Regional Estimates of Reproduction Numbers — the ITWW model

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recap reproduction equation

- the epidemic spread can be modeled by an reproduction equation, e.g.

$$I(t) \mid I(t-1), \; \cdots \sim \text{Pois}\left(R(t)\sum_{\tau=1}^{\infty} I(t-\tau)w(\tau)\right)$$

where $I(t)$ is the amount of **incident cases** on day t, $R(t)$ is the **(instantaneous) reproduction number** on day t and $w(\tau)$ is the distribution of the **generation time**

- many estimators of $R(t)$ are available, we start with frequentist approach

$$\hat{R}(t) = \frac{I(t)}{\sum_{\tau=1}^{\infty} I(t-\tau)w(\tau)},$$

which works well when denominator is large, e.g. on the country level

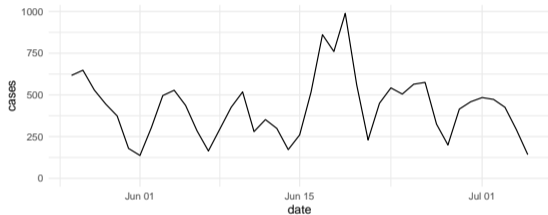The **SPIRIT** of science

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local outbreaks: Germany in summer 2020

Figure: Daily reported SARS-CoV-2 infections in May – July 2020 in Germany.
Data source: Robert-Koch Institut.

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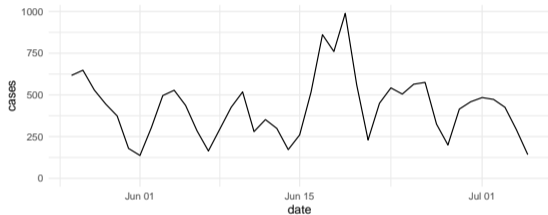ILMENAU

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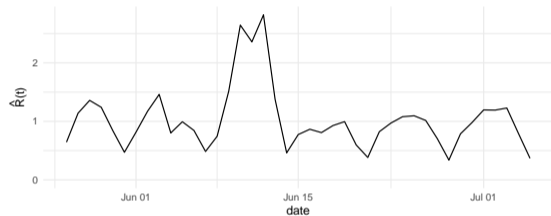

Figure: $\hat{R}(t) = I(t)/\sum_{\tau=1}^{\infty} I(t-\tau)w(\tau)$ for Germany in May – July 2020. Estimates are backdated by one week to account for reporting delay.

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monitoring epidemic spread on subnational level

- large, but localized, outbreaks are regional events which may lead to undesirable estimates of $\hat{R}(t)$
- many other aspects of an epidemic are also heterogeneous within one country:
  - immunity,
  - implemented countermeasures and
  - other socio-economic factors.

  ⇝ model and estimate reproduction numbers on the county level
- county level data pose additional challenges: low case numbers, high variability and imported / exported cases between counties

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model

$$I_c(t) \mid I_c(t-1), \; \cdots \sim \text{Pois}\left(R_c(t)\Phi_c(t)\right)$$

where $I_c(t)$ is the amount of incident cases in county c on day t,
$\Phi_c(t) = \sum_{\tau=1}^{\infty} I_c(t-\tau)w(\tau)$ is the amount of currently infectious on day t in county c

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- to deal with low and highly variable case counts, we use techniques from **small-area estimation**: model $R_c(t)$ as random with common distribution

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model

$$I_c(t) \mid R_c(t), I_c(t-1), \ \cdots \sim \text{Pois}\left(R_c(t)\left((1-p_t)\Phi_c(t) + \frac{p_t}{K-1}\sum_{c'\neq c}\Phi_{c'}(t)\right)\right)$$

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- to deal with low and highly variable case counts, we use techniques from **small-area estimation**: model $R_c(t)$ as random with common distribution
- to deal with imported and exported cases we add p_t, the proportion of imported infections which we assume to be evenly distributed among all other $K-1$ counties
- here and in the following we tacitly condition on all past incidences

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$$I_c(t) \mid R_c(t), I_c(t-1), \; \cdots \sim \mathrm{Pois}\left(R_c(t)\left((1-p_t)\Phi_c(t) + \frac{p_t}{K-1}\sum_{c'\neq c}\Phi_{c'}(t)\right)\right)$$

