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FACULTY OF MEDICINE

Spatio-temporal modelling and probabilistic forecasting of infectious disease counts

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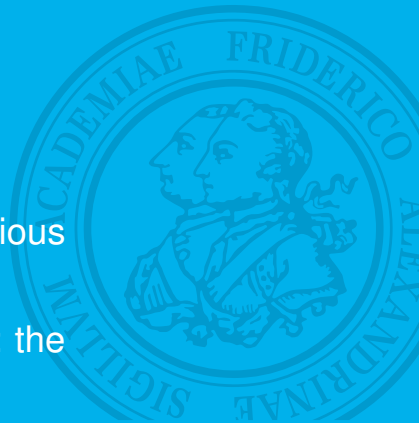
Joint work with Johannes Bracher and Leonhard Held (University of Zurich):

Meyer and Held (2017): Incorporating social contact data in spatio-temporal models for infectious disease spread. *Biostatistics* 18:338–351. DOI:10.1093/biostatistics/kxw051

Held, Meyer and Bracher (2017): Probabilistic forecasting in infectious disease epidemiology: the 13th Armitage lecture. *Statistics in Medicine* 36:3443–3460. DOI:10.1002/sim.7363



World Health Organization 2014

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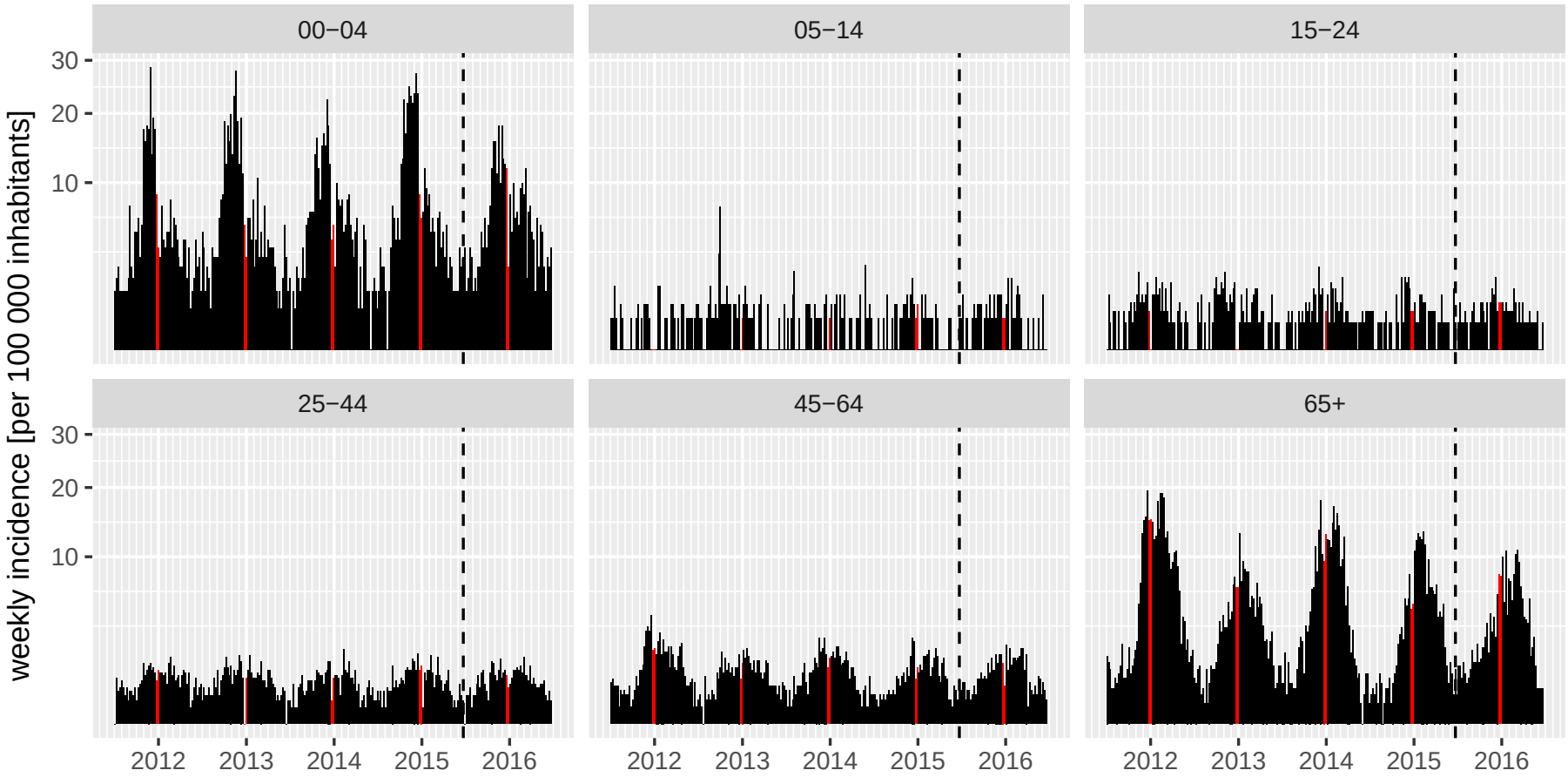
2. Stratified count time series from routine public health surveillance
3. Useful statistical models for such dependent data
4. Suitable measures for the evaluation of probabilistic forecasts

