Estimate of the instantaneous reproduction number (R_t) of an ongoing epidemic incorporating nowcasting and back-projection corrections

Flávia M. D. Marquitti
Pesquisadora de Pós Doutorado - Unicamp
Observatório COVID-19 BR

flamarquitti@gmail.com

Obrigada

OBSERVATÓRIO COVID-19 BR

Henrique dos Santos Flores
Marcelo Eduardo Borges
Rafael Lopes Paixão da Silva
Tatiana Pineda Portella
Silas Poloni Lyra
Diogo Melo
Renato Mendes Coutinho
Paulo Inácio K. L. Prado
Roberto André Kraenkel

UNICAMP

CAPES

Basic reproduction number (R_0)

- R_0 is the basic number (ratio) of reproduction and it characterizes the transmission potential of a disease
- It represents expected number of secondary cases produced by a typical primary case in an entirely susceptible population
- The R_0 of a disease is function of human social behavior and organization, as well as the innate biological characteristics of particular pathogens
  - Transmissibility
  - Contact rate
  - Infectious period
- Constant review
  - Measles: estimate: 12-18
  - Systematic review by Guerra et al (2017): 3-200 (!!)

Instantaneous (effective) reproduction number (R_t ,R_{eff})

R_t is the actual average number of secondary cases per primary case and it is usually a fraction of the R_0:

$$R_t = R_0 x$$

where, in a simple model, ***x*** is the frequency of susceptible individuals in a population at a given time ***t***

Why calculate R_{eff}?

It is commonly used to characterize pathogen transmissibility during an epidemic.

The monitoring of R over time provides feedback on the effectiveness of interventions and on the need to intensify control efforts.

To stop an epidemic, R needs to be persistently reduced to a level below 1.

Instantaneous (effective) reproduction number (R_t ,R_{eff})

- $R_{eff} > 1$: number os new cases increases
- $R_{eff} = 1$: equilibrium of cases (endemic)
- $R_{eff} < 1$: number os new cases decreases

R_{eff} (and R_0) is not a rate!

It is a number, a ratio.

Estimate the R_{eff} for a local community, where contacts/transmissions occur

How to estimate the R_{eff}

Ratio between the incidence number of new cases at a time ***t*** and the incidence number of new cases at time ***t-1***

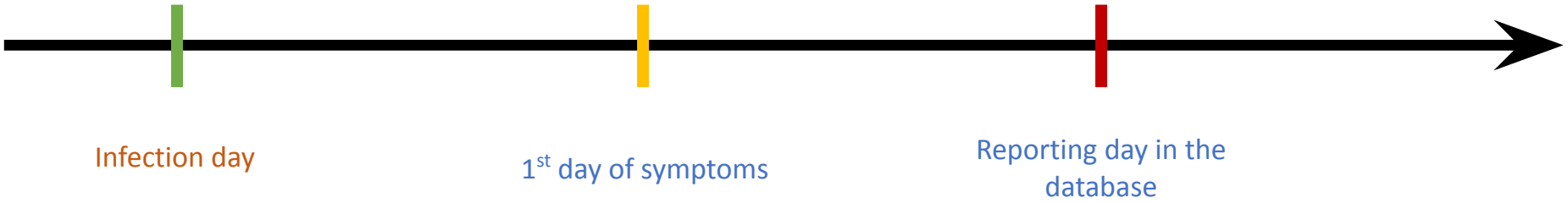
day	Incidence number	Ratio N(t)/N(t-1)
1	10	-
2	12	1.2
3	18	1.5
4	26	1.4
5	44	1.7

However we must consider that the expected number of incidence cases at a given time ***t*** depends on the number of incidence cases in previous time steps ***t-s*** weighted an infectivity function $\mathbf{w_s}$

$$\mathbf{E}[I_t] = R_t \sum_{s=1}^{t} I_{t-s} w_s$$

Database and dates

There are 3 important dates for a given a case:

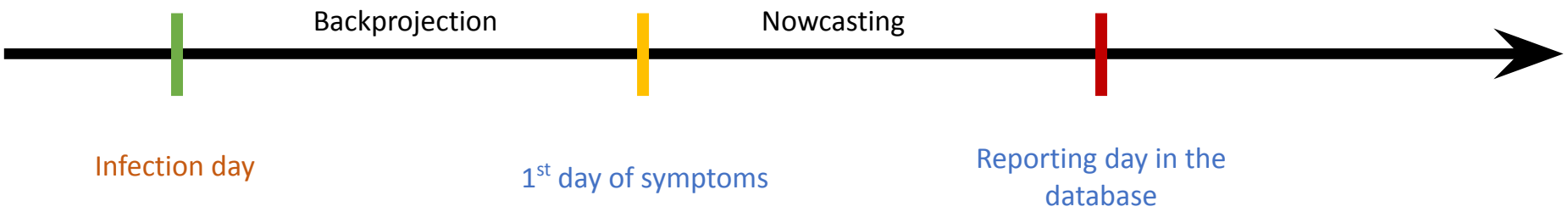


Brazilian national health surveillance of hospitalized individuals (SIVEP-Gripe) we have access to at least 2 of them:

- Date of 1st of symptoms
- Reporting date

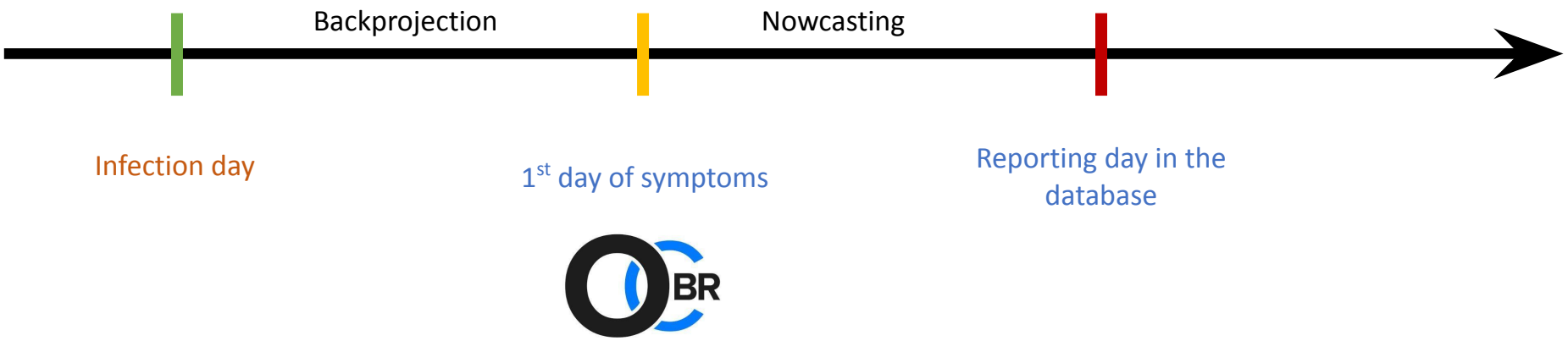
Delays!!

Correcting delays



Correcting delays

- Corrections:



Methods to estimate R_{eff}

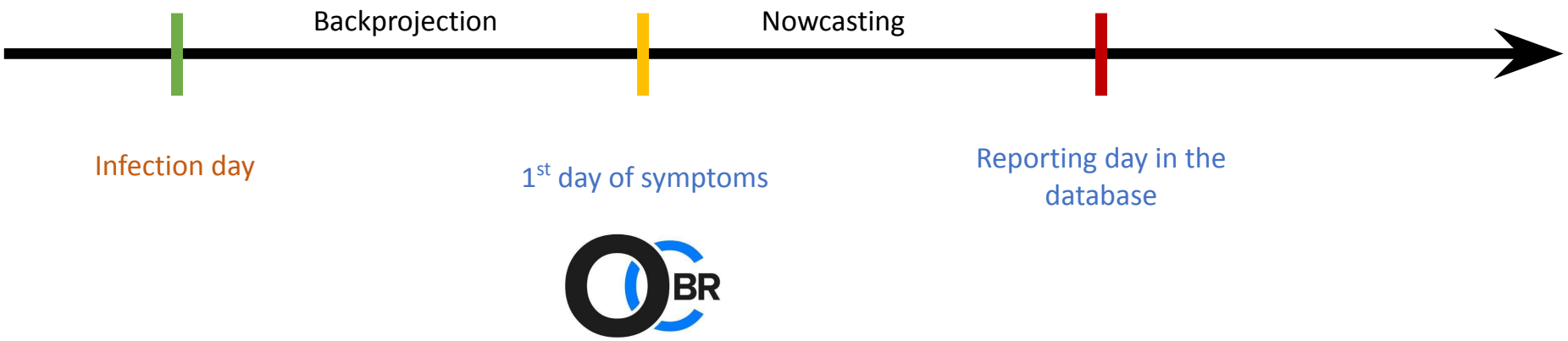
- Robert Koch Institute 2020
- Wallinga e Teunis 2004
- Bettencourt e Ribeiro 2008
- Cori et al 2013

Methods to estimate R_{eff}

- Robert Koch Institute 2020
- Wallinga e Teunis 2004
- Bettencourt e Ribeiro 2008
- **Cori et al 2013**
  - Time series of cases
  - Serial interval distribution (trasmission tree) - incorporates uncertainty in the distribution the time between the onset of symptoms in a primary case and the onset of symptoms in secondary cases

