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A model of covid-19 transmission to understand the effectiveness of the containment measures: application to data from France

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SUMMARY

The main objective of this paper is to address the following question : are the containment measures imposed by most of the world governments effective and sufficient to stop the epidemic of COVID-19 beyond the lock-down period? In this paper we propose a mathematical model which allows to investigate and analyze this problem. We show by means of the reproductive number, \mathcal{R}_0 that the containment measures appear to have slowed the growth of the outbreak. Nevertheless, these measures remain only effective as long as a very large fraction of population, p , greater than the critical value $1 - 1/\mathcal{R}_0$ remains confined. Using French current data, we give some simulation experiments with five scenarios including: (i) the validation of model with p estimated to 93%, (ii) the study of the effectiveness of containment measures, (iii) the study of the effectiveness of the large scale testing, (iv) the study of the social distancing and wearing masks measures as well as (v) the study taking into account the combination of the large scale test of detection of infected individuals and the social distancing with linear progressive easing of restrictions. The latter scenario was shown to be effective to overcome the outbreak if the transmission rate is decreased to 75% and the number of tests of detection is multiplied by three. We also noticed that if the measures studied in our five scenarios are taken separately then the second wave might occur at least as far as the parameter values remain unchanged.

Key words: COVID-19, Basic reproduction ratio, containment measures, new wave

1 INTRODUCTION

In December 2019, a disease that appeared in central China precisely in the city of Wuhan (Hubei Province) started to take its toll. On January 7, 2020, Chinese authorities admitted that the country was facing an epidemic caused by a new virus from the coronavirus family. First named "2019-nCoV", this virus and disease was named COVID-19 or SARS-COV-2 by the World Health Organization (WHO) [36]. COVID-19 disease has passed in a few weeks from a localized epidemic to a pandemic. This disease is now a public health emergency of international level and is currently affecting more than 200 countries with more than 350,000 deaths and nearly 6 millions people infected according to WHO. It is contagious with human-to-human transmission via respiratory droplets or by touching contaminated surfaces and then touching one's face. The most common symptoms are fever, cough, and difficulty breathing, but it can cause acute respiratory distress, which is often fatal.

The spread of the disease has enormous consequences for all sectors of society, endangering economics of almost all countries in the world. In the current state of knowledge, there is no preventive vaccine, biomedical means of prevention or specific therapeutic means. International, national and local control strategies are essentially based on barrier measures, social distancing, wearing masks, confinement, screening and diagnosis according to various methods and symptomatic treatment. Today in different countries, research in all its dimensions has become an absolute priority. In particular any research which can help to understand, prevent and treat Covid 19 is encouraged at the highest political level of many countries. Following this urgency, models have already been proposed in order to study the dynamics and to control the pandemic [2, 12, 22, 28, 24, 25, 29, 5, 35]. In this paper, we propose a new model which could help to understand the effectiveness of the containment measures adopted across countries. The model will be used to predict different scenarios of the possible resurgences of the new waves of epidemic in France.

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The paper is organized as follows. The next section presents the model. The basic reproduction ratio is established in Section 3. Section 4 is devoted to the formulation of the function which regulates the containment measures. In section 5, we identified the values of model parameters. The Section 6 presents the Simulation experiments for which five scenarios will be implemented: validation of model by comparison with the actual available data in France, testing the effectiveness of containment measures and Longer term forecasting of epidemic, study of the effectiveness of the large scale testing, study of social distancing measures and the combined study of the large scale testing and Social distancing and/or wearing masks measures. Concluding remarks will follow in Sections 7.

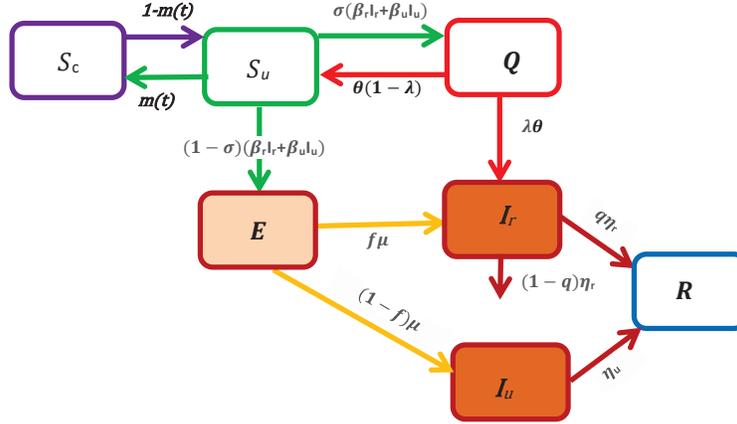


Figure 1: A schematic of the model for COVID-19 transmission. In this Figure, S_u represents the number of unconfined susceptible, S_c denotes the number of confined susceptible, E depicts the number of exposed, I_r denotes the number of reported Infectious, I_u represents the number of unreported infectious or silent carriers, R denotes the number of recovered, Q denotes the number of quarantined. The arrow show the people moving between the compartments.

2 MODEL FORMULATION

To model the COVID-19 transmission, we divide the human population into seven classes. Susceptible unconfined $S_u(t)$, susceptible confined $S_c(t)$, exposed $E(t)$, reported infectious $I_r(t)$, unreported infectious or silent carriers, $I_u(t)$, quarantined $Q(t)$, recovered $R(t)$ at any time t , see in Figure 1.

In this paper, the unreported infectious individuals depict mainly the individuals with no clinical symptoms (asymptomatic or silent carriers) during their infectious period. They also include some infectious individuals with mild symptoms who thus often go unrecognized.

In what follows, we assume that these individuals don't die of the disease, while the reported infectious can die of disease at a rate $(1-q)\eta_r$, where $1-q$ is the fraction of reported individuals that die, q is the fraction of reported individuals that recover and $1/\eta_r$ is the average length of infectious period of reported individuals (see Figure 1).

An individual moves to the susceptible unconfined class, S_u , either from the confined class at a rate $1-m(t)$ or from the quarantined class at a constant rate $\theta(1-\lambda)$. The fundamental parameter that we have introduced in our model to study the containment measures is the parameter $m(t)$, it can be interpreted as the fraction of confined susceptible individuals at any time t . When the susceptible individuals are exposed to the virus, then the exposition provides either the reported class, I_r or the unreported class, I_u . Without making any distinction about the origin of the infection, we assume that a fraction σ of Susceptible unconfined individuals which has been in contact with an infectious individual is quarantined with contact tracing while the other fraction $(1-\sigma)$ who was not detected by the contact tracing move to the exposed class E once effectively infected or stay in compartment S_u otherwise. Then, the quantities $(1-\sigma)(\beta_r I_r + \beta_u I_u)S$ and $\sigma(\beta_r I_r + \beta_u I_u)S$ represent the inflow of new individuals into the exposed class E and quarantined class Q respectively. The parameters β_r and β_u are the transmission rate of reported and unreported cases respectively. We assume that reported individuals will participate into the infections with a lower rate than those unreported because they are generally isolated at the hospital or at home. However, they can transmit the infection to caregivers or their entourage. Moreover, they may have first been asymptomatic carriers contributing to the transmission of the virus. To simplify the notation, we set $\beta_u = \beta$ and $\beta_r = \varrho\beta_u = \varrho\beta$ where $\varrho \in [0, 1]$. The parameter ϱ represents the infectivity of the reported cases and for $\varrho = 1$, the reported and unreported have the same level of infectivity. Among the quarantined individuals, a fraction λ of individuals are effectively infected and moves in the reported infectious class, I_r , after an average duration of isolation, $1/\theta$, and a fraction $1-\lambda$ returns to the susceptible class without being reported infectious. We assume that only a fraction

f of the individuals of exposed class becomes reported infectious and enters to the class I_r at a rate μ where $1/\mu$ represents the average length of the exposed period while the other fraction $(1 - f)$ moves to the infectious unreported infectious class I_u at a rate μ .

