbol{u} \sim \mathrm{G}(\mathbf{1}/\phi, \phi) \tag{8b}$$

Probability function for Y

$$
\begin{aligned}
P[Y = y_i] &= g_Y(y; \lambda, \phi) \\
&= \frac{\lambda^y}{y!\Gamma(1/\phi)\phi^{1/\phi}} \frac{\phi^{y+1/\phi}\Gamma(y+1/\phi)}{(\lambda\phi+1)^{y+1/\phi}} \\
&= \frac{\Gamma(y+1/\phi)}{\Gamma(1/\phi)y!} \frac{1}{(\lambda\phi+1)^{1/\phi}} \left(\frac{\lambda\phi}{\lambda\phi+1}\right)^y \\
&= \binom{y+1/\phi-1}{y} \frac{1}{(\lambda\phi+1)^{1/\phi}} \left(\frac{\lambda\phi}{\lambda\phi+1}\right)^y, \ for\ y = 0, 1, 2, \ldots
\end{aligned} \tag{9}
$$

where we have used the convention

$$
\binom{z}{y} = \frac{\Gamma(z+1)}{\Gamma(z+1-y)y!} \tag{10}
$$

The marginal distribution of Y is a negative binomial distribution, $Y \sim \mathrm{NB}\left(1/\phi, 1/(\lambda\phi+1)\right)$

Inference on individual group means

Consider the hierarchical Poisson-Gamma model in (8), and assume that a value $Y = y$ has been observed. Then the conditional distribution of u for given $Y = y$ is a Gamma distribution,

$$u|Y = y \sim \mathrm{G}\left(y + 1/\phi, \phi/(\lambda\phi + 1)\right) \tag{11}$$

