Real-time monitoring the COVID-19 pandemic

The point of view of a physicist

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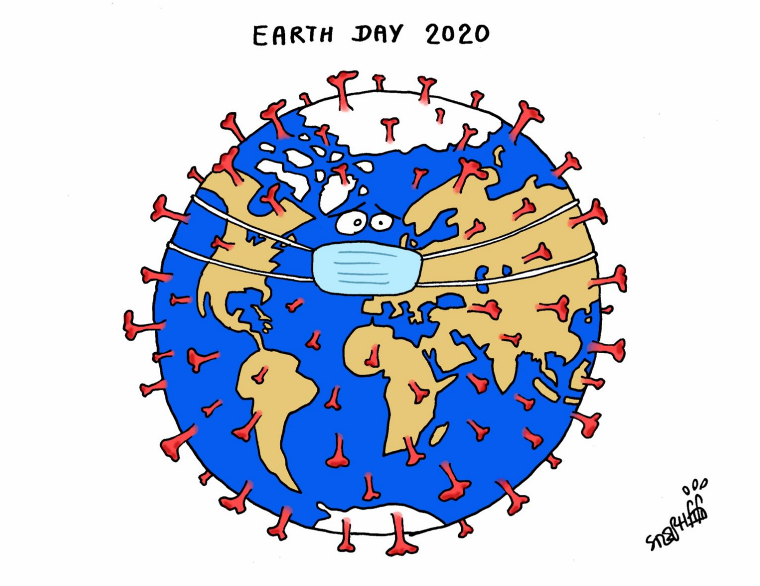

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Preamble

- This work was initiated primarily for a personal use :

  - Have the clearest possible picture of the pandemic situation from the end of February 2020 and check the consistency of the many announcements : publications, news, authorities,…

  - Perform medium or long term projections when possible : business and personal travels, daily life, family, work, investments …

  - *Understand the dynamics of the COVID-19 pandemic which is a unique event on this scale in a human life (primarily for non-specialists).*

- After the first developments, all the results were online from mid-March 2020 on my personal page, then updated daily or weekly, depending on the situation.

- A paper is under submission in a peer review journal.

- **The kind support of many colleagues, friends and internet followers is greatly acknowledged. Their encouragements and help were a great motivation to continue this work despite the lack of time !!**

Main questions

- Could we describe the COVID-19 pandemic with a minimum set of assumptions ?
- Could we have robust predictions ?
- Can we have a consistent picture of the pandemic worldwide ?
- Where is the major source of uncertainty in the modeling ?
- Can we have a consistent view between R_0 and herd immunity ?
- …

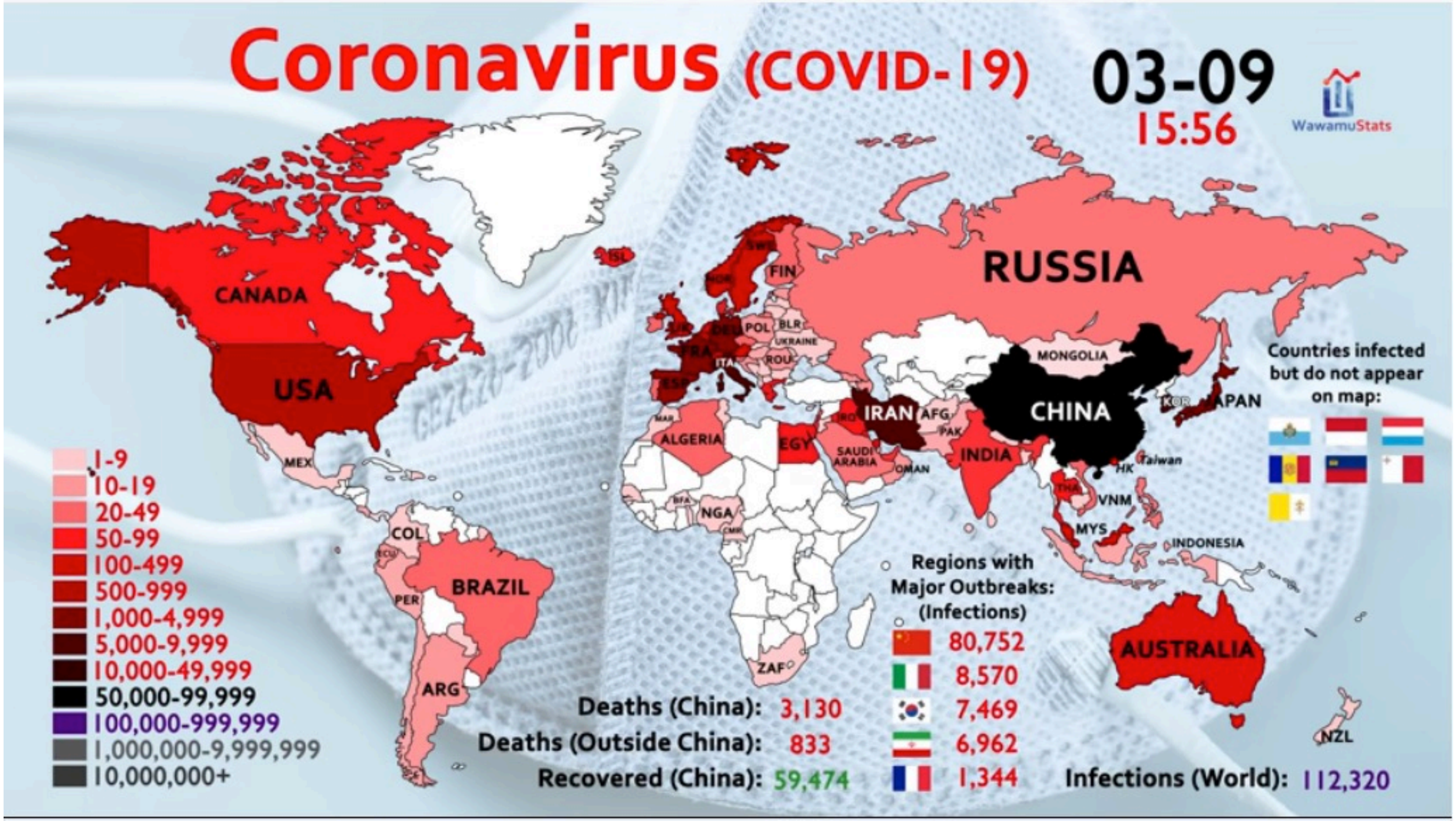
Outline

- **Timeline and some key dates**
- **Challenges in outbreak modeling**
- **Outbreak modeling**
  - *Code description: SIR model + social distancing function*
  - *Computing procedure and validation (Hemorrhagic fever, Ebola)*
- **Global modeling parameters**
  - *Main time lags*
  - *Infection fatality rate (IFR) model (Diamond-Princess)*
  - *Mean IFR in the world*
- **COVID-19 pandemic monitoring**
  - *Dynamics of the COVID-19 for a set of representative countries.*
  - *Estimation of R_0 and the level of the collective immunity.*
  - *Lockdown : impact of the date and comparison between countries*
  - *Secondary waves and variants*
  - *Monitoring the vaccination efficiency*

Timeline and some key dates

- COVID-19 outbreak started officially at the end of December 2019 at Wuhan, Hubei province, China
- It spreads rapidly around the world in January 2020 (maps from John Hopkin's University)
- *Human-to-human contaminations officially announced by China on January 22, 2020*
- Lockdown of Wuhan and Hubei province on January 23, 2020
- Diamond-Princess cruise liner officially in quarantine on February 1st, 2020 (cruise departure on January 20, 2020) for COVID-19 onboard.
- Fast spread of COVID-19 in Europe, especially in Italy and Spain, then in France during February 2020. Respective lockdowns : the 9th,13th and 16th of March 2020
- WHO announced the **pandemic nature of COVID-19** on March 11, 2020
- …

Timelapse of COVID-19 in the world up to the 30-Oct-2020



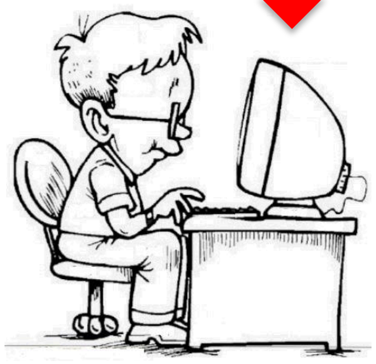
Link : https://www.youtube.com/watch?v=NxUgD6T_RIA

Challenges in outbreak modeling

- **Get reliable public data** : from WHO and some domestic health organizations (daily updated) : cumulative numbers of infections (I) and fatalities (F) + number of people in intensive care units (ICU) in some countries.

- **Calculate some important generic quantities which must be determined prior to simulations** : *mean infection to fatality rate (IFR), infection + recovery + fatality times,…*

- **Take into account of the COVID-19 specificities** : *age dependence of the IFR* → age-stratified structure per country from UNO (+ population density of major cities), *most infected persons have no symptoms.*

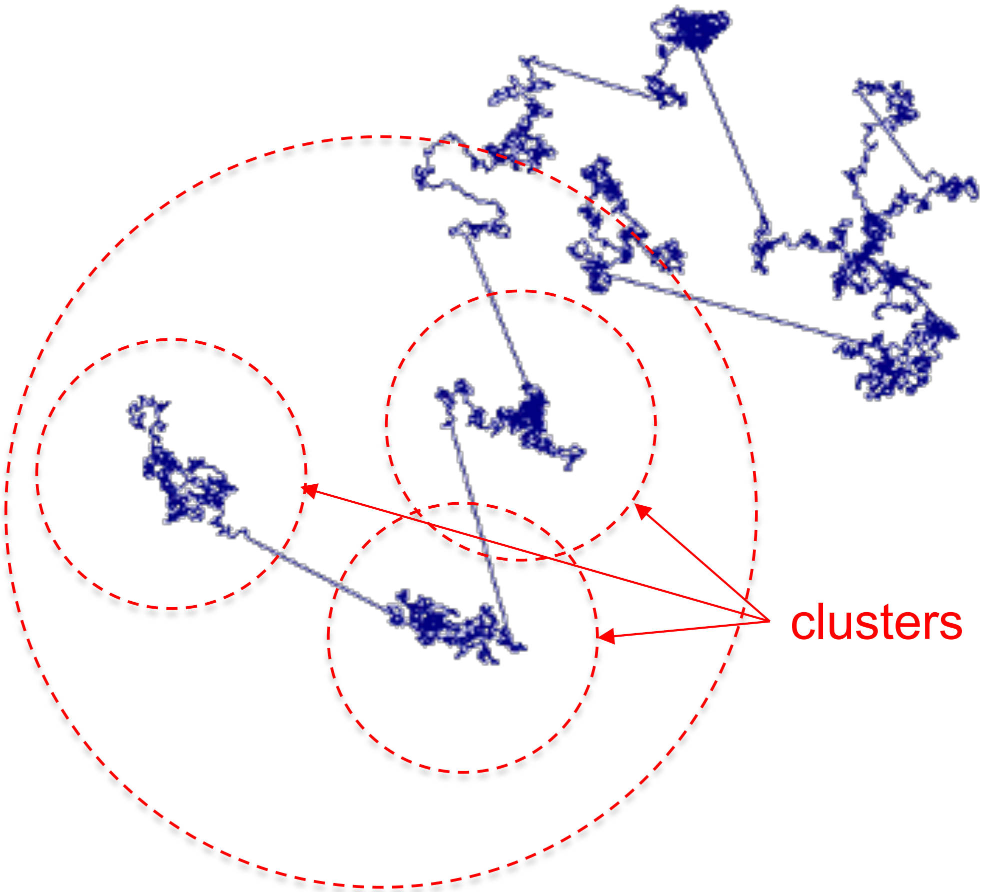


- Basic reproduction factor R_0 and the effective one R(t).
- Impact of lockdown/curfew → date of the outbreak peak.
- Daily numbers of infections, fatalities and people in ICU at important dates (10 days, …)
- Dates of symbolic thresholds (1000, 10000, 100000,… fatalities).
- Level of population immunity → *risk of secondary waves*
- Outbreak duration (*very rough estimate*)
- Impact of a vaccination campaign

Outbreak modeling

- *Code description: SIR model + social distancing function*
- *Computing procedure and code validation (Ebola outbreak, Western Africa 2014-2015)*

Why a 0-D approach is valid for the COVID-19 pandemic ?



2-D spatial diffusion of the virus

- The spatial diffusion of the SARS-CoV-2 looks like a Lévy flights diffusion process (Johns Hopkins data).
- Formations of **multiple almost independent clusters.**

- The dynamics of the disease may be considered as **scale invariant.**
- The general properties of the COVID-19 may be obtained regardless of the size of the considered population.
- One can compare countries, states, cities and boats (0-D approach)

Modeling COVID-19 : which method to consider ?

- Modeling outbreaks is a long standing activity → works of Anderson Gray McKendrick and William Ogilvy Kermack developed in 1927 (compartmental concept)

- Two categories of model : **deterministic** or stochastic.

- **Deterministic approach is appropriate for large populations** that can be assigned to different subgroups, named as susceptible (S), infected (I) or recovered (R) or SIR-type model.

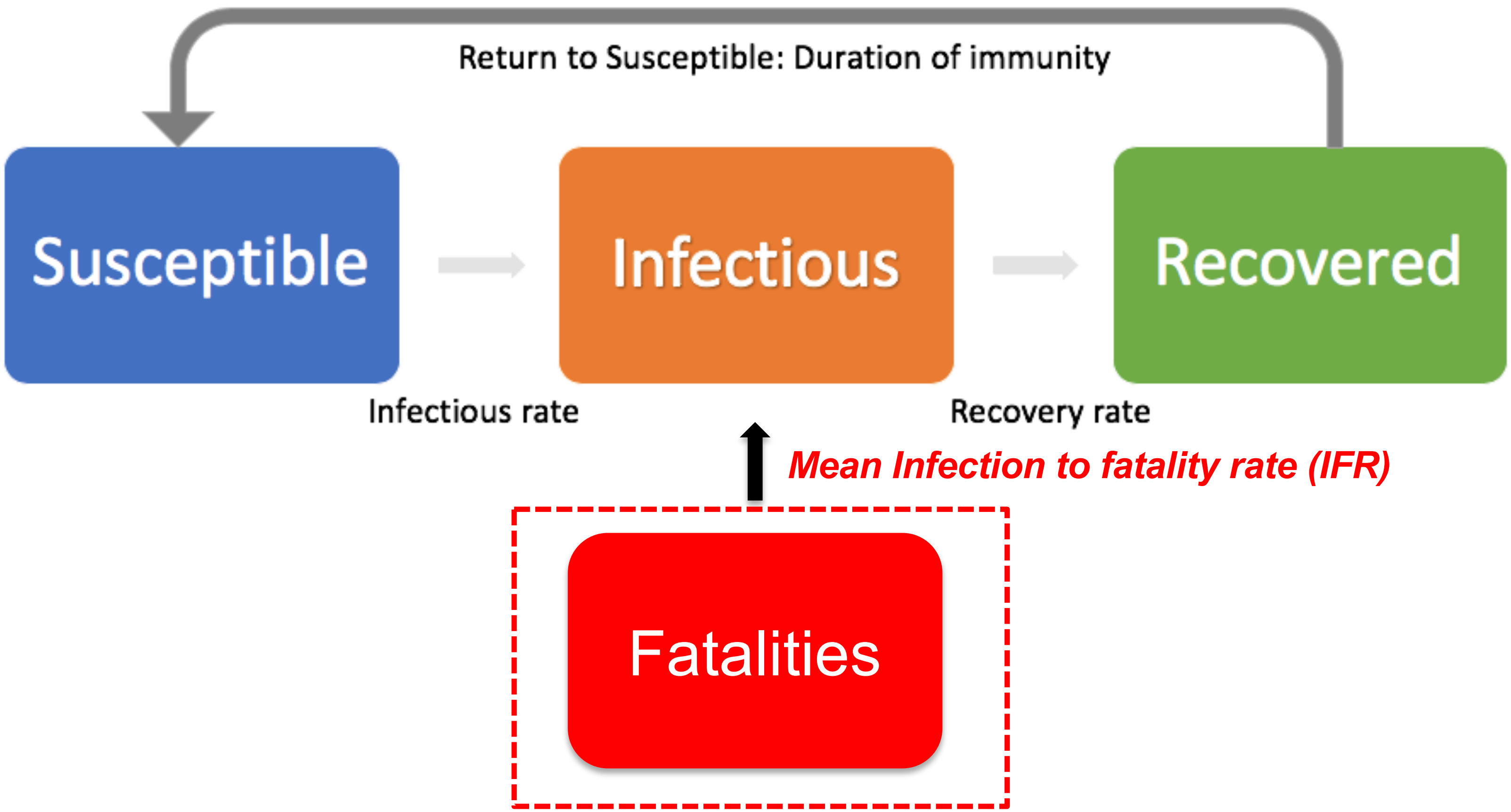
- In a standard approach, the transition rates from one group to another are described by an ordinary differential equation, so the simplest SIR model is made of three coupled differential equations whose solutions give the time evolution of the number of people in each group.

- Many refined models are existing, some of them mixing deterministic and stochastic methods, with more compartments, and spatial description (inhomogeneity).

- *A general statement* : very complex codes with many coupling between different reservoirs is rarely able to be predictive accurately (too many free parameters)

The SIR model for the COVID-19

A SIR approach has been considered → simple + fast + large infected population



COVID-19 specificity because many people are infected without symptoms

The simplified SIR model : main equation

- ***The COVID-19 is mainly driven by infections → a single delay differential equation is solved.***

- Daily incremental increase of infected people where q_I^j is the infection rate per day (day j) :

$$\boxed{\triangle N_I^j = q_I^{j-1}\left(N_I^{j-1} - N_R^{j-1} - N_F^{j-1}\right)\Delta t}$$

- Cumulative number (day j) : $\boxed{N_I^j = \triangle N_I^j + N_I^{j-1}}$

- With a constant q_I, N_I is a simple geometric time series (*exponential growth*) → the dynamics of the outbreak comes from the time dependence of q_I *and* N_R *(recovery time). Approximation : infected people are immediately contagious once infected, and cannot be reinfected (long immunity)*

- *When* N_I and N_F contain the same information (cross-correlation ≈ auto-correlation), *other compartments can be simply described by lags and proportional coefficients to the population I* (δ_F **= mean Infection to Fatality Rate (IFR)**, $j_F \times \Delta t$ = fatality time, $j_R \times \Delta t$ = recovery time).

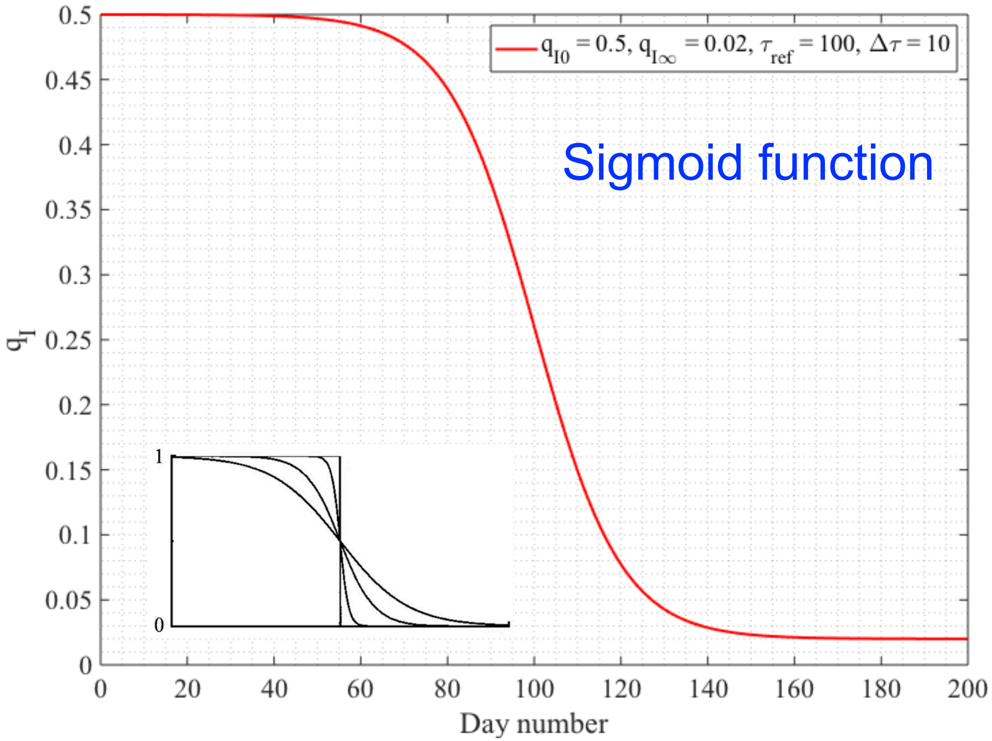
$$\boxed{N_F^j = \delta_F N_I^{j-j_F}} \qquad \boxed{N_R^j = (1-\delta_F)\, N_I^{j-j_R}}$$

The social distancing law

- The infection rate is described by a *sigmoid function* (may be chained if change of slope in N_I dynamics, secondary waves) :

$$\boxed{q_I^j = \left(q_{I0}^j - q_{I\infty}^j\right)\left(\frac{1+\exp\left(-\tau_{ref}^j/\Delta\tau^j\right)}{1+\exp\left(\left(j\Delta t - \tau_{ref}^j\right)/\Delta\tau^j\right)}\right) + q_{I\infty}^j}$$

⟷ Social distancing



- **An effective reproduction number** may be naturally introduced (day j) :

$$\boxed{R^j \equiv q_I^j \tau_i}$$

- τ_i is a time during which infected people can contaminate R^j susceptible ones (compartment S)

- Basic reproduction number (from the 1st wave only) :

$$\boxed{R_0 = q_{I0}\tau_i}$$

Basic reproduction number R_0

- **The basic reproduction number R_0** is a dimensionless number that characterizes the natural contagiousness of a virus: it gives the expected number of secondary cases produced by a single (typical) infection in a completely susceptible (S) population. (seasonal flu → $R_0 \approx 1.5$).

- R_0 gives informations on transmissibility, contact rates, and the mean expected duration of infection τ_i. So, in the simplified model, the infection rate is

$$\boxed{q_I = (\text{transmission/contact}) \times (\text{contact/time})}$$

  - transmission/contact : reduction by wearing mask, washing hands, ventilation
  - contact/time : confinement, curfew, population density

- By definition, R_0 can only be determined during the initial phase of the outbreak, because social distancing is supposed to be small at that time (constant rates, no demography and well-mixed population), while the reservoir of susceptible people is almost infinite.

R_0 and herd immunity : finite reservoir effect

- The susceptible population (S) is given by

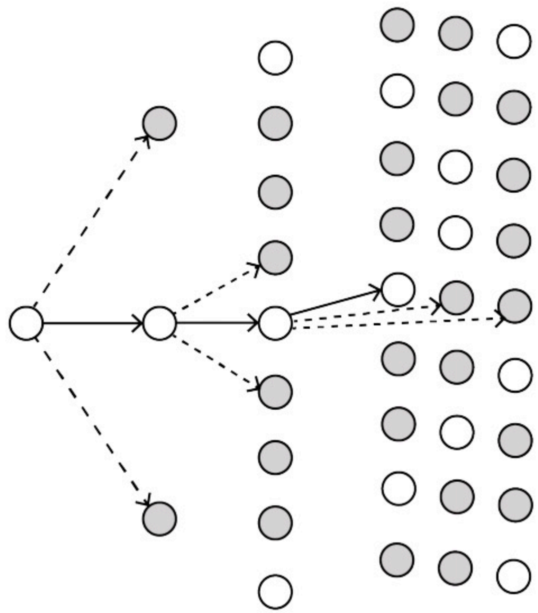
$$N_S = N_{tot} - N_I - N_R - N_V - N_F$$

where N_{tot} is the total number of people, N_V the number of vaccinated people.

- As the outbreak develops, the susceptible population is decreasing → the mean number of people that can be infected by someone contaminated is progressively lower : the **effective reproduction number is $R = R_0 \times N_S/N_{tot}$.**
(at t = 0, $N_S = N_{tot}$ and $R = R_0$, and $R = 0$ when $N_S = 0$)

- The outbreak starts to vanish when $R < 1$. When it is fully over, $N_I = 0$, and supposing that $N_F << (N_{tot}, N_R, N_V)$, the immunited fraction of the population is $f^\infty = (N_R + N_V)/ N_{tot}$:

$$\boxed{R < 1 \rightarrow R_0 \times (1- f^\infty) < 1 \rightarrow f^\infty > 1 - 1/R_0}$$



$R_0 = 3$, grey points → already immunited

Computing procedure

- The four parameters of the social distancing law (sigmoid-like function) and day #0 are determined from the constraint to obtain the best fit of the **fatalities time series used as a proxy of the COVID-19 outbreak before large vaccination** because of the *difficulty to know the infected population* → Maximizing the coefficient of determination $\mathcal{R}$ ranging between 0 (no agreement) and 1 (perfect agreement).

$$\boxed{\mathcal{R}^2 = 1 - \delta_{res}/\delta_{tot}}$$

Residual sum of squares →

$$\delta^j_{res[I,F]} = \sum_{k=1}^{k=j} \left(\underbrace{\boxed{\mathbf{n}^k_{[I,F]}}}_{\text{observations}} - \underbrace{\boxed{n^k_{[I,F]}}}_{\text{simulations}} \right)^2$$

Explained sum of squares →

$$\delta^j_{tot[I,D]} = \sum_{k=1}^{k=j} \left(\mathbf{n}^k_{[I,F]} - \overline{\mathbf{n}}^j_{[I,F]} \right)^2$$

$\mathbf{n}_{[I,F]}$ are measured daily numbers of infections and fatalities ($n_{[I,F]}$ calculated ones)

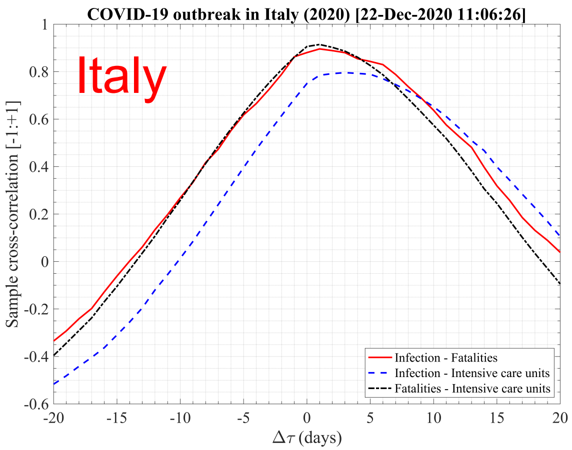
- *Other times series (people in ICU and positive tests) may be used **qualitatively** in particular to identify changes in the outbreak dynamics (important for sudden secondary waves).*

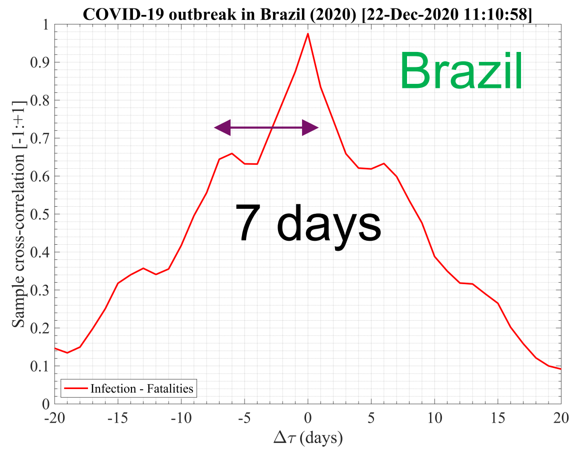
- Daily updated set of parameters → allow to estimate the robustness of the predictions.

- Data quality → sample cross-correlations $\Gamma_{X-Y}(\Delta\tau) = \int X(t)\, Y(t - \Delta\tau_{xy})\, dt$

Data quality : sample cross-correlations (1st wave)

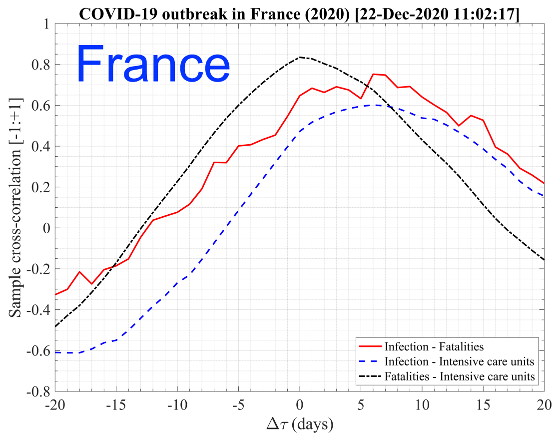
Clean.
Stable
with time.

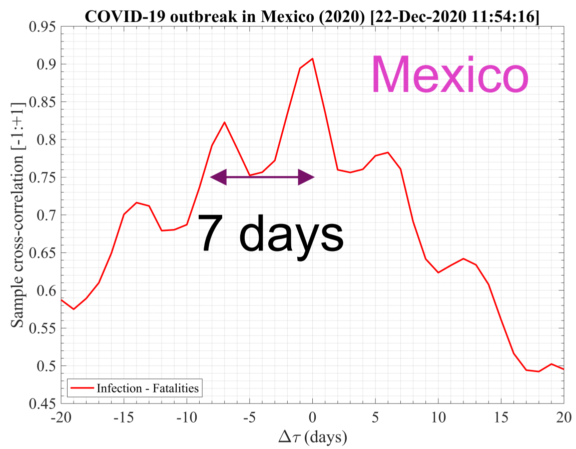




Slightly
periodic
cross-
correlation.
*Degradation
with time.*

Slightly
noisy.
*Degradation
with time.*

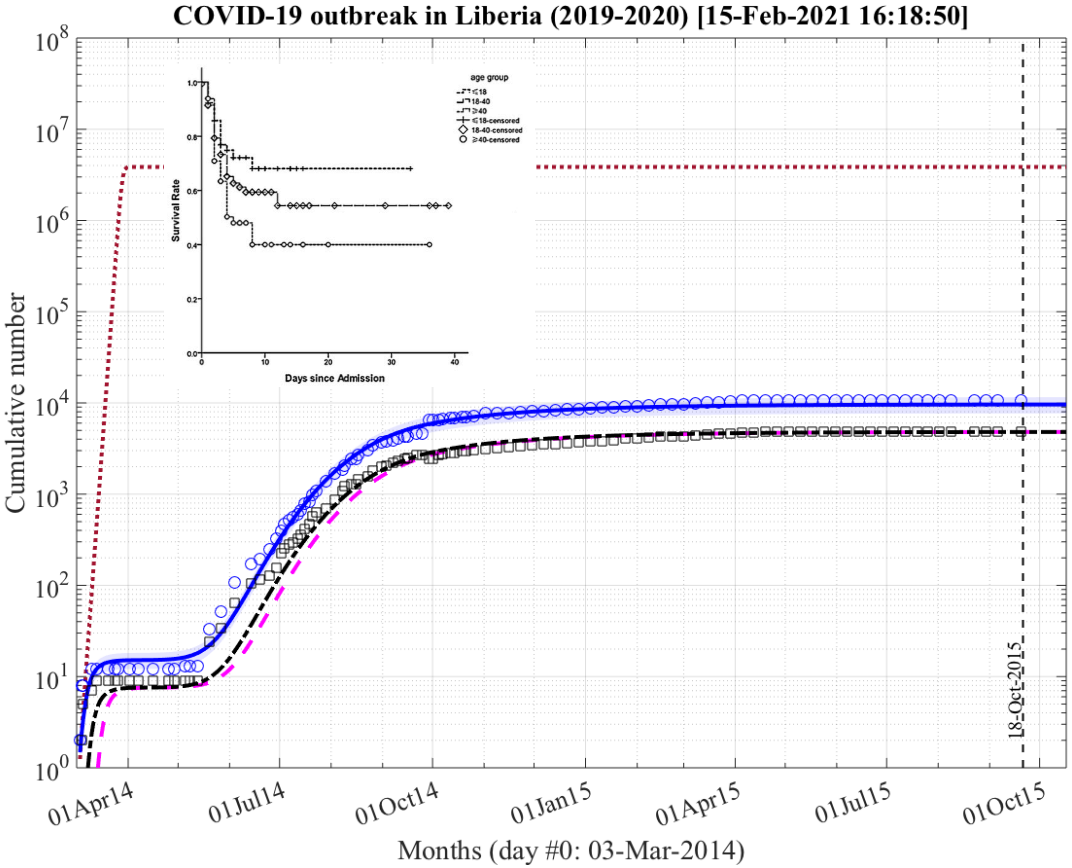


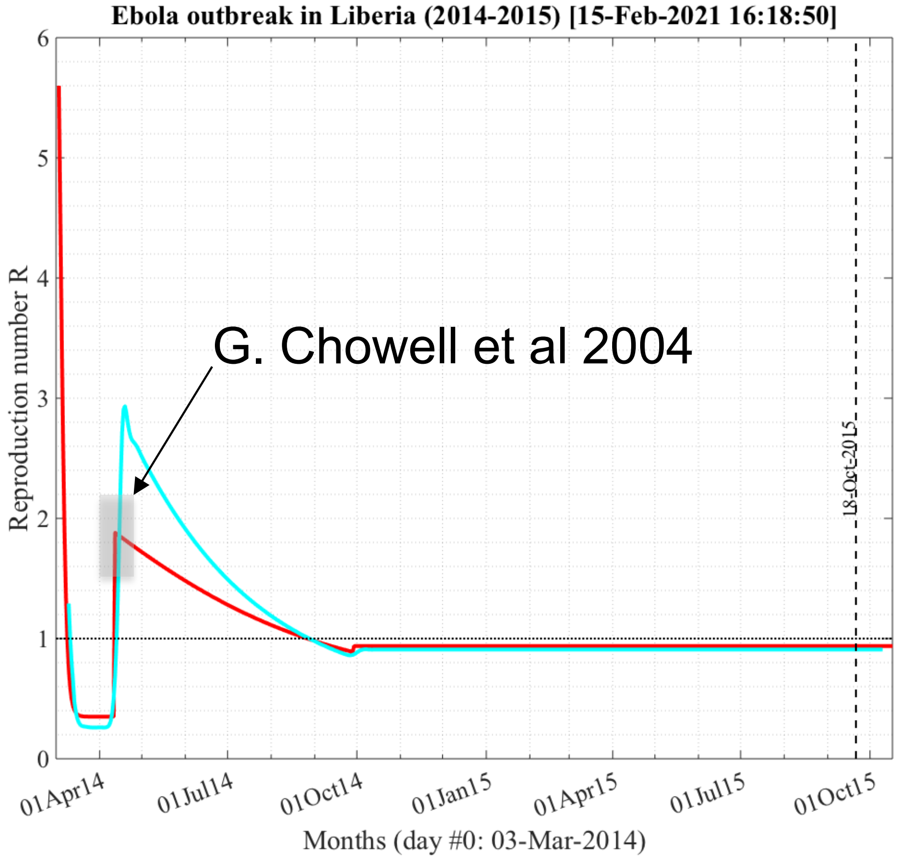


Strongly
periodic
cross-
correlation.
*Degradation
with time.*

Lags deduced from cross-correlations are not related to intrinsic characteristics of the disease but result from administrative organization. In addition, ***reported fatality dates are not the actual fatality dates which can lead to some marginal bias in data analysis.***

Code validation : Hemorrhagic fever (Ebola)





- τ_i = 7 days (R = 1 when $dN_I/dt = 0$), mean incubation time : 6.5 days from Refs.
- Different slopes between first and second wave (like for COVID-19)

G. Chowell et al. Journal of Theoretical Biology 229 (2004) 119-26
M. Eichner et al. Public Health Res Perspect 2 (2011), 3-7
J. Li et al., International Journal of Infectious Diseases 42 (2016) 34–39

Global modeling parameters

- *Main time lags*
- *Infection to fatality rate (IFR) model (Diamond-Princess)*
- *IFR in the world*

Main time lags

Two delays linear differential equation

$$\boxed{\dot{N}_I = q_I \left(N_I - (1-\delta_F)\, N_I\,(t-\tau_R) - \delta_F N_I\,(t-\tau_F)\right)}$$

- **τ_R = 12 days :** close to the 95th percentile of the distribution of patients at hospital in Wuhan, and close to the two weeks official « quarantine » duration for WHO. *R(t) of the model consistent with Cori's method using* τ_R *= 12 days, while it is not consistent with* τ_R *= 6 days.*

- **τ_F = 6-7 days** at the begining of the outbreak (from Russel et al.) and **20-30 days** later from time series analysis (Arizona,…), and the correlations between outbreak contamination peak and the date of the lockdowns (France, Italy, Switzerland,…).

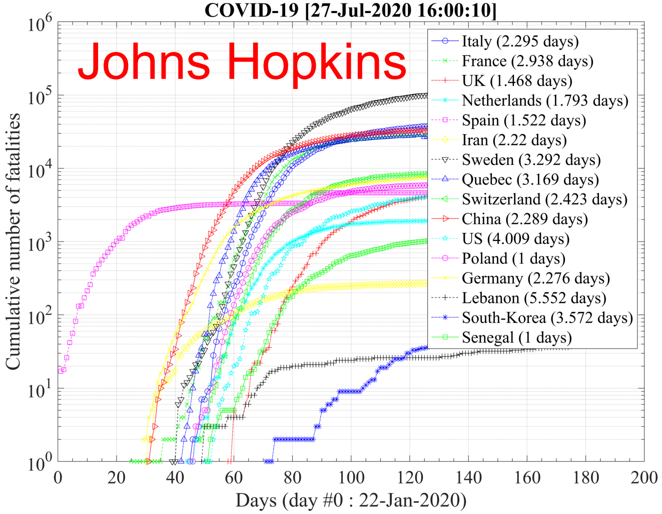
- In the limit of a very low IFR or $\delta_F \ll 1$, valid for COVID-19, $\tau_I = \tau_R$ and **$R = q_I\tau_R$** (from the characteristic equation).

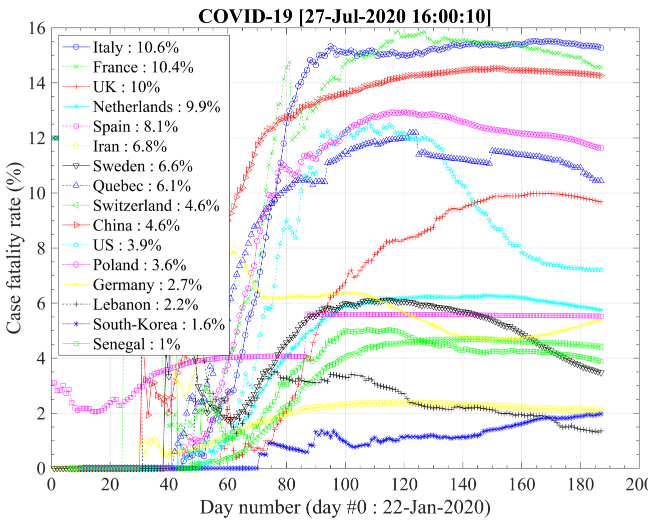
- The time lag τ_{ICU} of the ICU time series as well as the fraction of the infected people requiring intensive care δ_{ICU} are obtained from the best fit of observations : $\tau_{ICU} \sim \tau_F$ within one or two days.

$$\boxed{\frac{n^j_{ICU}}{n^j_F} \simeq \frac{\delta_{ICU}}{\delta_F}}$$

O. Arino et al., Delay Differential Equations and Applications (2002), Springer
T. W. Russell et al, Euro Surveill. 25 (2020); Q. Li, New England Journal Medicine 382 (2020) 1199-1207, DOI: 10.1056/NEJMoa2001316

COVID-19 infection fatality rate (IFR) determination





$$\boxed{R_0 = \tau_i \left(\exp\left(\ln 2/\tau_{\times 2}\right) - 1\right)}$$

- Fast rise of the cumulative number of fatalities, first in China, then in many countries.

- **Initial rises of fatalities are similar for all countries** (including China), all corresponding to a rough averaged doubling time $\tau_{x2} \approx 2.5 \pm 0.8$ days → first estimate from the 8-10 first days : $\mathbf{R_{0(x2)} \sim 3.6 \pm 1.2}$ (τ_i = 12 days)

- **The case to fatality rate (CFR) from the number of positive tests N_c is useless** : it varies strongly from country to country, and with time for a given country → *a lot of infected people are asymptomatic and missed by tests* → large underestimation of the number of of infections N_I leading to overestimate the IFR → *impact on determination of the level of collective immunity.*

- **The fatalities are used as the main proxy of the outbreak.**

- **Calibration of the IFR when $N_c \approx N_I$ → COVID-19 in Diamond-Princess cruise liner.**

Mean IFR for the COVID-19 : calculation procedure

Diamond-Princess

- Determination of the mean IFR from time series analysis of the COVID-19 in the Diamond-Princess cruise liner.

- **Calibration of the IFR model** to find consistently the mean IFR deduced from the time series analysis and the observed age structure of the fatalities, using the known age-structure of the infected population on board.

- Calculation of the mean IFR worldwide using the calibrated IFR model and the age structure of the population (assumed to be similar to the infected population)

- Calculate the actual number of infected people from the fatalities time series, and estimate the level of collective immunity with respect to the theoretical herd immunity ($1 - 1/R_0$) → check the overall consistency (must include also the effect of an artificial immunity provided by vaccination, and its progressive reduction with time)

COVID-19 in Diamond-Princess cruise liner

- COVID-19 model was developed by end of February 2020. Few available data for calibrating the model : *IFR, lags, proportional coefficients,…*

- *Diamond-Princess cruise liner offered a unique opportunity to do it* : almost isolated environment, large number of passengers (2666) and crew members (1045), two populations well separated in median age : passengers (69y), crew (36y).

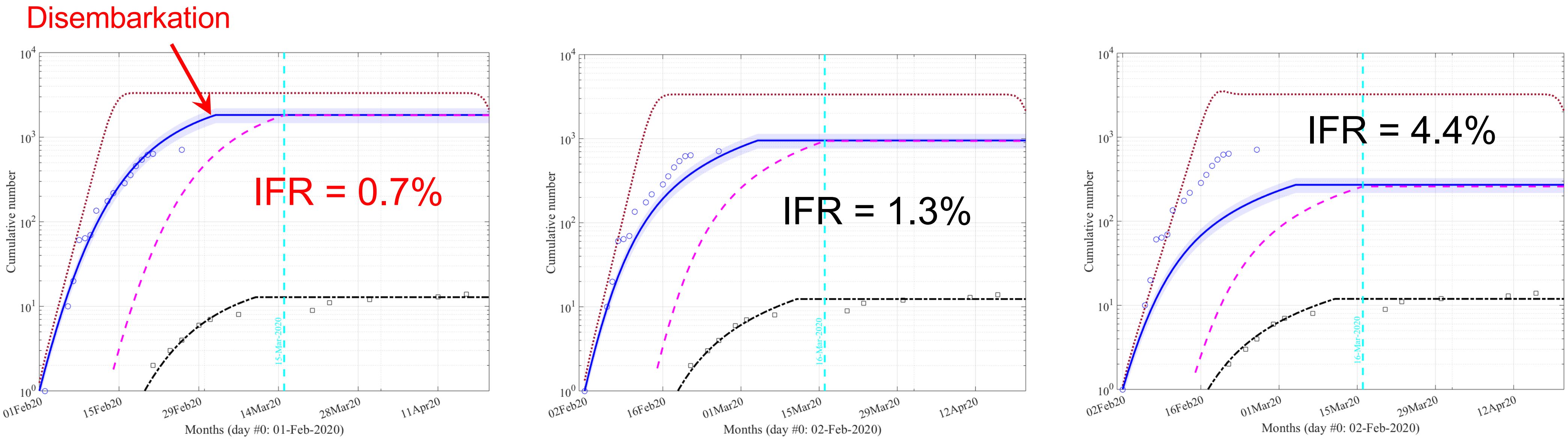
- All population tested (PCR tests mostly) : large number of infected people (712), 7 fatalities (1st of March 2020), but 7 more later (14th of April 2020) → total 14 fatalities.

- No fatalities in the crew population → **clear evidence of the IFR age dependence** (seen also in the fully isolated Shackleton expedition with less people (217), and Charles-de Gaulle aircraft carrier with a young population → 1050 infected over 1950 people, no fatalities)

- Cruise start : 20th of January 2020. One Chinese passenger already infected was disembarked the 25th of January. Everybody disembarked the 1st of March 2020.

