StatGroup19 empirical models for the Italian epidemic indicators

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F. Divino   A. Farcomeni   G. Jona Lasinio   G. Lovison   A. Maruotti

ECDC Forecast Hub Seminar

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Outline

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Common modeling strategies

Compartmental models - **SIR** (Diekmann et al., 2012)

- **Features**
  - **Epidemiologically** correct models
  - **Mechanistically** describe the underlying **dynamic**
  - Can model the pandemic **all-round**

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  - Based on **chaotic systems**
  - Rely on **hypothetical constants** and **require accurate data**
  - **Bias** and **misspecification** lead to completely different results

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At the beggining of the Italian pandemic
most **forecasts** proved to be completely **wrong**!

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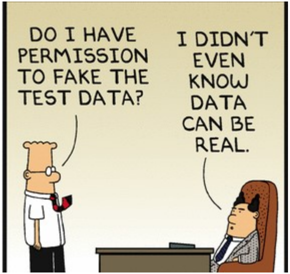
Data issues

Errors and heterogeneity

- Different transmission and data collection system
- Measurement errors and errors in data entry
- Delays in reporting
- Temporal misalignment between indicators
- Tracking was highly symptoms driven



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Phenomenological models (Chowell et al., 2016)

- **Features**
  - **Macroscopic** models
  - Draw inference from **global statistical properties** of the data
  - **Statistical artifacts** modeling the observables' mean

Common modeling strategies

Phenomenological models (Chowell et al., 2016)

- **Features**
  - **Macroscopic** models
  - Draw inference from **global statistical properties** of the data
  - **Statistical artifacts** modeling the observables' mean
- **Pitfalls**
  - Entirely ignore the **nature of the data**
  - Assume **Gaussianity**
  - Use flexible (non-semiparametric) models to **extrapolate**

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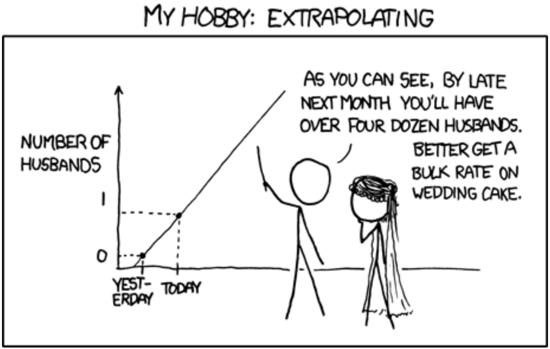
Common conceptual mistakes

Pick a model, validate its performances, but **be aware of its limitations**!

- Never ignore **confidence intervals**
- Good fit does not imply good **extrapolation**
- Predictions at **unreasonable time horizons** are **unreliable**



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Italian available data

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- **Type** (main):
  - **Prevalence:** current positives, intensive care occupancy (stock)

$$Y_t = Y_{t-1} + I_t - O_t$$

  - **Incidence:** cumulative positives, cumulative deceased (flow)

$$Y_t^c = Y_{t-1}^c + \mathbf{Y_t}$$

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Logistic curves

- *S-shaped* curves
- Widely used to model various **growth** phenomena (biological, population, etc.)
- **Exponential** growth followed by a sudden **level off**

Cumulative incidence indicators: logistic growth

Logistic curves

- *S-shaped* curves
- Widely used to model various **growth** phenomena (biological, population, etc.)
- **Exponential** growth followed by a sudden **level off**

In the **epidemic** context

- Finite elements solutions/approximations to epidemiological **ode**
- Describe the **macroscopic** behavior of an **infection trajectory**
- Fit **globally** on the data respecting their **epidemic** nature

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Richards' driven GLM

Cumulative counts follow a **Logistic Growth**

- Model the mean as a **modified Richards' curve**

$$\mathbb{E}[Y_t^c] = \lambda_\gamma(t) = b \cdot t + \frac{r}{\left[1 + 10^{h(p-t)}\right]^s}, \quad \gamma = [b, r, h, p, s]^\top$$

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- Innovations follow **first differences**

$$\mathbb{E}\left[\mathbf{Y_t}\right] = \mathbb{E}[Y_t^c] - \mathbb{E}[Y_{t-1}^c] = \lambda_\gamma(t) - \lambda_\gamma(t-1) \approx$$
$$\approx \frac{d}{dt}\lambda_\gamma(t) = \widetilde{\lambda}_\gamma(\mathbf{t}) = \mathbf{b} + \mathbf{f}_\lambda(\mathbf{t})$$