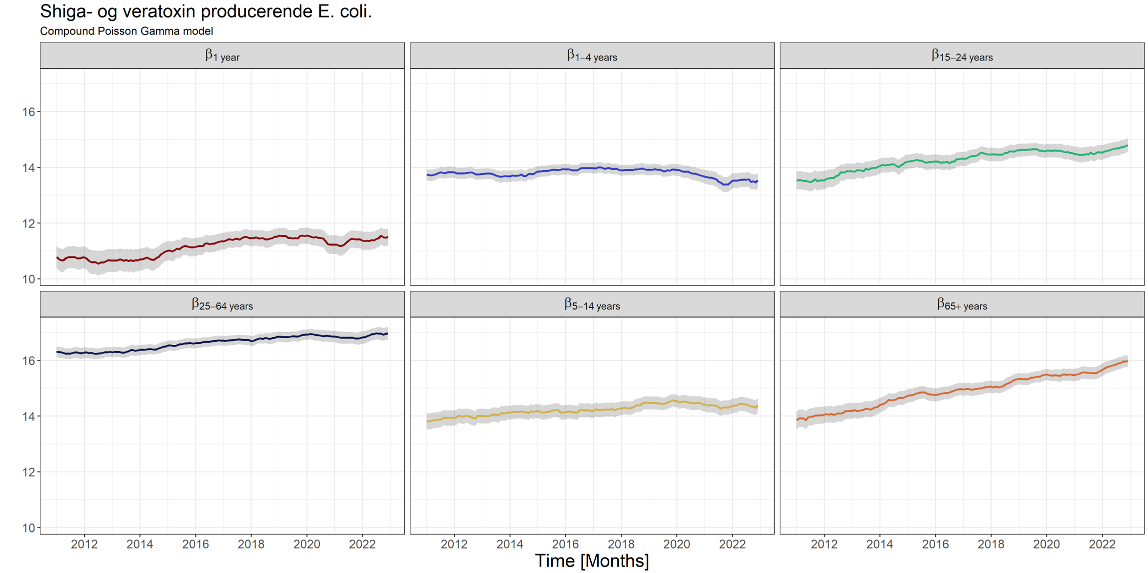
with mean

$$\mathrm{E}[u|Y = y] = \frac{y\phi + 1}{\lambda\phi + 1} \tag{12}$$

and variance

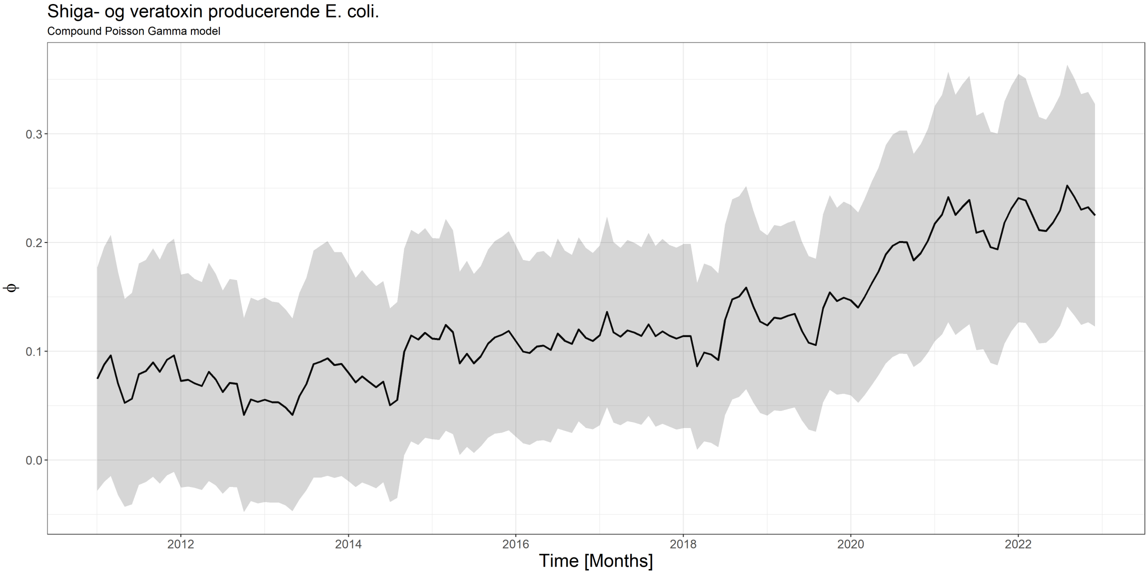
$$\mathrm{V}[u|Y = y] = \frac{(y\phi^2 + \phi)}{(\lambda\phi + 1)^2} \tag{13}$$

Results


Shiga- og veratoxin producerende E. coli.
Compound Poisson Gamma model
β1 year
β1–4 years
β15–24 years
β25–64 years
β5–14 years
β65+ years
10
12
14
16
2012
2014
2016
2018
2020
2022
Time [Months]