T. W. Russell et al, *Euro Surveill.* 25 (2020) K. Mizumoto and G. Chowell, *Infectious Disease Modelling* 5 (2020) 264-270 Ing AJ, et al. *Thorax 75* (2020) 693-694

COVID-19 in Diamond-Princess : mean IFR value from time series

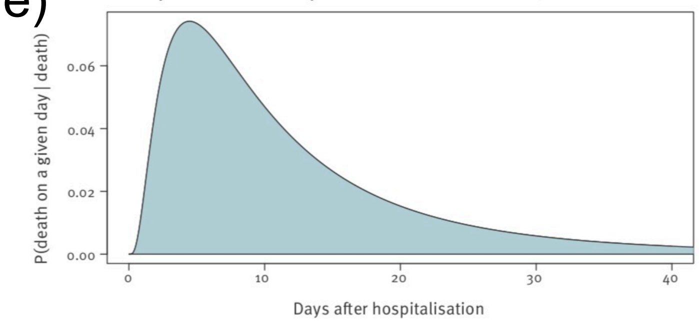


- Single solution fully consistent with data : mean IFR = **0.7%** ***(upper limit, since asymptomatic infected population is assumed to be small < 15%. See refs.)***

- Day #0 : 1st of February 2020 (10 days after cruise departure)

- j_F = 7 days (consistent with Wuhan hospital data) but the tail of fatalities may be very long (~2 months)

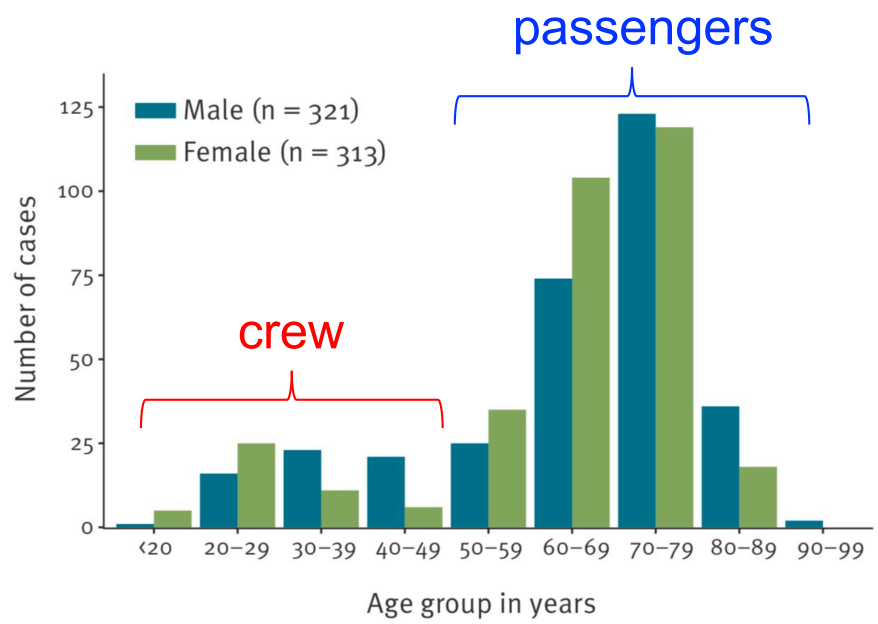
A. Delay distribution of hospitalisation to death in Wuhan, China



T. W. Russell et al, *Euro Surveill.* 25 (2020)
K. Mizumoto and G. Chowell, *Infectious Disease Modelling* 5 (2020) 264-270

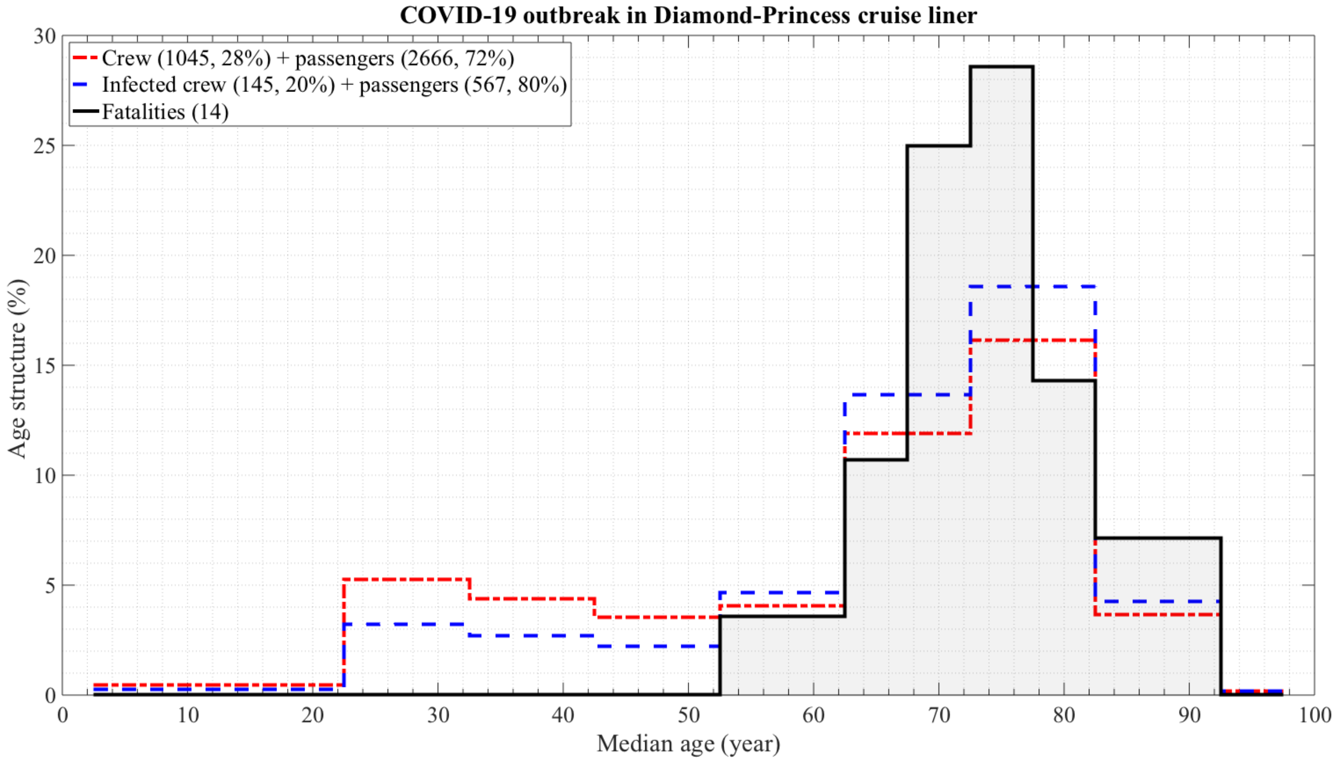
COVID-19 in Diamond-Princess : age-structure of the infected population

- No age-stratified structure available for the whole population of the Diamond-Princess
- 567 out of 2666 passengers and 145 out of 1045 crew have been infected.
- Age-stratified structure for infected people only, but does not reflect the actual one (bias) → median age : 69 years old
- Age-stratified structure of the whole population on the cruise liner *rebuild from sparse details* :
  - crew [20y-50y], median age of 36y
  - passenger [50y-90y] has median age of 69y
- Reconstruction possible because the two populations (crew, passengers) are well separated in age



K. Mizumoto and G. Chowell, *Infectious Disease Modelling* 5 (2020) 264-270

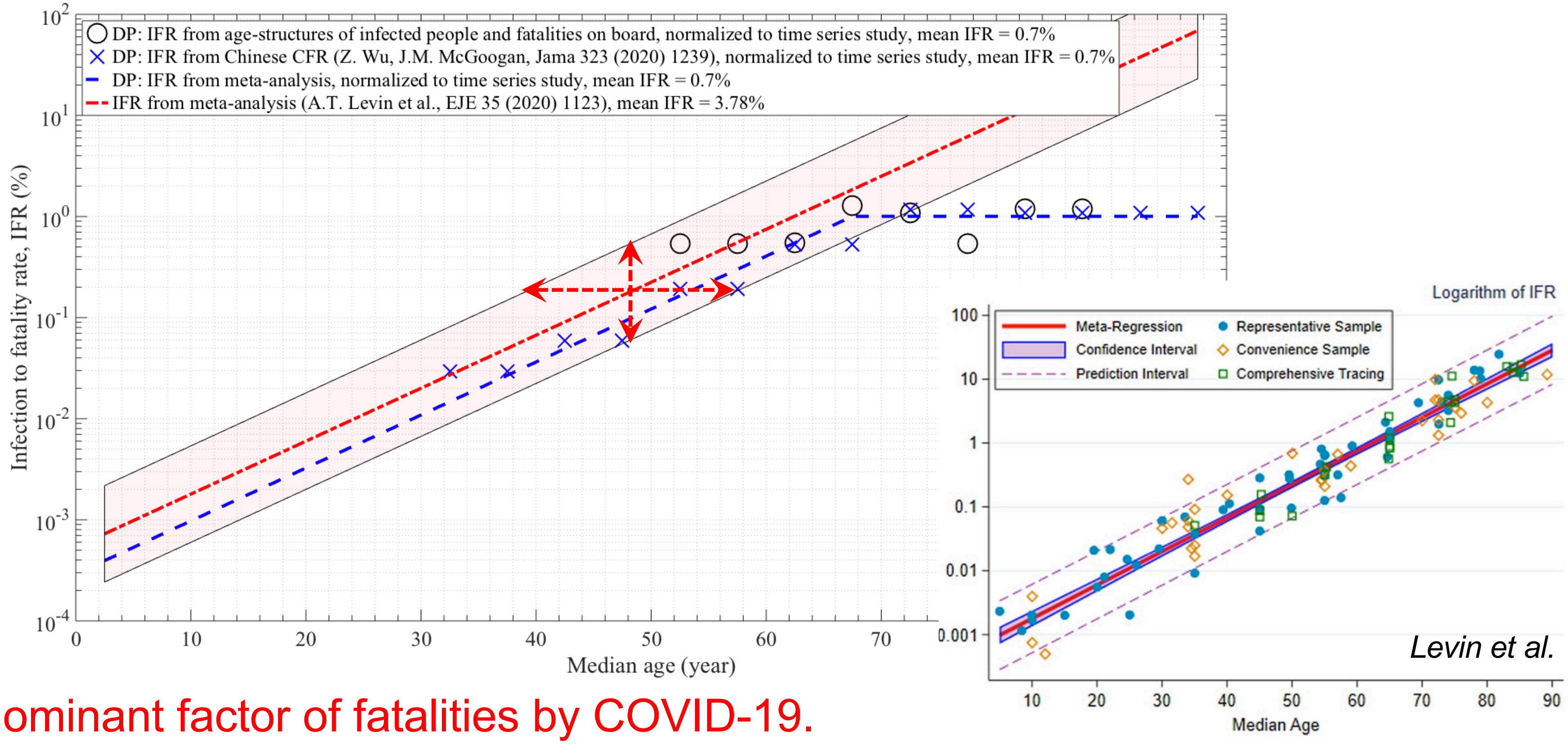
COVID-19 in Diamond-Princess cruise liner



- Passengers slightly more contaminated than crew, 8% variation → *consistent with viral load increase with age (Ref.)*
- **The whole population onboard and the infected one have close age-structures**.
- Age-structure of fatalities similar to age-structure of old infected passengers → *IFR should be almost flat with age onboard.*
- Poor statistics : 14 fatalities → *large uncertainty*

S. Euser et al, (2020) https://doi.org/10.1101/2021.01.15.21249691

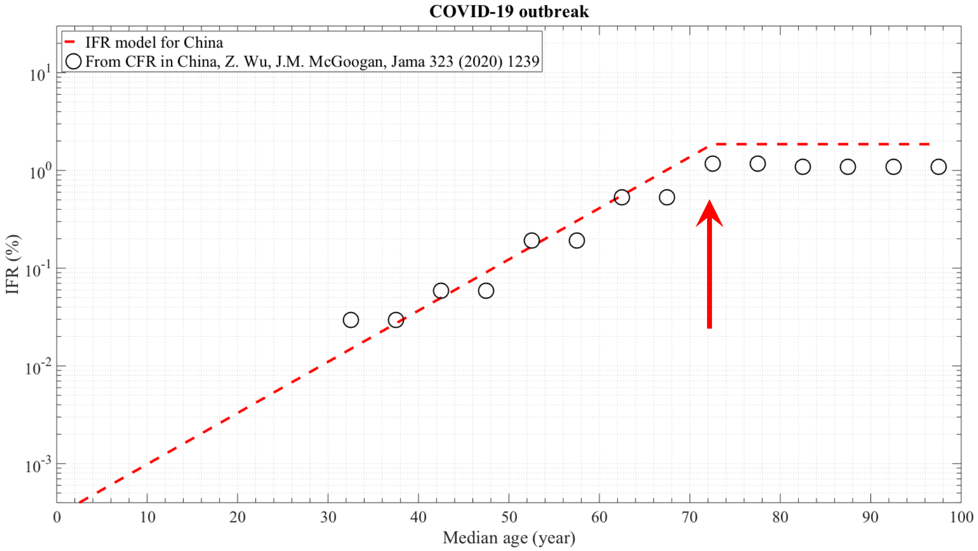
IFR per class of age for the COVID-19

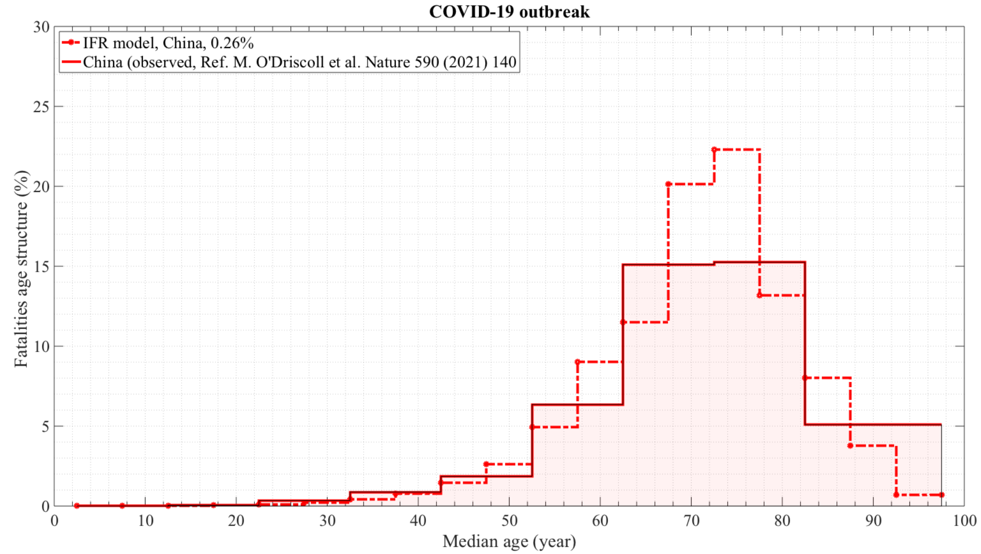


- Age is the dominant factor of fatalities by COVID-19.
- **The exponential dependence** with age of the CFR was early identified in China.
- Very large interval of prediction : the meta-regression is inaccurate. *Is the exponential law universal for all ages and everywhere ?*
- **The age distribution of fatalities calculated by the IFR model using the age-structure of the infected population should match observations.**

A.T. Levin et al, European Journal of Epidemiology 35 (2020) 1123

IFR and mean IFR in China



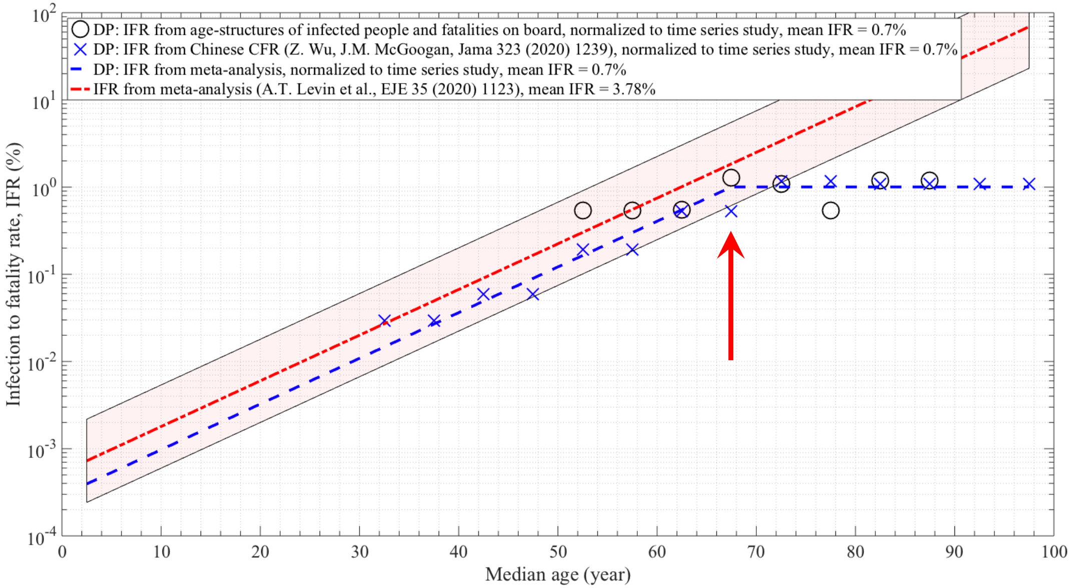


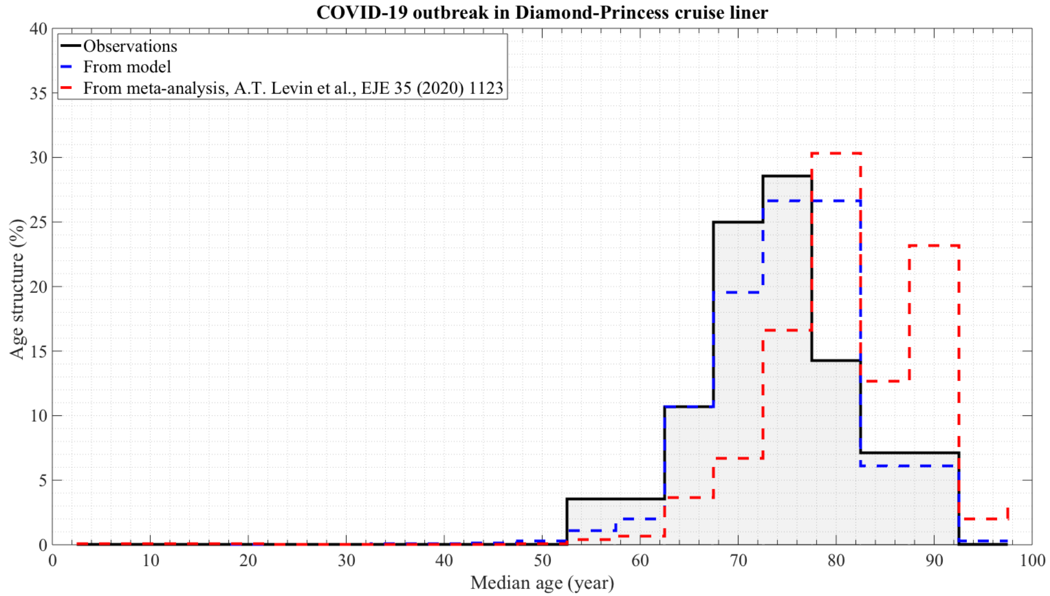
- The case to fatality rate (CFR) in China (March 2020) is growing exponentially up to 75y and is flat for older people. Same slope as the meta-analysis of the IFR below 70y
- When the exponential growth is adjusted on the law to gives a mean IFR of 0.7% on the Diamond-Princess (consistent with time series), the age distribution of the fatalities by COVID-19 calculated from the age-structure of the population in China is close to observations → mean IFR (China) = 0.26%.
- *A purely exponential growth with age of the IFR up to 100y (meta-analysis) would shift the maximum in the fatalities age-structure well beyond observations.*

T. W. Russell et al, *Euro Surveill.* 25 (2020)

A.T. Levin et al, European Journal of Epidemiology 35 (2020) 1123

IFR for the Diamond-Princess

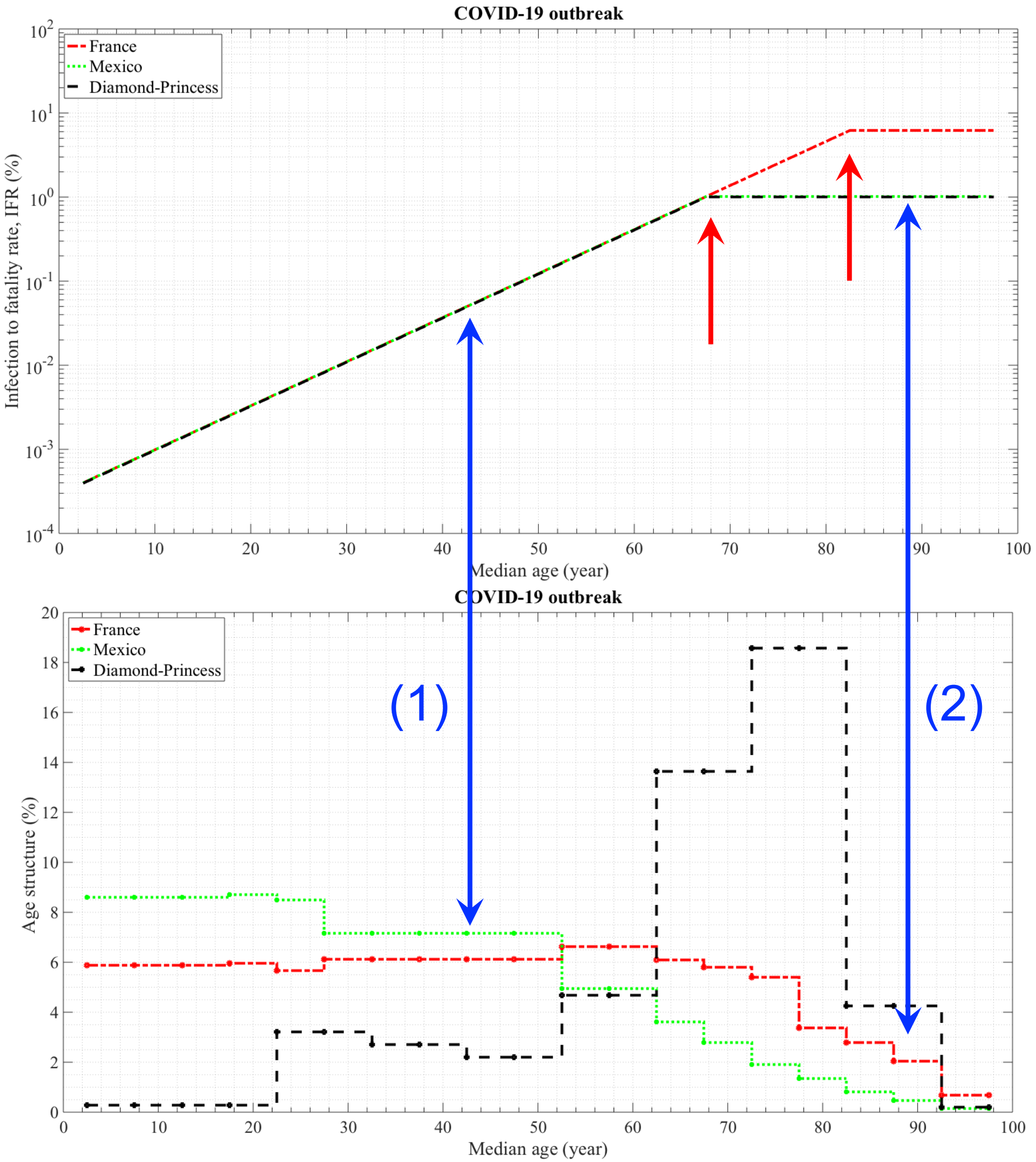


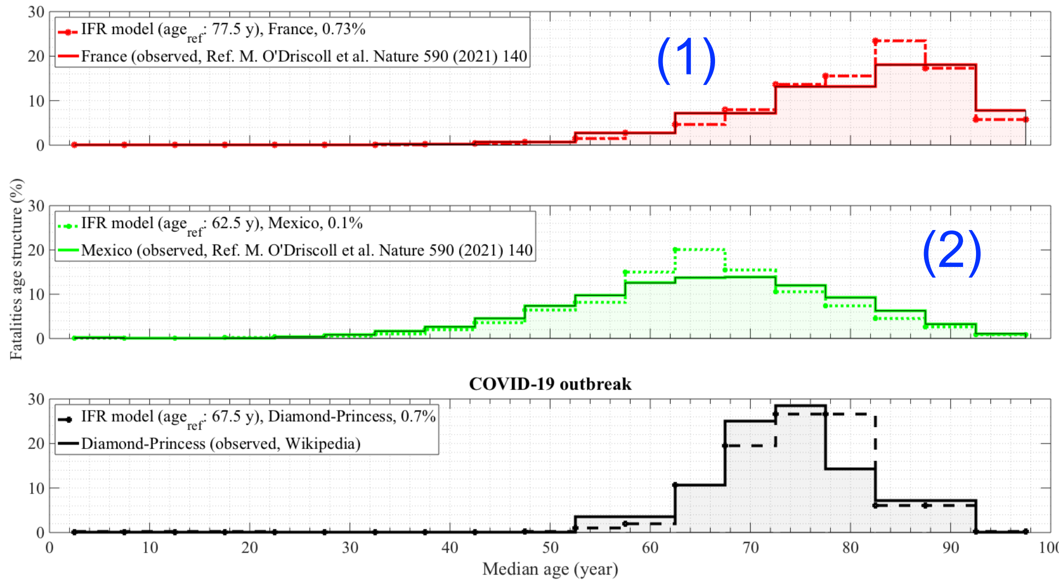


- IFR age dependence from meta-analysis (full exponential) not consistent with age distribution of fatalities on the Diamond-Princess, mean IFR = 3.8% not consistent with time series, more than 30 fatalities expected while 14 observed (but poor statistics).
- **IFR model** :
  - Exponential law of the IFR with age (consistent with meta-analysis) up to the age at which the age-structure of the fatalities is maximum .
  - Above this age of reference, the IFR is set constant.
  - The exponential law is multiplied by a factor to recover the mean IFR in the Diamond-Princess cruise liner from time series.

A.T. Levin et al, European Journal of Epidemiology 35 (2020) 1123

Mean IFR in France, Mexico and Diamond-Princess



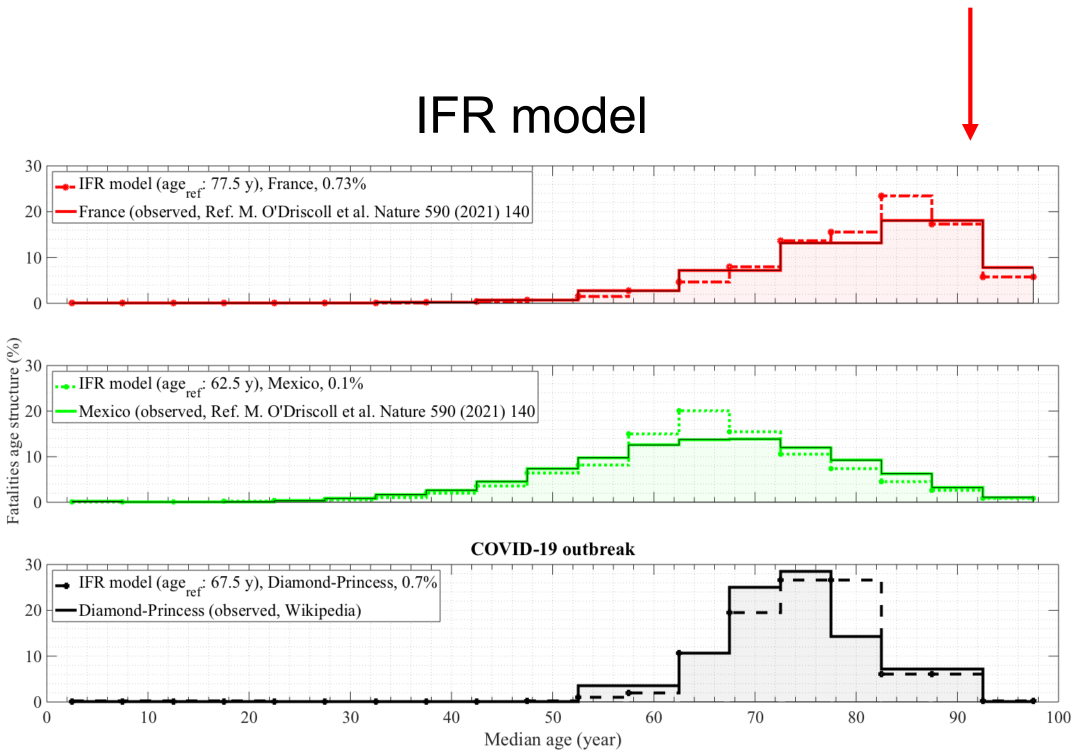


The age distribution of fatalities is driven by the exponential growth of the IFR up the age of reference (1) and then by the decrease of the population with age (2).

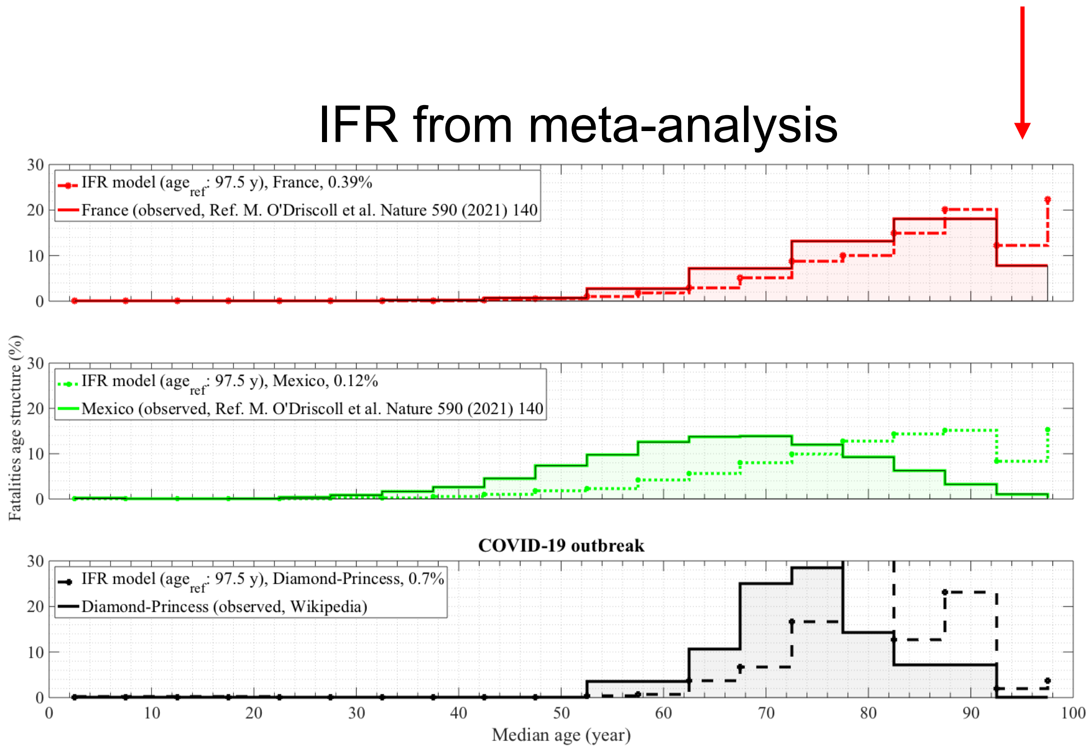
A.T. Levin et al, European Journal of Epidemiology 35 (2020) 1123
M. O'Driscoll et al. Nature 590 (2021) 140

IFR and age-distribution of the fatalities (France, Mexico and Diamond-Princess)

IFR model



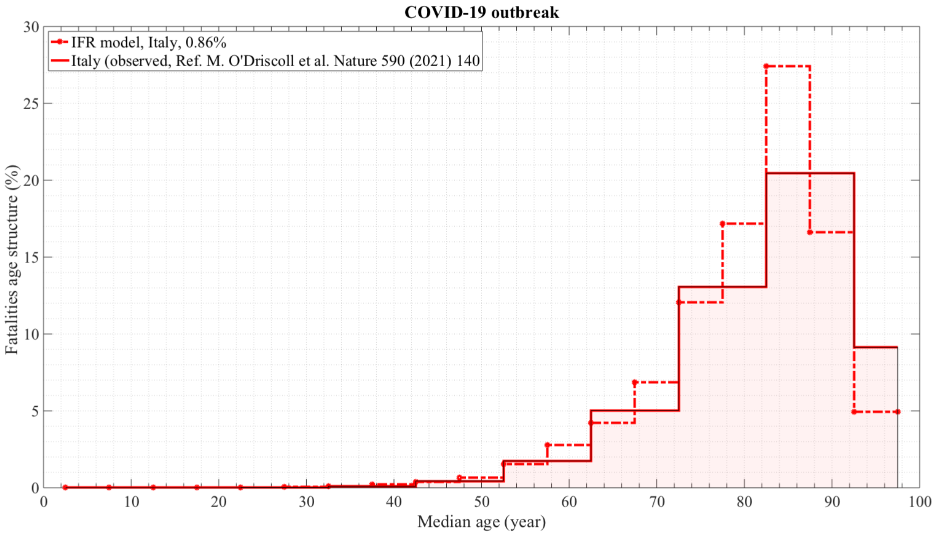
IFR from meta-analysis

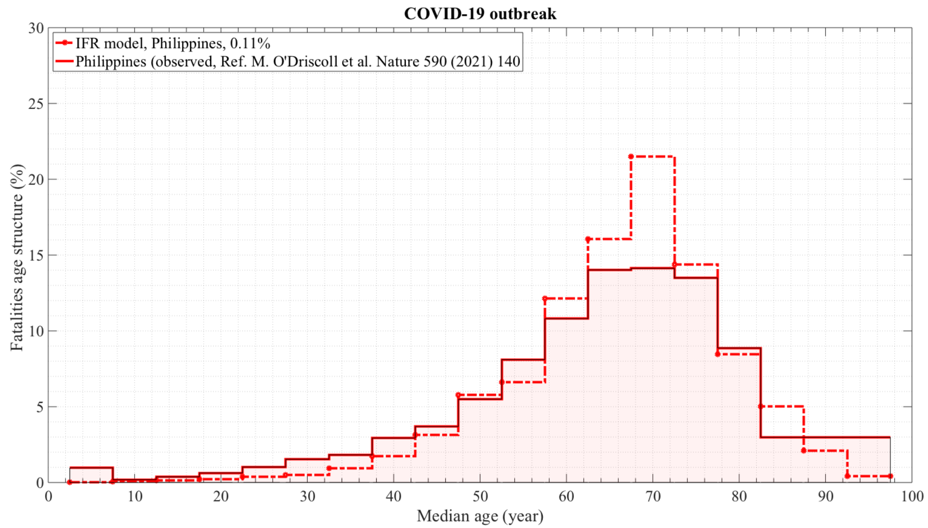


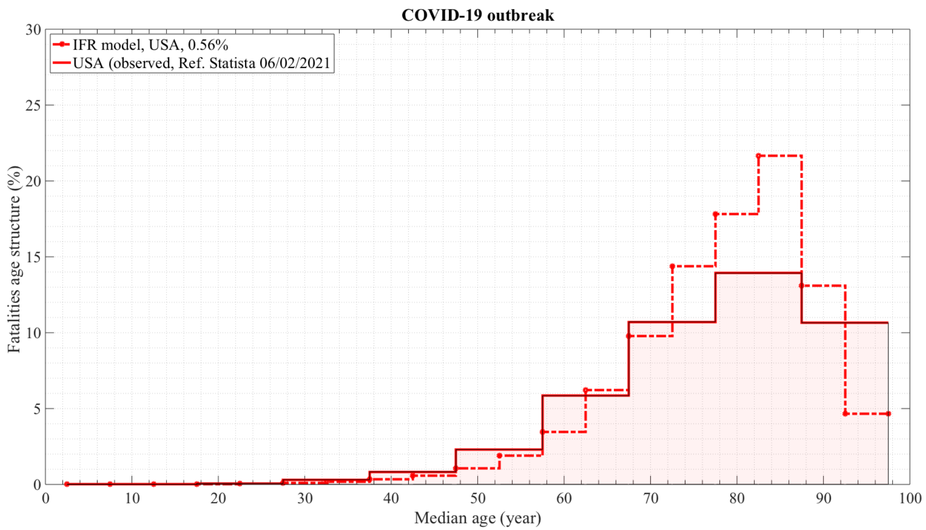
Pure exponential age-dependence

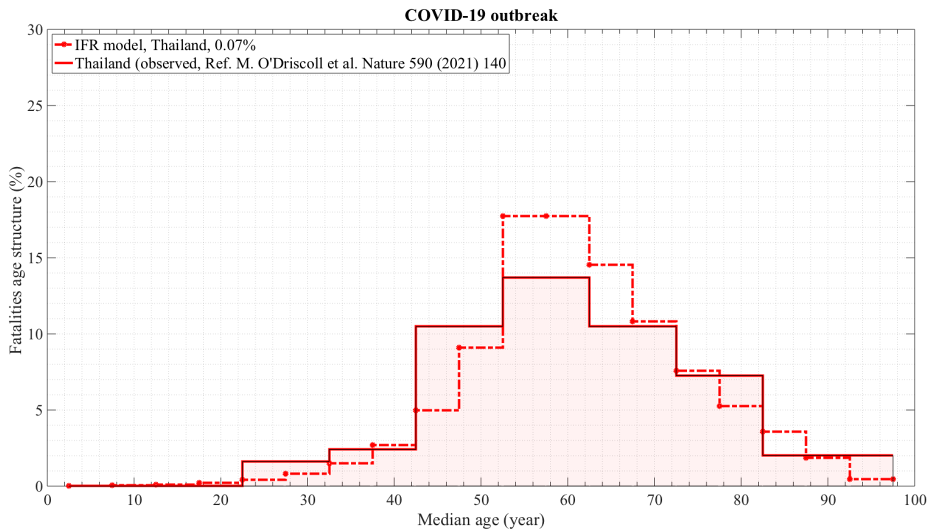
A.T. Levin et al, European Journal of Epidemiology 35 (2020) 1123
M. O'Driscoll et al. Nature 590 (2021) 140

IFR and age-distribution of the fatalities (Italy, USA, Thailand, Philippines)



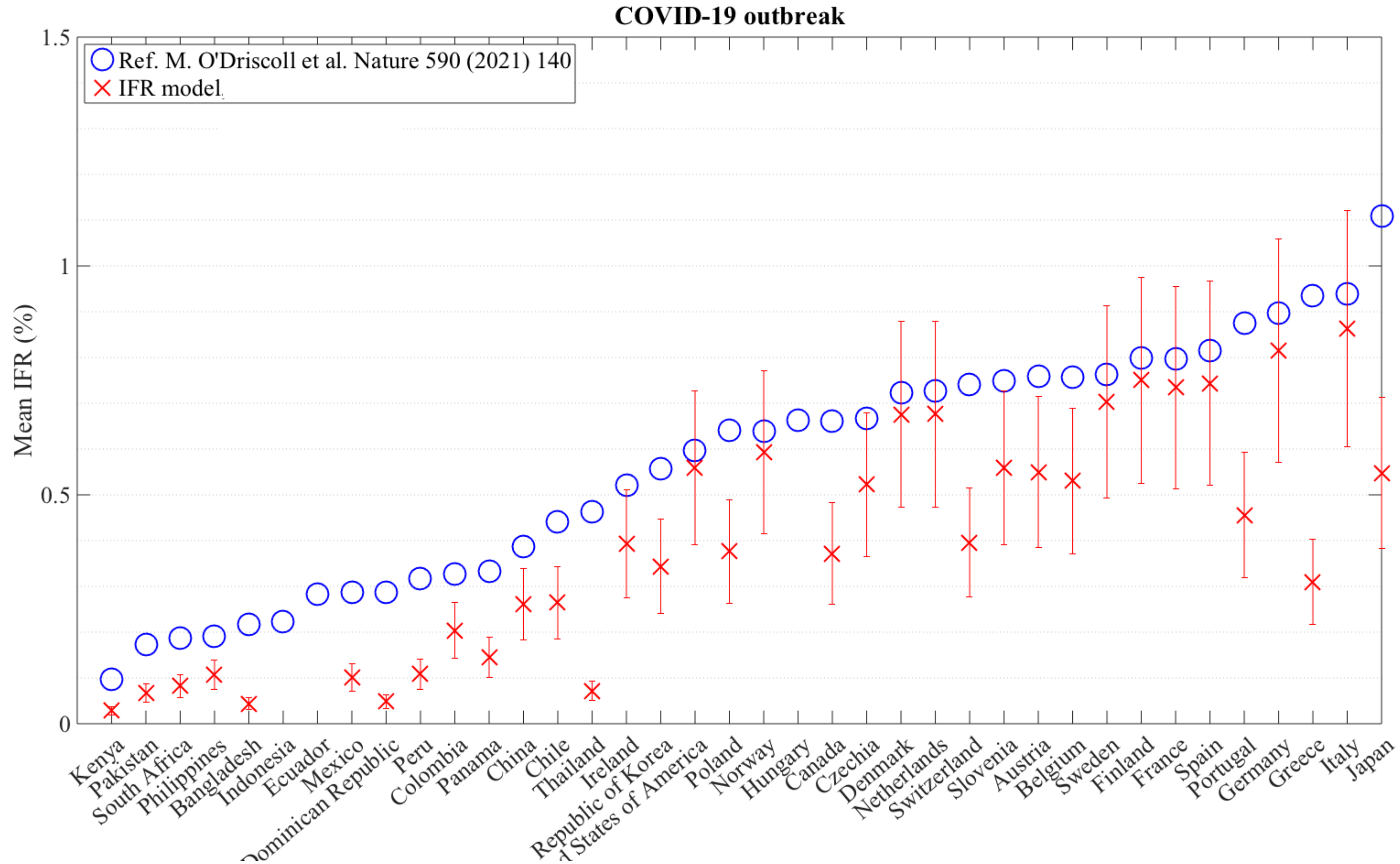






A.T. Levin et al, European Journal of Epidemiology 35 (2020) 1123
M. O'Driscoll et al. Nature 590 (2021) 140

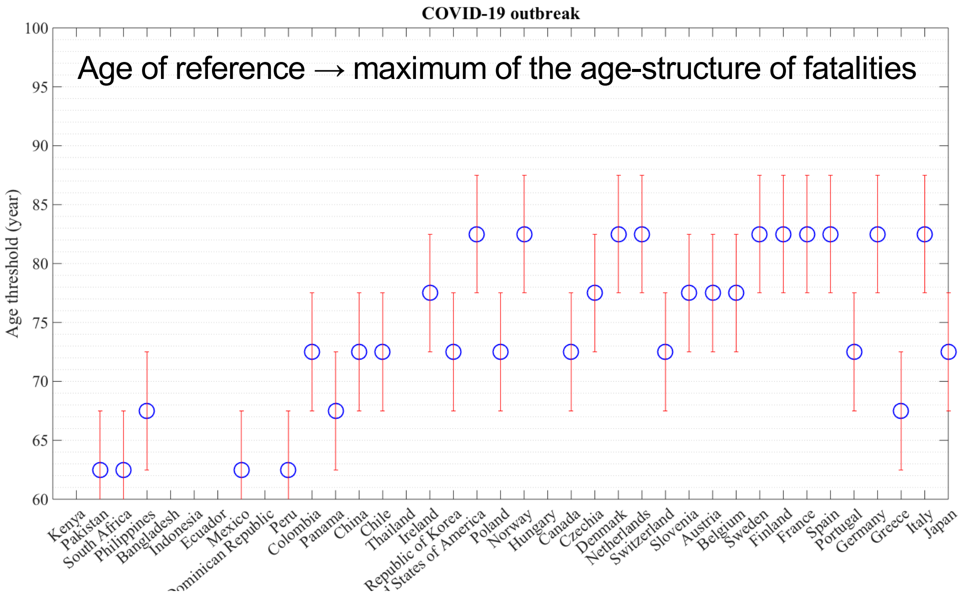
Mean IFR depending upon the model

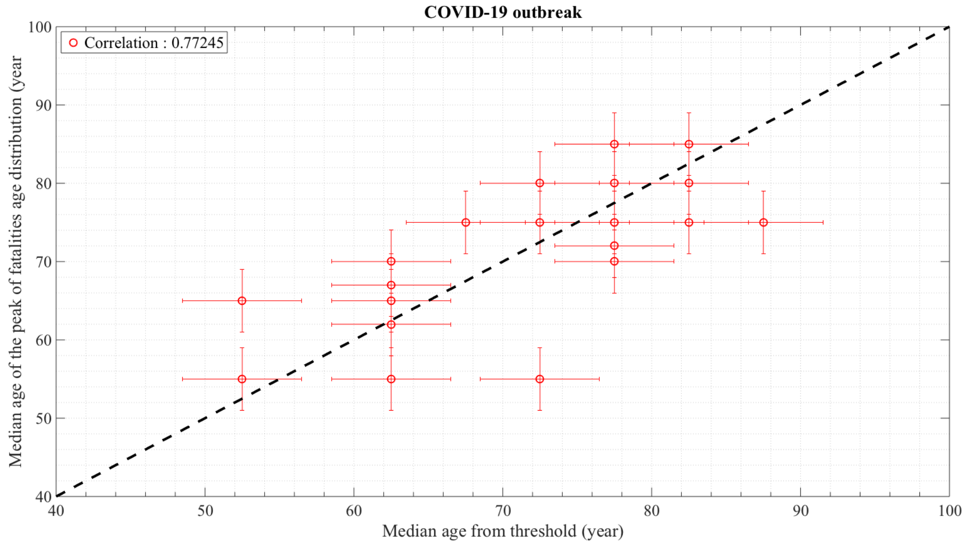


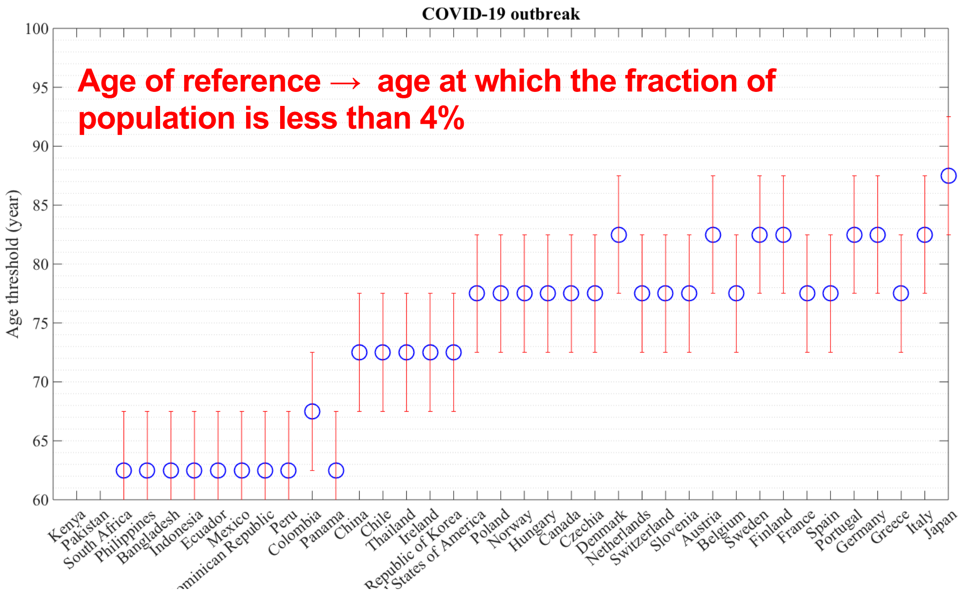
- Same trend between of the mean IFR calculated with an exponential age-dependence or the IFR model taking the age of reference at the maximum of the fatalities age-structure (dominant law).
- Almost exponential IFR with age for European countries, not in other continents.
- Large uncertainty of the mean IFR.

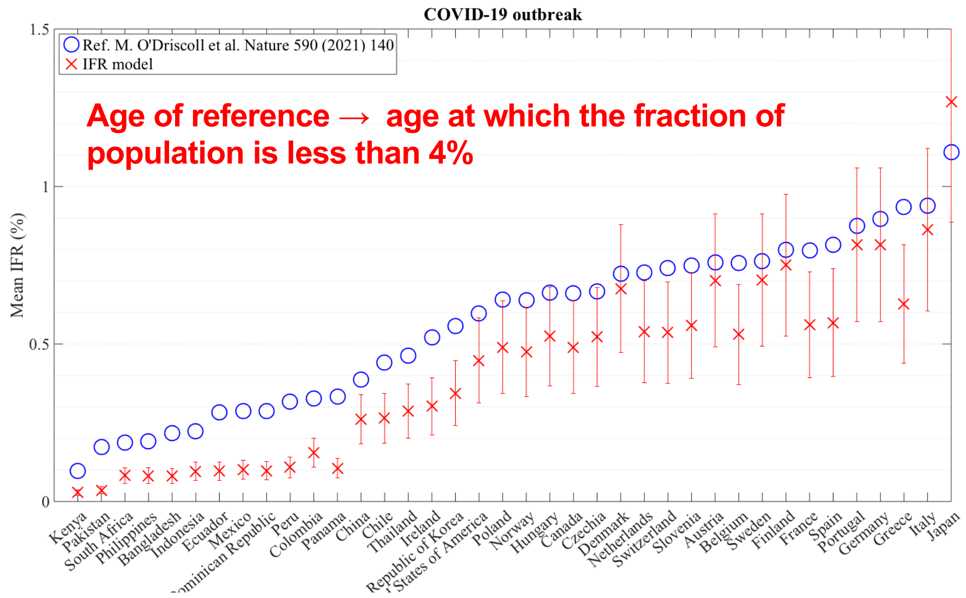
A.T. Levin et al, European Journal of Epidemiology 35 (2020) 1123
M. O'Driscoll et al. Nature 590 (2021) 140

Age of reference : correlation with the age-structure of the population









IFR model for worldwide COVID-19 simulations

- The mean IFR worldwide is calibrated from the times series of the COVID-19 on the Diamond-Princess, since IFR ≈ CFR, the age distribution of fatalities and the infected population onboard. *Mean IFR in Diamond-Princess = 0.7%.*

- From Diamond-Princess analysis, the age-structure of the infected population is close to that of the whole population onboard : assumed to be valid worldwide. Note : *the age distribution of the population may change with time (vacation period,…).*

- **The IFR model is an exponential function of age until an age of reference beyond which it becomes constant :** necessary to describe the observed age-structures of the fatalities from the distribution in age of the population (for European countries, the full exponential law for the IFR is almost valid).

