

Bayesian Hierarchical Model Algorithm for Automated Detection of Infectious Disease Outbreaks

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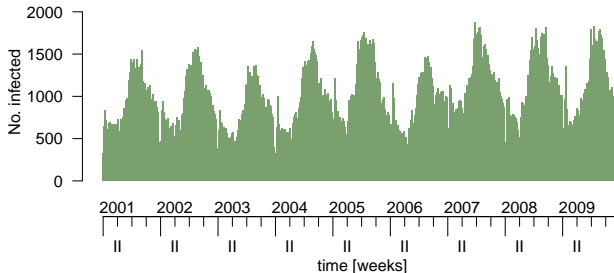
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Motivation: German routine surveillance of Campylobacter

- ▶ Leading cause of enteritis illnesses in industrial countries (Robert Koch-Institut, 2005)
- ▶ Absolute humidity has been proven to influence the incidence
- ▶ Typical characteristics of surveillance time series

Process of Campylobacter infections in Germany

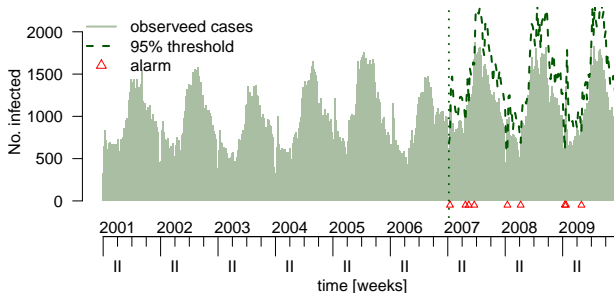


Aim of Surveillance

Public health view: Early-warning system to detect health risks, such as outbreaks of infectious diseases

Statistical view: Real-time online monitoring in routine surveillance data to detect aberrations for public health events

Process of Campylobacter infections in Germany



Outline

Theoretical Framework

Statistical Foundation: Heisterkamp et al. (2006)

Bayesian Version: Definition of Prior

Threshold Calculation: Predictive Posterior

Implementation

Simulation & Application

Simulation Studies

Campylobacter data

Conclusion

Statistical Foundation: Heisterkamp et al. (2006)

- Generalised additive quasi-Poisson model (GAM) of the number of cases

$$y_t | \mu_t \stackrel{\text{iid}}{\sim} \text{Po}(\mu_t), \quad t = 1, \dots, T$$

$$\log(\mu_t) = \eta_t = \beta_{0t} + \mathbf{x}'_t \boldsymbol{\beta}_x, \quad t = 1, \dots, T$$

with overdispersion $\text{Var}(y_t | \mu_t) = \phi \cdot \text{E}(y_t | \mu_t) = \phi \cdot \mu_t$

- Time varying intercept as smoothed time effect

$$\beta_{0t} = \beta_0(t) = g_m(t) + u_t, \quad u_t \stackrel{\text{iid}}{\sim} \text{N}(0, \lambda^{-1})$$

stationary model (IID): $g_{iid}(t) = \beta_0$

neighbour model (RW1): $g_{rw1}(t) = \beta_{0,t-1}$

linear model (RW2): $g_{rw2}(t) = 2\beta_{0,t-1} - \beta_{0,t-2}$

Heisterkamp et al. (2006): Advantages & Disadvantages

- ▶ Opposite to Farrington et al. (1996) all available data is used for modelling
- ▶ Likelihood inference for the GAM
- ▶ Threshold calculation using a plug-in prediction interval
 - ⇒ Uncertainty by parameter estimation is ignored
 - ⇒ Normal distribution assumption for MLE is questionable
- ▶ Alarm is triggered if observed y_t is exceeding treshold
- ▶ Enhanced computational efficiency by sequential model update procedure

Our Work: Bayesian Hierarchical Model Algorithm

- ▶ Improvement of Heisterkamp et al. (2006) approach by using Bayesian inference for GAM: Deduce results only from posterior distribution

$$p(\beta|\mathbf{y}_t) \propto p(\mathbf{y}_t|\beta)p(\beta).$$

- ▶ Time varying intercept as random walk prior $p(\beta)$
- ▶ Regression modelling, i.e. covariates such as absolute humidity can be taken into account
- ▶ Threshold calculation using predictive posterior $p(y_T|y_1, \dots, y_{T-1})$ as in Höhle (2007) which
 - ▶ includes directly uncertainty due to prediction and estimation
 - ▶ does not assume any further distribution properties

Definition of Prior

Time varying intercept: $\beta_{0t} \propto N(g_m(t), \lambda^{-1})$ random walk
 Covariate paramters: $\beta'_x \propto N(0, \mathbf{B}^{-1})$ non-informative

I.e. the prior for $\beta = (\beta_{01}, \dots, \beta_{0T}, \beta'_x)'$ given λ is

$$p(\beta) \propto \lambda^{\frac{\text{rk}(\mathbf{A}_m)}{2}} \exp\left(-\frac{\lambda}{2} \beta' \mathbf{A}_m \beta\right),$$

where $\mathbf{A}_m = \begin{pmatrix} \boxed{\mathbf{D}'_m \mathbf{D}_m} & 0 \\ 0 & \mathbf{B} \end{pmatrix}$, with difference matrix \mathbf{D}_m .