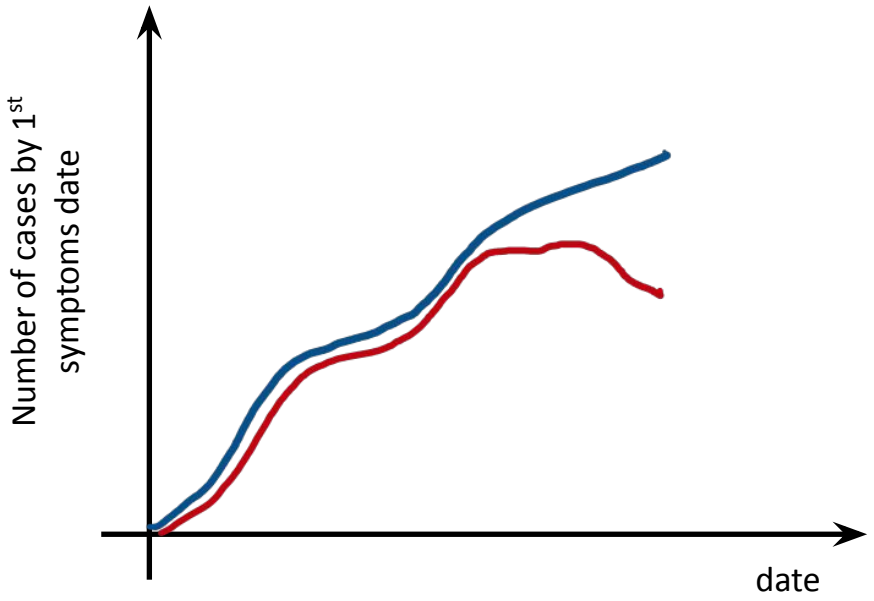
Correcting delays

- Corrections:



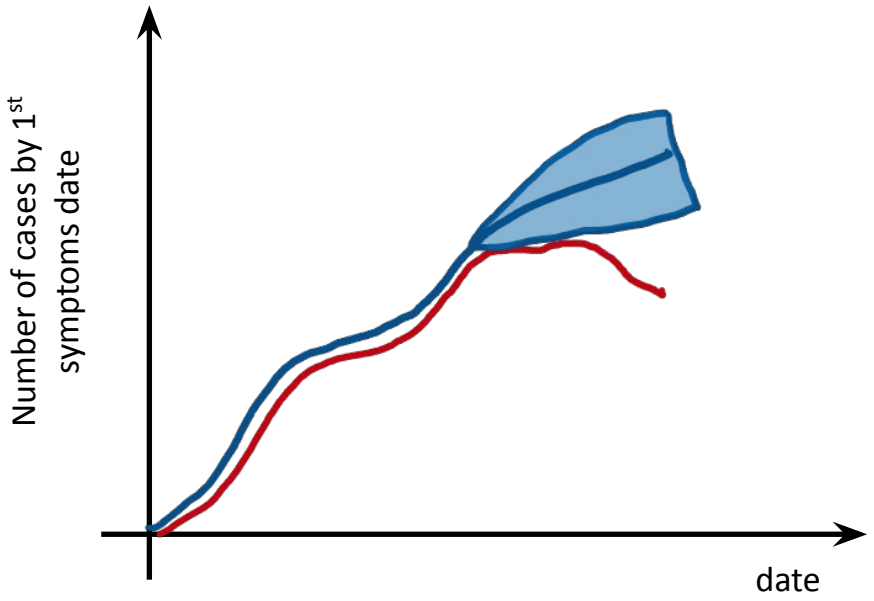
Nowcasting

Nowcasting estimates the number of cases that have already occurred (that already have a 1st day of symptoms) but that have not been reported in the database.



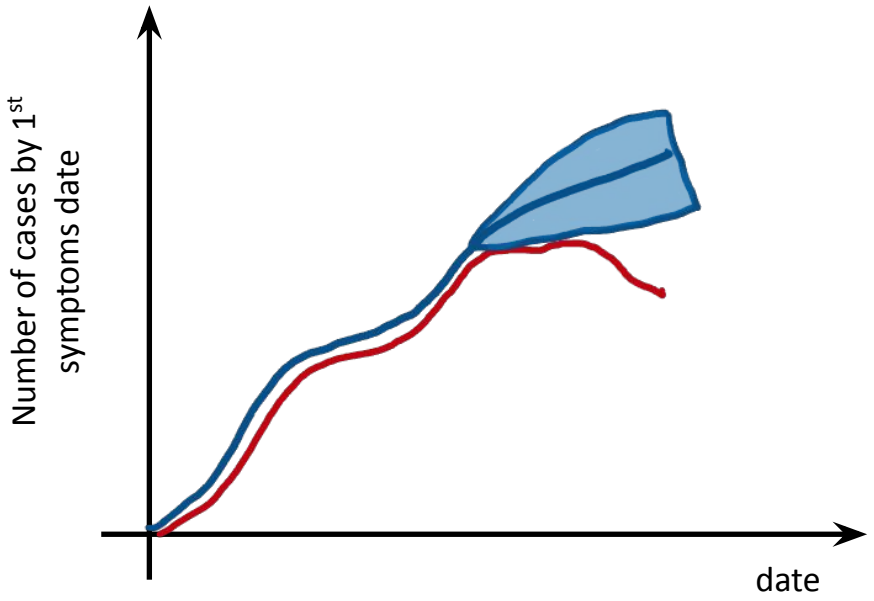
Nowcasting

Nowcasting estimates the number of cases that have already occurred (that already have a 1st day of symptoms) but that have not been reported in the database.



Nowcasting

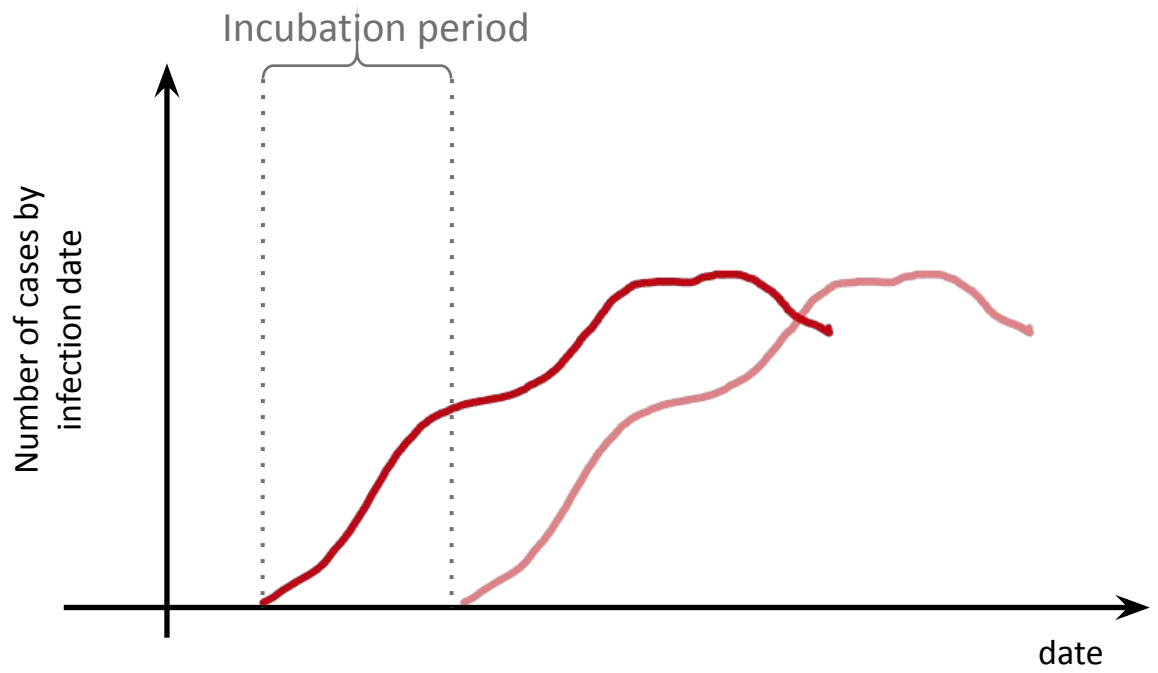
Nowcasting estimates the number of cases that have already occurred (that already have a 1st day of symptoms) but that have not been reported in the database.



- Nowcasting by Bayesian Smoothing (McGough et al 2020)
- Posterior series

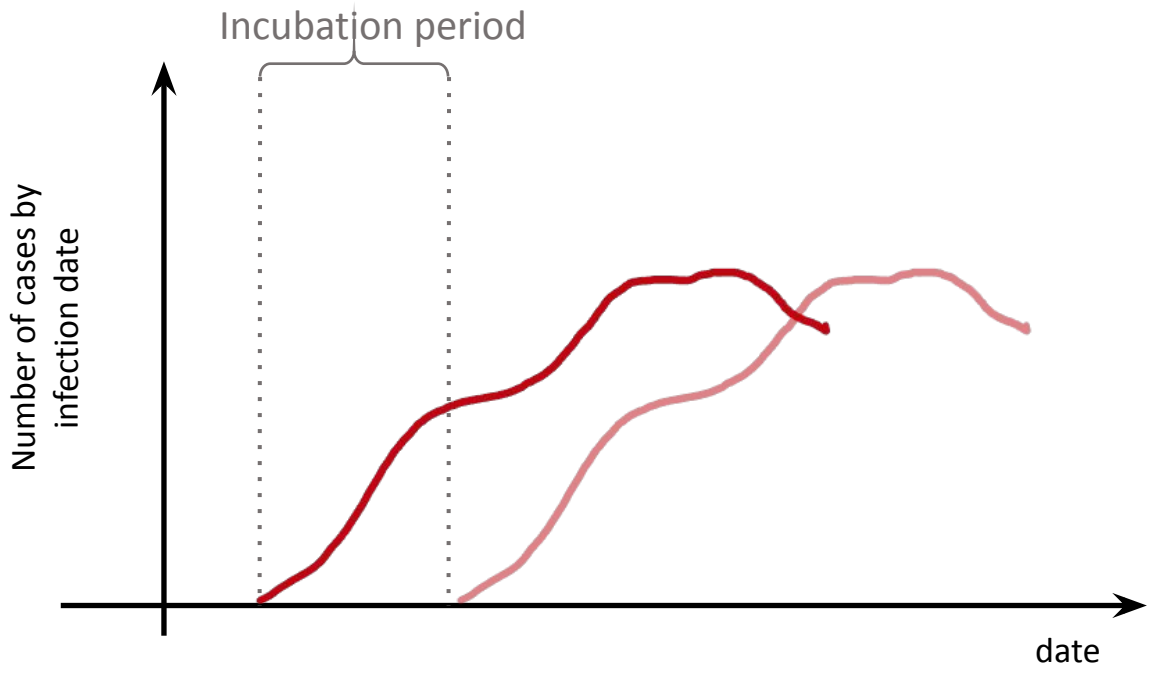
Back-projection

Back-projection estimates the number of cases by infection date, therefore including the incubation period (SARS-CoV2 ~ 5 days)