Case study: norovirus gastroenteritis in Berlin, 2011–2016

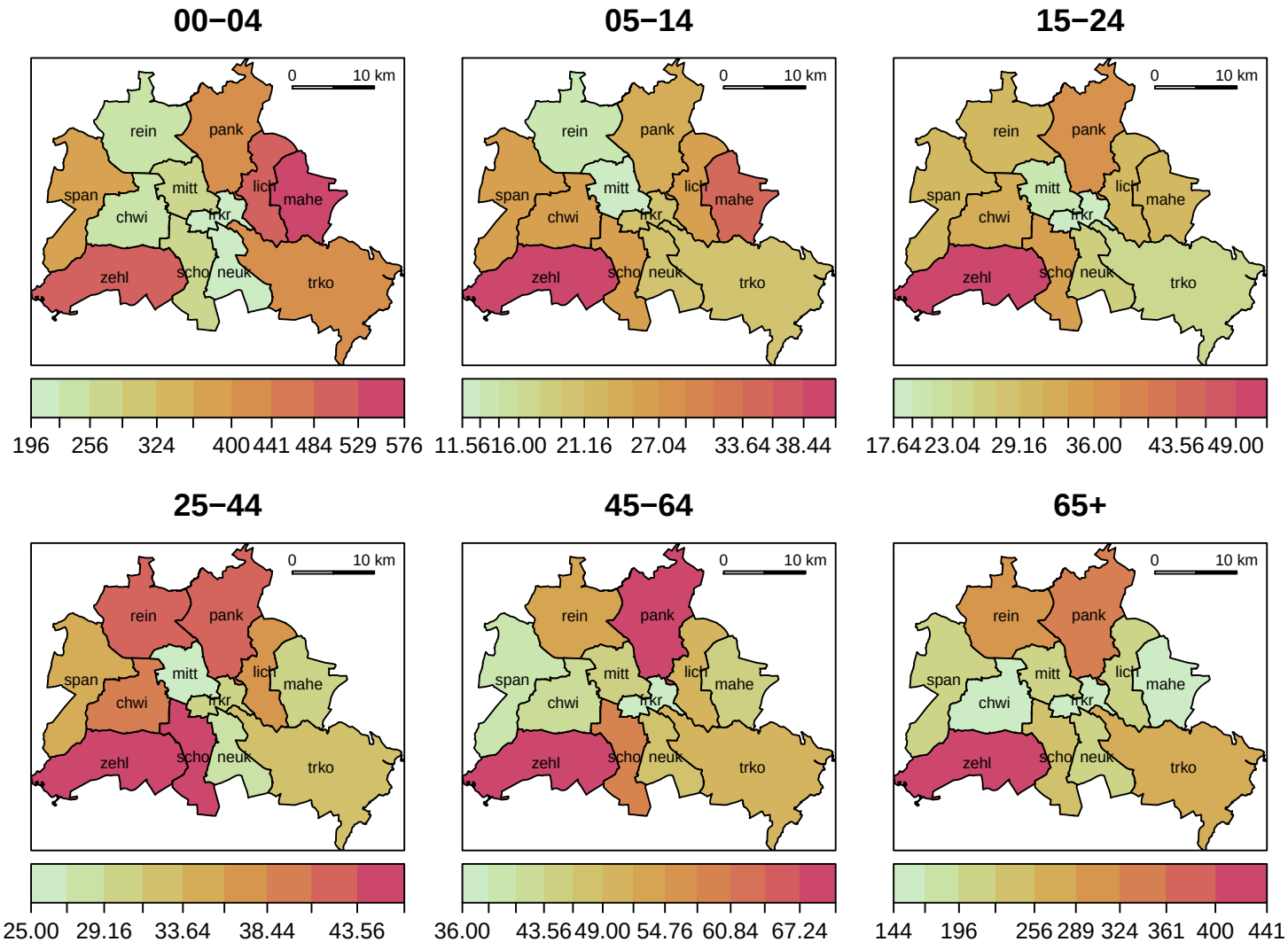
— Weekly time series by age group, aggregated over all 12 city districts



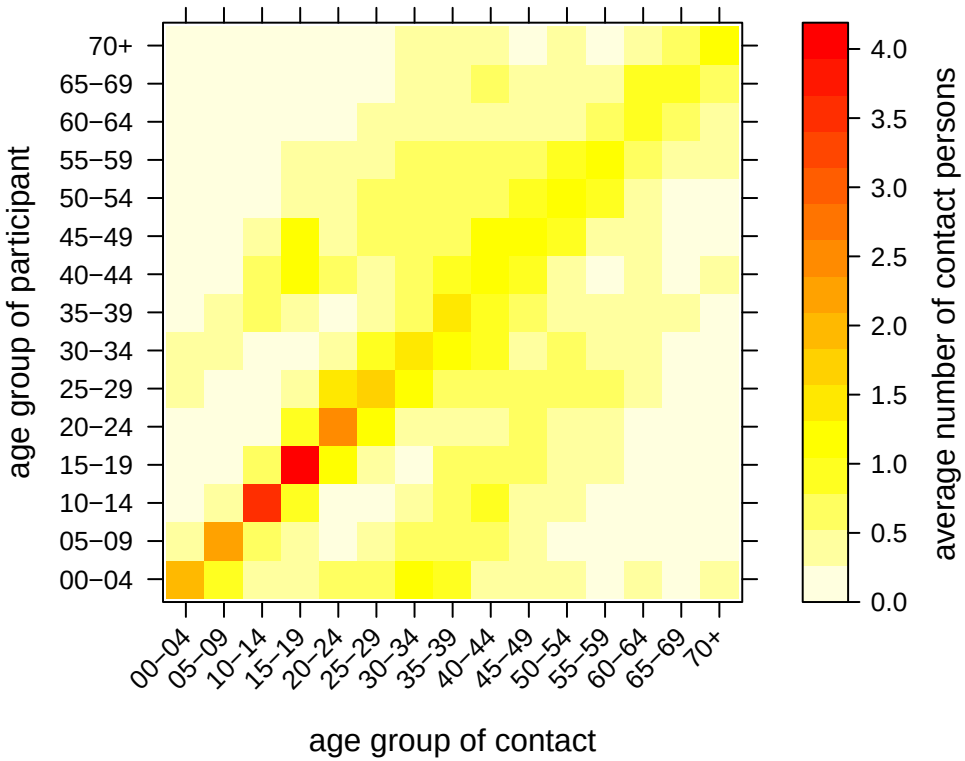
[Stratified lab-confirmed counts obtained from `survstat.rki.de`]

Case study: norovirus gastroenteritis in Berlin, 2011–2016

— Disease incidence maps by age group, aggregated over time



Infectious disease spread ~ social contacts



EU-funded POLYMOD study [Mossong et al. 2008]:

- 7 290 participants from eight European countries recorded contacts during one day
- Contact characteristics were similar across countries
- Remarkable mixing patterns with respect to age

Starting point for our statistical modelling framework

We have:

- Public health surveillance counts Y_{grt} indexed by *g*roup, *r*egion, *t*ime period
- Social contact matrix $C = (c_{g'g})$
- Maybe additional covariates (climate, socio-demographics, ...)