- assume $R_c(t) \sim \mathrm{Gamma}(a_t, s_t)$ with shape a_t and scale s_t such that

$$I_c(t) \mid I_c(t-1), \; \cdots \sim \mathrm{NegBinom}\left(a_t, q_t(s_t, p_t, \; \dots)\right)$$

  has known distribution

- assuming cond. independence we obtain maximum-likelihood estimators $(\hat{a}_t, \hat{s}_t, \hat{p}_t)$

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  $\rightsquigarrow$ Empirical Bayes

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estimated reproduction numbers

on the county level

- conditional on incidences

$$R_c(t) \mid I_c(t), I_c(t-1), \ldots$$

  is again gamma distributed (conjugate prior)

- estimate $\mathbb{E}(R_c(t) \mid I_c(t), I_c(t-1), \ldots)$ by Plug-in using ML estimates $\hat{a}_t, \hat{s}_t$ and $\hat{p}_t$

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on the country level

- estimate prior mean $\mathbb{E}R_c(t) = a_t s_t$ by Plug-in $\hat{a}_t \hat{s}_t$

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simulation study

- simulate point process on $\mathbb{T} = \mathbb{R}^2/(20\mathbb{Z})^2$, unit square represent counties

Figure: One primary case and the secondary cases it generates over time.

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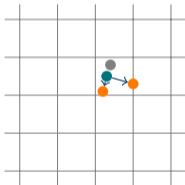- position of secondary cases are gaussian, centered around the position of primary case

Figure: One primary case and the secondary cases it generates over time.

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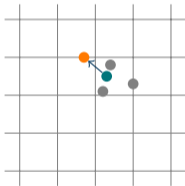- position of secondary cases are gaussian, centered around the position of primary case

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simulation study: results
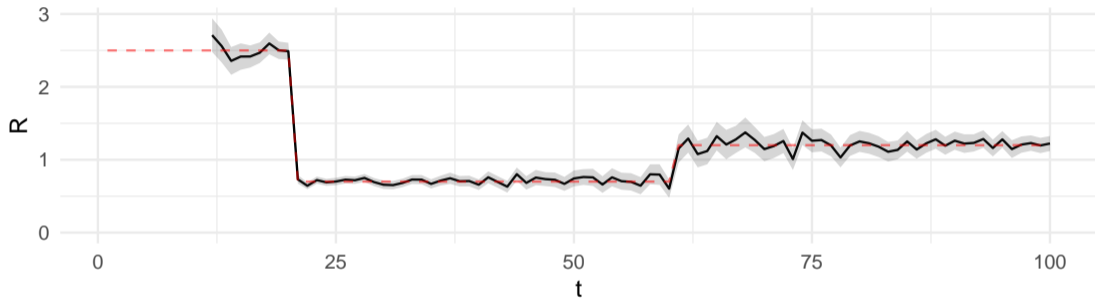
Figure: Estimated country-wide reproduction number (black) with asymptotic 95% confidence intervals (grey ribbons) and true value (dashed red line).

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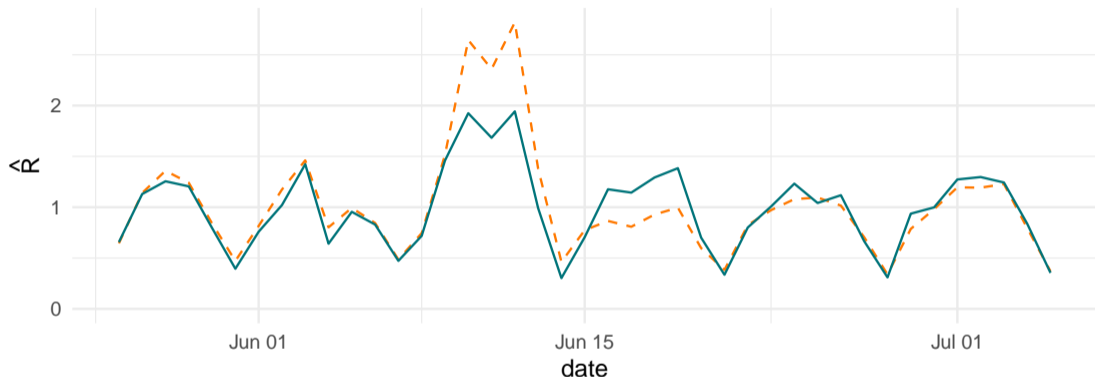
application to the COVID-19 epidemic in Germany

Figure: Comparison of country wide reproduction number estimates based on county and country level incidences. Estimates are backdated by one week to account for reporting delay.