With the above considerations, the model describing the spread of COVID-19 takes the form:

$$\begin{cases} \frac{dS_c}{dt} = m(t)S_u - (1 - m(t))S_c \\ \frac{dS_u}{dt} = (1 - m(t))S_c - m(t)S_u - \beta(\varrho I_r + I_u)S_u + \theta(1 - \lambda)Q \\ \frac{dE}{dt} = (1 - \sigma)\beta(\varrho I_r + I_u)S_u - \mu E \\ \frac{dI_r}{dt} = \mu f E + \theta \lambda Q - \eta_r I_r \\ \frac{dI_u}{dt} = \mu(1 - f)E - \eta_u I_u \\ \frac{dR}{dt} = \eta_r \varrho I_r + \eta_u I_u \\ \frac{dQ}{dt} = \sigma \beta(\varrho I_r + I_u)S_u - \theta Q. \end{cases} \quad (1)$$

This model (1) is supplemented together with initial data $S_c(\tau_0), S_u(\tau_0), E(\tau_0), I_r(\tau_0), I_u(\tau_0), R(\tau_0)$ and $Q(\tau_0)$.

Let $DI_r(t), DI_u(t), CI_r(t)$ and $CI_u(t)$ denotes the daily number of reported cases, unreported one, the cumulative number of reported cases and unreported cases respectively at any time t . These quantities are obtained by solving the following equations

$$\begin{cases} \frac{dDI_r(t)}{dt} = \mu f E(t) + \theta \lambda Q(t) - DI_r(t) \\ \frac{dDI_u(t)}{dt} = \mu(1 - f)E(t) - DI_u(t) \\ \frac{dCI_r(t)}{dt} = \mu f E(t) + \lambda \theta Q(t) \\ \frac{dCI_u(t)}{dt} = \mu(1 - f)E(t). \end{cases} \quad (2)$$

with initial conditions $DI_r(\tau_0), DI_u(\tau_0), CI_r(\tau_0)$ and $CI_u(\tau_0)$

3 BASIC REPRODUCTION NUMBER

The fundamental key concept in epidemiology is the basic reproduction number. Commonly denoted by \mathcal{R}_0 , it is the expected number of secondary cases produced by a typical infective individual introduced into a completely susceptible population, in the absence of any control measure [10, 34]. Mathematically, \mathcal{R}_0 is the spectral radius of the next generation matrix. The next generation matrix can be obtained by construction (cf. for instance [1, 11, 14]). Using the method developed in [34], we obtain explicit formula for \mathcal{R}_0 as follows:

$$\mathcal{R}_0 = [(1 - \sigma)f + \sigma \lambda] \frac{\varrho \beta S_u(0)}{\eta_r} + (1 - \sigma)(1 - f) \frac{\beta S_u(0)}{\eta_u} \quad (3)$$

where $\beta_u = \beta$ and $\beta_r = \varrho \beta$. In Appendix we give some details about the derivation of \mathcal{R}_0 .

The quantity $\mathcal{R}_r := [(1 - \sigma)f + \sigma \lambda] \varrho \beta S_u(0) / \eta_r$ represents the average number of secondary infections produced by one reported infective individual during its infectious period, $1/\eta_r$; $\mathcal{R}_u := (1 - \sigma)(1 - f) \beta S_u(0) / \eta_u$ represents the average number of secondary infections produced by one unreported infective individual during its infectious period, $1/\eta_u$;

To take into account the containment measures, the large scale testing, the social distancing and wearing masks measures, some constant parameters such as f, σ, β and $S_u(0)$ will be replaced in equation (3) with the aforementioned time-dependent parameters. In this case, we can define the effective daily reproduction number, $\mathcal{R}_0(t)$ which measures the number of new infections produced by a single infected individual per day. This quantity are obtained by solving the following equation

$$\frac{\mathcal{R}_0(t)}{dt} = [(1 - \sigma(t))f(t) + \sigma(t)\lambda] \frac{\varrho \beta(t) S_u(t)}{\eta_r} + (1 - \sigma(t))(1 - f(t)) \frac{\beta(t) S_u(t)}{\eta_u} - \mathcal{R}_0(t) \quad (4)$$

with initial condition $\mathcal{R}_0(0) = \mathcal{R}_0$ defined in Equation (3).

4 CONSTRUCTION OF THE CONTAINMENT RATE

To analyze the effectiveness of containment measures, we assume that a fraction $m(t)$ of susceptible individuals in the population is confined at any time t . Furthermore, we introduce a parameter p which indicates the maximum percentage of the population that the government confines. This fraction should be greater than the quantity $1 - 1/\mathcal{R}_0$ to be sure of its effectiveness [40, 11]. This parameter varies from country to country and can be set in advance for a given country. Let τ_0 denotes the starting date of epidemic, τ_1 represents the date at which a government decides to apply the containment measures, τ_2 denotes the date at which a fraction p of the population is confined, τ_3 stands for the date at which the government decides to exit progressively the containment measures because either the restrictions take effect or there are budget or social limitations and τ_f denotes the date for the end of the containment measures. Now, we divide the containment rate $m(t)$ into four phases:

Phase 0: Period without containment measures (from date τ_0 to τ_1), then $m(t) = 0$.

Phase 1: Period when containment is taking place until the government reaches its maximum containment effort (from date τ_1 to τ_2). In this phase we assume that the function m increases exponentially and reach the value p at date τ_2 . It follows that m takes the form $m(t) = 1 - \exp(-a(t - \tau_1))$ where $a = -\ln(1 - p)/(\tau_2 - \tau_1)$.

Phase 2: Period where the maximum effort is maintained (from date τ_3 to τ_4) and $m(t) = p$.

Phase 3: Period at which the government decides to relax the containment measures (from date τ_3 to τ_f). This drop is linearly depending on the time so that the value of m at date τ_f equals to 0. Then m is described as follows $m(t) = p + b(t - \tau_3)$, where $b = -p/(\tau_f - \tau_3)$.

5 MODEL PARAMETERS

Before to go further, let us point out that in our paper, the values of the parameters $f, \sigma, \mu, \theta, \tau_0, \tau_3, \tau_f$, as well as the initial values $S_u(\tau_0), S_c(\tau_0)$ and $I_r(\tau_0)$ were chosen from expert opinions. The values of the parameters $\tau_2, \lambda, \varrho, p, \beta, \sigma, \eta_r, \eta_u$ as well as the initial values $CI_u(\tau_0), Q(\tau_0), E(\tau_0)$ were unknown. However, it is possible to identify them from specific time data. The value of the parameter q can be easily computed from current data. By setting $x = (\tau_2, \lambda, \varrho, p, \beta, \sigma, \eta_r, \eta_u, I_u(\tau_0), Q(\tau_0), E(\tau_0), \tau_2)$, we estimated an optimal value of x that fit with the data from France by minimizing the following error function

$$\chi^2(x) = \frac{\sum_{l=1}^n (obs(t_l) - sim(t_l, x))^2}{n} \quad (5)$$

where n is the number of observed data, $obs(t_l)$ and $sim(t_l, x)$ are the observed and calculated data at time t_l respectively.