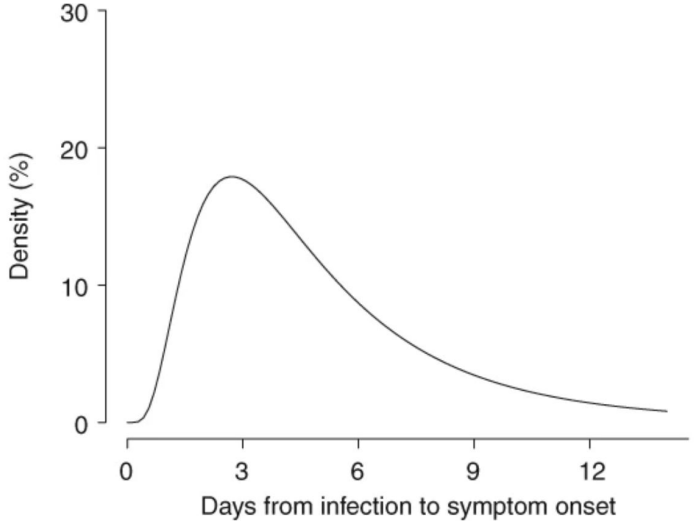


Back-projection

Back-projection deconvolution estimates the number of cases by infection date, therefore including the incubation period (SARS-CoV2 ~ 4-5 days)



- Expectation-Maximization Smoothing procedure (Becker et al 1991)
- Bootstrap simulation

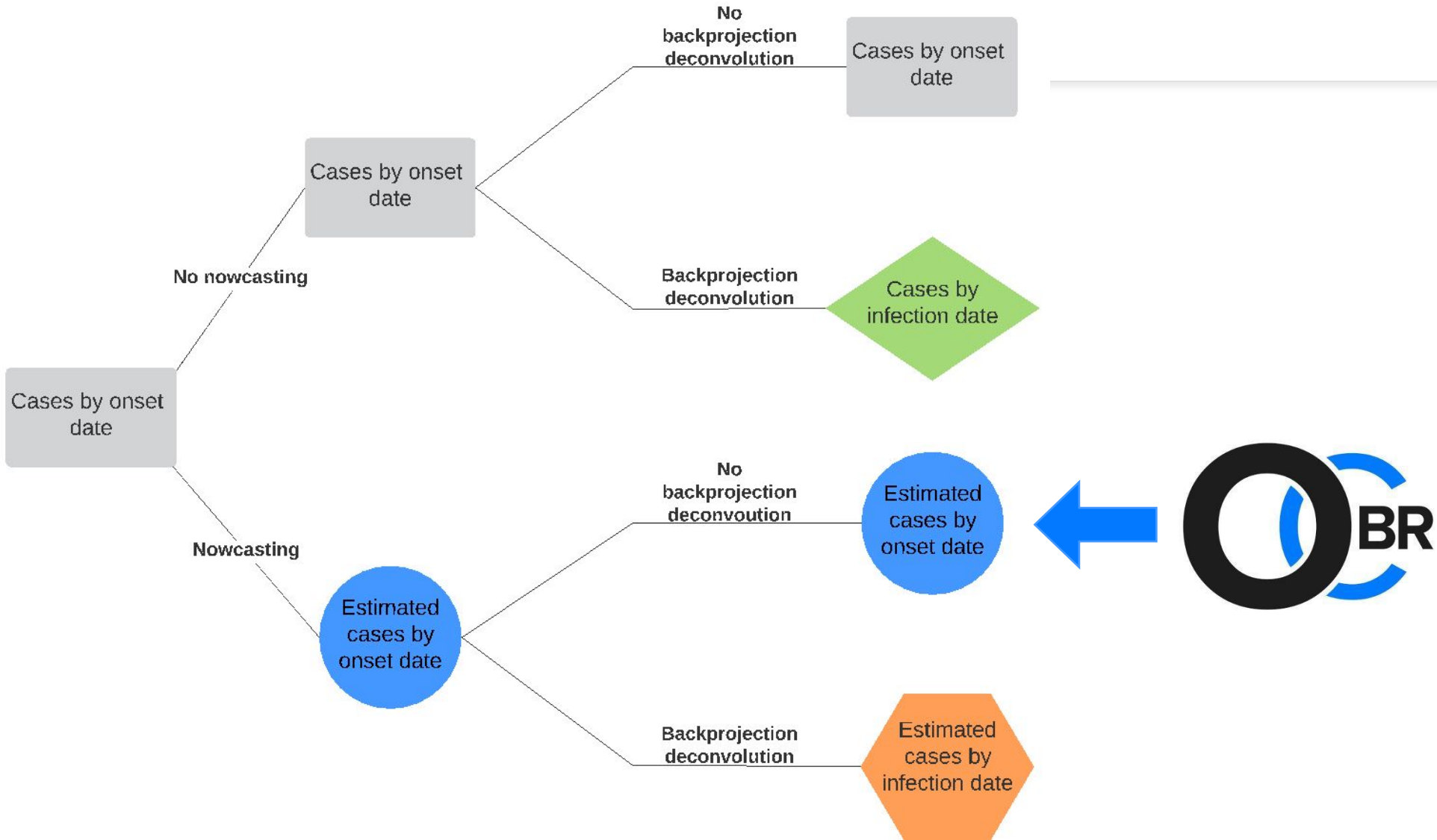


He et al 2020

Credible intervals of the R_{eff}

- ***Nowcasting CI:*** delays from de reporting system
- ***Backprojetion CI:*** delay from the incubation period.
- ***Transmission tree CI*****:** from the method proposed by Cori et al 2013 based on cases that will come from the transmission tree

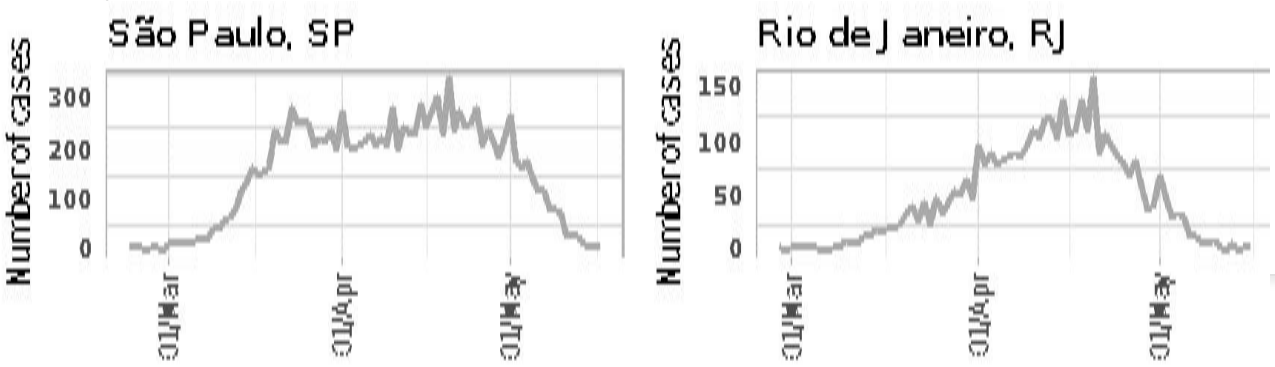
Different delay corrections



Results

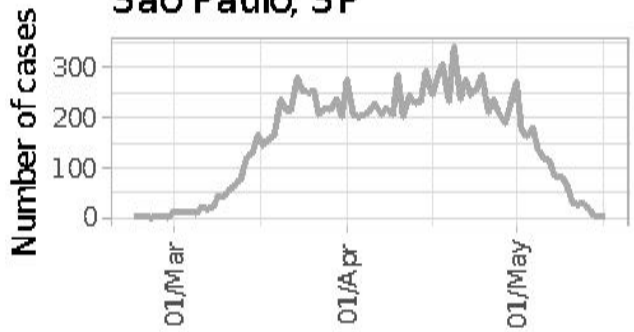
- SIVEP-Gripe (hospitalized cases)
- Positive cases diagnosed by RT-PCR
- Base from May 18,2020 (with a consolidated base of June 30,2020)
- State capitals:

  São Paulo (SP), Rio de Janeiro (RJ), Manaus (AM), Fortaleza (CE)

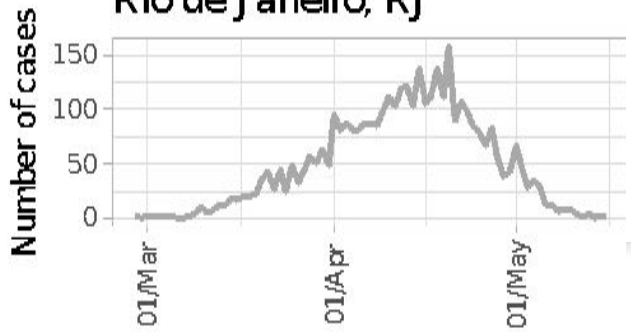

São Paulo, SP
Number of cases
300
200
100
0
01/Mar
01/Apr
01/May

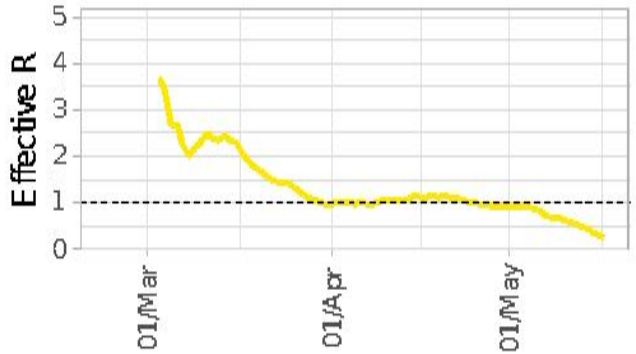
Rio de Janeiro, RJ
Number of cases
150
100
50
0
01/Mar
01/Apr
01/May

