III SIGMAT

Simpósio Integrado de Matemática

Universidade Estadual de Ponta Grossa

Ponta Grossa, PR, Novembro de 2020

Notas sobre *números de reprodução*

para Covid-19 ou outras epidemias

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MAIS DETALHES:

P. Zingano, J. Zingano, A. Silva and C. Zingano,
Defining and computing reproduction numbers to monitor the outbreak of Covid-19 or other epidemics, DOI: 10.20944/preprints202006.0370.v1

https://www.preprints.org/manuscript/202006.0370/v1

PROGRAMA MATLAB:

https://drive.google.com/drive/u/1/folders/16kLxlZyqH-QATOLQI6QWTx7qZnL3IoCP

Anne Cori, Neil M. Ferguson, C. Fraser and S. Cauchemez, *A new framework and software to estimate time-varying reproduction numbers during epidemics*, American Journal of Epidemiology, **178** (2013), 1505-1512.

R. N. Thompson, J. E. Stockwin, R. D. van Gaalen, J. A. Polonsky, Z. N. Kamvar, P. A. Demarsh, E. Dahlqwist, S. Li, E. Miguel, T. Jombart, J. Lessler, S. Cauchemez and A. Cori, *Improved inference of time-varying reproduction numbers during infectious disease outbreaks*, Epidemics, **29** (2019), DOI: 10.1016/j.epidem.2019.100356.

K. M. Gostic, L. Mcgough, E. Baskerville, S. Abbott, K. Joshi, C. Tedijanto, R. Kahn, R. Niehus, J. Hay, P. de Salazar, S. Meakin, J. Munday, N. I. Bosse, K. Sherrat, N. Robin, L. F. White, J. S. Huisman, T. Stadler, J. Wallinga, S. Funk, M. Lipsitch and S. Cobey, *Practical considerations for measuring the effective reproductive number Rt*, MedRxiv (2020), 1-21, DOI: 10.1101/2020.06.18.20134858.

B. Ridenhour, J. M. Kowalik and D. K. Shay, *Unraveling R_0: Considerations for public health applications*, American Journal of Public Health, **108** (2018), S445-S454, DOI: 10.2105/AJPH.2013.301704.

M. Martcheva, *An Introduction to Mathematical Epidemiology*,
Springer, New York, 2015.

Modelo matemático (SEIR determinístico):

$$
\begin{cases}
\dfrac{dS}{dt} = -\beta(t)\,\dfrac{S(t)}{N}\,I(t), \\[2mm]
\dfrac{dE}{dt} = \beta(t)\,\dfrac{S(t)}{N}\,I(t) - \delta\,E(t), \\[2mm]
\dfrac{dI}{dt} = \delta\,E(t) - (r(t) + \gamma)\,I(t), \\[2mm]
\dfrac{dR}{dt} = \gamma\,I(t), \\[2mm]
\dfrac{dD}{dt} = r(t)\,I(t),
\end{cases}
$$

A informar: $\beta(t)$, δ, $r(t)$, γ,
$S(t_0)$, $E(t_0)$, $I(t_0)$, $R(t_0)$, $D(t_0)$

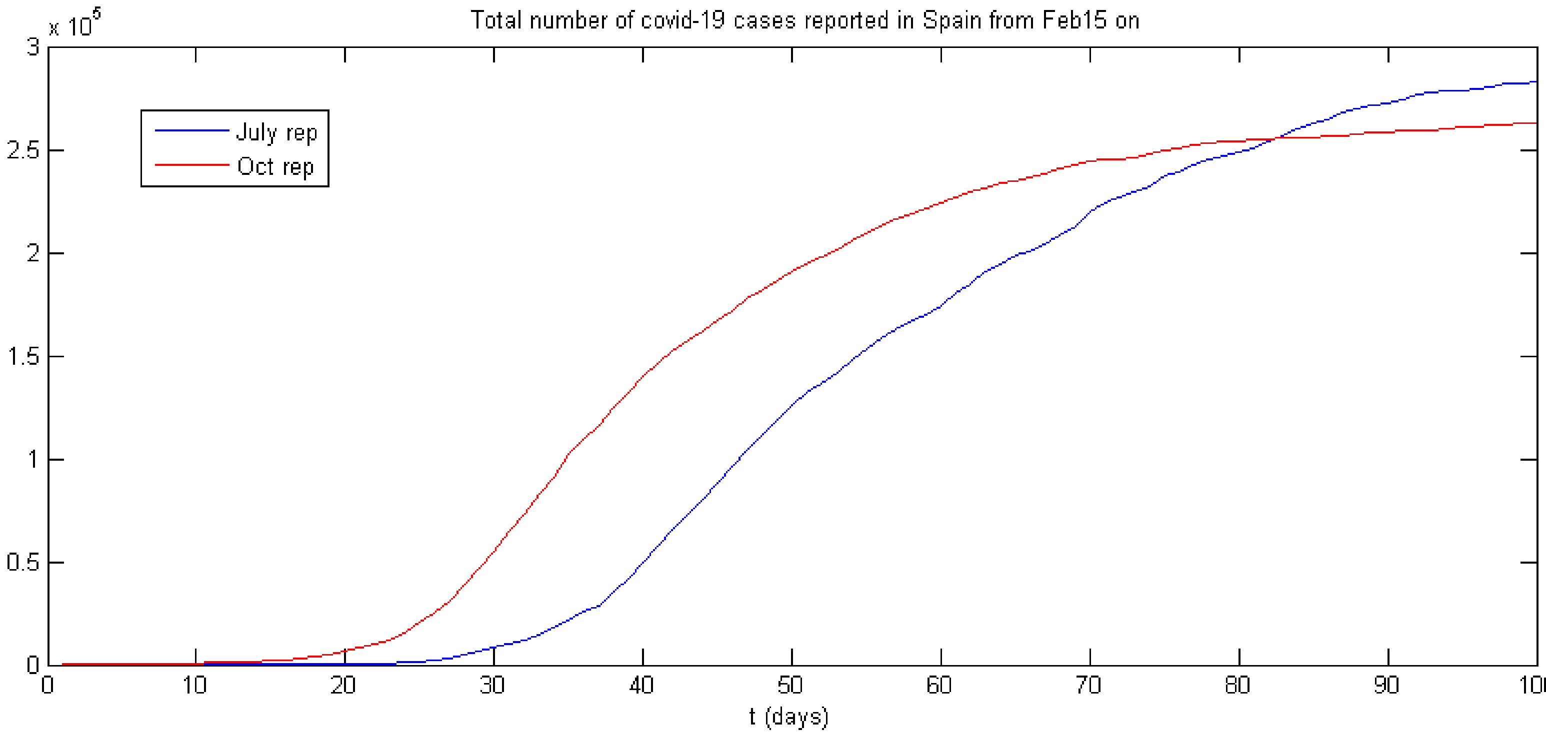
Dados: N, $D(t_i)$, $S(t_i)$, $1 \leq i \leq m$

Modelo matemático (SEIR determinístico):

$$\begin{cases} \dfrac{dS}{dt} = -\beta(t)\,\dfrac{S(t)}{N}\,I(t), \\[2mm] \dfrac{dE}{dt} = \beta(t)\,\dfrac{S(t)}{N}\,I(t) - \delta\,E(t), \\[2mm] \dfrac{dI}{dt} = \delta\,E(t) - (r(t) + \gamma)\,I(t), \\[2mm] \dfrac{dR}{dt} = \gamma\,I(t), \\[2mm] \dfrac{dD}{dt} = r(t)\,I(t), \end{cases}$$

A informar: $\beta(t)$, δ, $r(t)$, γ,
$S(t_0)$, $E(t_0)$, $I(t_0)$, $R(t_0)$, $D(t_0)$

Dados: N, $D(t_i)$, $S(t_i)$, $1 \leq i \leq m$



Mais detalhes:

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Defining and computing reproduction numbers to monitor the outbreak of Covid-19 or other epidemics, DOI: 10.20944/preprints202006.0370.v1

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Programa matlab:

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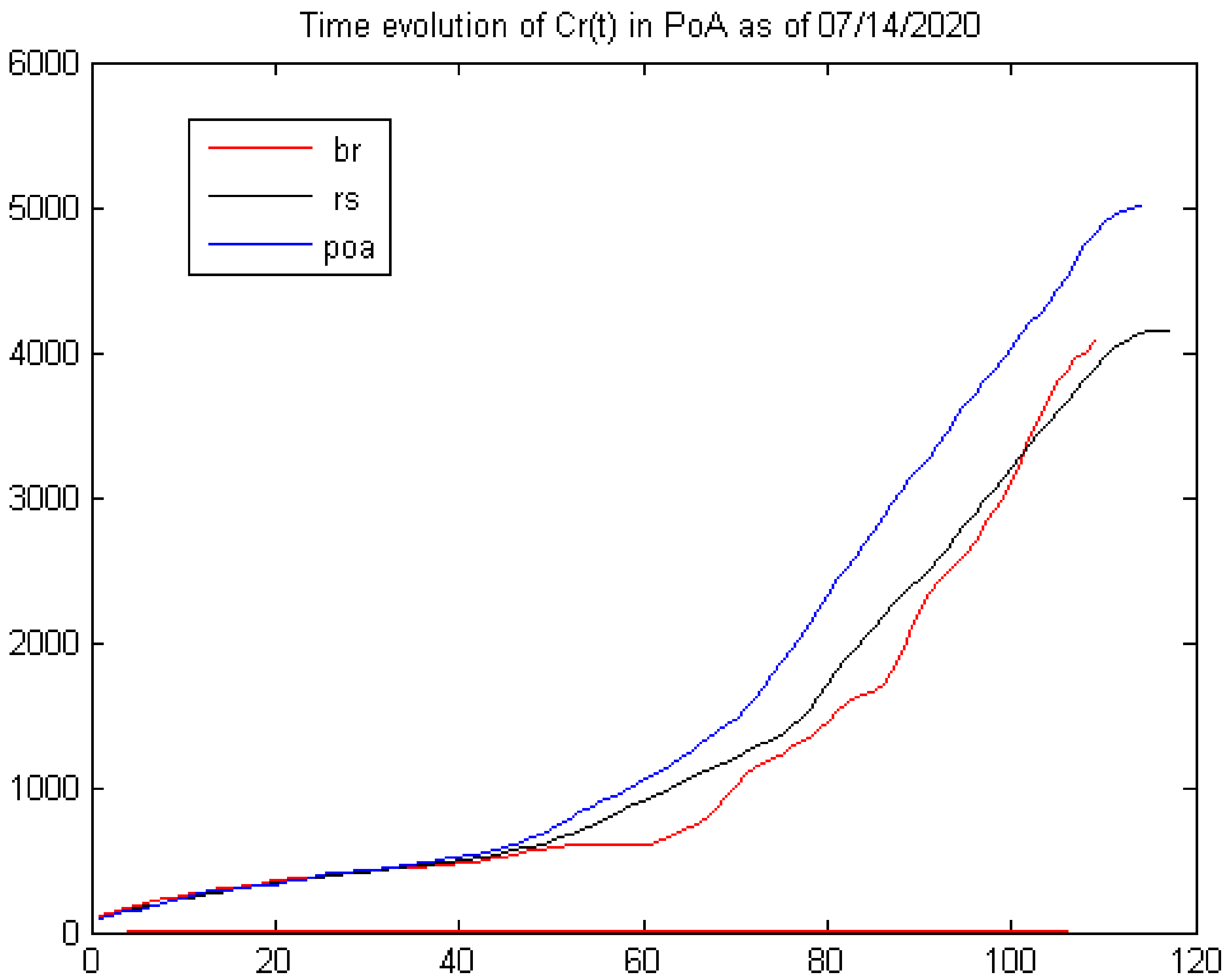
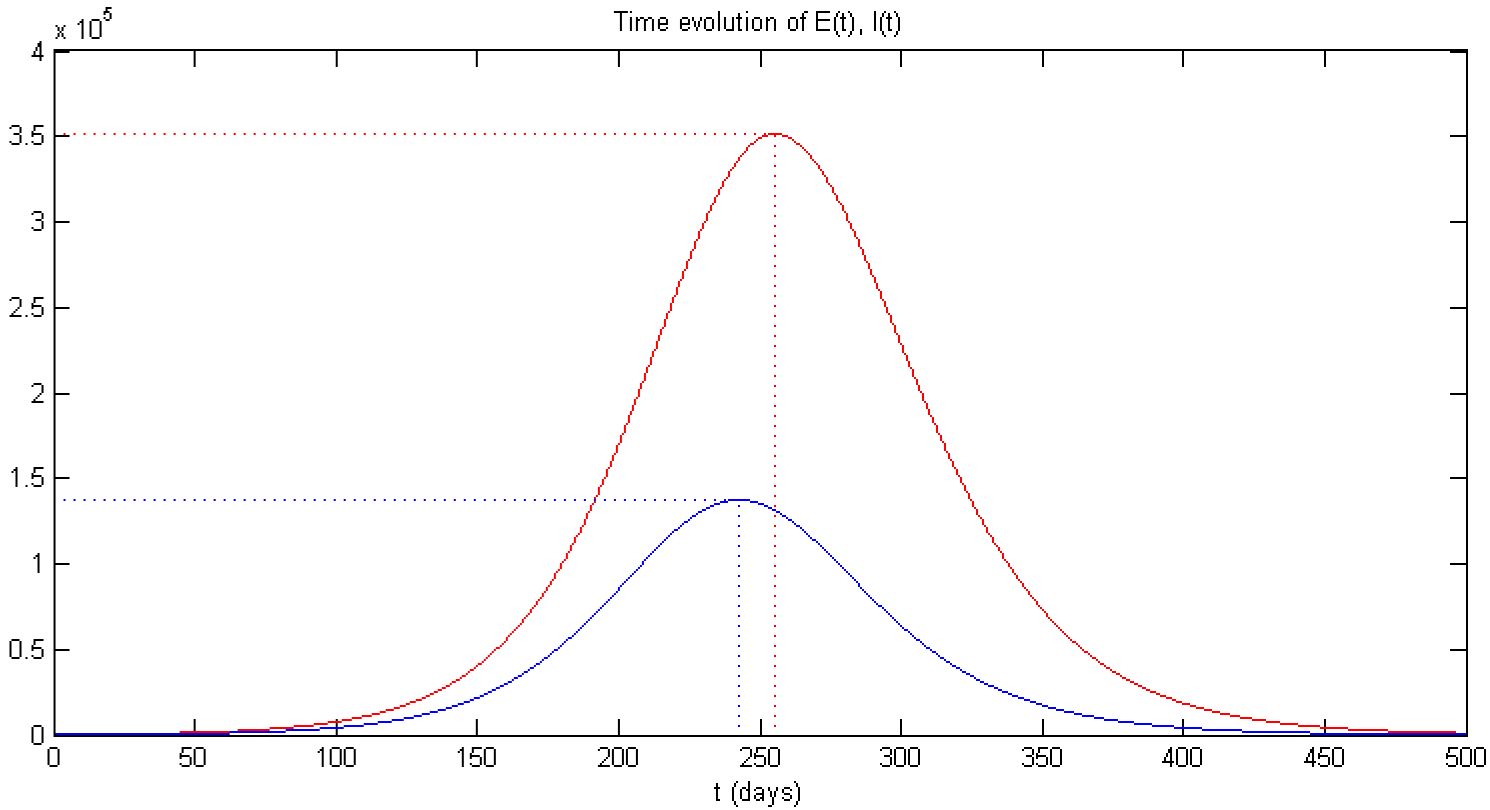
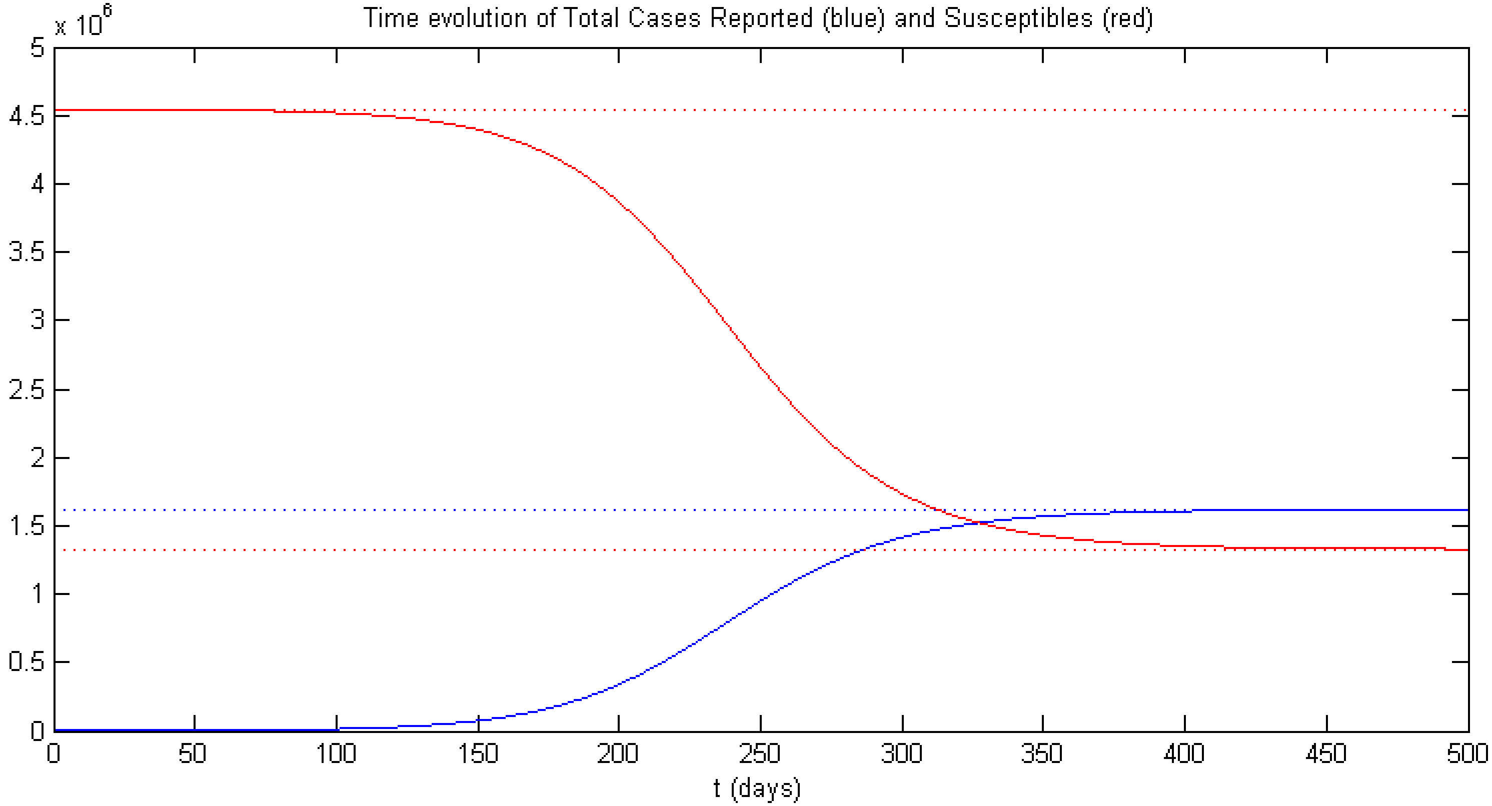
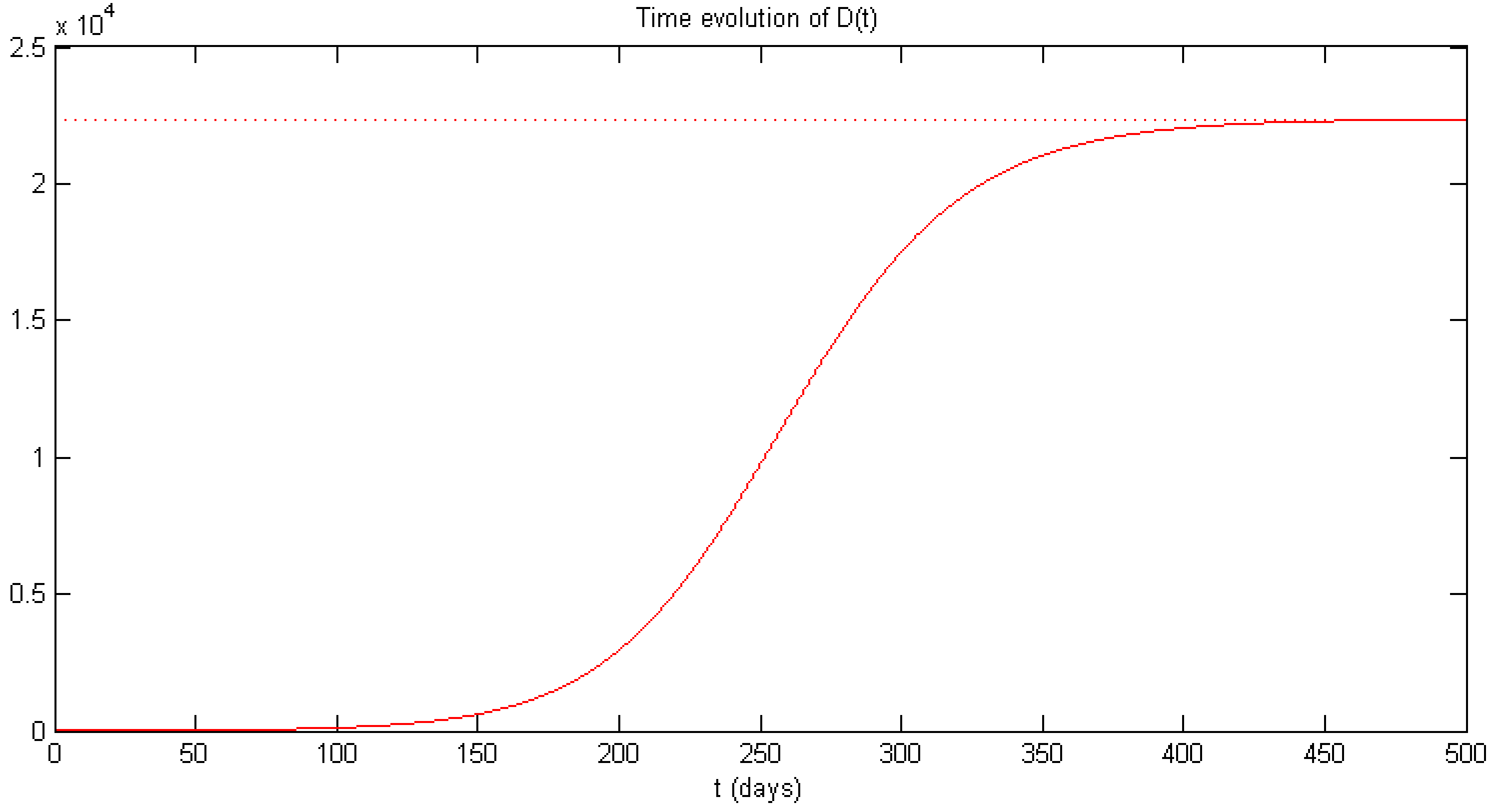


