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

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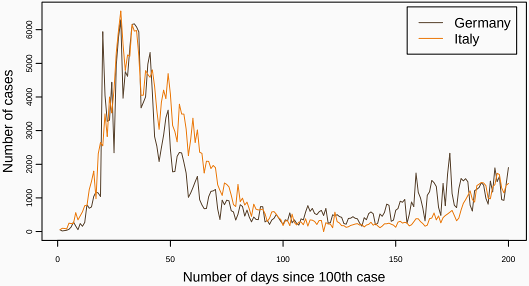
Introduction

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 epidemic time trends.

Model

Model

We can model the count data using a Poisson distribution $X_{it} \sim P_{\lambda_i(t/T)}$.Since $\lambda_i(t/T) = \mathbb{E}[X_{it}] = \mathrm{Var}(X_{it})$, we can rewrite X_{it} as

$$X_{it} = \lambda_i\Big(\frac{t}{T}\Big) + u_{it} \quad \text{with} \quad u_{it} = \sqrt{\lambda_i\Big(\frac{t}{T}\Big)}\eta_{it}.$$

In empirical applications, however, the variance tends to be larger than the mean. Hence, quasi-Poisson models are used.

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

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

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).

Studies of COVID-19:

- SIR 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 rescaled time intervals on $[0,1]$, and let $H_0^{(ijk)}$ be the hypothesis that the functions λ_i and λ_j are equal on an interval $\mathcal{I}_k$, i.e.

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

We want to test $H_0^{(ijk)}$ simultaneously for all pairs of countries i and j and all intervals $\mathcal{I}_k$ in the family $\mathcal{F}$ and we want to control the familywise error rate (FWER) at level α.

Let $\mathcal{M}_0 := \big\{(i,j,k) : H_0^{(ijk)} \text{ holds true}\big\}$. Then, FWER is defined as

$$\text{FWER}(\alpha) = \mathrm{P}\Big(\exists (i,j,k) \in \mathcal{M}_0 : \text{we reject } H_0^{(ijk)}\Big).$$

Test statistic

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

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

where h_k is the length of $\mathcal{I}_k$. $\hat{s}_{ijk,T}$ estimates the average distance between λ_i and λ_j on $\mathcal{I}_k$. Under certain assumptions,

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

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

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

with $\hat{\sigma}^2$ being an appropriate estimator of σ^2. Details

Test statistic

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

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

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

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

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

Critical values

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

- Traditional approach: $c_{ijk,T}(\alpha) = c_T(\alpha)$ for all (i, j, k).
- 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 chosen such that we control FWER.

Critical values, part 2

We want to control FWER:

$$\begin{aligned}
\text{FWER}(\alpha) &= \mathrm{P}\Big(\exists(i,j,k) \in \mathcal{M}_0 : |\widehat{\psi}_{ijk,T}| > c_{ijk,T}(\alpha)\Big) \\
&= 1 - \mathrm{P}\Big(\forall(i,j,k) \in \mathcal{M}_0 : |\widehat{\psi}_{ijk,T}| \le c_{ijk,T}(\alpha)\Big) \\
&= 1 - \mathrm{P}\Big(\forall(i,j,k) \in \mathcal{M}_0 : a_k\big(|\hat{\psi}_{ijk,T}| - b_k\big) \le q_T(\alpha)\Big) \\
&= 1 - \mathrm{P}\Big(\max_{(i,j,k)\in\mathcal{M}_0} a_k\big(|\hat{\psi}_{ijk,T}| - b_k\big) \le q_T(\alpha)\Big) \\
&\le \alpha.
\end{aligned}$$

Hence, we choose $q_T(\alpha)$ as the $(1-\alpha)$-quantile of the statistic

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

where $\hat{\psi}^0_{ijk,T}$ is equal to $\hat{\psi}_{ijk,T}$ under the null.

Test procedure

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.

2. Compute a $(1-\alpha)$-quantile $q_{T,\text{Gauss}}(\alpha)$ of Φ_T by Monte Carlo simulations.
3. Adjust $q_{T,\text{Gauss}}(\alpha)$ by the scale-dependent constants:

$$c_{T,\text{Gauss}}(\alpha, h_k) = b_k + q_{T,\text{Gauss}}(\alpha)/a_k.$$

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: $|\lambda_i(u) - \lambda_i(v)| \leq L|u - v|$ for all $u, v \in [0, 1]$.