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We would like to model all three data dimensions (g, r, t) and account for their dependent nature:

g: social mixing patterns between age groups

r: spatial dynamics through human travel

t: temporal dependencies inherent to communicable diseases

An age-stratified, spatio-temporal, endemic-epidemic model

$$Y_{grt} = \text{NegBin}(\mu_{grt}, \psi_{gr})$$

$$\mu_{grt} = \nu_{grt} + \phi_{grt} \sum_{g',r'} c_{g'g} \, w_{r'r} \, Y_{g',r',t-1}$$

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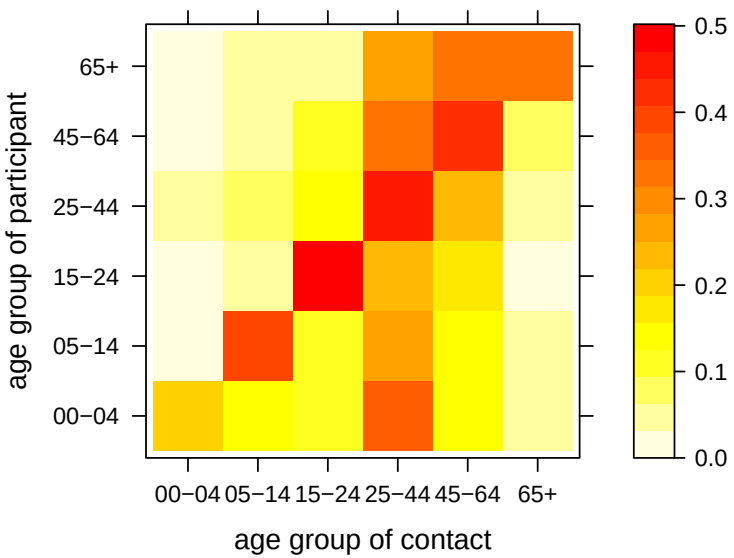
Contact matrix $(c_{g'g})$ for $g' \to g$, aggregated from POLYMOD



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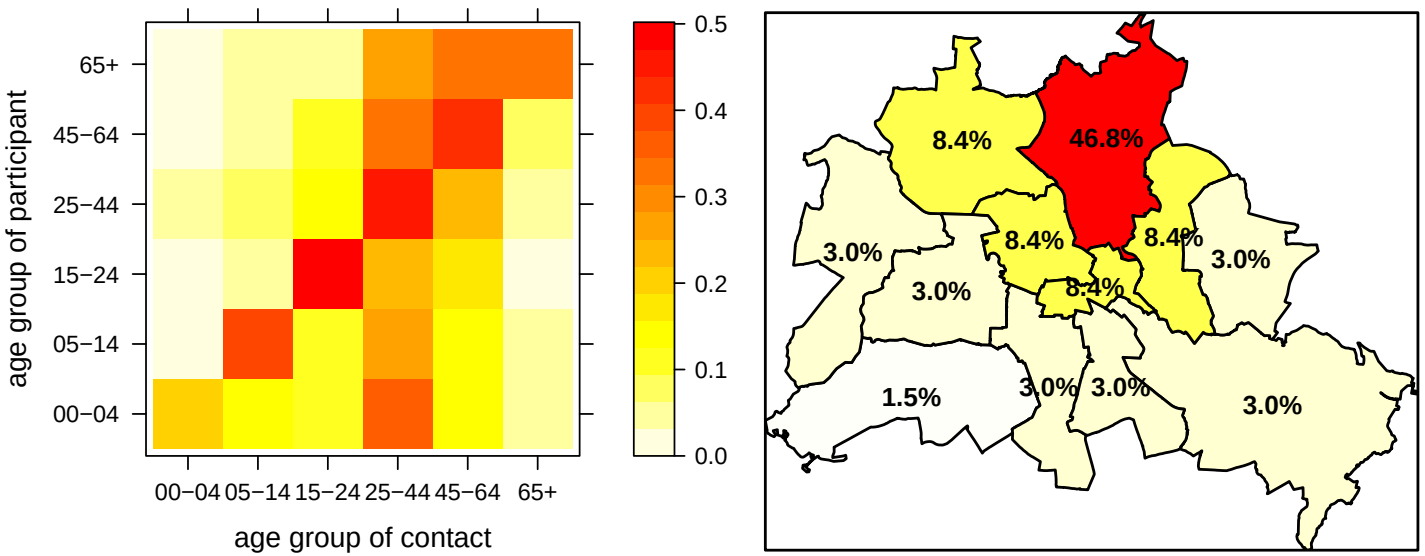
Spatial weights for $r' \to r$, power-law decay $w_{r'r} = (o_{r'r} + 1)^{-\rho}$