- The age of reference is determined from : (i) the maximum of the observed age-structure of the fatalities if available, or (ii) at the age beyond which the fraction of the population is less than 4% (best correlation).

- Mean IFR → Italy : 0.86%, France : 0.73%, USA : 0.45%, China : 0.26%

Mean IFR for the COVID-19 in the world

- Population age-structures from UNO database.
- IFR seasonal flu : 0.05 %, CDC (COVID-19 is a much more severe disease)

Country	Mean IFR (%)
Italy	0.86
Germany	0.81
Quebec (Canada)	0.76
Spain	0.74
France	**0.73**
Sweden	0.70
Netherlands	0.68
Belgium	0.53
United Kingdom	0.51
USA	0.45

Country	Mean IFR (%)
Switzerland	0.39
Poland	0.38
South-Korea	0.34
China	0.26
Israel	0.25
Brazil	0.22
Mexico	0.20
Lebanon	0.10
Iran	0.11
India	0.093

M. Biggerstaff et al., BMC Infectious Diseases, 14 (2014) 480

Some evidences for a low mean IFR (<< 1%)

- At Bergamo (Italy), almost isolated with strong lockdown from beginning of March 2020, **f = 57 %** of the local population was in contact of the virus SARS-Cov-2 from antibody analysis, 9965 tests, random sample (source : www.reuter.com/, 8th of June 2020)

- Antibody analysis at New-York city suggested that IFR is significantly less than 0.5% (local estimate). From statistical analysis (IFR@DP = 2%), IFR@NY = 0.7% and from time series analysis (IFR@DP = 0.6-0.7%), **IFR@NY = 0.25%** (Source: www.futura-sciences.com, 27th of April 2020)

- Charles-de-Gaulle aircraft carrier : **f = 54 %** but IFR@CdG = 0% (young crew)

- Ernest Shackleton expedition : **f = 59 %** and IFR@ES = 0.8% (very large uncertainty because of the small number of the passengers (217)

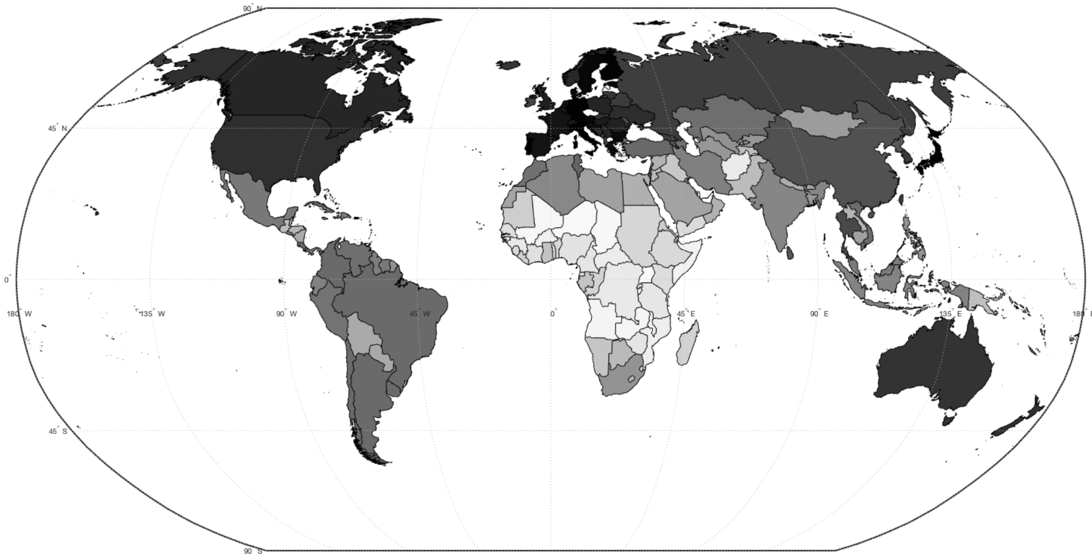
- Mumbay (India) : **f = 75 %** from measurements of antibodies in the the slum (40% of $20 \times 10^{+6}$ inhabitants with 6000 fatalities observed, 6300 calculated for the mean IFR of India = 0.14%)

- Manaus (Brazil) : **f ~ 66 % [74% beginning October 2020]** from measurements of antibodies (mid of June 2020), code results : **f_{code} ~ 65 % [78% beginning October 2020]**

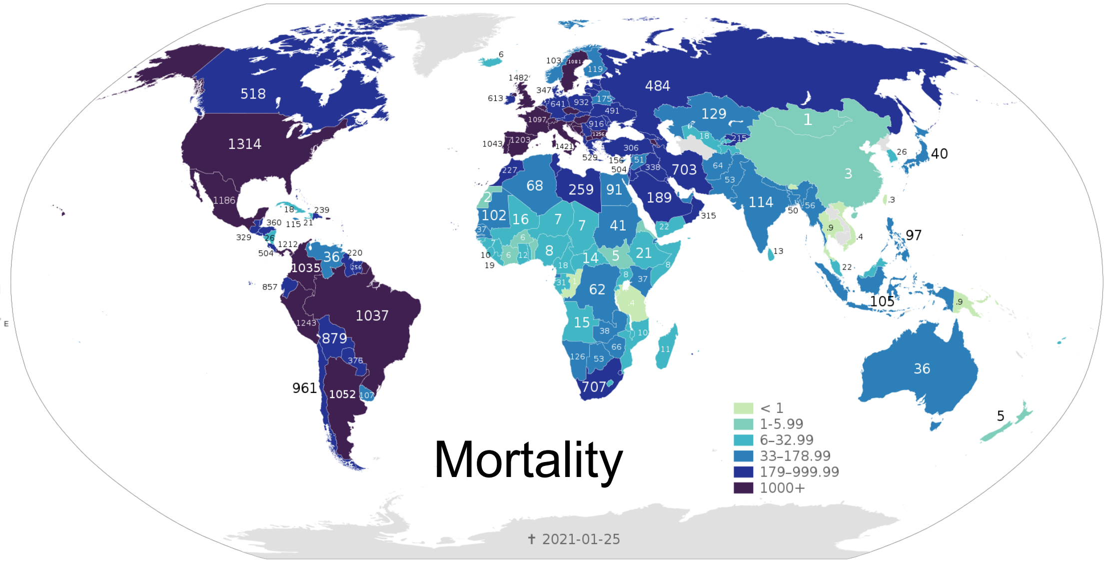
A. Malani, et al., (2020) https://doi.org/10.1016/S2214-109X(20)30467-8

L. F. Buss et al., Science (2020) 10.1126/science.abe9728

World map of mean IFR



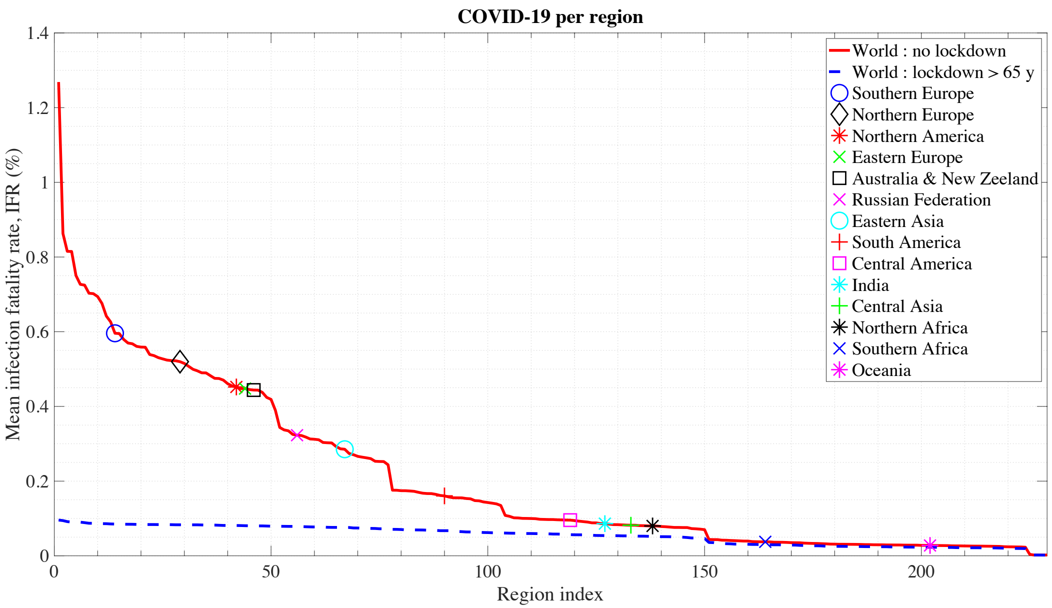
From the IFR model

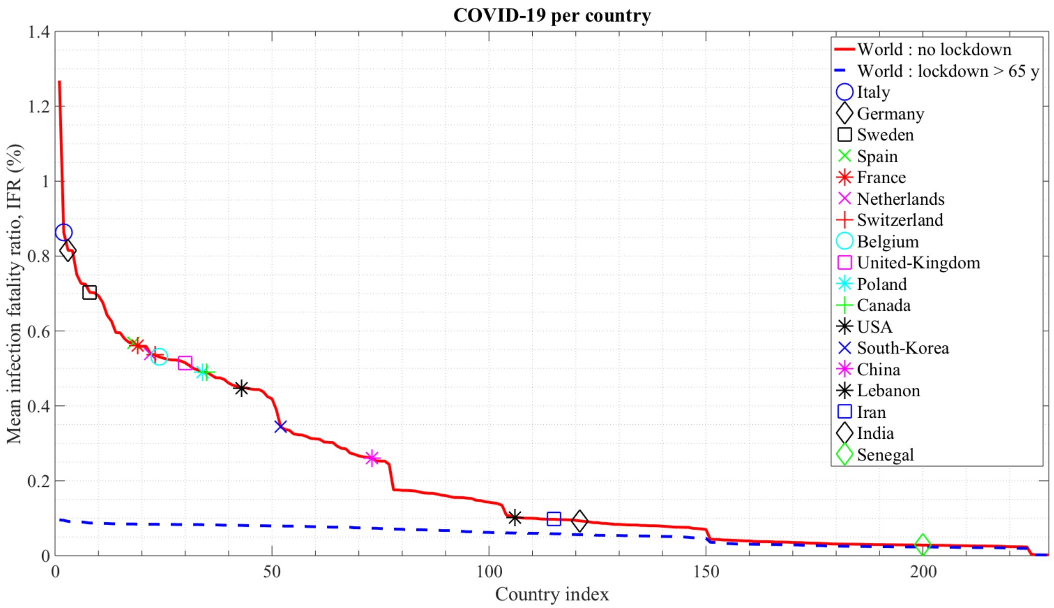


https://en.wikipedia.org/wiki/COVID-19_pandemic_by_country_and_territory

- **Mean IFR of the world : 0.2±0.2%. Median mean IFR of the world : 0.1%.**
- The mean IFR indicates that African countries should be less impacted by the COVID-19 because of the favorable age-structure of the population (young population) : good agreement with observed mortality despite warnings in March 2020 by the WHO.
- The virus SARS-CoV-2 should nevertheless propagate as in all other countries.

Mean IFR in the world by regions and countries

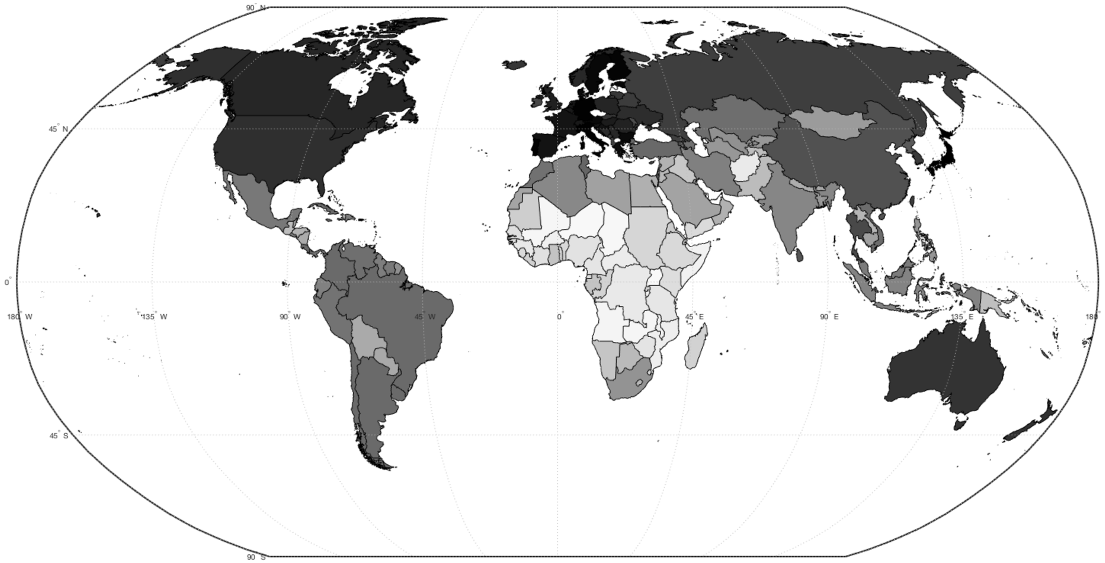




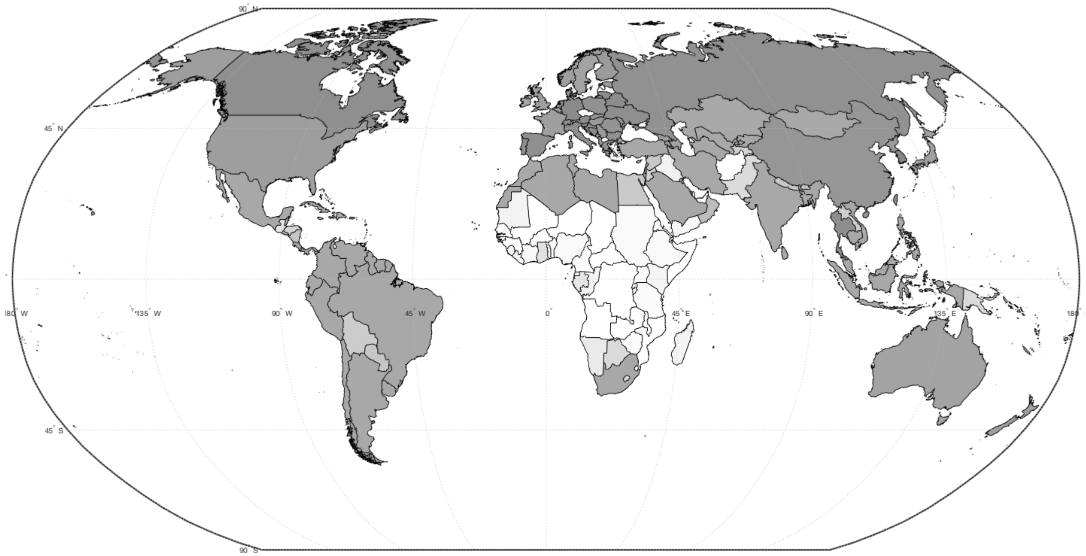
- Southern Europe is the most exposed to COVID-19 in term of fatalities (Italy in particular).
- Oceania, Africa and India are the less exposed in terms of fatalities *(but the COVID-19 spread like in other places)* → Confirmed as outbreak is developing (announced mid-April 2020).
- Highest IFR : *Japan (1.27%)*, lowest IFR : *Uganda (0.047%)*
- South-America has a medium exposure to COVID-19 in terms of fatalities.
- China is less exposed than Europe and USA.
- *A strict lockdown for people older than 65y leads to a considerable reduction of the mean IFR (but unapplicable because of asymptomatic cases)*

World map of mean IFR : impact of a differential lockdown

Mean IFR, no lockdown



Mean IFR, lockdown > 65y



- **Mean IFR of the world : 0.2±0.2%.**
- **Median mean IFR of the world : 0.1%.**

- **Mean IFR of the world : 0.054±0.025%.**
- **Median mean IFR of the world : 0.058%.**

COVID-19 pandemic monitoring

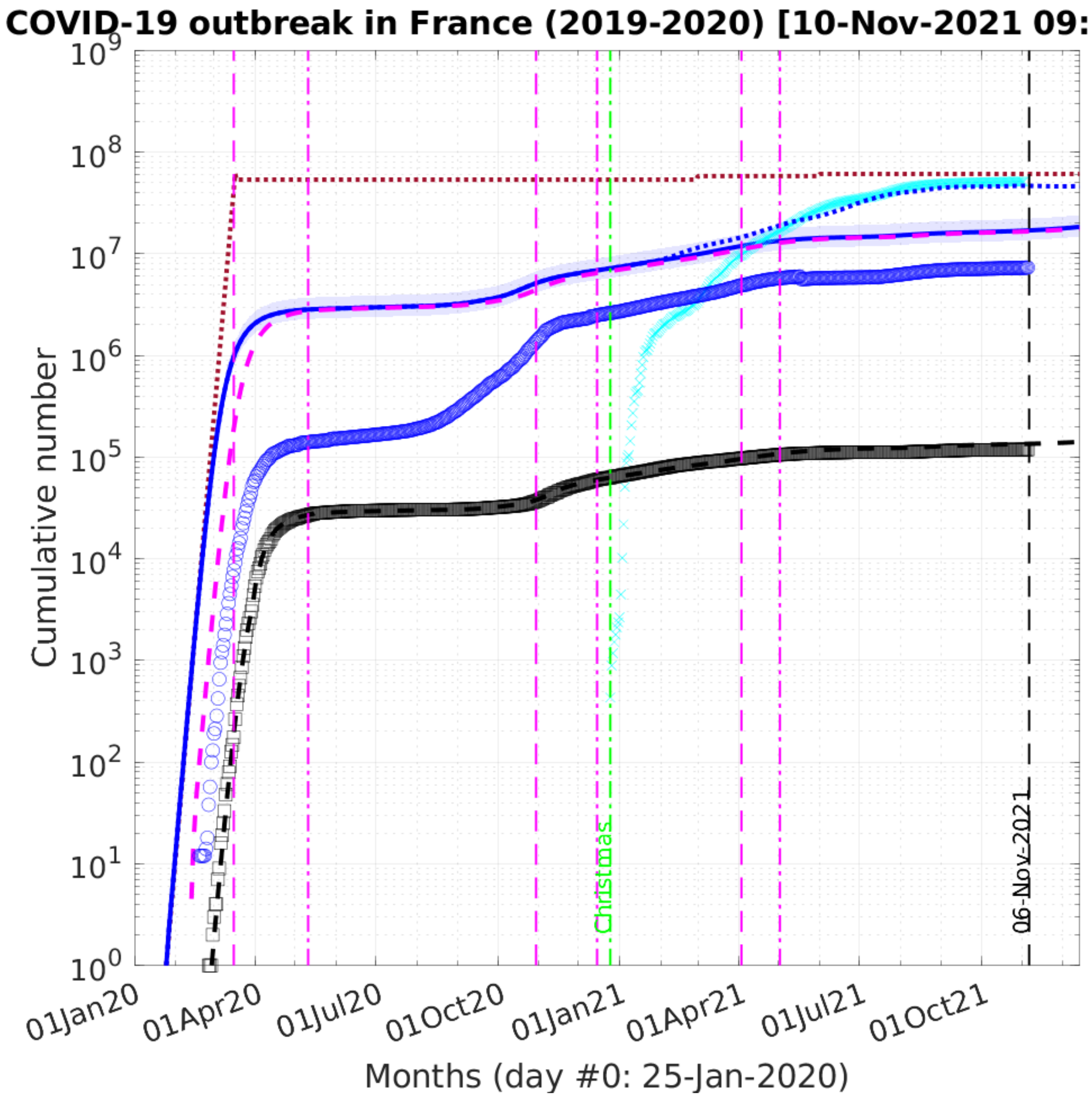
- *Dynamics of the COVID-19 for a set of representative countries*
- *Estimation of R_0 and the level of the collective immunity.*
- *Lockdown : impact of the date and comparison between countries*
- *Secondary waves and variants*
- *Monitoring the vaccination efficiency*

Representative countries for COVID-19 study

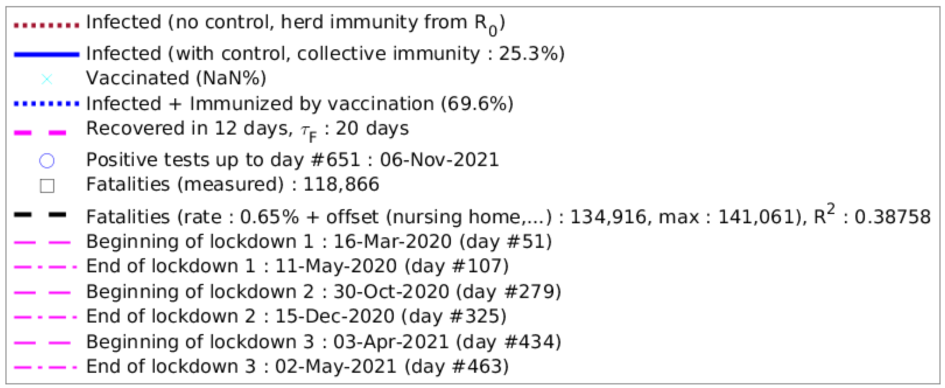
Large set of countries or places where climatic, social, economical and health conditions are very different.

- **Europe** : Belgium , France, Germany, Italy, the Netherlands, Poland, Spain, Sweden, Switzerland, United Kingdom.
- **North-America** : USA and Arizona, California and Florida states , Quebec (Canada).
- **Central and South-America** : Mexico, Brazil and some Brazilian cities and states (Manaus, Sao Paulo city ad state, Fortaleza).
- **Asia** : China, India and South-Korea.
- **Middle-East** : Iran, Israel, Lebanon, Turkey.
- **Africa** : Senegal.
- **Other countries** : Russian federation

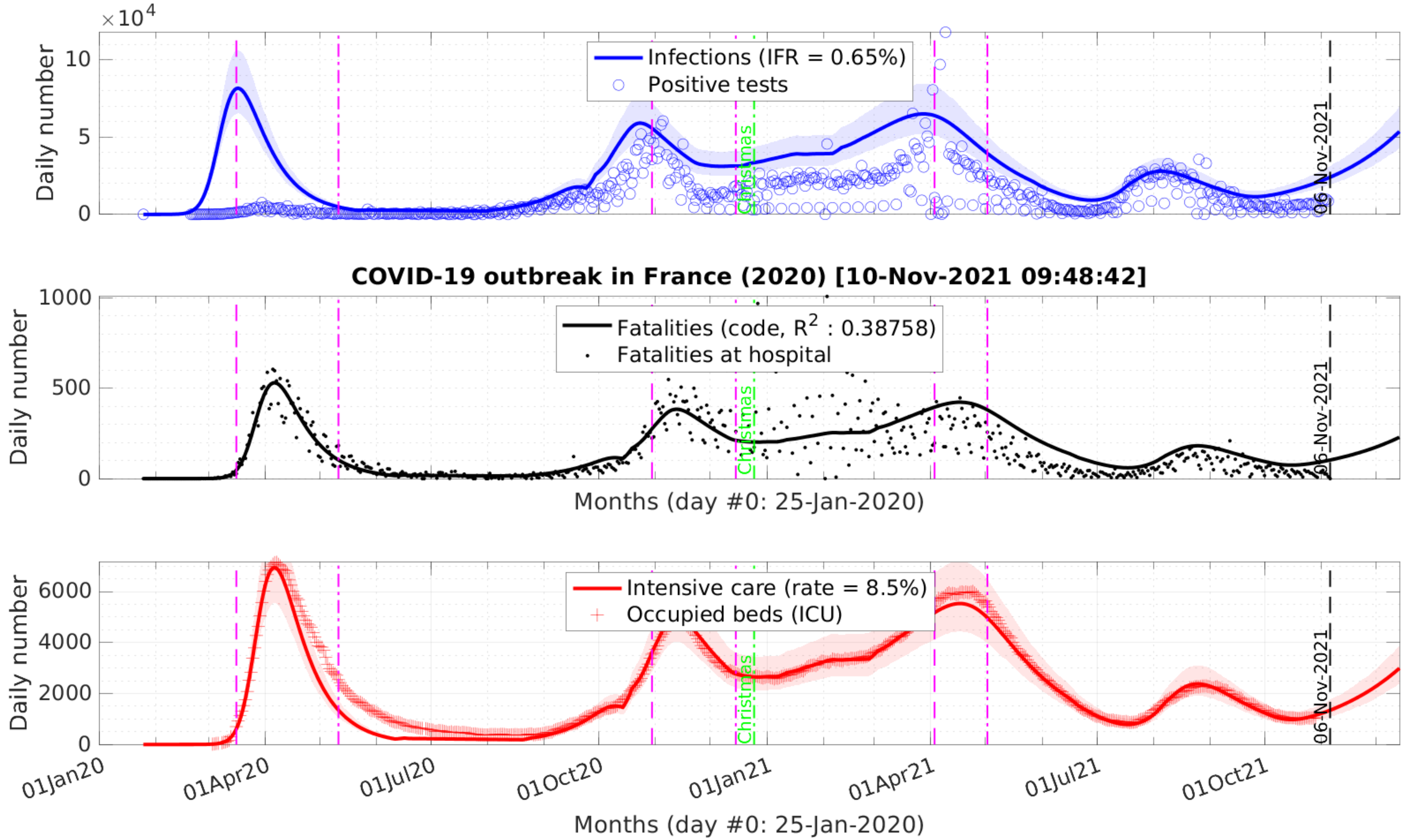
COVID-19 in France : cumulative time series



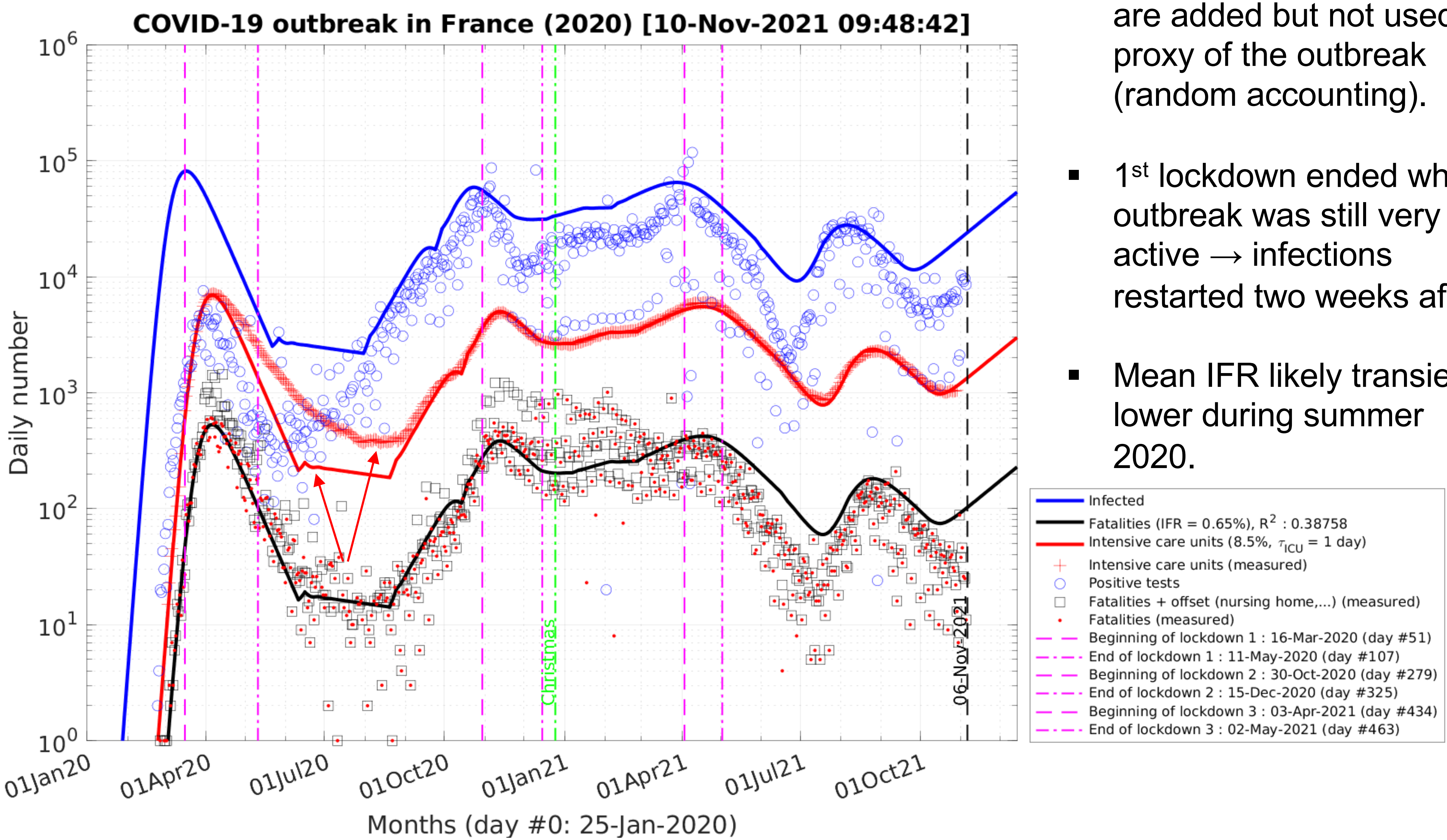
- Far from theoretical herd immunity by end of 2020 → still high risk of secondary waves even after a year a pandemic
- Vaccination campaign improves collective immunity
- Mean IFR for population at hospital (nursing home excluded)
- Occurrence of more contagious variants increases the theoretical level of herd immunity



COVID-19 in France : daily time series

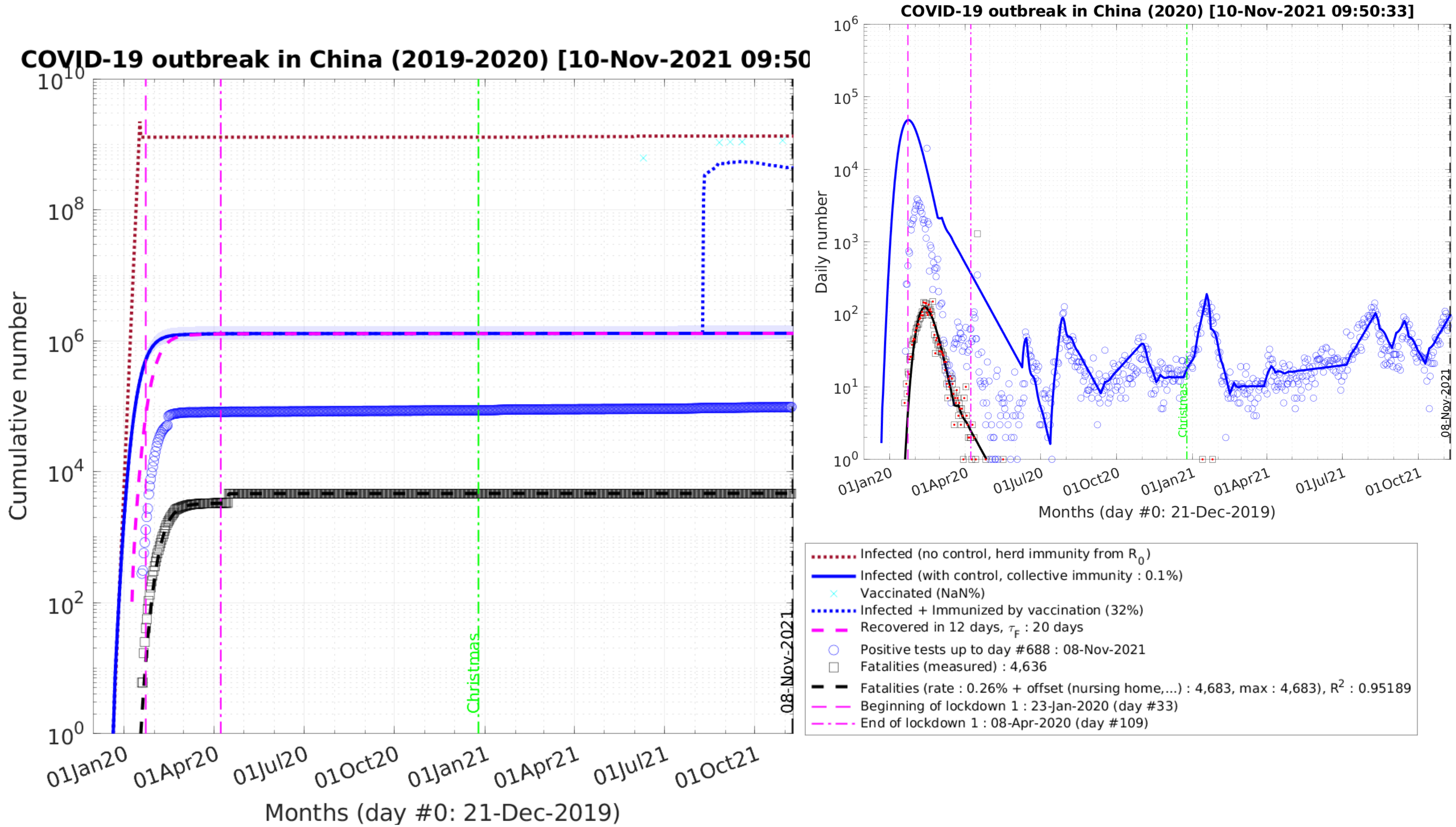


COVID-19 in France : daily time series

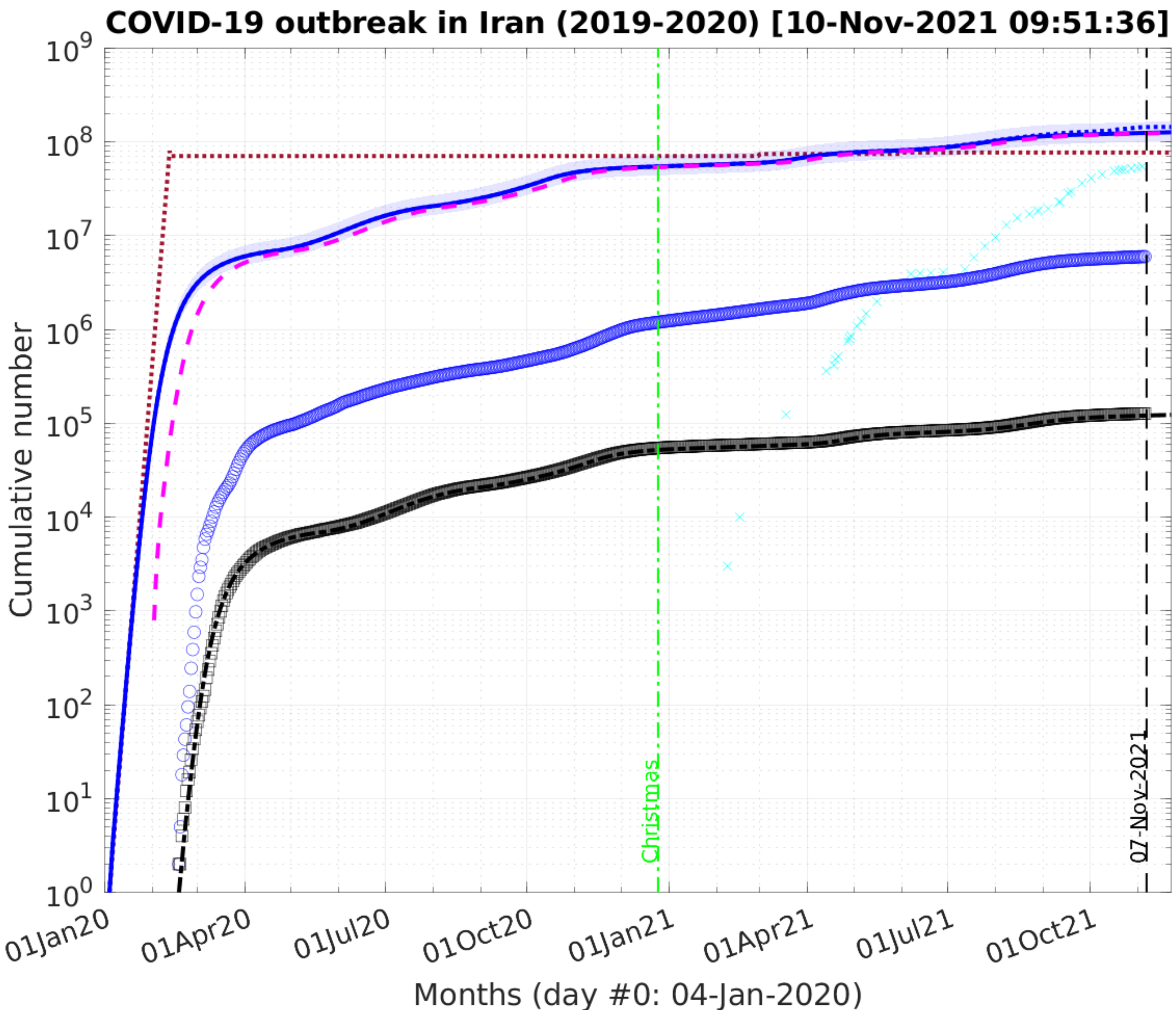


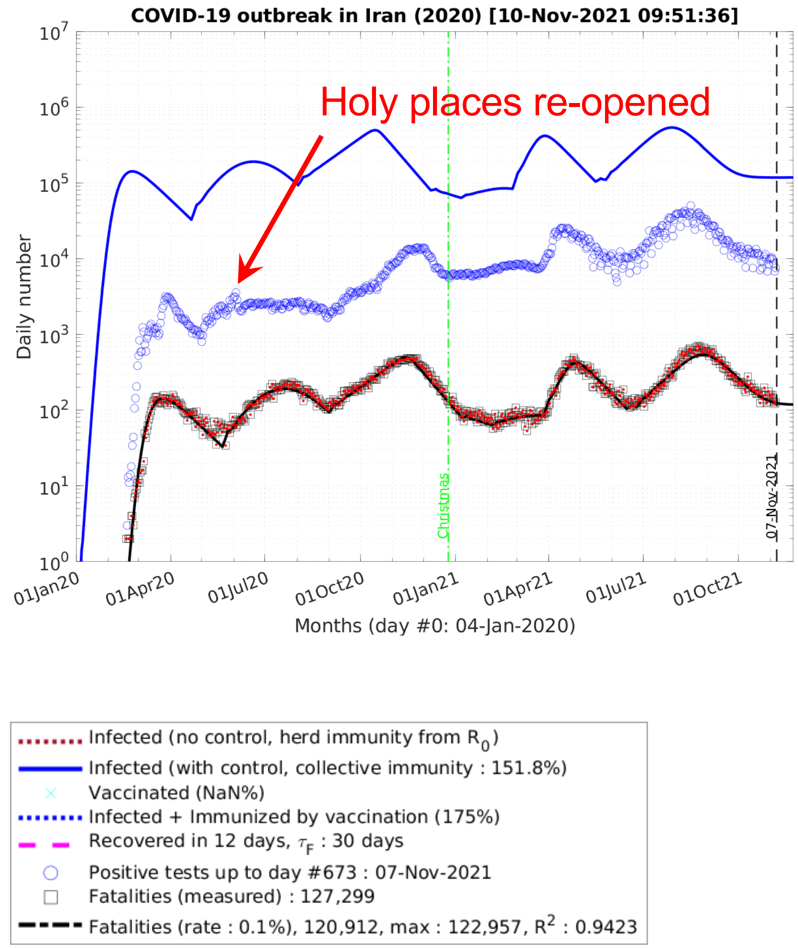
- Fatalities in nursing homes are added but not used as proxy of the outbreak (random accounting).
- 1st lockdown ended while outbreak was still very active → infections restarted two weeks after.
- Mean IFR likely transiently lower during summer 2020.