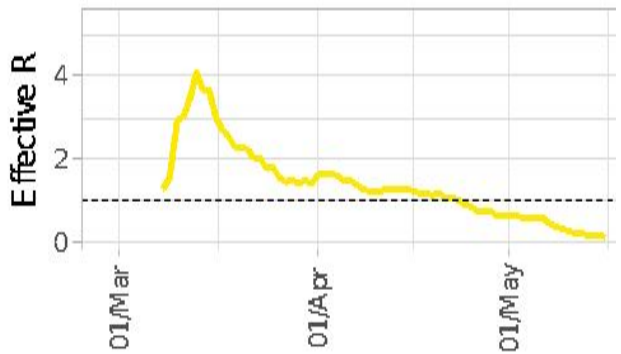
São Paulo, SP



Rio de Janeiro, RJ

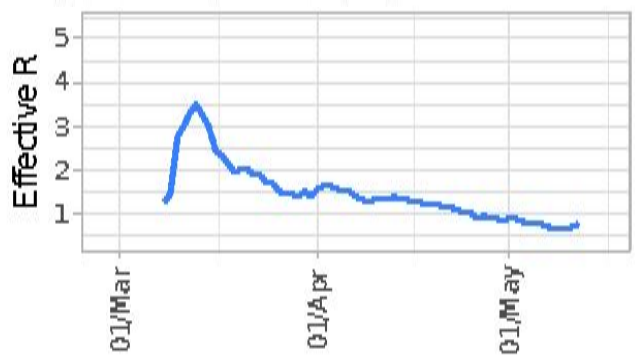


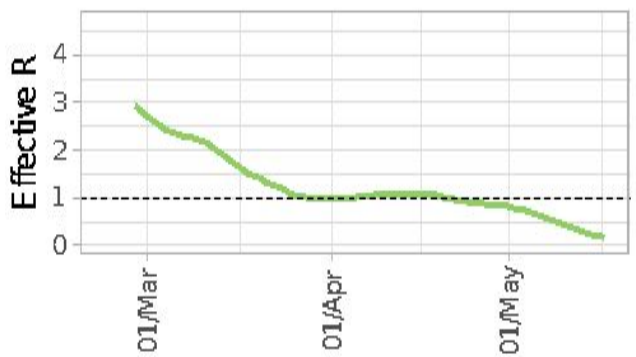


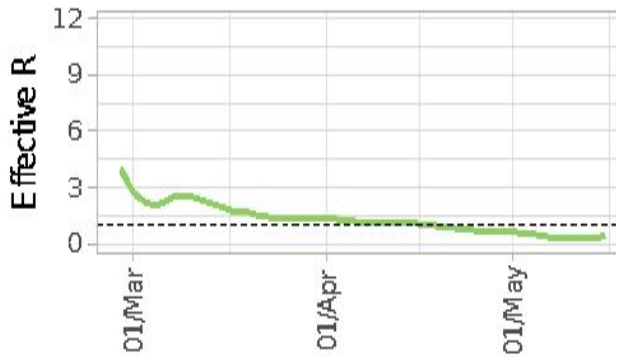


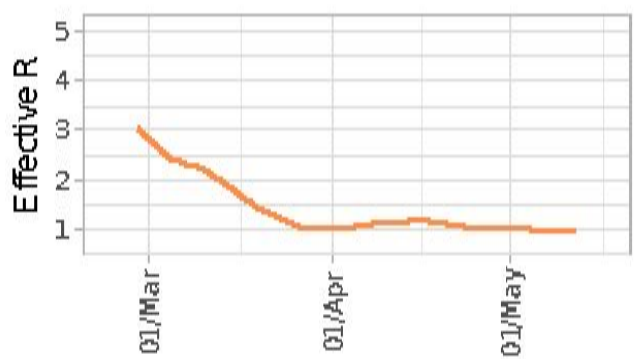
São Paulo, SP

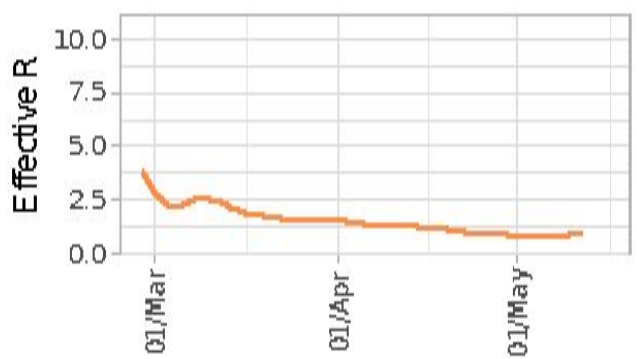
Rio de Janeiro, RJ



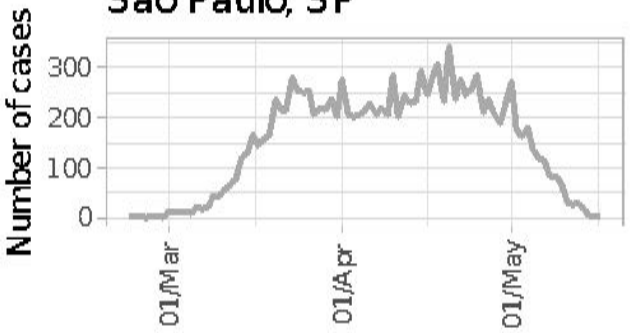




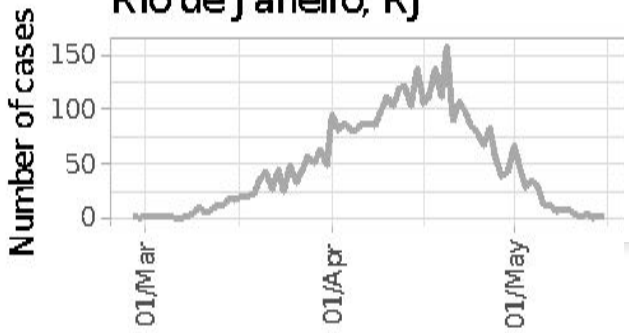


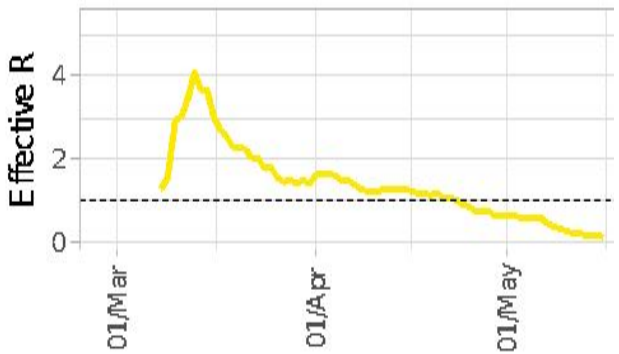


São Paulo, SP

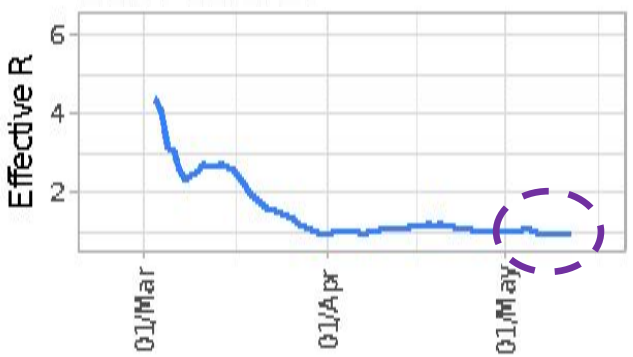


Rio de Janeiro, RJ

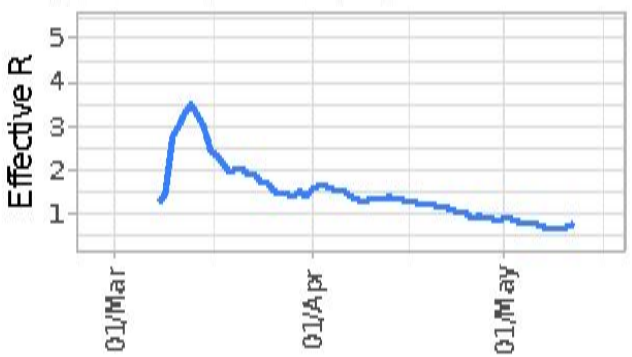


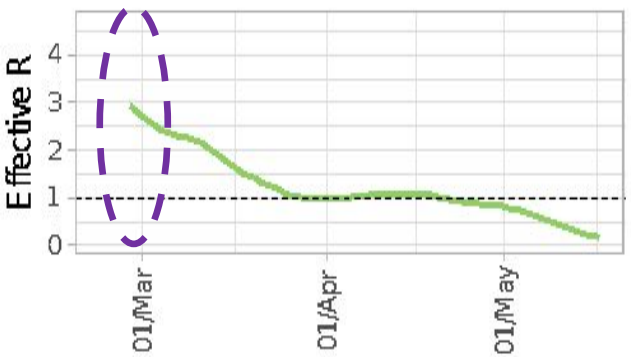


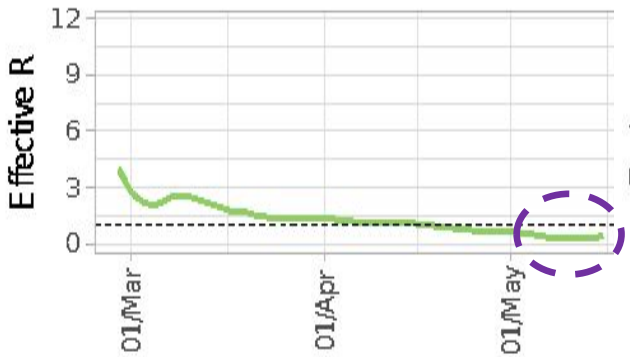
São Paulo, SP

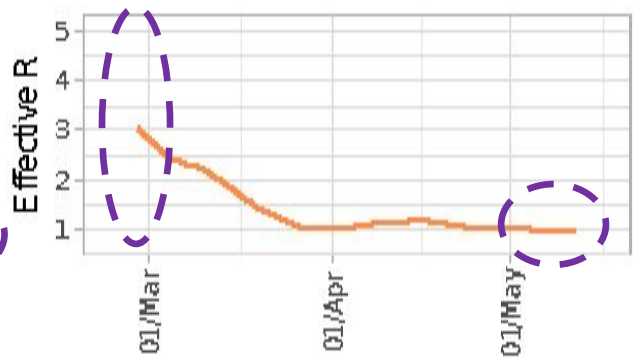


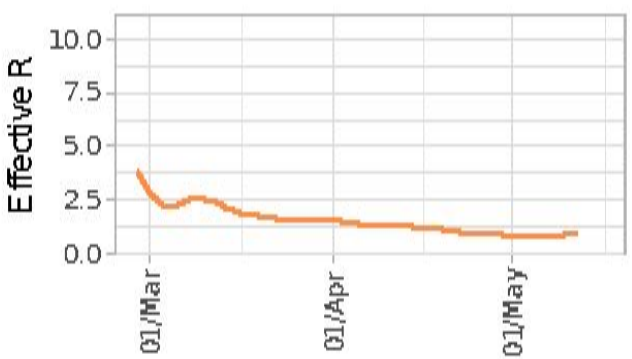
Rio de Janeiro, RJ

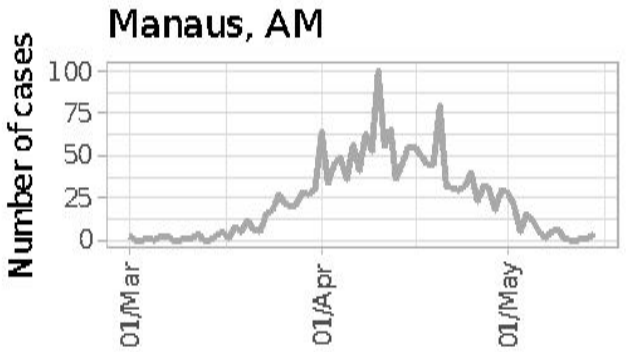




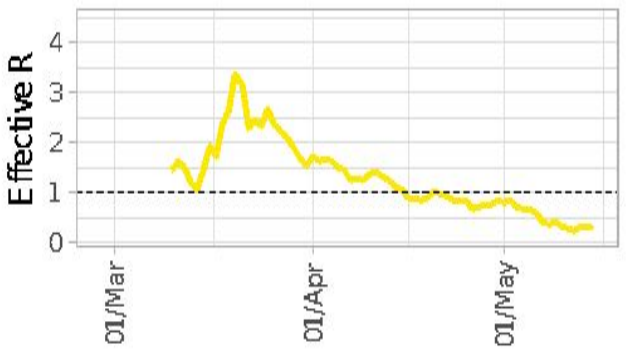


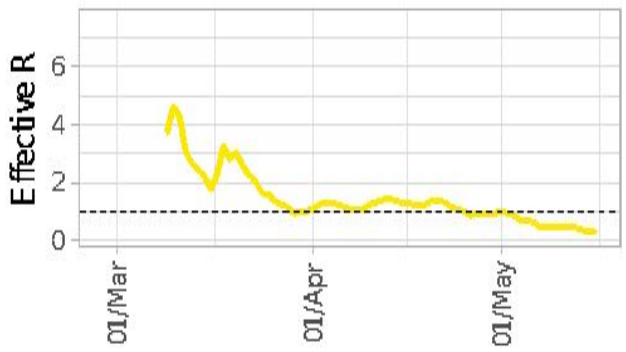


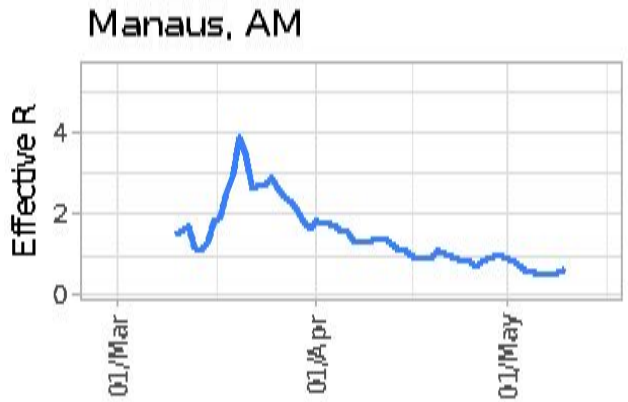


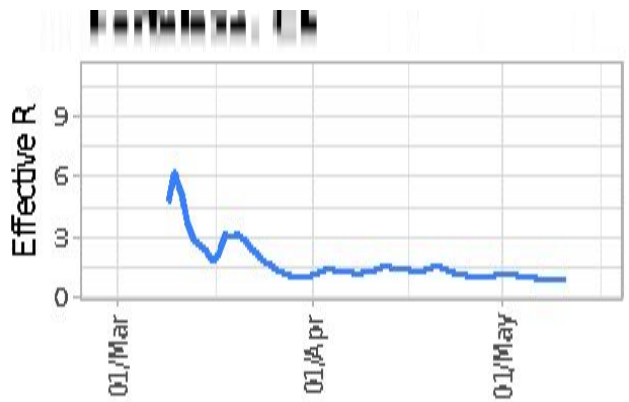

Manaus, AM
Number of cases
100
75
50
25
0
01/Mar
01/Apr
01/May