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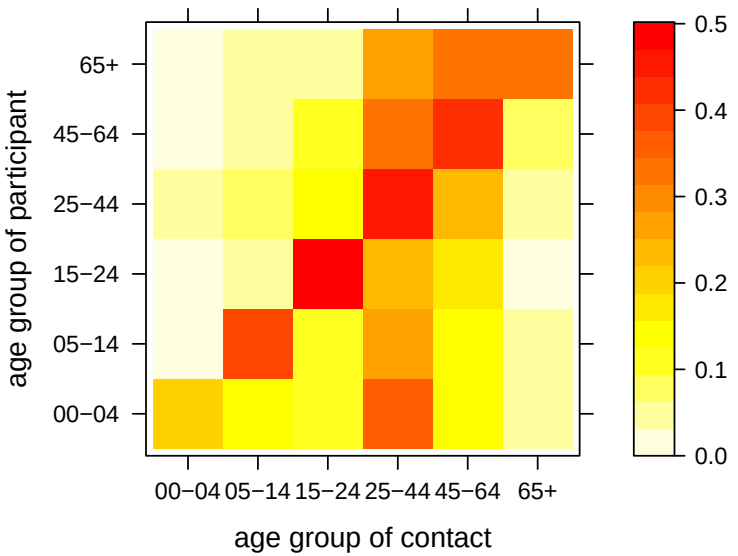
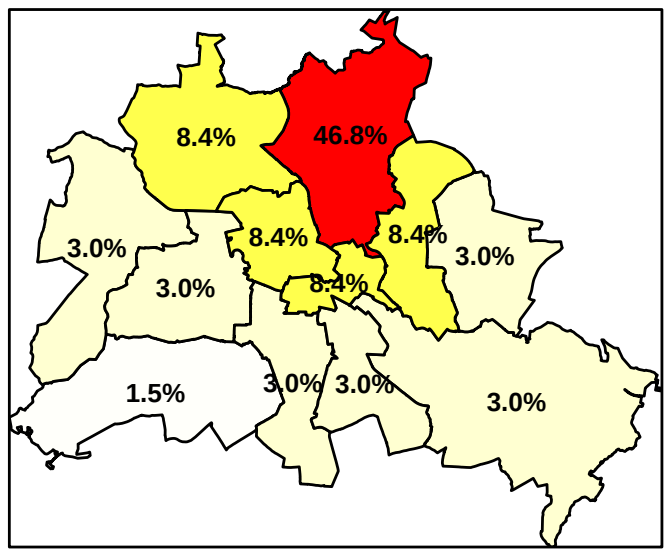
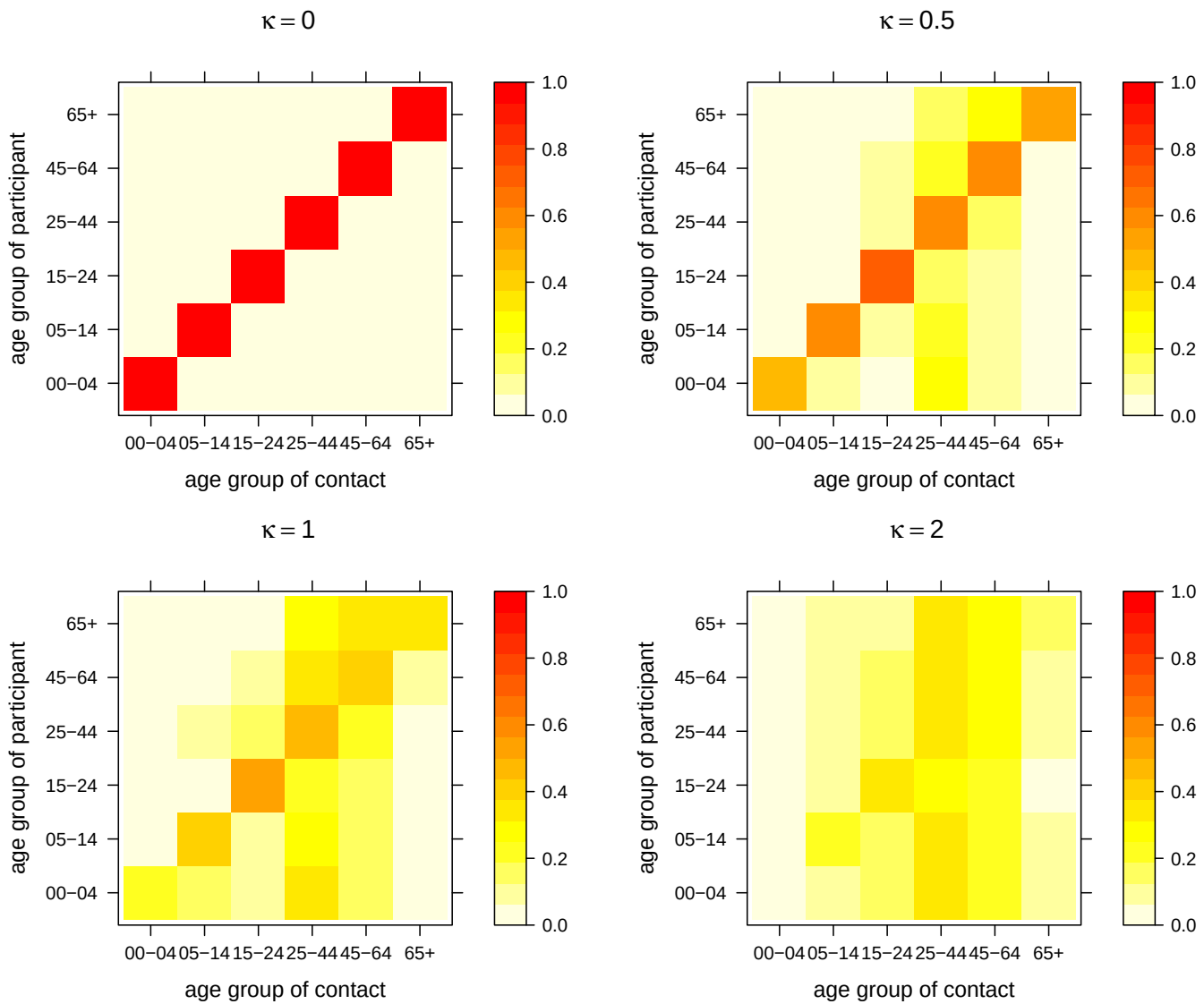
Log-linear predictors ν_{grt} and ϕ_{grt}



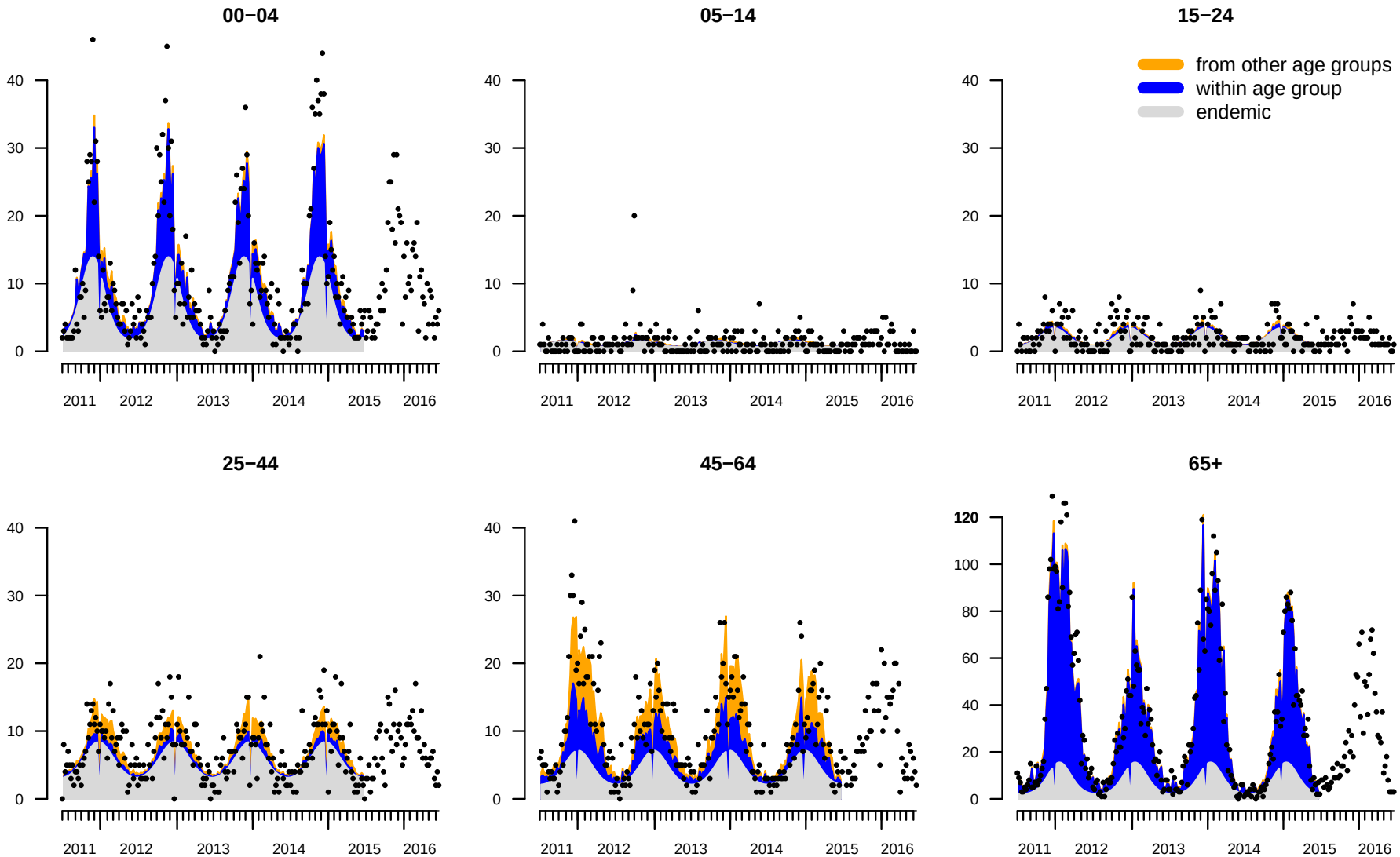


- Population
- Seasonality
- Group-specific susceptibility
- (Covariates)