$\mathcal{C}2$ $0 < \lambda_{\min} \leq \lambda_i(w) \leq \lambda_{\max} < \infty$ for all $w \in [0, 1]$ and all i.

$\mathcal{C}3$ η_{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 $\theta > 4$.

$\mathcal{C}5$ $h_{\max} = o(1/\log T)$ and $h_{\min} \geq CT^{-b}$ for some $b \in (0, 1)$.

$\mathcal{C}6$ $p := \{\#(i, j, k)\} = O(T^{(\theta/2)(1-b)-(1+\delta)})$ for some small $\delta > 0$.

Theoretical properties

Proposition

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

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

Proposition

Consider a sequence of functions $\lambda_i = \lambda_{i,T}$, $\lambda_j = \lambda_{j,T}$ such that

$$\exists \mathcal{I}_k : \lambda_{i,T}(w) - \lambda_{j,T}(w) \geq c_T \sqrt{\log T/(T h_k)} \; \forall w \in \mathcal{I}_k,$$

and $c_T \to \infty$ faster than $\frac{\sqrt{\log T}\sqrt{\log \log T}}{\log \log \log T}$. Let $\mathcal{M}_1$ be the set of triplets (i, j, k) for which this holds true. Then under $\mathcal{C}1 - \mathcal{C}6$, it holds that

$$\mathrm{P}\Big(\forall (i, j, k) \in \mathcal{M}_1 : |\hat{\psi}_{ijk,T}| > c_{T,\mathrm{Gauss}}(\alpha, h_k)\Big) = 1 - o(1).$$

Notation

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

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

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

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

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

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

$$\sup_{q \in \mathbf{R}} \left| \mathrm{P}\big(\Psi_T \leq q\big) - \mathrm{P}\big(\Phi_T \leq q\big) \right| = o(1).$$

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. It can be shown that $\mathrm{P}(\Phi_T \leq q_{T,\text{Gauss}}(\alpha)) = 1 - \alpha$. 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

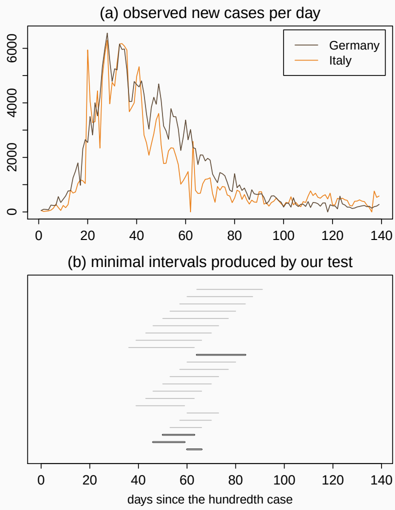
An interval $\mathcal{I}_k \in \mathcal{F}_{\text{reject}}(i,j)$ is called **minimal** if there is no other interval $\mathcal{I}_{k'} \in \mathcal{F}_{\text{reject}}(i,j)$ with $\mathcal{I}_{k'} \subset \mathcal{I}_k$. The set of minimal intervals is denoted $\mathcal{F}^{\min}_{\text{reject}}(i,j)$.

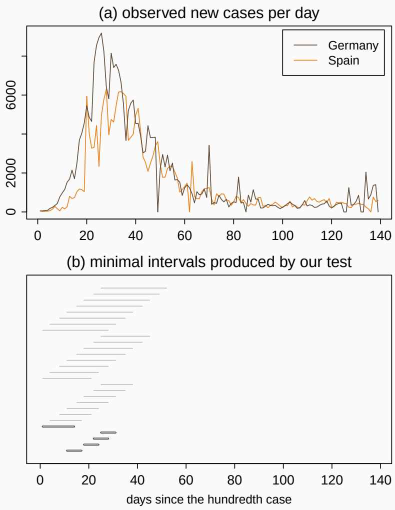
We can make very similar confidence statement about the set of minimal intervals as well:

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

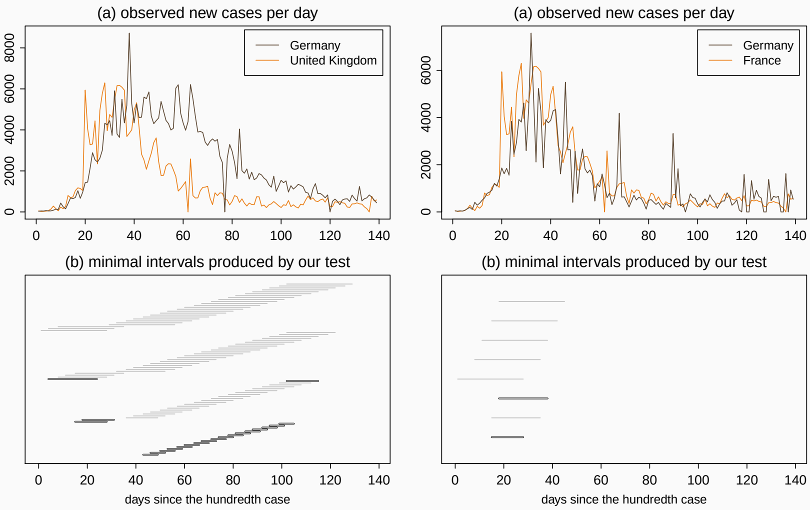
Application

Application results





Application results, part 2



Discussion

We can claim, with confidence of about 95%, that the null hypothesis is violated for all intervals (and all pairs of countries) for which our test rejects the null.

However, we can not say anything about the causes of such differences. This question requires further (probably not purely statistical) analysis.

Further possible extensions:

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

Thank you!

Simulation results for the size of the test

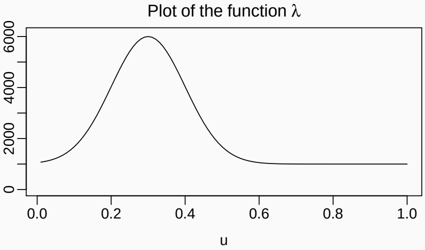
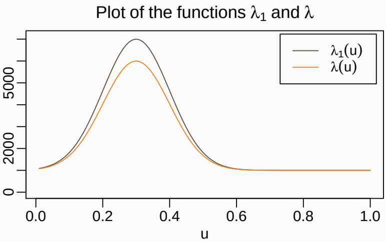


Table 1: Size of the multiscale test

	$n = 5$			$n = 10$			$n = 50$		
	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

Simulation results for the power of the test



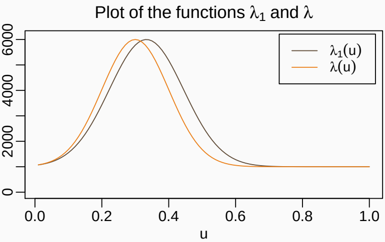


Table [illegible]: Power of the multiscale test for scenario [illegible]

	$n = 5$			$n = 10$			$n = 50$		
	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
$T = 100$	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
$T = 250$	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0.920	[illegible]	[illegible]	[illegible]
$T = 500$	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Idea behind $\hat{\sigma}$

We estimate the overdispersion paramter σ^2 by

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

We assume that λ_i is Lipschitz continuous. Then

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

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

Idea behind the additive correction

Consider the uncorrected Gaussian statistic

$$\Phi_T^{\text{uncor}} = \max_{(i,j,k)} |\phi_{ijk,T}|$$

and let the family of intervals be

$$\mathcal{F} = \big\{[(m-1)h_l, mh_l] \text{ for } 1 \leq m \leq 1/h_l, 1 \leq l \leq L\big\}.$$

Then we can rewrite the uncorrected test statistic as

$$\Phi_T^{\text{uncor}} = \max_{i,j} \max_{\substack{1 \leq l \leq L, \\ 1 \leq m \leq 1/h_l}} \left| \frac{1}{\sqrt{2Th_l}} \sum_{t=1}^{T} 1\Big(\frac{t}{T} \in [(m-1)h_l, mh_l]\Big)(Z_{it} - Z_{jt}) \right|$$

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