COVID-19 in China

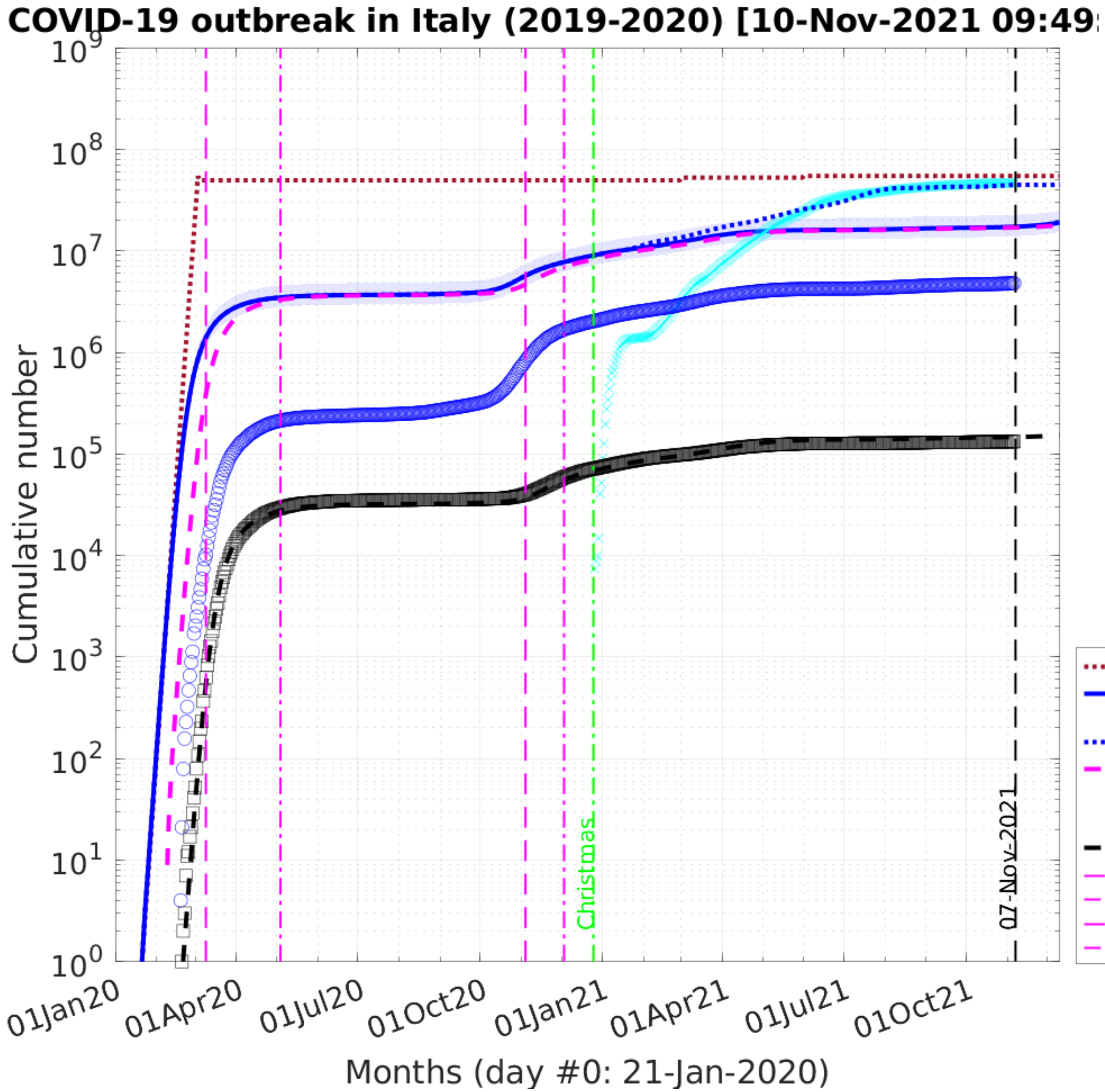


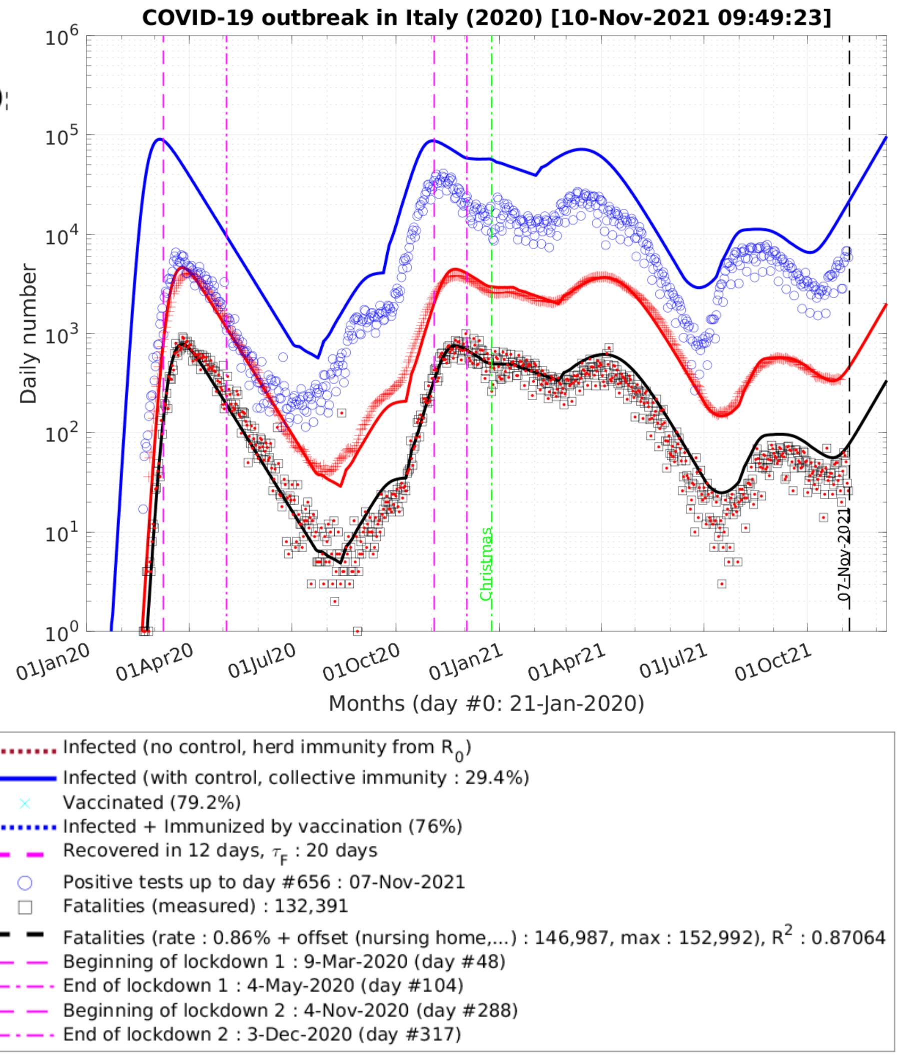
COVID-19 in Iran



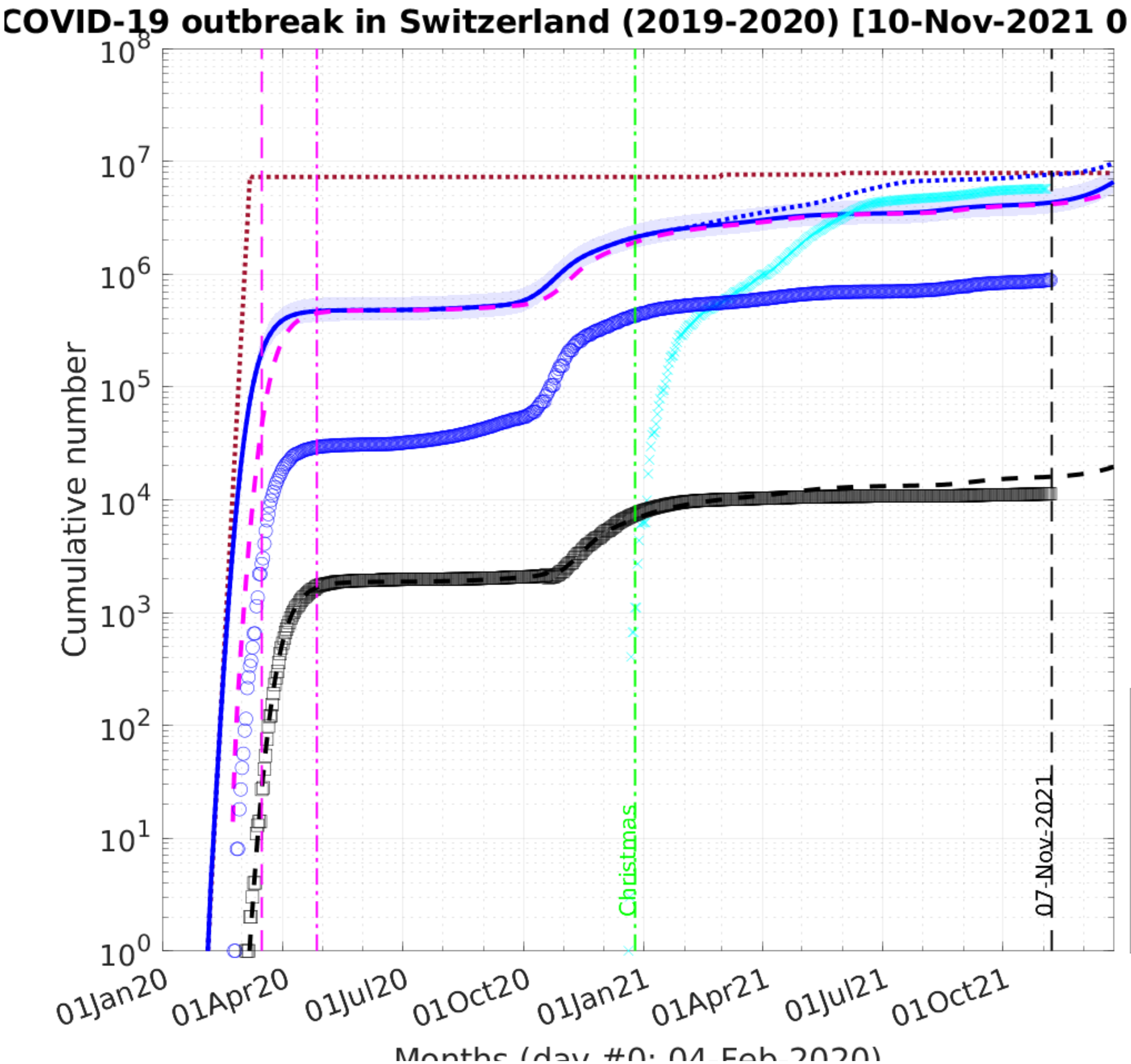


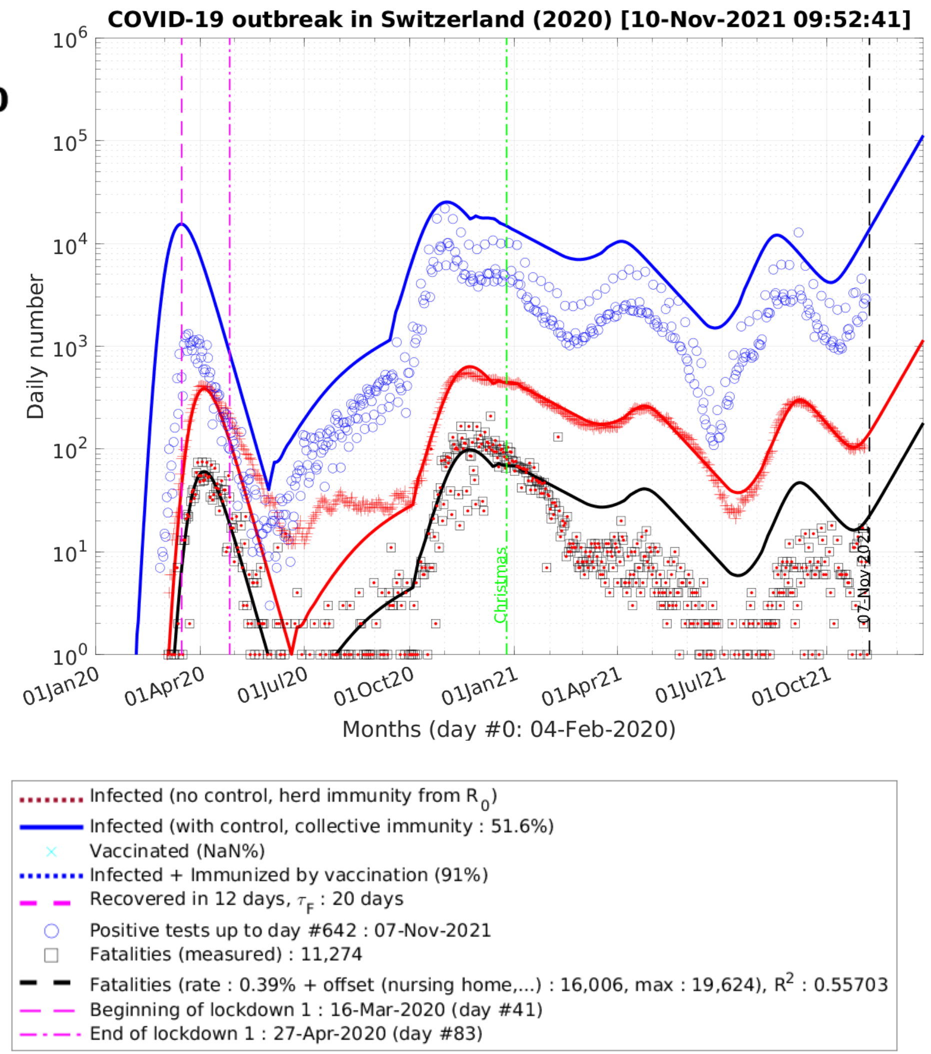
COVID-19 in Italy



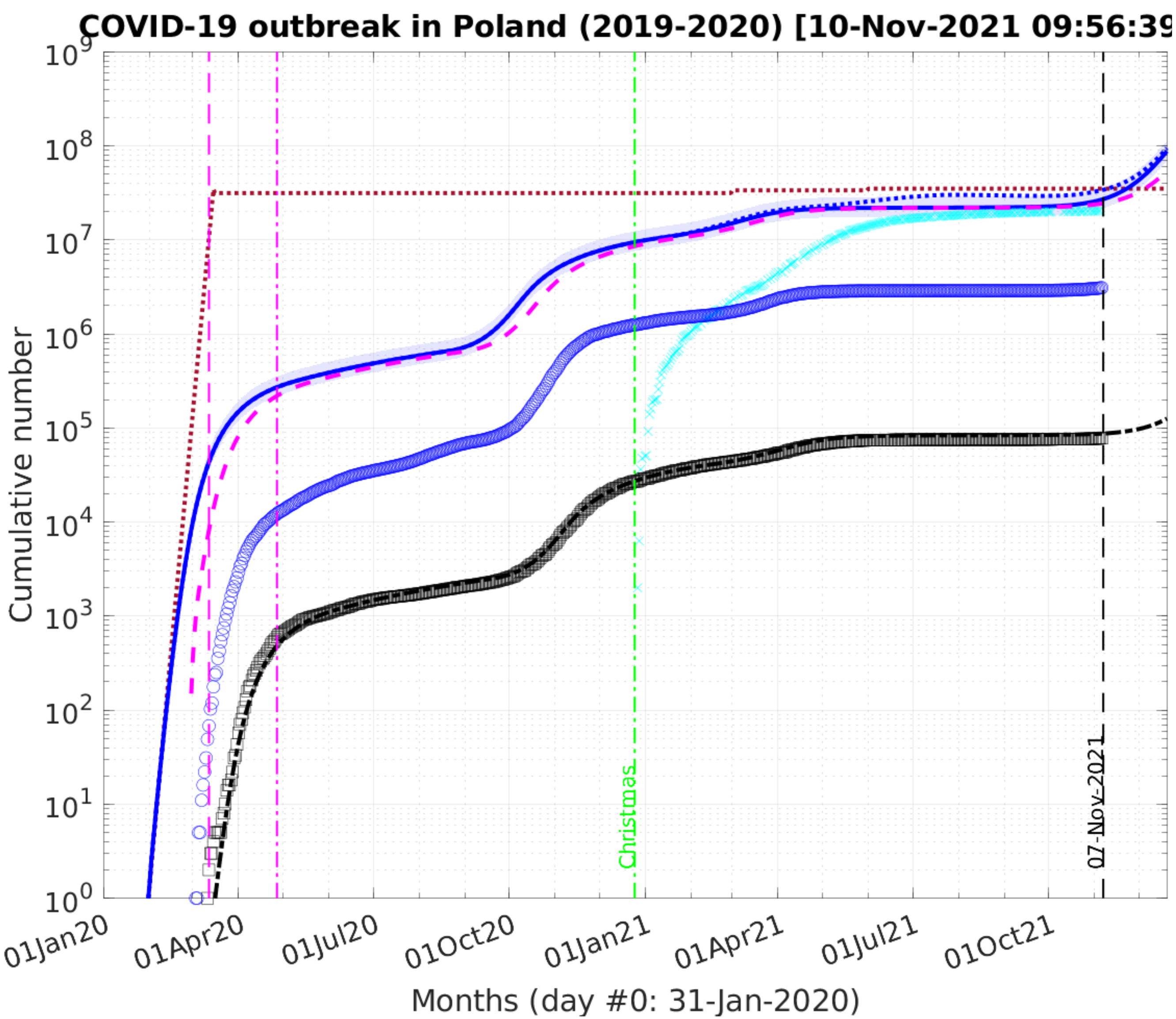


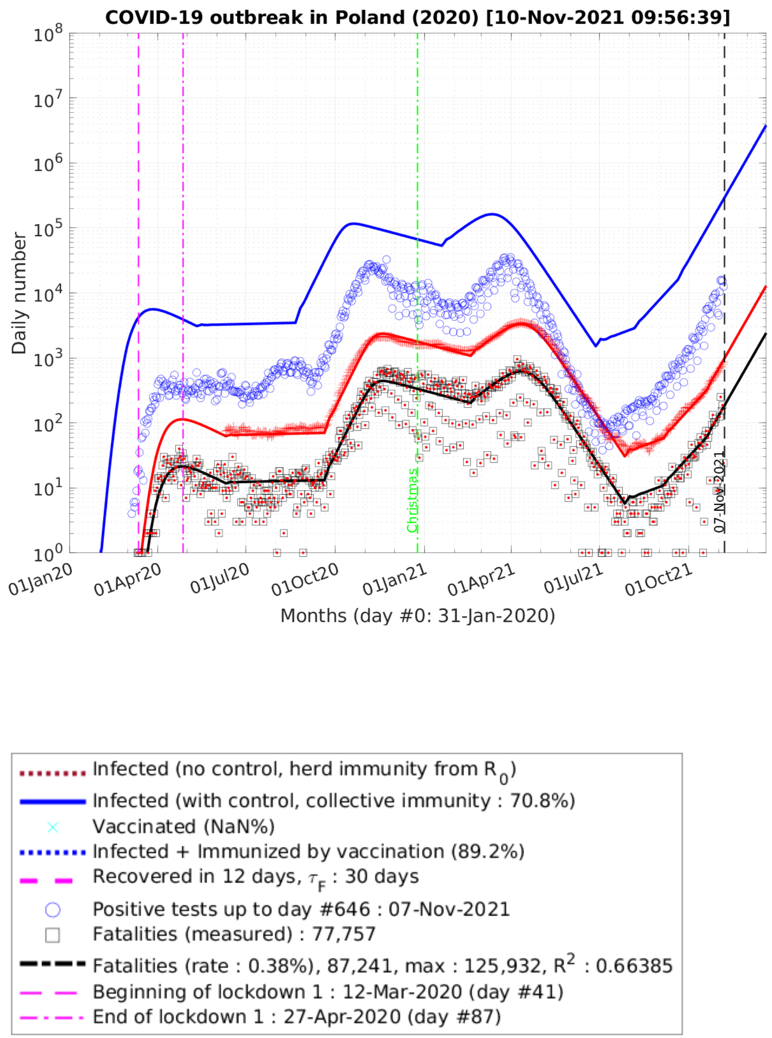
COVID-19 in Switzerland



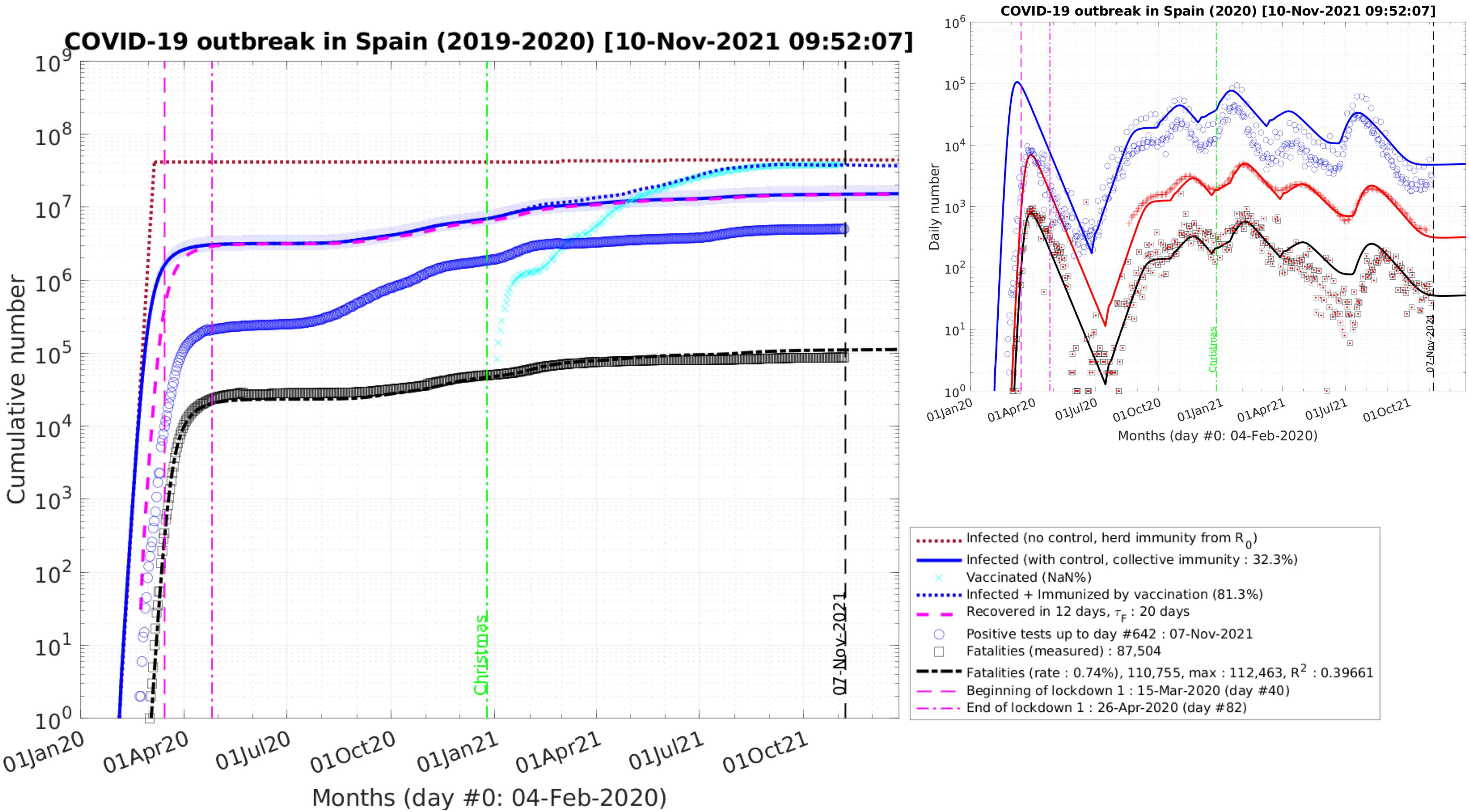


COVID-19 in Poland

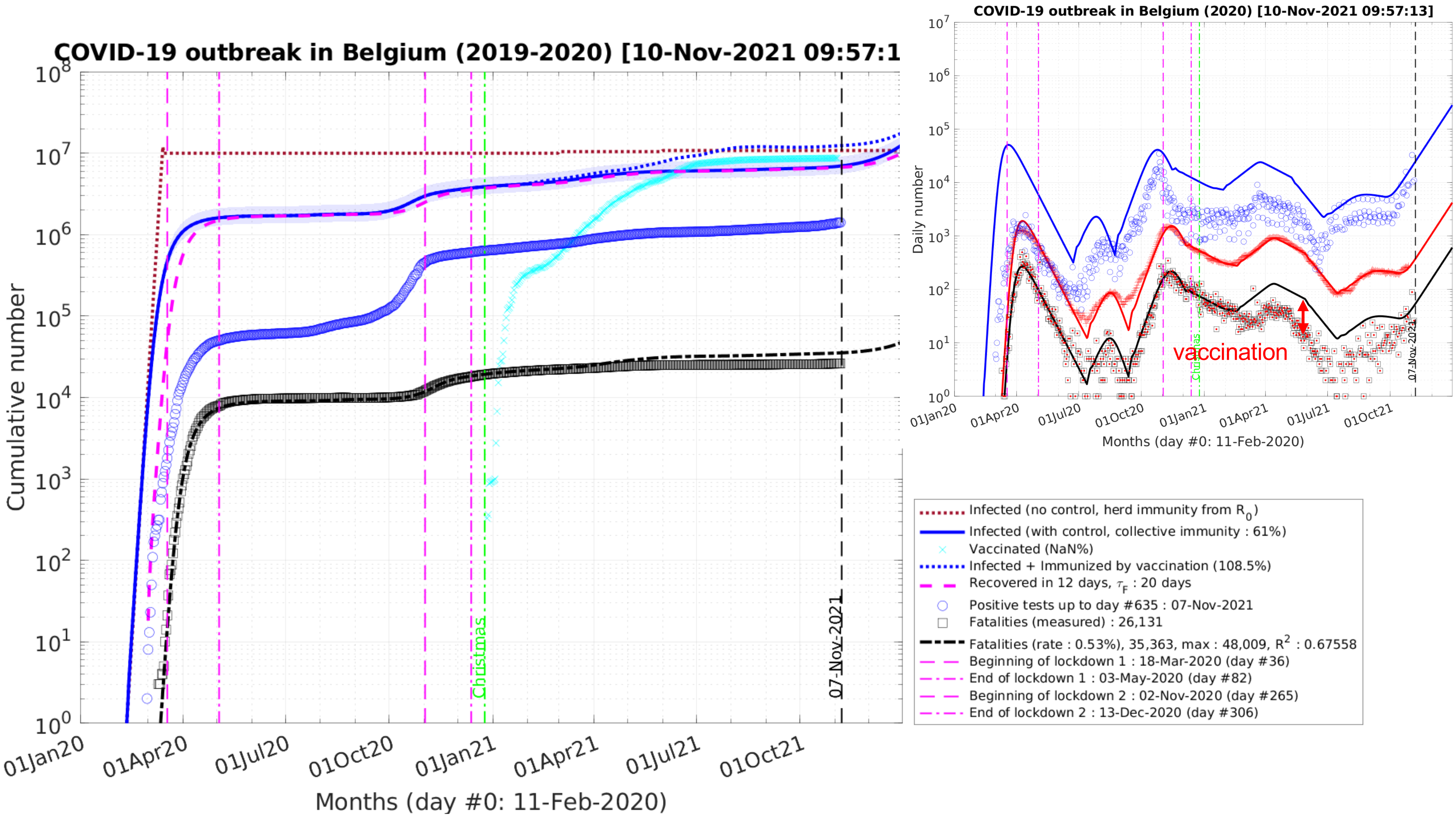




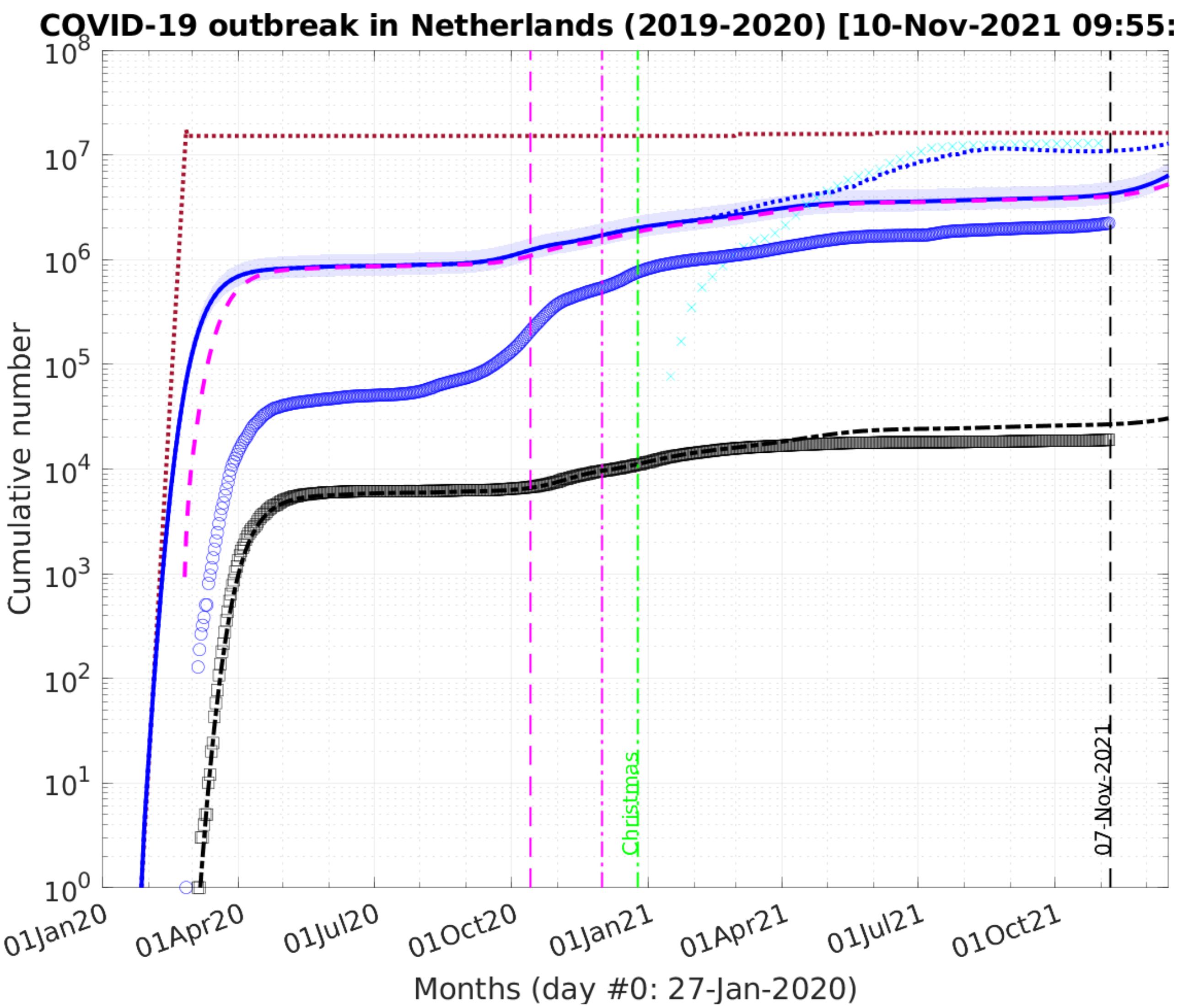
COVID-19 in Spain

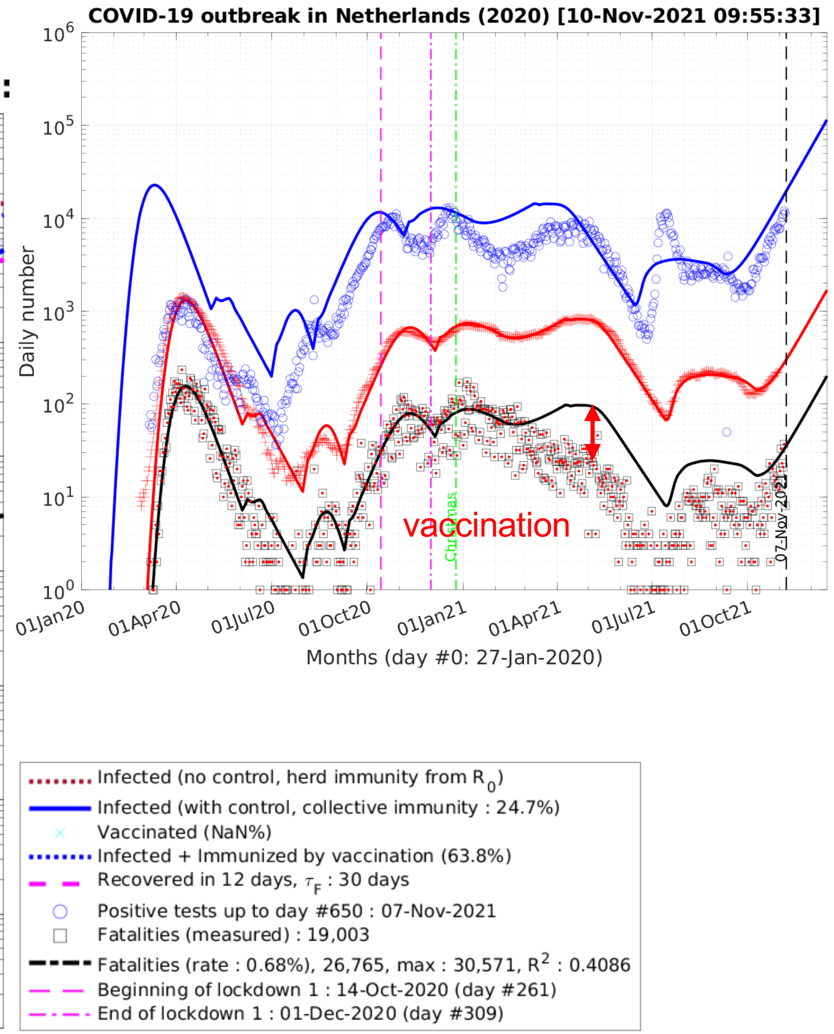


COVID-19 in Belgium

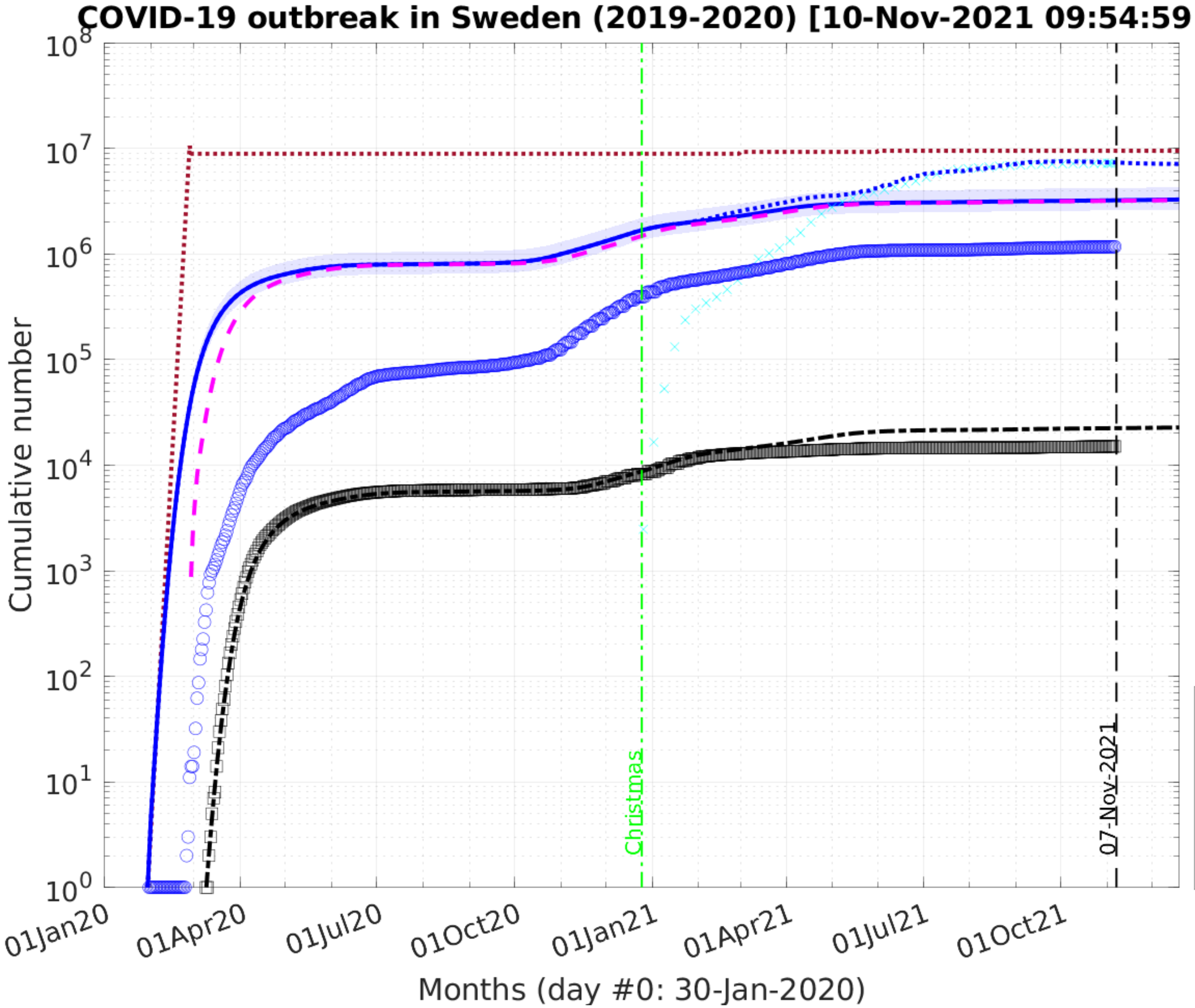


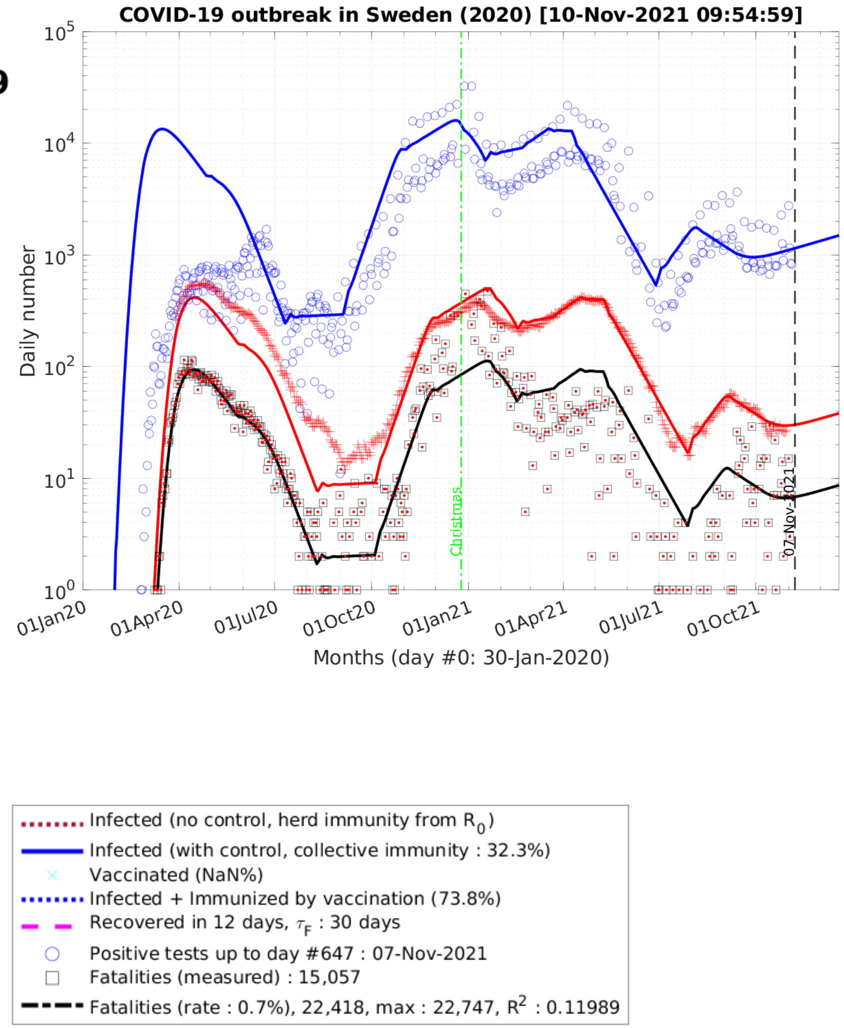
COVID-19 in the Netherlands



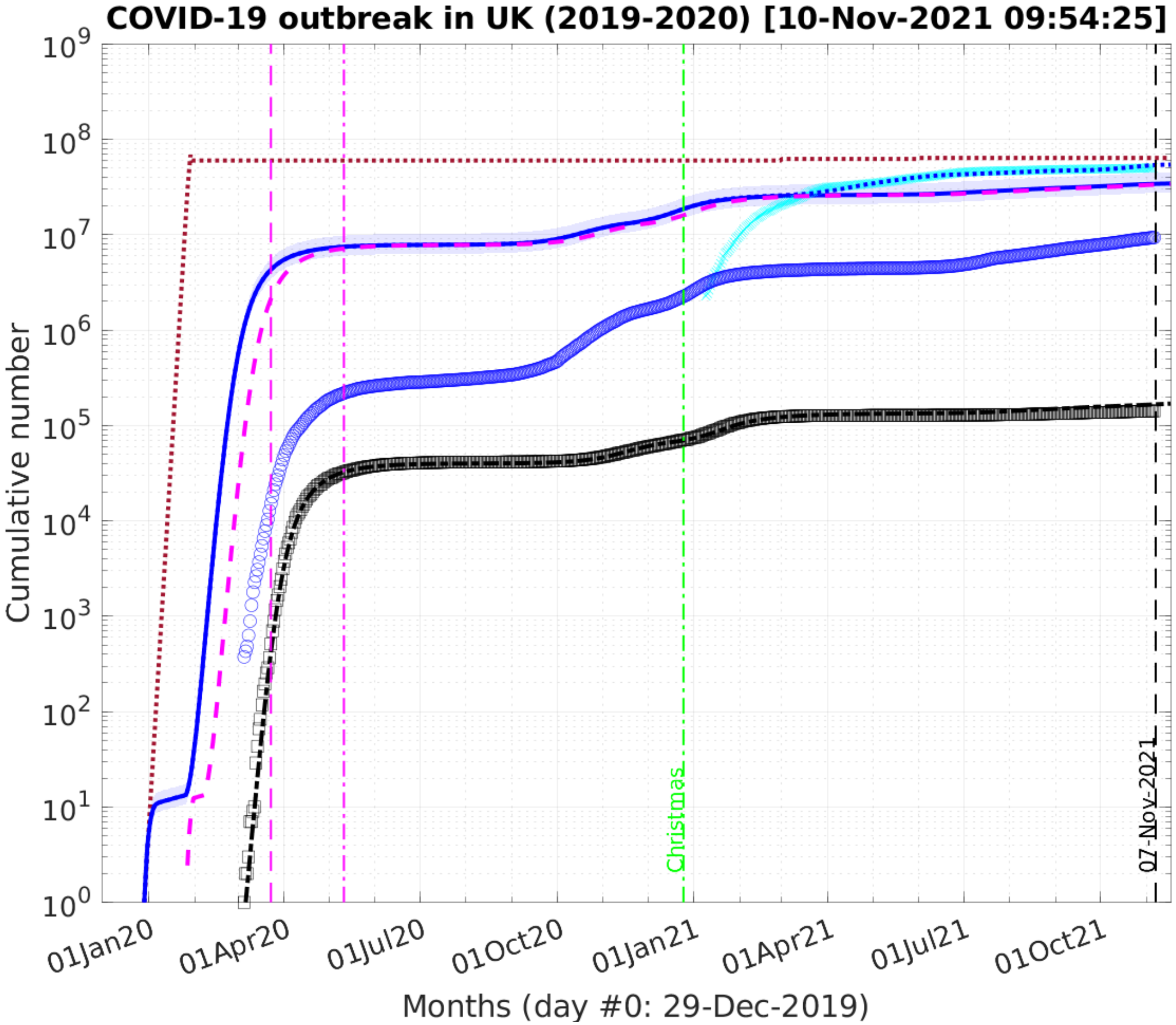


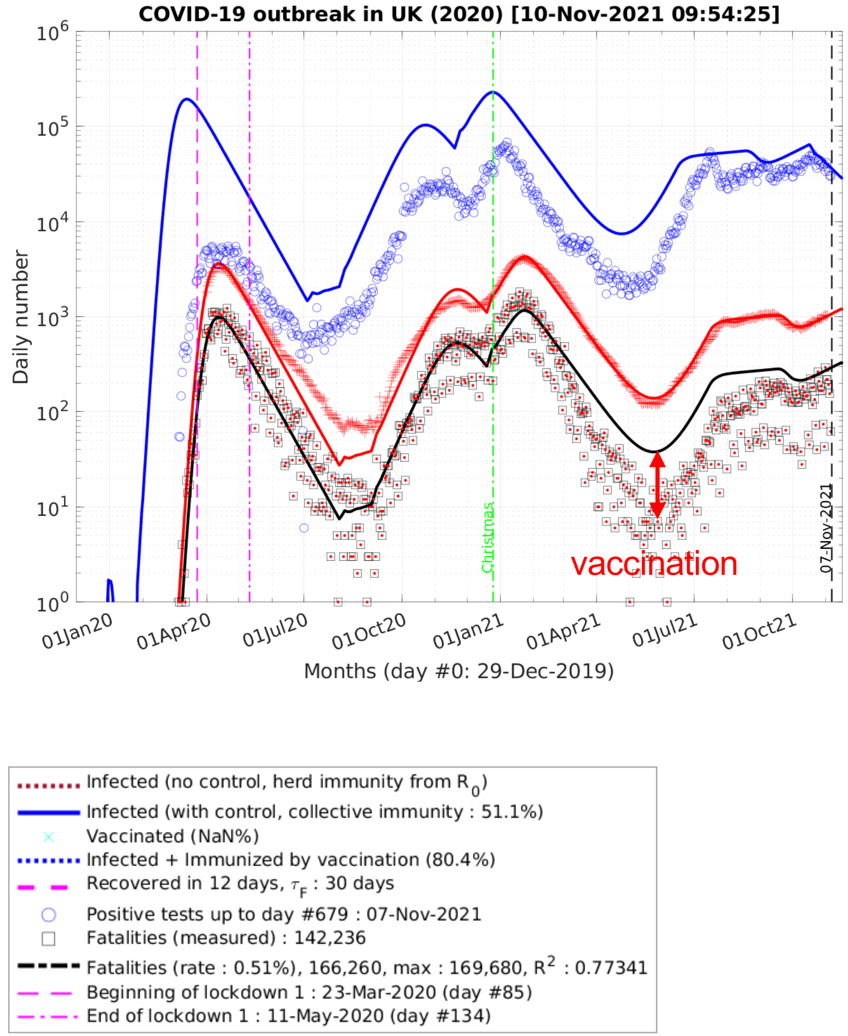
COVID-19 in Sweden



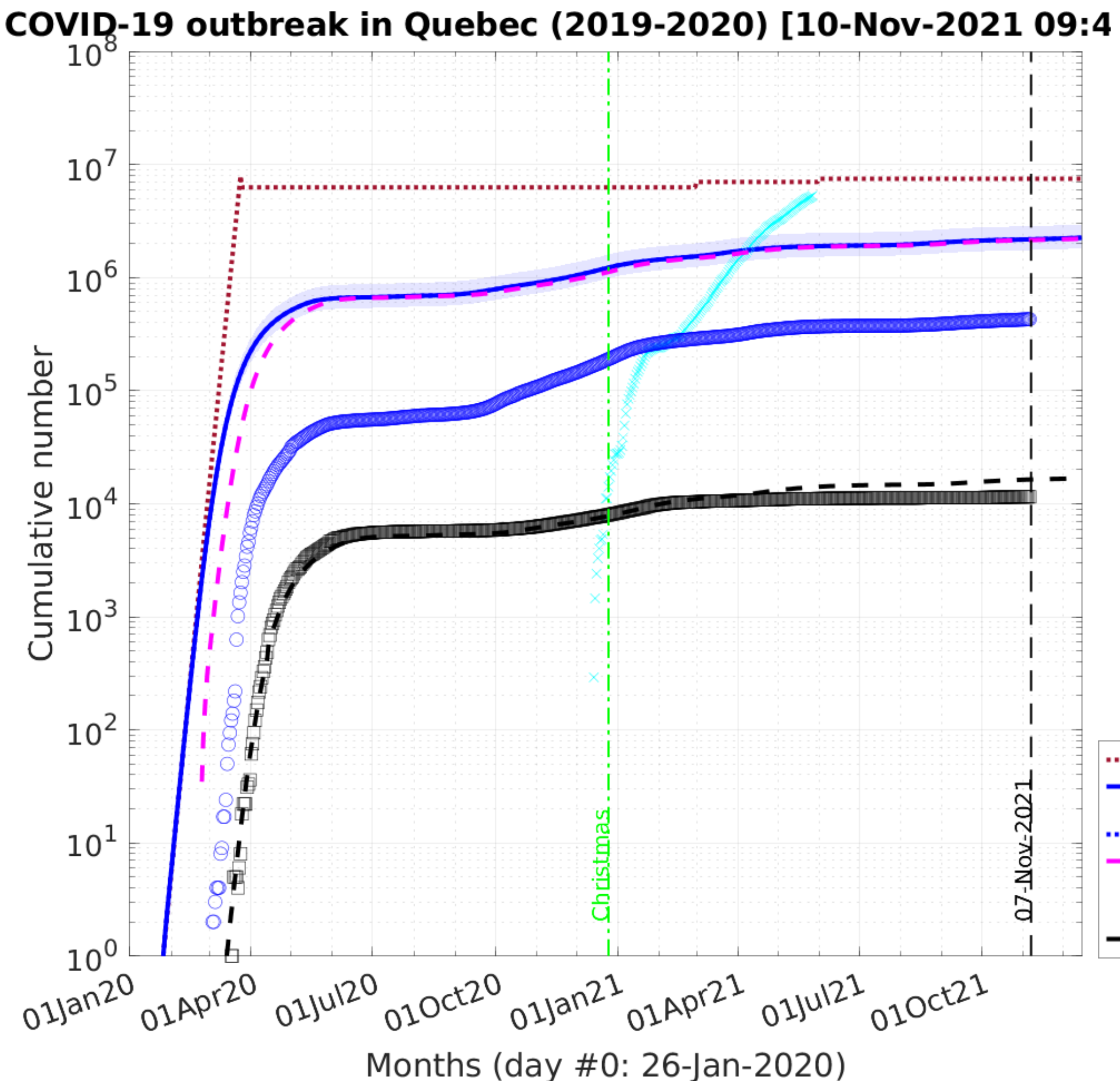


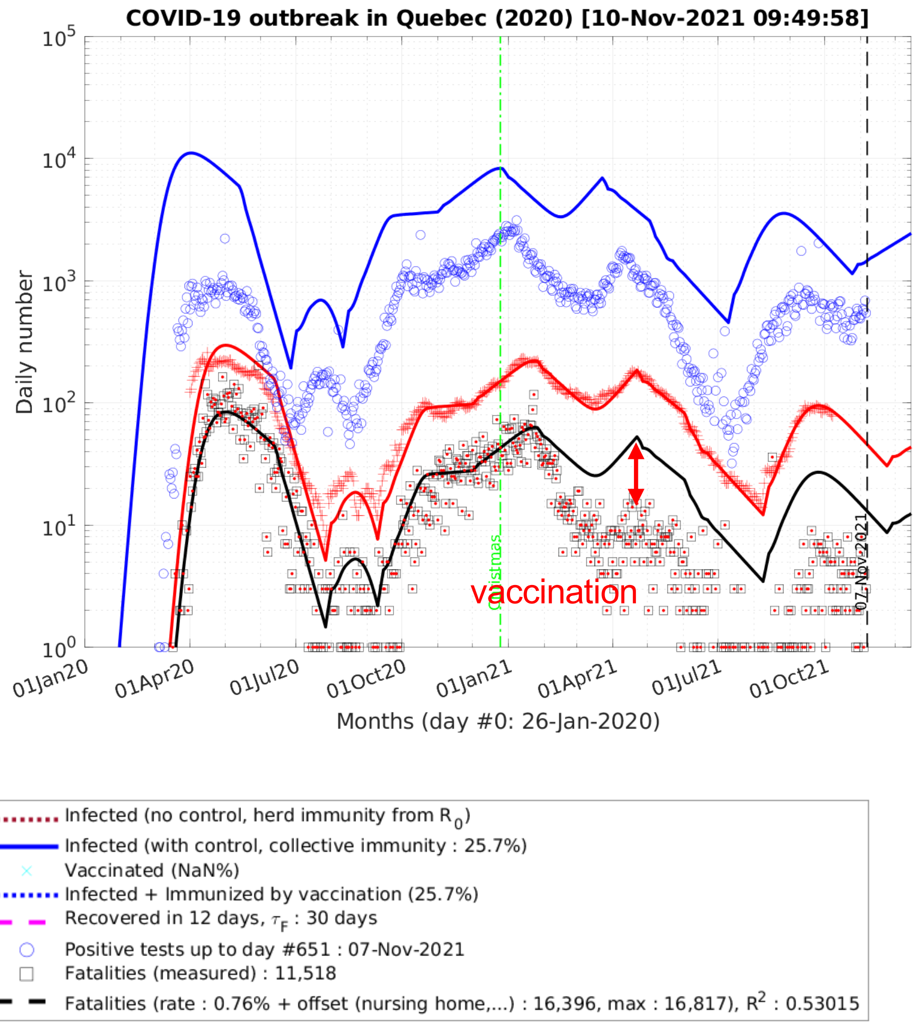
COVID-19 in United-Kingdom





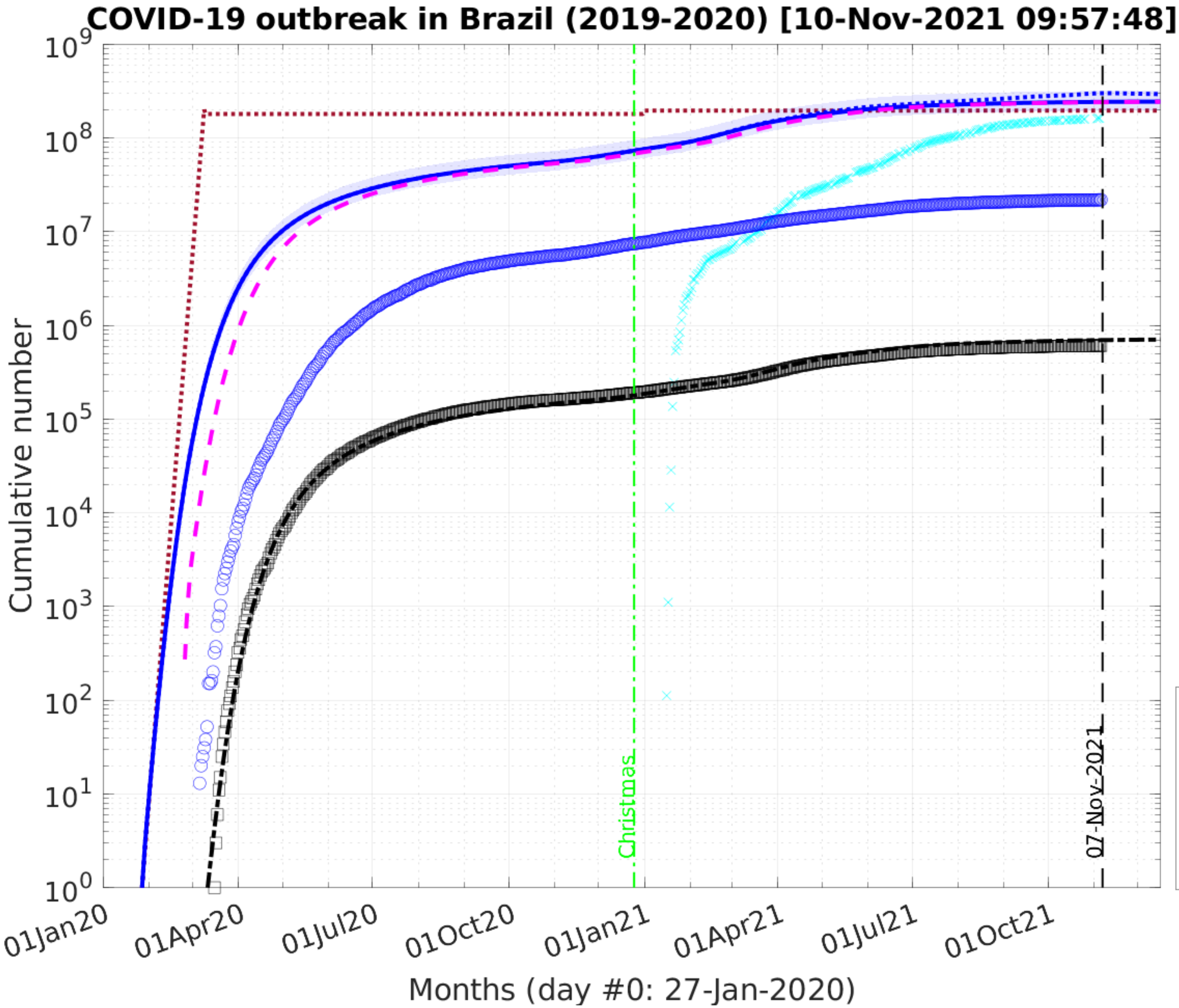
COVID-19 in Quebec (Canada)