Time evolution of Cr(t) in PoA as of 07/14/2020
6000
5000
4000
3000
2000
1000
0
0
20
40
60
80
100
120
br
rs
poa


Time evolution of E(t), I(t)
x 10^5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
50
100
150
200
250
300
350
400
450
500
t (days)


Time evolution of Total Cases Reported (blue) and Susceptibles (red)
x 10^6
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
50
100
150
200
250
300
350
400
450
500
t (days)


Time evolution of D(t)
x 10^4
2.5
2
1.5
1
0.5
0
0
50
100
150
200
250
300
350
400
450
500
t (days)

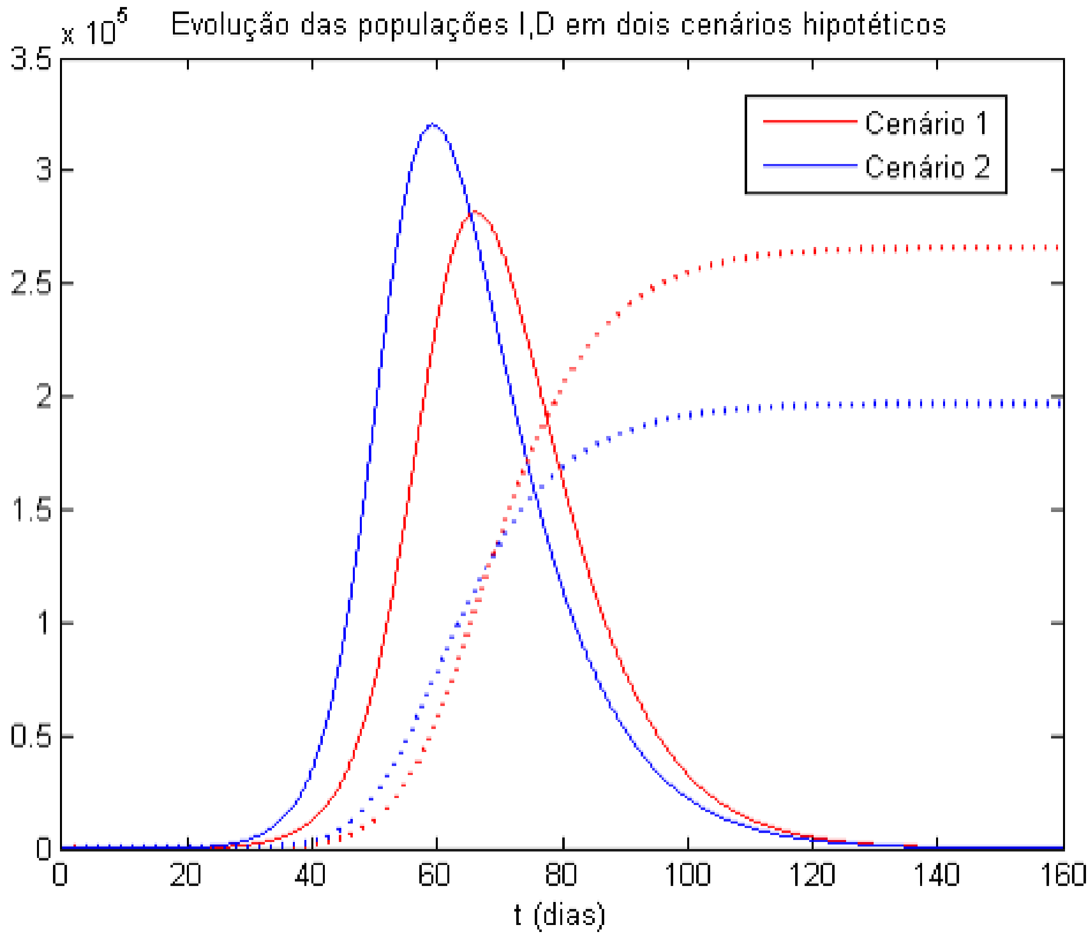
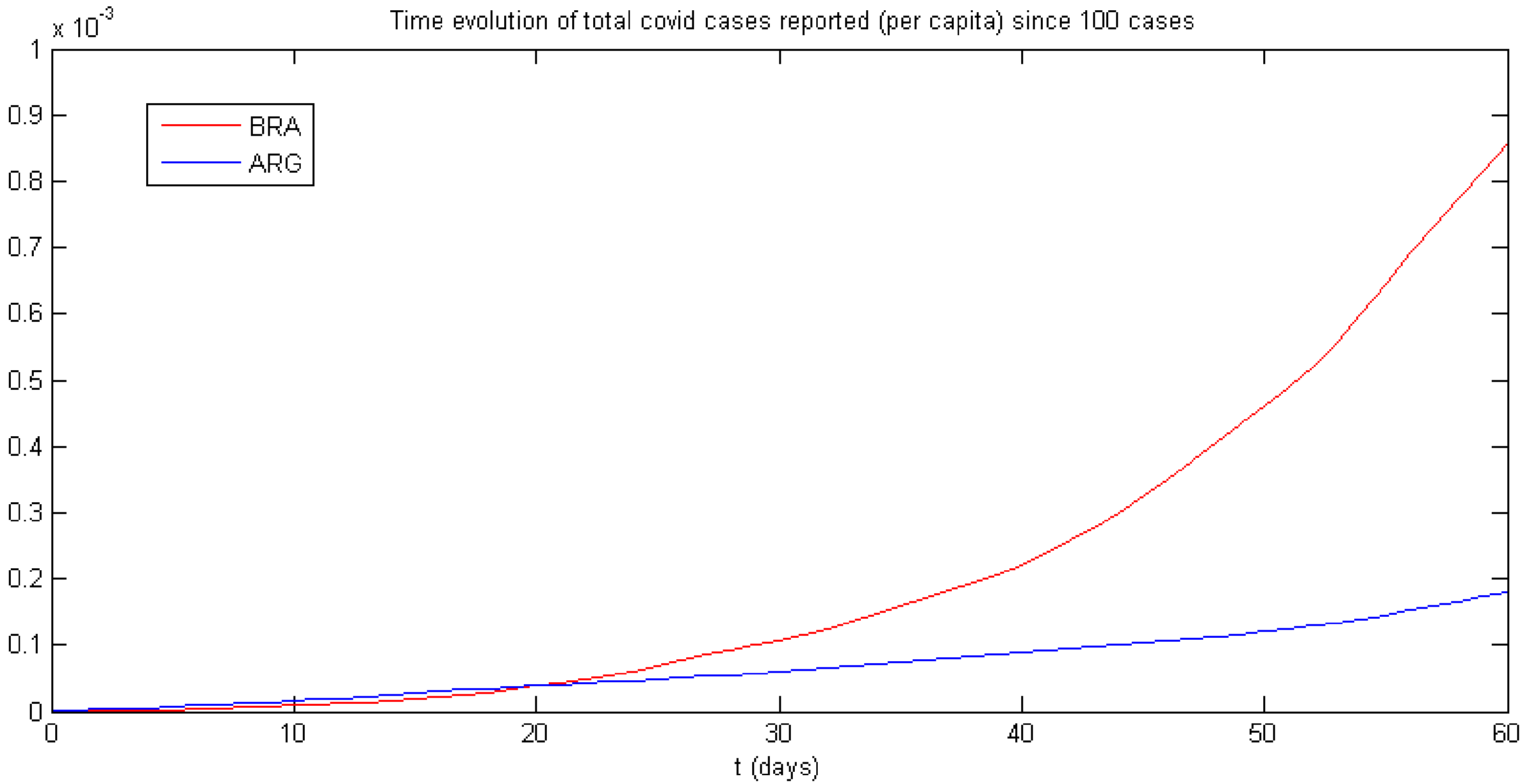
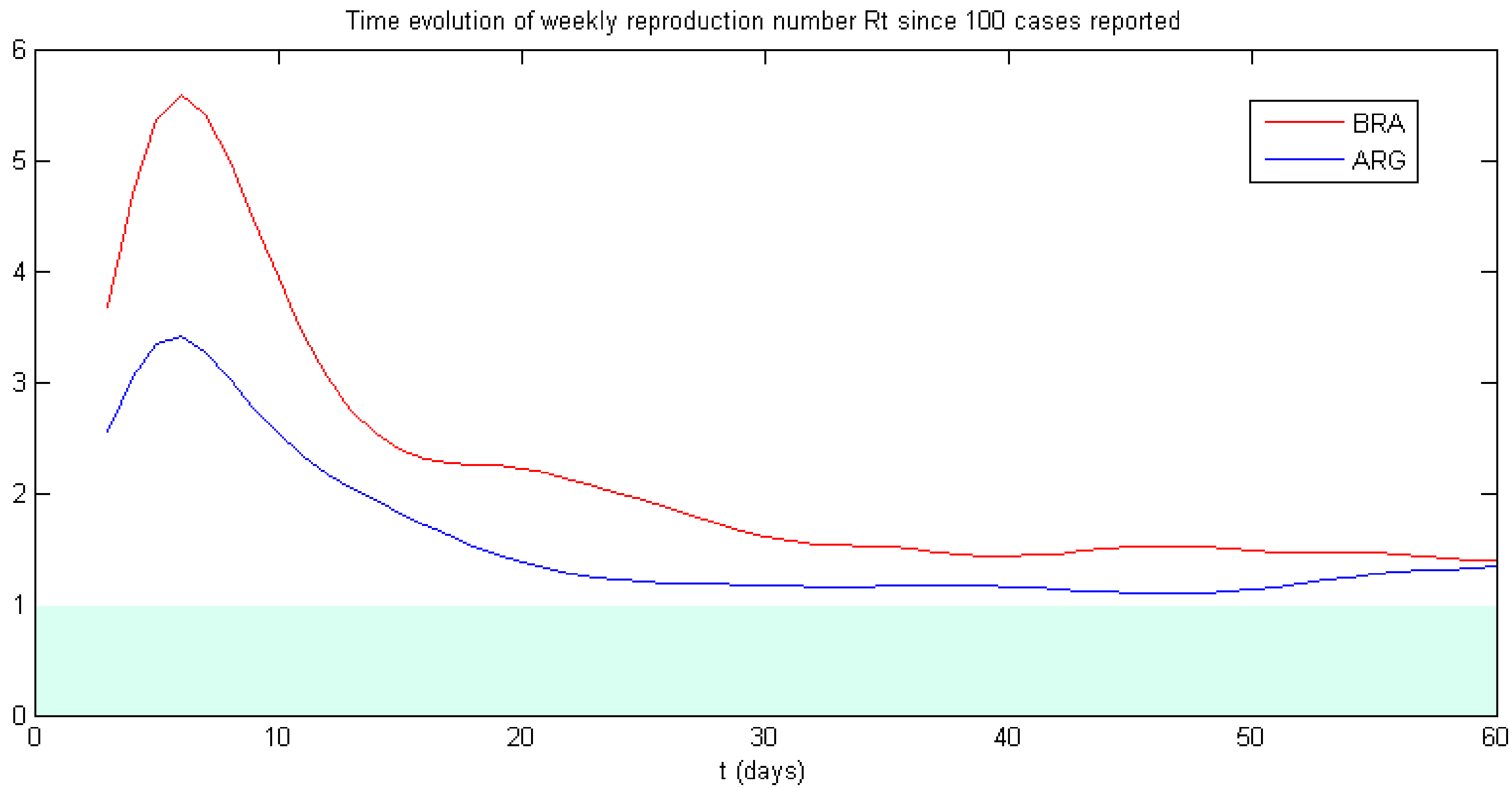
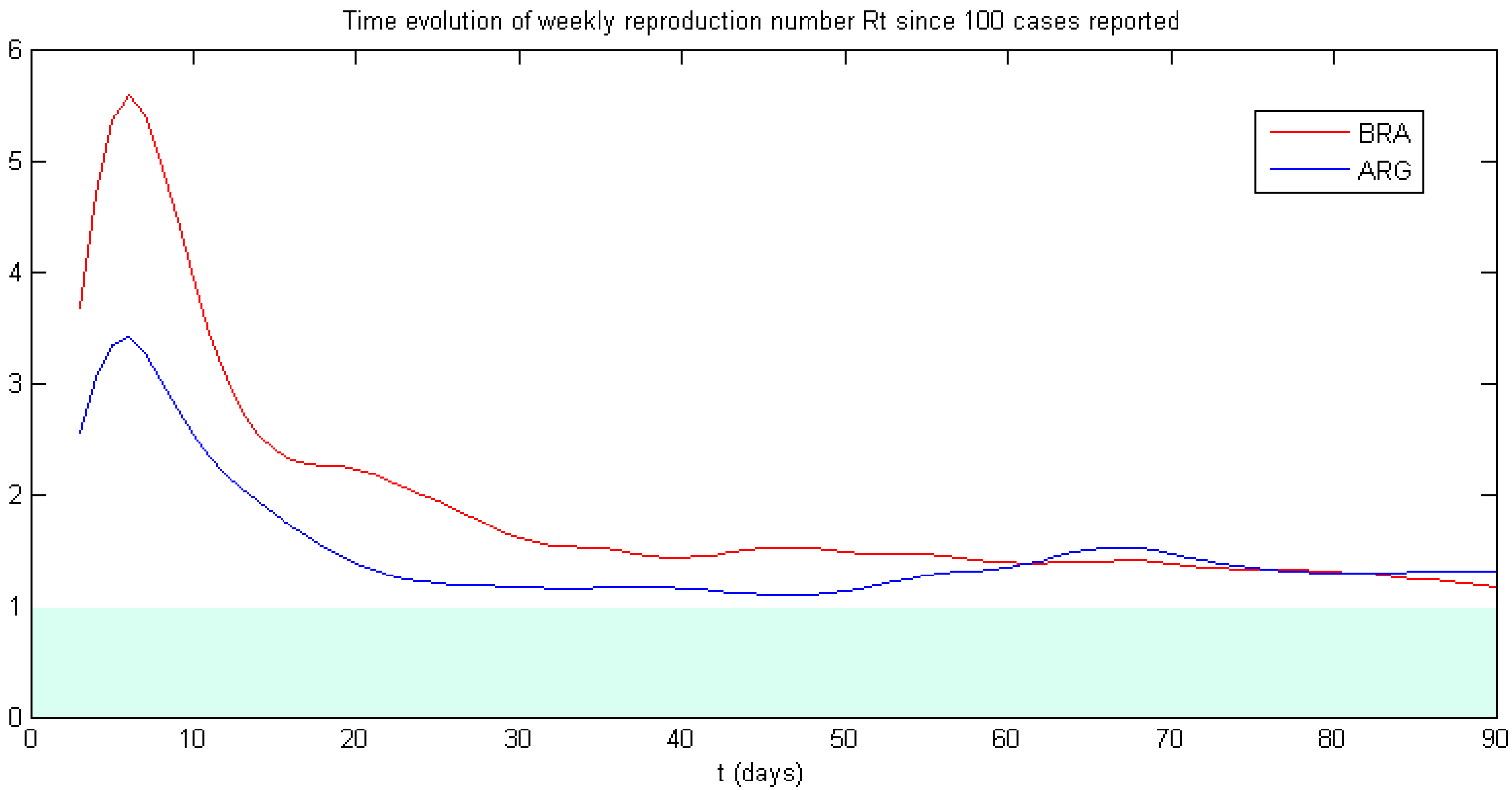