5.1 Chosen Values: $f, \sigma, \mu, \theta, \tau_0, \tau_3, \tau_f, S_u(\tau_0), S_c(\tau_0)$ and $I_r(\tau_0)$

Initial conditions: We started the simulations at the moment where in France, the number of reported cases were identified with 12 individuals, ie precisely on the date $\tau_0 = 25$ February. Then $I_r(\tau_0) = 12$. The population of France is around 66 999 000 inhabitants [4], thus, we set $S_c(\tau_0) = 66 999 000$. At that date, there were no confined individuals, thus $S_c(\tau_0) = 0$.

Value of parameter f : Recall that, $(1 - f)$ stands for the fraction of exposed individuals that becomes unreported infectious and corresponds to the proportion of asymptomatic or silent carriers or mild infectious. $(1 - f)$ is ranging from 17.9%-86% [36, 8, 9, 26, 16] and some reviews therein [41]. The fractions of unreported individuals in these previous studies is derived from the number of tests performed. Therefore, the current fraction may be seriously underestimated. During the onset of covid-19 in France, there was very little screening tests. That's why, we estimated that $1 - f = 0.8$ (ie. $f = 0.2$). Furthermore, we make it vary in the scenario 3 (effectiveness of the large scale testing), as soon as the number of tests increases.

Value of parameter σ : The value of parameter σ was calibrated to 0.2 so that $\sigma = f$. In scenario 3, we assume that f increases in the same order as σ when the time evolves (see Figure 2(c)), because when the number of tests increases, the fraction of reported cases increases and thus the fraction σ of Susceptible unconfined individuals that is quarantined increases with contact tracing.

Value of parameter τ_1 : The starting date of the containment was fixed on March 17, then $\tau_1 = 17$ March.

Value of parameter τ_3 : According to the announcement of French government of April 13, a gradual deconfinement started on May 11. So for model validation, we fixed $\tau_3 = 11$ May.

Value of parameter τ_f : We fixed the end date of containment measures on September 1.

Value of parameter μ : The mean incubation period $1/\mu$ was fixed to 5 days see [36, 19, 3].

Value of parameter θ : We considered 14 days to isolate the quarantined individuals, therefore, $1/\theta = 14$ days.

5.2 Estimated values: $\tau_2, \lambda, \varrho, p, \beta, \sigma, \eta_r, \eta_u, I_u(\tau_0), Q(\tau_0), E(\tau_0), \tau_2$ and q .

By calibrating the model with the data corresponding to the cumulated reported cases for France, we identified some values of model parameters giving a good fit of the observed data obtained in [7]. The parameter values and initial conditions estimated are listed in Table 1.

Value of parameters τ_2 and p : we estimate that the government has successfully confined 93% of the population on the date April 12, thus, $\tau_2 = 12$ April and $p = 0.93$. This value means that 93% of the population was confined on date τ_2 equals to April 12th, thus $S_c(\tau_2) = 62\,300\,700$. In this case, 7% of the population that remained active and we set $S_u(\tau_2) = 4\,689\,300$. Note that this number corresponds approximately to 15.78% of active population in France which was 29 700 000 according to INSEE in 2017 [32].

Value of parameters η_r and η_u : By fitting with data from France, we estimate that the mean duration of infectious period for unreported individuals, $1/\eta_u = 4$ days and for reported ones, $1/\eta_r = 10$ days.

Value of parameters β_r, β_u and ϱ : we estimated that the infectivity of reported cases ϱ is equals to 0.40 compared to infectivity of unreported which is 1. The transmission rate $\beta_u = \beta$ of unreported individuals is estimated to 2.115×10^{-8} day⁻¹, then the transmission rate of reported individuals equals to $\beta_r = \beta\varrho = 0.846 \times 10^{-8}$ day⁻¹.

Value of parameter q : Since $1 - q$ represents the fraction of reported individuals that dies, thus

$$1 - q = \frac{\text{Cumulative number of death among the reported individuals}}{\text{Cumulative number of reported individuals}}.$$

From current data (July 31), we find $1 - q = 30254/186573 = 0.1622$. It follows that the disease-induced death rate of reported individuals, $(1 - q)\eta_r$, equals to $0.1622 \times 1/10 = 0.0162$ day⁻¹. Furthermore, the fraction of reported individuals that becomes recovered equals to $q = 0.8378$.

Value of parameters $E(\tau_0), Q(\tau_0)$ and $I_u(\tau_0)$: we estimate that at date τ_0 , we have $Q(\tau_0) = 36, I_u(\tau_0) = 50$ and $E(\tau_0) = 112$.

6 SIMULATION EXPERIMENTS: APPLICATION TO DATA FROM FRANCE

6.1 Scenario 1: validation of model with Data from France

We selected for model validation, the data obtained for daily reported (DRI_r) and cumulative reported (CRI_r) cases for France see [7]. Some constants and parameters involved in the model were listed in Table 1. The results of this scenario are illustrated on the figures 3.

6.2 Scenario 2: effectiveness of containment measures

The objective of this scenario is to analyse if the outbreak might stop for different values of the date at which the containment measures are relaxed, namely τ_3 . Then, the value of the latter is assumed varying from May 11, June 01 and 30. The end date of containment measures τ_f , is fixed to September 1. The values of the parameters used are listed in tables 1 excepted the containment function m that varies (see Figure 2(b)).

The results of this scenario are illustrated on the figures 4.

6.3 Scenario 3: effectiveness of the large scale testing

To investigate the effectiveness of the large scale test of detection of infected individuals, the date at which the containment measures are relaxed, τ_3 , is fixed to May 11; the end date of containment measures, τ_f , is fixed to September 01. We assume that between the dates τ_3 , and τ_f , the fraction of reported cases f increases linearly and reach 200% of its initial value and the fraction of susceptible individuals which is quarantined σ is also increased linearly to reach 200% of its initial value (see Figure 2(c)), the initial values is estimated in scenario 1. The values of the other parameters is listed in tables 1 excepted the containment function m that varies (see Figure 2(b)).

The results of this scenario are illustrated on the figures 5.

6.4 Scenario 4: Social distancing and/or wearing masks measures

To study the social distancing and/or wearing masks measures, the date at which the containment measures are relaxed, τ_3 , was fixed to May 11; the end date of containment measures, τ_f , is fixed to September 01. We assume that between the dates τ_3 , and τ_f , the transmission rate β decreases linearly to reach 75% of its initial value (see Figure 2(d)). The values of the other parameters is listed in tables 1 excepted the containment function m that varies (see Figure 2(b)).

The results of this scenario are illustrated on the figures 6.