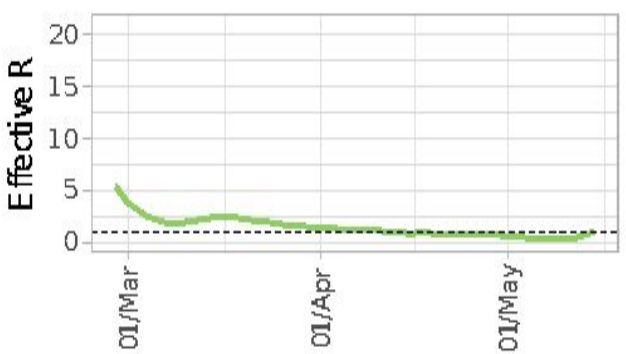

Fortaleza, CE
Number of cases
100
75
50
25
0
01/Mar
01/Apr
01/May

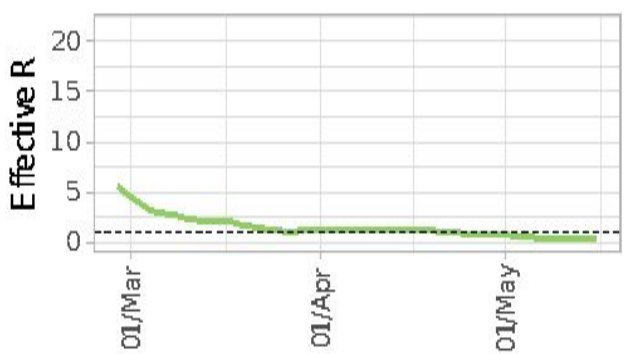

Effective R
4
3
2
1
0
01/Mar
01/Apr
01/May

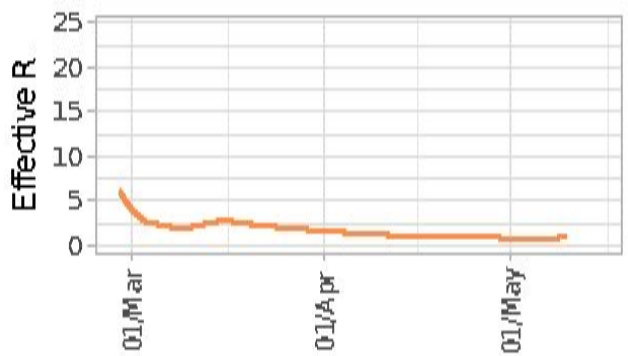

Effective R
6
4
2
0
01/Mar
01/Apr
01/May


Manaus, AM
Effective R
4
2
0
01/Mar
01/Apr
01/May


Effective R
9
6
3
0
01/Mar
01/Apr
01/May

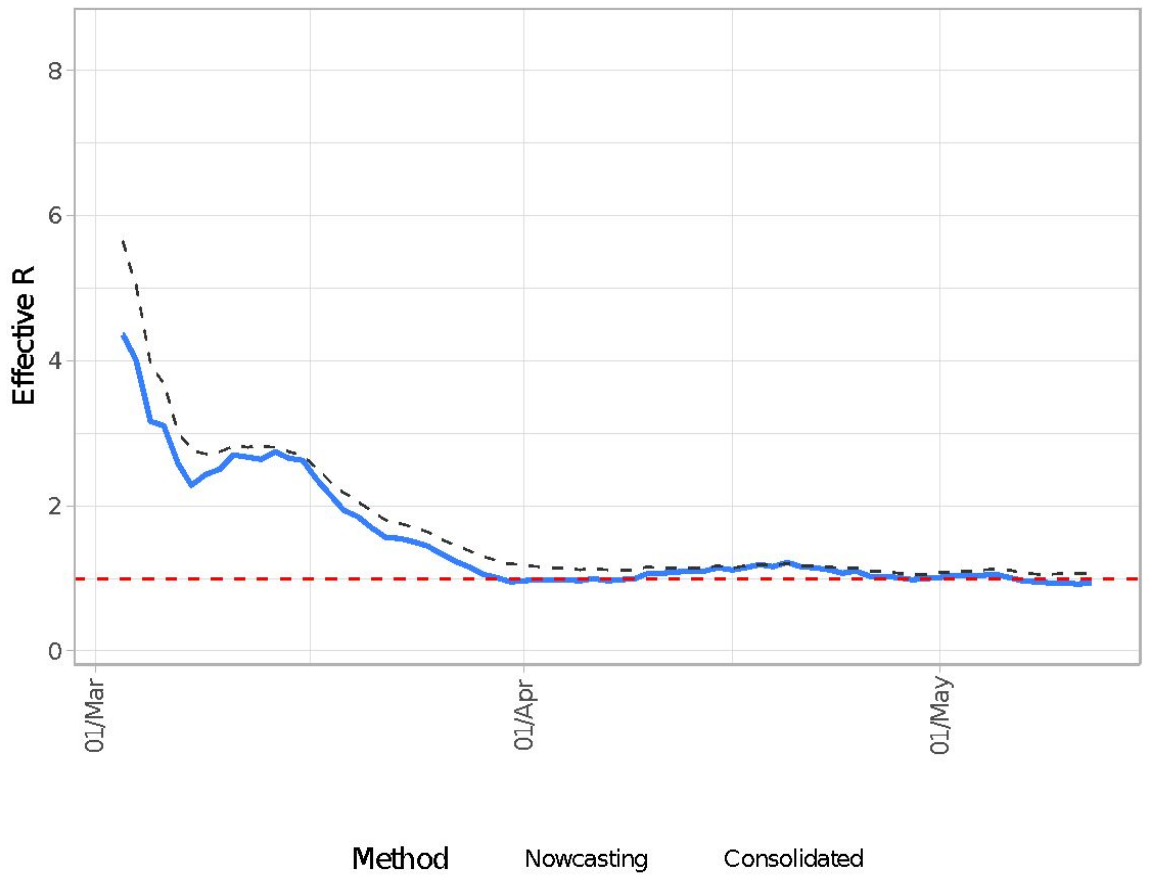

Effective R
20
15
10
5
0
01/Mar
01/Apr
01/May


Effective R
20
15
10
5
0
01/Mar
01/Apr
01/May

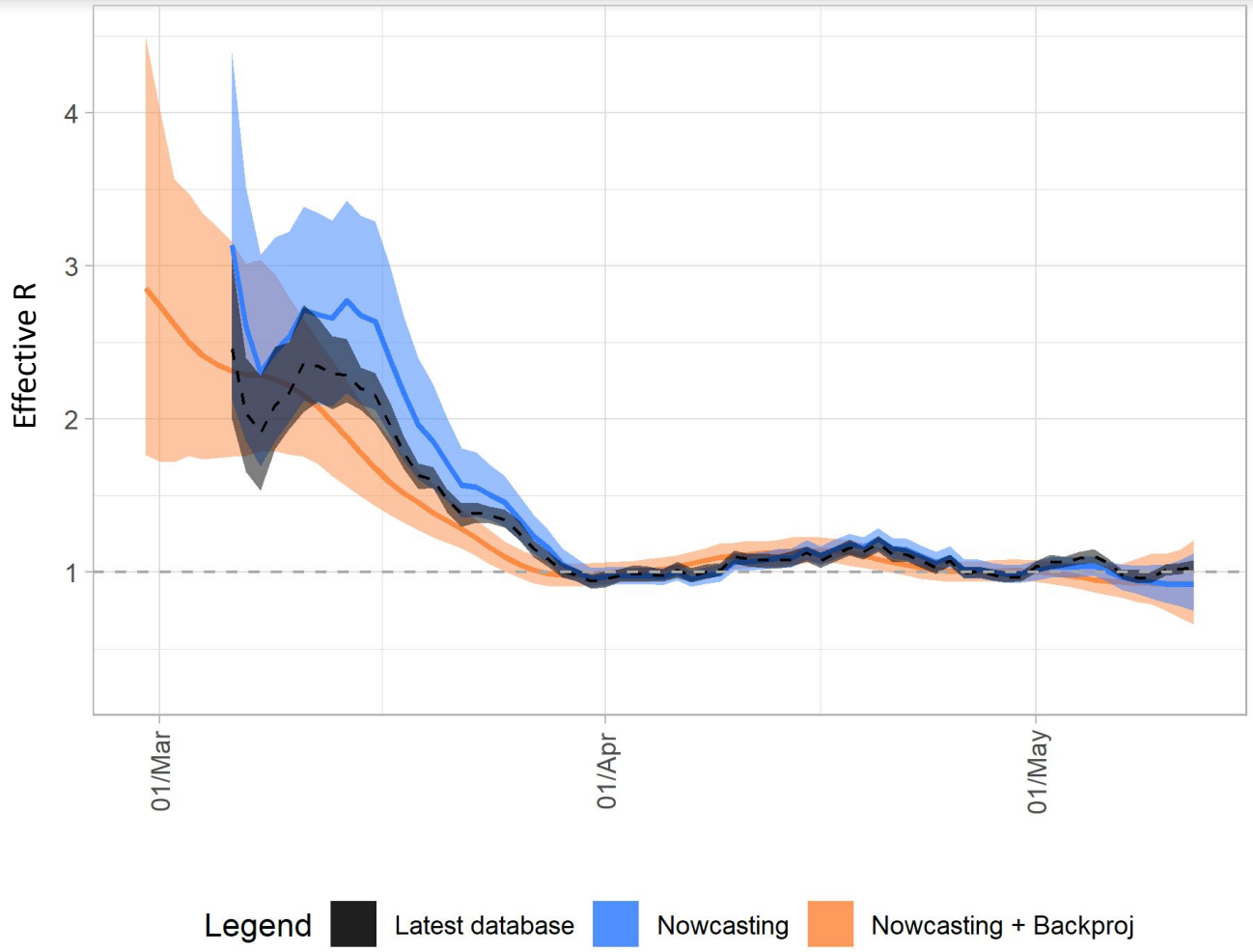

Effective R
25
20
15
10
5
0
01/Mar
01/Apr
01/May


Effective R
20
15
10
5
0
01/Mar
01/Apr
01/May

Results


Effective R
8
6
4
2
0
01/Mar
01/Apr
01/May
Method
Nowcasting
Consolidated

Results


Effective R
4
3
2
1
01/Mar
01/Apr
01/May
Legend
Latest database
Nowcasting
Nowcasting + Backproj

Discussion

- Estimate the R_t based on the notification date is not accurate
- Important delays that can be corrected: reporting system and incubation period
