# Simultaneous statistical inference for epidemic trends: the case of COVID-19

Marina Khismatullina Michael Vogt 01/10/2020

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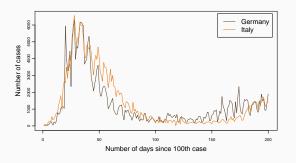
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Introduction

# **Motivation**

# Research question:

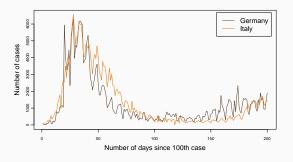
How do outbreak patterns of COVID-19 compare across countries?



# **Motivation**

#### Research question:

How do outbreak patterns of COVID-19 compare across countries?



# Aim of the paper

To develop new inference methods that allow to *identify* and *locate* differences between time trends.

# Model

#### Model

We observe *n* time series  $\mathcal{X}_i = \{X_{it} : 1 \leq t \leq T\}$  of length T:

$$X_{it} = \lambda_i \left(\frac{t}{T}\right) + \sigma \sqrt{\lambda_i \left(\frac{t}{T}\right)} \eta_{it},$$

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#### where

- $\lambda_i$  are unknown trend functions on [0, 1];
- $\bullet$   $\sigma$  is the overdispersion parameter;
- η<sub>it</sub> are error terms that are independent across i and t and have zero mean and unit variance.

#### Literature

Curve comparisons

• Park et al. (2009)

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Studies of COVID-19

• SEIR models

The multiscale testing method

# **Testing problem**

Let  $\mathcal{F} = \{\mathcal{I}_k \subseteq [0,1] : 1 \leq k \leq K\}$  be a family of intervals on [0,1], and for a given interval  $\mathcal{I}_k$  we want to test whether the functions  $\lambda_i$  and  $\lambda_j$  are the same on this interval. Formally, the testing problem is

$$H_0^{(ijk)}: \quad \lambda_i(w) = \lambda_j(w) \text{ for all } w \in \mathcal{I}_k.$$

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We want to test these hypothesis  $H_0^{(ijk)}$  simultaneously for all pairs of countries i and j and all intervals  $\mathcal{I}_k$  in the family  $\mathcal{F}$ .

For the given interval  $\mathcal{I}_k$  and a pair of time series i and j we calculate

$$\hat{s}_{ijk,T} = \frac{1}{\sqrt{Th_k}} \sum_{t=1}^{T} \mathbf{1} \left( \frac{t}{T} \in \mathcal{I}_k \right) (X_{it} - X_{jt}),$$

where  $h_k$  is the length of the interval  $\mathcal{I}_k$ .

For the given interval  $\mathcal{I}_k$  and a pair of time series i and j we calculate

$$\hat{s}_{ijk,T} = \frac{1}{\sqrt{Th_k}} \sum_{t=1}^{I} \mathbf{1} \left( \frac{t}{T} \in \mathcal{I}_k \right) (X_{it} - X_{jt}),$$

where  $h_k$  is the length of the interval  $\mathcal{I}_k$ . Under certain assumptions,

$$\operatorname{Var}(\hat{s}_{ijk,T}) = \frac{\sigma^2}{Th_k} \sum_{t=1}^{T} \mathbf{1}\left(\frac{t}{T} \in \mathcal{I}_k\right) \left\{\lambda_i\left(\frac{t}{T}\right) + \lambda_j\left(\frac{t}{T}\right)\right\}.$$

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In order to normalize the variance of the statistic  $\hat{s}_{ijk,T}$ , we scale it by an estimator of its variance:

$$\widehat{\mathrm{Var}(\hat{s}_{ijk}, \tau)} = \frac{\hat{\sigma}^2}{Th_k} \sum_{t=1}^T \mathbf{1}(\frac{t}{T} \in \mathcal{I}_k)(X_{it} + X_{jt}),$$

with 
$$\hat{\sigma}^2=n^{-1}\sum_{i=1}^n\hat{\sigma}_i^2$$
 and  $\hat{\sigma}_i^2=rac{\sum_{t=2}^T(X_{it}-X_{it-1})^2}{2\sum_{t=1}^TX_{it}}$ .