Table 1: *List of parameters meanings and the parameter ranges for which the model was solved*

Name	Meaning	Value
p	Maximum fraction of the susceptible that a government can confine	0.93
f	Fraction of Exposed that becomes reported infectious	0.4
ϱ	Infectivity of reported individuals	0.5
λ	Fraction of quarantined individuals that becomes infectious	0.3
q	Fraction of reported individuals that becomes recovered	0.83
σ	Fraction of individuals which is quarantined with contact tracing	0.2
$\beta_r = \varrho\beta$	Transmission rate of reported individuals	0.846×10^{-8}
$\beta_u = \beta$	Transmission rate of unreported individuals	2.115×10^{-8}
$(1 - q)\eta_r$	Disease-induced death rate of reported individuals	0.016
$1/\mu$	Average length of the exposed period	5
$1/\eta_r$	Average length of infectious period of reported individuals	10
$1/\eta_u$	Average length of infectious period of unreported individuals	4
$1/\theta$	Average length of the quarantine period	14
$m(t)$	The fraction of confined susceptible at any time t	$[0 - p]$, see Fig. 2
τ_0	Starting date of the epidemic	February 25
τ_1	Starting date of the containment	March 17
τ_2	Date at which a fraction p of the population is confined	April 12
τ_3	Decision date of relaxation of the containment measures	May 11-June 28
τ_f	End date of containment measures	Sep. 01
Initial values	Meaning	Value
$S_c(\tau_0)$	Initial confined susceptible population	0
$S_u(\tau_0)$	Initial unconfined susceptible population	66990000
$E(\tau_0)$	Initial exposed population	112
$I_r(\tau_0)$	Initial reported population	12
$I_u(\tau_0)$	Initial unreported population	50
$R(\tau_0)$	Initial recovered population	0
$Q(\tau_0)$	Initial quarantined population	36

6.5 Scenario 5: Combined effects of large scale testing and Social distancing measures

To test the combined effects of large scale testing and Social distancing social and/or wearing masks measures, we combine the conditions of scenario 1 and 2. The date at which the containment measures are relaxed, τ_3 , is fixed to May 11; the end date of containment measures, τ_f , is fixed to September 01. Between the dates τ_3 and τ_f , we assume that f increases linearly to reach 200% of its initial value, σ increases linearly to reach 200% of its initial value and β decreases of 75% of its initial value see Figure 2(d) for these different variations of parameter values.

The results of this scenario are illustrated on the figures 7.

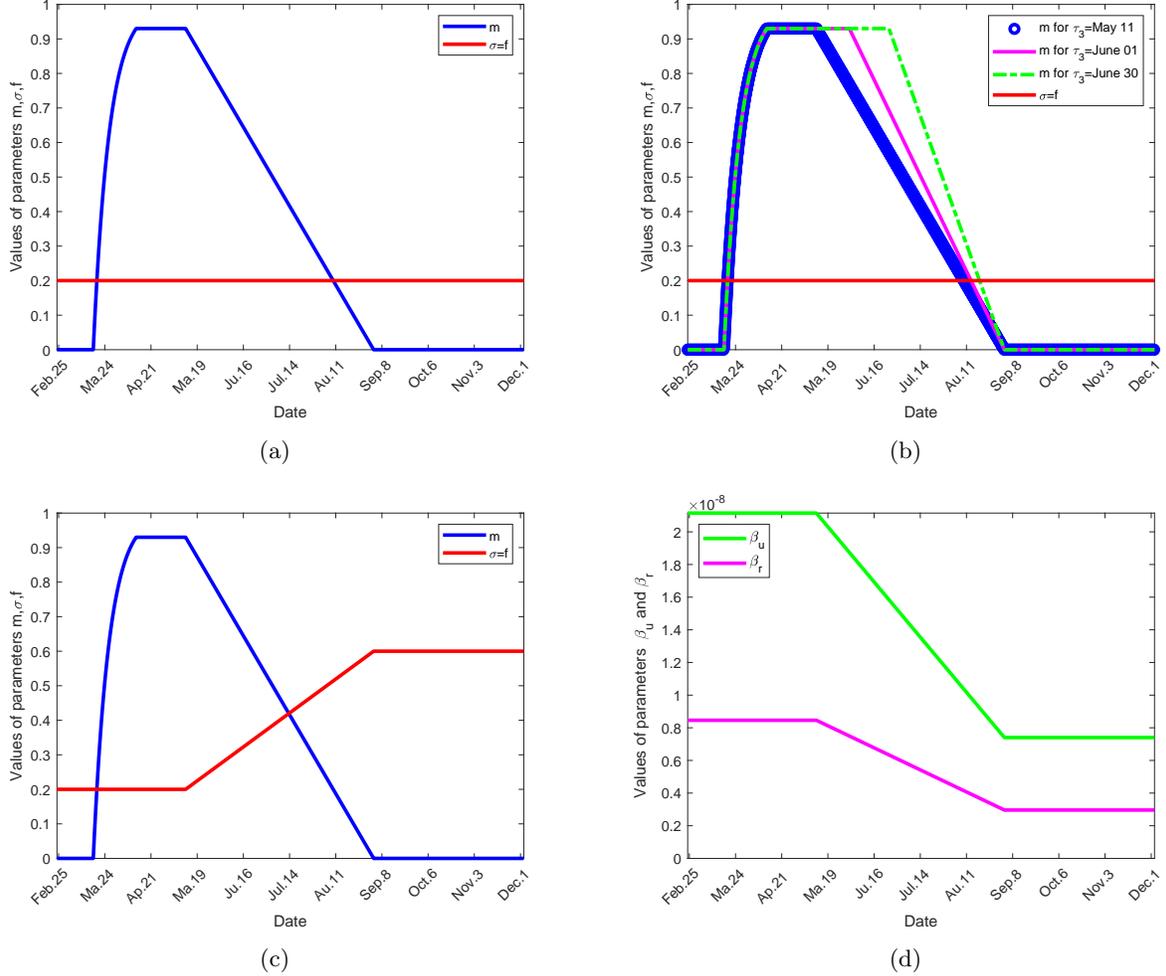


Figure 2: Evolution over time of parameters m , σ , f , β_r , β_u and τ_3 according to each scenario; the other parameters of model are fixed in Table 1. (a) for scenario 1, only the parameter m is time depending, $f = \sigma = 0.2$, $\beta_r = 0.846 \times 10^{-8}$, $\beta_u = 2.115 \times 10^{-8}$ and $\tau_3 = \text{May 11}$ for all time. (b) for scenario 2, $f = \sigma = 0.2$, $\beta_r = 0.846 \times 10^{-8}$, $\beta_u = 2.115 \times 10^{-8}$ for all time, only the parameter m is time depending for three different values of the date at which the containment measures are relaxed, τ_3 , more precisely when τ_3 takes the values May 11, June 01 and 30. (c) for scenario 3, we set $\tau_3 = \text{May 11}$, m , f and σ evolve over time, $\beta_r = 0.846 \times 10^{-8}$, $\beta_u = 2.115 \times 10^{-8}$. (d) for scenario 4, $\tau_3 = \text{May 11}$, $f = \sigma = 0.2$, m evolves as in (a), in addition, the transmission rate β_r and β_u evolve. (e) for scenario 5, $\tau_3 = \text{May 11}$, f, σ, m evolve as in (c), moreover β_r and β_u evolve as in (d)