- Backprojection can affect the end of the R_t time series, decreasing the R_t values due to the lack of data feeding the end of the time series
- The nowcasting increases the CI of the R_t

Discussion

- Decisions made by policy makers and health authorities must consider the CI and not only the mean value. The entire range of the CI must be lower than 1 to be considered controlled.

- When using the back-projection correction, one should avoid using the most recent estimates of R_t (final temporal series).

- Other metrics should also be taken into account for public health decisions.

  values of R_t around 1 associated with a high number of new cases per day can easily fuel a new rise

Questions?

Reff estimate by Cori et al 2013 method

- We use a modified estimate_R function from EpiEstim R package
- We use a sliding window of 6 days
- Serial interval by Nishiura et al 2020 for MCMC estimation for the transmission tree

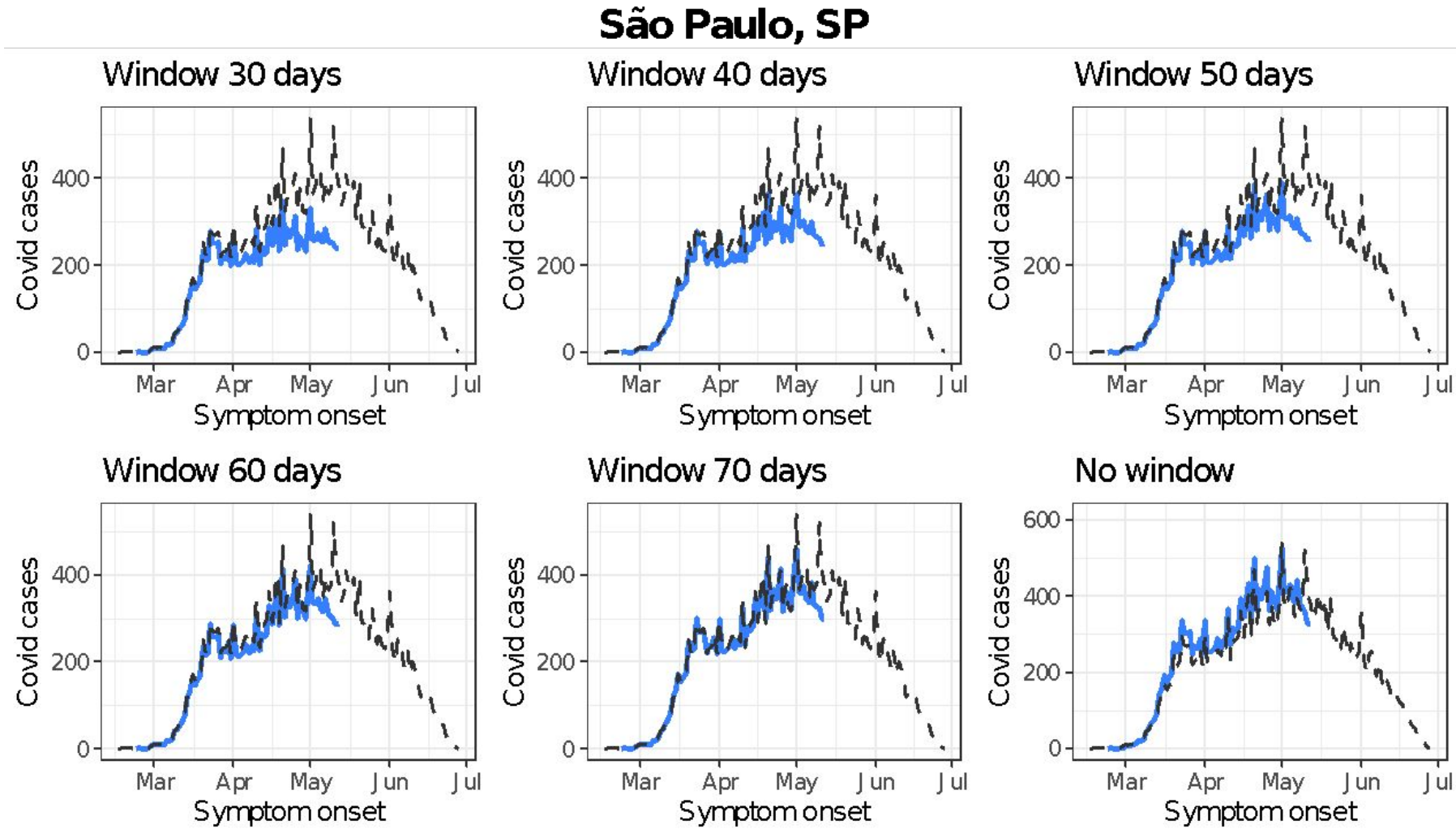
Nowcasting

- We use a modified function from the NobBs R package (McGough et al 2020)
- Trim of 5 days in the time series end
- Time window of delay:

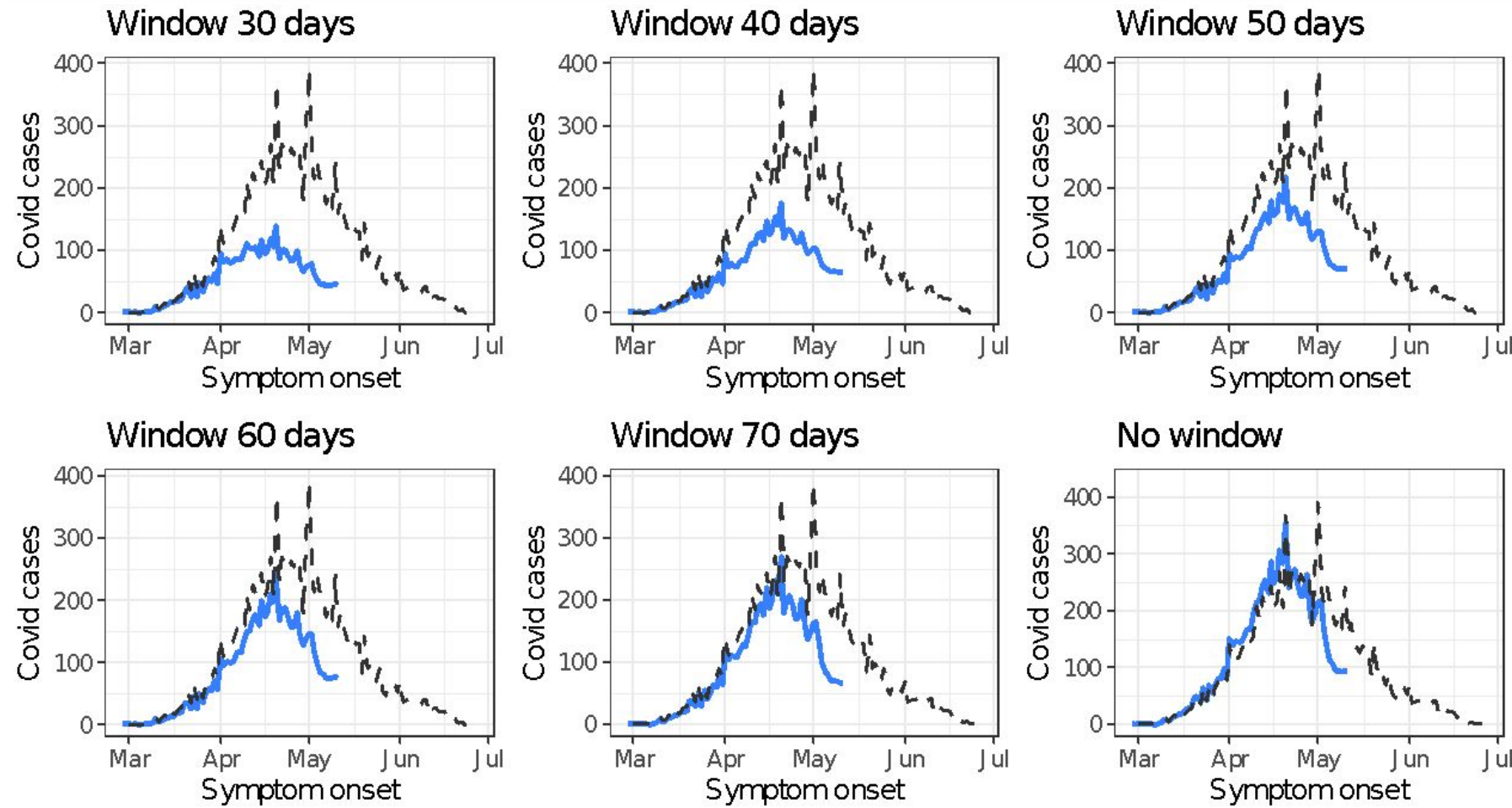
  São Paulo (SP): 70 days

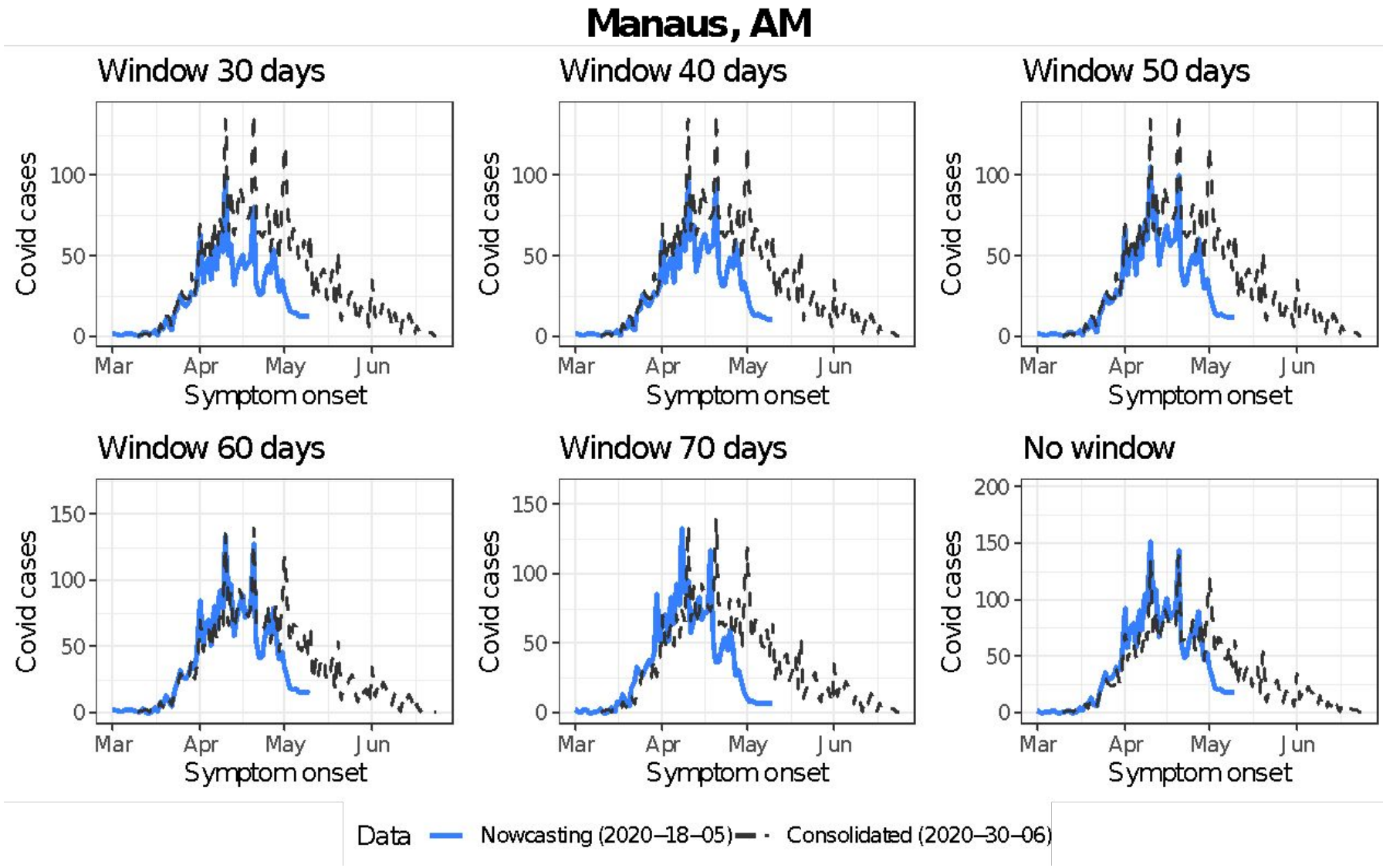
  Manaus (AM): 60 days.

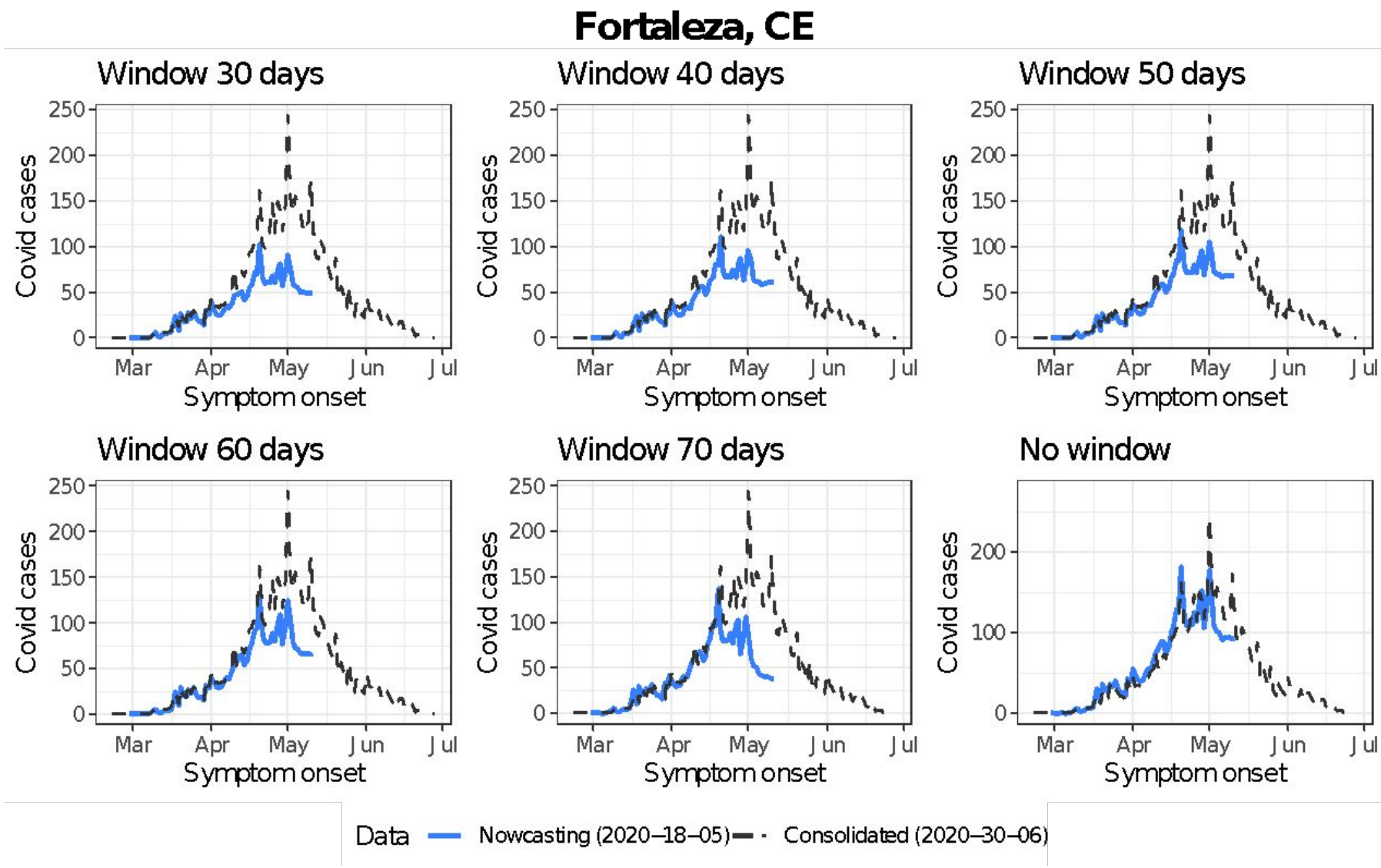
  Rio de Janeiro (RJ) and Fortaleza (CE) no window.