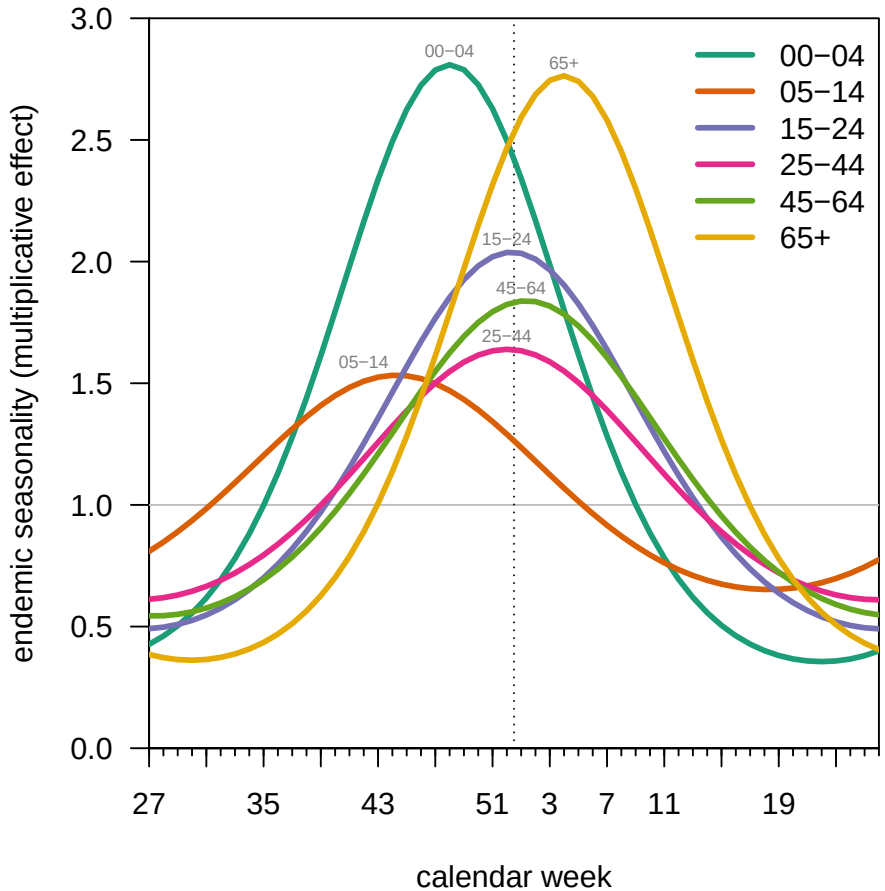
Power-adjustment of the contact matrix: $C^\kappa := E\Lambda^\kappa E^{-1}$