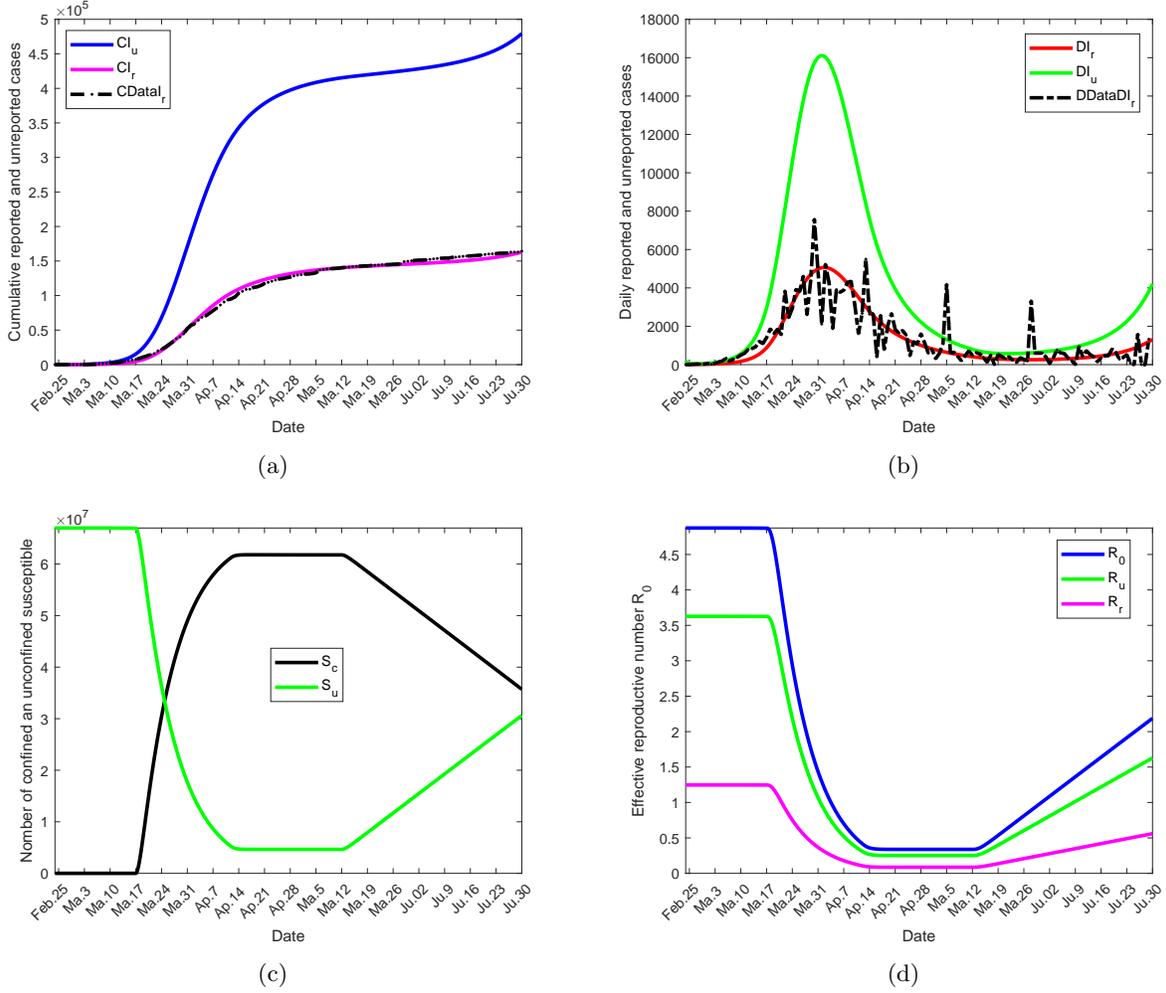


Figure 3: Scenario 1: validation of model with currently data from France. The date at which the containment measures are relaxed, τ_3 , was fixed to May 11; the end date of containment measures, τ_f , was fixed to September 01. (a) The cumulative number of reported CI_r and unreported CI_u cases simulated, and observed data $CData_r$. (b) The daily number of reported DI_r and unreported DI_u cases from the model and observed data $DData_{DI_r}$. (c) The confined and unconfined susceptible S_c and S_u . (d) The daily reproductive number R_0 . In this scenario, the values of the parameters were estimated and listed in tables 1 excepted the containment function m which varies between 0 and 1 (see Figure 2(a))

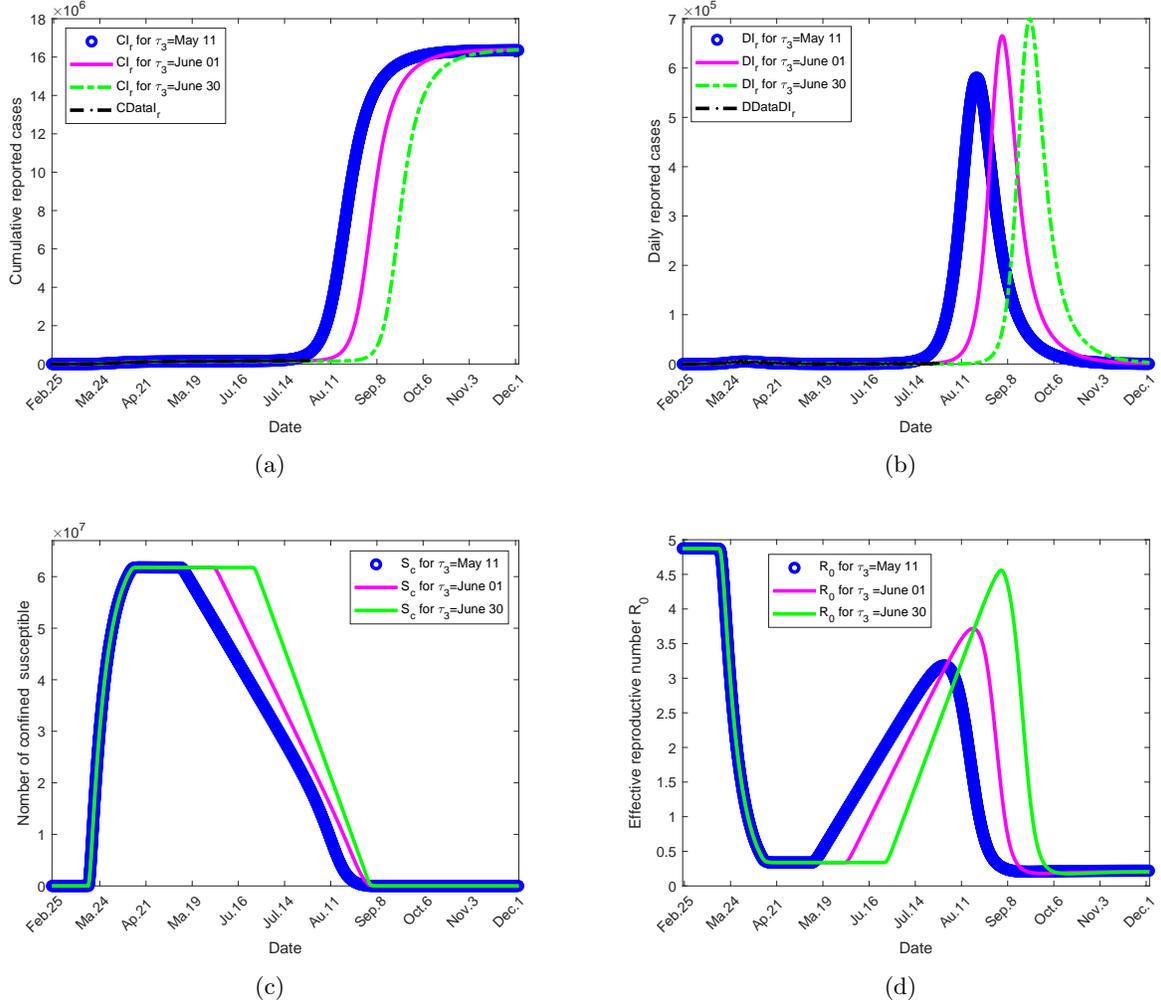


Figure 4: Scenario 2: longer term forecasting of epidemic spreading according to different values of the date at which the containment measures are relaxed, τ_3 that varies between May 11, June 01 and 30. The end date of containment measures τ_f , was fixed to September 1. (a) The cumulative number of reported CI_r cases simulated. (b) The daily number of reported DI_r cases from the model. (c) The number of confined susceptible S_c . (d) The daily (effective) reproductive number R_0 . In this scenario, the values of the parameters were estimated and listed in tables 1 excepted the containment function m which varies between 0 and 1 for different values of τ_3 (see Figure 2(b))