Test statistic for the hypothesis  $H_0^{(ijk)}$  is defined as

$$\widehat{\psi}_{ijk,T} = \frac{\sum_{t=1}^{T} \mathbf{1}(\frac{t}{T} \in \mathcal{I}_k)(X_{it} - X_{jt})}{\widehat{\sigma}\{\sum_{t=1}^{T} \mathbf{1}(\frac{t}{T} \in \mathcal{I}_k)(X_{it} + X_{jt})\}^{1/2}}.$$

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Under certain conditions and under the null,  $\widehat{\psi}_{ijk,T}$  can be approximated by the Gaussian version of the test statistic:

$$\phi_{ijk,T}(u,h) = \frac{1}{\sqrt{2Th_k}} \sum_{t=1}^{T} \mathbf{1}\left(\frac{t}{T} \in \mathcal{I}_k\right) (Z_{it} - Z_{jt}),$$

where  $Z_{it}$  are independent standard normal random variables.

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For the given significance level  $\alpha \in (0,1)$  and for each (i,j,k), reject  $H_0^{(ijk)}$  if  $|\widehat{\psi}_{ijk,T}| > c_{T,\mathsf{Gauss}}(\alpha,h_k)$ 

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- $q_{T,Gauss}(\alpha)$  is  $(1-\alpha)$ -quantile of the Gaussian test statistic  $\Phi_T$ ;
- and  $\Phi_T = \max_{(i,j,k)} a_k (|\phi_{ijk,T}| b_k)$  the Gaussian test statistic.

Theoretical properties

 ${\cal C}1$  The functions  $\lambda_i$  are uniformly Lipschitz continuous:

$$|\lambda_i(u) - \lambda_i(v)| \le L|u - v|$$
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C2 
$$0 < \lambda_{\min} \le \lambda_i(w) \le \lambda_{\max} < \infty$$
 for all  $w \in [0,1]$  and all  $i$ .

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- C3  $\eta_{it}$  are independent both across i and t.

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- $\mathcal{C}4 \ \mathbb{E}[\eta_{it}] = 0, \ \mathbb{E}[\eta_{it}^2] = 1 \ \text{and} \ \mathbb{E}[|\eta_{it}|^\theta] \leq C_\theta < \infty \ \text{for some} \ \theta > 4.$

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- C1 The functions  $\lambda_i$  are uniformly Lipschitz continuous:  $|\lambda_i(u) \lambda_i(v)| < L|u v|$  for all  $u, v \in [0, 1]$ .
- $|\mathcal{M}(a)| = 2|a| \quad \forall |a| \quad a, v \in [a, 1].$
- C2  $0 < \lambda_{\min} \le \lambda_i(w) \le \lambda_{\max} < \infty$  for all  $w \in [0,1]$  and all i.
- C3  $\eta_{it}$  are independent both across i and t.
- $\mathcal{C}4$   $\mathbb{E}[\eta_{it}] = 0$ ,  $\mathbb{E}[\eta_{it}^2] = 1$  and  $\mathbb{E}[|\eta_{it}|^{\theta}] \leq C_{\theta} < \infty$  for some  $\theta > 4$ .
- $\mathcal{C}5$   $h_{\mathsf{max}} = o(1/\log T)$  and  $h_{\mathsf{min}} \geq CT^{-b}$  for some  $b \in (0,1)$ .
- C6  $p := \{\#(i,j,k)\} = O(T^{(\theta/2)(1-b)-(1+\delta)})$  for some small  $\delta > 0$ .

# Theoretical properties

#### **Proposition**

Denote  $\mathcal{M}_0$  the set of triplets (i,j,k) where  $H_0^{(ijk)}$  holds true. Then under  $\mathcal{C}1-\mathcal{C}6$ , it holds that

$$P\Big(orall (i,j,k) \in \mathcal{M}_0: |\hat{\psi}_{ijk,T}| \leq c_{T,\mathsf{Gauss}}(lpha,h_k)\Big) \geq 1-lpha + o(1)$$

# Strategy of the proof

• Replace the statistic  $\widehat{\Psi}_{\mathcal{T}}$  under  $H_0: m=0$  by a statistic  $\widetilde{\Phi}_{\mathcal{T}}$  with the same distribution and the property that

$$\left|\widetilde{\Phi}_{T}-\Phi_{T}\right|=o_{p}(\delta_{T}),$$

where  $\delta_T = o(1)$ . To do so, we make use of strong approximation theory for dependent processes as derived in Berkes et al. (2014)

# Strategy of the proof

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• Using the anti-concentration results for Gaussian random vectors (Chernozhukov et al. 2015), prove that  $\Phi_T$  does not concentrate too strongly in small regions of the form  $[x-\delta_T,x+\delta_T]$ , i.e.