Novel methods based on general mixed effect models

Results

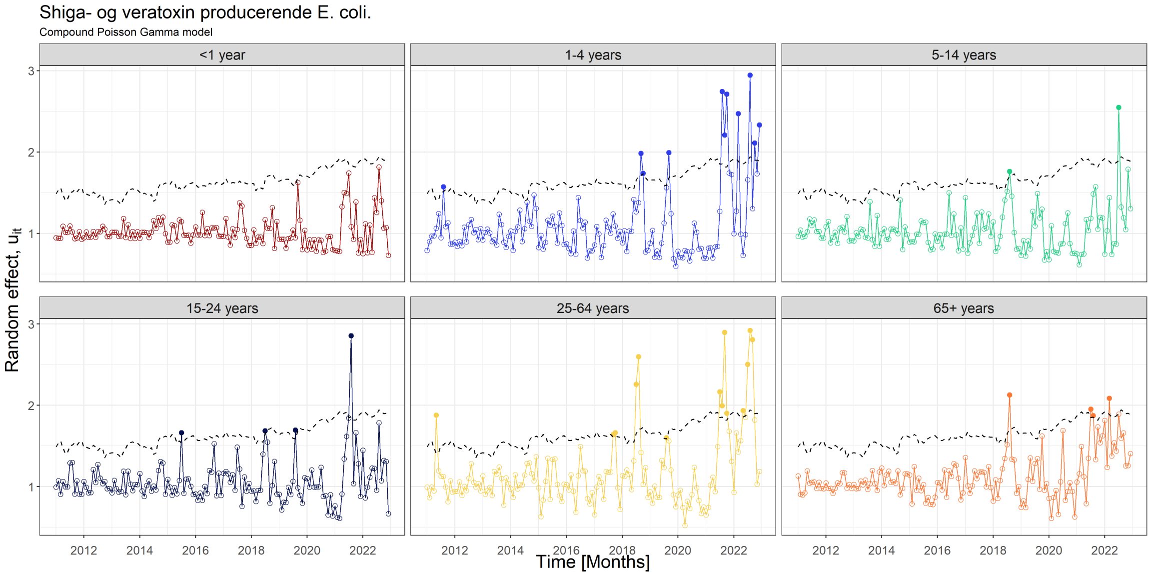


Threshold calculation

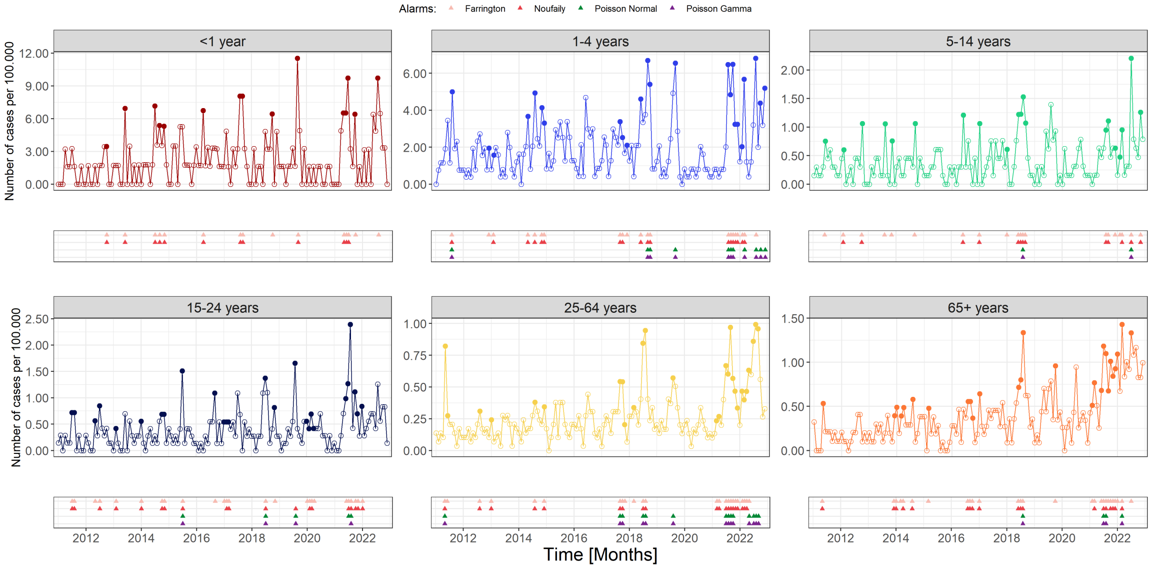
The critical value, C_α, is computed from the $1-\alpha$-quantile of the reparametrized Gamma distribution with the maximum-likelihood estimate for the variance, $\hat{\phi}$.

$$C_\alpha = \mathrm{G}(\mathbf{1}/\hat{\phi}, \hat{\phi})_{1-\alpha} \tag{14}$$

Results - Out-of-sample random effects



Comparison of methods



References

Farrington, C. P. et al. (1996). "A Statistical Algorithm for the Early Detection of Outbreaks of Infectious Disease". In: *Journal of the Royal Statistical Society. Series A (Statistics in Society)* 159.3, pp. 547–563. ISSN: 09641998, 1467985X. URL: http://www.jstor.org/stable/2983331 (visited on 01/27/2023).

