Nonparametric comparison of epidemic time trends: the case of COVID-19

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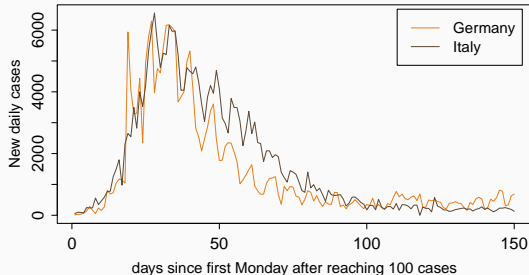# Introduction

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Aim of the paper

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

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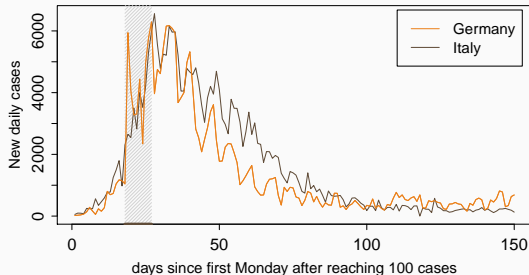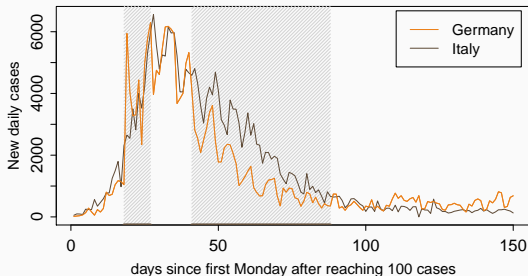
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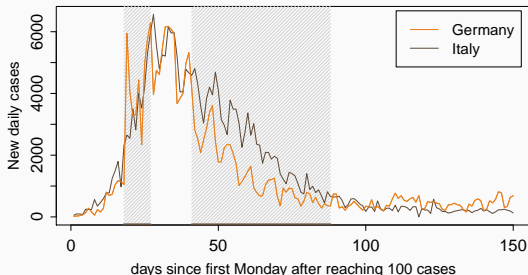**Aim of the paper**

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

Research question: Out of many given intervals, how to find those where the trends are significantly different?

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Why is it relevant?

Finding systematic differences between trends $=$ basis for further research

$\Rightarrow$ understanding which government policies are more effective.

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Testing many hypotheses at the same time = multiple testing problem

    ⇒ large probability of one true null hypothesis being rejected.

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Is it limited to COVID-19?

No! Our method = general method for comparing nonparametric trends

⇒ new statistical test for equality of nonparametric trend curves.

Comparison of deterministic trends:

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

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Since $\lambda_i(t/T) = \mathbb{E}[X_{it}] = \mathrm{Var}(X_{it})$, we can rewrite X_{it} as

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In applications the variance can be larger than the mean $\Rightarrow$ quasi-Poisson models.

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- 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.

Testing procedure

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 for each triplet (i,j,k) consider the null hypothesis that the functions λ_i and λ_j are equal on an interval $\mathcal{I}_k$

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$$\text{FWER}(\alpha) = \text{P}\Big(\exists (i,j,k) : \text{we wrongly reject } H_0^{(ijk)}\Big)$$

Test statistic

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

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

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$$+ \frac{\sigma}{Th_k} \sum_{t=1}^{T} \mathbf{1}\left(\frac{t}{T} \in \mathcal{I}_k\right)\left(\sqrt{\lambda_i\left(\frac{t}{T}\right)}\eta_{it} - \sqrt{\lambda_j\left(\frac{t}{T}\right)}\eta_{jt}\right)$$

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\hat{s}_{ijk} =& \frac{1}{Th_k} \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) \\
&+ \frac{\sigma}{Th_k} \sum_{t=1}^{T} \mathbf{1}\Big(\frac{t}{T} \in \mathcal{I}_k\Big)\Big(\sqrt{\lambda_i\Big(\frac{t}{T}\Big)}\eta_{it} - \sqrt{\lambda_j\Big(\frac{t}{T}\Big)}\eta_{jt}\Big) \\
=& \frac{1}{Th_k} \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) + o_P(1)
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=& \frac{1}{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) + o_P(1)
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Test statistic, part 2