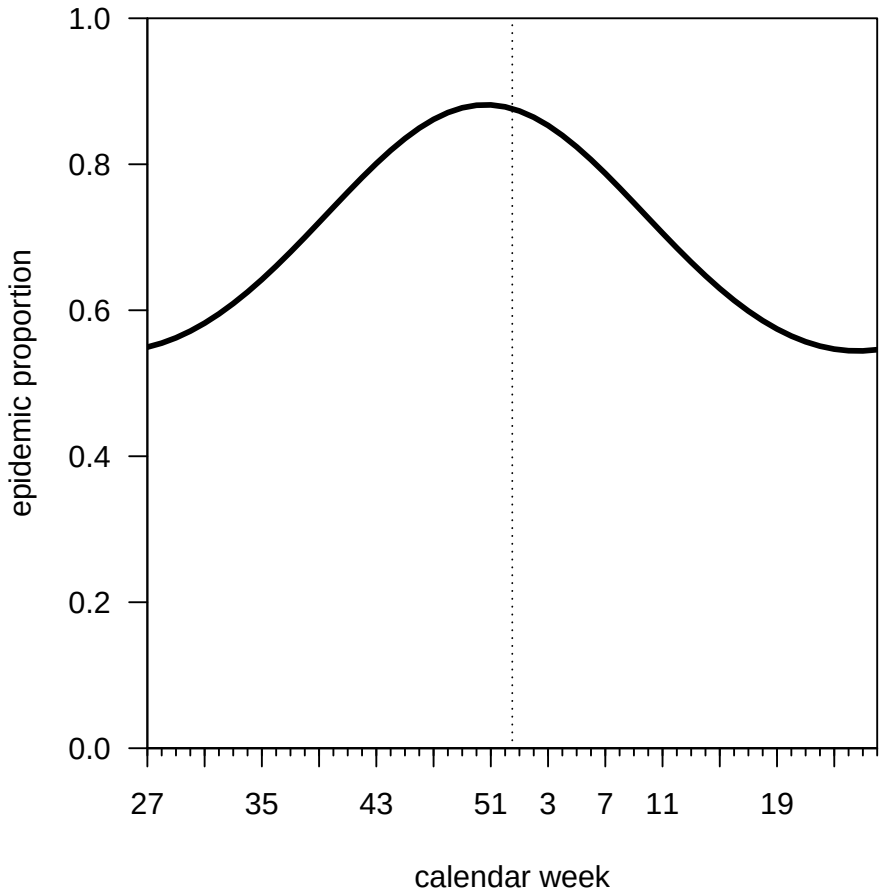


Fitted mean by age group aggregated over districts

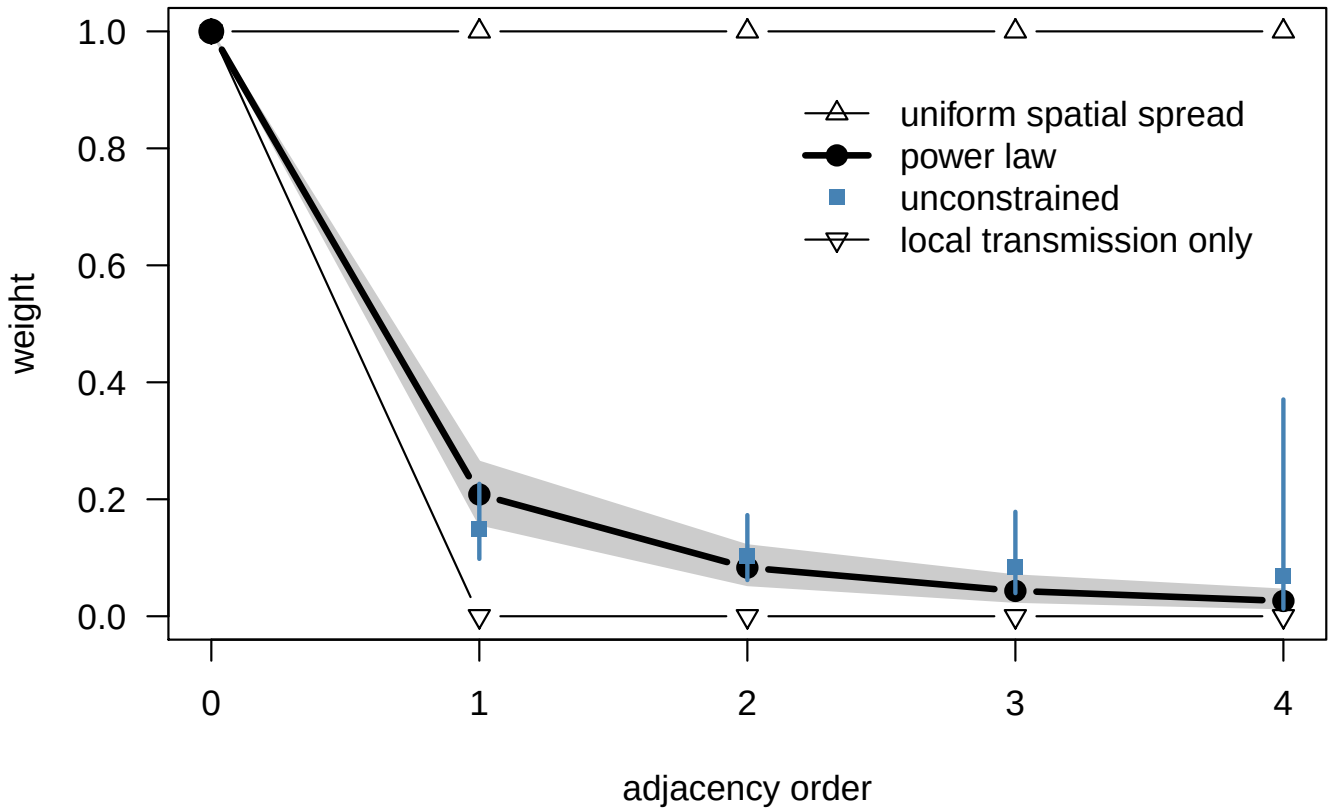


Estimated seasonality





Spatial power-law weights



Power transformation of the contact matrix

$\hat{\kappa} = 0.41$ (95% CI: 0.29 to 0.60)

Predictive model assessment

- AIC-based model comparison selects the most complex model (including the spatial power law and the adjusted contact matrix)
- Does this model also yield the best forecasts for the last season?
  - one-week-ahead: predictive distributions are negative binomial
  - long-term: via Monte Carlo simulation
- Various forecast targets exist, e.g., overall epidemic curve (weekly counts), final size (aggregated over the whole season)

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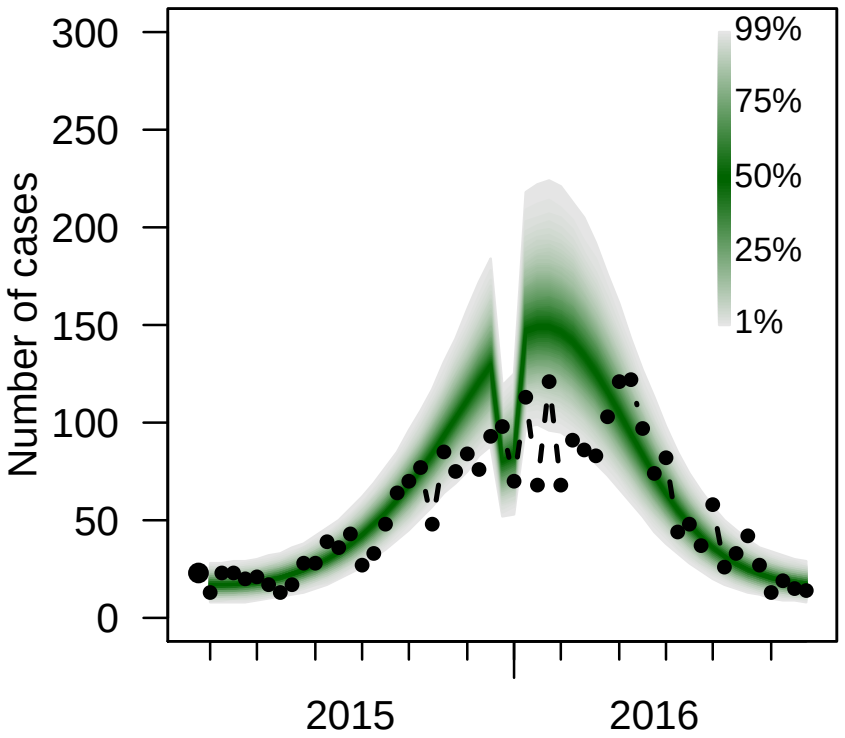
  - one-week-ahead: predictive distributions are negative binomial
  - long-term: via Monte Carlo simulation
- Various forecast targets exist, e.g., overall epidemic curve (weekly counts), final size (aggregated over the whole season)
- "Best" is quantified in terms of sharpness and calibration of the forecasts
- Proper scoring rules serve as overall performance measures [Gneiting and Katzfuss 2014]
  - Assign penalty score based on the predictive distribution F and the actual observation y_{obs}
  - Example: Dawid-Sebastiani score

$$\mathrm{DSS}(F, y_{obs}) = \log|\boldsymbol{\Sigma}| + (y_{obs} - \boldsymbol{\mu})^\top \boldsymbol{\Sigma}^{-1} (y_{obs} - \boldsymbol{\mu})$$