E.g. for 2nd order random walk is $\mathbf{D}_{rw2} = \begin{pmatrix} 1 & -2 & 1 & & \\ & 1 & -2 & 1 & \\ & & \ddots & \ddots & \\ & & & & \ddots \end{pmatrix}$.

Predictive Posterior

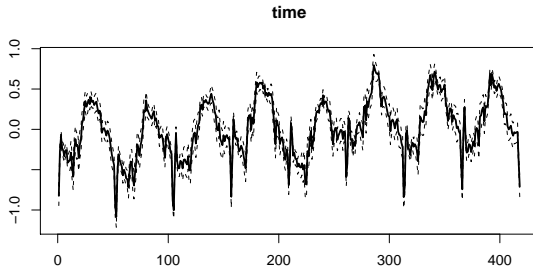
The predictive posterior is the pdf for a new observation y_T at current time point T given the past

$$\begin{aligned} f(y_T | y_1, \dots, y_{T-1}) &= \int f(y_T, \beta_{0T} | y_1, \dots, y_{T-1}) d\beta_{0T} \\ &= \int f(y_T | \beta_{0T}) p(\beta_{0T} | y_1, \dots, y_{T-1}) d\beta_{0T}. \end{aligned}$$

Alarm threshold $\xi_{1-\alpha}$ is defined as 100% $\cdot (1 - \alpha)$ -quantile of the predictive posterior.

Implementation using INLA

- ▶ Bayesian inference is usually very computer-intensive using MCMC methods
- ▶ Modern, efficient, and accurate GAM fitting by using Integrated Nested Laplace Approximation (INLA, Rue et al., 2009)



PostMean 0.025% 0.5% 0.975%

Implementation in R

- ▶ The realization with R `inla` is simple, but partially unstable
- ▶ Calculation of predictive posterior is done by Monte Carlo integration
- ▶ Implementation available as `algo.hts()` into R package `surveillance` (Höhle, 2007)

```
> algo.hts(disProgObj,  
+          control=list(range=NULL, co.arg=NULL,  
+                        prior='iid', family='poisson',  
+                        alpha=0.05, mc.betaT1=100, mc.yT1=10))
```

Simulation Studies

Bayesian hierarchical model algorithm was compared with RKI method (inspired by Stroup et al., 1993), simple Bayes algorithm (Höhle, 2007), Farrington algorithm (Farrington et al., 1996) regarding

- ▶ Percentage of false alarm
- ▶ Realistic simulation data of different scenarios regarding trend, seasonality and distribution parameters for outbreak (Hutwagner et al., 2005)
- ▶ Computing time

Results for Bayesian hierarchical model algorithm

- ▶ 3.5-3.9% false alarms \Rightarrow not overly conservative
- ▶ 1-2 sec. per time point \Rightarrow slow, but still reasonable computing time
- ▶ approach is stable and well working in all scenarios, e.g. overall outbreak detection rates with trend and medium seasonality

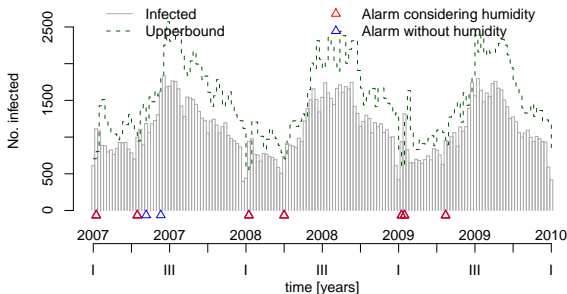
	Bayesian Hierarchical Model						Farrington		Bayes	RKI
	Poisson			neg. Binomial			(4,0,2)		(4,0,2)	(4,0,2)
	iid	rw1	rw2	iid	rw1	rw2	rew			
spec	0.27	0.12	0.02	0.60	0.10	0.10	0.64	0.89	1.00	0.71
sens	0.76	0.94	0.99	0.49	0.95	0.95	0.83	0.56	0.01	0.75
mlag	5.86	12.26	18.46	2.80	12.50	12.50	4.14	0.88	0.00	2.80

\Rightarrow our method could not be shown to be superior

Application to Campylobacter data including covariates

```
> control <- list(range=which(date>=as.Date('2007-01-01')),
+               co.arg=cbind(11.hum,12.hum,13.hum,14.hum,15.hum),
+               prior='rw1', family='poisson')
> hts.hum <- algo.hts(cam.disProg, control=control))
```

Analysis of Campylobacter using hts(prior=rw1)



Conclusion and Discussion

- ▶ Consideration of all available knowledge
 - ▶ All past observations
 - ▶ Model includes covariates
 - ▶ Time series structure as prior knowledge
- ▶ Seamless inference
 - ▶ Simultaneous inclusion of estimate and prediction uncertainty
 - ▶ No further assumptions for calculation of threshold needed
 - ▶ Probabilistic decision making possible
- ▶ Stage of development
 - ▶ Instabilities in numerical execution by R `inla`
 - ▶ Efficient update procedure needed
 - ▶ Superior performance compared to established methods could not be shown
- ▶ Potential for improvements and further developments

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