Figura 1: ilustração da sensibilidade de previsões de longo termo com respeito a incertezas nos parâmetros β e r usando o modelo (1). No cenário 1, tem-se β = 0.7 e r = 0.03, observando-se 67 dias para a ocorrência do pico de indivíduos infecciosos (curva vermelha cheia) e um total de 266 mil óbitos (curva vermelha tracejada). No cenário 2, com β = 0.8 e r = 0.02, os resultados mudam significativamente (curvas azuis).

Boa ideia: *indicadores de crescimento*




Time evolution of weekly reproduction number Rt since 100 cases reported
BRA
ARG
t (days)
0
10
20
30
40
50
60
0
1
2
3
4
5
6



Time evolution of weekly reproduction number Rt since 100 cases reported
BRA
ARG
t (days)
0
10
20
30
40
50
60
70
80
90
0
1
2
3
4
5
6

Usando modelo SEIR (determinístico):

$$
\begin{cases}
\dfrac{dS}{dt} = -\beta(t)\,\dfrac{S(t)}{N}\,I(t), \\
\dfrac{dE}{dt} = \beta(t)\,\dfrac{S(t)}{N}\,I(t) - \delta\,E(t), \\
\dfrac{dI}{dt} = \delta\,E(t) - (r(t)+\gamma)\,I(t), \\
\dfrac{dR}{dt} = \gamma\,I(t), \\
\dfrac{dD}{dt} = r(t)\,I(t),
\end{cases}
$$

Somando a segunda e terceira equações:

$$
\frac{d(E+I)}{dt} = \beta(t)\,\frac{S(t)}{N}\,I(t) - (r(t)+\gamma)\,I(t) = \left\{\beta(t)\,\frac{S(t)}{N} - (r(t)+\gamma)\right\} I(t)
$$

$$
\Longrightarrow E(t)+I(t) \quad \text{cresce se:} \quad \beta(t)\,\frac{S(t)}{N} > r(t)+\gamma,
$$

ou seja, se:

$$
R_t^{(0)} := \frac{\beta(t)\,S(t)/N}{r(t)+\gamma} > 1
$$

Mais possibilidades:

$$\begin{cases} \dfrac{dS}{dt} = -\beta(t)\,\dfrac{S(t)}{N}\,I(t), \\ \dfrac{dE}{dt} = \beta(t)\,\dfrac{S(t)}{N}\,I(t) - \delta\,E(t), \\ \dfrac{dI}{dt} = \delta\,E(t) - (r(t) + \gamma)\,I(t), \\ \dfrac{dR}{dt} = \gamma\,I(t), \\ \dfrac{dD}{dt} = r(t)\,I(t), \end{cases}$$

Usando a terceira equação:

$$\frac{dI}{dt} = \delta\,E(t) - (r(t) + \gamma)\,I(t) = \Big\{\delta\,E(t)/I(t) - (r(t) + \gamma)\Big\}\,I(t)$$

$\Longrightarrow I(t)$ cresce se: $\delta\,\dfrac{E(t)}{I(t)} > r(t) + \gamma,$

ou seja, se:

$$R_t^{(1)} := \frac{\delta\,E(t)/I(t)}{r(t) + \gamma} > 1$$

etc etc.

Há mais possibilidades!

$$\begin{cases} \dfrac{dS}{dt} = -\beta(t)\,\dfrac{S(t)}{N}\,I(t), \\ \dfrac{dE}{dt} = \beta(t)\,\dfrac{S(t)}{N}\,I(t) - \delta\,E(t), \\ \dfrac{dI}{dt} = \delta\,E(t) - (r(t)+\gamma)\,I(t), \\ \dfrac{dR}{dt} = \gamma\,I(t), \\ \dfrac{dD}{dt} = r(t)\,I(t), \end{cases}$$

Considerando uma janela de tempo $[\,t, t+d\,]$:

$$R_t^{(2)} := \frac{I(t+d)}{I(t)},$$

$$R_t^{(3)} := \frac{E(t+d)+I(t+d)}{E(t)+I(t)},$$

etc etc.

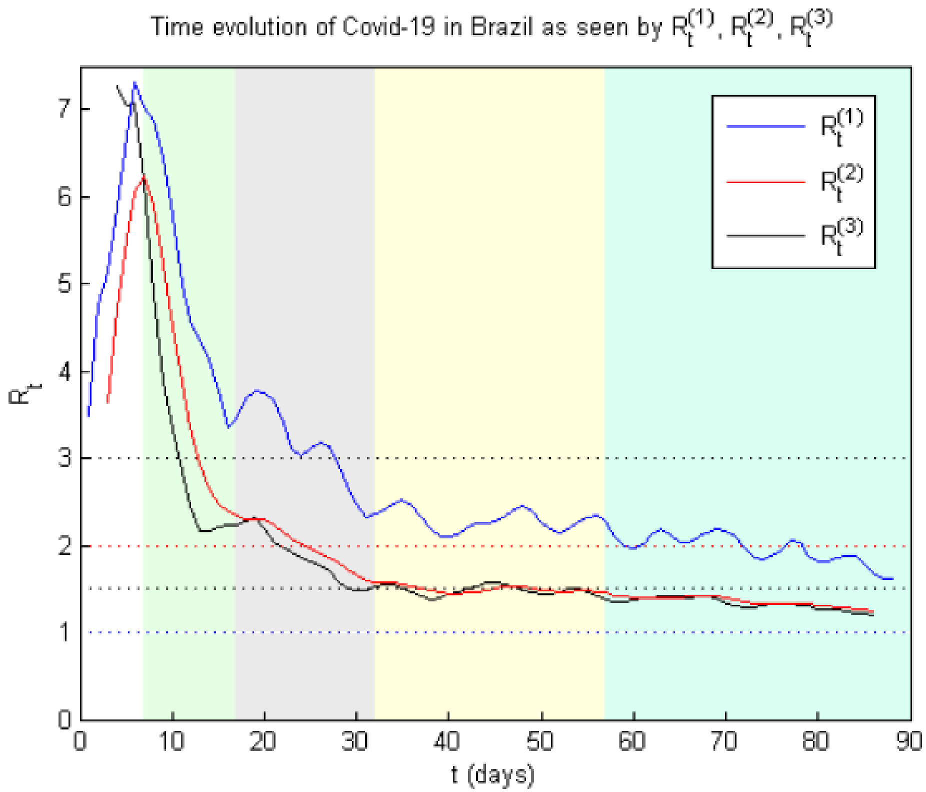


Fig. 5: Comparison of the time evolution of Covid-19 in Brazil (since 100 cases reported) as seen by the indicators defined in (3.3), (3.4), pointing to similar scenarios. In the three cases it is clear that Brazil has not yet reached a state of control of the epidemic ($R_t < 1$)

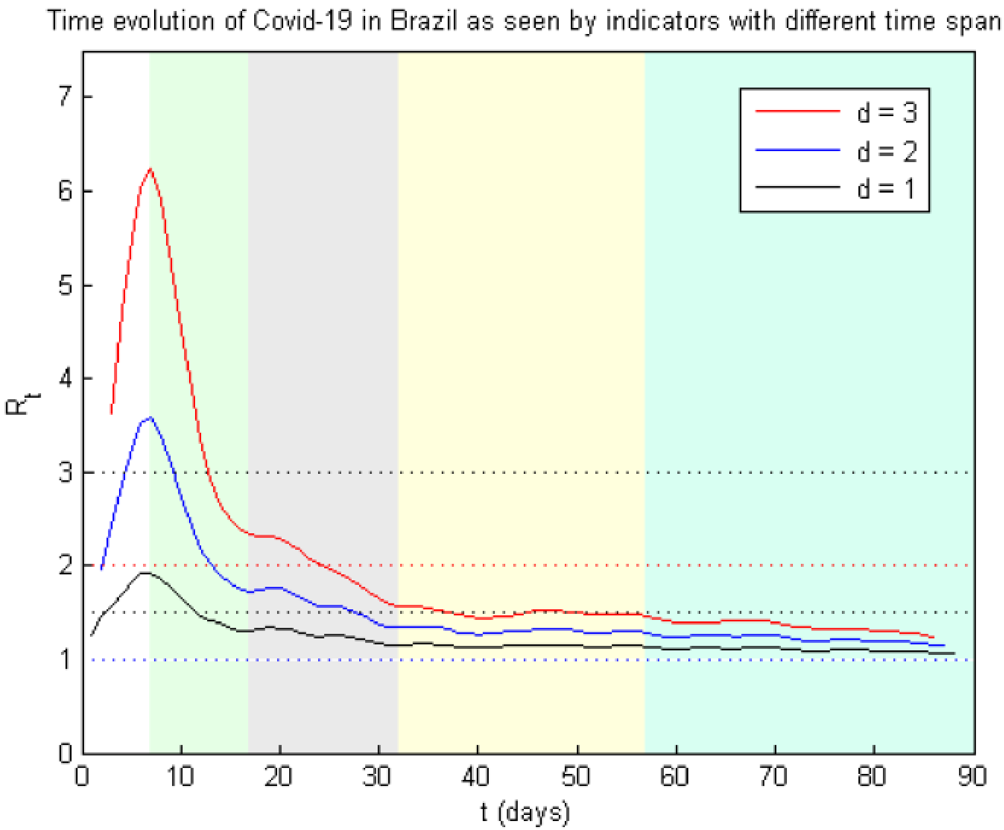


Fig. 6: Comparison of the time evolution of Covid-19 in Brazil (since 100 cases reported) as seen by $R_t = I(t+d)/I(t-d)$ for different values of d, showing similar scenarios. In the three cases it is clear that Brazil has not yet reached a state of control of the epidemic ($R_t < 1$)

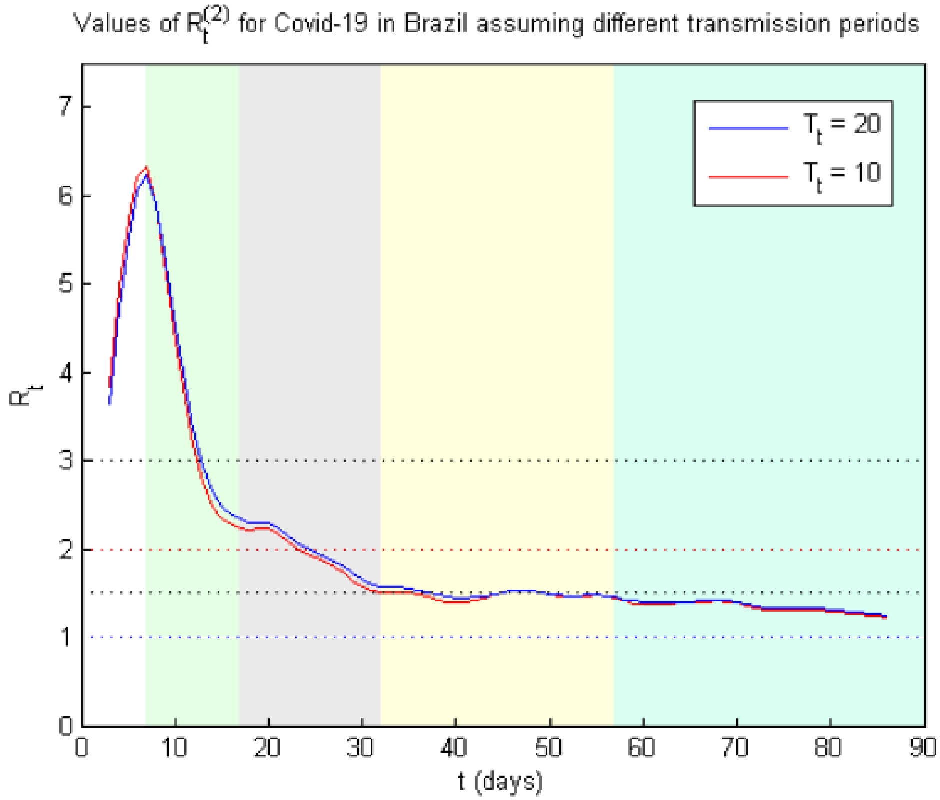
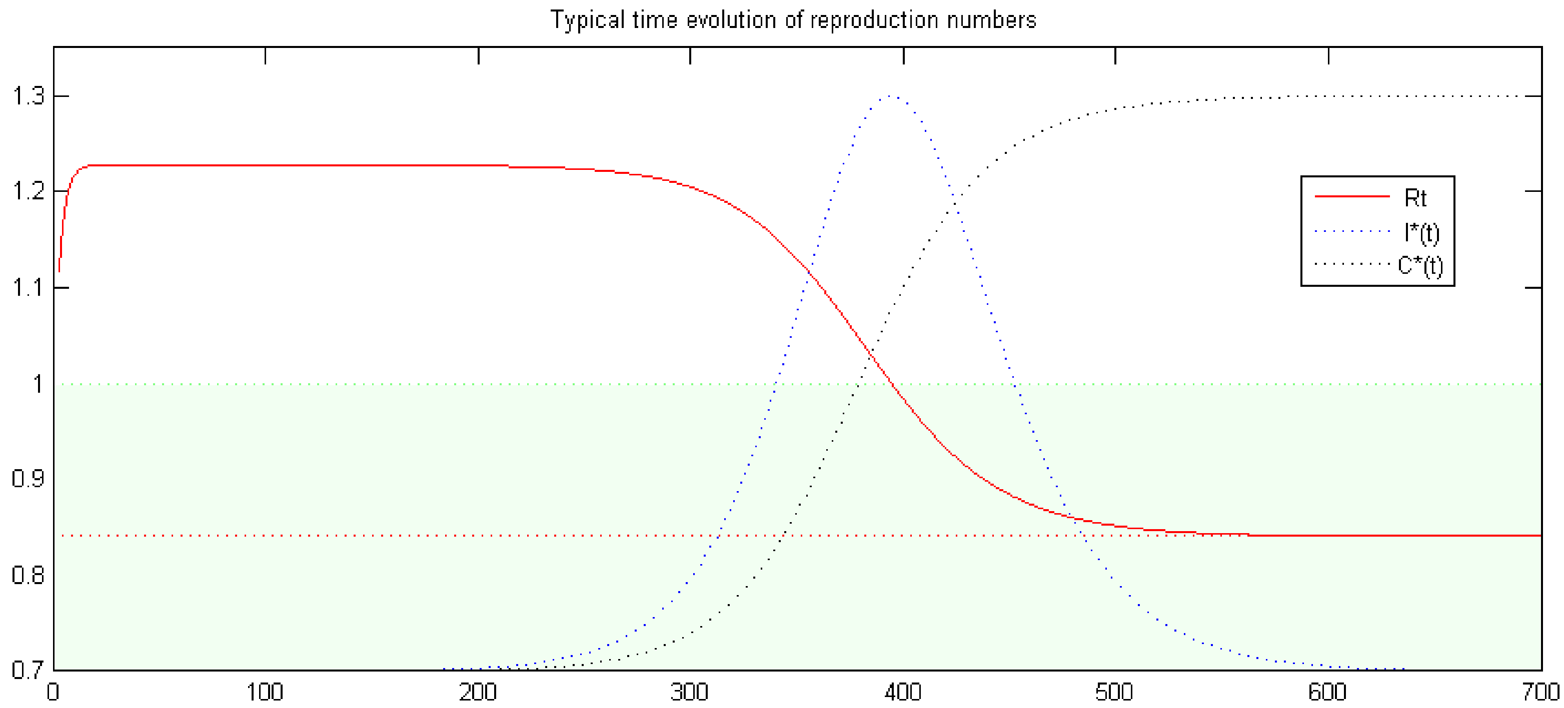
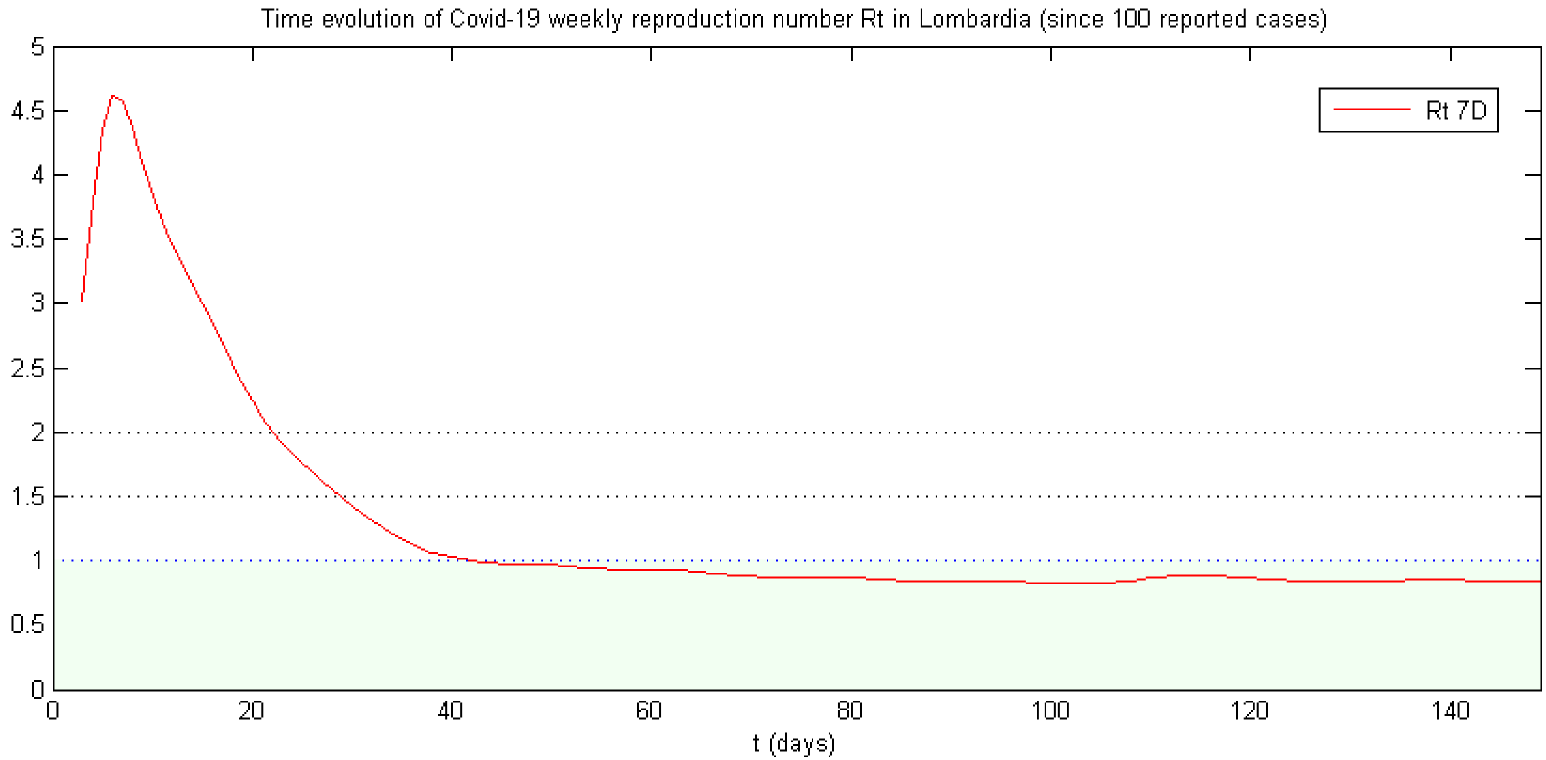