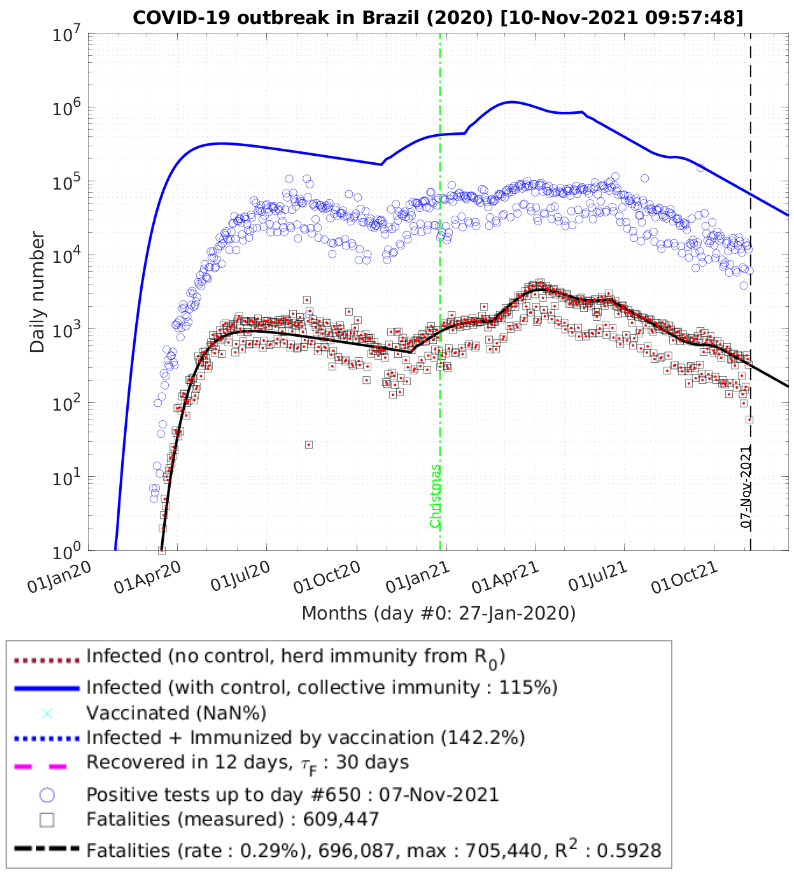




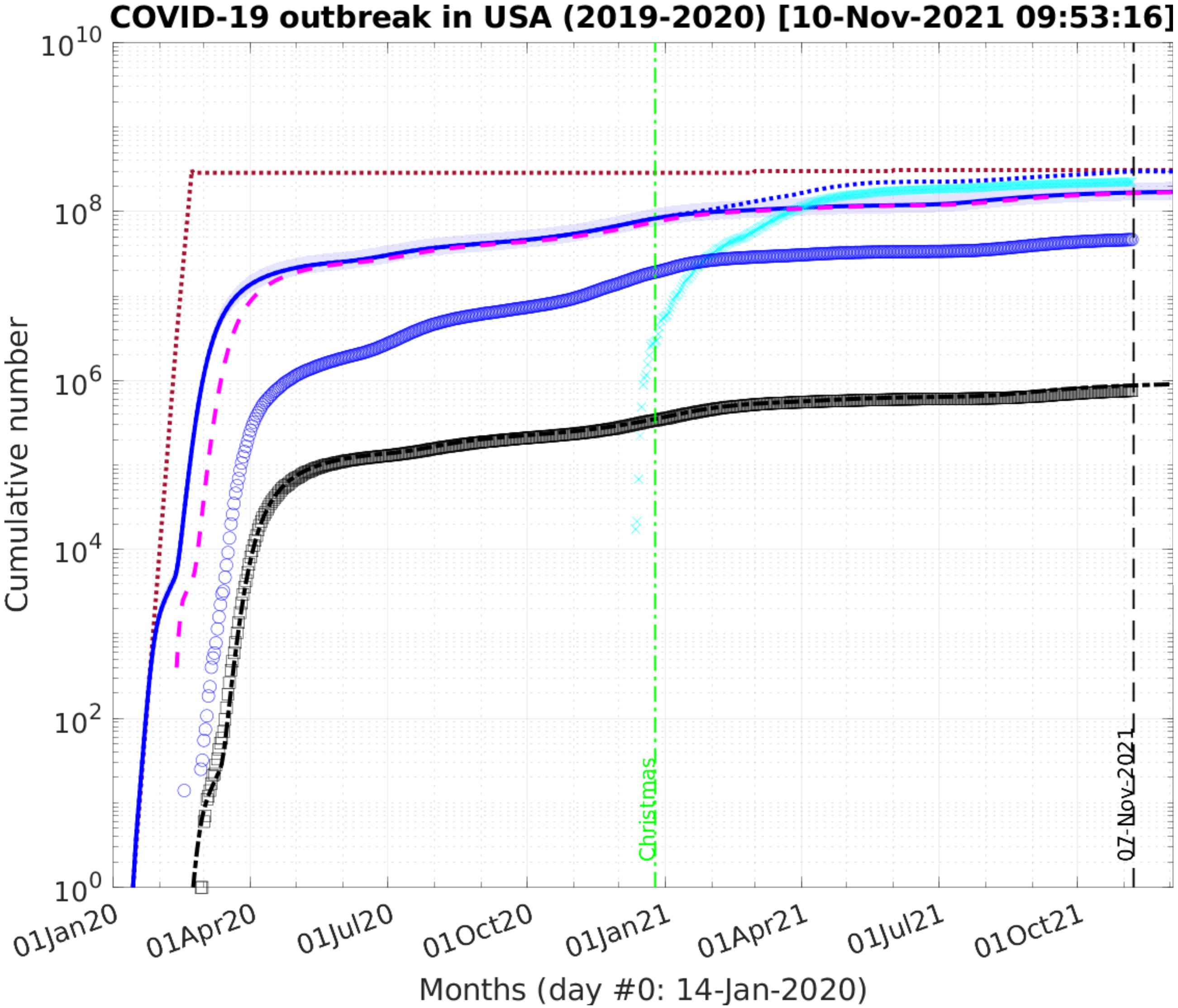
COVID-19 in Brazil

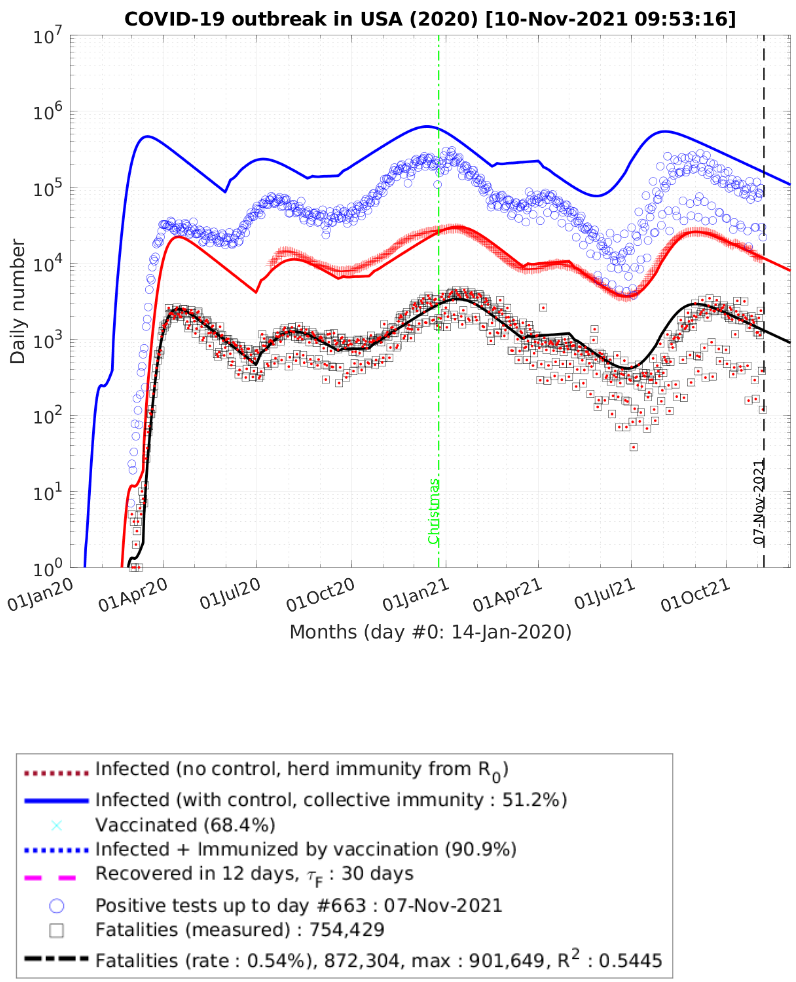
Effect of collective immunity may explain the roll-over, despite marginal impact of vaccinations.



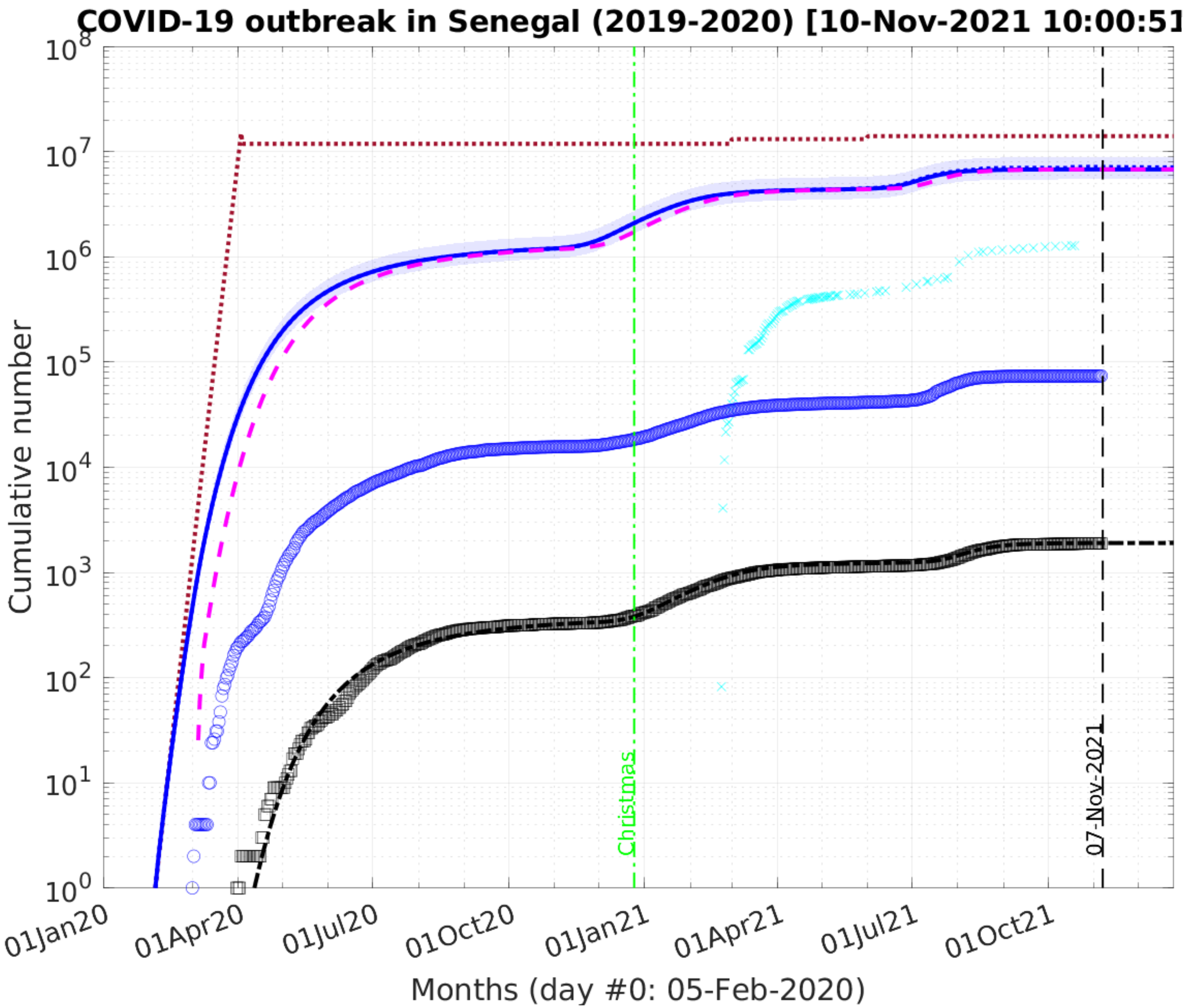


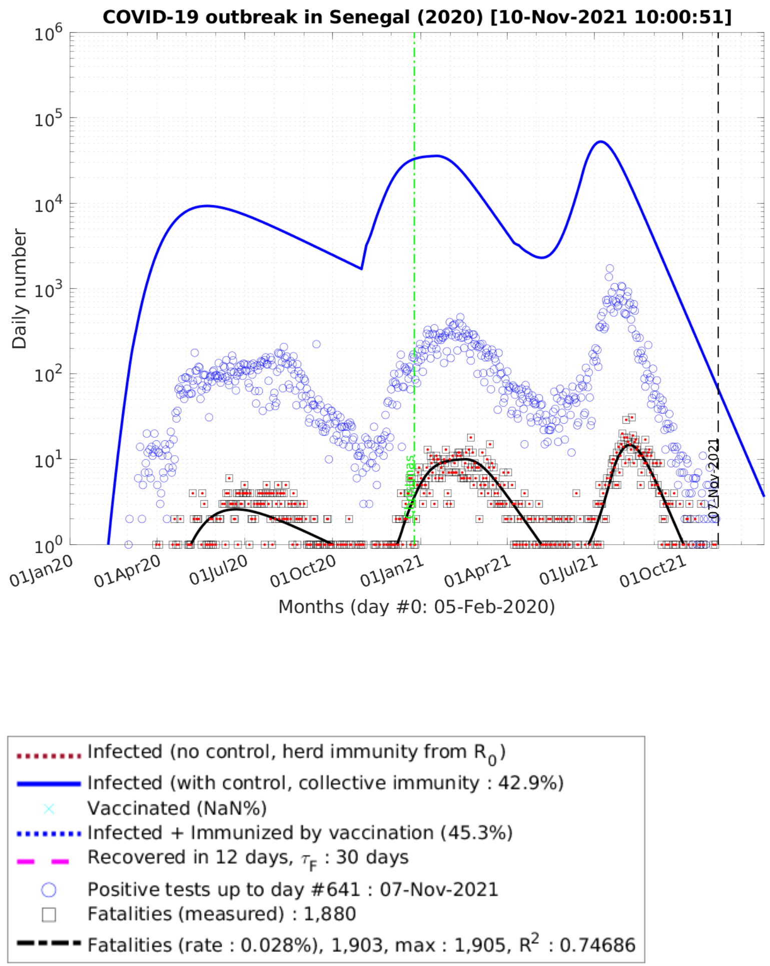
COVID-19 in USA



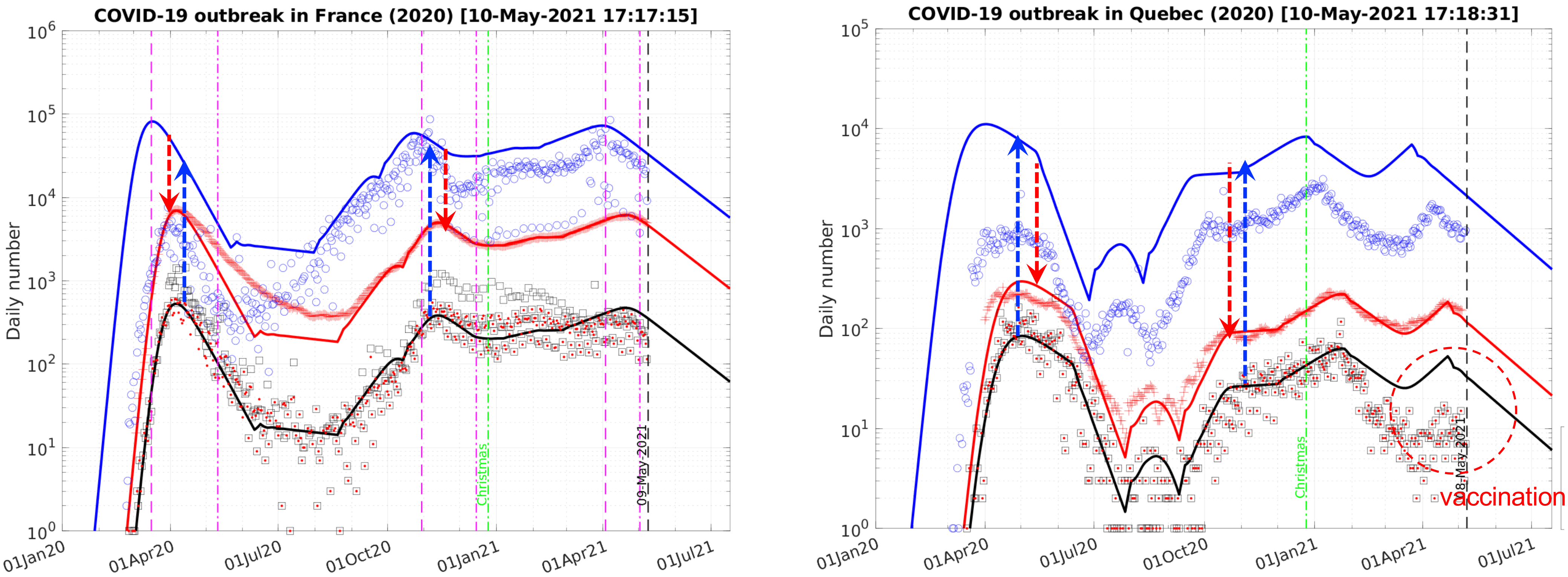


COVID-19 in Senegal



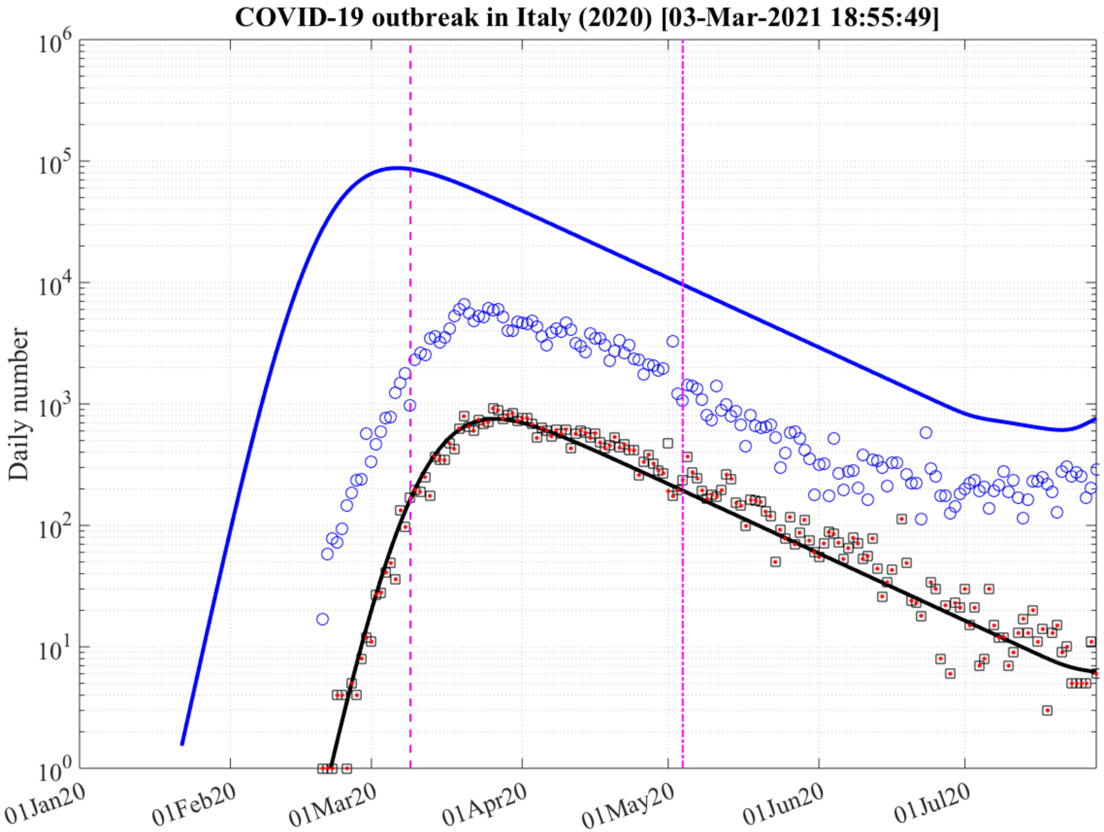


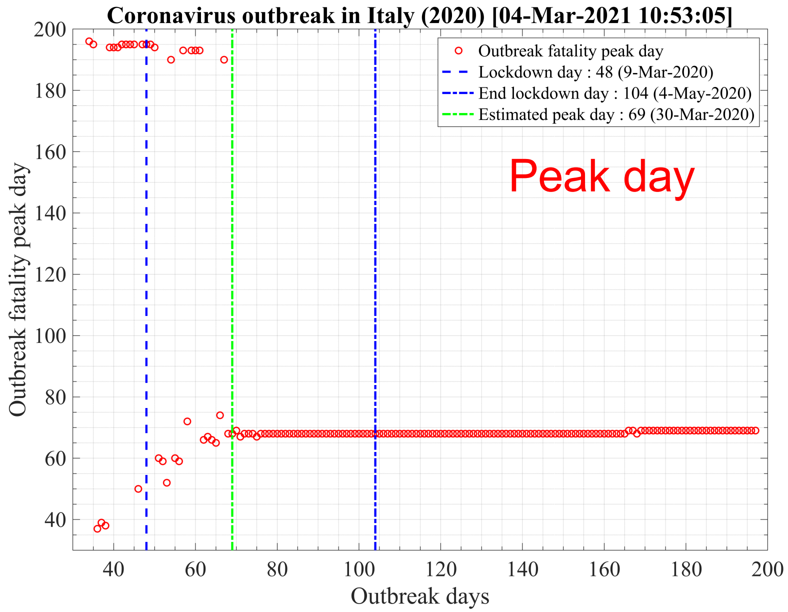
COVID-19 characteristics are unchanged during 2020

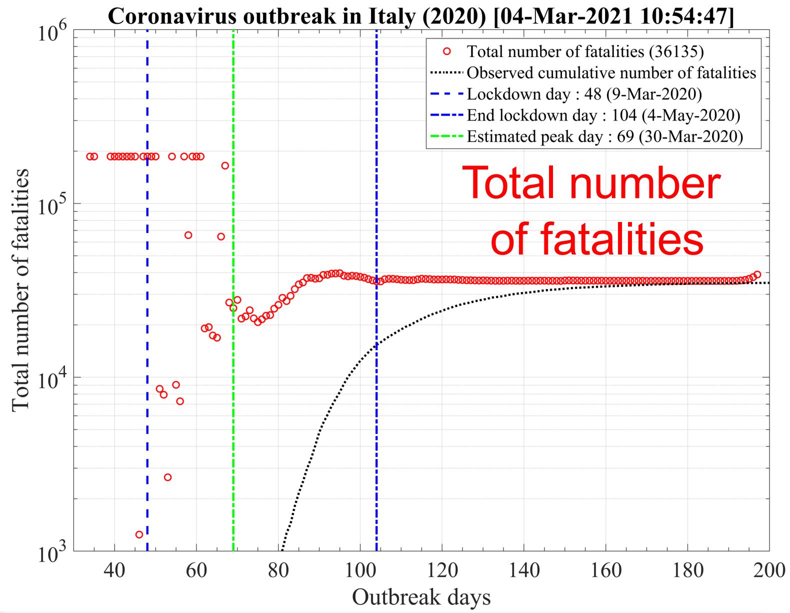


- The number of people in ICU can be quantitatively reproduced in March-April 2020 and later in the year without changing any parameters of the outbreak → ***the parameters characterizing COVID-19 are almost unchanged : mean IFR + the fraction of the infected population in ICU.***
- The transient discrepancy between the calculated and observed ICU time series (red) for France during summer 2020 may result from a younger infected population → lower mean IFR.

Robusteness of the predictions with time (Italy, 1st wave)

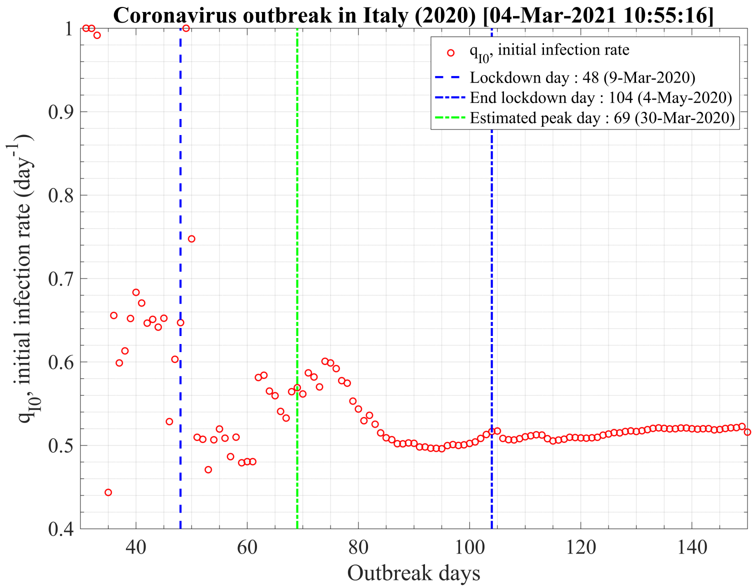


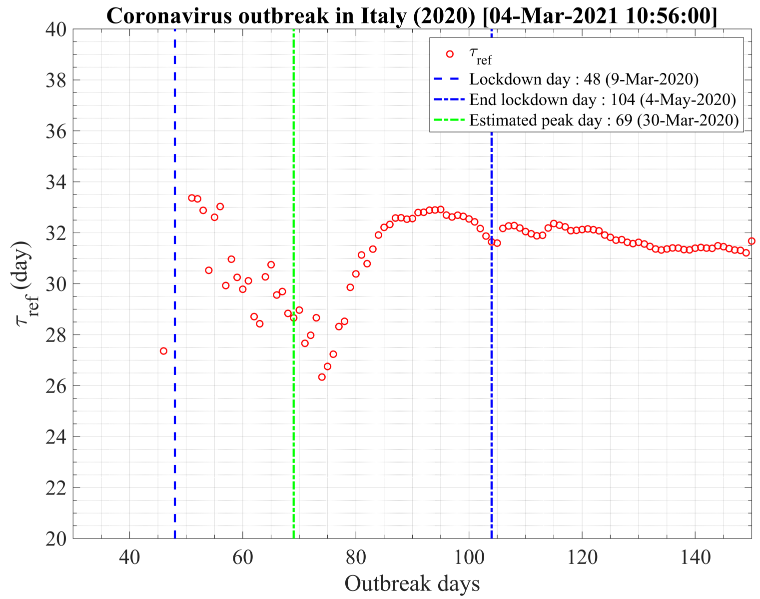


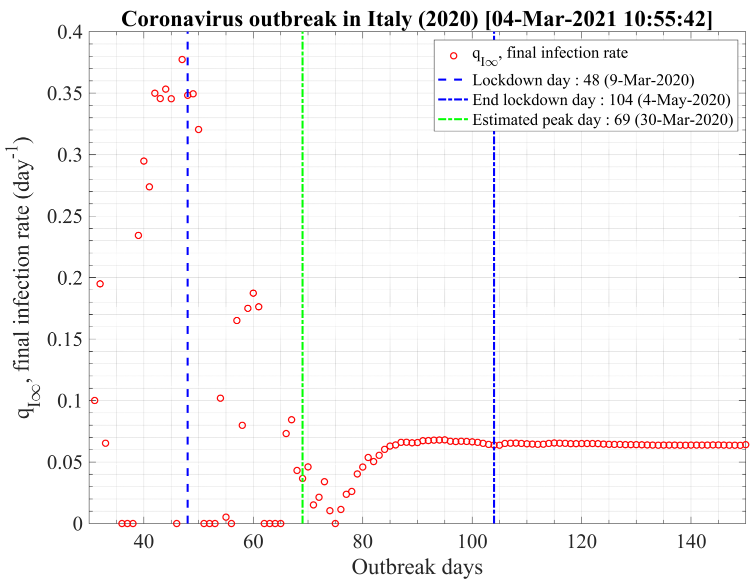


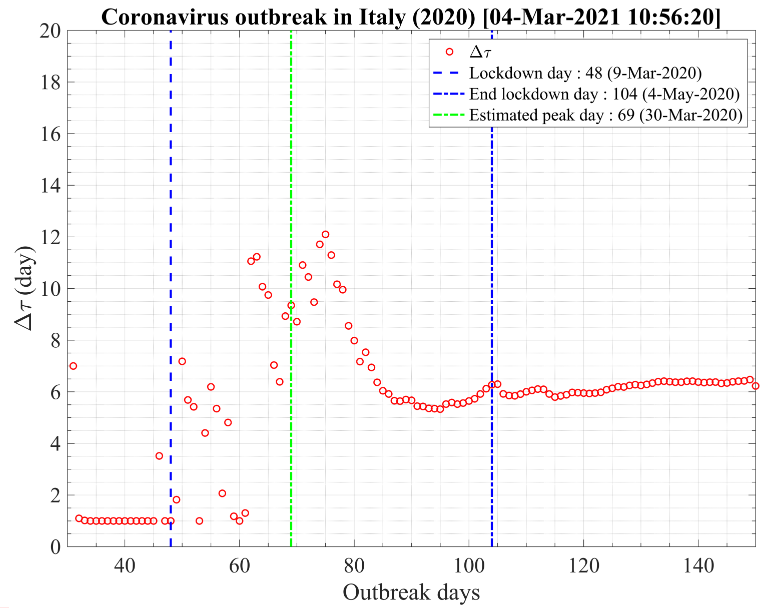
- Peak of the outbreak arises ~20 days after lockdown.
- Before outbreak peak → free epidemic growth : large number of fatalities (200,000), herd immunity rapidly reached (190 days). **Noisy data → very difficult to predict accurately the peak day prior its occurrence.**
- After the peak → very stable predictions.

Evolution of social distancing parameters with time (Italy, 1st wave)









COVID-19 pandemic monitoring

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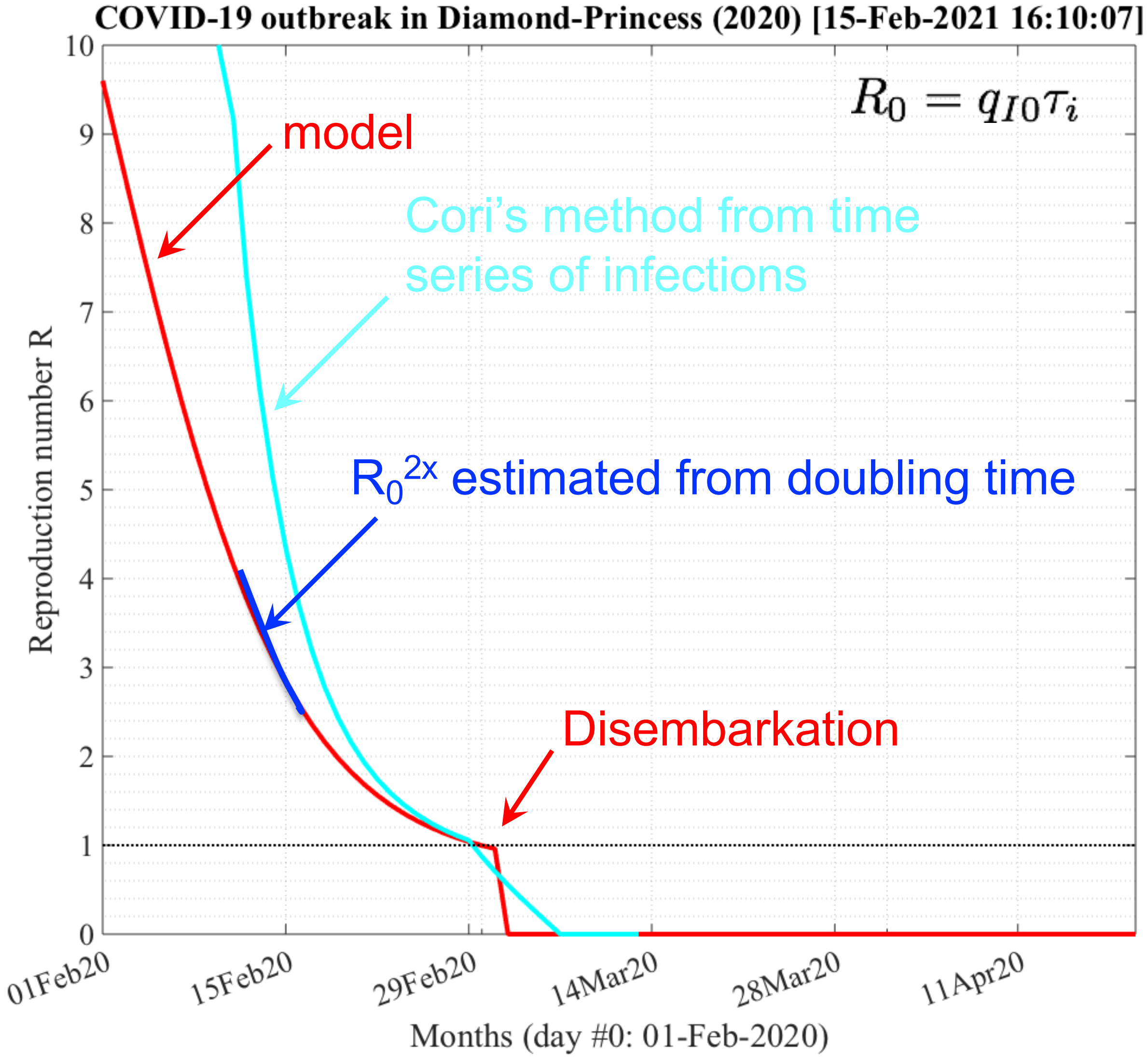
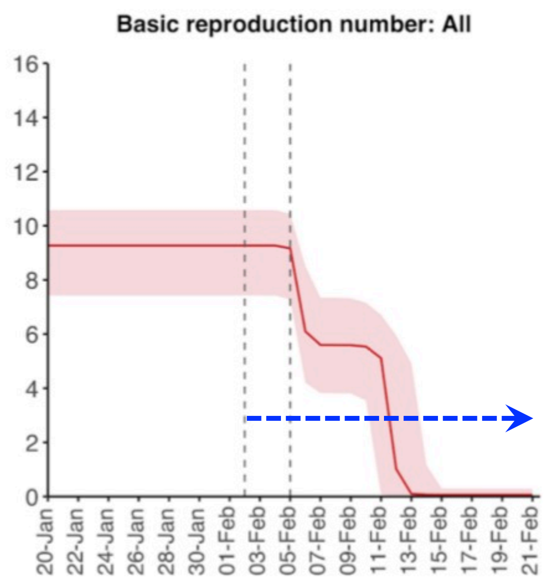
COVID-19 in Diamond-Princess cruise liner : R_0 and R(t)

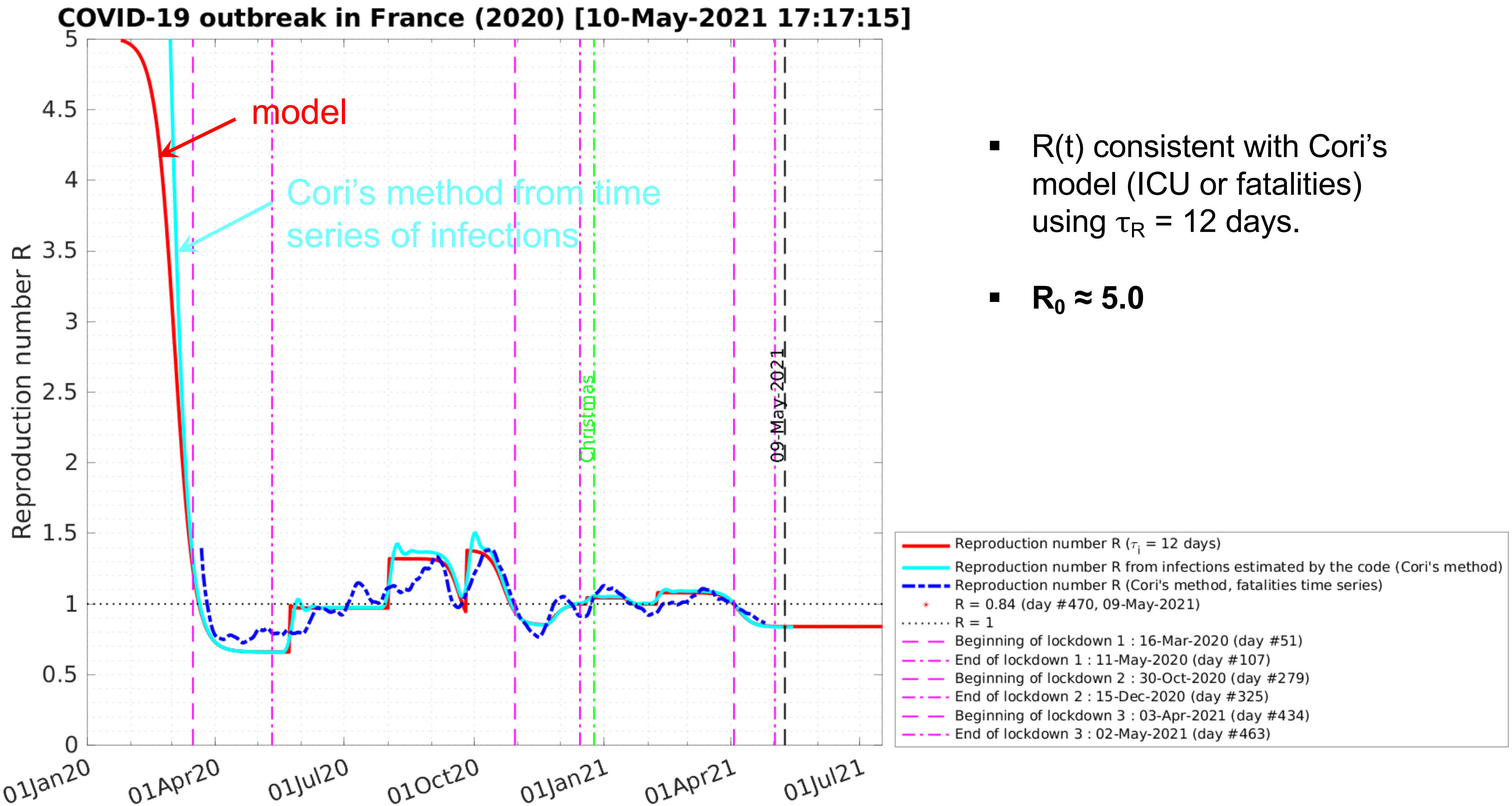


- R_0 consistent with expected herd immunity (not reached because of disembarkation)
- **R_0 ~ 9.6** (τ_i = 12 days) and R(t) consistent with a statistical study of the COVID-19 on the Diamond-Princess cruise line.