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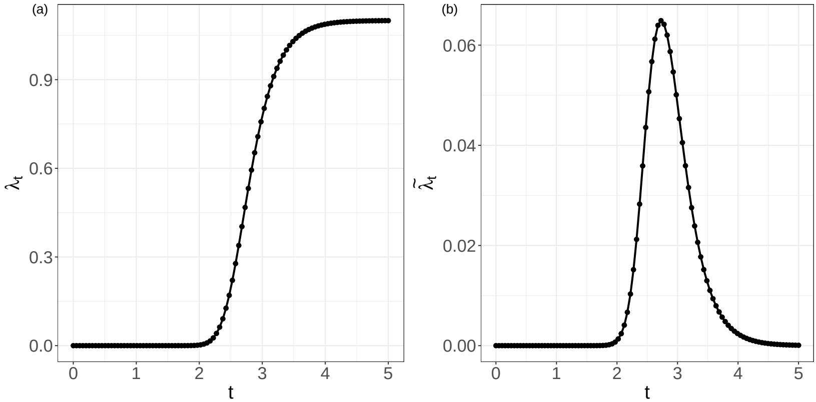
Richards' driven GLM



Example of a Richards' curve (a) and its first differences (b).

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Modeling key-points of Alaimo Di Loro et al. (2021)

- Consider the effect of **covariates** through a link function

$$\eta_{\boldsymbol{\beta}}(\boldsymbol{X}) = \boldsymbol{\beta}\boldsymbol{X} \quad \Rightarrow \quad g_{\boldsymbol{\beta}}(\boldsymbol{X}) = \exp\left\{\eta_{\boldsymbol{\beta}}(\boldsymbol{X})\right\}$$

  - **Additive**:

$$\mu_{\boldsymbol{\theta}}(t, \mathbf{X}) = b_{\boldsymbol{\beta}}(\mathbf{X}) + r \cdot \widetilde{\lambda}_{\boldsymbol{\gamma}}(t), \quad b_{\boldsymbol{\beta}}(\mathbf{X}) = g_{\boldsymbol{\beta}}(\boldsymbol{X})$$

  - **Multiplicative**:

$$\mu_{\boldsymbol{\theta}}(t, \mathbf{X}) = b + r_{\boldsymbol{\beta}}(\mathbf{X}) \cdot \widetilde{\lambda}_{\boldsymbol{\gamma}}(t), \quad r_{\boldsymbol{\beta}}(\mathbf{X}) = g_{\boldsymbol{\beta}}(\boldsymbol{X})$$

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Modeling key-points (Alaimo Di Loro et al., 2021)

- Behold to the **discrete** nature of counts
  Negative Binomial

$$Y_t|\boldsymbol{\theta}, \nu \sim NegBin(\mu_{\boldsymbol{\theta}}(t),\, \nu)$$

Modeling key-points (Alaimo Di Loro et al., 2021)

- Behold to the **discrete** nature of counts
  Negative Binomial

$$Y_t|\boldsymbol{\theta}, \nu \sim NegBin(\mu_{\boldsymbol{\theta}}(t),\ \nu)$$

- Given $\mu_{\boldsymbol{\theta}}(\cdot)$ the Y_t's is **stochastically independent** from Y^c_{t-1}:

$$Y_t \perp Y^c_\tau \quad \forall\, \tau < t$$

Cumulative counts **likelihood**:

$$f_{Y^c}(y^c_1, \ldots, y^c_T | y_0; \boldsymbol{\theta}) = \prod_{t=1}^{T} f_{Y^c_t}(y^c_t | y^c_{t-1}; \boldsymbol{\theta}) = \prod_{t=1}^{T} f_{Y_t}(y_t | \boldsymbol{\theta})$$

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Estimation of Alaimo Di Loro et al. (2021)

Optimal parameters $\hat{\theta}$:

- **Log-Likelihood maximization**
- **Multi-start** routine based on **Fisher-scoring**
- Gradient $\nabla(\cdot)$ and Hessian $\mathcal{H}(\cdot)$ **computed analytically**