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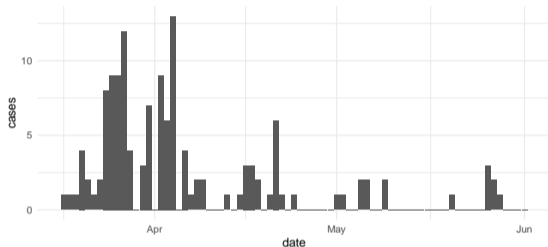# application to the COVID-19 epidemic in Germany

Figure: Daily reported SARS-CoV-2 cases in Ilm-Kreis county in March – June 2020 in Germany.

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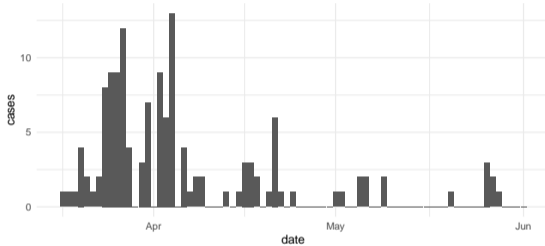
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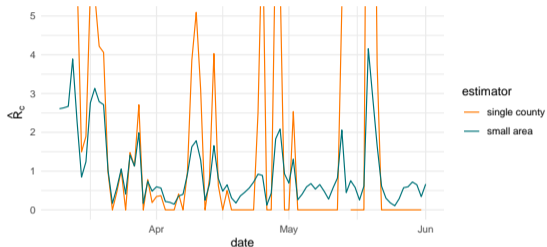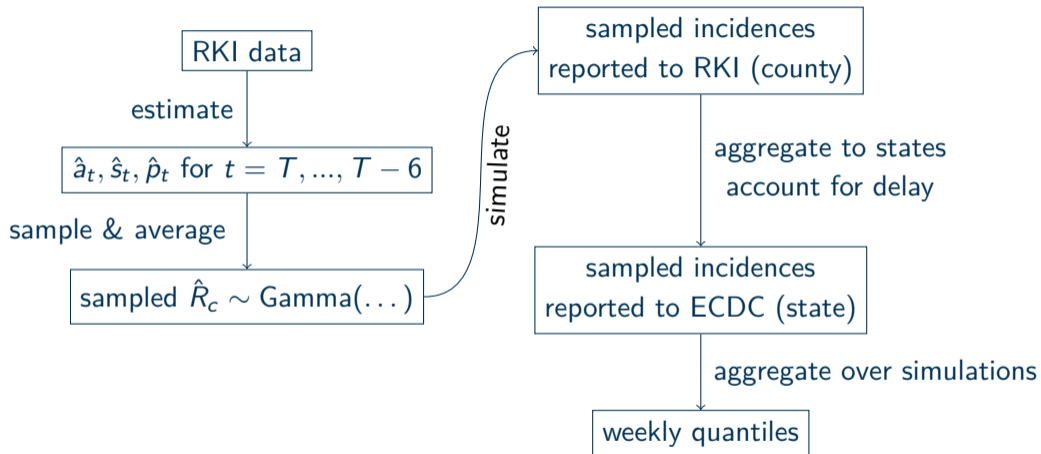Figure: Daily reported SARS-CoV-2 cases in Ilm-Kreis county in March – June 2020 in Germany.

Figure: Estimated reproduction numbers for Ilm-Kreis county between March and June 2020.

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forecasting incidences in Germany

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forecasting deaths in Germany

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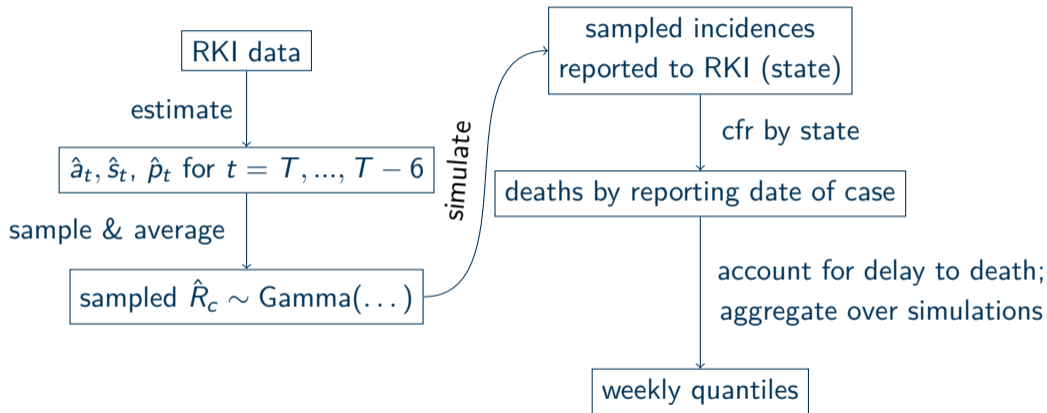
dealing with overconfidence