J.C. Emery et al. eLife 2020;9:e58699 DOI: 10.7554/ELIFE.58699

COVID-19 in France : reproduction number R(t)

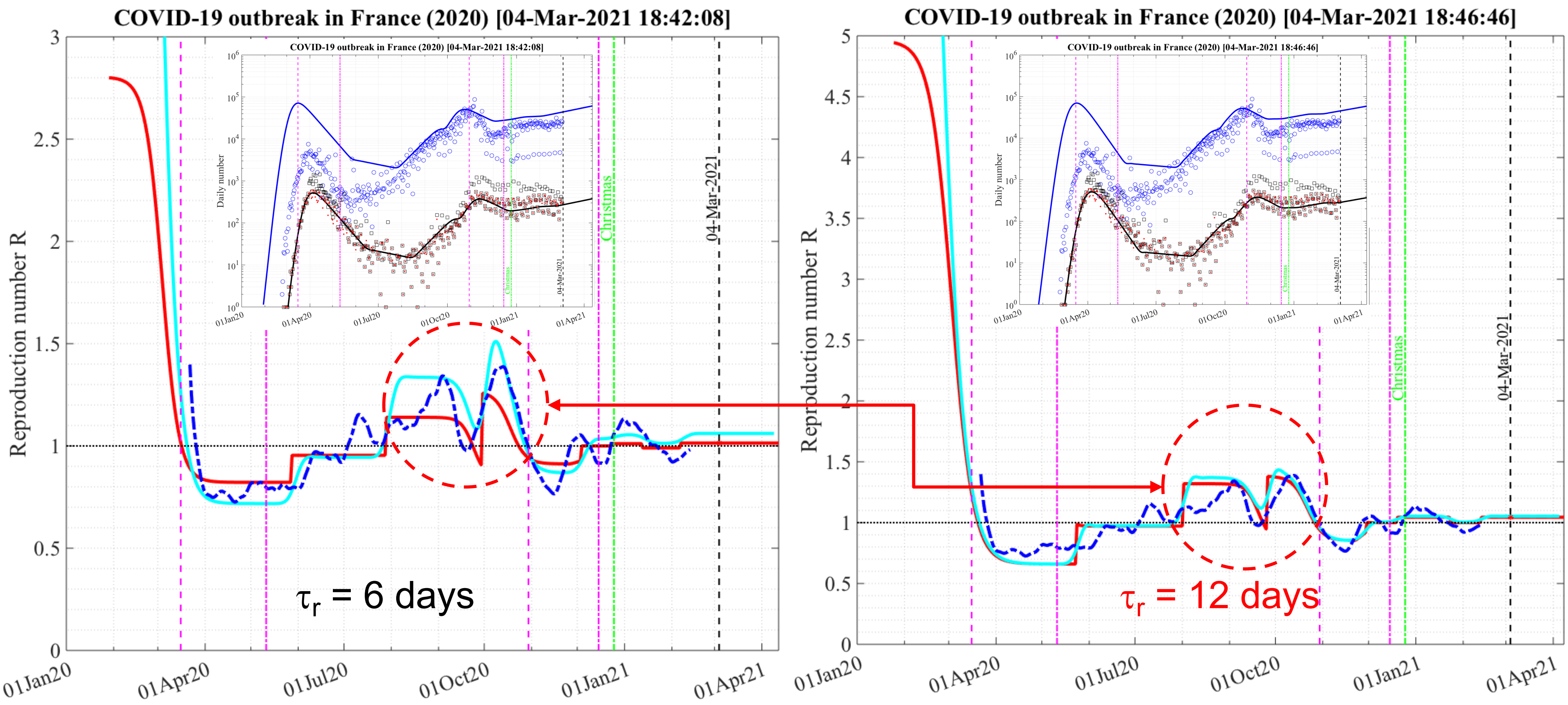


- R(t) consistent with Cori's model (ICU or fatalities) using τ_R = 12 days.
- **$R_0 \approx 5.0$**

Cori A et al. Am J Epidemiol. 178 (2013) 1505

J. S. Huisman et al., (2020) https://doi.org/10.1101/2020.11.26.20239368.

Impact of recovery time on the reproduction number R(t)

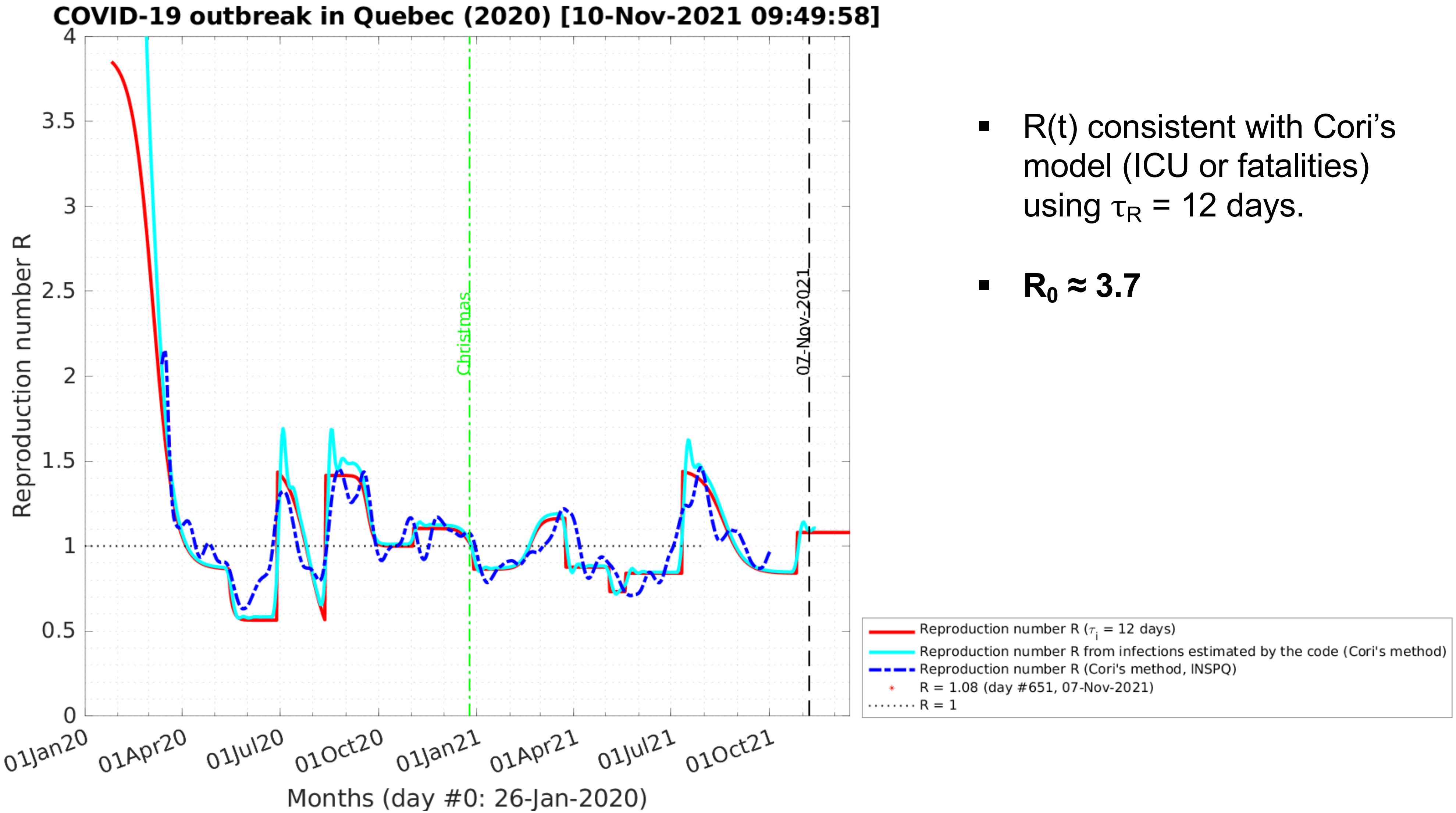


R(t) inconsistent with Cori's method for infection time series (cyan) if τ_r = 6 days, which confirms the choice of τ_r = 12 days.

Cori A et al. Am J Epidemiol. 178 (2013) 1505

J. S. Huisman et al., (2020) https://doi.org/10.1101/2020.11.26.20239368.

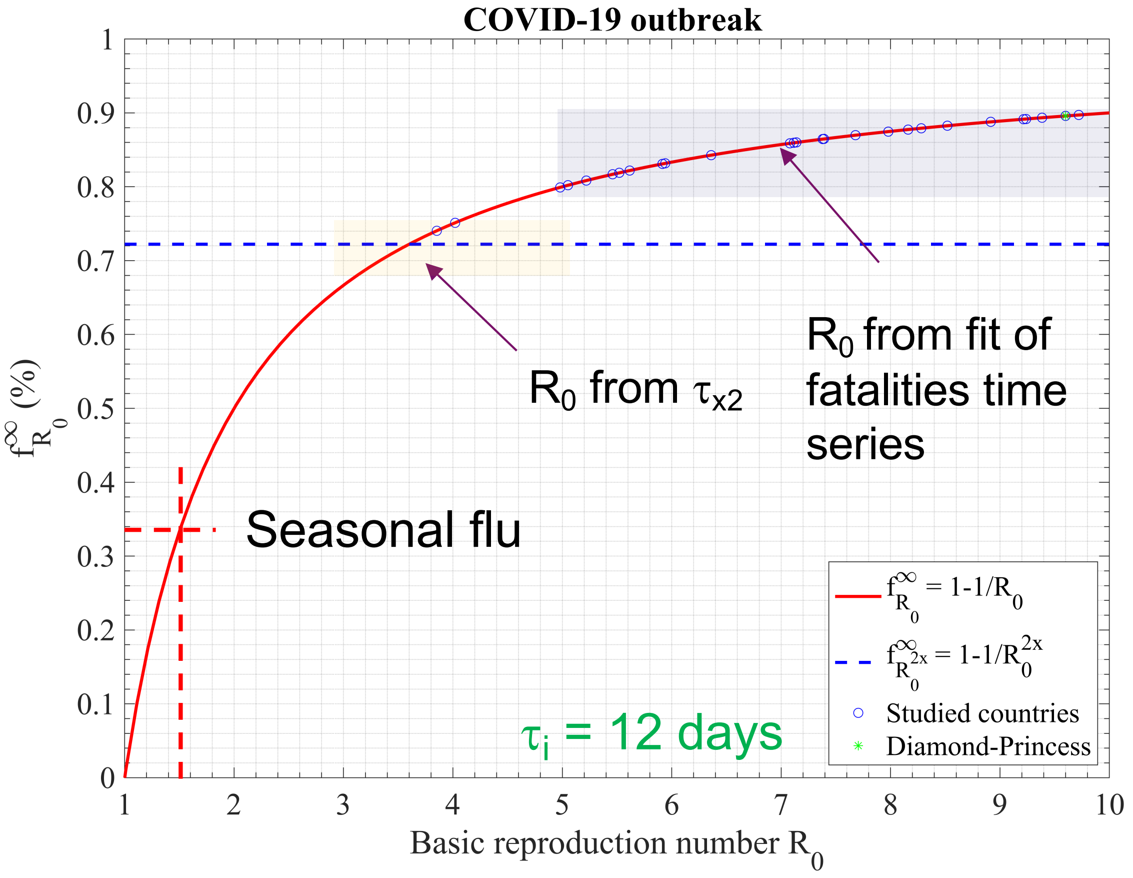
COVID-19 in Quebec : reproduction number R(t)



- R(t) consistent with Cori's model (ICU or fatalities) using τ_R = 12 days.
- **$R_0 \approx 3.7$**

Cori A et al. Am J Epidemiol. 178 (2013) 1505

Basic reproduction number R_0 and herd immunity



- The measles, $R_0 \approx$ 12-18 → f^{∞} = 95%
- Varicella or Delta variant, $R_0 \approx$ 10-12 → f^{∞} = 90%
- ***Original SARS-CoV-2, $\langle R_0 \rangle = 7.5 \pm 2.3$ → $f^{\infty} >$ 80%***
- *Original SARS-CoV-2, $\langle R_0^{2x} \rangle = 3.6 \pm 1.2$ →* f^{∞} > 70%
- Seasonal flu, $R_0 \approx$ 1.4 → f^{∞} = 35%

SARS-CoV-2 is very contagious

- *R_{0x2} from τ_{x2} is determined far from day #0 (first fatalities) → Not relevant for* f^{∞} calculations.
- $\Delta f^{\infty}/f^{\infty} = \Delta R_0/(R_0-1)$ → if $R_0 > 5$, $f^{\infty} >$ 80%.

Original SARS-CoV-2 R_0 and collective immunity

Country	Day #0	R_0	Fatalities N_F *01-Mar-2021*	Immunity f^{∞} (%)	f (%) *01-Mar-2021*
Italy	21-Jan-2020	6.4	97,227	84	20.0
Germany	03-Jan-2020	9.2	69,939	89	12.0
France	**25-Jan-2020**	**5.0**	**86,803**	**80**	**13.0**
Spain	04-Feb-2020	9.2	69,142	89	23.7
Sweden	30-Jan-2020	9.4	12,826	89	21.8
Netherlands	27-Jan-2020	8.9	15,503	89	15.4
Switzerland	04-Feb-2020	7.7	9,961	87	32.5
Belgium	11-Feb-2020	8.0	22,034	88	38.5
United Kingdom	29-Dec-2019	9.7	122,415	90	37.9
Poland	31-Jan-2020	5.9	43,353	83	35.7
Israel	03-Feb-2020	5.5	5,697	82	30.4

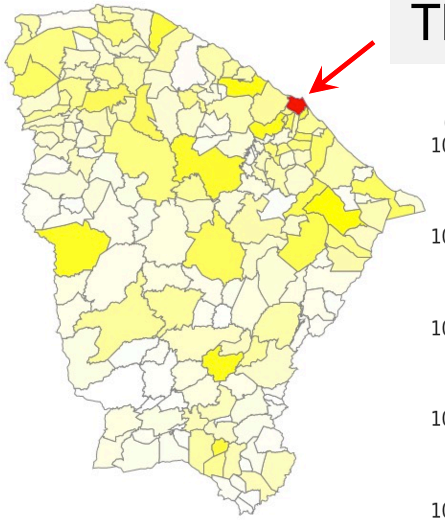
Red : low, Blue: medium, Green : high collective immunity

Original SARS-CoV-2 R_0 and collective immunity

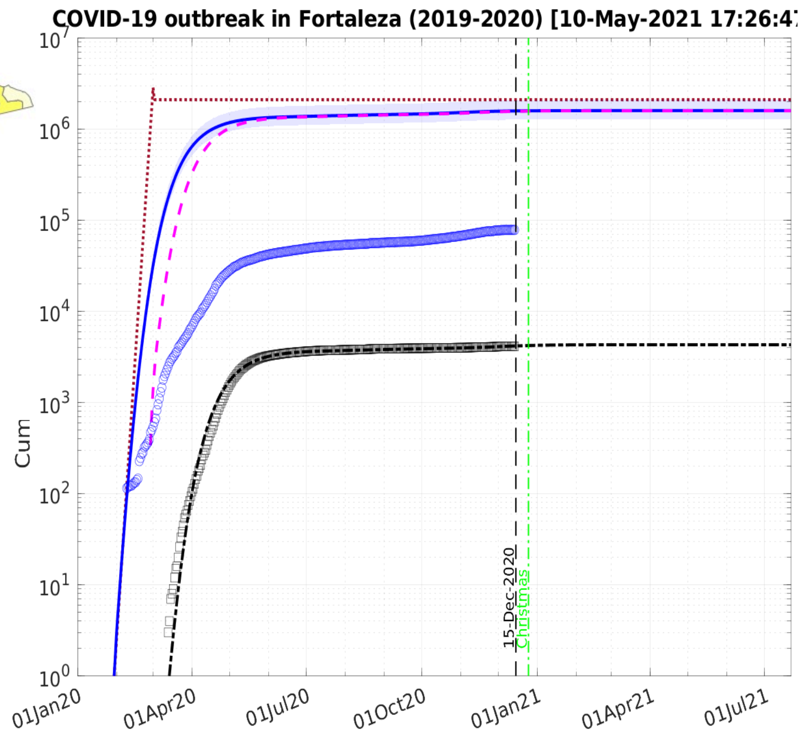
Country	Day #0	R_0	Fatalities N_F *01-Mar-2021*	Immunity f^{∞} (%)	f (%) *01-Mar-2020*
Quebec (Canada)	26-Jan-2020	3.8	10,372	74	17.2
South-Korea	06-Jan-2020	7.7	1,595	87	1.0
USA	14-Jan-2020	8.2	510,458	88	32,4
China	21-Dec-2019	14.6	4,636	93	0.1
Brazil	27-Jan-2020	7.1	252,835	86	62.2
Mexico	30-Jan-2020	5.9	184,474	83	80.1
Lebanon	23-Jan-2020	5.6	4,610	82	96.9
Iran	04-Jan-2020	7.1	59,899	86	72.7
India	20-Jan-2020	5.1	156,938	80	12.2
Senegal	05-Feb-2020	4.0	857	75	26.0

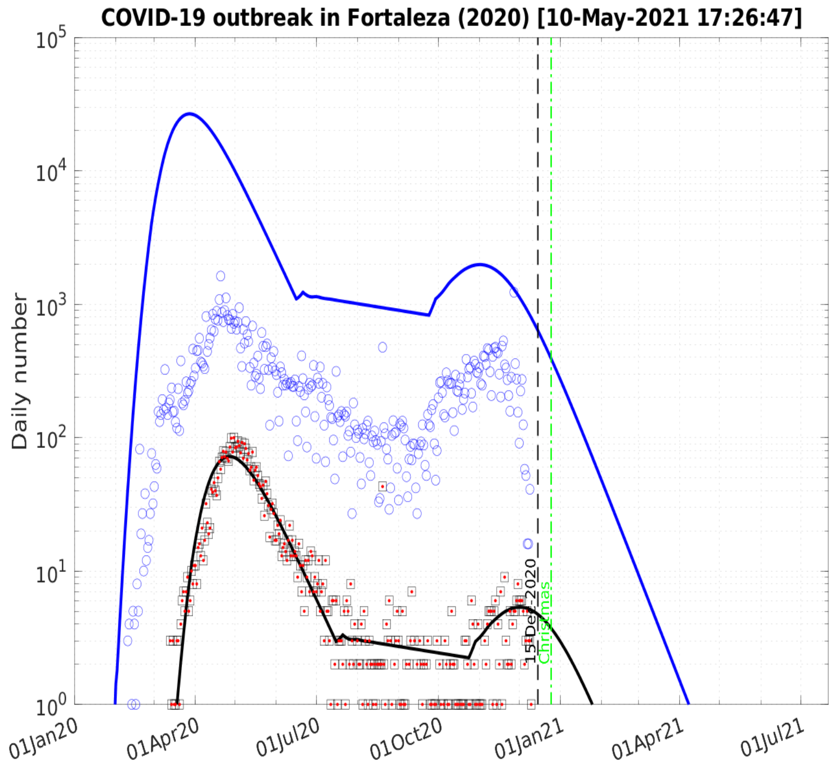
- France is one of the countries with the lowest initial **R_0 ($\langle R_0 \rangle = 7.4 \pm 2.3$).**
- Days #0 are consistent with observed dates when outbreak started.

Brazilian cities and herd immunity: Fortaleza



The city of Fortaleza (Brazil, 2.36 millions inhabitants, density 7768 km^{-2})

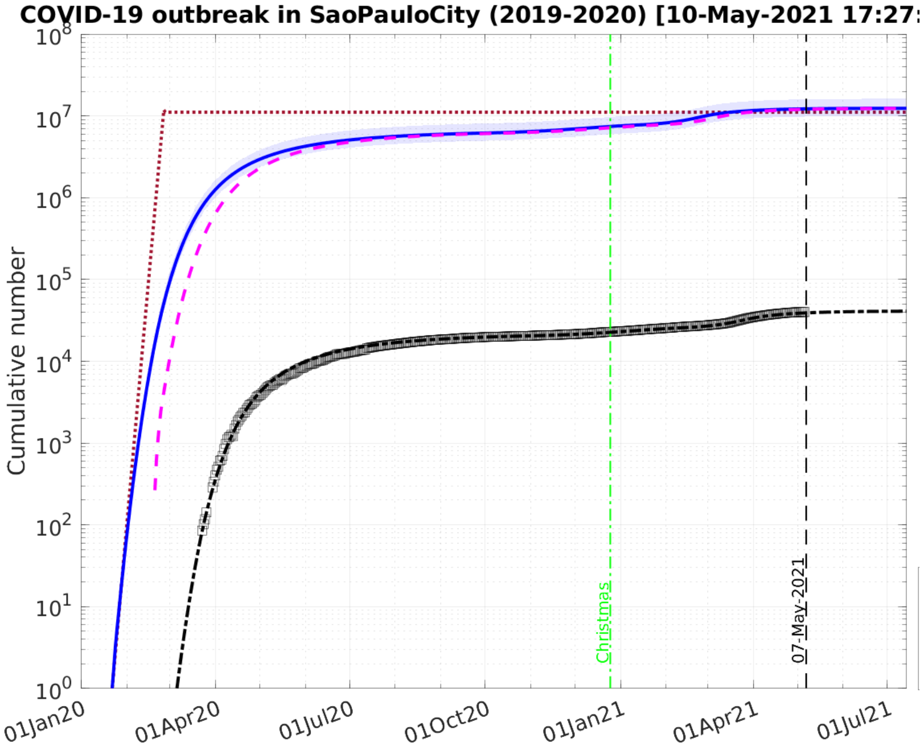


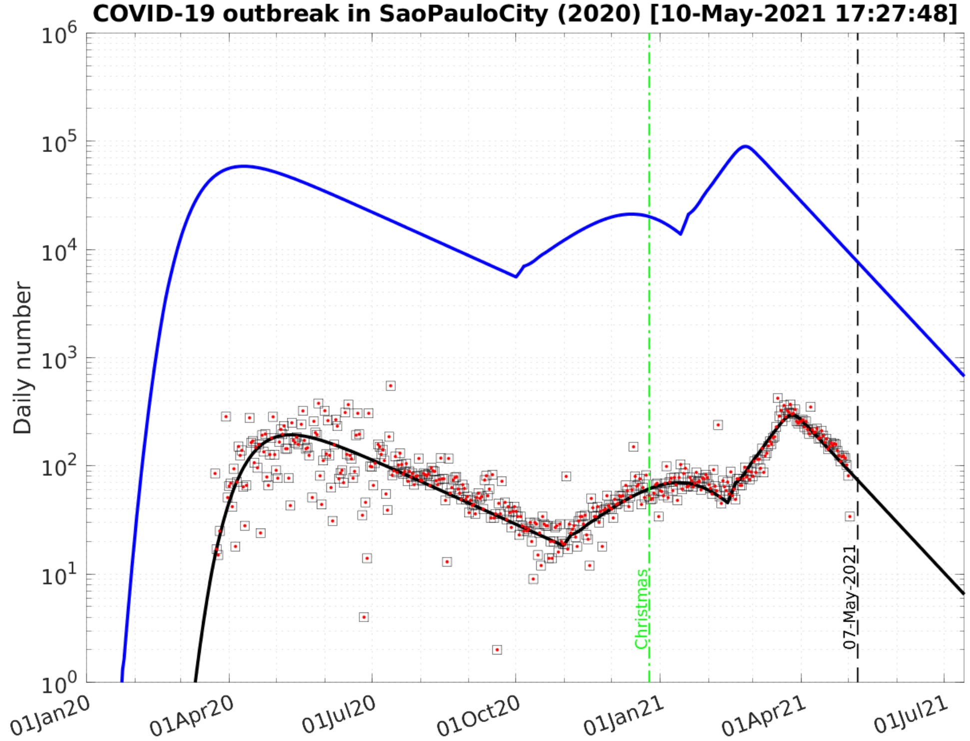


- Population is older than the mean age of brazilian (specific mean IFR)
- The collective immunity is reaching the estimated theoretical herd immunity in around 100 days.
- Despite the probable high level of collective immunity, a small secondary surge is observed after *a flat plateau of fatalities which lasted 100 days at low level.*

Brazilian cities and herd immunity: Sao Paulo

City of Sao Paulo (Brazil, 11.8 millions inhabitants)

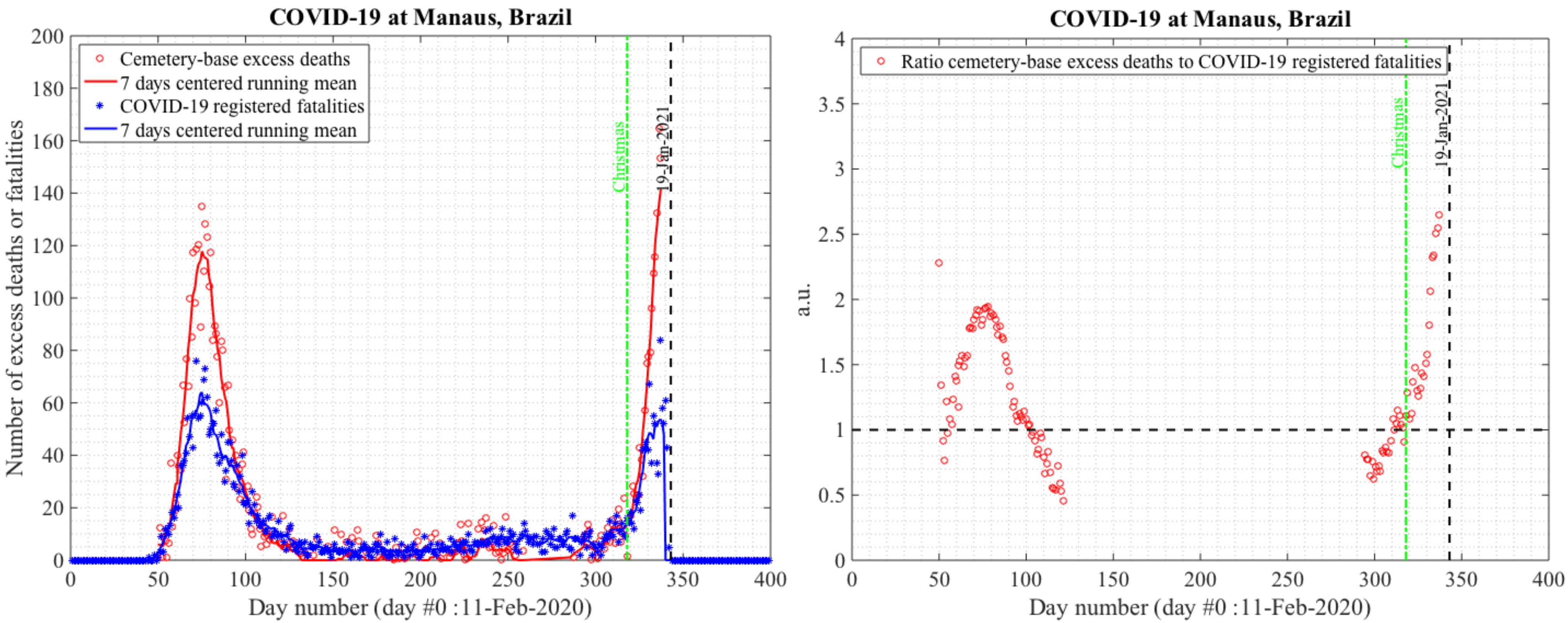




- The mean IFR is higher than in Brazil (specific mean IFR : 0.33%)
- The theoretical herd immunity seems to be reached after the P.1 surge. May explain the drop.
- A long secondary waves is observed despite the estimated high level of collective immunity.
- *Serology studies suggest a rather high mean IFR (~0.5%)*

Brazilian cities and herd immunity : Manaus

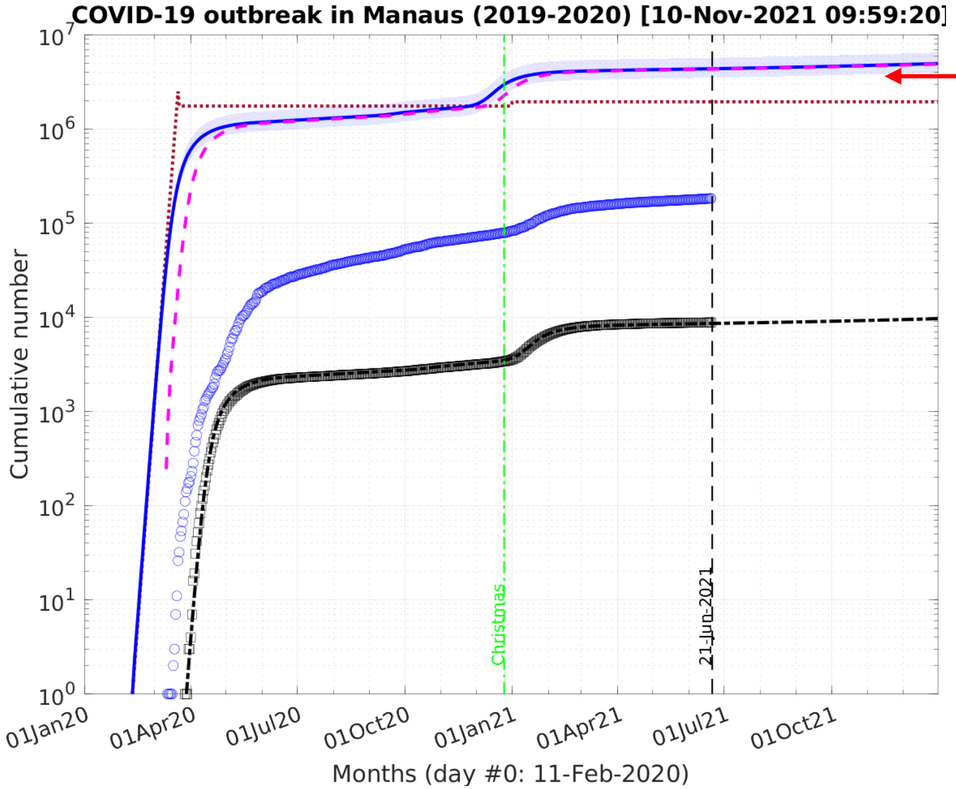
The city of Manaus (Brazil, 2.14 millions inhabitants)

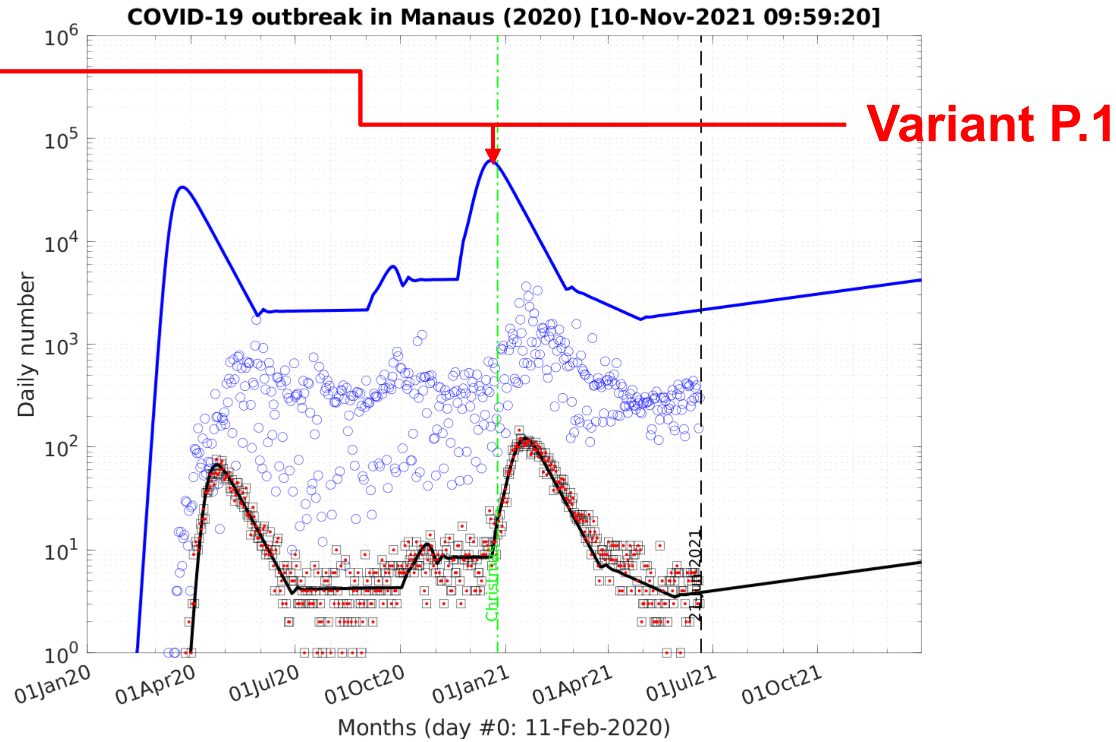


Mean IFR ≈ 0.2% taking into account of cemetery-base exceed deaths, age structure of the population and the age distribution of fatalities by COVID-19

Brazilian cities and herd immunity : Manaus

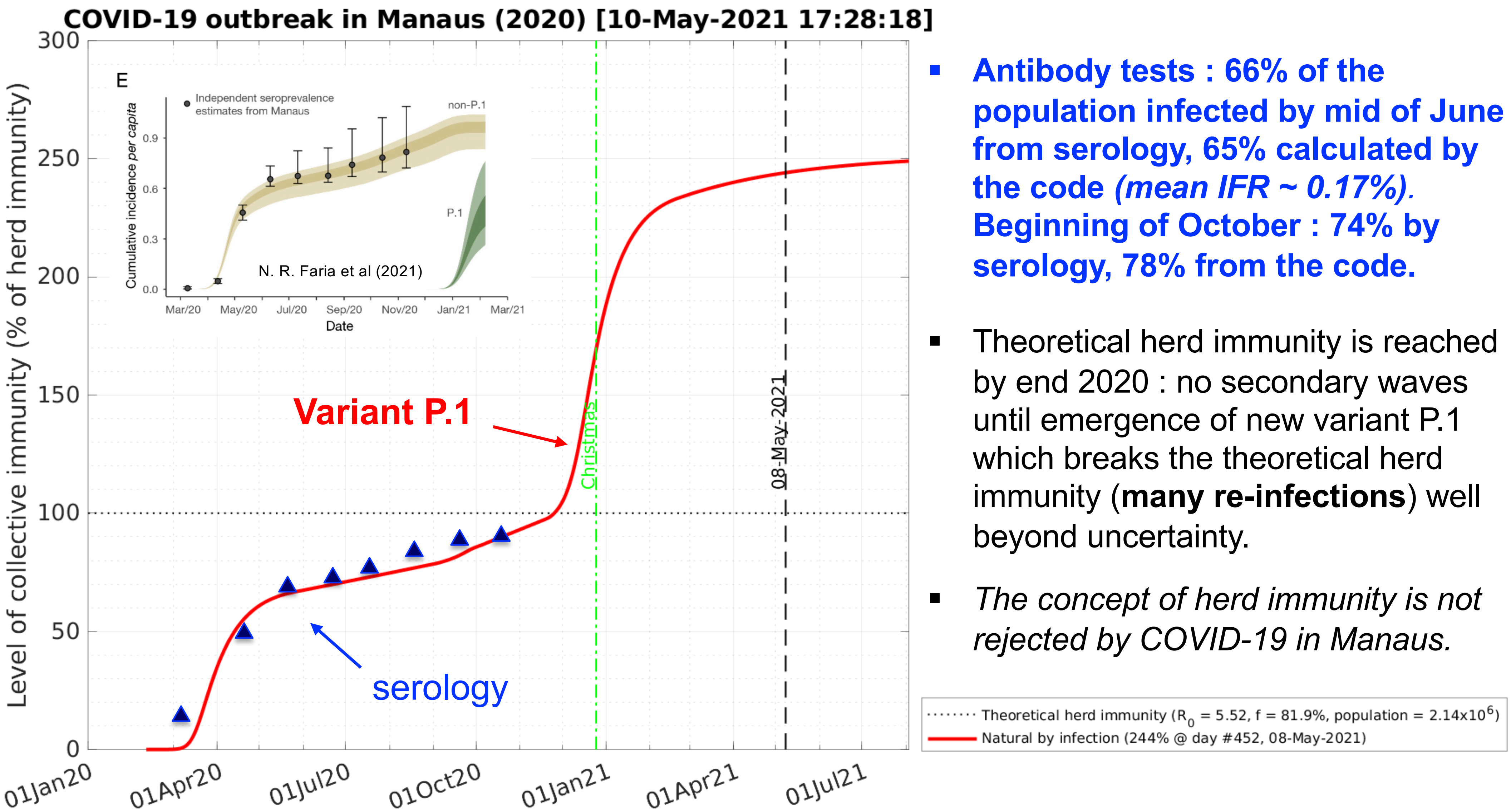
The city of Manaus (Brazil, 2.14 millions inhabitants)





- Theoretical herd immunity is reached in December 2020 : no secondary waves until end 2020.
- Emergence of the new variant P.1 breaks the theoretical herd immunity : **re-infections**. Local social behaviour may have also contributed to the fast rise of the outbreak in January 2021

Brazilian cities and herd immunity : Manaus



- **Antibody tests : 66% of the population infected by mid of June from serology, 65% calculated by the code *(mean IFR ~ 0.17%)*. Beginning of October : 74% by serology, 78% from the code.**
- Theoretical herd immunity is reached by end 2020 : no secondary waves until emergence of new variant P.1 which breaks the theoretical herd immunity (**many re-infections**) well beyond uncertainty.
- *The concept of herd immunity is not rejected by COVID-19 in Manaus.*

L.F. Buss et al, https://doi.org/10.1101/2020.09.16.20194787 L. F. Buss et al., Science (2020) 10.1126/science.abe9728 N. R. Faria et al., Science 10.1126/science.abh2644 (2021)

New variants : Gamma and Delta

- Occurrence of variants of the initial virus is a normal evolution.

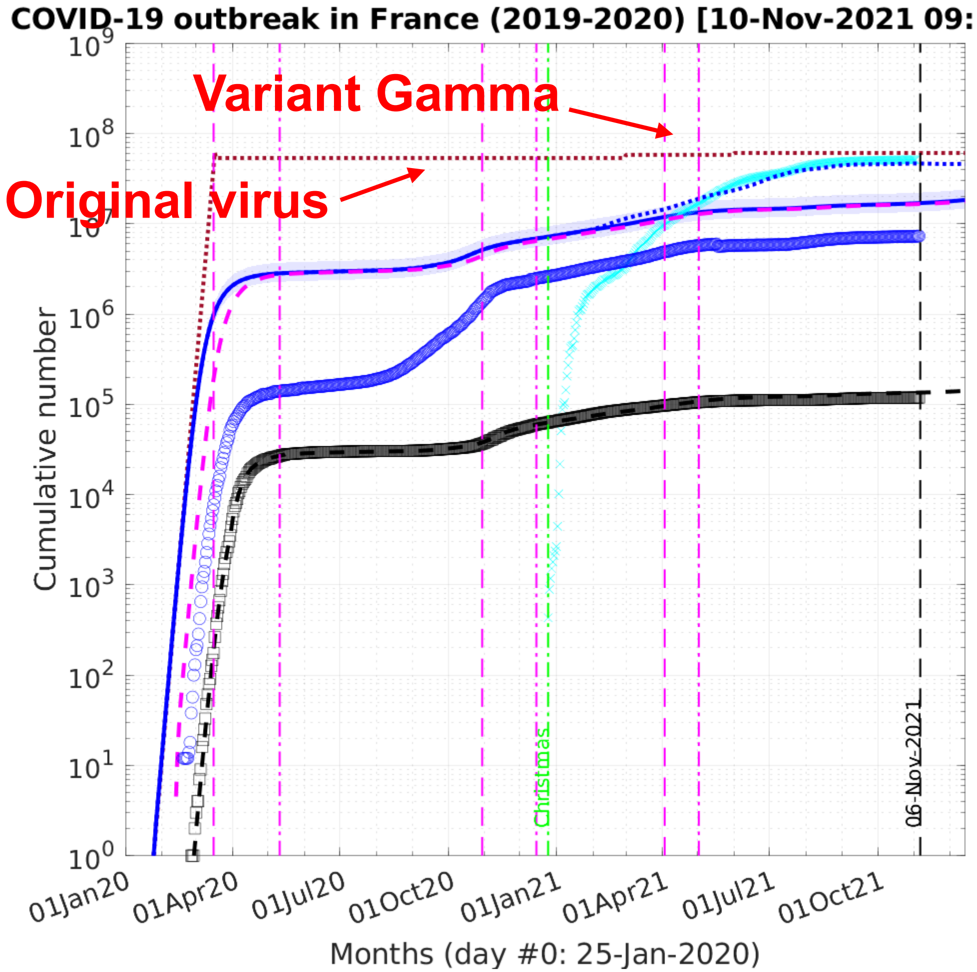
- Variants more contagious (R_0) becomes progressively dominant : Gamma variant (English, March 2020) is 50% more contagious than the original virus, Delta variant (Indian, June 2020) is 50% more contagious than the Gamma variant, so x2.25 more contagious than the original virus.

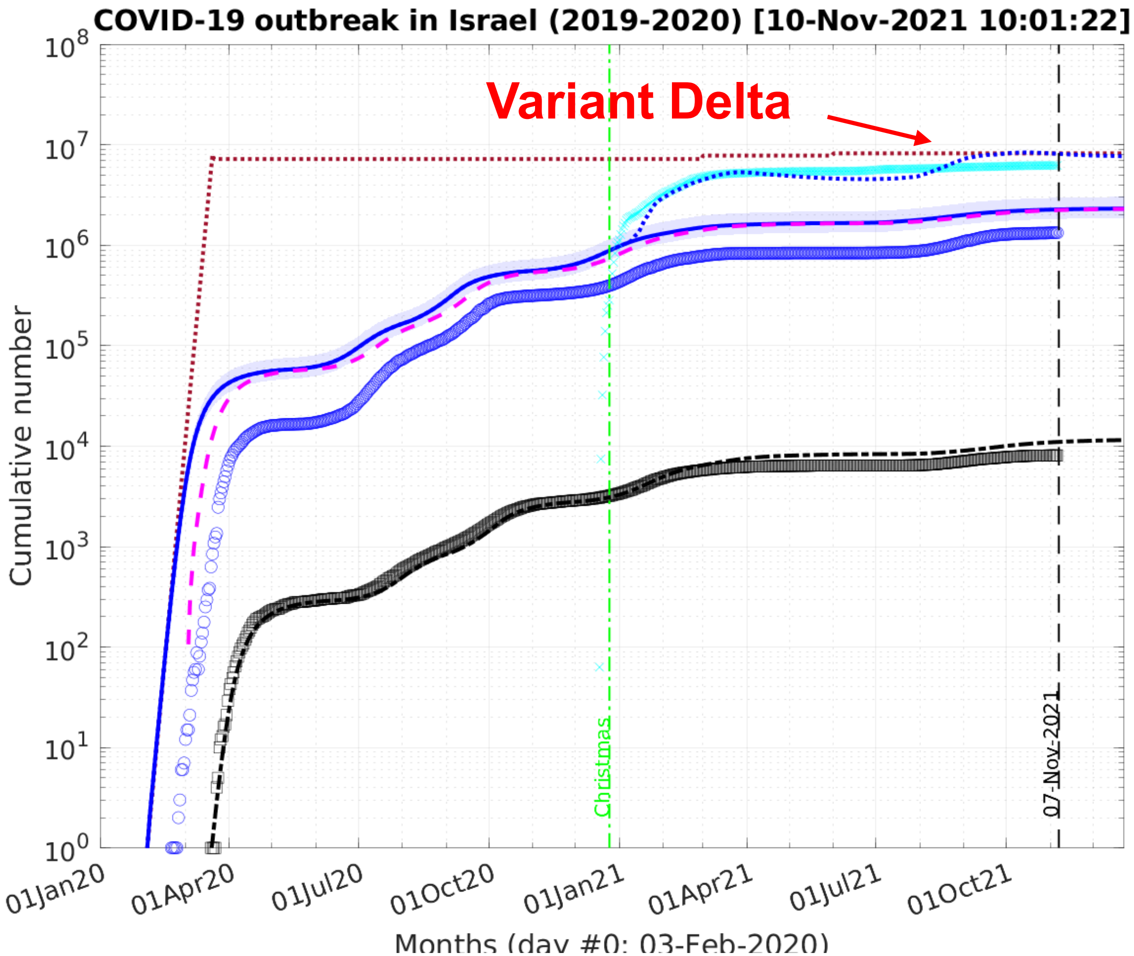
- Despite the large increase of R_0, the theoretical level of herd immunity is weakly affected $\rightarrow f = 1 - 1/R_0$

- For France :

  - Original virus : $R_0 \approx 5$, $f = 80\%$
  - Gamma variant : $R_0 \approx 7.5$, $f = 87\%$
  - Delta variant : $R_0 \approx 11.25$, $f = 91\%$

Gamma and Delta variants : impact on theoretical herd immunity





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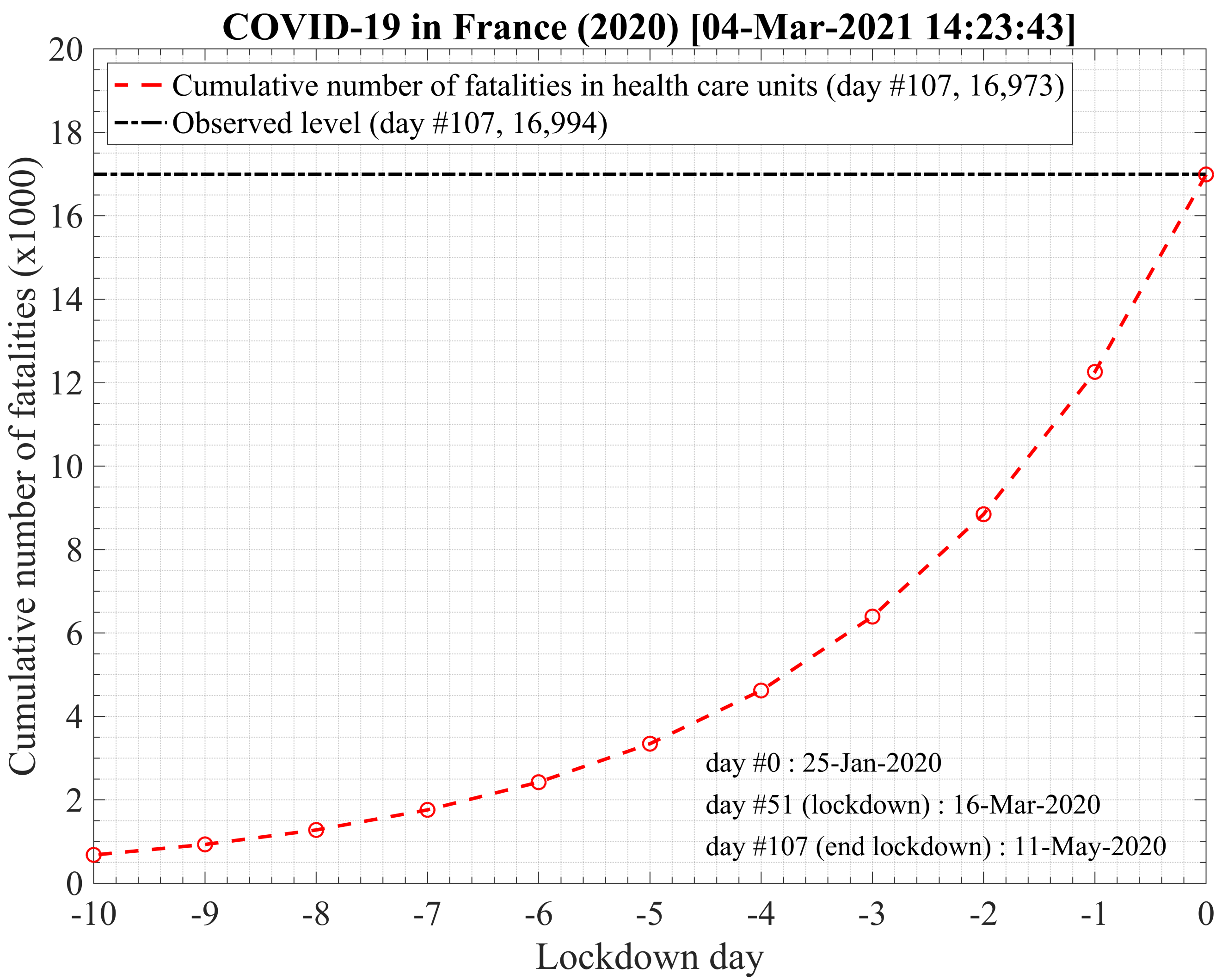
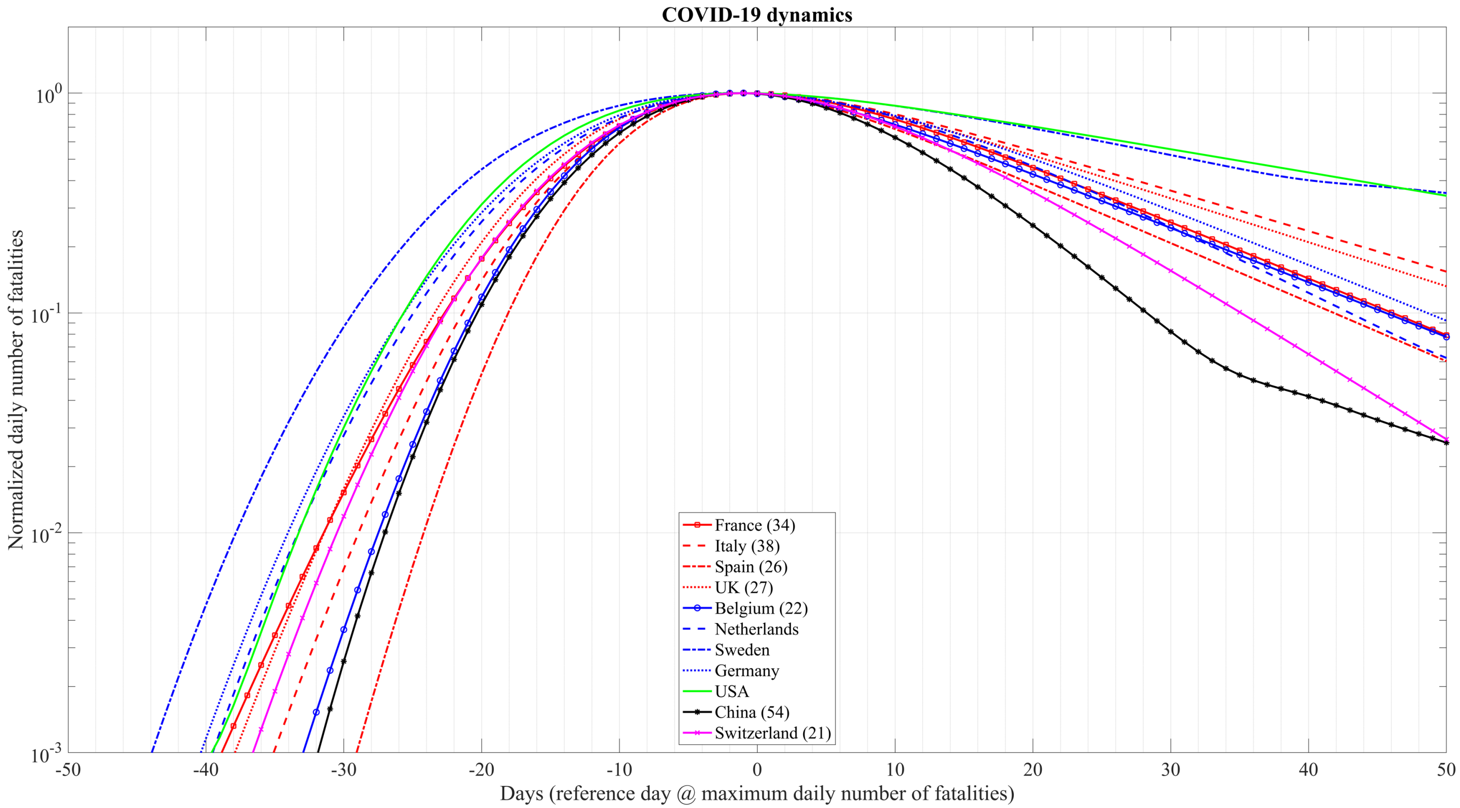
Impact of lockdown date (1st wave, France)



- Simulation parameters unchanged during almost 80 days during the first outbreak wave
- Anticipated lockdown date by shifting τ_{ref}^{J}
- If lockdown would have been decided one week earlier → more than 15,000 lives would have been saved at hospital…
- **With a lockdown four days later, 62904 fatalities would have been observed the 11th of May 2020 instead of 16,989.**

Strict vs soft lockdown (1st wave)



- Strict lockdown in China → best control of the outbreak (rise and decrease)
- *Sweden has the slowest rise and decrease of the outbreak (specific health policy)*
- Most European countries have similar outbreak dynamics whatever their policy against COVID-19 : strict lockdown or soft one : *social distancing* + *some restrictions*.