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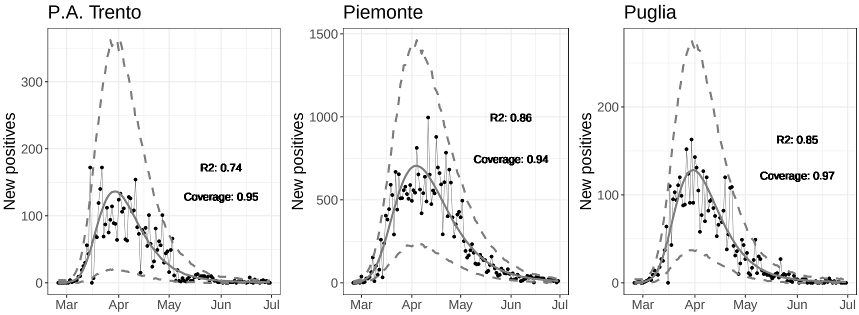
Uncertainty:

- Parameters' uncertainty quantified by the **Hessian**
- **Huber Sandwich** correction

$$\boldsymbol{V}\left[\hat{\boldsymbol{\theta}}\right] = \left(\mathcal{H}(\hat{\boldsymbol{\theta}})\right)^{-1} \nabla(\hat{\boldsymbol{\theta}})\nabla(\hat{\boldsymbol{\theta}})^{\top} \left(\mathcal{H}(\hat{\boldsymbol{\theta}})\right)^{-1}$$

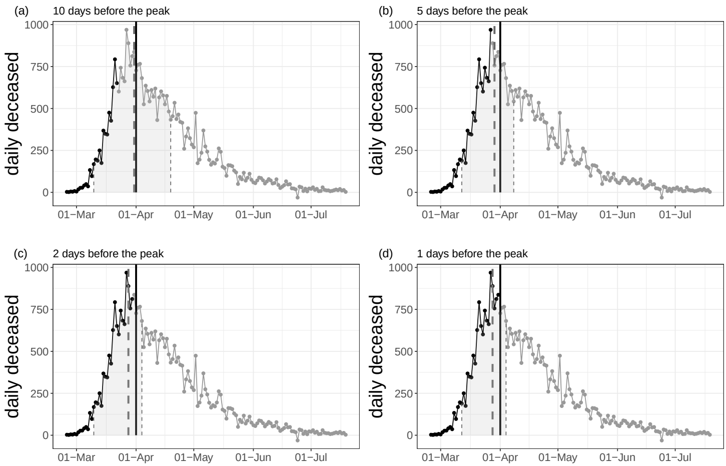
- Mean and prediction **intervals** obtained by bootstrap.

Model results - Fitting



Model fitting - Daily positives - Negative Binomial.

Model validation - peak detection



Estimation of the date of the peak for *daily deceased* at different steps-before.

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Introducing dependence in Mingione et al. (2021)

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Disease mapping

$$Y_{gt}|\mu_{gt} \sim Pois(\mu_{gt})$$
$$\log(\mu_{gt}) = \log(E_g) + \log(m_{gt}), \quad g = 1, \ldots, G, \quad t = 1, \ldots, T$$

- E_g is an offset accounting for area-specific exposures levels
- m_{gt} is a relative measure of the risk of area g at time t

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The relative risk

$$\log(m_{gt}) = \log\left(\widetilde{\lambda}_{\gamma_g}(t)\right) + \boldsymbol{x}_{gt}^{\top}\boldsymbol{\beta} + \phi_{gt}$$

- $\widetilde{\lambda}_{\gamma_g}(t)$ logistic growth temporal trend
- $\boldsymbol{x}_{gt}^{\top}\boldsymbol{\beta}$ a linear predictor based on K covariates
- ϕ_{gt} is a random effect for the g-th area at time t

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Introducing dependence in Mingione et al. (2021)

Spatial dependence (Stern and Cressie, 1999)

- Neighborhood graph $\boldsymbol{W}$ s.t. $w_{ii} = 0$, $w_{ij} > 0$ iff $i \sim j$
- **CAR proper prior**

$$\phi_t \sim \mathcal{N}_G \left(\mathbf{0}, \, \sigma^2 \cdot (\boldsymbol{D} - \alpha \boldsymbol{W})^{-1} \right)$$

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Temporal dependence (Rushworth et al., 2014)

- 1-st order dependence on the past
- **AR(1)** over the space-vectors $\{\phi_t\}_{t=1}^T$

$$\phi_t \,|\, \phi_{1:t-1} \sim \mathcal{N}_G\left(\rho \cdot \phi_{t-1},\ \sigma^2 \cdot (\boldsymbol{D} - \alpha \boldsymbol{W})^{-1}\right)$$

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Alternative settings of Mingione et al. (2021)