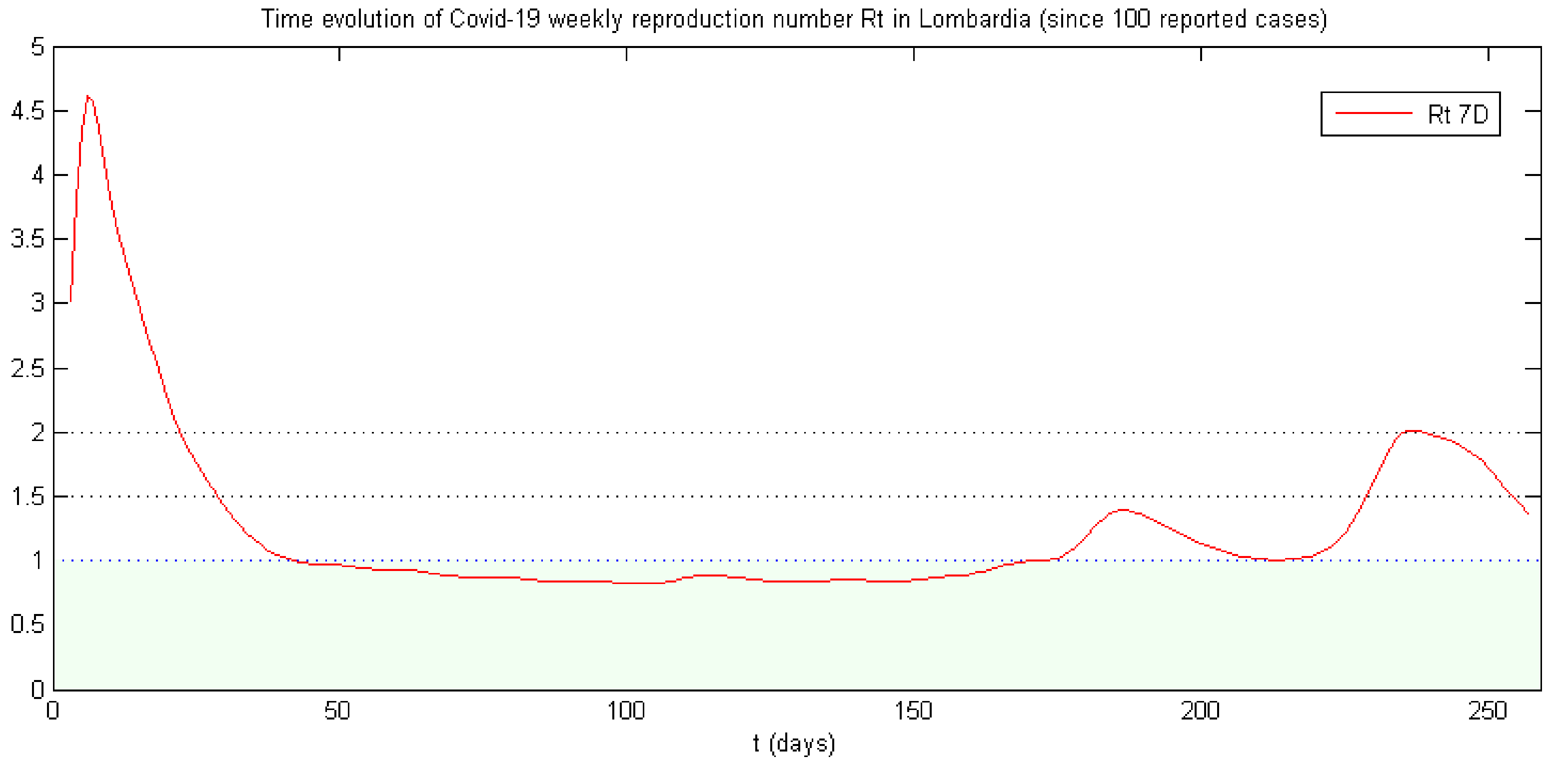
Fig. 7: Robustness of $R_t^{(2)}$ with respect to large uncertainties on the value of transmission time. Date zero refers to 100 cases reported, that is: 03/13/2020. (As in Fig. 5 and Fig. 6 above, calculations were based upon official data reported at https://covid.saude.gov.br.)

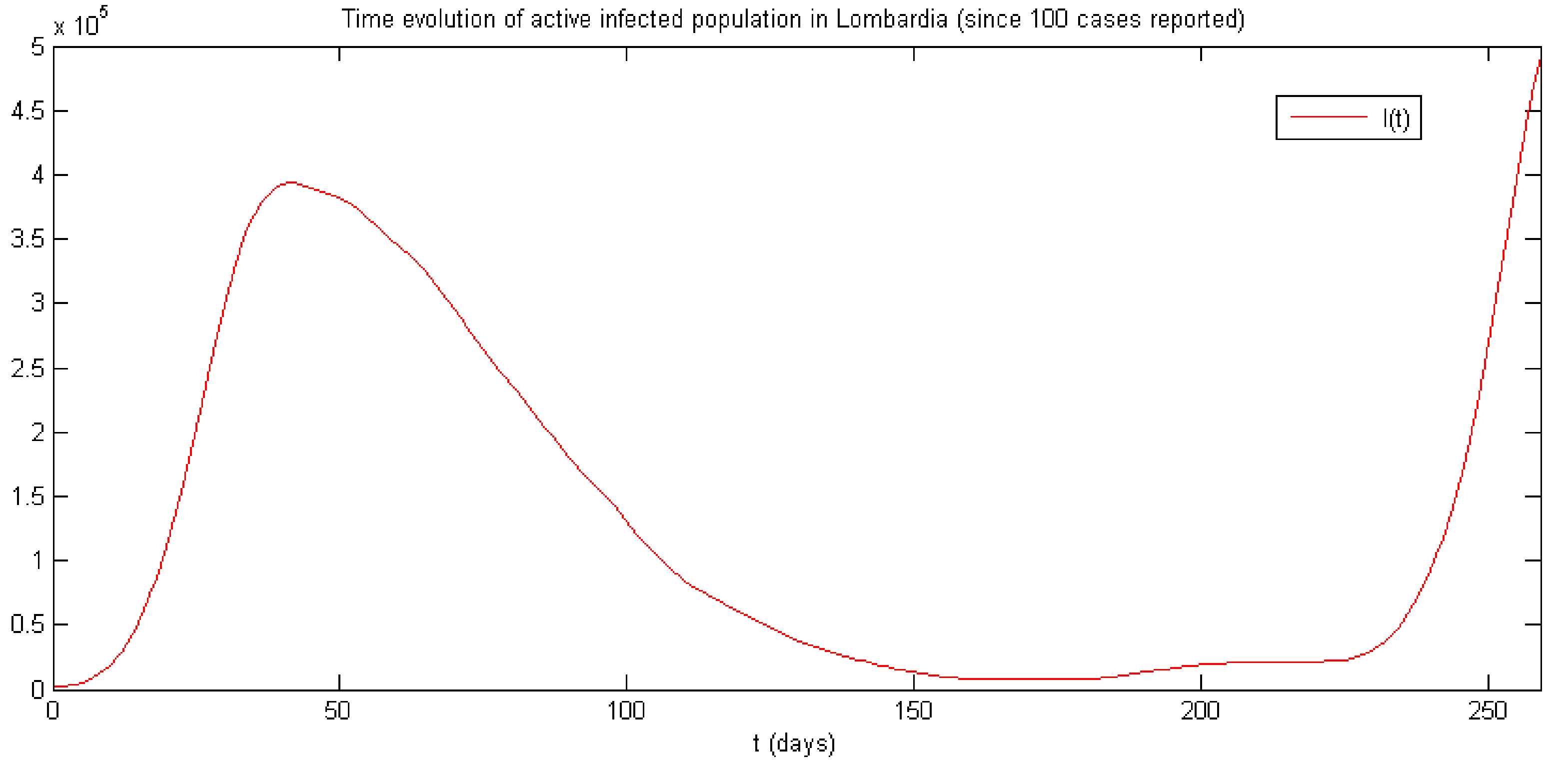


Typical time evolution of reproduction numbers
1.3
1.2
1.1
1
0.9
0.8
0.7
0
100
200
300
400
500
600
700
Rt
I*(t)
C*(t)

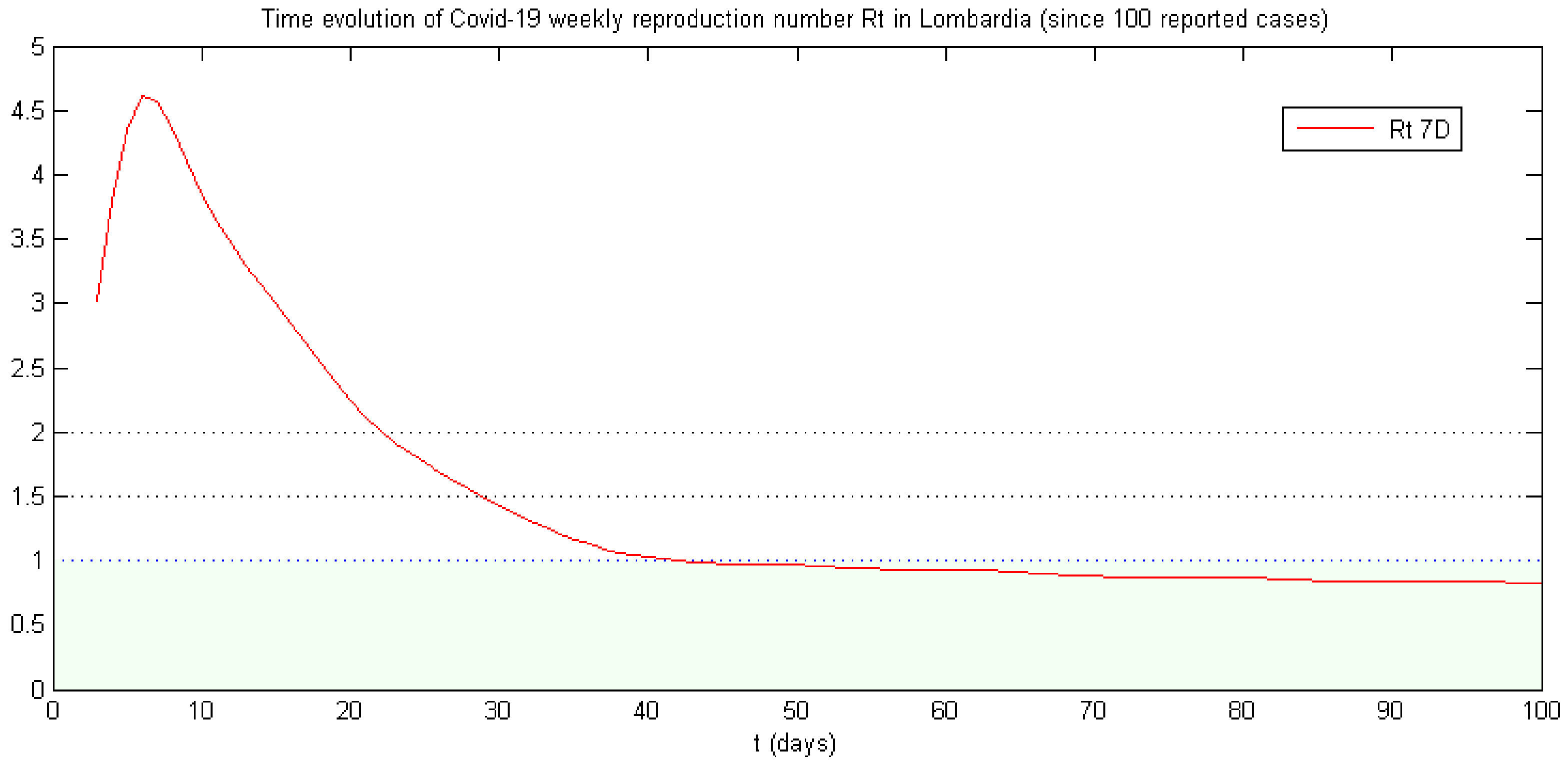


Time evolution of Covid-19 weekly reproduction number Rt in Lombardia (since 100 reported cases)
Rt 7D
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
20
40
60
80
100
120
140
t (days)

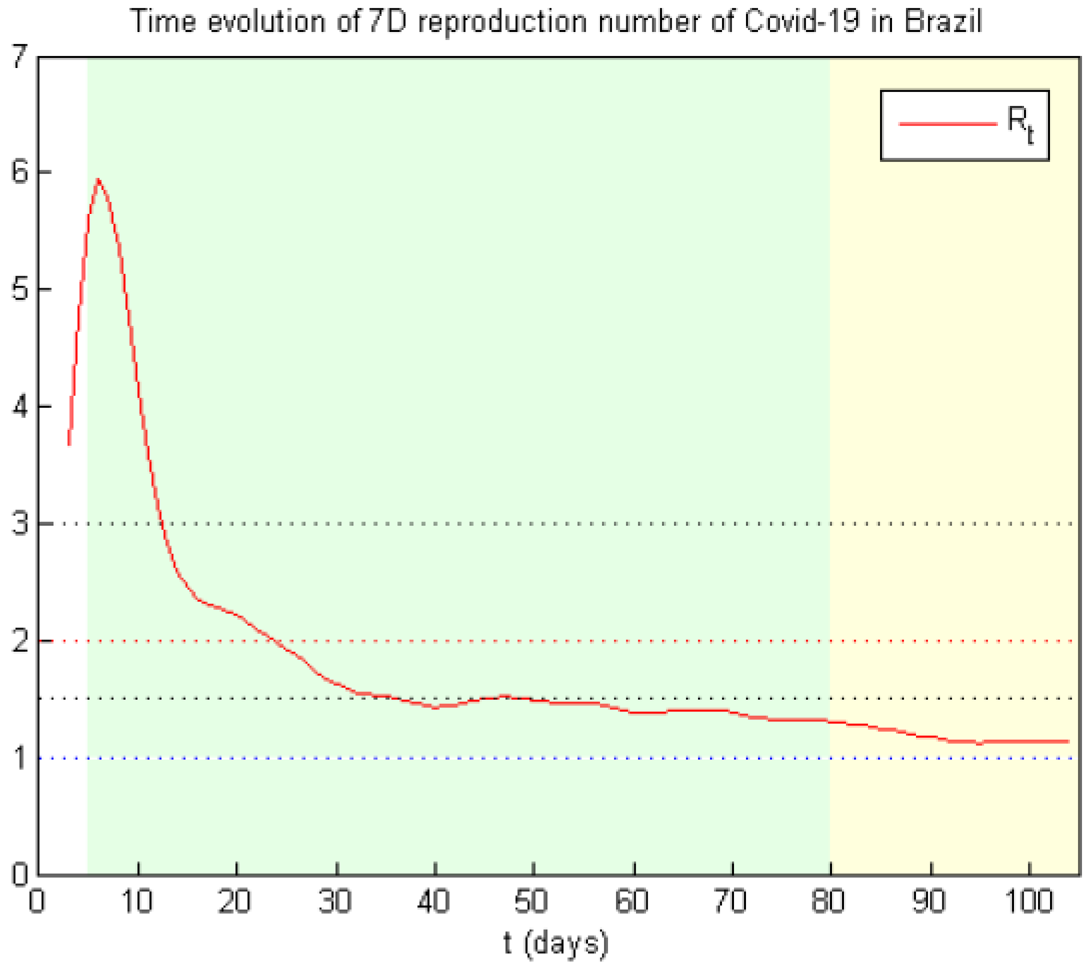

Time evolution of Covid-19 weekly reproduction number Rt in Lombardia (since 100 reported cases)
Rt 7D
t (days)
0
50
100
150
200
250
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5