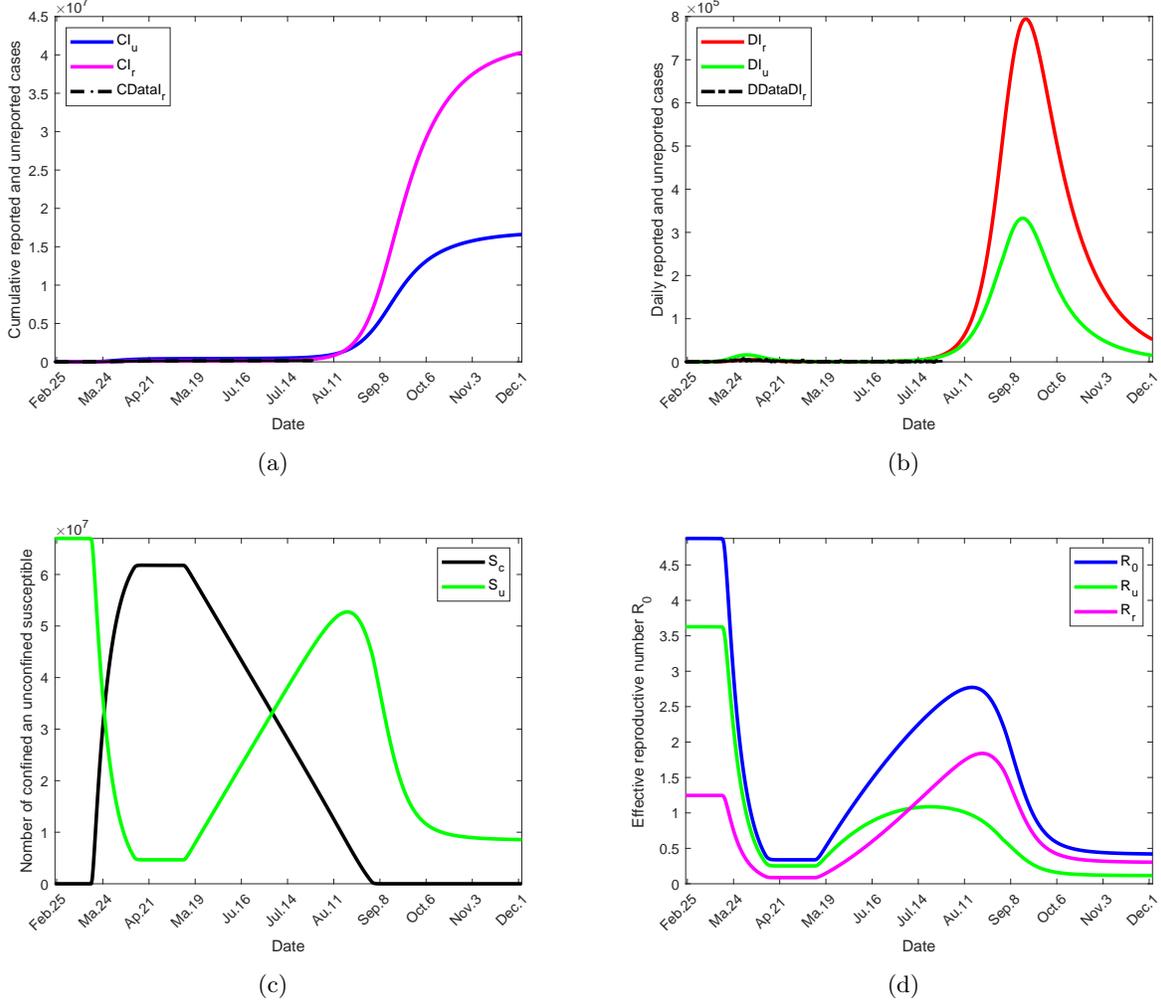


Figure 5: Scenario 3: Longer term forecasting of epidemic spreading in case of large scale tests of detection on infected individuals. τ_3 , was fixed to May 11; τ_f , was fixed to September 01. Between the dates τ_3 and τ_f , the parameter f was assumed increase linearly to reach 200% of its initial value, σ increased linearly to reach 200% of its initial value (see Figure 2(c)). The values of the other parameters were listed in tables 1 excepted m that varies (see Figure 2(b)). (a) The cumulative number of simulated reported CI_r and unreported CI_u cases, and observed data $CData_r$. (b) The daily number of simulated reported DI_r and unreported DI_u cases, and observed data $DDataDI_r$. (c) The number of simulated confined and unconfined susceptible S_c and S_u . (d) The daily reproductive number R_0 .