Common factors

- $\log(E_g) = \log(residents_g)$ scaled by a factor of 10^5
- Number of total weekly swabs (standardised) as covariate

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"Global VS Individual" growth

- One **common Richards** for all regions $\lambda_\gamma(\cdot)$
- **Individual Richards** for each region $\lambda_{\gamma_g}(\cdot)$

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Alternative spatial dependence graphs $\boldsymbol{W}$

- $\boldsymbol{W}_{Ind} = \mathbf{0} \rightarrow$ spatial independence
- $\boldsymbol{W}_{Flow}$ based on proximity flows (direct HV trains, flights, ferries) as in Della Rossa et al. (2020)
- $\boldsymbol{W}_{Geo}$ based on regions' geographical position

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Estimation in Mingione et al. (2021): Bayesian

Prior setting

$$\log(b), \log(r) \sim \mathcal{N}(0, 100) \quad \log(h), \log(s) \sim \mathcal{N}(0, 1)$$
$$p \sim \mathcal{N}\left(T/2,\ T/(2 \cdot 1.96)\right) \quad \boldsymbol{\beta} \sim \mathcal{N}_K\left(\mathbf{0}, 100 \cdot \boldsymbol{I}_K\right)$$

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Implementation using `STAN` (Carpenter et al., 2017)

- Hamiltonian Monte Carlo → **NUTS** (Hoffman and Gelman, 2014)
- **Exact-sparse** CAR (Joseph, 2016) for computational efficiency
- 70%/30% **in-sample/out-of-sample** split

Codes at https://github.com/minmar94/Covid19-Spatial

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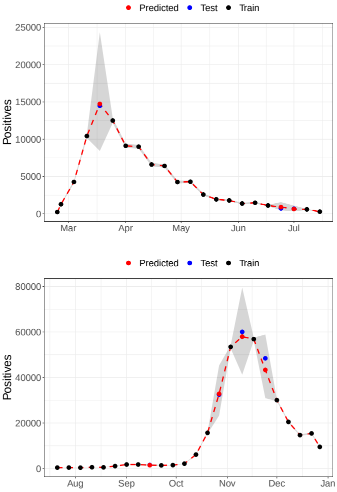
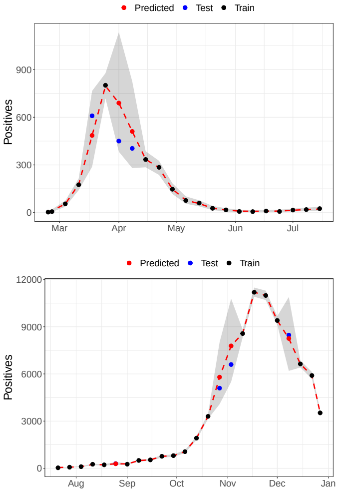
Out-of-sample predictions



(a) Lombardia



(b) Sicilia

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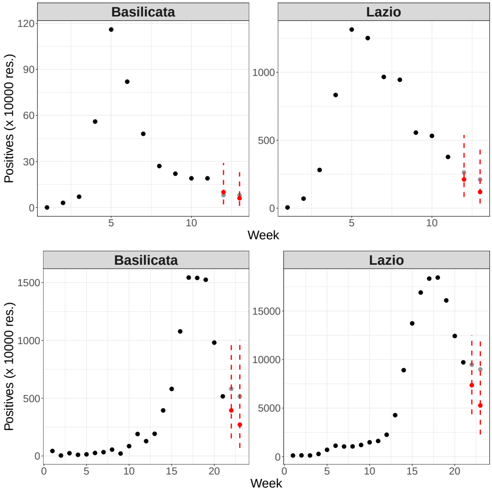
Forecasting ability of the best model



Black dots in-sample, grey dots out-of-sample, red dots predicted values, red dashed 95% prediction intervals.