Madsen, Henrik and Poul Thyregod (2011). *Introduction to general and generalized linear models*. English. Texts in statistical science. CRC Press. ISBN: 9781420091557.

Noufaily, Angela et al. (2013). "An Improved Algorithm for Outbreak Detection in Multiple Surveillance Systems". en. In: *Online Journal of Public Health Informatics* 32.7, pp. 1206–1222.

Salmon, Maëlle, Dirk Schumacher, and Michael Höhle (2016). "Monitoring Count Time Series in R: Aberration Detection in Public Health Surveillance". In: *Journal of Statistical Software* 70.10, pp. 1–35. DOI: 10.18637/jss.v070.i10. URL: https://www.jstatsoft.org/index.php/jss/article/view/v070i10.

Proof - Probability function for Y

The probability function for the conditional distribution of Y for given u

$$f_{Y|u}(y;\lambda,u) = \frac{(\lambda u)^y}{y!}\exp(-\lambda u) \tag{15}$$

and the probability density function for the distribution of u is

$$f_u(u;\phi) = \frac{1}{\phi\Gamma(1/\phi)}\left(\frac{u}{\phi}\right)^{1/\phi-1}\exp(-u/\phi) \tag{16}$$

Proof - Probability function for Y

Given (15) and (16), the probability function for the marginal distribution of Y is determined from

$$\begin{aligned} g_Y(y;\lambda,\phi) &= \int_{u=0}^{\infty} f_{Y|u}(y;\lambda,u) f_u(u;\phi)\,du \\ &= \int_{u=0}^{\infty} \frac{(\lambda u)^y}{y!} \exp(-\lambda u) \frac{1}{\phi \Gamma(1/\phi)} \left(\frac{u}{\phi}\right)^{1/\phi - 1} \exp(-u/\phi)\,du \\ &= \frac{\lambda^y}{y!\Gamma(1/\phi)\phi^{1/\phi}} \int_{u=0}^{\infty} u^{y+1/\phi-1} \exp\big(-u(\lambda\phi+1)/\phi\big)\,du \end{aligned} \tag{17}$$

Proof - Probability function for Y

In (17) it is noted that the integrand is the *kernel* in the probability density function for a Gamma distribution, $\mathrm{G}\left(y + 1/\phi, \phi/(\lambda\phi + 1)\right)$. As the integral of the density shall equal one, we find by adjusting the norming constant that

$$\int_{u=0}^{\infty} u^{y+1/\phi-1} \exp\left(-u/\Big(\phi/(\lambda\phi+1)\Big)\right) du = \frac{\phi^{y+1/\phi}\Gamma(y+1/\phi)}{(\lambda\phi+1)^{y+1/\phi}} \tag{18}$$

and then (9) follows

Proof - Conditional distribution of Y

The conditional distribution is found using Bayes Theorem

$$\begin{aligned} g_u(u|Y=y) &= \frac{f_{y,u}(y,u)}{g_Y(y;\lambda,\phi)} \\ &= \frac{f_{y|u}(y;u)g_u(u)}{g_Y(y;\lambda,\phi)} \\ &= \frac{1}{g_Y(y;\lambda,\phi)}\left(\frac{(\lambda u)^y}{y!}\exp(-\lambda u)\frac{1}{\phi\Gamma(1/\phi)}\left(\frac{u}{\phi}\right)^{1/\phi-1}\exp(-u/\phi)\right) \\ &\propto u^{y+1/\phi-1}\exp\big(-u(\lambda\phi+1)/\phi\big) \end{aligned} \tag{19}$$

We identify the *kernel* of the probability density function

$$u^{y+1/\phi-1}\exp(-u(\lambda\phi+1)/\phi) \tag{20}$$

as the kernel of a Gamma distribution, $\mathrm{G}(y+1/\phi,\phi/(\lambda\phi+1))$