Time evolution of active infected population in Lombardia (since 100 cases reported)
x 10^5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
50
100
150
200
250
t (days)
I(t)

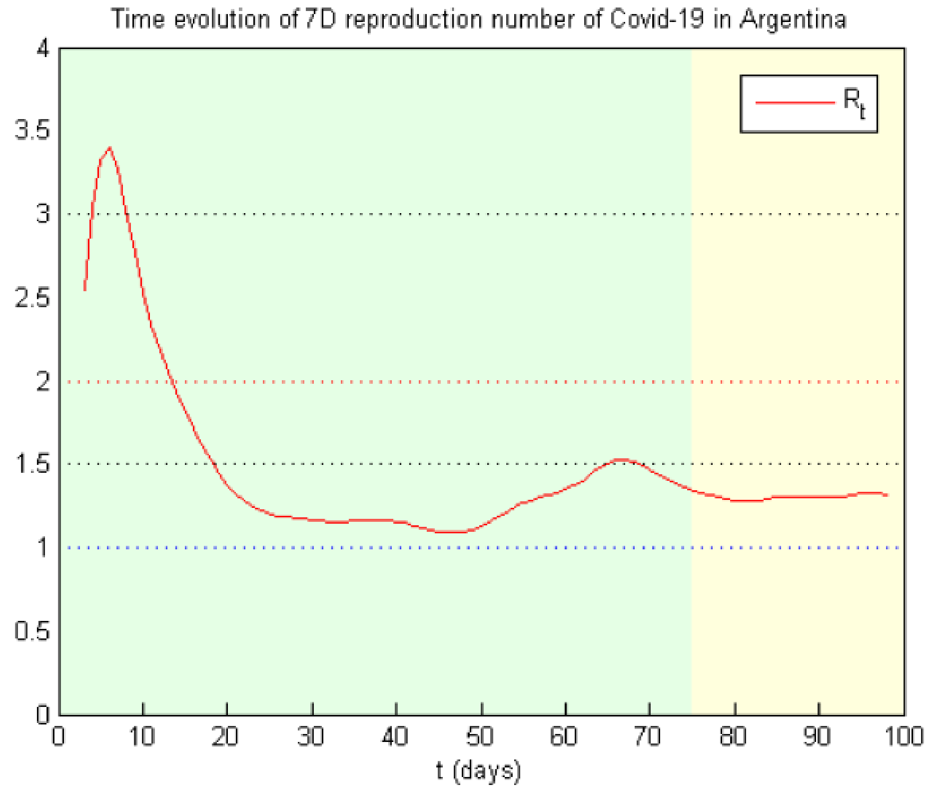


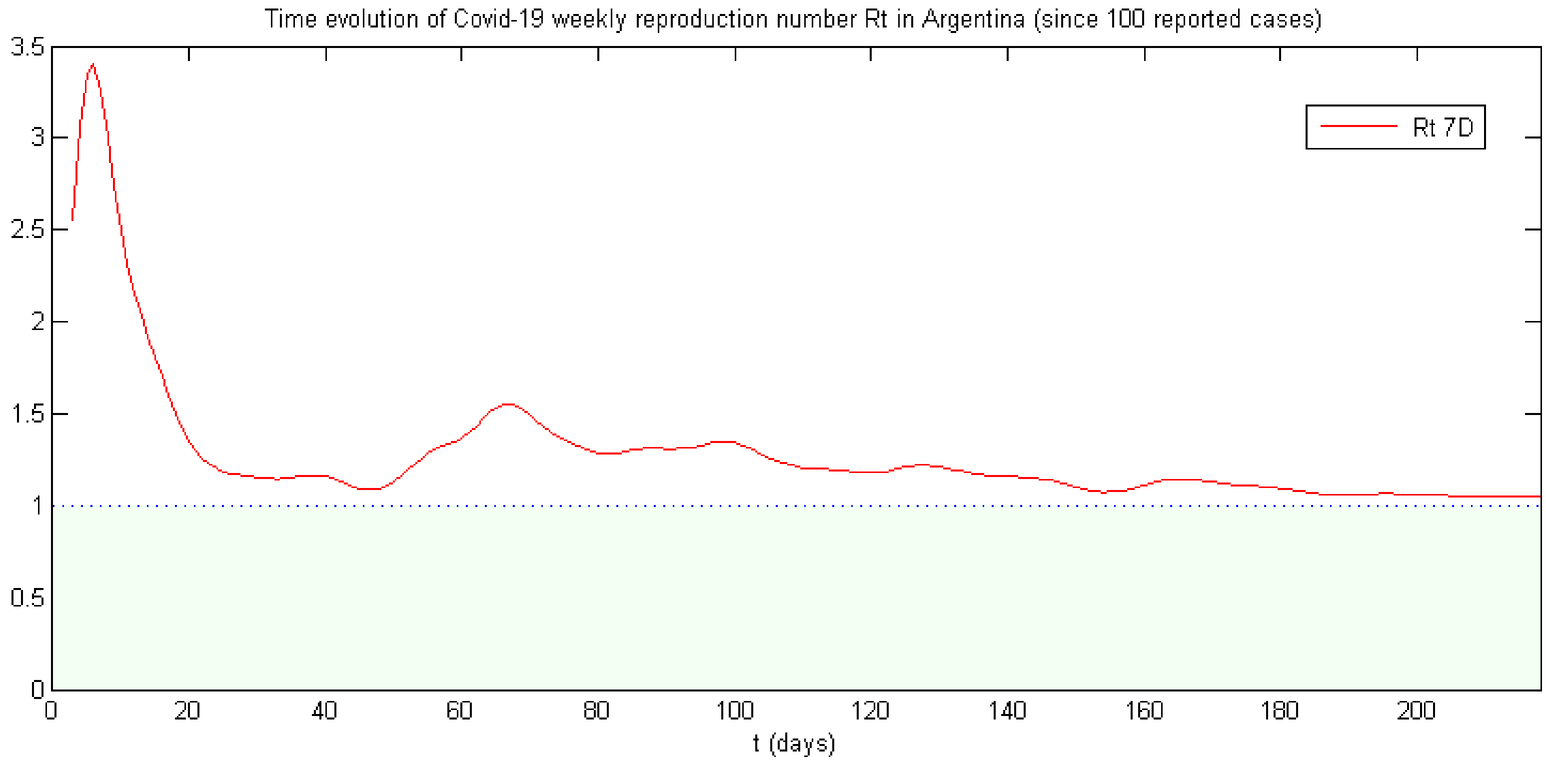
Time evolution of Covid-19 weekly reproduction number Rt in Lombardia (since 100 reported cases)
Rt 7D
t (days)
0
10
20
30
40
50
60
70
80
90
100
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5



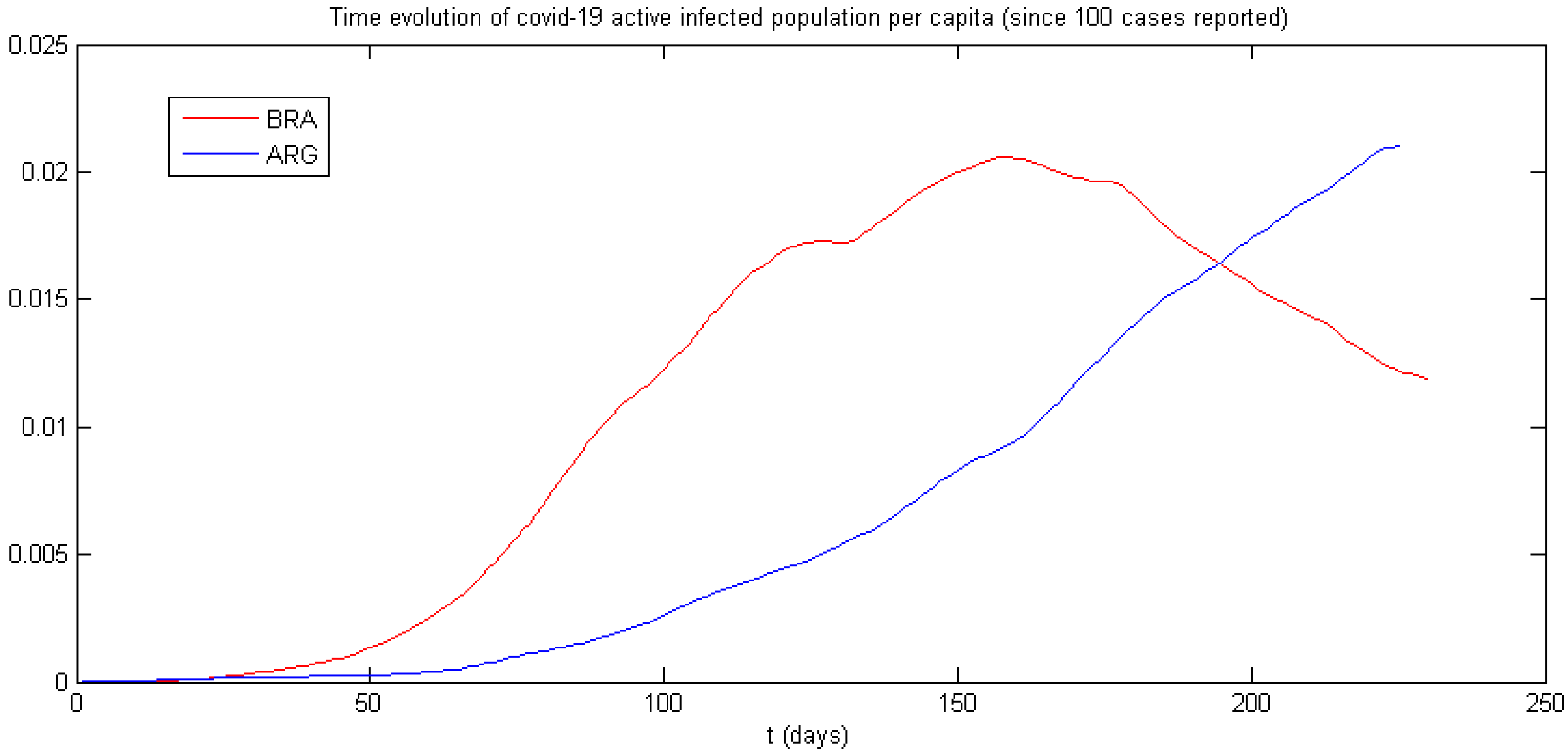
Time evolution of 7D reproduction number of Covid-19 in Brazil
7
6
5
4
3
2
1
0
0
10
20
30
40
50
60
70
80
90
100
t (days)
R_t

Example 1: Time evolution of Covid-19 in Argentina since 03/18/2020 ($t = 0$), the date of 97 total cases reported. Strong containment measures had begun 3 days earlier ($t = -3$) and managed to keep the number of cases and deaths down low, with R_t decreasing continually until 05/04/2020 ($t = 47$), when it reached a minimum value of 1.08. Following that, the situation deteriorated with R_t increasing to 1.54 on 05/24/2020 ($t = 67$), despite the reinforcement of most intervention procedures. Partial relaxation of some of these measures was introduced on 06/01/2020 ($t = 75$) and, in this new period, R_t has remained relatively stable at 1.30 (yellow band), but tending to slowly increase (present value is 1.32). Bringing the epidemic to a state of nationwide control ($R_t < 1$) still seems far away. This example illustrates the unfortunate fact that having low numbers of infections does not necessarily mean having the epidemic under control.

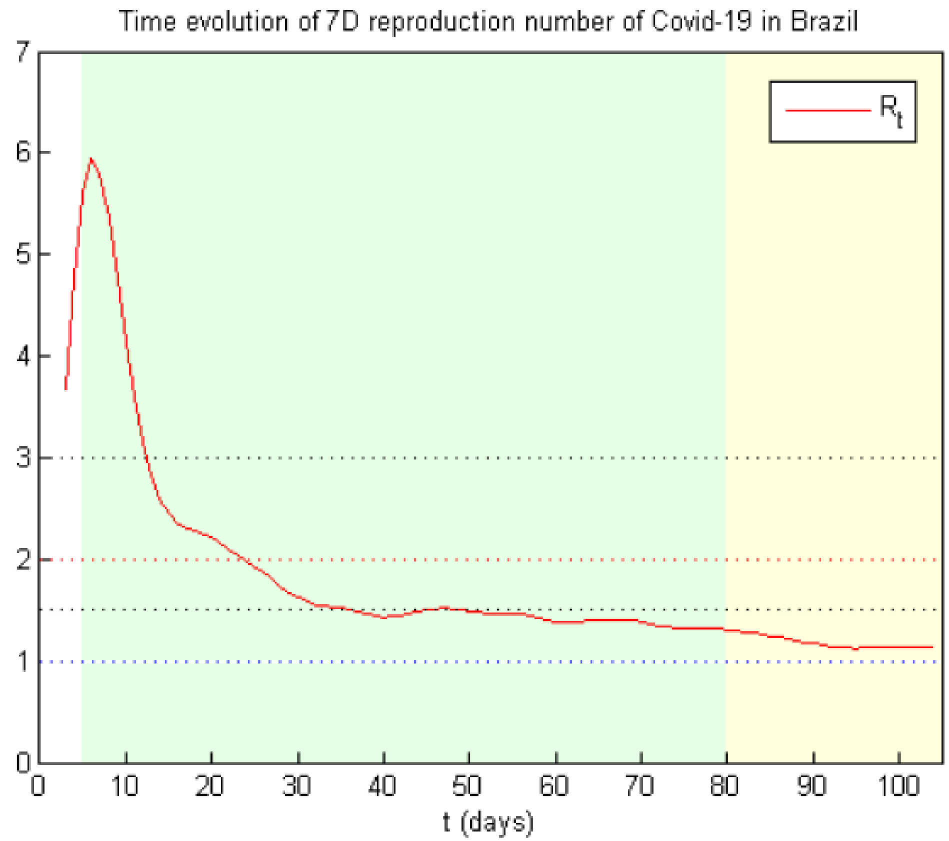


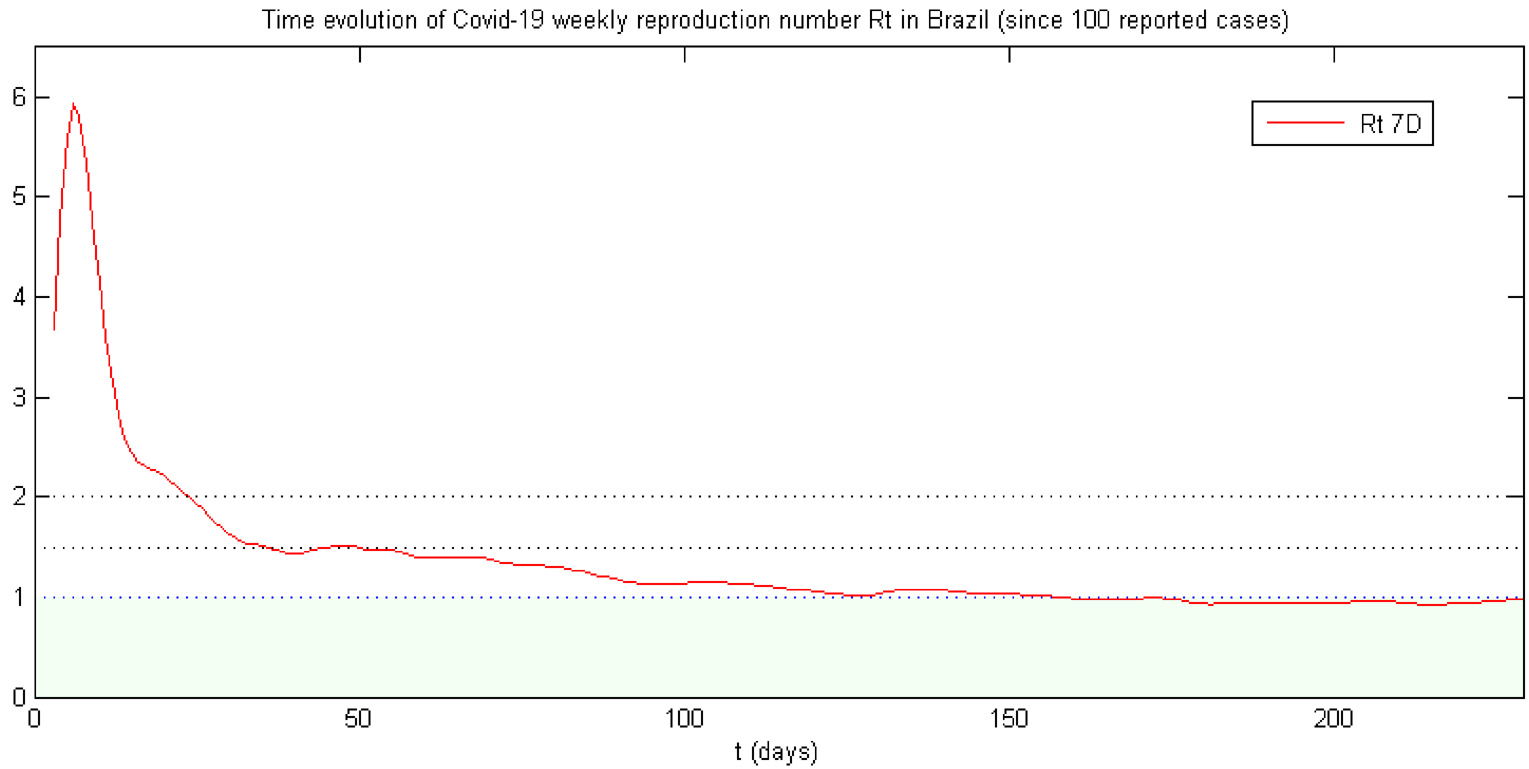


Time evolution of Covid-19 weekly reproduction number Rt in Argentina (since 100 reported cases)
Rt 7D
3.5
3
2.5
2
1.5
1
0.5
0
0
20
40
60
80
100
120
140
160
180
200
t (days)