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Nowcasting of ICUs in Farcomeni et al. (2021)

Focus on **ICU occupancy**

- $Y_{gt} \in \{0, \ldots, B_g\}$ **occupied beds** at time t in area g, with **capacity** B_g
- **Key** for **planning and allocating** health resources

Provide **1 to 5 days-ahead** predictions

- Use only data from the most **recent two weeks**
- Optimal **ensemble** of two methods
- Validate **short-term** performances on the run

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Nowcasting of ICUs in Farcomeni et al. (2021)

First model

- **Generalized Linear Mixed Effect Model (GLMM)**
- Fit through `glmer` in the `lme4` package (Bates et al., 2007)

Second model

GLMM

$$Y_{gt} \sim Poisson(\lambda_{gt})$$

where

$$\log(\lambda_{gt}/R_g) = \beta_{g0} + \beta_{g1} t + \beta_{g2} t^2$$

and

$$(\beta_{g0}, \beta_{g1}, \beta_{g2}) \sim MVN((\beta_0, \beta_1, \beta_2), \Sigma)$$

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- Fit through `tsglm` in the `tscount` package (Liboschik et al., 2015)

INGARCH

$$Y_{gt} \sim Pois\,(\mu_{gt})$$
$$\log\,(\mu_{gt}) = \alpha_{0g} \cdot \log\,(\mu_{g,t-1}) + \alpha_{1g} \cdot \log\,(Y_{g,t-1} + 1) + \eta_{\boldsymbol{\beta}}(t)$$

where

$$\eta_{\boldsymbol{\beta}}(t) = \beta_{0g} + \beta_{1g}t + \beta_{2g}t^2 + \beta_{3g}t^3$$

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Model averaging

- **Convex combination** of predictions
- **Leave-last-out** optimal weight

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Model averaging

Ensemble predictor

$$\hat{Y}_{g,t+1} = w_{gt}\,\hat{Y}_{g,t+1}^{(INGARCH)} + (1 - w_{gt})\,\hat{Y}_{g,t+1}^{(GLMM)}$$

where

- $w_{gt} \in (0, 1)$ and $w_{gt} = 0.5$ for $t < 15$
- **Prediction intervals** are obtained as the **weighted average** of the limits of prediction intervals
- **Jensen's inequality** show that this conservatively guarantees the **nominal level**

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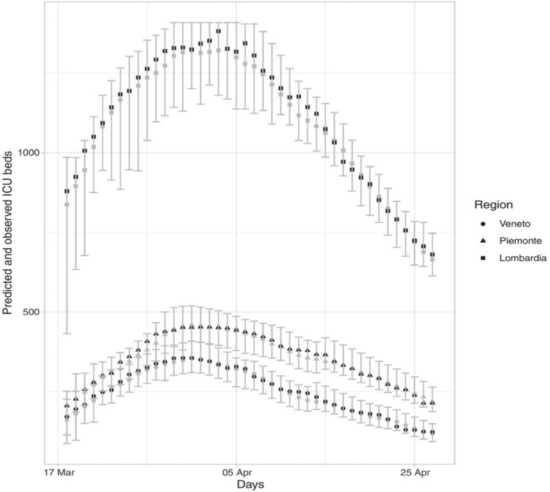
Results (Farcomeni et al., 2021)



Predicted (grey) vs observed (black) number of ICU beds during the first outbreak in Lombardia, Vento and Piemonte. Grey solid lines are 99% confidence intervals.

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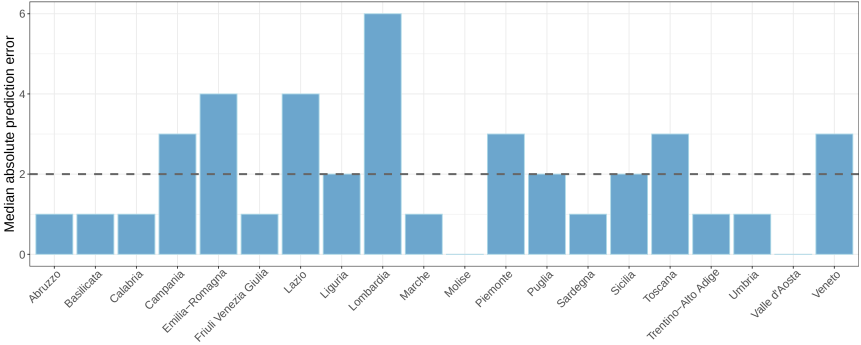
Results



Median absolute prediction error by region for ICU occupancy since March 12, 2020.

