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

Marina Khismatullina Michael Vogt

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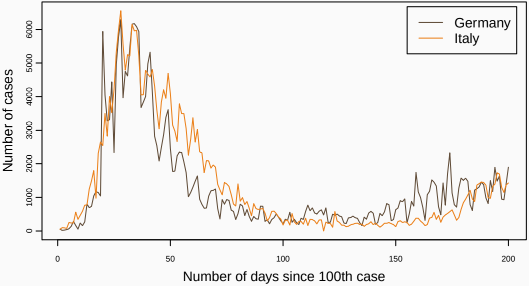
Table of contents

Introduction

Motivation

Research question:

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



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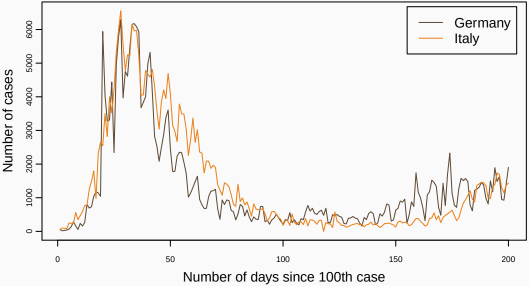

Aim of the paper

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

Model

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

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

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where

- λ_i are unknown trend functions on $[0,1]$;
- σ is the overdispersion parameter;
- η_{it} are error terms that are independent across i and t and have zero mean and unit variance.

Literature

Comparison of deterministic trends:

- Park et al. (2009), Degras et al. (2012), Zhang et al. (2012), Hidalgo and Lee (2014), Chen and Wu (2019).

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- Park et al. (2009), Degras et al. (2012), Zhang et al. (2012), Hidalgo and Lee (2014), Chen and Wu (2019).

Studies of COVID-19:

- SEIR models: Yang et al. (2020), Wu et al. (2020), De Brouwer et al. (2020).
- Time series analysis: Gu et al. (2020), Li and Linton (2020).
- Dong et al. (2020).

Testing

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 λ_i and λ_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 $\mathcal{F}$.

Test statistic

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

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

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

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$$\mathrm{Var}(\hat{s}_{ijk,T}) = \frac{\sigma^2}{T^2 h_k^2} \sum_{t=1}^{T} 1\Big(\frac{t}{T} \in \mathcal{I}_k\Big)\Big\{\lambda_i\Big(\frac{t}{T}\Big) + \lambda_j\Big(\frac{t}{T}\Big)\Big\}.$$

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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:

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

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

Test statistic

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

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

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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:

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

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

Test procedure

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1. Consider the Gaussian test statistic $\Phi_T = \max_{(i,j,k)} a_k \big(|\phi_{ijk,T}| - b_k \big)$, 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.

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Test procedure

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

Theoretical properties

Assumptions

$\mathcal{C}1$ The functions λ_i are uniformly Lipschitz continuous:
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$\mathcal{C}4$ $\mathbb{E}[\eta_{it}] = 0$, $\mathbb{E}[\eta_{it}^2] = 1$ and $\mathbb{E}[|\eta_{it}|^\theta] \leq C_\theta < \infty$ for some $\theta > 4$.

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$\mathcal{C}6$ $p := \{\#(i, j, k)\} = O(T^{(\theta/2)(1-b)-(1+\delta)})$ 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

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

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Proposition

Consider any sequence of functions $\lambda_i = \lambda_{i,T}$, $\lambda_j = \lambda_{j,T}$ with the following property: There exists an interval $\mathcal{I}_k$ such that $\lambda_{i,T}(w) - \lambda_{j,T}(w) \geq c_T\sqrt{T\log T/h_k}$ for all $w \in \mathcal{I}_k$, and $c_T \to \infty$. Then under $\mathcal{C}1-\mathcal{C}6$, it holds that

$$\mathrm{P}\big(|\hat{\psi}_{ijk,T}| \leq c_{T,\mathrm{Gauss}}(\alpha,h_k)\big) = o(1).$$

Notation

In order to proceed with the proof, we will need the following notation:

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

$$\hat{\psi}^0_{ijk,T} = \frac{\sum_{t=1}^{T} 1\big(\frac{t}{T} \in \mathcal{I}_k\big)\,\sigma\overline{\lambda}_{ij}^{1/2}(\frac{t}{T})(\eta_{it} - \eta_{jt})}{\hat{\sigma}\{\sum_{t=1}^{T} 1\big(\frac{t}{T} \in \mathcal{I}_k\big)(X_{it} + X_{jt})\}^{1/2}} \qquad \hat{\Psi}^0_T = \max_{(i,j,k)} a_k\big(|\hat{\psi}^0_{ijk,T}| - b_k\big),$$

$$\psi^0_{ijk,T} = \frac{1}{\sqrt{2Th_k}} \sum_{t=1}^{T} 1\Big(\frac{t}{T} \in \mathcal{I}_k\Big)(\eta_{it} - \eta_{jt}) \qquad \Psi_T = \max_{(i,j,k)} a_k\big(|\psi^0_{ijk,T}| - b_k\big),$$

$$\phi_{ijk,T} = \frac{1}{\sqrt{2Th_k}} \sum_{t=1}^{T} 1\Big(\frac{t}{T} \in \mathcal{I}_k\Big)(Z_{it} - Z_{jt}) \qquad \Phi_T = \max_{(i,j,k)} a_k\big(|\phi_{ijk,T}| - b_k\big).$$