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$$\sup_{x\in\mathbb{R}}\mathrm{P}\big(|\Phi_{\mathcal{T}}-x|\leq\delta_{\mathcal{T}}\big)=o(1).$$

Show that

$$\sup_{x \in \mathbb{R}} \left| P(\widetilde{\Phi}_{\mathcal{T}} \le x) - P(\Phi_{\mathcal{T}} \le x) \right| = o(1).$$

# Theoretical properties

Define

$$\Pi_{\mathit{T}}^{+} = \big\{\mathit{I}_{u,h} = [u-h,u+h] : (u,h) \in \mathcal{A}_{\mathit{T}}^{+} \text{ and } \mathit{I}_{u,h} \subseteq [0,1] \big\}$$

with

$$\mathcal{A}_{T}^{+} = \left\{ (u, h) \in \mathcal{G}_{T} : \frac{\widehat{\psi}_{T}(u, h)}{\widehat{\sigma}} > q_{T}(\alpha) + \lambda(h) \right\}$$

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$$\Pi_{T}^{-} = \left\{ I_{u,h} = [u - h, u + h] : (u,h) \in \mathcal{A}_{T}^{-} \text{ and } I_{u,h} \subseteq [0,1] \right\}$$

with

$$\mathcal{A}_{T}^{+} = \left\{ (u, h) \in \mathcal{G}_{T} : \frac{\widehat{\psi}_{T}(u, h)}{\widehat{\sigma}} > q_{T}(\alpha) + \lambda(h) \right\}$$
$$\mathcal{A}_{T}^{-} = \left\{ (u, h) \in \mathcal{G}_{T} : -\frac{\widehat{\psi}_{T}(u, h)}{\widehat{\sigma}} > q_{T}(\alpha) + \lambda(h) \right\}$$

# Theoretical properties

### **Proposition**

Under our assumptions, for events

$$E_T^+ = \left\{ \forall I_{u,h} \in \Pi_T^+ : m'(v) > 0 \text{ for some } v \in I_{u,h} \right\}$$
 it holds that

$$P(E_T^+) \ge (1 - \alpha) + o(1)$$

# Theoretical properties

### **Proposition**

Under our assumptions, for events  $E_T^+ = \left\{ \forall I_{u,h} \in \Pi_T^+ : m'(v) > 0 \text{ for some } v \in I_{u,h} \right\} \text{ and }$   $E_T^- = \left\{ \forall I_{u,h} \in \Pi_T^- : m'(v) < 0 \text{ for some } v \in I_{u,h} \right\} \text{ it holds that }$   $P(E_T^+) \ge (1 - \alpha) + o(1)$   $P(E_T^-) \ge (1 - \alpha) + o(1)$ 

# **Graphical representation**

### Minimal intervals

An interval  $\mathcal{I}_k \in \mathcal{F}_{\text{reject}}(i,j)$  is called **minimal** if there is no other interval  $\mathcal{I}_{k'} \in \mathcal{F}_{\text{reject}}(i,j)$  with  $\mathcal{I}_{k'} \subset \mathcal{I}_k$ . The set of minimal intervals is denoted  $\mathcal{F}_{\text{reject}}^{\min}(i,j)$ .

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### Define

$$\begin{split} &\Pi_T^{min,+} = \text{ set of minimal intervals from } \Pi_T^+, \\ &E_T^{min,+} = \left\{ \forall I_{u,h} \in \Pi_T^{min,+} : m'(v) > 0 \text{ for some } v \in I_{u,h} \right\} \end{split}$$

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Since 
$$E_T^{min,+} = E_T^+$$
, we have

$$P(E_T^{min,+}) \ge (1-\alpha) + o(1).$$

# Conclusion

### Conclusion

We developed multiscale methods to test qualitative hypotheses about nonparametric time trends:

- whether the trend is present at all;
- whether the trend function is constant;
- in which time regions there is an upward/downward movement in the trend.

We derived asymptotic theory for the proposed tests.

As an application of our method, we analyzed the behavior of the yearly mean temperature in Central England from 1659 to 2017.

# Thank you!

Long-run error variance estimator

Estimate the long-run error variance  $\sigma^2 = \sum_{\ell=-\infty}^{\infty} \operatorname{Cov}(\varepsilon_0, \varepsilon_\ell)$  of the error terms  $\{\varepsilon_t\}$  in the model

$$Y_t = m\left(\frac{t}{T}\right) + \varepsilon_t,$$

where  $\{\varepsilon_t\}$  is a stationary and causal AR(p) process of the form

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- p is known.

Yule-Walker equations yield

$$\mathbf{\Gamma}_{q}\mathbf{a}=\boldsymbol{\gamma}_{q}+\nu^{2}\boldsymbol{c}_{q},$$

where

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### Note

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 for large values of  $q$ .