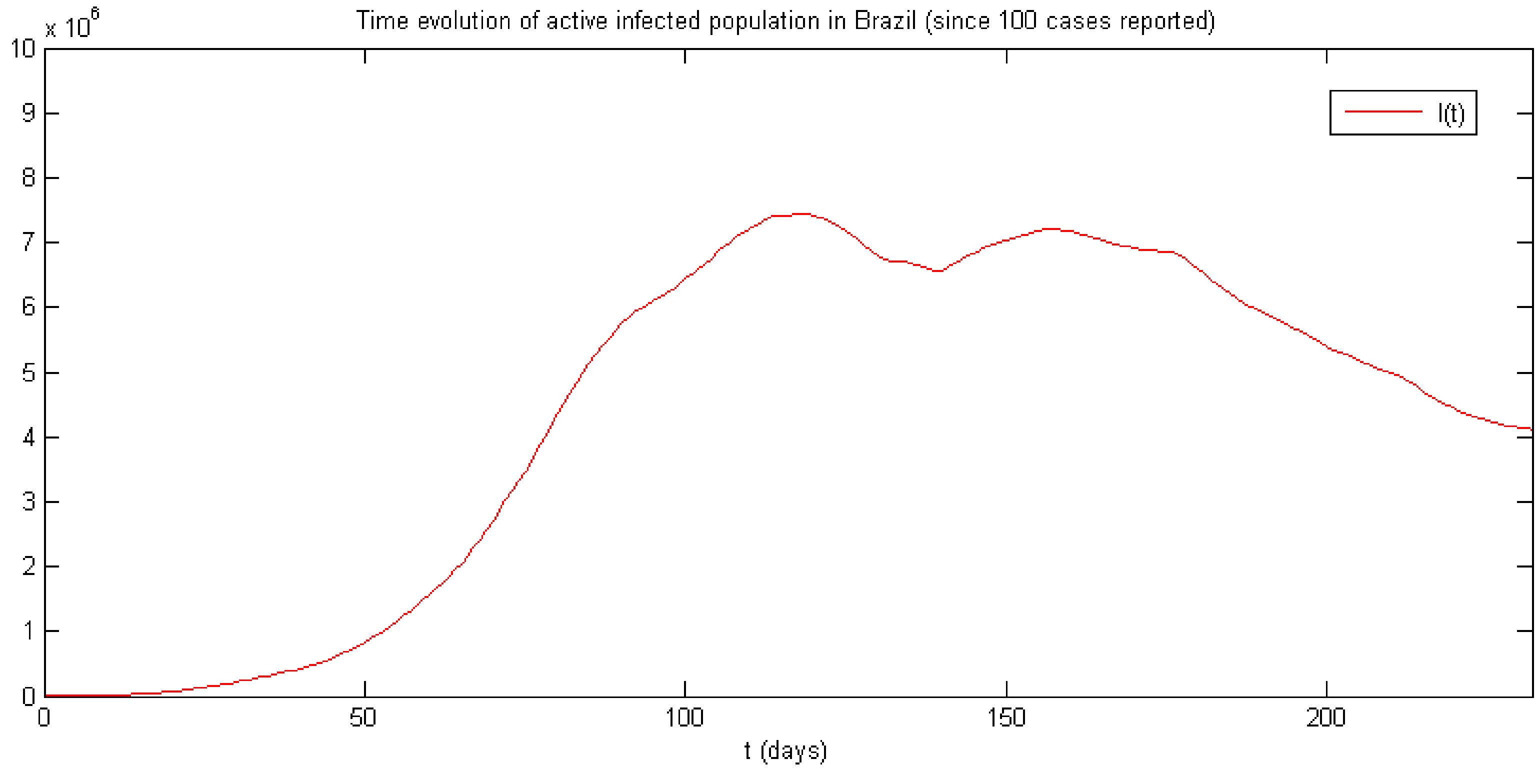

Time evolution of covid-19 active infected population per capita (since 100 cases reported)
BRA
ARG
0.025
0.02
0.015
0.01
0.005
0
0
50
100
150
200
250
t (days)

Example 2: Time evolution of Covid-19 in Brazil since 03/13/2020, the date of 98 total cases reported ($t = 0$). With very poor coordination between the central and local authorities and with different levels of intervention in the various states of the country, the decreasing of R_t after reaching 1.5 by mid-April proceeded very slowly (green band) due to the spread of the epidemic and the emergence of new infection foci. Relaxation measures began to be implemented on different dates according to the individual regions, but can be traced on average back to 06/01/2020 ($t = 80$). Despite the encouraging behavior of R_t shown in the following fortnight (yellow band),



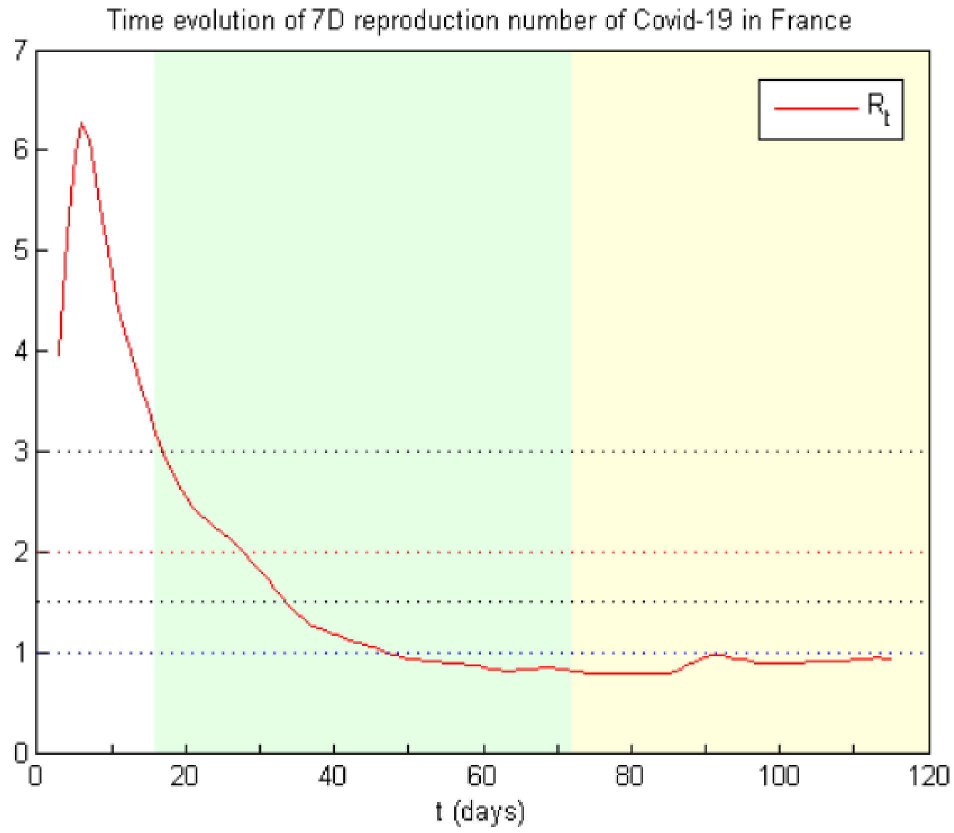


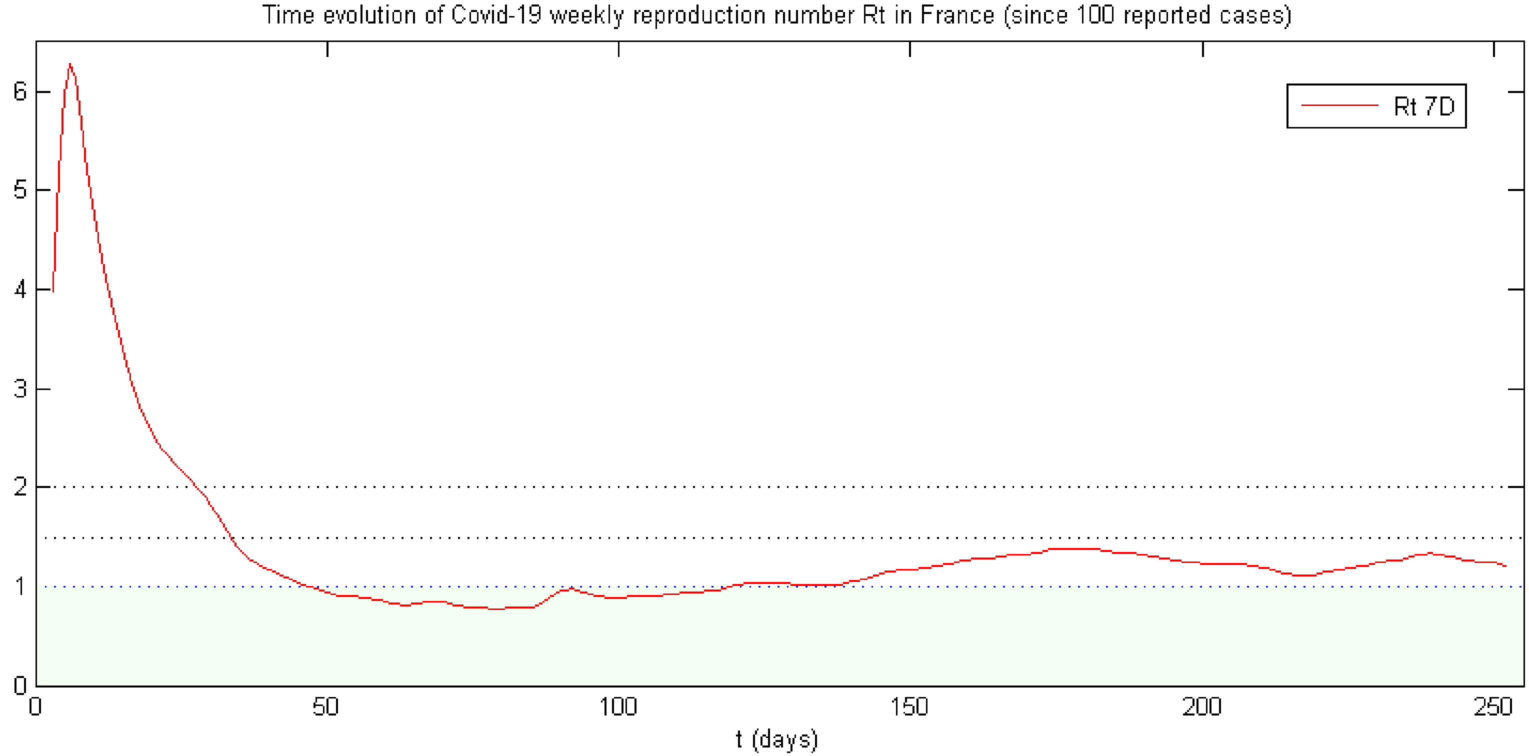
Time evolution of Covid-19 weekly reproduction number Rt in Brazil (since 100 reported cases)
Rt 7D
0
1
2
3
4
5
6
0
50
100
150
200
t (days)



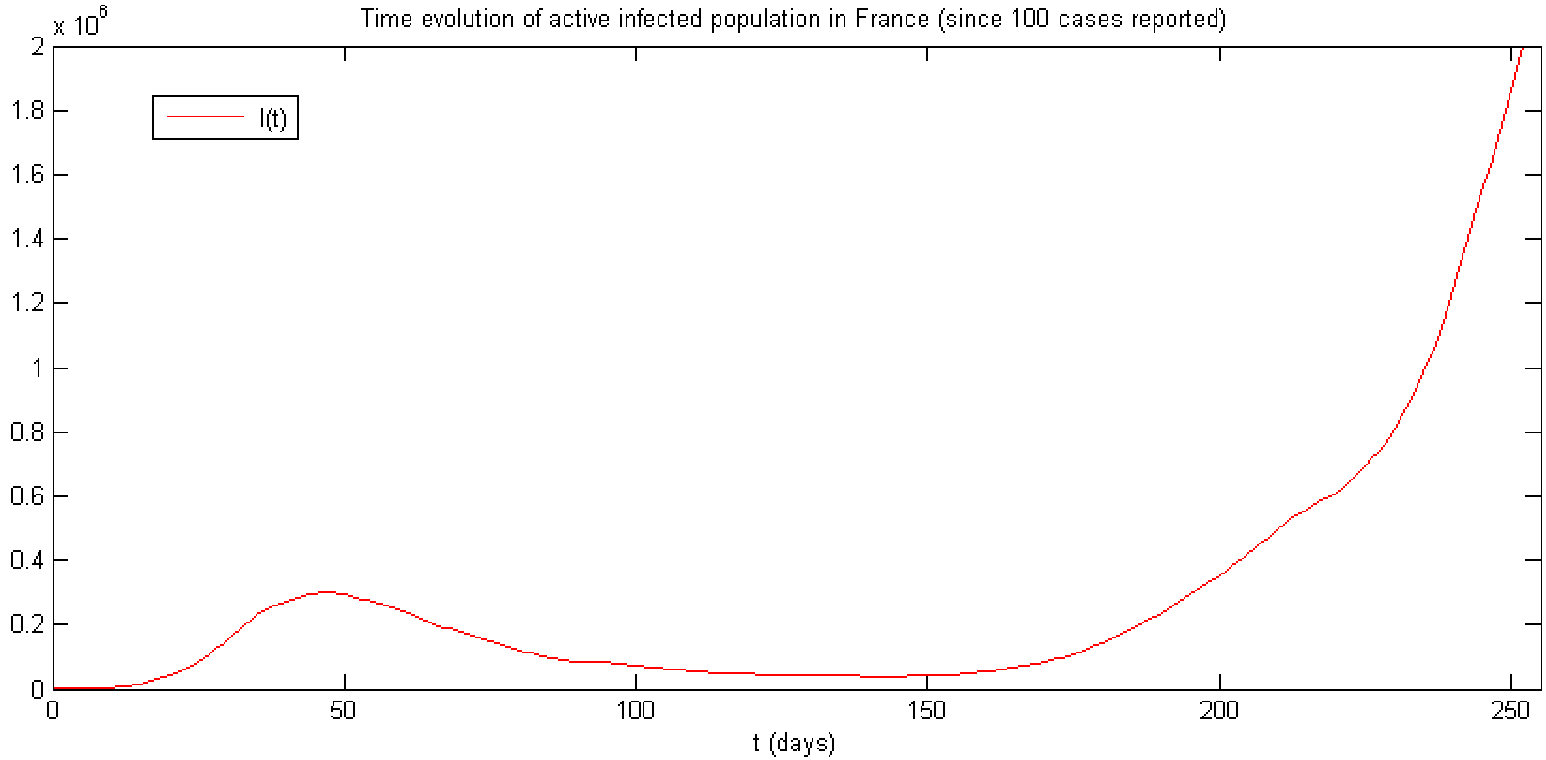
Time evolution of active infected population in Brazil (since 100 cases reported)
x 10^6
10
9
8
7
6
5
4
3
2
1
0
0
50
100
150
200
t (days)
I(t)

Example 3: Time evolution of Covid-19 in France since 02/29/2020 ($t = 0$), the date of 100 total cases reported. Containment measures began relatively late on 03/16/2020 ($t = 16$), with a strict eight-week lockdown that reduced the value of R_t down to 0.81 (green band). Restrictions were afterwards relaxed (yellow band), with R_t stable for a couple of weeks, when it began increase. A peak value of 0.99 was reached on 05/30/2020, followed by a reduction to 0.89 on 06/08/2020