Strategy of the proof

1. We prove that $\left|\hat{\Psi}_T^0 - \Psi_T\right| = o_p(r_T)$, where $\{r_T\}$ is some null sequence.
2. With the help of results from Chernozhukov et al. (2017), we prove
$$\sup_{q \in \mathrm{R}} \left| \mathrm{P}\big(\Psi_T \leq q\big) - \mathrm{P}\big(\Phi_T \leq q\big) \right| = o(1).$$
3. By using these two results, we now show that
$$\sup_{q \in \mathbb{R}} \left| \mathrm{P}\big(\hat{\Psi}_T^0 \leq q\big) - \mathrm{P}\big(\Phi_T \leq q\big) \right| = o(1). \tag{1}$$
4. $\mathrm{P}(\Phi_T \leq q_{T,\text{Gauss}}(\alpha)) = 1 - \alpha$ by definition of the quantile $q_{T,\text{Gauss}}(\alpha)$. From this and (1), it immediately follows that
$$\mathrm{P}\big(\hat{\Psi}_T^0 \leq q_{T,\text{Gauss}}(\alpha)\big) = 1 - \alpha + o(1),$$
which in turn implies the desired statement.

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 $\mathcal{F}^{\text{min}}_{\text{reject}}(i,j)$.

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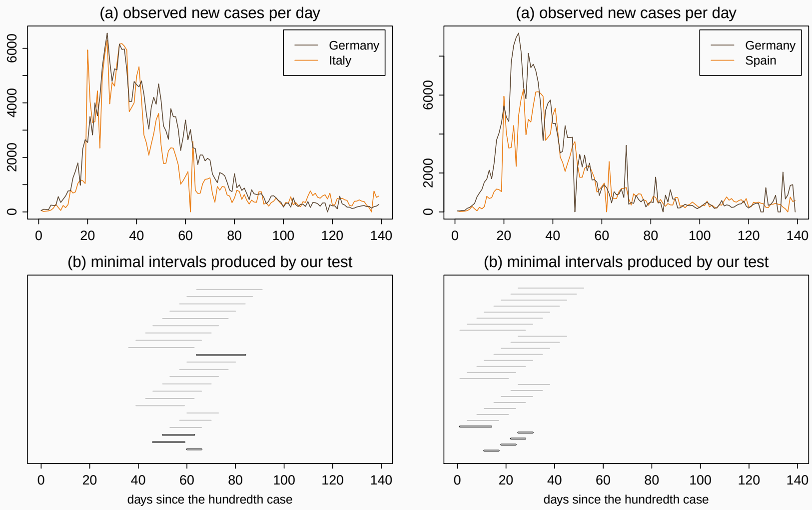
We can make very similar confidence statement about the set of minimal intervals as well:

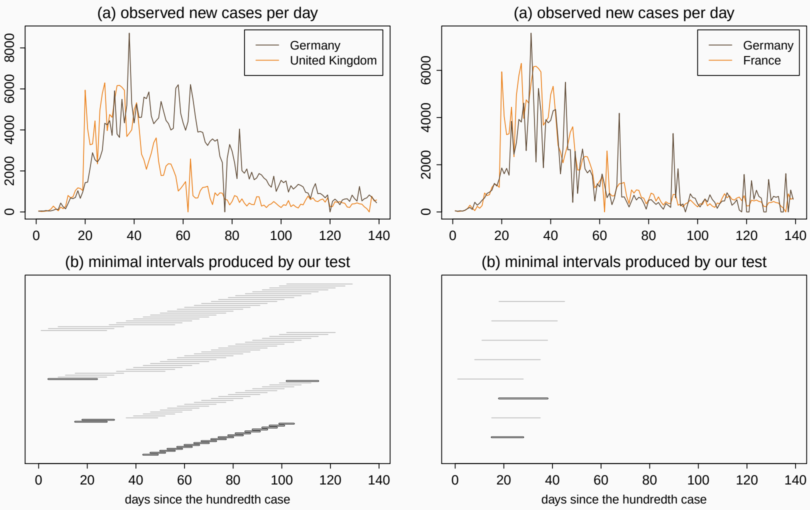
$$\mathrm{P}\Big(\forall (i,j,k) \in \mathcal{M}_0 : \mathcal{I}_k \notin \mathcal{F}^{\text{min}}_{\text{reject}}(i,j)\Big) \geq 1 - \alpha + o(1).$$

Application

Application results



Application results, part 2



Discussion

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- to introduce scaling factor in the trend function, that allow for adjusting for the size of the country (population, density, testing regimes, etc.);

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Further possible extensions:

- to introduce scaling factor in the trend function, that allow for adjusting for the size of the country (population, density, testing regimes, etc.);
- to connect with data-driven techniques such as machine learning;
- to build in some policy changes.