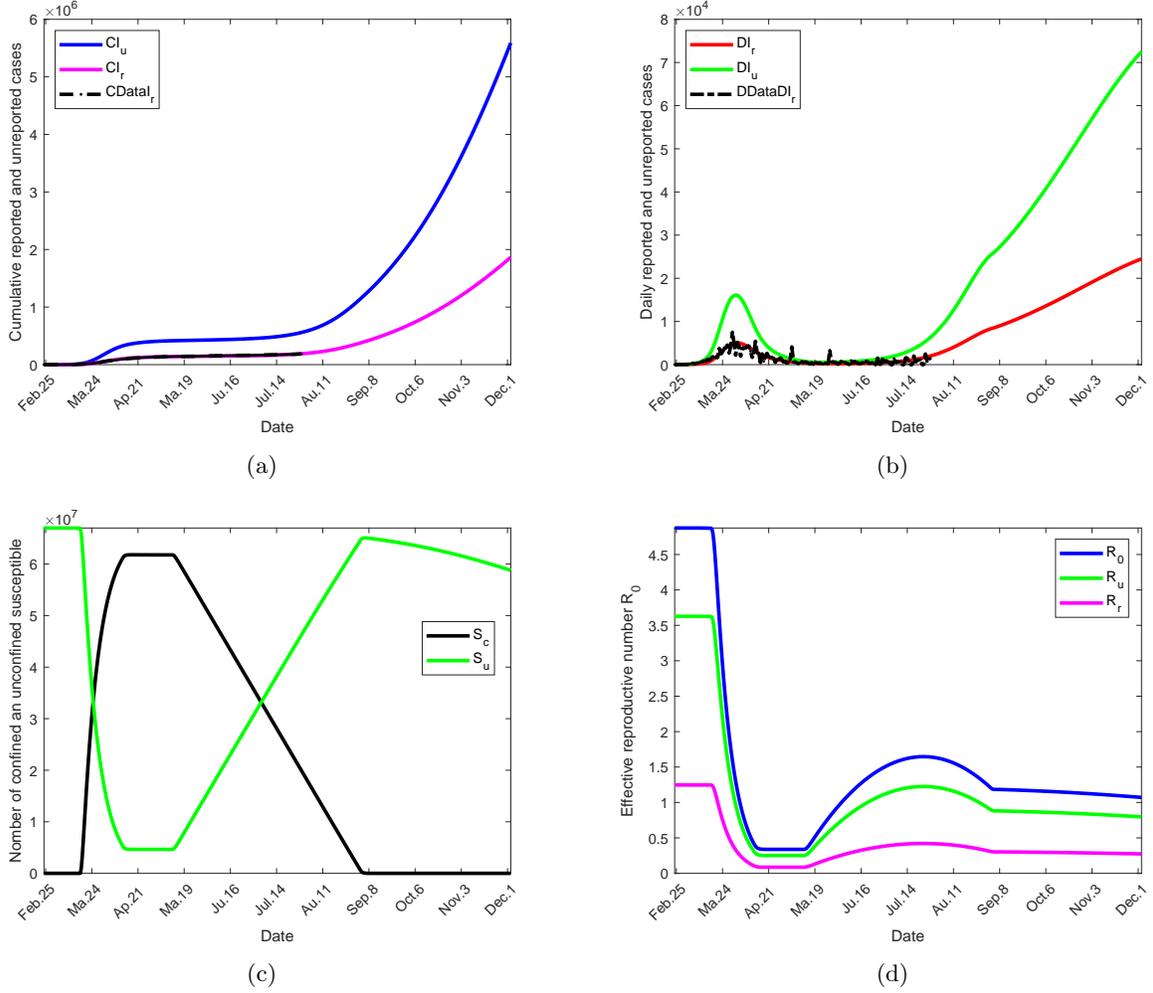
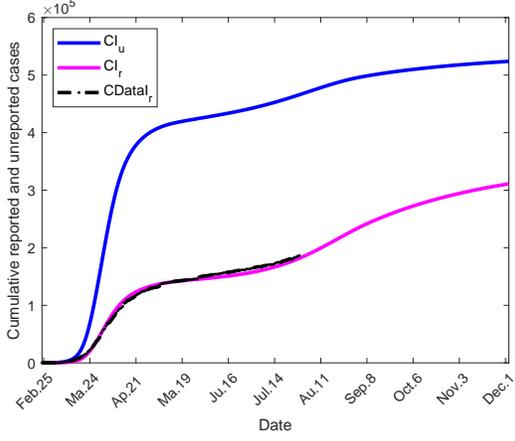
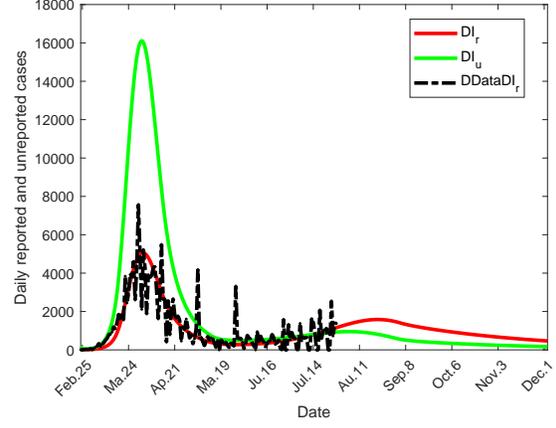


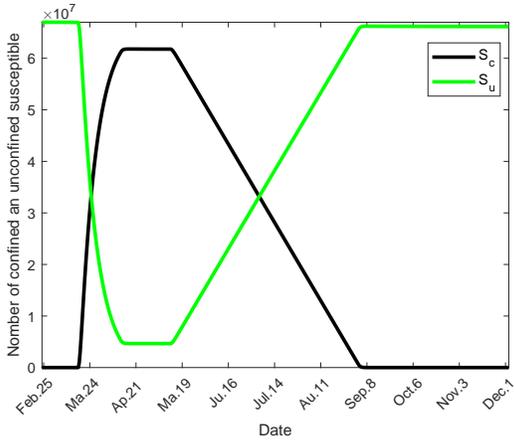
Figure 6: scenario 4: Longer term forecasting of epidemic spreading in case of the social distancing and wearing masks measures. τ_3 , was fixed to May 11; τ_f , was fixed to September 01. Between the dates τ_3 and τ_f , the parameter β decreases of 75% of its initial value see Figure 2(d). The values of the other parameters are listed in tables 1 excepted m that varies (see Figure 2(b)). (a) The cumulative number of simulated reported CI_r and unreported CI_u cases, and observed data $CDataI_r$. (b) The daily number of simulated reported DI_r and unreported DI_u cases, and observed data $DDataI_r$. (c) The number of simulated confined and unconfined susceptible S_c and S_u . (d) The daily reproductive number R_0 .



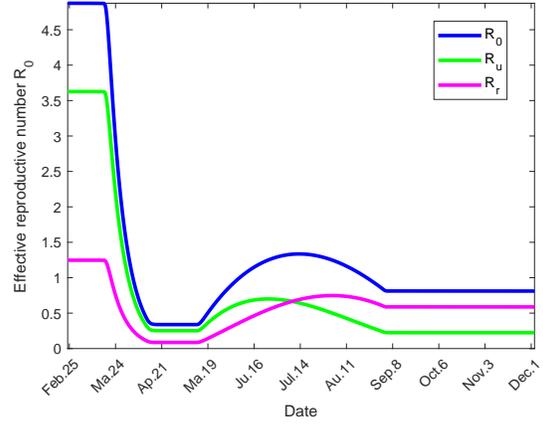
(a)



(b)



(c)



(d)

Figure 7: Scenario 5: Longer term forecasting of epidemic spreading in case of both social distancing and/or wearing masks and large scale tests. τ_3 , was fixed to May 11; τ_f , was fixed to September 01. Between the dates τ_3 and τ_f , the parameter f increases linearly to reach 200% of its initial value, σ increases linearly to reach 200% of its initial value (see Figure 2(c)). β decreases to 75% of its initial value see Figure 2(d). The values of the other parameters are listed in table 1 excepted m that varies (see Figure 2(b)). (a) The cumulative number of simulated reported CI_r and unreported CI_u cases, and observed data CI_rData . (b) The daily number of simulated reported DI_r and unreported DI_u cases, and observed data $DDataI_r$. (c) The number of simulated confined and unconfined susceptible S_c and S_u . (d) The daily reproductive number \mathcal{R}_0 .

7 DISCUSSION AND CONCLUSION

This model takes into account the measures of confinement, distinguishing between confined individuals, quarantined individuals and isolated individuals. Many values were estimated to fit the beginning of expansion of disease in France, other were inferred from expert opinions, see Section 5. The proportion $(1 - f)$ is ranging from 17.9%-86% [36, 8, 9, 26, 16] and some reviews therein [41]. The lower value was observed on board of the Diamond princess, i.e. in conditions which are not representative of large scale populations living in larger surfaces. At the other hand, in [20] and in a WHO report, it was estimated that between 80 and 86% of all infections were undocumented. Since this fraction is dependant on the number of tests performed and since during the onset of covid-19 in France, there was very little screening tests, we eventually chose $f = 0.2$.