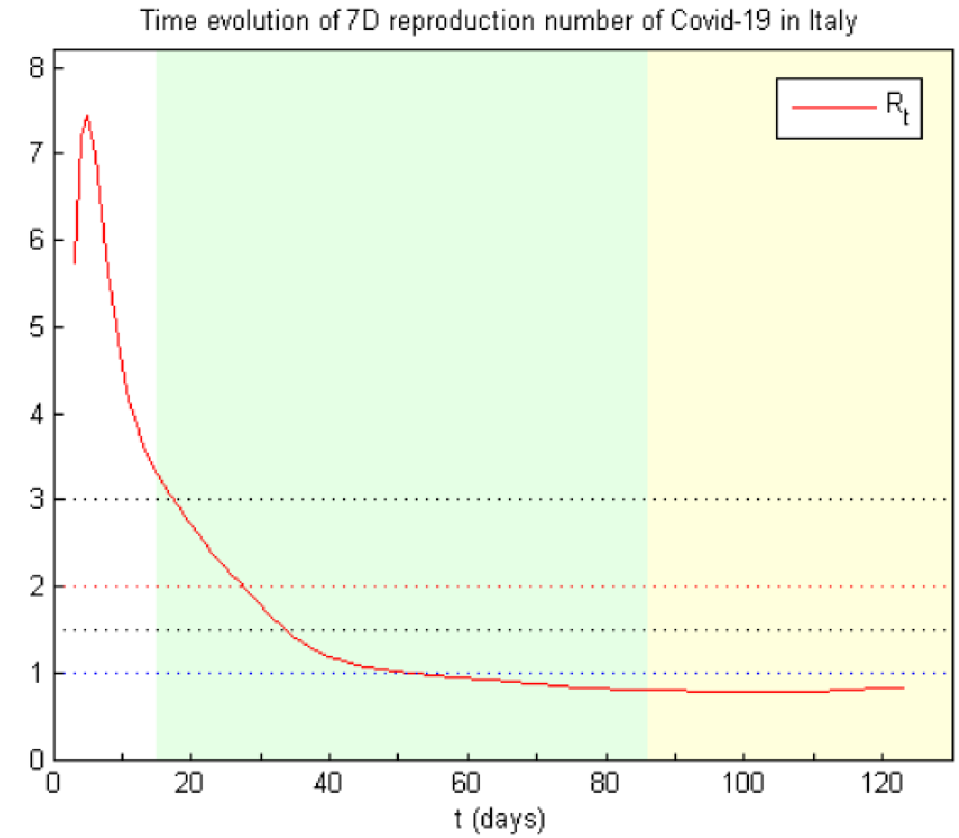


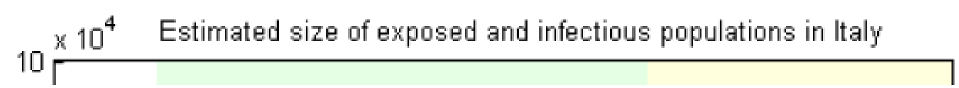
Time evolution of Covid-19 weekly reproduction number Rt in France (since 100 reported cases)
Rt 7D
0
1
2
3
4
5
6
0
50
100
150
200
250
t (days)

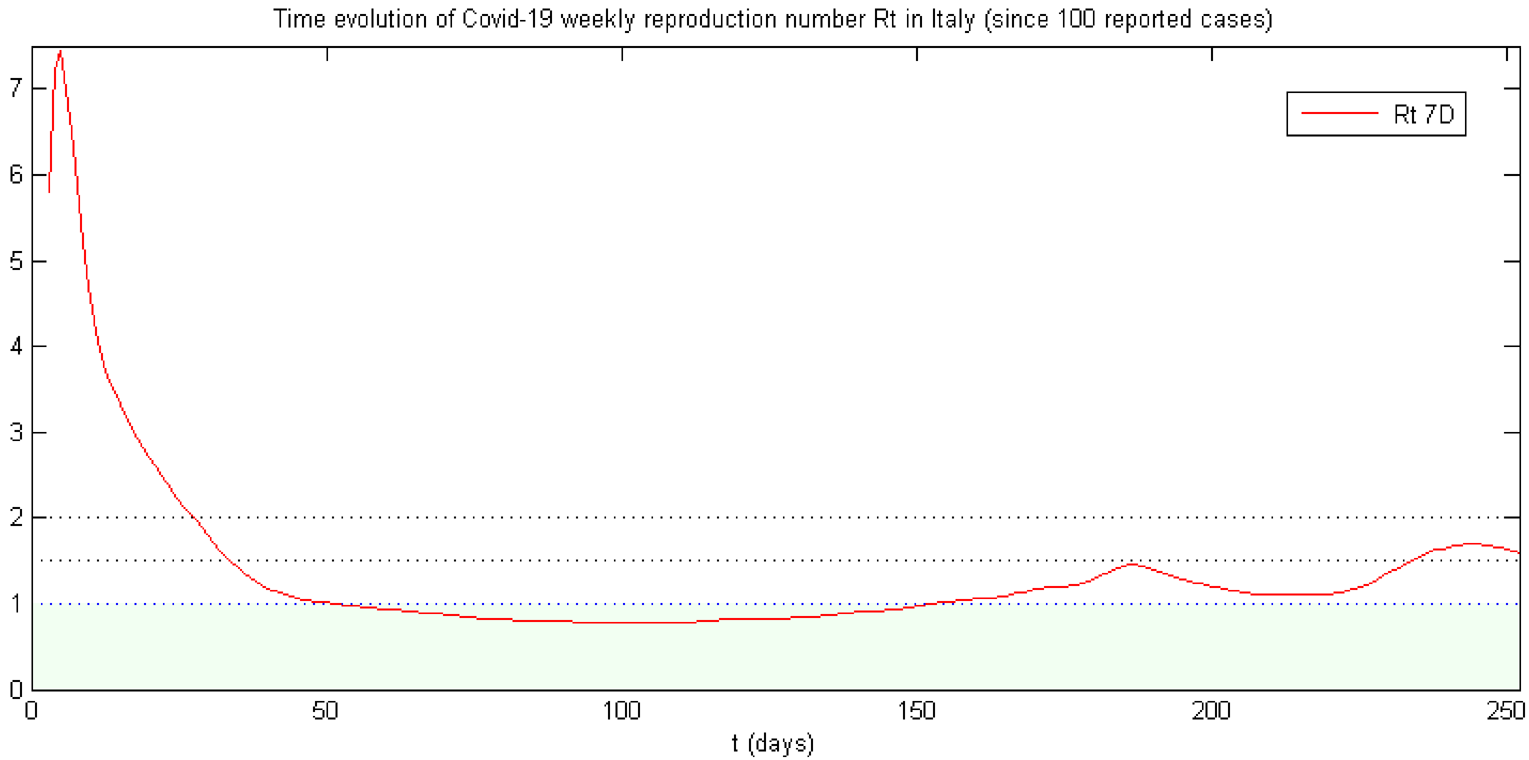


Time evolution of active infected population in France (since 100 cases reported)
x 10^6
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
I(t)
0
50
100
150
200
250
t (days)

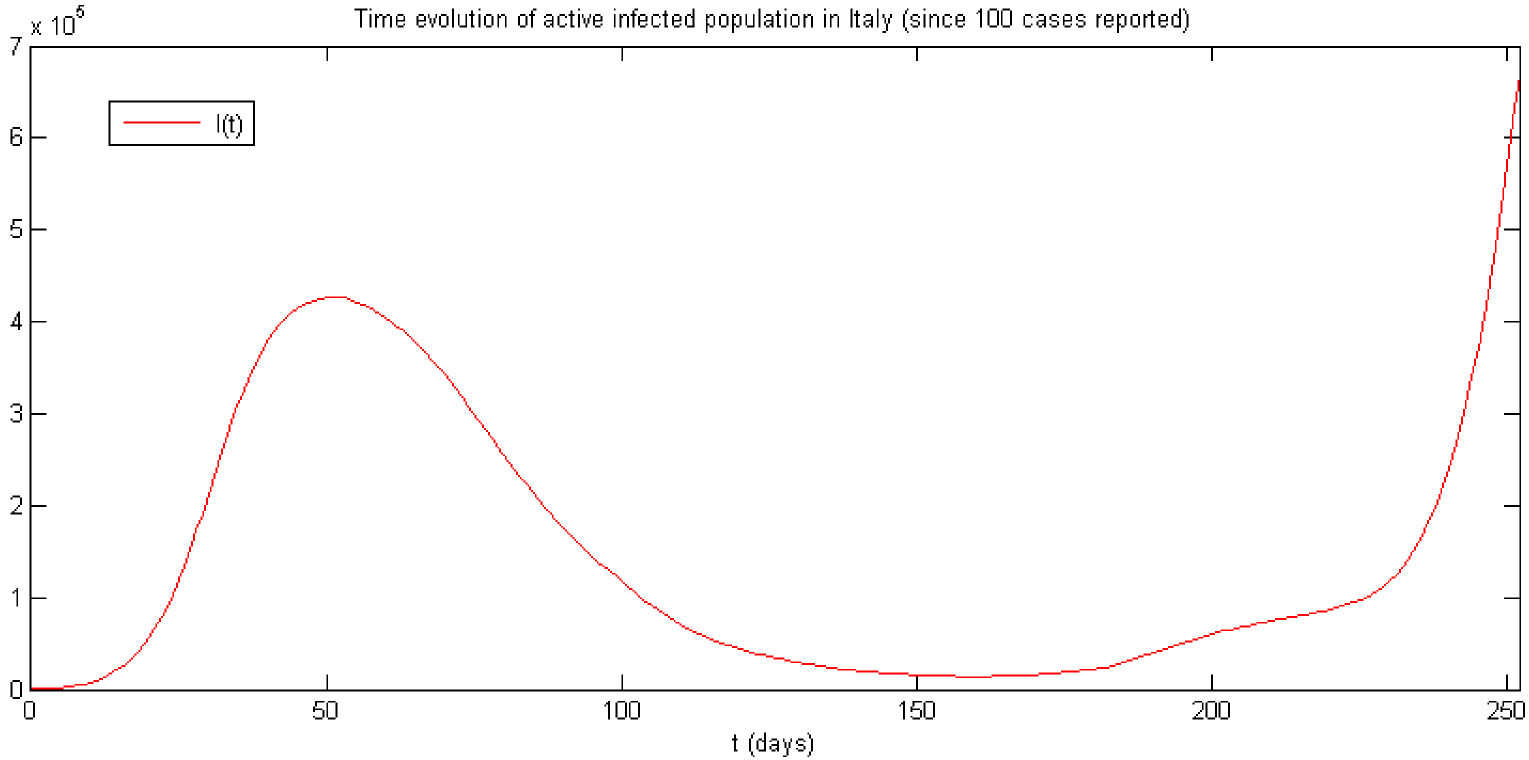
Example 4: Time evolution of Covid-19 in Italy since 02/22/2020, the date of 79 total cases reported ($t = 0$). Containment measures began fifteen days later, with a strict eight-week national lockdown imposed on 03/10/2020 ($t = 17$). The strong intervention, embraced by the population and maintained for the whole period, succeeded in reducing R_t continually down to a safe value of 0.80 on 05/18/2020 ($t = 86$), when some of the contention rules began being relaxed



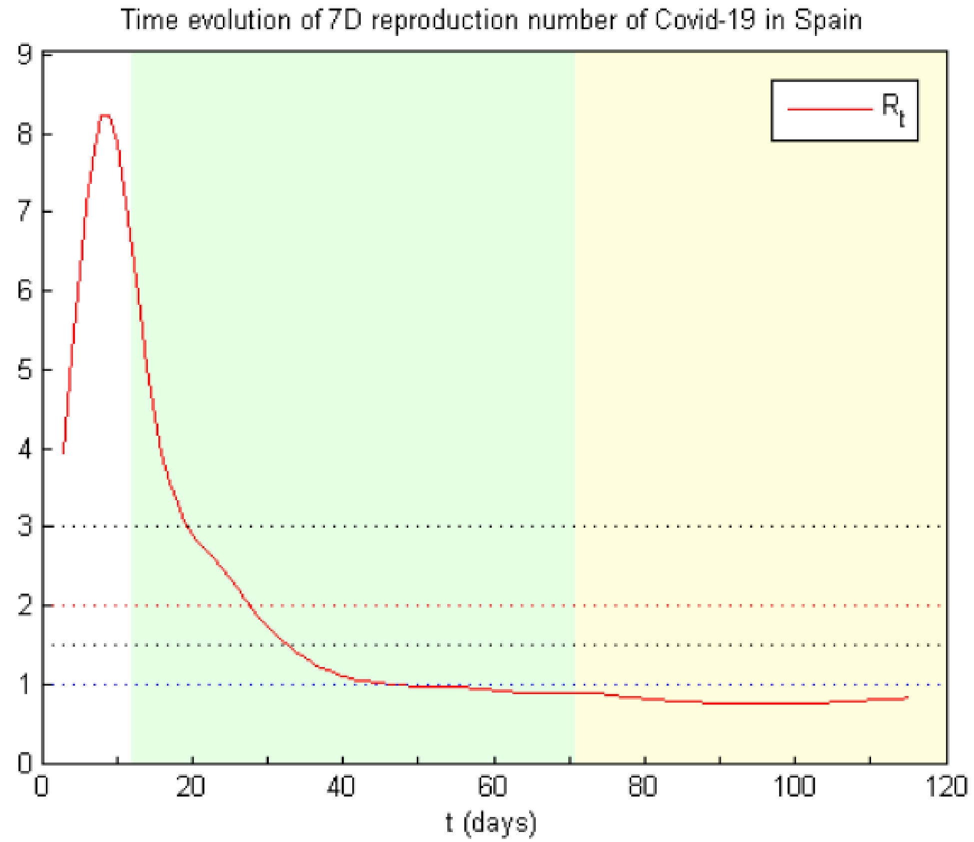


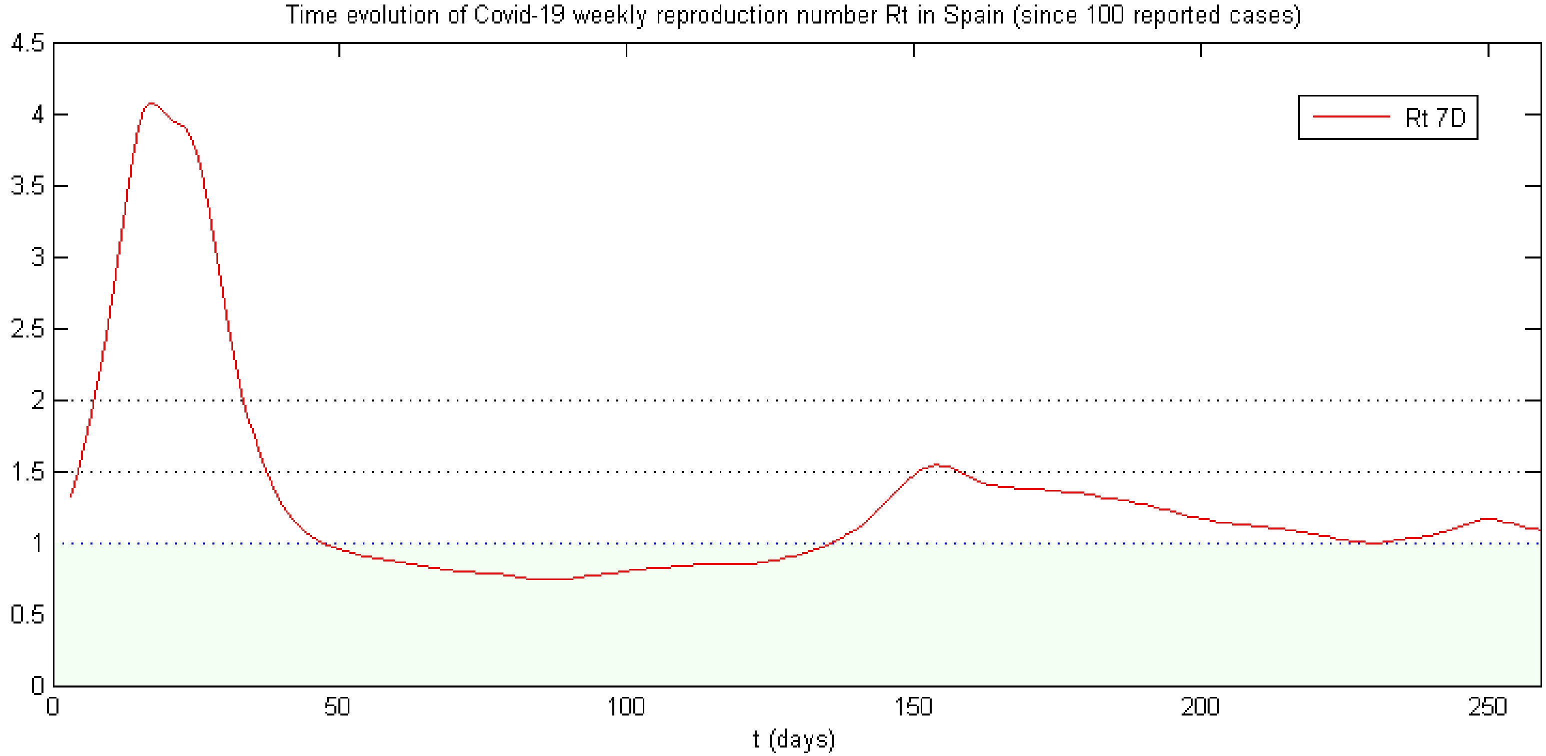


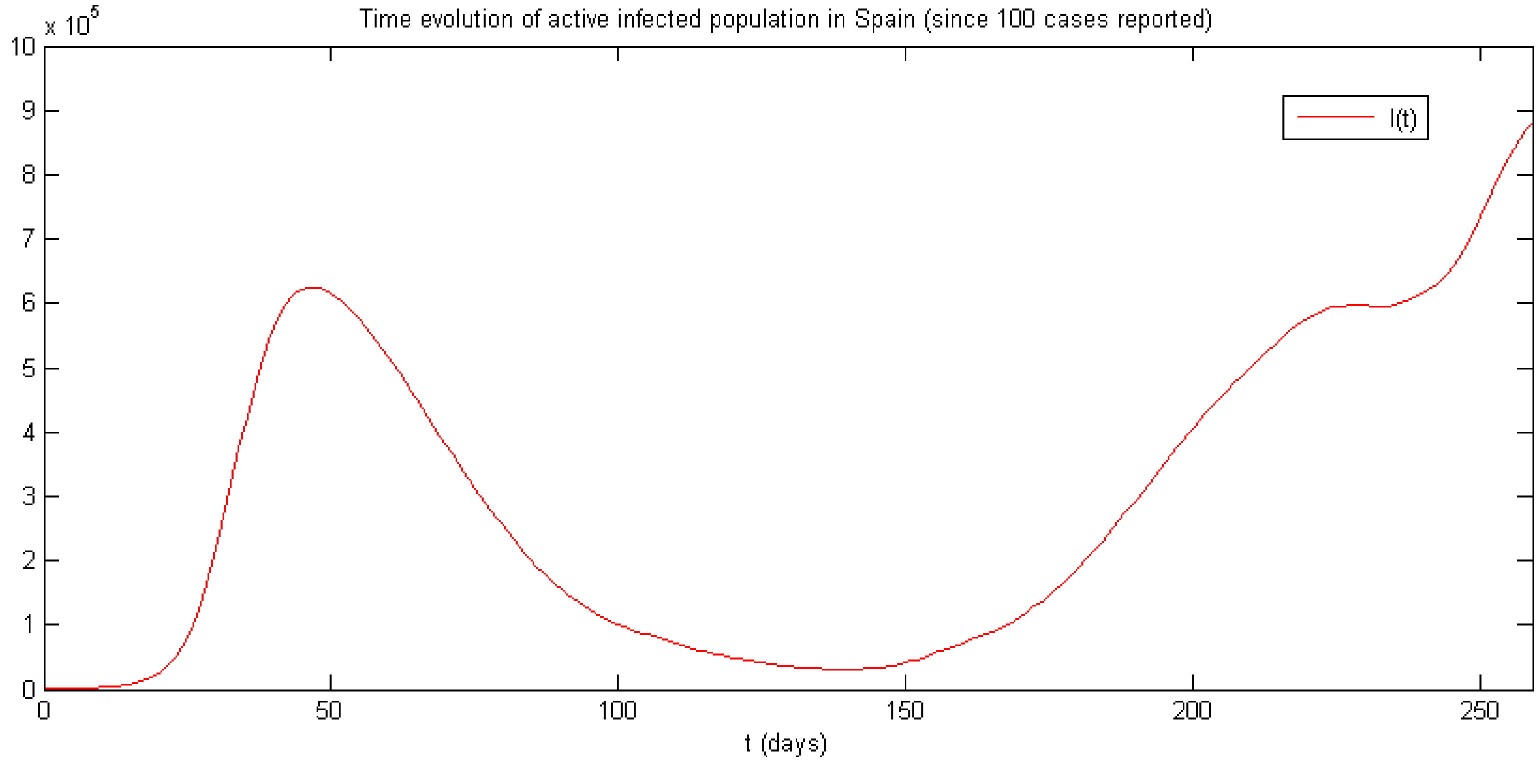
Time evolution of Covid-19 weekly reproduction number Rt in Italy (since 100 reported cases)
Rt 7D
0
1
2
3
4
5
6
7
0
50
100
150
200
250
t (days)