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Concluding remarks

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Conclusion

- ✓ Development of a coherent framework for the growth dynamic of counts
- ✓ Inclusion of desirable space-time dependence in the residuals
- ✓ Development of a reliable ensemble predictor of ICU occupancy

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Work in progress

- × Growth model for prevalence indicators using INAR perspective
- × Include space-time dependence in the ICU ensemble model
- × Include the effects of external policies in the model

Main references

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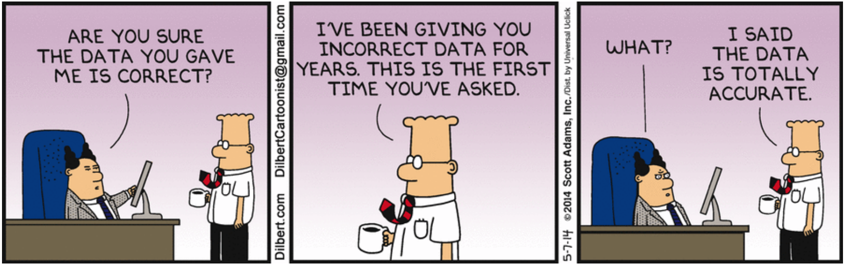

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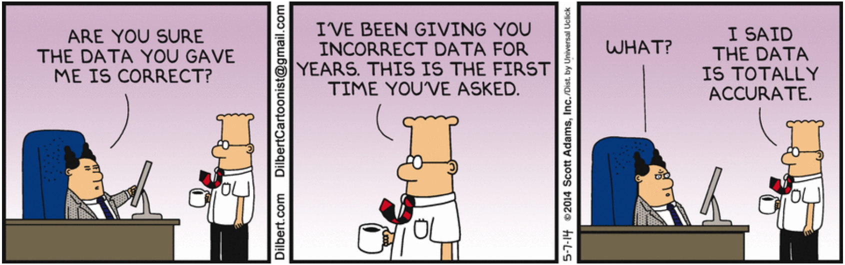

Questions?

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APPENDIX

Deviance residuals (Svetliza and Paula, 2003)

Poisson

$$\hat{d}_t^{\text{Poi}} = \text{sgn}\left(y_t - \mu_{\hat{\boldsymbol{\theta}}}(t)\right) \cdot \sqrt{2y_t \log\left(\frac{y_t}{\mu_{\hat{\boldsymbol{\theta}}}}\right) - \left(y_t - \mu_{\hat{\boldsymbol{\theta}}}(t)\right)}$$

Negative Binomial

$$\hat{d}_t^{\text{NB}} = \text{sgn}\left(y_t - \mu_{\hat{\boldsymbol{\theta}}}(t)\right) \cdot \sqrt{2\left[y_t \log\left(\frac{y_t}{\mu_{\hat{\boldsymbol{\theta}}}(t)}\right) - (y_t + \nu) \cdot \log\left(\frac{y_t + \nu}{\mu_{\hat{\boldsymbol{\theta}}}(t) + \nu}\right)\right]}$$

Pearson residuals

$$\hat{\phi}_t = \frac{y_t - \hat{y}_t}{\widehat{\mathrm{Var}}\left[Y_t\right]}, \qquad t = 1, \ldots, T.$$

where:

$$\widehat{\mathrm{Var}}_{\mathrm{Poi}}\left[Y_t\right] = \mu_{\hat{\boldsymbol{\theta}}}(t), \qquad \widehat{\mathrm{Var}}_{\mathrm{NB}}\left[Y_t\right] = \mu_{\hat{\boldsymbol{\theta}}}(t) + \frac{\mu_{\hat{\boldsymbol{\theta}}}(t)^2}{\hat{\nu}}$$

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Model validation

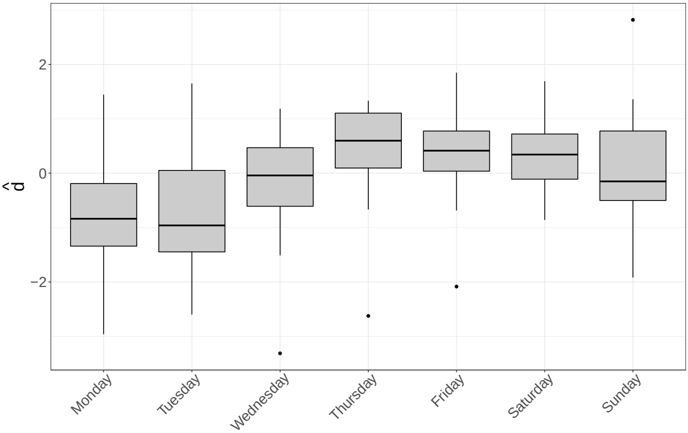

Figure: Deviance residuals distribution aggregated by day of the week for *daily positives*.

