

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

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# Table of contents

1. Introduction
2. Model
3. Testing procedure
4. Theoretical properties
5. Application

# Introduction

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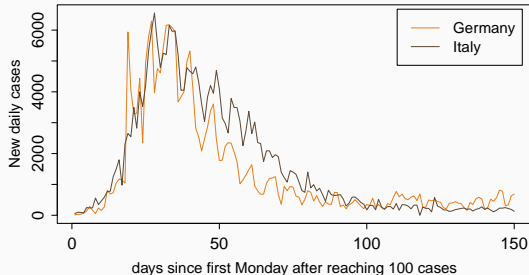
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To develop new inference methods that allow to *identify* and *locate* differences between epidemic time trends.

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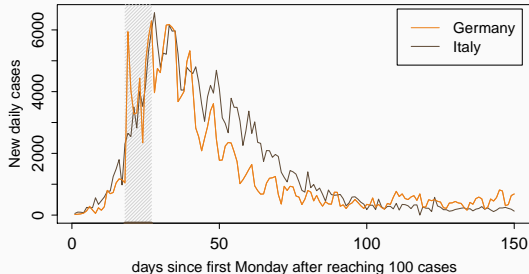
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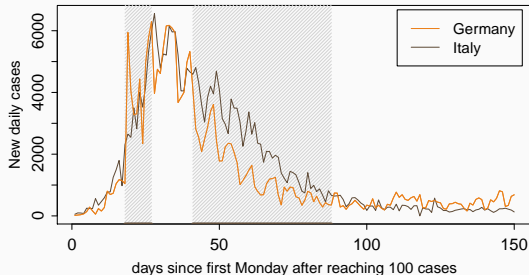
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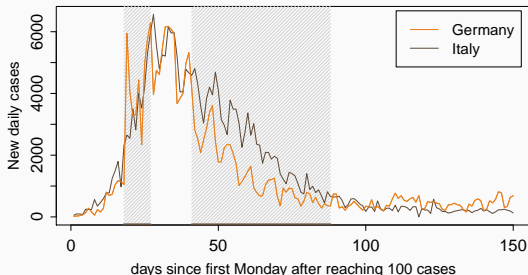
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# Motivation

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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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Finding systematic differences between trends = basis for further research

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

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- $\sigma$  is the overdispersion parameter;
- $\eta_{it}$  are error terms that are independent across  $i$  and  $t$  and have zero mean and unit variance.

# Testing procedure

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# 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  $\lambda_i$  and  $\lambda_j$  are equal on an interval  $\mathcal{I}_k$

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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  $\alpha$

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

# Test statistic

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

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

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Under certain assumptions,

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

## Test statistic, part 2

Under certain assumptions,

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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:

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

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

## Test statistic, part 3

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

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



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

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

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

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

where  $a_k$  and  $b_k$  are scale-dependent constants and  $q(\alpha)$  is chosen such that we control FWER. [Details](#)

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## Critical values, part 2

We want to control FWER. Let  $\mathcal{M}_0 := \{(i, j, k) | H_0^{(ijk)} \text{ is true}\}$ , then

$$\begin{aligned}\text{FWER}(\alpha) &= P\left(\exists(i, j, k) \in \mathcal{M}_0 : |\hat{\psi}_{ijk}| > c_{ijk}(\alpha)\right) \\&= 1 - P\left(\forall(i, j, k) \in \mathcal{M}_0 : |\hat{\psi}_{ijk}| \leq c_{ijk}(\alpha)\right) \\&= 1 - P\left(\forall(i, j, k) \in \mathcal{M}_0 : a_k(|\hat{\psi}_{ijk}| - b_k) \leq q(\alpha)\right) \\&= 1 - P\left(\max_{(i, j, k) \in \mathcal{M}_0} a_k(|\hat{\psi}_{ijk}| - b_k) \leq q(\alpha)\right) \\&\leq 1 - P\left(\max_{(i, j, k)} a_k(|\hat{\psi}_{ijk}^0| - b_k) \leq q(\alpha)\right)\end{aligned}$$

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

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

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

# Test procedure

1. Consider the Gaussian test statistic

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

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

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

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



# Test procedure

1. Consider the Gaussian test statistic

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

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

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

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

## Test procedure

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

# Theoretical properties

---

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

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

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



## 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*

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

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

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

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

# Theoretical properties

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and  $c_T \rightarrow \infty$  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