1st wave lockdown in China, France and Italy

- **Estimated number of daily infections at the first day of the 1st lockdown :**
  - China : 44,800 *[23th of January 2020]*
  - France : 68,500 *[16th of March 2020]*
  - Italy : 87,000 *[9th of March 2020]*
- **Estimated number of daily infections at the last day of the 1st lockdown :**
  - China : 390 *[8th of April 2020] (76 days)*
  - France : 4,600 *[11th of May 2020] (56 days)*
  - Italy : 10,000 *[4th of May 2020] (56 days)*
- **Estimated last day of the 1st lockdown to get Chinese levels of infections**
  - France : 17th of July 2020 *[11th of May 2020] (123 days instead of 56 days)*
  - Italy : 18th of July 2020 *[4th of May 2020] (136 days instead of 56 days)*

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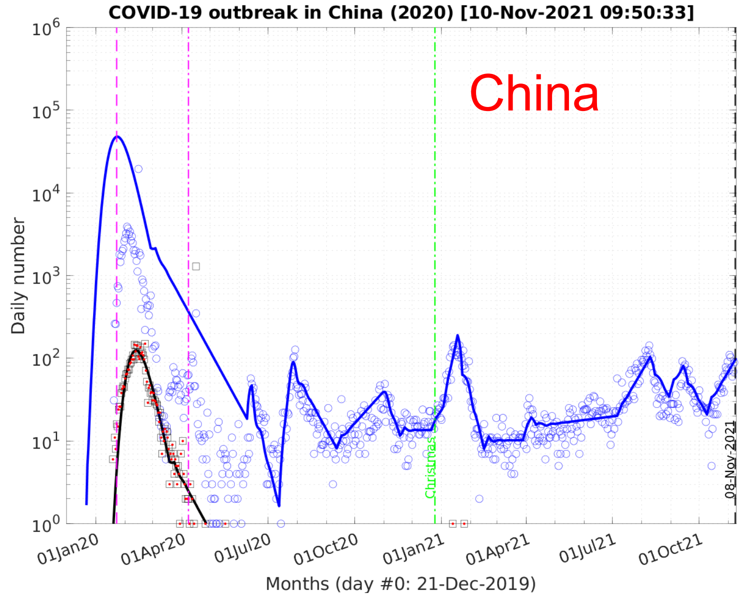
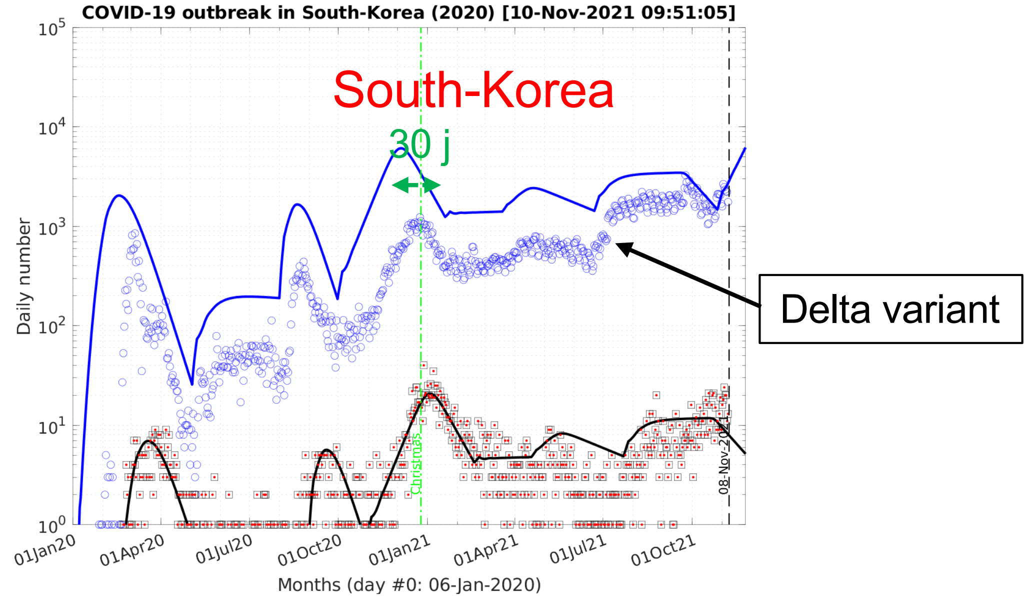
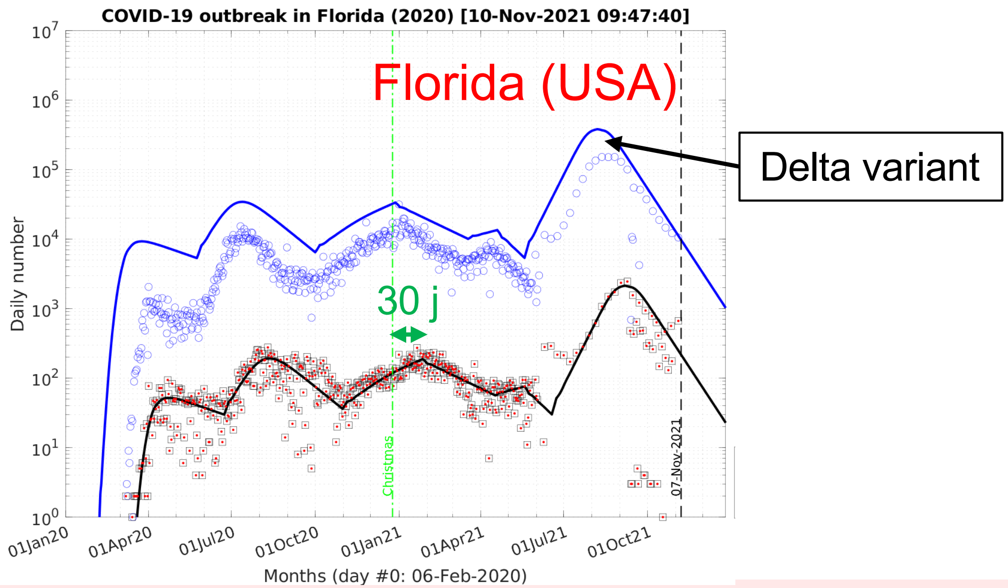
Secondary outbreak waves

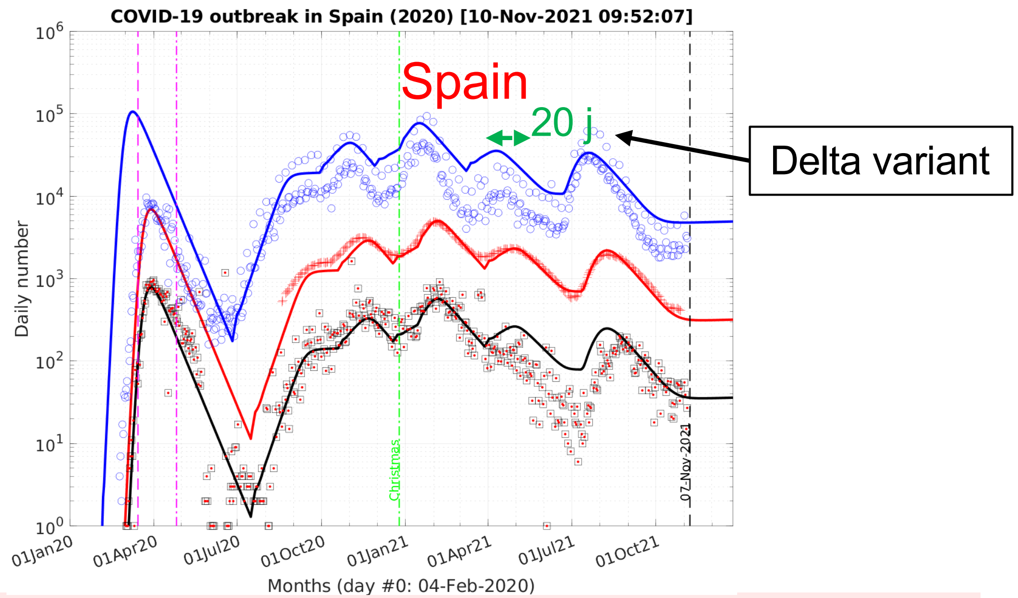
- The occurrence of secondary waves is a major concern for the population.
- The definition of a second wave is related to the proxy that is chosen: change in the derivative of the time series (fatalities) → *minor bursts of contaminations are not considered as signs a second wave if no impact on fatalities.*
- **Secondary waves may be stronger than the primary one if it is triggered by a <u>more contagious variant</u> and not only lack of correct application of social distancing rules.**
- The risk of secondary waves is potentially high when collective level of immunity is far from herd immunity
    - It is amplified by the very high contagiousness of the SARS-CoV-2 ($\langle R_0 \rangle \approx 7.4 \pm 2.3$) or variants
    - It is limited by social restrictions (masks, partial or full lockdown, curfew, …)
- Because of the high contagiousness of the virus or variants, bursts of infections are observed in many countries, indicating the weakness of the situation in most of them that tried to control the first wave outbreak by social restrictions.
- **Virus eradication**, has done by China and New Zeeland, is likely the single option that could allow a fast but local normal life recovery *but not valid for long term*→ *large local confinements (~2 weeks) when even very positive cases are identified followed by a massive campaign of tests with fast results.*

Secondary outbreak waves

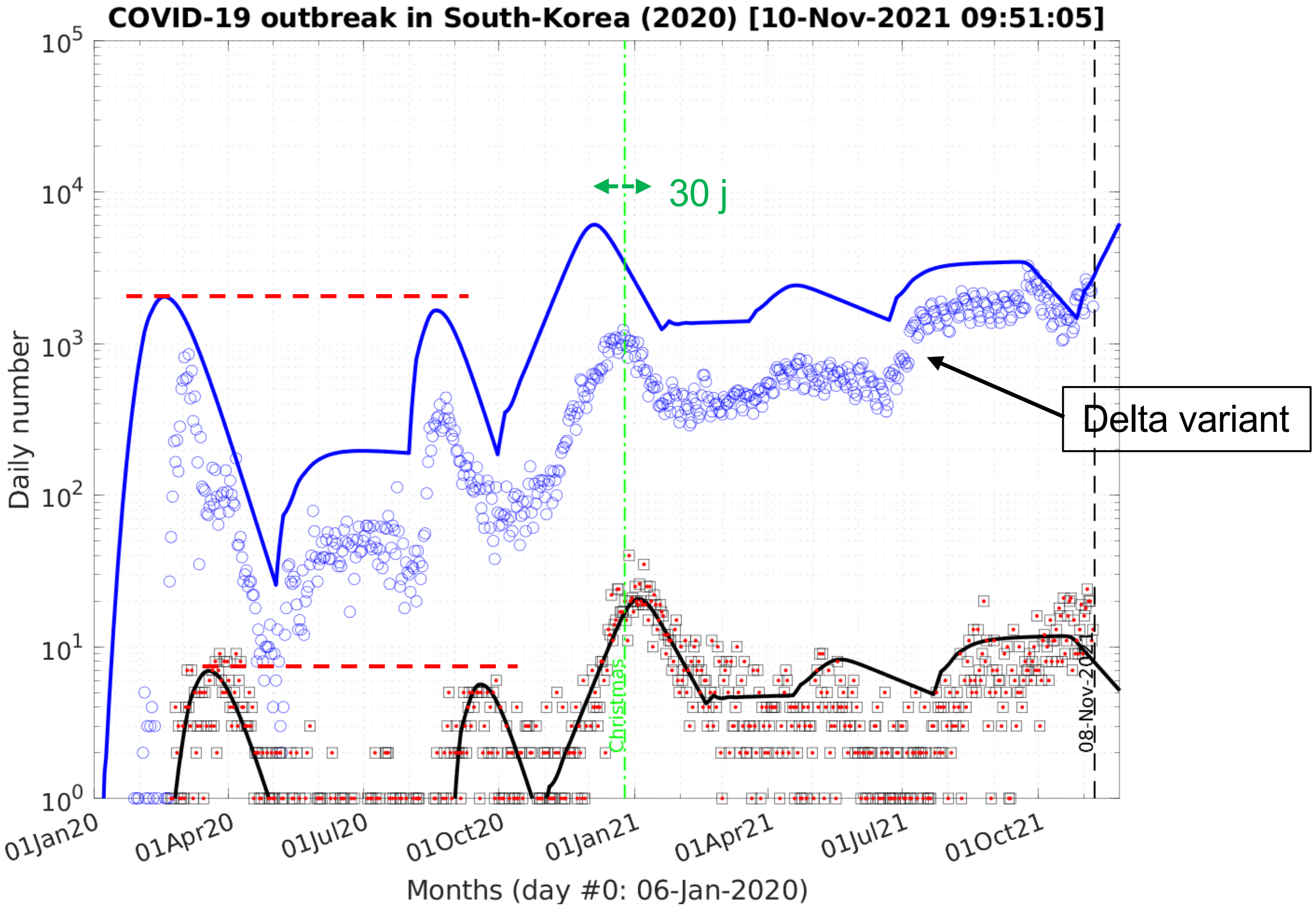






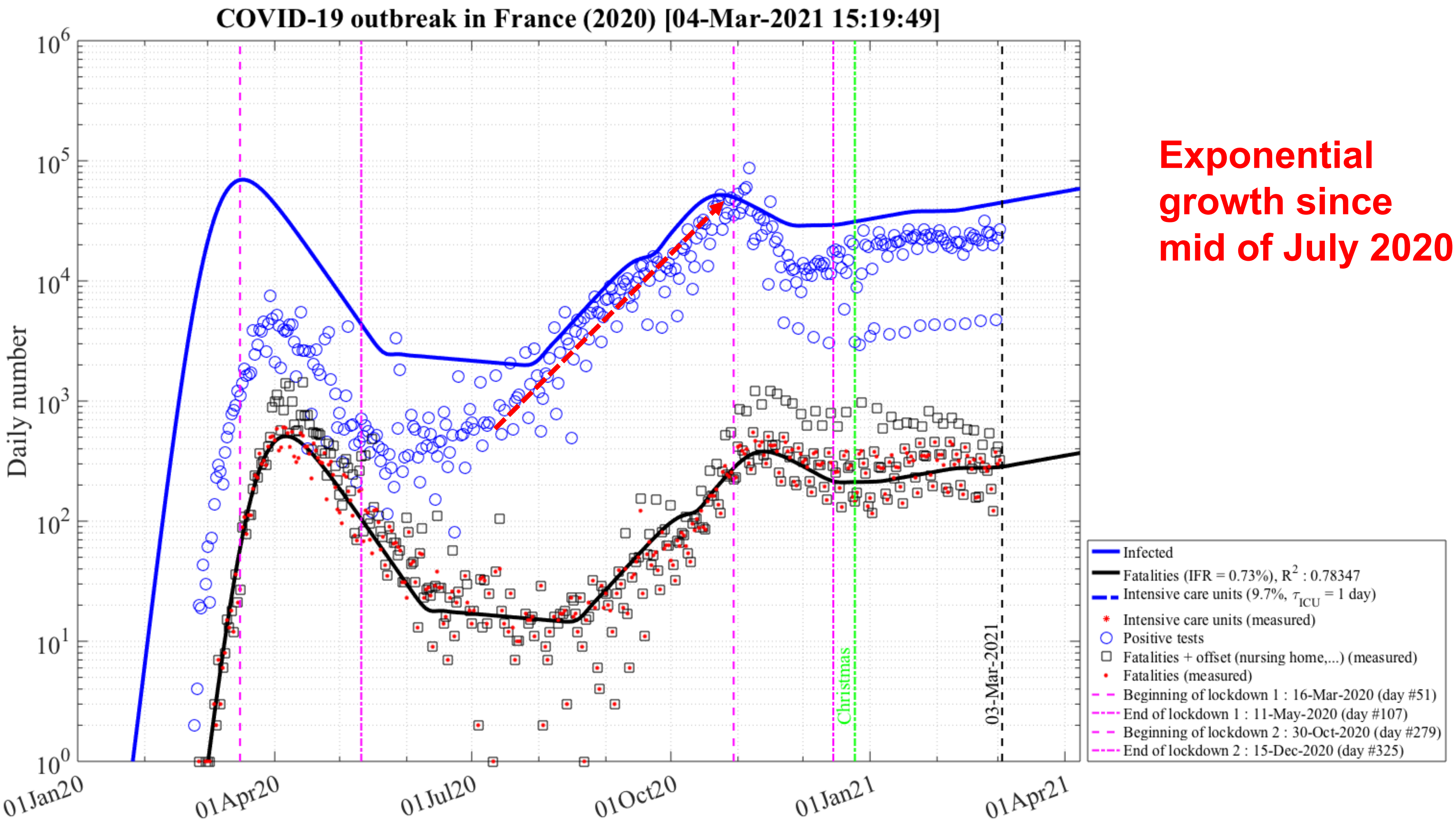


Multipe secondary waves in South-Korea



W separated multiple bursts with similar amplitudes in a country where massive tests have been performed since the early phase of the outbreak → **same impact on fatalities level, nothing has changed in the COVID-19 characteristics since first wave. Consistent with the others waves.**

Second wave in France (no new variant)



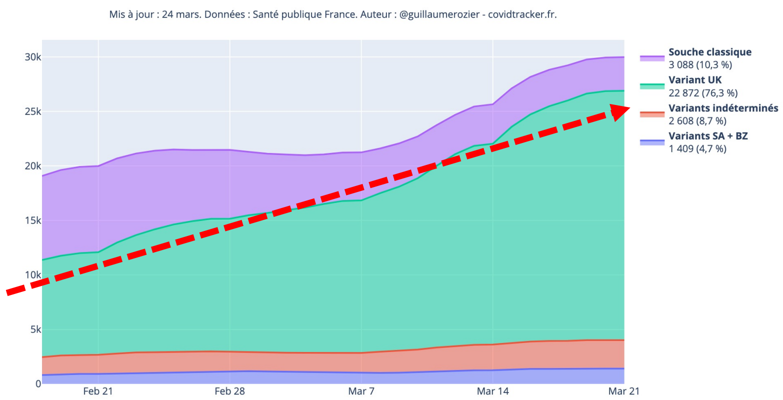
Exponential growth since mid of July 2020

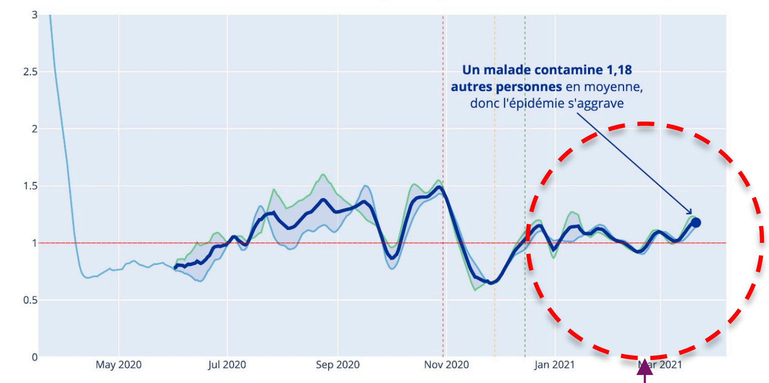
Third wave in France because of the Gamma (english) variant

- Impact of the Gamma variant on the occurrence of a third wave (**8th of February 2021**):
  - +50% more contagious → R_0 is 50% higher
  - Fraction is increasing 50% each week

Week	Fraction (%)	R(t)
#3	3	1.06
#4	4.5	1.04
#5	6.7	1.01
#6	10.1	1.00
#7	15.2	0.99
#8	22.8	0.98
#9	34.2	0.99
#10	51.3	1.02
#11	**76.9**	**1.07**
#12	**115**	**1.16**

covidtracker.fr





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Vaccination and modeling

- Because of the strong age dependence of the IFR, vaccinating old population should reduce rapidly the daily number of fatalities. The impact on the number of people in ICU is unclear (should be reduced too in principle), and weak on infections since there is no strong age dependence of infections.

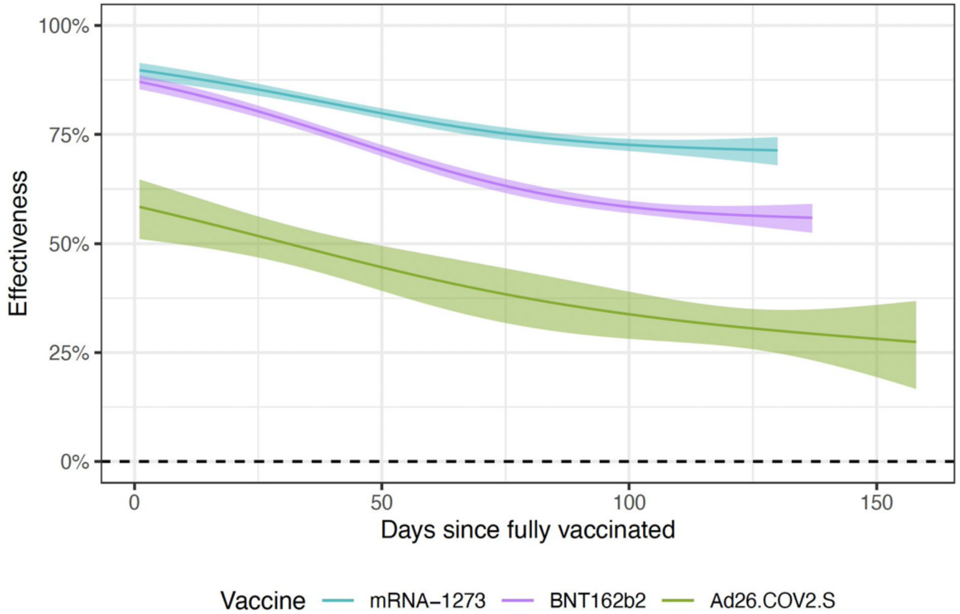
- People from the susceptible compartment (S) are supposed to be immunized N days after the first injection, whatever the type of vaccine. By default, N ≈ 40 *(25 days between the first and second injections if any, and full protection 15 days after the second one)*. It may be larger if time between two injections is enlarged. The cumulative number of immunized people is the sum of those which have recovered naturally after being infected and those which have been vaccinated with the lag of N days. **An important is the decrease of immunity with time once vaccinated.**

- Vaccination started beginning of 2021 in most countries, but Israel was the earliest to start the process with Pfizer-BioNTech® ARNm vaccine: 55% of the population had a first injection, 40% has two by March 2021. *The combination of vaccination, reduction of international travels, strong lockdown which lower the mean infection rate and vaccination makes and small population size makes it the best case to identify the impact of vaccine at a country scale.*

Time decrease of the immunity provided by vaccination

- Maximum immunity obtained by vaccination is obtained about 2 weeks after the second injection whatever the type of vaccine.

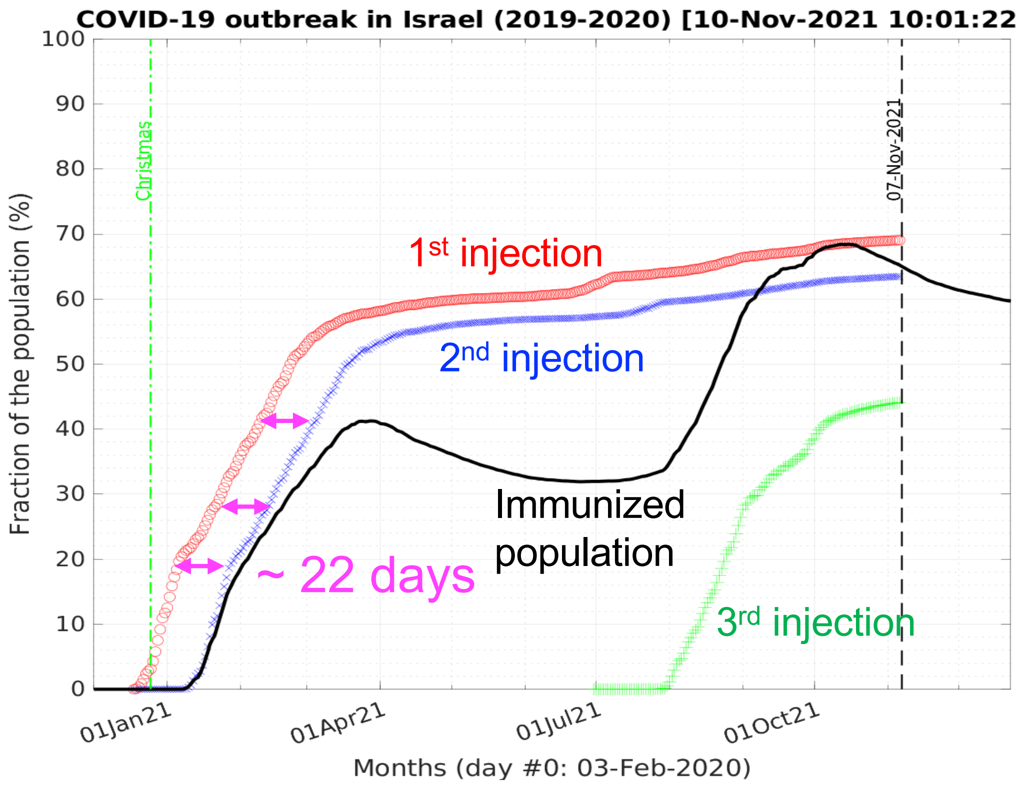
- Immunity decreases progressively with time since specific antibodies against SARS-CoV-2 are vanishing → this leads to a reduction of the protection against severe form of the COVID-19, such that people with the full scheme of vaccination may become severely sick again.



- ***This effect is modeled to fit observations in the calculation of the level of immunity of the population provided by vaccination.***

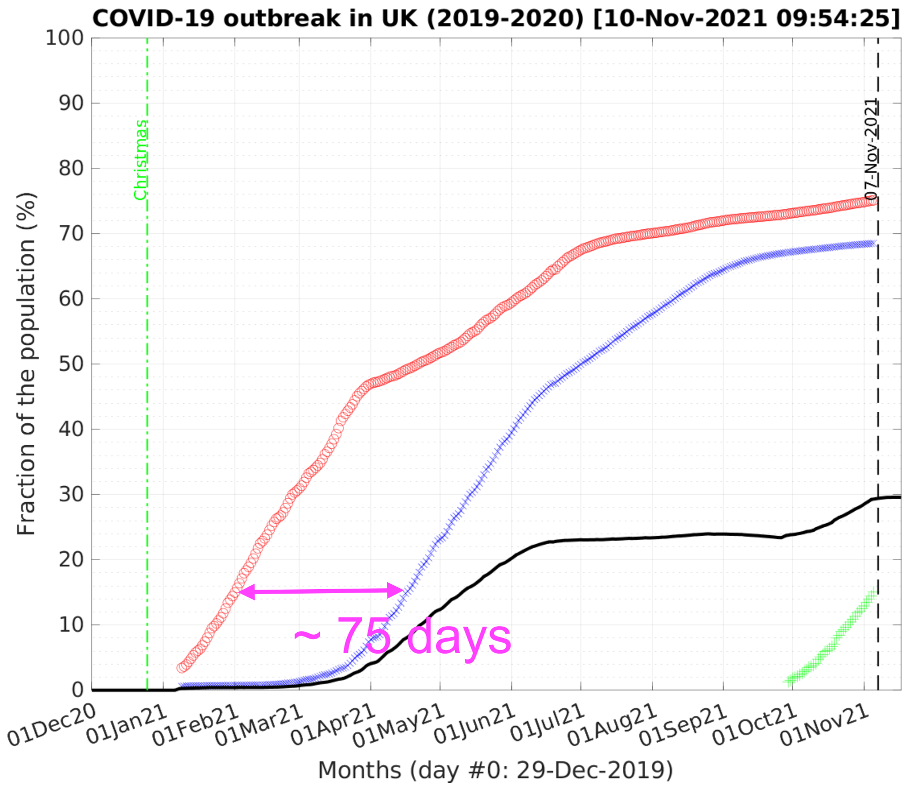
Vaccination policy (Israel and United-Kingdom)

Israel



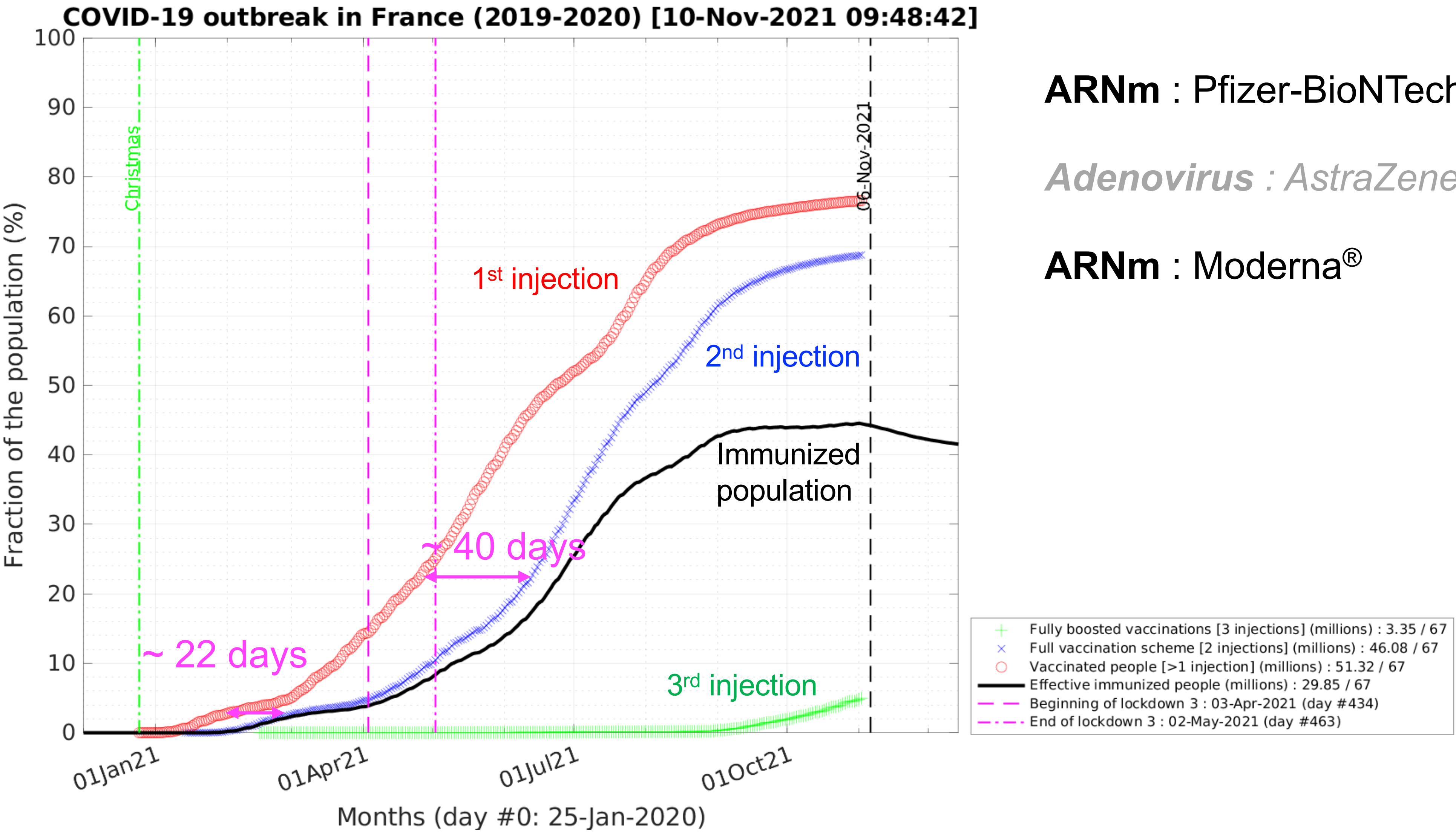
ARNm : Pfizer-BioNTech®

United-Kingdom



Adenovirus : AstraZeneca®

Vaccination policy in France



ARNm : Pfizer-BioNTech®

***Adenovirus** : AstraZeneca®*

ARNm : Moderna®

Vaccination policy

Decreasing age of vaccinated people

[100-85] →[85-75] → [75-65] → [65-50] → [50-30] → [30-20] → [20-0]

Individual benefit

Collective benefit

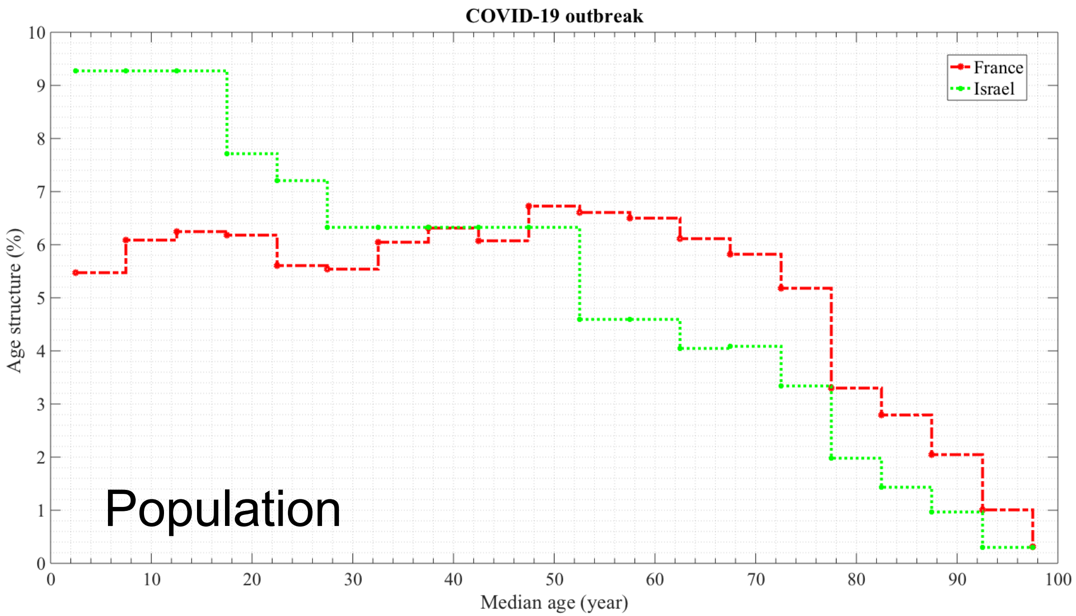
Collective benefit

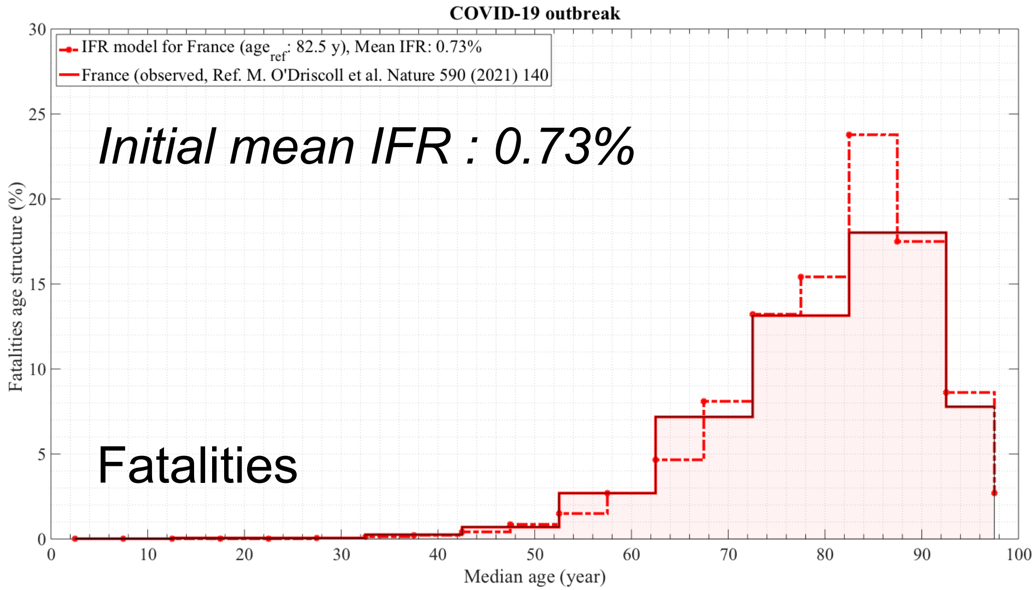
Individual benefit

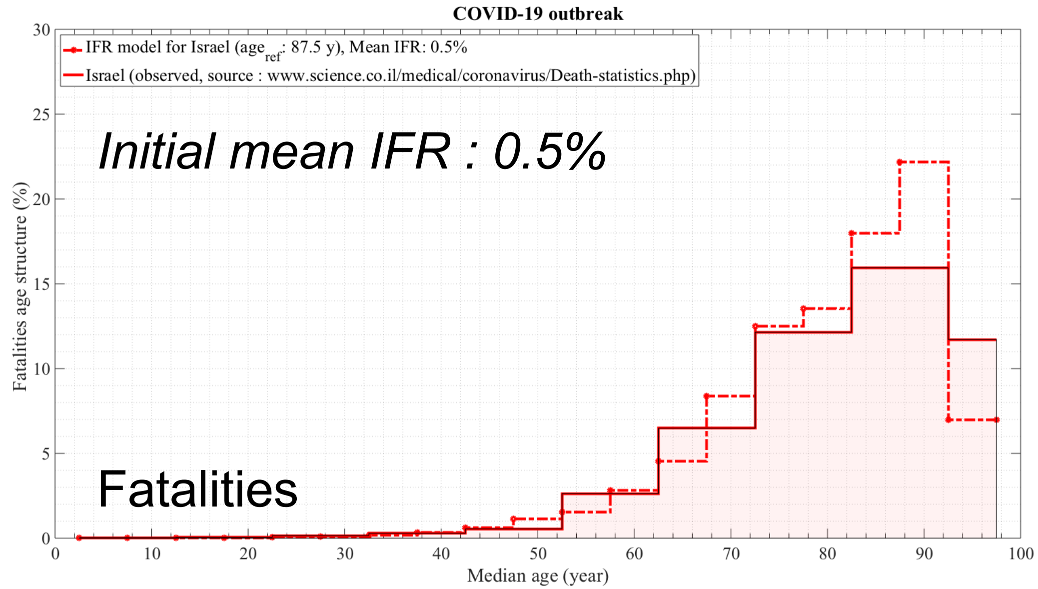
Time

Fast reduction of mean IFR in the initial phase of vaccination because of the strong age dependence of the IFR and the limited number of elderly at fixed vaccination rate.