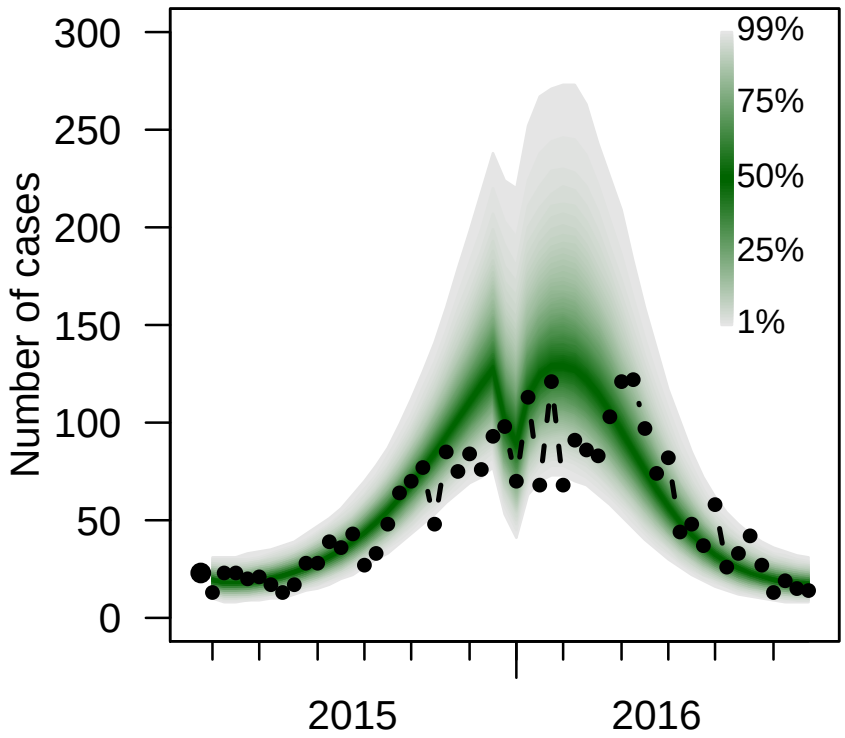
Target quantity: overall epidemic curve

purely endemic model



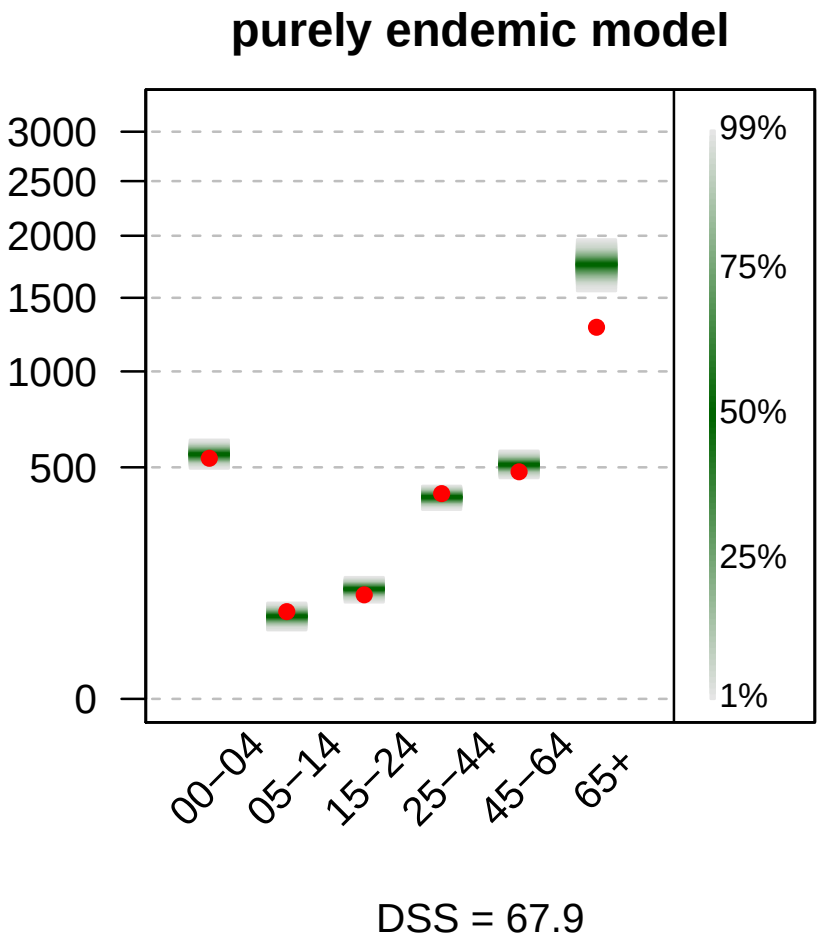
DSS = 346.5

full model

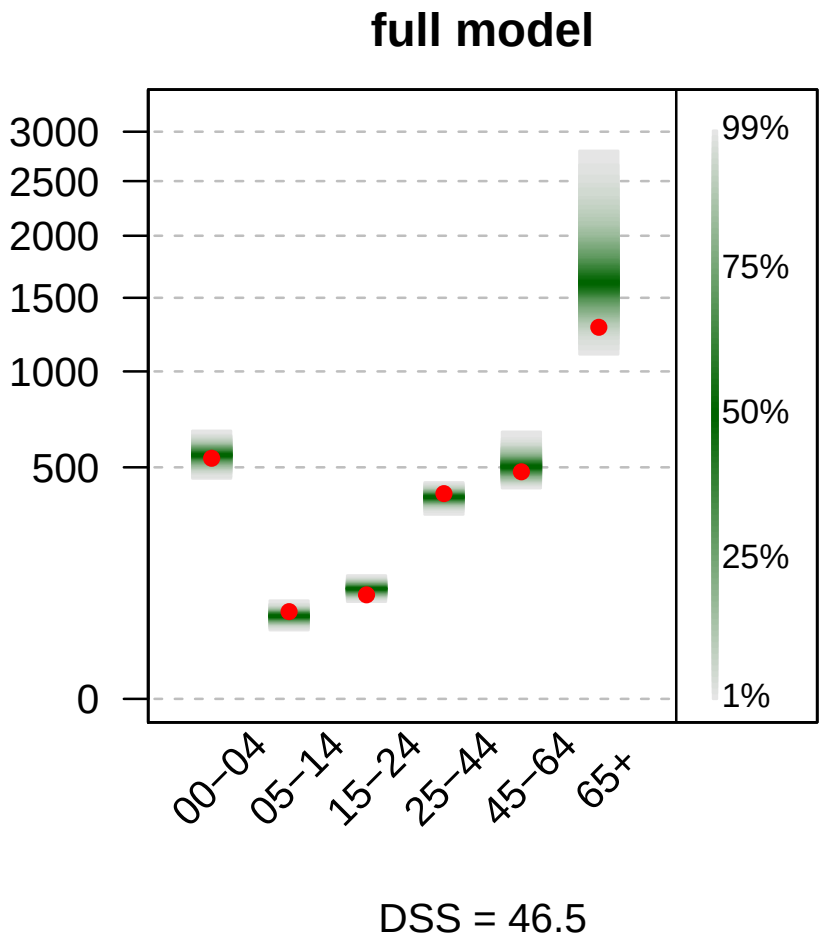


DSS = 334.0

Target quantity: final size by age group



DSS = 67.9



DSS = 46.5

Conclusion

- Models do not perfectly represent individual-level disease transmission, but are still useful for prediction of aggregate-level surveillance counts
- Endemic-epidemic modelling frameworks are implemented in `surveillance`, also for individual-level data on disease occurrence [Meyer, Held, and Höhle 2017]
- Spatial weights and social contact data improve model fit *and* predictions
- The data and code to reproduce some of the presented results is available in the supplementary package `hhh4contacts` [Meyer and Held 2017]
- If the modelling goal is forecasting, use proper scoring rules to assess the quality of probabilistic forecasts [Held, Meyer, and Bracher 2017]