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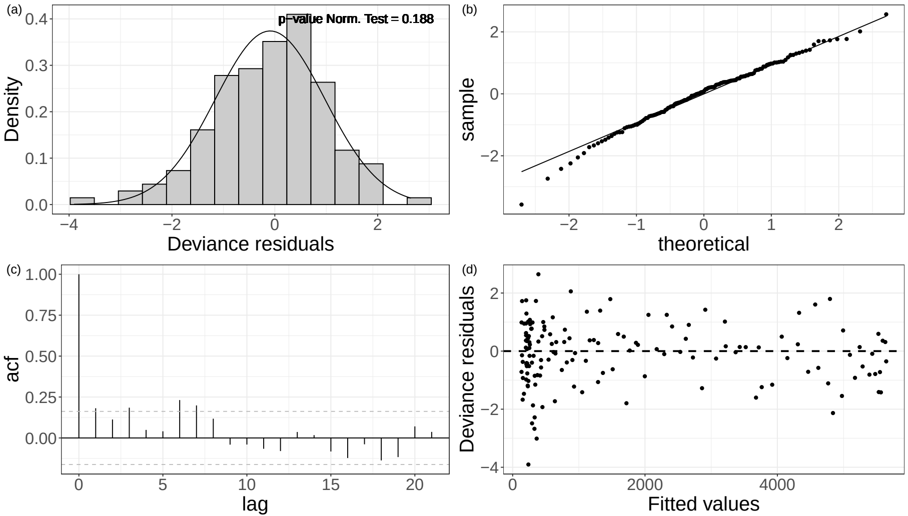

Figure: Residual diagnostic - Daily positives - Negative Binomial.

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Model results

Table: *Parameters' point estimates and 95% confidence intervals for the additive model on daily positives.*

Parameter	Point estimate	95% Interval
β_0	5.26	$(5.18, 5.34)$
β_{wd}	-0.46	$(-0.53, -0.38)$
r	224.57×10^3	$(224.13 \times 10^3, 225.01 \times 10^3)$
h	0.0289	$(0.0287, 0.0291)$
p	-23.26	$(-29.64, -16.88)$
s	44.42	$(-35.67, 124.51)$
ν	22.01	$(21.35, 22.70)$

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Parameters' estimates

Wave	Param.	M_{Ind}	M_{Flow}	M_{Geo}
I	α	–	**0.14 (0.02, 0.21)**	**0.76 (0.71, 0.81)**
	ρ	0.89 (0.87, 0.91)	**0.88 (0.90, 0.93)**	**0.86 (0.85, 0.89)**
	β	0.36 (0.26, 0.44)	0.34 (0.25, 0.42)	0.21 (0.14, 0.29)
II	α	–	**0.93 (0.92, 0.95)**	**0.87 (0.85, 0.90)**
	ρ	0.88 (0.86, 0.90)	**0.87 (0.85, 0.89)**	**0.82 (0.80, 0.85)**
	β	0.42 (0.38, 0.46)	0.27 (0.24, 0.30)	0.13 (0.09, 0.16)

Comparison of parameters' estimates for the spatial (α) and temporal (ρ) auto-correlation, and for the swabs' effect in the first and the second wave.

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Model selection and validation

Wave	Metric	M_{Ind}	M_{Flow}	M_{Geo}
I	Coverage	0.98	0.98	0.98
	PIW	1535	1178	1144
	RMSE	423	**184**	**272**
	WAIC	2869	**2650**	**2774**
	LOO	3087	**2849**	**2982**
II	Coverage	0.96	0.97	0.92
	PIW	33393	4497	4046
	RMSE	12841	**910**	**995**
	WAIC	4112	**3820**	**3971**
	LOO	4393	**4080**	**4252**

Out-of-sample predictive performances for the first and the second wave.

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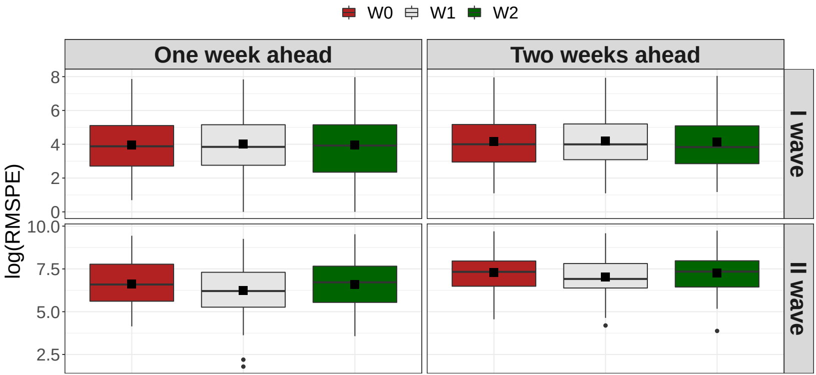
Parameters' estimates