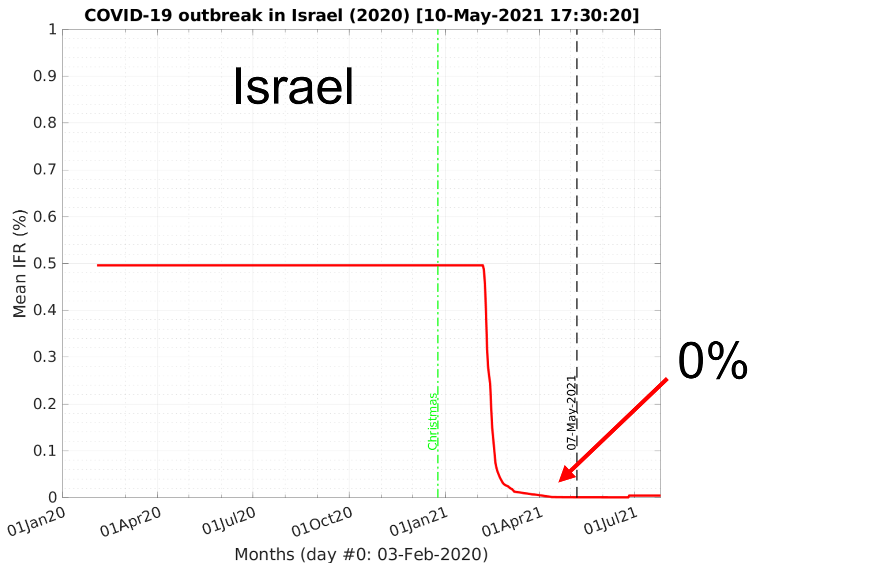
Population and fatalities age structures (France and Israel)

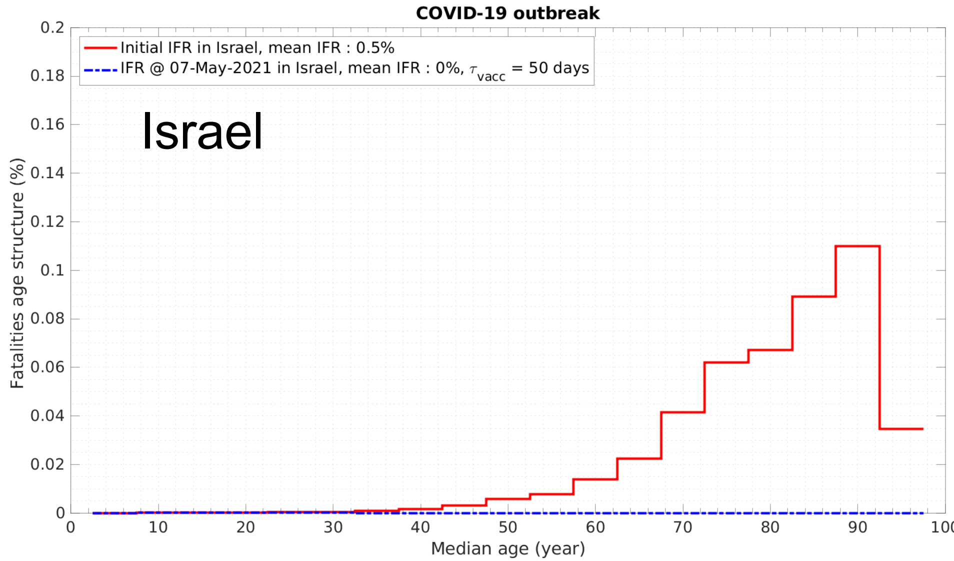


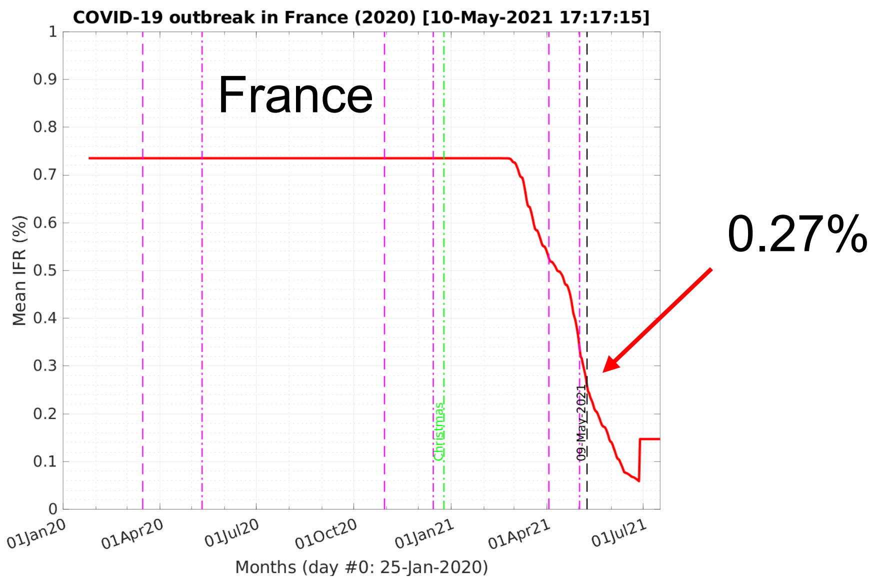


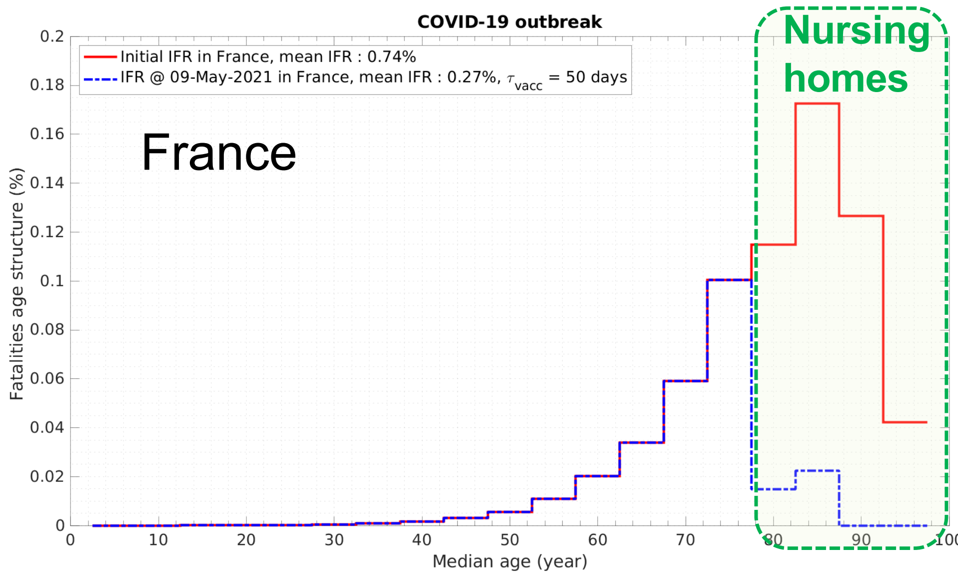


Mean IFR and vaccination for France and Israel (21th March 2021)



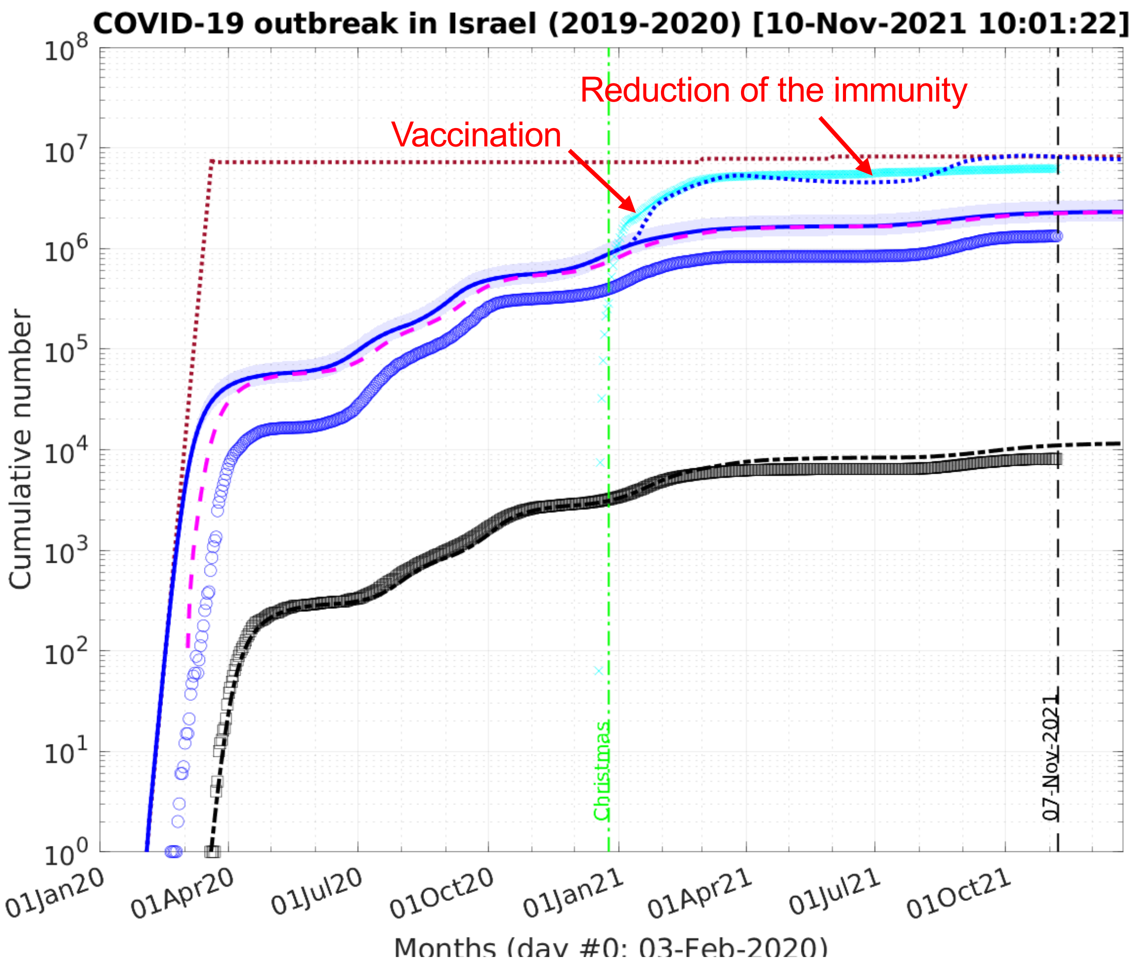


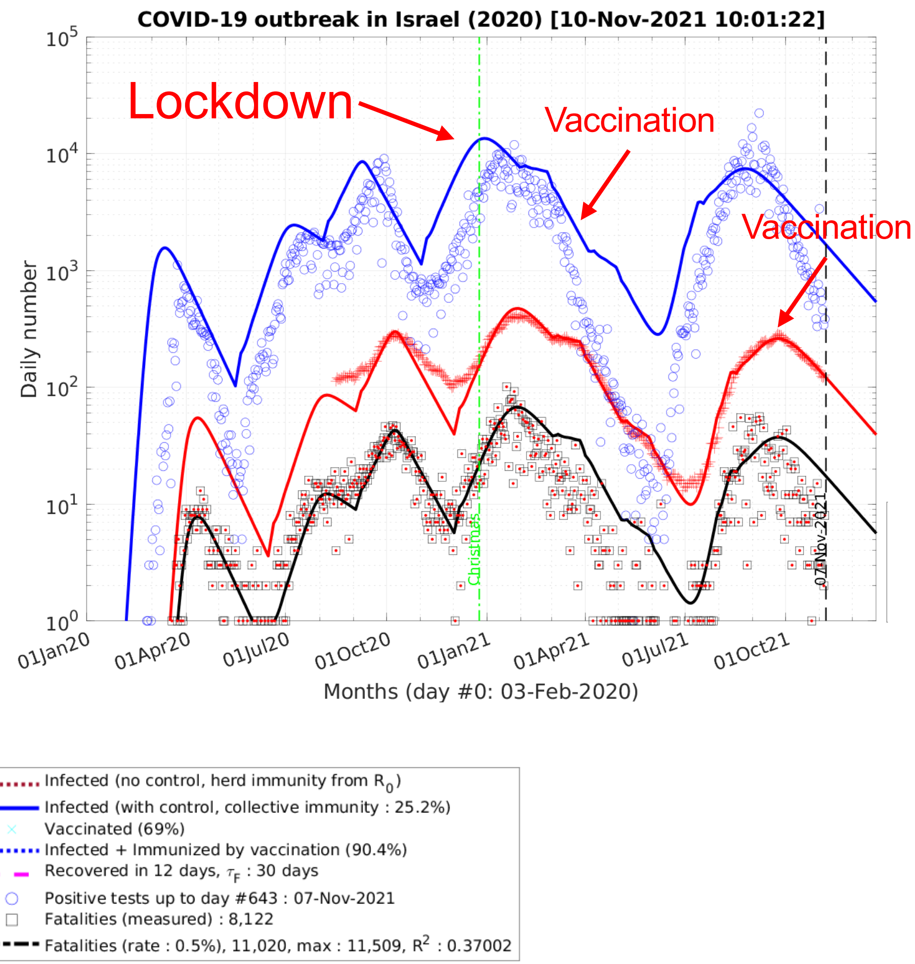




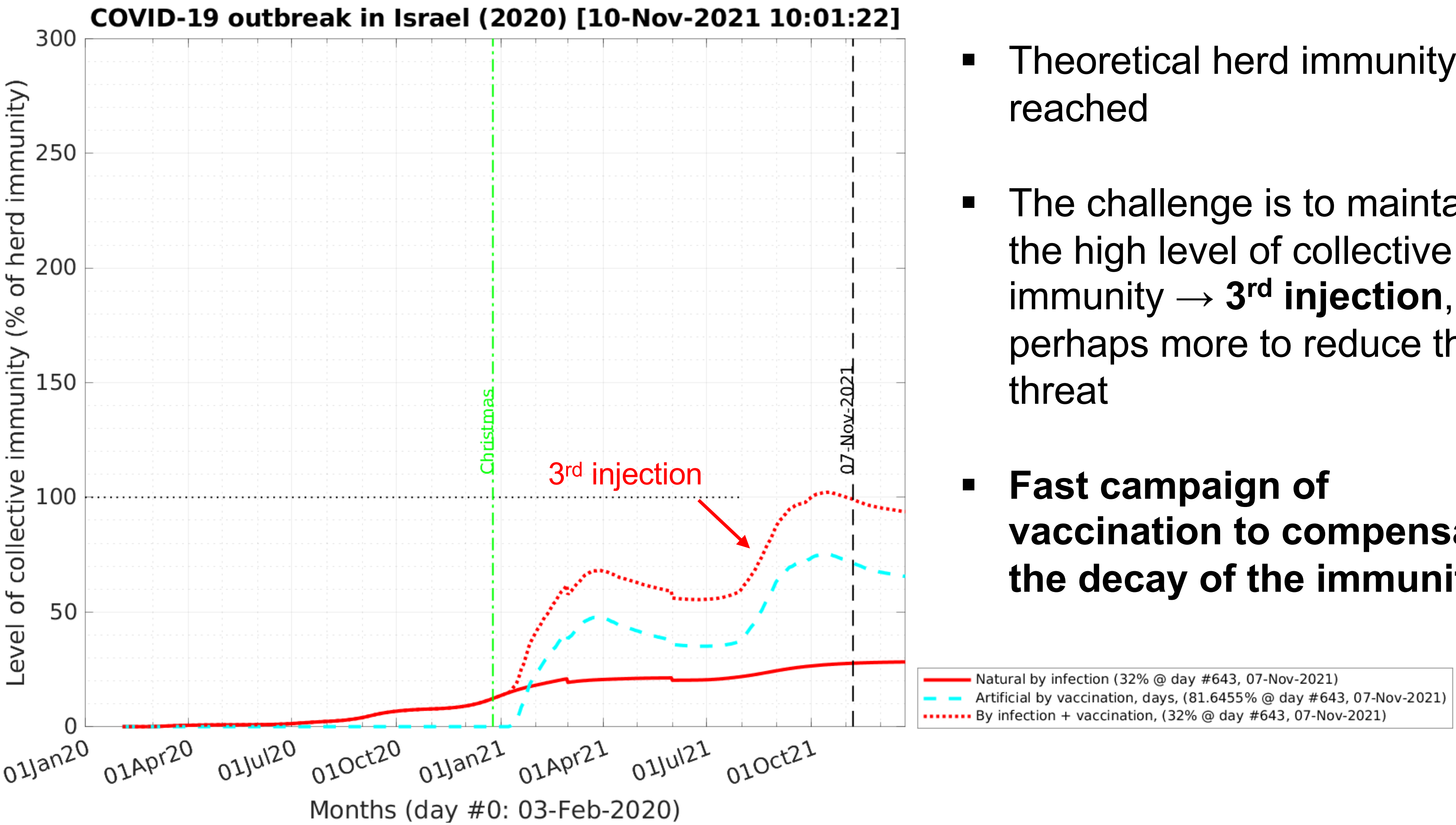
Monitoring vaccine efficiency : case of Israel (Pfizer-BioNTech vaccine)

Large global impact of vaccination by mid-May, but the occurrence of the Delta variant more contagious distanced the country from the theoretical herd immunity, while immunity by vaccination was decreasing → new strong wave.





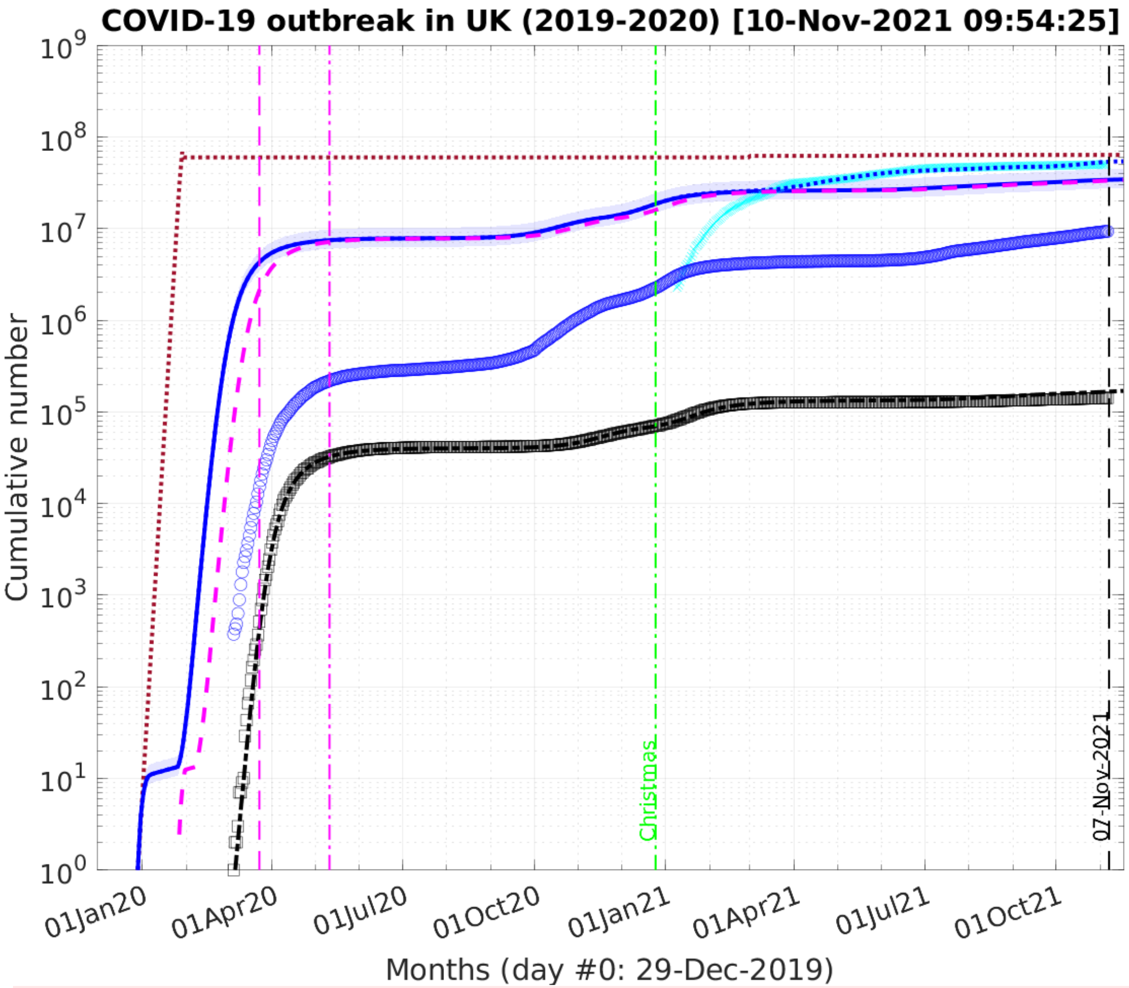
Monitoring vaccine efficiency : case of Israel (Pfizer-BioNTech vaccine)

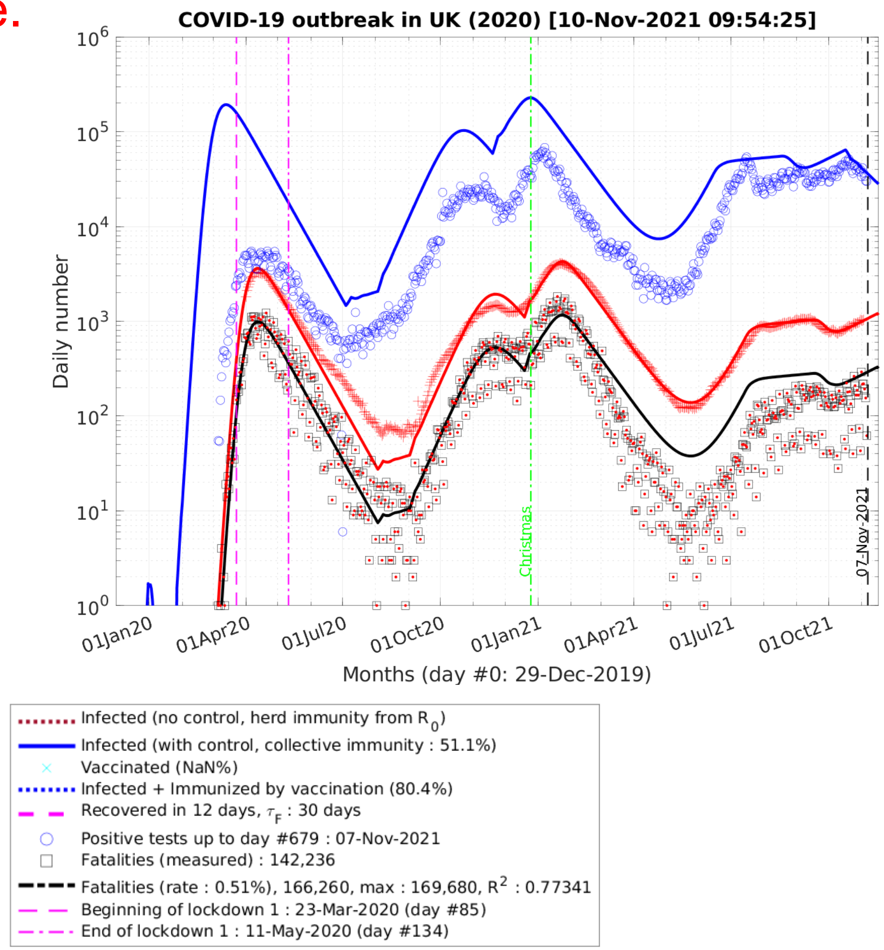


- Theoretical herd immunity is reached
- The challenge is to maintain the high level of collective immunity → **3rd injection**, perhaps more to reduce the threat
- **Fast campaign of vaccination to compensate the decay of the immunity**

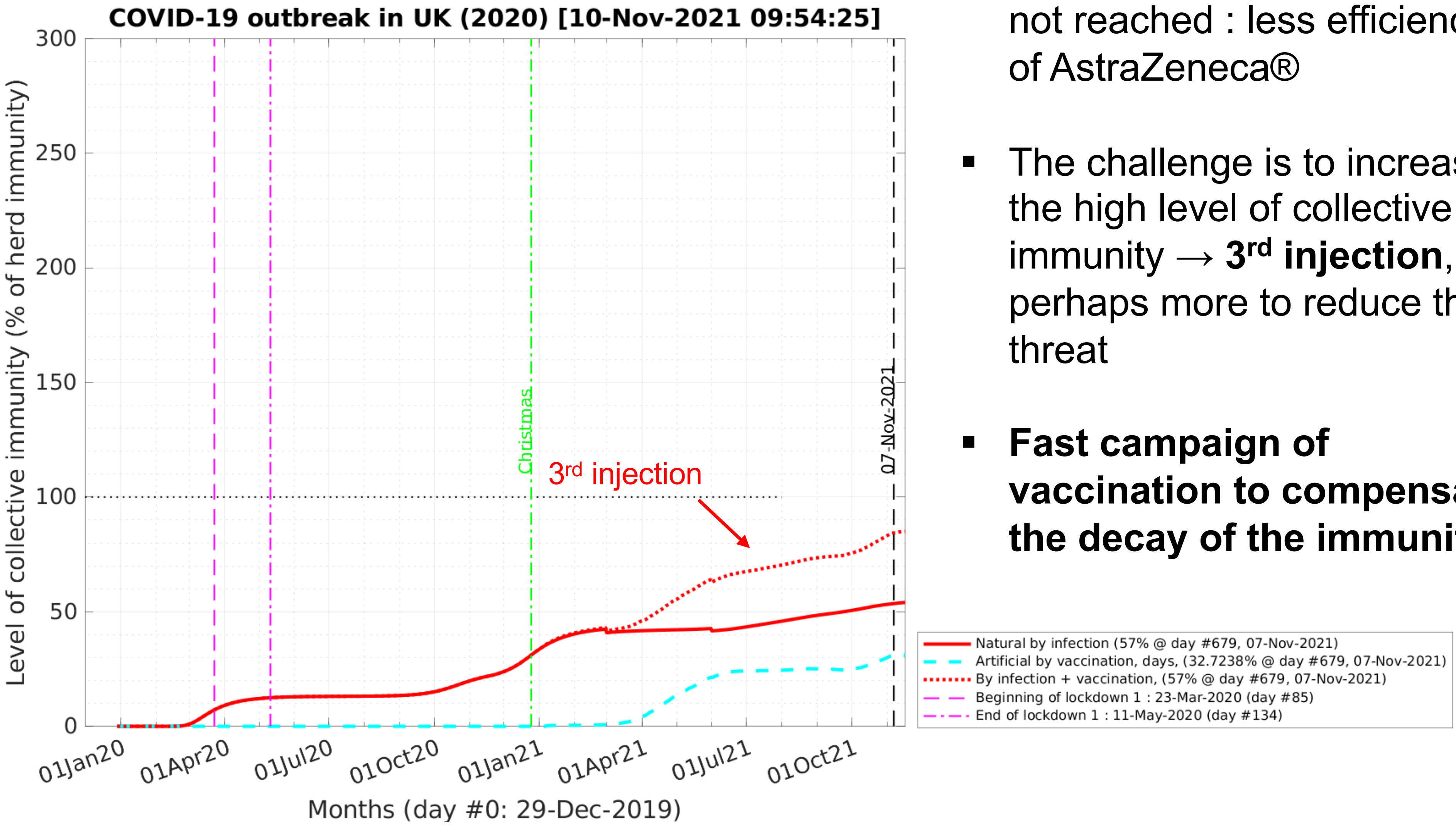
Monitoring vaccine efficiency : case of United-Kingdom (AstraZeneca vaccine)

Large global impact of vaccination by mid-May, but the occurrence of the Delta variant more contagious distanced the country from the theoretical herd immunity, while immunity by vaccination was becoming stagnant → new wave.





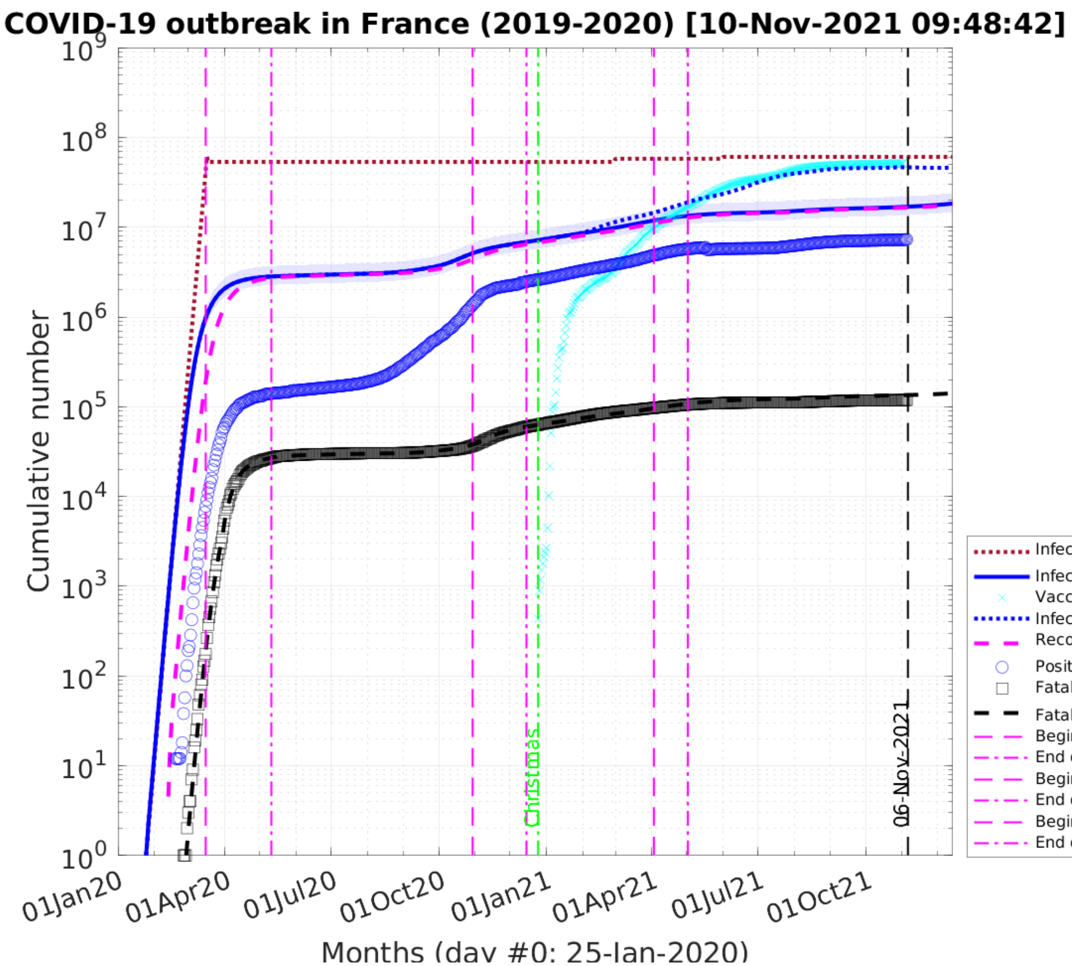
Monitoring vaccine efficiency : case of United-Kingdom (AstraZeneca vaccine)

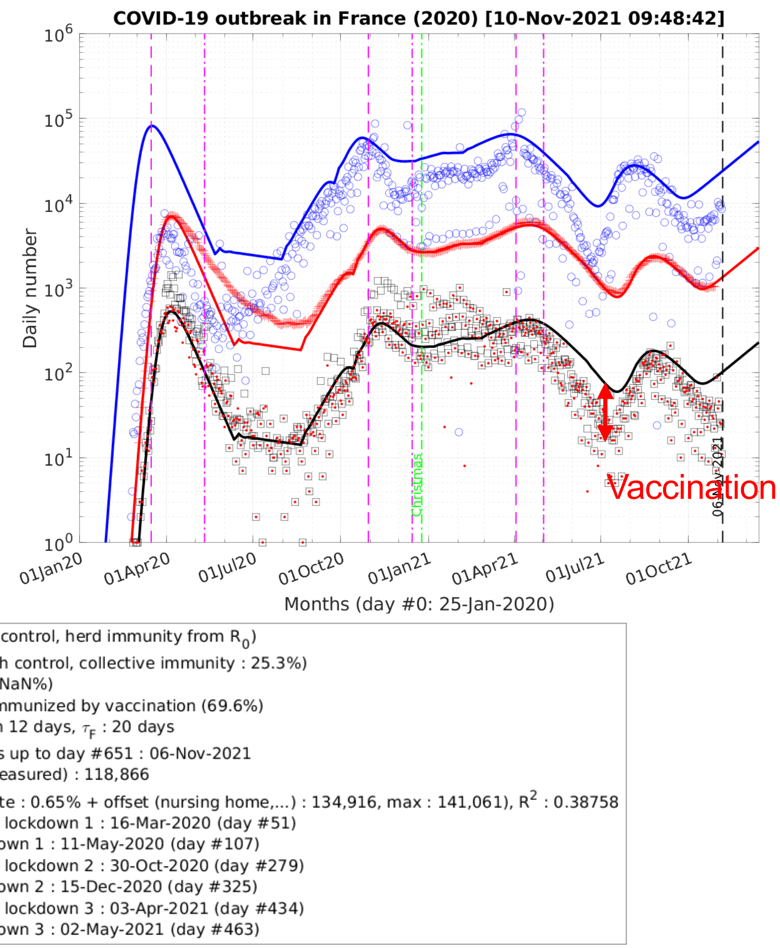


- Theoretical herd immunity is not reached : less efficiency of AstraZeneca®
- The challenge is to increase the high level of collective immunity → **3rd injection**, perhaps more to reduce the threat
- **Fast campaign of vaccination to compensate the decay of the immunity**

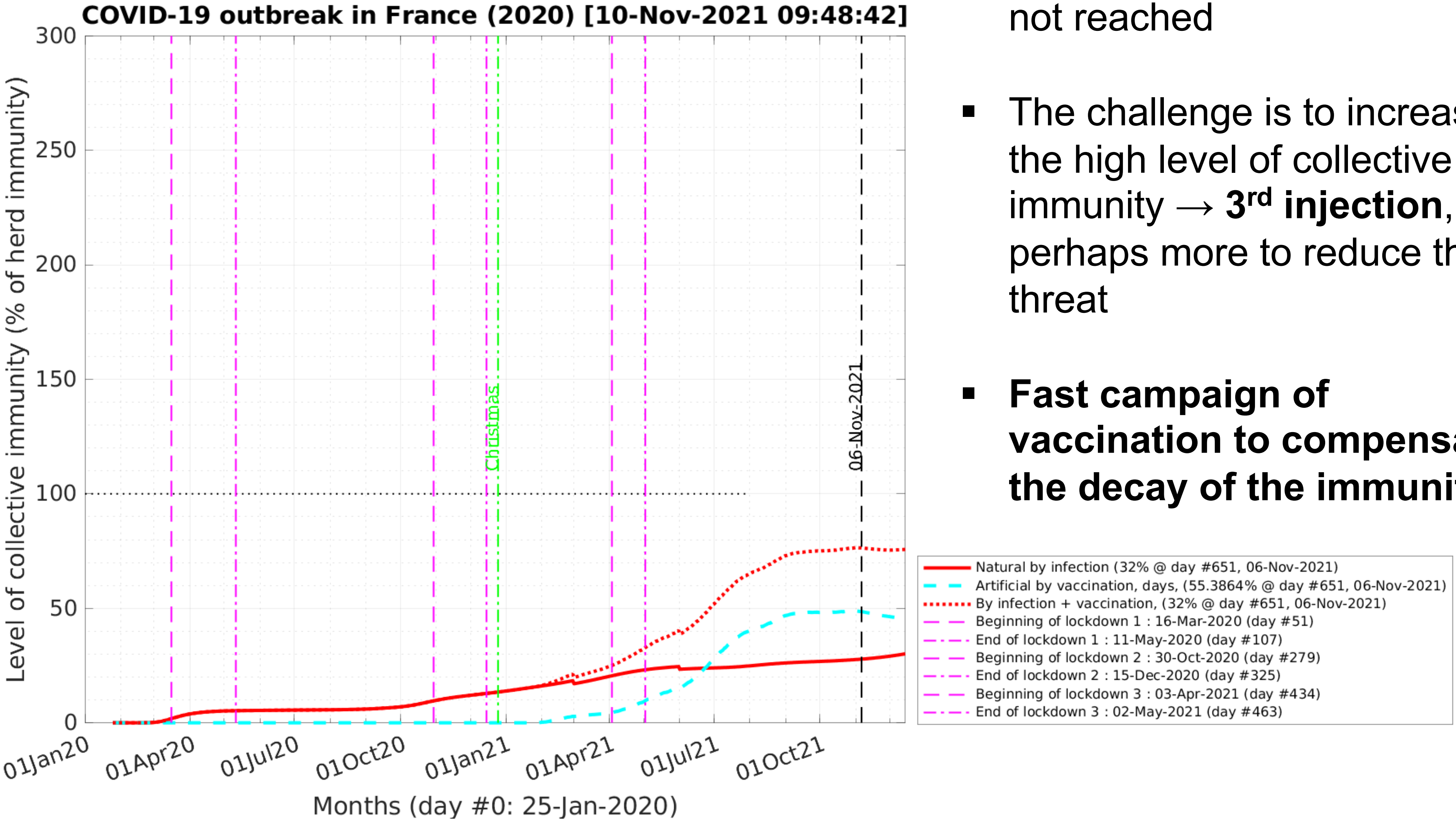
Monitoring vaccine efficiency : case of France (Pfizer-BioNTech, Moderna, AstraZeneca vaccines)

Significant impact of vaccination by mid-May, but the occurrence of the Delta variant more contagious distanced the country from the theoretical herd immunity, while immunity by vaccination was becoming stagnant → new waves.





Monitoring vaccine efficiency : case of France
(Pfizer-BioNtech, Moderna and AstraZeneca vaccines)

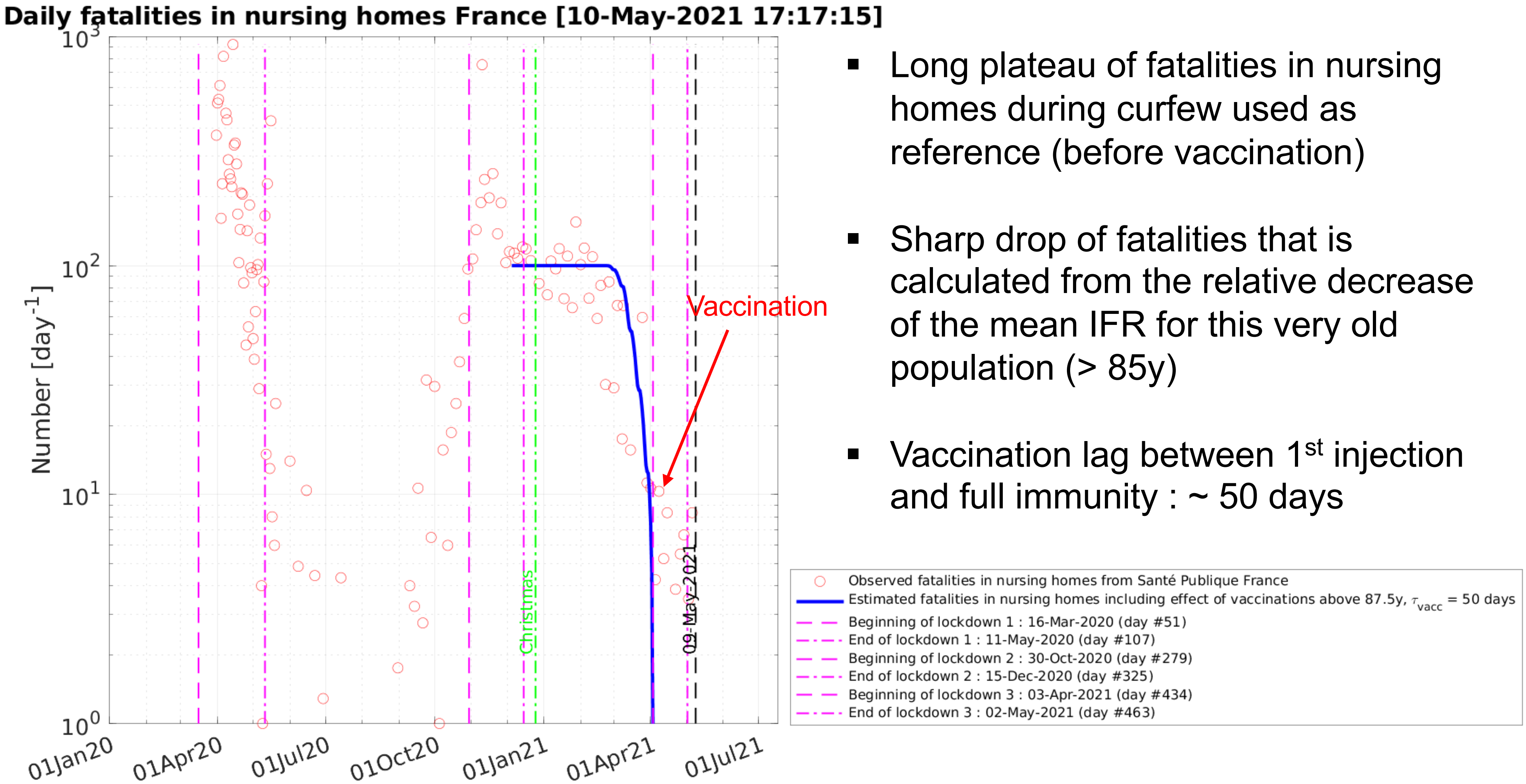


- Theoretical herd immunity is not reached

- The challenge is to increase the high level of collective immunity → **3rd injection**, perhaps more to reduce the threat

- **Fast campaign of vaccination to compensate the decay of the immunity**

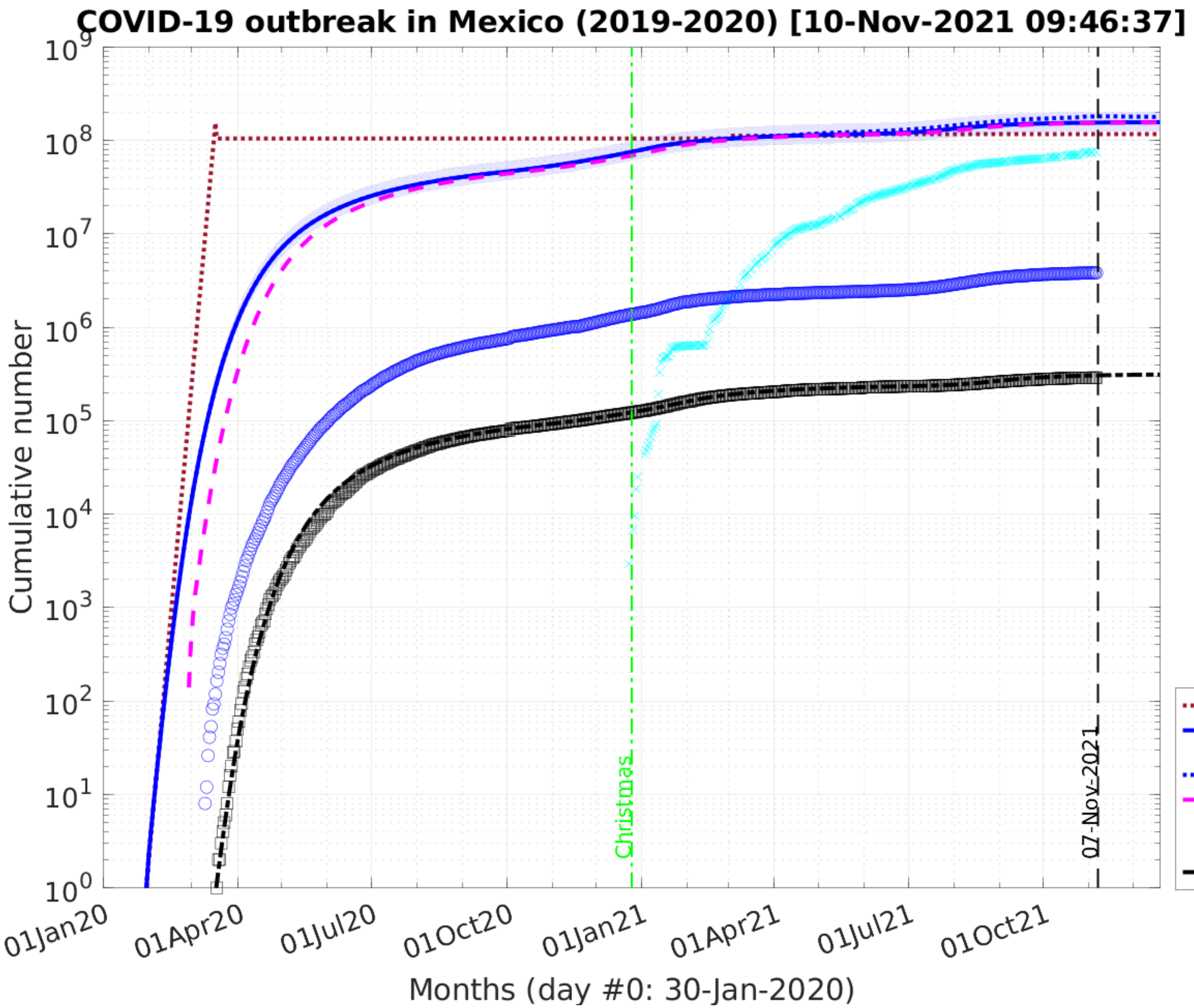
Monitoring vaccine efficiency in French nursing homes

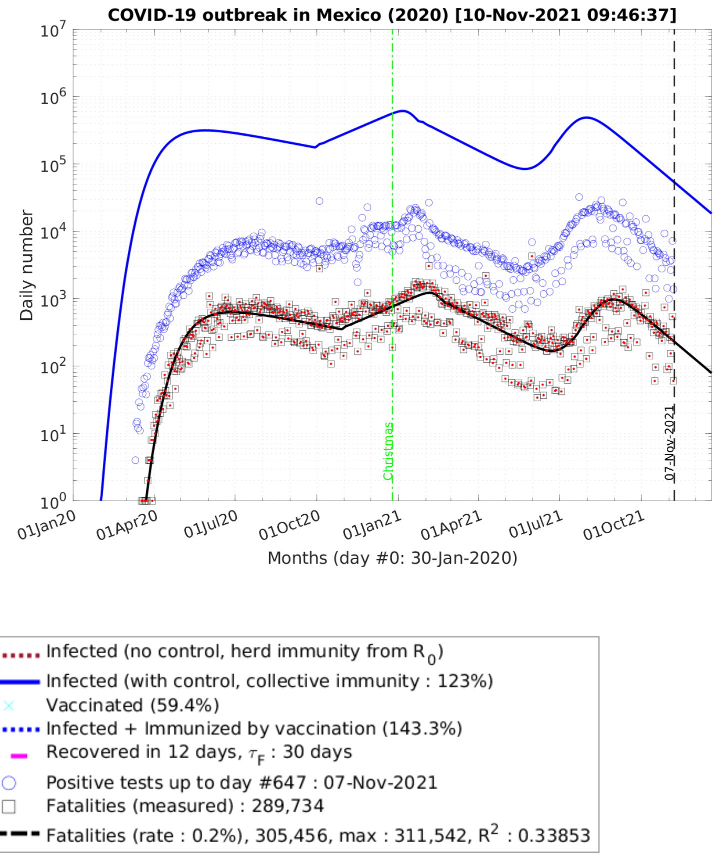


- Long plateau of fatalities in nursing homes during curfew used as reference (before vaccination)
- Sharp drop of fatalities that is calculated from the relative decrease of the mean IFR for this very old population (> 85y)
- Vaccination lag between 1st injection and full immunity : ~ 50 days

Vaccine vs natural herd immunity (Mexico)

- No roll-over in absence of variant
- Effect of vaccination is marginal
- IFR may be underestimated





Impact of vaccination on the COVID-19 pandemic

- **The vaccination policy (elderly first) leads to a progressive decreasing of the mean age of fatalities. Very effective in nursing homes in France (very old people).**

- *Modeling issues : when all the population will be immunized, the mean IFR is almost zero → **using the fatalities time series to estimate the actual number of infections is no more possible**. Replace fatalities time series by people in ICU time series.*

- The expected reduction of the number of people in ICU by vaccination seems to arise much more slowly.

- The decay of the immunity provided by vaccination combined with the occurrence of much more contagious variants led to distance countries from the theoretical herd immunity, leading to new waves, that may be quite strong (Israel, Poland, United-Kingdom).

- **The decay with time of the immunity provided by vaccination force authorities to perform an aggressive vaccination campaign (especially for the 3rd injection), otherwise, immunity will remain stagnant.**

Have we answered to the initial questions ?

- Could we describe the COVID-19 pandemic with a minimum set of assumptions ? Yes and worldwide with a SIR model. COVID-19 simulation parameters stay constant in 2020 (very few progresses to reduce severe forms of the disease)

- Could we have robust predictions ? Yes on short term if the outbreak is decreasing, *not in the increasing phase (the most important) because of noisy data. Statement valid whatever the type of model (ill-posed problem) → raise the question of political communication…*

- Can we have a consistent picture of the pandemic worldwide ? Yes, the original virus is very contagious, with a $\langle R_0 \rangle = 7.5 \pm 2.3$ and the variants are much more contagious.

- Where is the major source of uncertainty in the modeling ? Mean IFR calculation and therefore the expected level of collective immunity. But some places have likely reached the theoretical herd immunity like Manaus. Consistent with serology. Countries far from it exhibits many epidemic bursts or secondary waves.

- Can we have a consistent view between R_0 and herd immunity ? Yes is no new aggressive variant (reinfection) is emerging. Vaccination confirms the consistent picture of the modeling but the challenge is to maintain the global immunity of the population (+injections)

Conclusions

- An over-simplified SIR model with a minimalist approach is able to describe quite accurately the COVID-19 pandemic worldwide.

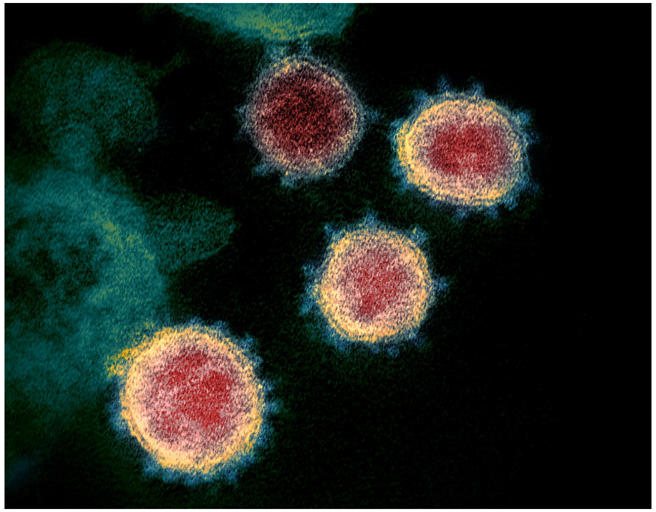
- The determination of the mean IFR is certainly the most difficult exercise. The approach considering the case of Diamond-Princess cruise liner, the distribution in age of the fatalities and assuming a distribution in age of the infected population similar to the whole population gives rather consistent results with observations (low mortality in Africa, consistency with some serology measurements in Brazil, Germany and India). *The IFR is likely not a full exponential at all ages, depending upon the countries. The age of reference where it becomes flat is roughly the age at which the fraction of the population is less than 4%.*

- **$\langle R_0 \rangle = 7.5 \pm 2.3$** for the original virus with a mean recovering time of 12 days. Consistent with some statistical studies. R(t) is close to the Cori's method. Lowering recovering time down to 6 days gives inconsistent amplitude of R(t). The value of R_0 is consistent with estimated herd immunity.

- The fraction of the infected population in ICU is **5-10%**. Constant in time during a year whatever the country.

- Clear difference in outbreak dynamics between very strong lockdown (China) and no-lockdown (Sweden). However, most European countries have similar dynamics despite different lockdown policies.

COVID-19 summary



Coronavirus SARS-CoV-2 (Wikipedia)

- **Mean recovery time $\tau_R \approx 12$ days.**
- **Mean infection to fatality rate (IFR) < 1.0% for all countries. World mean IFR = 0.2%. Strongly dependent of age structure.**
- **Averaged basic reproduction number $\langle R_0 \rangle \approx 7.5 \pm 2.3$ (original virus)**
- **Level of herd immunity $f^\infty = 1 - 1/\langle R_0 \rangle > 80\%$. Likely reached in Manaus before the variant P1 in January 2021.**
- **Fraction in intensive care units : $f_{ICU} \sim 5\text{-}10\%$**
- **Fatalities arise about ~20-30 days after infections.**
- **Most of the infected population has no symptom but may contribute to spread the virus.**
- **COVID-19 characteristics are almost unchanged during 2020-2021.**
- **A simplified SIR model catches well most of the characteristics of the outbreak dynamics in all studied countries, states and cities.**
- **Maintaining collective immunity close to the theoretical level by vaccination is a major challenge, thanks to the decay of the antibodies**

This work is dedicated in memory of my mother who passed away in January 2020.

She told me several times about the dramatic impact of the Spanish flu (H1N1) on my family in 1918-1920 and she, herself, was hit very hard by the Asian flu (H2N2) in 1957.

Major outbreaks are fully part of human history. We must never forget.