São Paulo, SP
Window 30 days
Window 40 days
Window 50 days
Window 60 days
Window 70 days
No window
Covid cases
0
200
400
600
Mar
Apr
May
Jun
Jul
Symptom onset
Data
Nowcasting (2020–18–05)
Consolidated (2020–30–06)

Rio de Janeiro, RJ




Manaus, AM
Window 30 days
Window 40 days
Window 50 days
Window 60 days
Window 70 days
No window
Covid cases
Symptom onset
Mar
Apr
May
Jun
Data
Nowcasting (2020–18–05)
Consolidated (2020–30–06)


Fortaleza, CE
Window 30 days
Window 40 days
Window 50 days
Window 60 days
Window 70 days
No window
Covid cases
Symptom onset
Mar
Apr
May
Jun
Jul
Data
Nowcasting (2020–18–05)
Consolidated (2020–30–06)

Back-projection

- The incidence data is corrected by discounting delays from infection to the first day of symptoms using an incubation distribution defined by a lognormal (mean=5.2 days and 95% CI = [4.1, 7.0] days (He et al 2020).

- In contrast to the nowcasting method, which includes cases considering the delay of the notification system, {\fla the back-projection method just estimate the shift in the time series backwards with no addition of cases

Back-projection

- The Expectation-Maximization-Smoothing procedure of Becker et al (1991} gives a sample estimation of the mean number of individuals infected at time ***t*** and is denoted by λ_t.

- The sample estimation must be accompanied by a confidence interval which can be estimated by a bootstrap method (see Yip 2008).

- We choose to return a sample draw from a Poisson distribution with mean λ_t after we have back-projected our data.

Back-projection

- This procedure is repeated for 1,000 posterior nowcasted series. The sample error for the λ_t computation is incorporated when we consider a large number of back-projected samples of a nowcasted series.

- The complete routine is implemented in C++ and is already integrated with R via the Rcpp package

More information and analysis in our website

https://covid19br.github.io/

Observatório COVID-19 BR

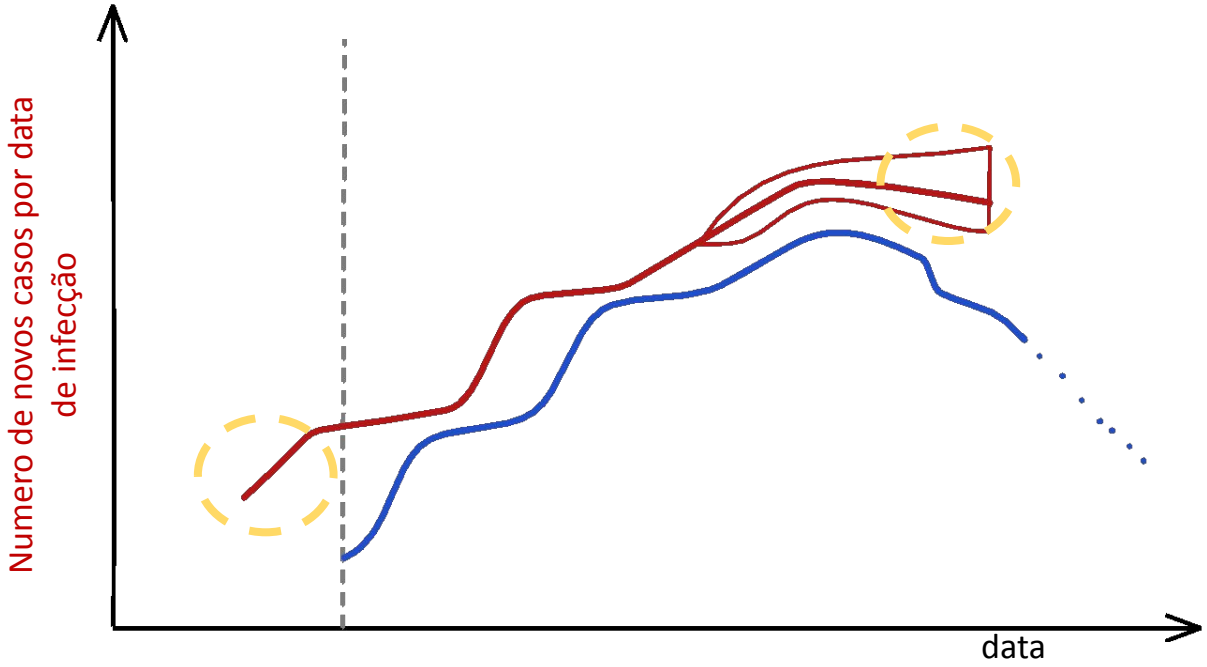
https://covid19br.github.io/

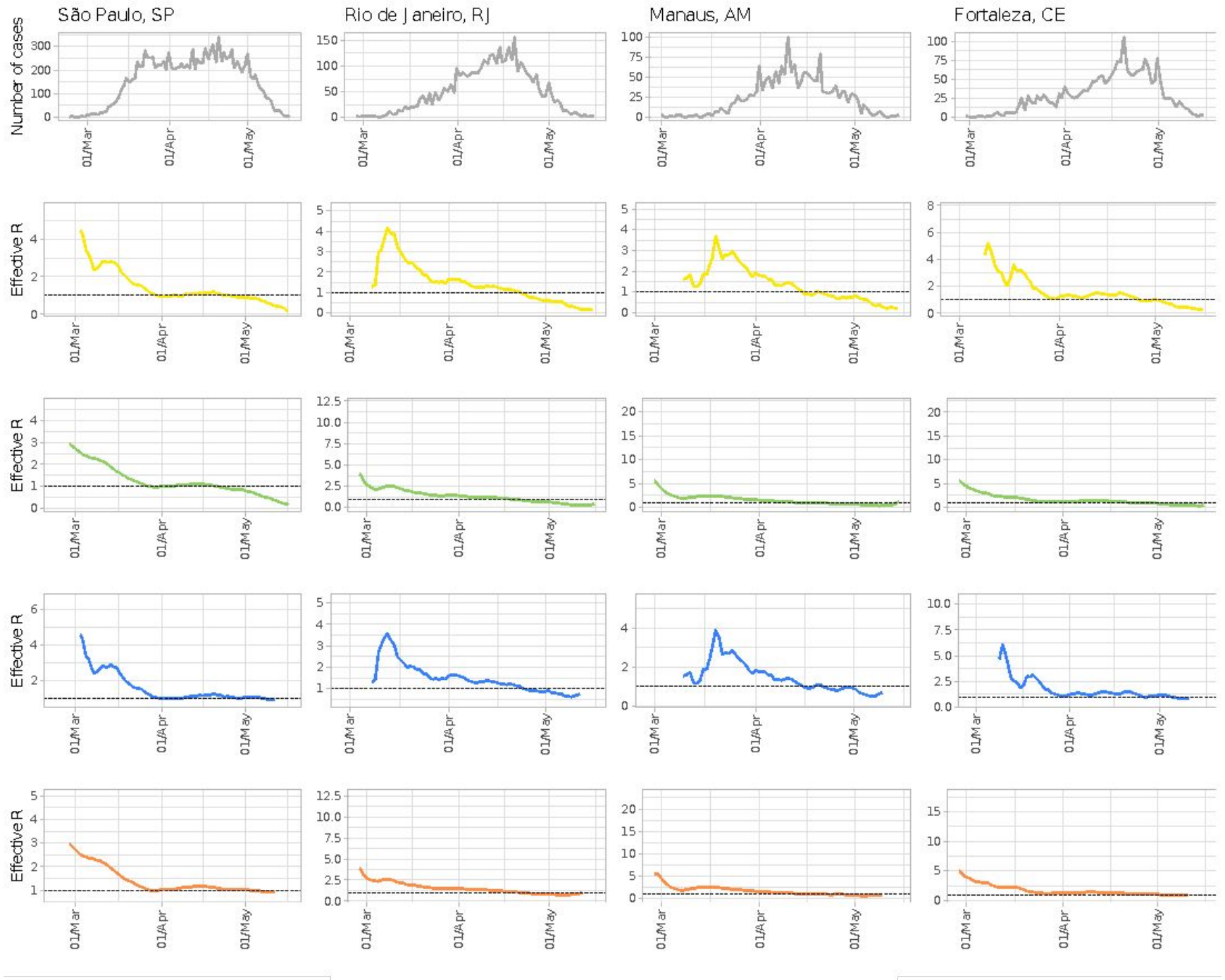
Contact:

Instagram, Facebook, **Twitter**: @obscovid19br

Correções do dia de ocorrência dos eventos

- Uma outra correção possível é deslocar a série para trás de acordo com um distribuição do número de dias entre o dia da infecção e o 1o sintoma. O método é geralmente chamado de *Backprojection deconvolution.*




São Paulo, SP
Rio de Janeiro, RJ
Manaus, AM
Fortaleza, CE
Number of cases
Effective R
01/Mar
01/Apr
01/May
Method
Cases
Backprojection
Nowcasting
Nowcasting + Backprojection