Under certain assumptions,

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

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

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

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

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

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

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

- More modern approach: $c_{ijk}(\alpha)$ depend on the length h_k of the time interval (Dümbgen and Spokoiny (2001)):

$$c_{ijk}(\alpha) = c(\alpha, h_k) := b_k + q(\alpha)/a_k,$$

where a_k and b_k are scale-dependent constants and $q(\alpha)$ is chosen such that we control FWER. $\boxed{\text{Details}}$

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

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

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

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Under our assumptions,

$$\hat{\psi}_{ijk}^0 \approx \frac{1}{\sqrt{2Th_k}} \sum_{t=1}^{T} \mathbf{1}\Big(\frac{t}{T} \in \mathcal{I}_k\Big)(\eta_{it} - \eta_{jt}),$$

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which can be approximated by a Gaussian version of the test statistic:

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

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

Test procedure

1. Consider the Gaussian test statistic

$$\Phi_T = \max_{(i,j,k)} a_k \big(|\phi_{ijk}| - b_k \big),$$

where a_k and b_k are scale-dependent constants and ϕ_{ijk} are weighted averages of the differences of standard normal random variables.

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

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

Test procedure

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

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 $u, v \in [0, 1]$.

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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

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

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

$$\exists \mathcal{I}_k : \lambda_i(w) - \lambda_j(w) \geq c_T \sqrt{\log T / (Th_k)} \ \forall w \in \mathcal{I}_k, \qquad (1)$$

and $c_T \to \infty$ faster than $\frac{\sqrt{\log T} \sqrt{\log \log T}}{\log \log \log T}$.

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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 (1) holds true. Then under $\mathcal{C}1 - \mathcal{C}6$, it holds that

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

Application

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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 $\mathcal{I}_{k'} \subset \mathcal{I}_k$.

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We can make similar confidence statements about minimal intervals:

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

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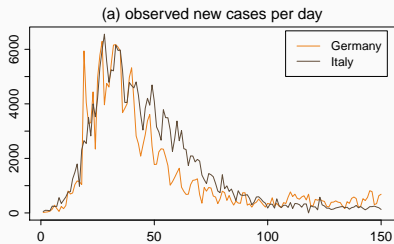
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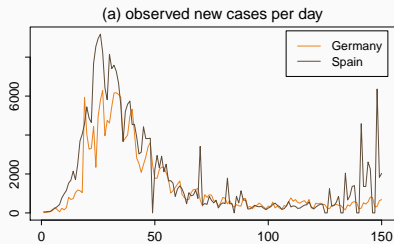
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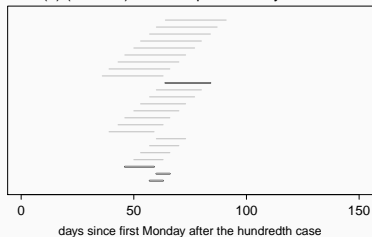
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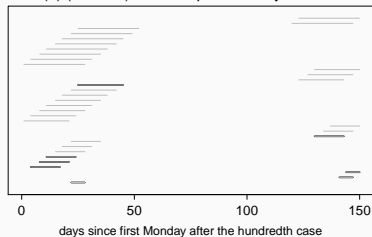
- 5000 Monte Carlo simulation runs to produce critical values.

(a) observed new cases per day — Germany, Italy

(b) (minimal) intervals produced by our test

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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.

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Further possible extensions:

- introduce scaling factor in the trend function, that will allow to adjust 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.

Thank you!

The family of intervals *F*

Nonparametric comparison of epidemic time trends: the case of COVID-19
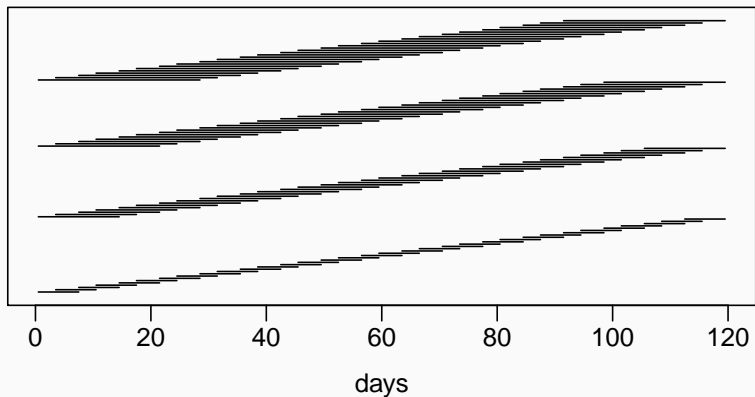
Simulation results for the size of the test