We construct the first-stage estimator by

$$\widetilde{\boldsymbol{a}}_q = \widehat{\boldsymbol{\Gamma}}_q^{-1} \widehat{\boldsymbol{\gamma}}_q,$$

where  $\widehat{\Gamma}_q$  and  $\widehat{\gamma}_q$  are constructed from the sample autocovariances  $\widehat{\gamma}_q(\ell) = (T-q)^{-1} \sum_{t=q+\ell+1}^T \Delta_q Y_{t,T} \Delta_q Y_{t-\ell,T}$ .

Simultaneous statistical inference for epidemic trends

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- Average the estimators  $\hat{a}_r$ :  $\hat{a} = \frac{1}{\bar{r}} \sum_{r=1}^{\bar{r}} \hat{a}_r$ .
- Estimate the long-run variance  $\sigma^2$  by

$$\widehat{\sigma}^2 = \frac{\widehat{\nu}^2}{(1 - \sum_{j=1}^p \widehat{a}_j)^2}.$$

### Motivation for the estimator

If  $\{\varepsilon_t\}$  is an AR(p) process, then the time series  $\{\Delta_q\varepsilon_t\}$  of the differences  $\Delta_q\varepsilon_t=\varepsilon_t-\varepsilon_{t-q}$  is an ARMA(p,q) process of the form

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Then  $\Delta_q Y_{t,T} = Y_{t,T} - Y_{t-q,T}$  is approximately an ARMA(p,q) process.

# Theoretical properties of the estimator

### Performance:

• Our estimator  $\hat{a}$  produces accurate estimation results even when the AR polynomial  $A(z) = 1 - \sum_{j=1}^{p} a_j z^j$  has a root close to the unit circle.

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### **Proposition**

Our estimators  $\tilde{a}_q$ ,  $\hat{a}$  and  $\hat{\sigma}^2$  are  $\sqrt{T}$ -consistent.

Consider the uncorrected statistic

$$\widehat{\Psi}_{T, \text{uncorrected}} = \max_{(u,h) \in \mathcal{G}_T} \Big| \frac{\widehat{\psi}_T(u,h)}{\widehat{\sigma}} \Big|$$

under the null hypothesis  $H_0$ : m = 0 and under simplifying assumptions:

- the errors  $\varepsilon_i$  are i.i.d. normally distributed;
- $\widehat{\sigma} = \sigma$ ;
- $\mathcal{G}_T = \{(u_k, h_l) | u_k = (2k-1)h_l \text{ for } 1 \le k \le 1/2h_l, 1 \le l \le L\}.$

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Simultaneous statistical inference for epidemic trends

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Simultaneous statistical inference for epidemic trends

# Idea behind $\hat{\sigma}$

We assume that  $\lambda_i$  is Lipschitz continuous. Then

$$X_{it} - X_{it-1} = \sigma \sqrt{\lambda_i \left(\frac{t}{T}\right)} (\eta_{it} - \eta_{it-1}) + r_{it},$$

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Together with

$$\frac{1}{T}\sum_{t=1}^{T}X_{it} = \frac{1}{T}\sum_{t=1}^{T}\lambda_{i}(t/T) + o_{p}(1),$$

we get that  $\hat{\sigma}_i^2 = \sigma^2 + o_p(1)$  for any i and thus  $\hat{\sigma}^2 = \sigma^2 + o_p(1)$ .

Go back

# Idea behind $a_k$ and $b_k$

How to construct critical values  $c_{ijk,T}(\alpha)$ ?

• Traditional approach:  $c_T(\alpha) = c_{ijk,T}(\alpha)$  for all (i,j,k).

# Idea behind $a_k$ and $b_k$

How to construct critical values  $c_{ijk,T}(\alpha)$ ?

- Traditional approach:  $c_T(\alpha) = c_{ijk,T}(\alpha)$  for all (i,j,k).
- A more modern approach:  $c_{ijk,T}(\alpha)$  depend on the length  $h_k$  of the time interval (Dümbgen and Spokoiny (2001)). In our context:

$$c_{ijk,T}(\alpha) = c_T(\alpha, h_k) := b_k + q_T(\alpha)/a_k,$$

where  $a_k = \{\log(e/h_k)\}^{1/2}/\log\log(e^e/h_k)$  and  $b_k = \sqrt{2\log(1/h_k)}$  are scale-dependent constants and  $q_T(\alpha)$  is the  $(1-\alpha)$ -quantile of the statistic

$$\hat{\Psi}_T = \max_{(i,j,k)} a_k \left( |\hat{\psi}^0_{ijk,T}| - b_k \right)$$

in order to ensure control of the FWER at level  $\alpha$ .

