Automated and Early Detection of Disease Outbreaks

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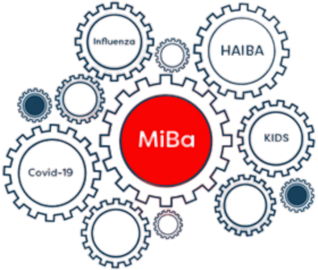
Motivation

- Establishment of the Danish Microbiology Database (MiBa) by Statens Serum Institut (SSI) in 2010
- Great opportunity for data analysis
- No fully automated procedures in place at SSI



Research goals

- Review of existing literature on statistical methods for detecting disease outbreaks
- Identification and implementation of state-of-the-art methods for detection of disease outbreaks
- Formulation of hierarchical models for the individually notifiable diseases
- Development of an automated method, based on the hierarchical models, for automated and early detection of disease outbreaks
- Comparison of the developed method and state-of-the-art methods in one or more case study
- Comparison of the developed method and state-of-the-art methods in a simulation study

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State-of-the-art algorithms

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

Novel algorithm

The novel algorithm utilizes a generalized mixed effects model or a hierarchical mixed effects model as a modeling framework to model the count case observations $\boldsymbol{y}$ and assess the unobserved random effects $\boldsymbol{u}$. These random effects are used directly to characterize an outbreak.

Step 1: Modeling framework

- Assume a hierarchical Poisson Normal or Poisson Gamma model to reference data using a log link
- Incorporate covariates by supplying a model formula on the form

$$\log(\lambda_{it}) = \boldsymbol{x}_{it}\boldsymbol{\beta} + \log(n_{it}), \quad i = 1, \ldots, m, \quad t = 1, \ldots, T \tag{1}$$

- Account for structural changes in the time series using a rolling window of width k

Step 2: Inference of random effects

- Infer one-step ahead random effects u_{it_0} for each group using the fitted model
- Define outbreak detection threshold U_{t_0} as a quantile of the second stage model's random effects distribution
- Use either a Gaussian or Gamma distribution with respective plug-in estimates

Step 3: Parameter estimations and outbreak detection

- Compare inferred random effects u_{it_0} to an threshold U_{t_0}
- Raise and alarm if the inferred random effect exceeds the threshold, i.e. $u_{it_0} > U_{t_0}$
- Omit outbreak related observations from future parameter estimation

Formulation of hierarchical models

Poisson Normal

$$\boldsymbol{Y}|\boldsymbol{u} \sim \mathrm{Pois}\left(\boldsymbol{\lambda}\exp(\boldsymbol{u})\right)$$
$$\boldsymbol{u} \sim \mathrm{N}(\boldsymbol{0}, I\sigma^2)$$

Poisson Gamma

$$\boldsymbol{Y}|\boldsymbol{u} \sim \mathrm{Pois}(\boldsymbol{\lambda}\boldsymbol{u})$$
$$\boldsymbol{u} \sim \mathrm{G}(\boldsymbol{1}/\phi, \phi)$$

Case study

Shiga toxin (verotoxin)-producing *Escherichia coli* (STEC)

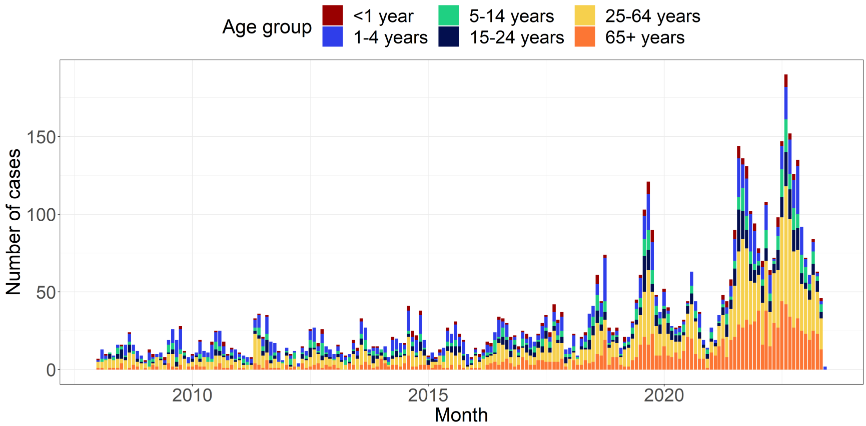

Figure: A stacked bar graph illustrating the number of monthly STEC cases observed in the period from 2008 to 2022 for the six age groups.

Constant model

$$\log(\lambda_{it}) = \beta(ageGroup_i) + \log(n_{it}) \tag{2}$$

- λ_{it} is the outbreak intensity at time t for age group i.
- $\beta(ageGroup_i)$ is the fixed effect specific to age group i.
- $\log(n_{it})$ acts as an offset, accounting for the population size at time t for age group i.

Trend model

$$\log(\lambda_{it}) = \beta(ageGroup_i) + \beta_{trend}t + \log(n_{it}) \quad (3)$$

- In addition to Model 1, includes a trend component.
- β_{trend} quantifies the rate of change in the outbreak intensity over time.

Seasonality model

$$\log(\lambda_{it}) = \beta(ageGroup_i) + \sin\left(\frac{2\pi \cdot \tau_t}{12}\right)\beta_{\sin} + \cos\left(2\frac{\pi \cdot \tau_t}{12}\right)\beta_{\cos} + \log(n_{it}) \tag{4}$$

- In addition to Model 1, incorporates an annual seasonality pattern.
- τ_t represents the time period t within a year (1-12).
- $\beta_{\sin}$ and $\beta_{\cos}$ capture the effect of the seasonal pattern.

Combined trend and seasonality model

$$\log(\lambda_{it}) = \beta(ageGroup_i) + \beta_{trend}t + \sin\left(\frac{2\pi \cdot \tau_t}{12}\right)\beta_{\sin} + \cos\left(\frac{2\pi \cdot \tau_t}{12}\right)\beta_{\cos} + \log(n_{it}) \quad (5)$$

- Builds upon previous models, combining trend and seasonality components.
- Includes both β_{trend}, $\beta_{\sin}$, and $\beta_{\cos}$ parameters.

Estimated one-step ahead random effects

- The upper bound U_{t_0} is calculated based on the 90% quantile of the distribution of the random effects
- If the one-step ahead random effects u_{it_1} exceeds the upper bound U_{t_0} an alarm is raised
- In the hierarchical Poisson Normal model (left), the random effects are exponentiated to transform them into the same domain as the hierarchical Poisson Gamma model (right)

- 30 alarms are generated using the hierarchical Poisson Normal framework, while 31 alarms are generated using the hierarchical Poisson Gamma framework.
- A great number of alarms are generated in the period from March 2021 to March 2022

Case study

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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).

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.