- recall that under our modelling assumptions, $R_c(t)|I_c(t), \cdots \sim \text{Gamma}\left(a_t + I_c(t), \dots\right)$
- sampling $R_c(t)$ independently in each county yields narrow prediction intervals on state and country level
- to introduce more variation, use copula for reproduction numbers of counties within one state:
  sample for each state l a probability $Q_l \sim \text{Unif}(0,1)$ i.i.d. and for any county c in state l set

  $$R_c(t) = F^{-1}(Q_l; \hat{a}_t + I_c(t), \dots)$$

  for the inverse cdf $F^{-1}(\cdot; a, s)$ of the gamma distribution $\text{Gamma}(a, s)$

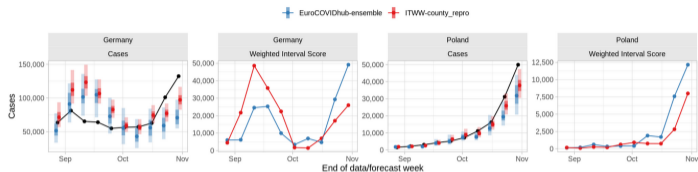The SPIRIT of science   TECHNISCHE UNIVERSITÄT ILMENAU

Model Performance - 2 week ahead forecasts

Figure: ECDC ForecastHub performance over time: cases
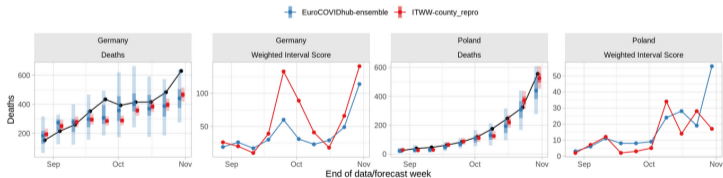
Figure: ECDC ForecastHub performance over time: deaths

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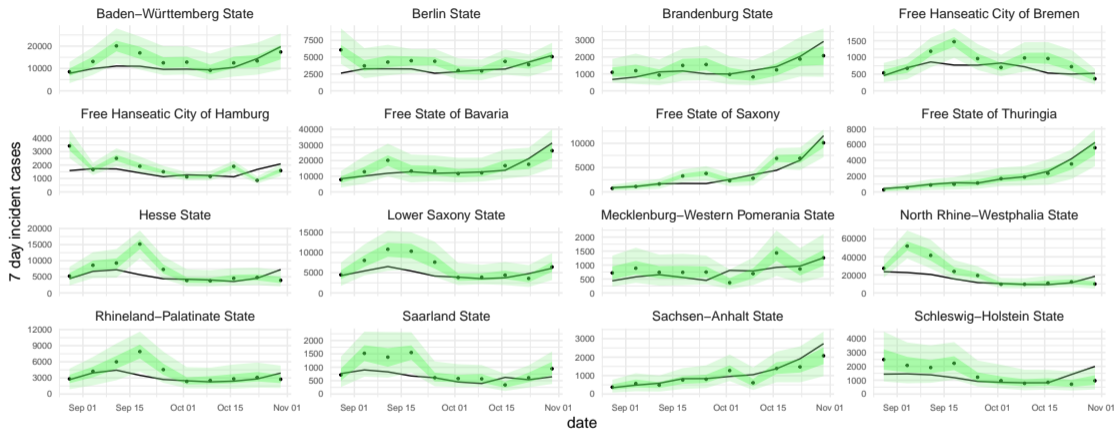
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Model Performance - State level

Figure: 95% and 50% prediction intervals, point forecast for **2 week ahead case forecasts** on the state level in Germany

Regional *R* — ITWW model 03 November 2021 @ weekly ECDC ForecastHub meeting
stefan.heyder@tu-ilmenau.de

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conclusion

- sub-national perspective allows to account for heterogeneity in spread
- good performance during phases of exponential growth
- problems: overshooting at peaks & overconfidence

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future research

- allow other prior distributions for $R_c(t)$: computationally intensive

- investigate and account for impact of socio-economic factors, week-day effects on $R_c(t)$

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