Thank you!

Simulation results for the size of the test

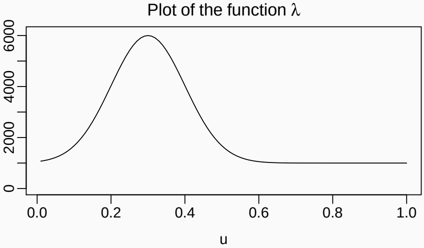

Table 1: Size of the multiscale test

	$n = 5$			$n = 10$			$n = 50$		
	significance level α			significance level α			significance level α		
	0.01	0.05	0.1	0.01	0.05	0.1	0.01	0.05	0.1
$T = 100$	0.011	0.047	0.093	0.010	0.044	0.087	0.008	0.037	0.075
$T = 250$	0.009	0.047	0.091	0.009	0.046	0.087	0.008	0.035	0.069
$T = 500$	0.010	0.044	0.083	0.008	0.048	0.093	0.007	0.035	0.077

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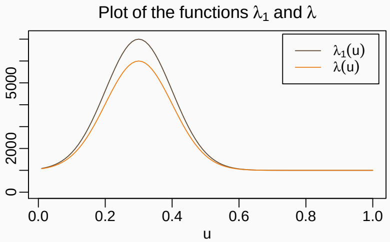

Table 2: Power of the multiscale test for scenario A

	$n = 5$			$n = 10$			$n = 50$		
	significance level α			significance level α			significance level α		
	0.01	0.05	0.1	0.01	0.05	0.1	0.01	0.05	0.1
$T = 100$	0.335	0.518	0.597	0.306	0.474	0.545	0.212	0.352	0.418
$T = 250$	0.615	0.790	0.836	0.580	0.764	0.800	0.470	0.648	0.705
$T = 500$	0.736	0.905	0.917	0.738	0.884	0.890	0.636	0.799	0.830

Simulation results for the power of the test

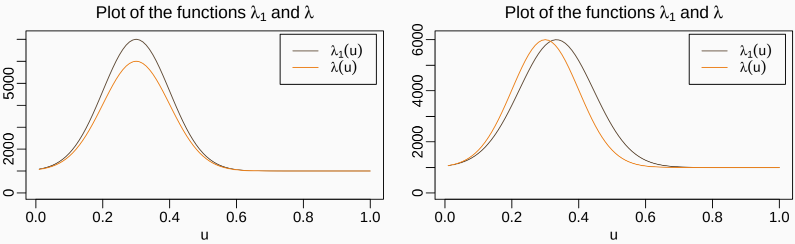

Table 3: Power of the multiscale test for scenario B

	$n = 5$			$n = 10$			$n = 50$		
	significance level α			significance level α			significance level α		
	0.01	0.05	0.1	0.01	0.05	0.1	0.01	0.05	0.1
$T = 100$	0.824	0.910	0.903	0.812	0.893	0.890	0.738	0.847	0.857
$T = 250$	0.991	0.972	0.941	0.991	0.960	0.920	0.991	0.965	0.933
$T = 500$	0.997	0.973	0.949	0.995	0.961	0.923	0.996	0.969	0.932

Idea behind $\hat{\sigma}$

We assume that λ_i is Lipschitz continuous. Then

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

where $|r_{it}| \leq C(1 + |\eta_{it-1}|)/T$ with a sufficiently large C.

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where $|r_{it}| \leq C(1 + |\eta_{it-1}|)/T$ with a sufficiently large C. Hence,

$$\frac{1}{T}\sum_{t=2}^{T}(X_{it} - X_{it-1})^2 = 2\sigma^2\Big\{\frac{1}{T}\sum_{t=2}^{T}\lambda_i(t/T)\Big\} + o_p(1).$$

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where $|r_{it}| \leq C(1 + |\eta_{it-1}|)/T$ with a sufficiently large C. Hence,

$$\frac{1}{T}\sum_{t=2}^{T}(X_{it} - X_{it-1})^2 = 2\sigma^2 \Big\{ \frac{1}{T}\sum_{t=2}^{T} \lambda_i(t/T) \Big\} + o_p(1).$$

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

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- 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

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

in order to ensure control of the FWER at level α.

Go back

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$\Rightarrow \quad \max_m \ldots = \sqrt{2\log(1/h_l)} + o_P(1) \to \infty$ as $h \to 0$ and the stochastic behavior of Φ_T^{uncor} is dominated by the elements with small bandwidths h_l. Go back