Plot of the function λ
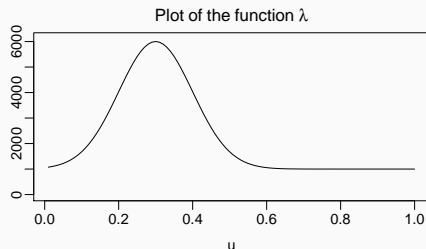
Table 1: Size of the multiscale test

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

Nonparametric comparison of epidemic time trends: the case of COVID-19

Simulation results for the power of the test

Plot of the functions λ_1 and λ
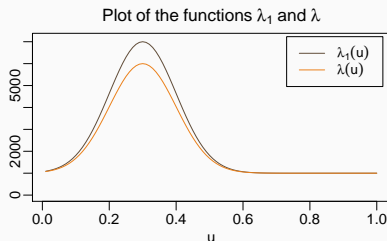
Table 2: Power of the multiscale test for scenario A

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

Nonparametric comparison of epidemic time trends: the case of COVID-19

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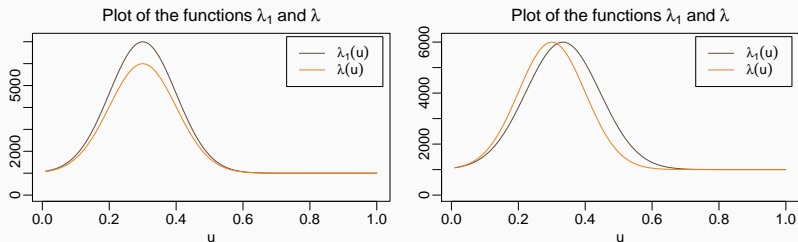
Table 3: Power of the multiscale test for scenario B

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

Nonparametric comparison of epidemic time trends: the case of COVID-19

Estimator of σ^2

We estimate the overdispersion paramter σ^2 by

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

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We assume that λ_i is Lipschitz continuous. Then

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

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

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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

Nonparametric comparison of epidemic time trends: the case of COVID-19

Notation

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

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

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

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

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

Strategy of the proof

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4. It can be shown that $P(\Phi_T \leq q_{\mathsf{Gauss}}(\alpha)) = 1 - \alpha$. From this and (2), it immediately follows that

$$P(\hat{\Psi}_T^0 \leq q_{\mathsf{Gauss}}(\alpha)) = 1 - \alpha + o(1),$$

which in turn implies the desired statement.

Idea behind a_k and b_k

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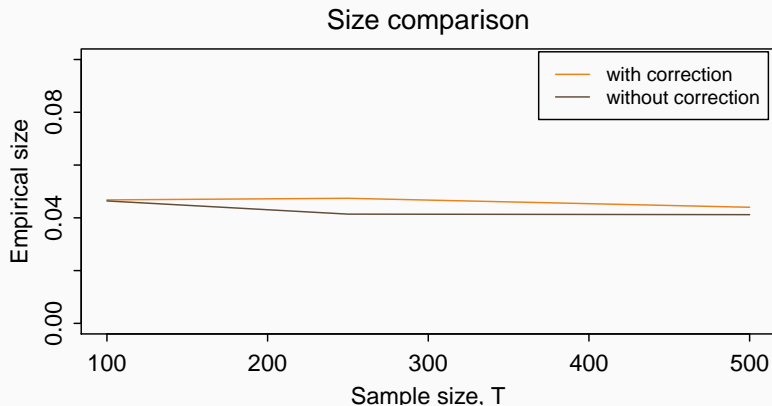
Specifically,

$$c_{ijk}(\alpha) = c(\alpha, h_k) := b_k + q(\alpha)/a_k,$$

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 $q(\alpha)$ is chosen such that we control FWER.

Idea behind a_k and b_k, part 2

This choice of scale-dependent constants helps us balance the significance of hypotheses between the time intervals of different lengths h_k:

Size comparison

Nonparametric comparison of epidemic time trends: the case of COVID-19

Idea behind the additive correction

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

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Then we can rewrite the uncorrected test statistic as

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

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Then we can rewrite the uncorrected test statistic as

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

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