Wave	Model	h	s
I	M_0	0.62 (0.60, 0.64)	7.8 (6.3, 9.9)
	M_1	0.62 (0.59, 0.65)	7.9 (5.5, 9.3)
	M_2	0.61 (0.58, 0.65)	7.8 (5.2, 9.3)
II	M_0	3.46 (3.26, 3.63)	0.06 (0.05,0.07)
	M_1	2.72 (2.33, 3.08)	0.09 (0.07,0.10)
	M_2	3.50 (3.20, 3.70)	0.06 (0.05, 0.07)

Wave	Model	b	r	p
I	M_0	0.05 (0.04, 0.06)	23 (20, 27)	2.0 (1.5, 2.5)
	M_1	0.06 (0.05, 0.07)	20 (17, 22)	2.2 (1.7, 2.8)
	M_2	0.05 (0.04, 0.06)	26 (21, 31)	2.2 (1.5, 2.9)
II	M_0	$7 \cdot 10^{-5}$ ($1 \cdot 10^{-6}$, $1 \cdot 10^{-3}$)	158 (143, 172)	23.2 (23.1, 23.3)
	M_1	$2 \cdot 10^{-4}$ ($3 \cdot 10^{-5}$, $7 \cdot 10^{-3}$)	178 (127, 215)	22.9 (22.8, 23.2)
	M_2	$4 \cdot 10^{-4}$ ($3 \cdot 10^{-6}$, $1 \cdot 10^{-2}$)	194 (163, 220)	23.1 (22.9, 23.2)

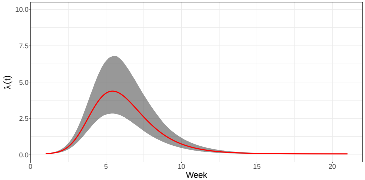
Table: Parameters' estimates of the Richards' curve for the waves I and II.

Forecasting comparisons between graphs

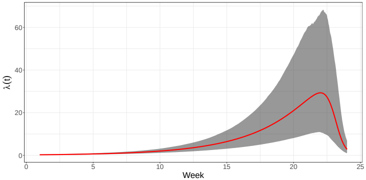


Prediction error (on the log scale) at different steps ahead, for each specification of ***W*** and for each wave.

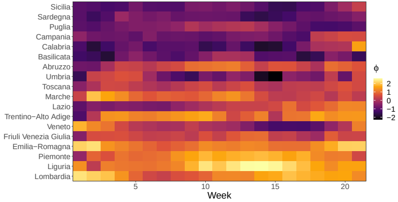
Common Richards' and latent effects



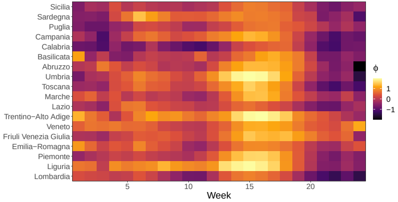
(a) M_{Flow} - I wave - $\widetilde{\lambda}_{\gamma}(t)$



(b) M_{Flow} - II wave - $\widetilde{\lambda}_{\gamma}(t)$



(c) M_{Flow} - I wave - ϕ_{gt}



(d) M_{Flow} - II wave - ϕ_{gt}

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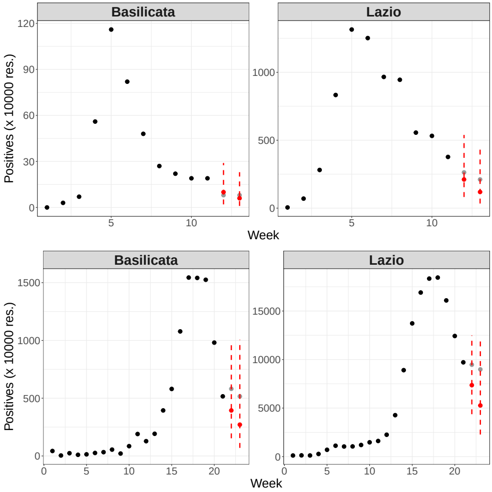
Forecasting ability of the best model



Black dots in-sample, grey dots out-of-sample, red dots predicted values, red dashed 95% prediction intervals.