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

# Application

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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:

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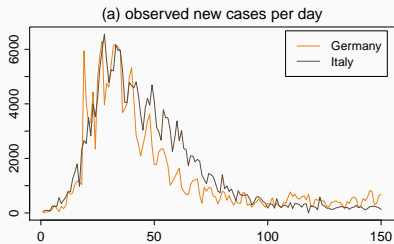
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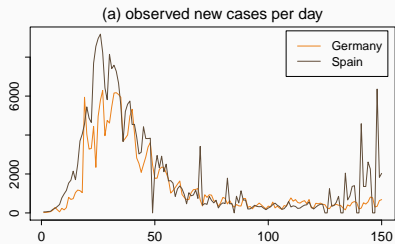
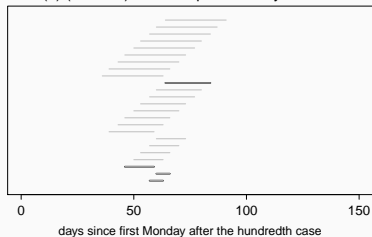
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- 5000 Monte Carlo simulation runs to produce critical values.

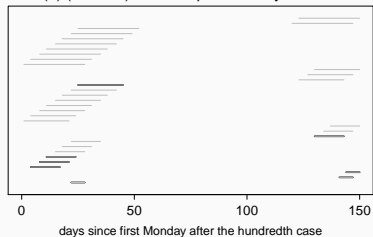
# Application results



(b) (minimal) intervals produced by our test

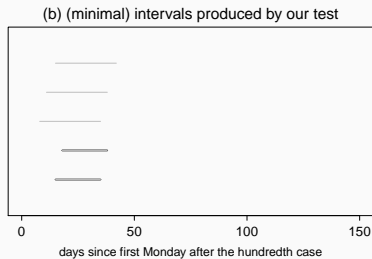
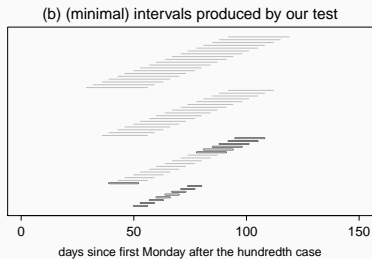
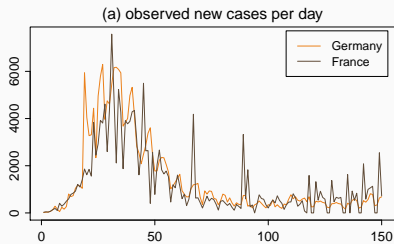
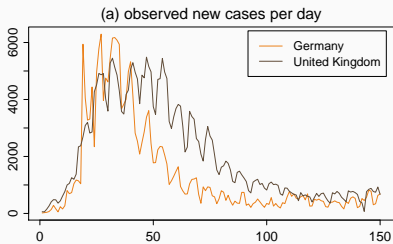


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# Application results, part 2



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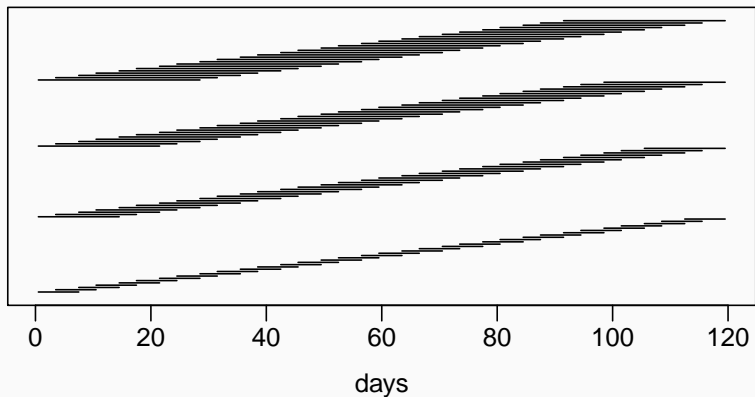
Further possible extensions:

- 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!**

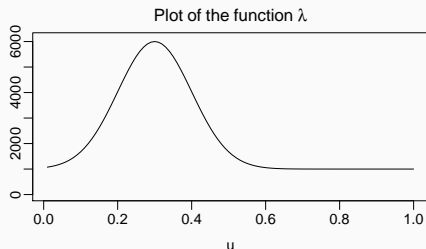
# Family of time intervals

The family of intervals  $F$





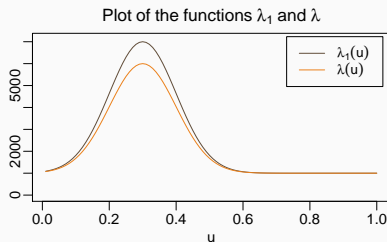
# Simulation results for the size of the test



**Table 1:** Size of the multiscale test

	$n = 5$			$n = 10$			$n = 50$		
	significance level $\alpha$			significance level $\alpha$			significance level $\alpha$		
	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

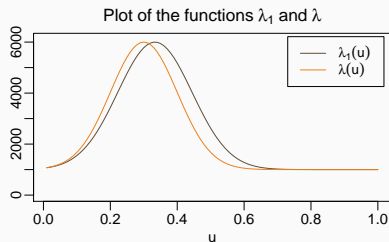
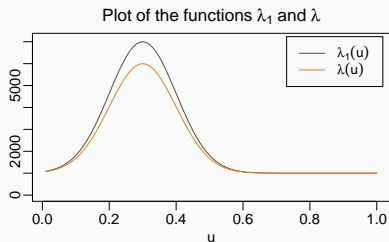
# Simulation results for the power of the test



**Table 2:** Power of the multiscale test for scenario A

	$n = 5$			$n = 10$			$n = 50$		
	significance level $\alpha$			significance level $\alpha$			significance level $\alpha$		
	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 $\alpha$			significance level $\alpha$			significance level $\alpha$		
	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

## Estimator of $\sigma^2$

We estimate the overdispersion parameter  $\sigma^2$  by

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

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

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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](#)

# Notation

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

$$\begin{aligned}\hat{\psi}_{ijk,T} &= \frac{\sum_{t=1}^T 1\left(\frac{t}{T} \in \mathcal{I}_k\right)(X_{it} - X_{jt})}{\hat{\sigma}\left\{\sum_{t=1}^T 1\left(\frac{t}{T} \in \mathcal{I}_k\right)(X_{it} + X_{jt})\right\}^{1/2}} \\ \hat{\psi}_{ijk,T}^0 &= \frac{\sum_{t=1}^T 1\left(\frac{t}{T} \in \mathcal{I}_k\right) \sigma \bar{\lambda}_{ij}^{-1/2}\left(\frac{t}{T}\right)(\eta_{it} - \eta_{jt})}{\hat{\sigma}\left\{\sum_{t=1}^T 1\left(\frac{t}{T} \in \mathcal{I}_k\right)(X_{it} + X_{jt})\right\}^{1/2}} & \hat{\Psi}_T &= \max_{(i,j,k)} a_k(|\hat{\psi}_{ijk,T}^0| - b_k) \\ \psi_{ijk,T}^0 &= \frac{1}{\sqrt{2Th_k}} \sum_{t=1}^T 1\left(\frac{t}{T} \in \mathcal{I}_k\right)(\eta_{it} - \eta_{jt}) & \Psi_T &= \max_{(i,j,k)} a_k(|\psi_{ijk,T}^0| - b_k) \\ \phi_{ijk,T} &= \frac{1}{\sqrt{2Th_k}} \sum_{t=1}^T 1\left(\frac{t}{T} \in \mathcal{I}_k\right)(Z_{it} - Z_{jt}) & \Phi_T &= \max_{(i,j,k)} a_k(|\phi_{ijk,T}| - b_k)\end{aligned}$$



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

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

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

which in turn implies the desired statement.

## Idea behind $a_k$ and $b_k$

A more modern approach of constructing the individual critical values  $c_{ijk}(\alpha)$  (Dümbgen and Spokoiny (2001)): let them depend on the scale of the testing problem, i.e. the length  $h_k$  of the time interval.

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

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  $q_T(\alpha)$  is chosen such that we control FWER. [Go back](#)

# Idea behind the additive correction

Consider the uncorrected Gaussian statistic

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

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and let the family of intervals be

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Then we can rewrite the uncorrected test statistic as

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

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