References

Gneiting, Tilmann and Katzfuss, Matthias (2014). "Probabilistic forecasting". In: *Annual Review of Statistics and Its Application* 1.1, pp. 125–151. DOI: 10.1146/annurev-statistics-062713-085831.

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Mossong, Joël et al. (2008). "Social contacts and mixing patterns relevant to the spread of infectious diseases". In: *PLoS Medicine* 5.3, e74. DOI: 10.1371/journal.pmed.0050074.

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Questions? Comments? ☞ seb.meyer@fau.de

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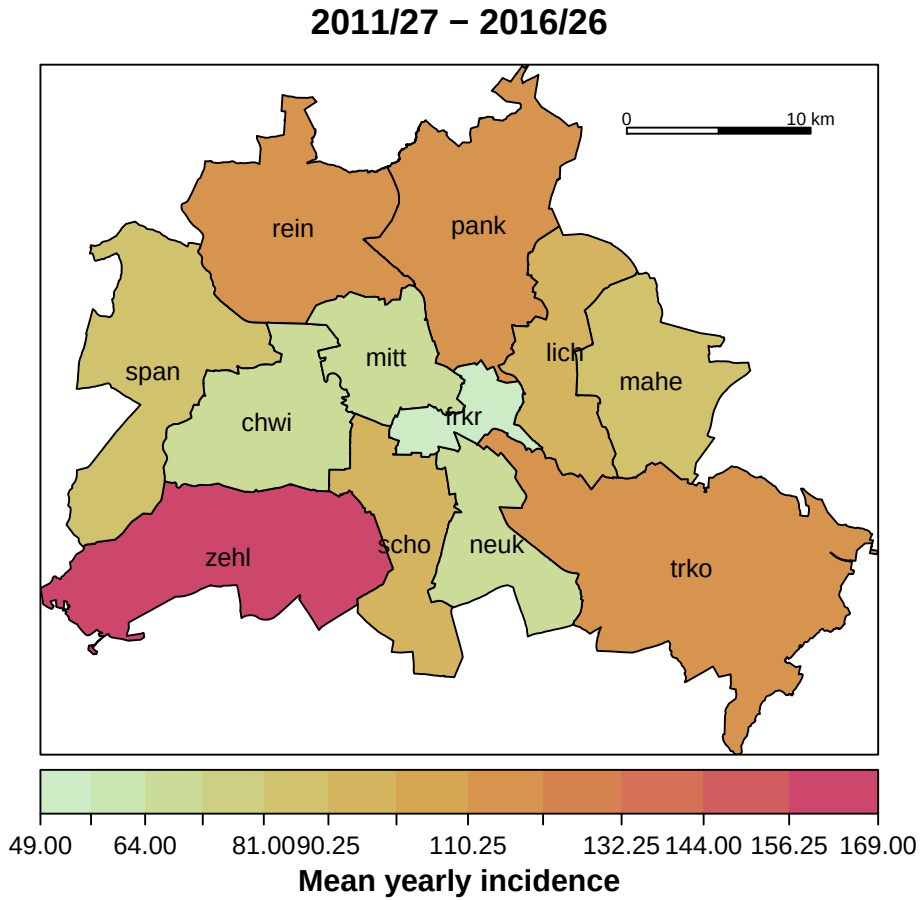
Appendix

Disease incidence map

```
noroBEr <- noroBE(by = "districts",
    timeRange=c("2011-w27","2016-w26"))
scalebar <- layout.scalebar(noroBEr@map,
    corner = c(0.7, 0.9), scale = 10,
    labels = c(0, "10 km"), cex = 0.6,
    height = 0.02)
plot(noroBEr, type = observed ~ unit,
     sub = "Mean yearly incidence",
     population = rowSums(pop2011) *
       (nrow(noroBEr)/52)/100000,
     labels = list(cex = 0.8),
     sp.layout = scalebar)
```



Example code for a “simple” version of the model

```
library("surveillance")  # basic "hhh4" modelling framework
library("hhh4contacts")  # norovirus and contact data

noroBEall <- noroBE(by = "all", flatten = TRUE,  # 6 x 12 = 72 columns
                    timeRange = c("2011-w27", "2016-w26"))

fit <- hhh4(stsObj = noroBEall, control = list(
    end = list(f = addSeason2formula(~1),
               offset = prop.table(population(noroBEall), 1)),
    ne = list(f = ~1 + log(pop),
              weights = W_powerlaw(maxlag = 5, log = TRUE),
              scale = expandC(contactmatrix(), 12)),
    data = list(pop = prop.table(population(noroBEall), 1)),
    family = "NegBin1", subset = 2:(4*52)))
```

Specific model formulation for the norovirus data

$$\mu_{grt} = e_{gr} \exp\left\{\alpha_g^{(\nu)} + \alpha_r^{(\nu)} + \beta x_t + \gamma_g^{(\nu)} \sin(\omega t) + \delta_g^{(\nu)} \cos(\omega t)\right\}$$
$$+ \exp\left\{\alpha_g^{(\phi)} + \alpha_r^{(\phi)} + \tau \log(e_{gr}) + \gamma^{(\phi)} \sin(\omega t) + \delta^{(\phi)} \cos(\omega t)\right\}$$
$$\sum_{g',r'} \lfloor (C^\kappa)_{g'g} (o_{r'r} + 1)^{-\rho} \rfloor \, Y_{g',r',t-1}$$

- Group- and district-specific effects $\alpha_g^{(\cdot)}$ and $\alpha_r^{(\cdot)}$
- Christmas break indicator $x_t \longrightarrow$ reduced reporting
- Group-specific endemic seasonality (sinusoidal log-rates, $\omega = 2\pi/52$)
- "Gravity model" $e_{gr}^\tau \longrightarrow$ force of infection scales with population size
- C^κ: power-adjusted contact matrix
- Power-law weights $w_{r'r} = (o_{r'r} + 1)^{-\rho}$

+ group-specific overdispersion parameters ψ_g