Time evolution of active infected population in Italy (since 100 cases reported)
x 10^5
7
6
5
4
3
2
1
0
I(t)
0
50
100
150
200
250
t (days)

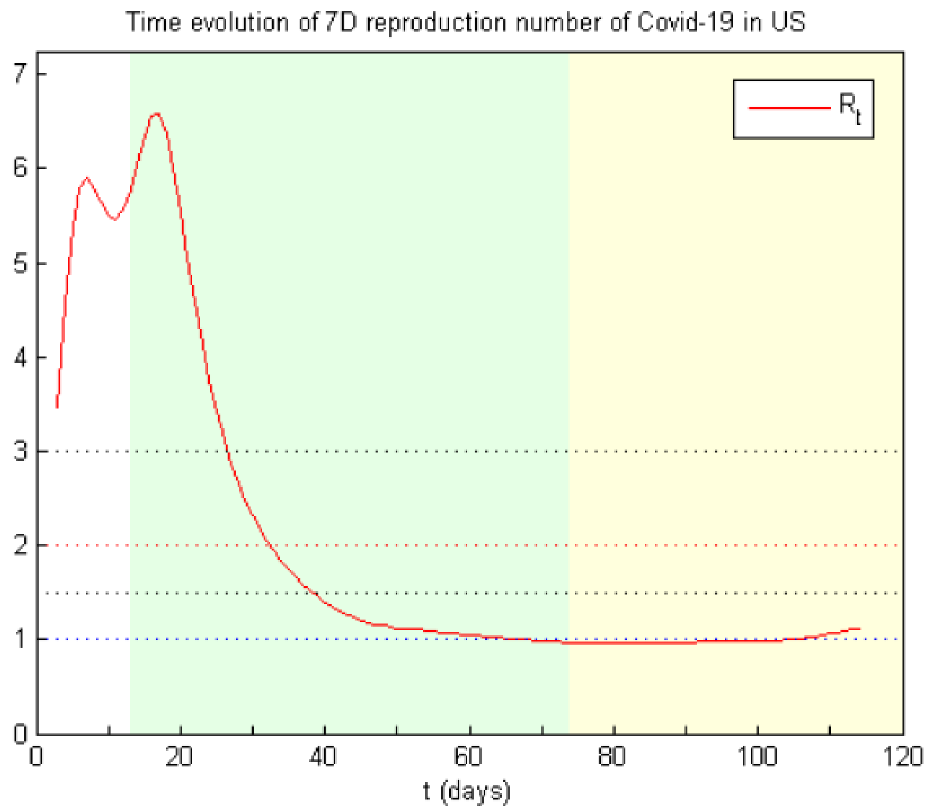
Example 6: Time evolution of Covid-19 in Spain since 03/01/2020, the date of 84 total cases reported ($t = 0$). After containment measures began on 03/13/2020 ($t = 12$), the value of R_t continually decreased to 0.89 on 05/11/2020 ($t = 71$), when restrictions began to be relaxed (yellow band). A minimum value of 0.75 was finally reached on 06/07/2020 ($t = 98$), after which a slow, steady increase set in towards the present value of 0.83 ($t = 115$), in much the same way as Italy.



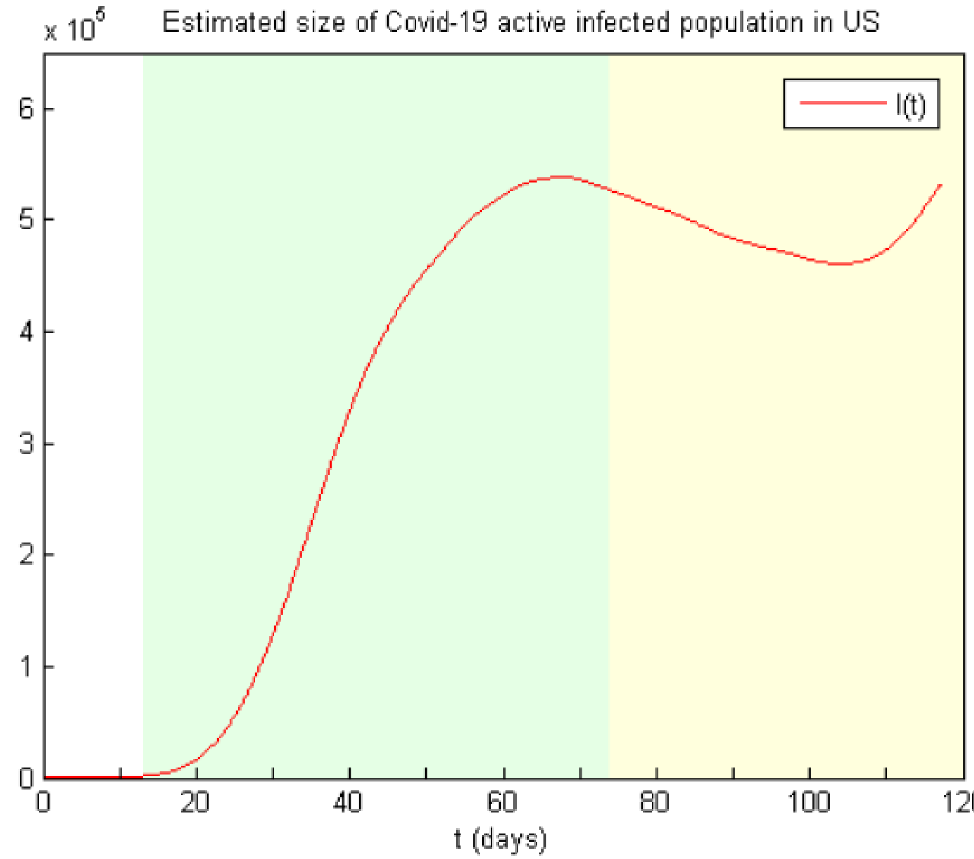

Time evolution of Covid-19 weekly reproduction number Rt in Spain (since 100 reported cases)
Rt 7D
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
0
50
100
150
200
250
t (days)

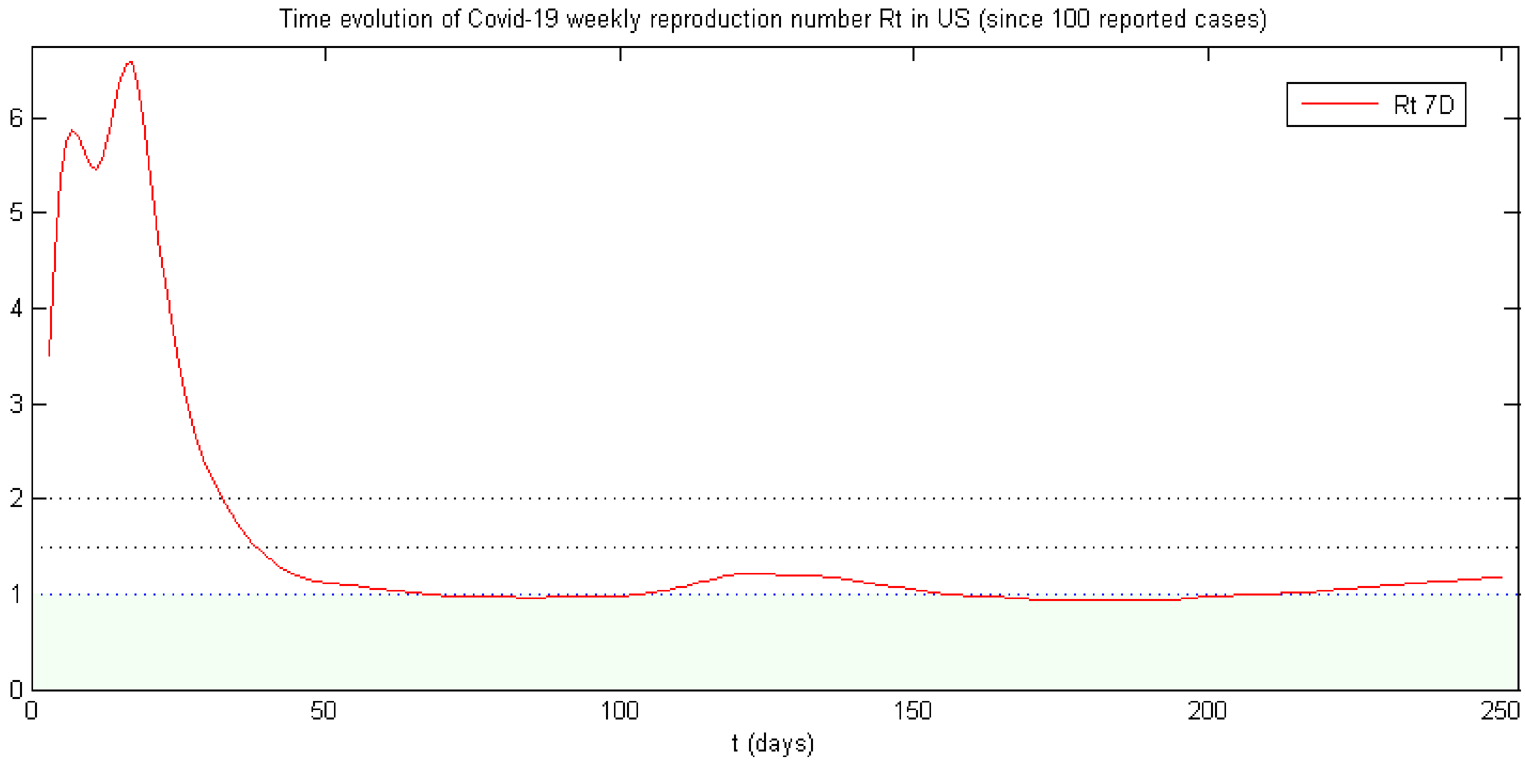

Time evolution of active infected population in Spain (since 100 cases reported)
x 10^5
10
9
8
7
6
5
4
3
2
1
0
0
50
100
150
200
250
t (days)
I(t)

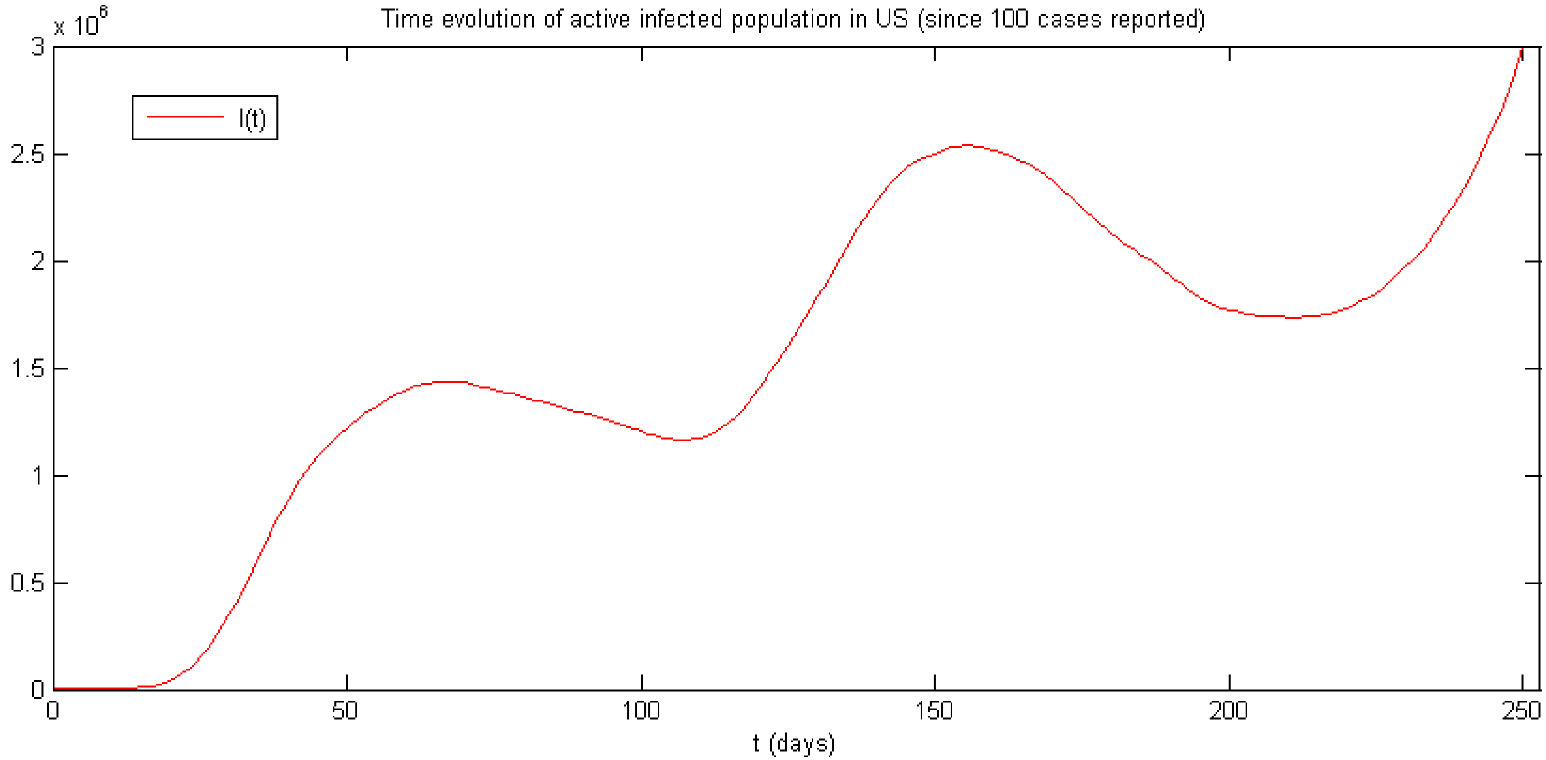
Example 8: Time evolution of Covid-19 in the US since 03/02/2020, the date of 100 total cases reported ($t = 0$). After containment measures began on 03/15/2020 ($t = 13$), R_t successfully decreased continually to 0.97 on 05/15/2020 ($t = 74$), when restrictions began to be relaxed, and then slightly down to 0.96 on 05/27/2020 ($t = 86$), followed by a slow and steady increase to the present value of 1.11 (yellow band). With a poor coordination between central and local authorities in the



beginning of the epidemic, the country suffered a high mortality rate (0.0388 %) and number of infections (more than 2.6 million cases reported). As of 06/27/2020, the US have not succeeded in bringing down the epidemic under nationwide control. A second peak ("second wave") in the size of the active infected population is now clear to happen sometime in the future, as indicated by the curve of $I_0(t)$ shown on the right.




Time evolution of Covid-19 weekly reproduction number Rt in US (since 100 reported cases)
Rt 7D
0
1
2
3
4
5
6
0
50
100
150
200
250
t (days)



Time evolution of active infected population in US (since 100 cases reported)
x 10^6
3
2.5
2
1.5
1
0.5
0
I(t)
0
50
100
150
200
250
t (days)

Um resultado final:

$$\begin{cases} \dfrac{dS}{dt} = -\beta(t)\,\dfrac{S(t)}{N}\,I(t), \\ \dfrac{dE}{dt} = \beta(t)\,\dfrac{S(t)}{N}\,I(t) - \delta\,E(t), \\ \dfrac{dI}{dt} = \delta\,E(t) - (r(t)+\gamma)\,I(t), \\ \dfrac{dR}{dt} = \gamma\,I(t), \\ \dfrac{dD}{dt} = r(t)\,I(t), \end{cases}$$

Teorema. *Existindo os limites*

$$\beta_* = \lim_{t\to\infty}\beta(t) \quad \text{e} \quad r_* = \lim_{t\to\infty} r(t),$$

então existem (e são positivos) os limites

$$\sigma = \lim_{t\to\infty}\frac{S(t)}{N}, \quad \alpha = \lim_{t\to\infty}\frac{E(t)}{I(t)}, \quad \text{e} \quad \lim_{t\to\infty}\frac{I(t+d)}{I(t)} = e^{(\alpha\delta - (r_* + \gamma))\,d}$$

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http://miba-srv01.nuvem.ufrgs.br:8080/shiny/simcovid19 (Gabriela Cybis, IME/UFRGS)
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Obrigado!