As for f , the mean duration of infectious period, is a debatable point. In [30], the authors estimate that the asymptomatic individuals had median virus persistence duration of 8.87 days (95% CI: 7.65-10.27). This duration varies also between asymptomatic and symptomatic individuals [39], even when mildly affected. By contrast, all severe cases were still tested positive at or beyond day 10 post-onset [38]. This longer virus persistence in severe cases as compared to milder cases has been also demonstrated by [31] but not by all authors, see some reviews therein [41]. Note also that in the literature, the estimate of the mean duration of infectious period of reported individuals is not always clear, since some authors include hospitalization or isolation period, others do not. Results vary between 2 and 8 days, [20, 6, 17]. Our model implicitly takes into account a combined effect of duration of infectivity and viral load, which results in risk of transmission. Indeed, the mean duration of infectious period estimated to be 10 days for reported individuals is coherent with the estimation in [27] based on clinical, microbiologic, epidemiologic and clinical data. Since we estimate the infectivity of the reported cases to be equal to 0.4, that of unreported cases in term of duration of infectious period, it means that reported individuals are infectious for 40% of their infectious period, ie 4 days. If the infectivity is interpreted in term of viral load, it means that 40% of the viral load excreted by the infectious reported cases is infective. Such a link between duration of infectious period and infectivity (ie interpreted in term of viral load) also holds in literature except in [42] where the authors observed no difference in viral load between asymptomatic and symptomatic patients. In [23] the virus level in the asymptomatic group was significantly lower than in the symptomatic group in the acute phase.

Figure 3 shows the adequacy of the model for predicting the evolution of number of cases in the beginning of the crisis until end of June. It also shows that as soon as confinement is reduced or stopped, the daily reproduction number \mathcal{R}_0 value increases again and a new wave of epidemics is to be expected as soon as its value is higher than 1. As observed on Figures 4 (for longer term forecasting), such waves are expected to appear very shortly after reduction of confinement, once the incubation period is spent. These values will allow predicting the effectiveness of the containment measures as well as risk and the intensity of possible resurgences of the new waves of epidemic in France. Indeed, the measures of confinement have a strong impact on the value of the daily reproduction number \mathcal{R}_0 . Figures 4 shows that, while it was equal to nearly 5 in the beginning of the disease, before confinement, it decreased to about 0.5 as long as confinement of most people takes place and increased to a lower value, between 2 and 2.5, that is about half its former value. But even if its value is reduced, it remains higher than 1. It is also to note that, unexpectedly, its value was lower when end of confinement was earlier. Figure 3-4 show that the current increase in number of cases could be expected as soon as containment was relaxed from Mid-May to September. However, number of cases are expected to decrease if a higher proportion of infected people are detected and confined, which is currently the case. Delaying the very starting date of deconfinement to 30 June would have resulted in a later and higher wave but not as late as could be expected for a starting date to 11 May. All French people are expected to be either reported or unreported infected individuals at the end of 2020, i.e. before expected development of vaccines. However, some of those values may change with evolution of measures of prevention such as social distancing and/or wearing masks, large scale testing, treatment of the disease.

Social distancing and wearing masks measures directly influences the transmission rate which is expected to dramatically decrease with the increasing tendency to wear masks. Its effect was investigated in scenario 3 where the transmission rate was assumed to decrease linearly to reach the value 75 % of its initial one as shown on Figure 2(d). The results of this scenario are shown on Figures 5. The transmission rate may be dramatically decreased. But the results show that this measure alone is insufficient to eliminate the disease.

The effectiveness of the *large scale test of detection* of infected individuals was analysed and shown on Figures 6. The fraction of reported cases, from date τ_3 to date τ_f , the fraction of reported cases f was assumed increase linearly to reach the value 200% of its initial one and the fraction of susceptible individuals which is quarantined σ was also increased linearly to reach the value 200% of its initial one (see Figure 2(c)), see Figure 2b These values may be observed by tracking all former contacts of any newly reported case, and systematically testing them, As in the former scenario dates of relaxation and end of containment measures were fixed to May 11th and September 1th respectively. Results show that this measure without further action is also insufficient to control the outbreak.

The *combined measures* of large scale testing and social distancing and/or wearing masks measures was studied in scenario 5. The transmission rates (reported and unreported individuals) were assumed to decrease from 75% to the date τ_2 to the date τ_f (see Figure 2(d)). The Figures 7, show the effectiveness of these combined measures and the potential of such a strategy. In particular, it shows that predicted data are compatible with the current situation with no evidence

yet of a second wave. This result also shows that protective measures must be maintained for a long term before the hypothesis of a second wave may be discarded.

In the absence of any control measure, the basic reproduction number \mathcal{R}_0 is equal to 4.8739. Most of this value is due to the weight of transmission by unreported individuals ($\mathcal{R}_u = 3.6271$) and the weight of transmission by reported cases accounts for much less ($\mathcal{R}_r = 1.2468$). These values show that the major number of secondary infections is produced by the unreported individuals. With increasing use of appropriate tests, reported individuals will be more precisely diagnosed, thus the fraction of reported cases f will increase and thus the importance of \mathcal{R}_r in the total value of \mathcal{R}_0 . Since the infectivity of reported individuals was estimated at 0.4 compared to infectivity of unreported the increase in \mathcal{R}_r will be very small showing the importance of detecting infectious individuals, see the evolution over time of the effective reproductive number $\mathcal{R}_0(t)$ and effective weight of transmission $\mathcal{R}_r(t)$ and $\mathcal{R}_u(t)$ on Figures 7(d). Therefore, the reported individuals will have a lower propensity to transmit the virus. Through stronger measures of prevention, the probability of contaminating other people will be lower.

With the confinement measures, the minimal percentage (critical fraction) of susceptible individuals that should be confined to eliminate the COVID-19 equals to $1 - 1/\mathcal{R}_0$ (see for instance [11, 40]). By confining more susceptible individuals, we increase the kinetics of elimination of the disease. By fitting the model with the French data, we estimated this fraction to $p = 93\%$. This value belongs to the critical interval, namely $]1 - 1/\mathcal{R}_0, 1] \simeq]0.8, 1]$.

By analyzing the results of simulations, we can conclude that the containment measures appear to have slowed the growth of the COVID-19 outbreak. Our model predicts that a second big wave of the epidemic may not be avoided if the situation remains unchanged and if the French government does not maintain the current efforts on large scale tests, obligation of wearing masks inside and in some cases outside and other prophylactic measures. However it also shows that these measures are efficient to avoid such a risk, thus preserving public health and avoiding a new confinement and all its terrible consequences, see Figure 3 and Figure 4. While if no measures were implemented, even only one infected individual in the population would result in a new wave of infections and a new period of confinement. Some obligations will succeed in avoiding a second wave of Covid-19.

In this article, we formulated a new model to describe the spread of COVID-19 to understand the effectiveness of the containment and quarantine measures. It is able to reproduce observed data from France and probably other countries.

8 APPENDIX. Some details about the derivation of \mathcal{R}_0

In order to define \mathcal{R}_0 , for model (1), we begin to find the disease-free equilibrium point by letting the compartments S_c, Q, E, I_r, I_u , and R be zero and $S_u = S_u(0)$.

Let $\mathcal{F}(I_r, I_u, E, Q)$ denotes the inflow of new individuals into the infected classes I_r, I_u, E and Q

$$\mathcal{F} = (0, 0, (1 - \sigma)\beta(\varrho I_r + I_u)S_u, \sigma\beta(\varrho I_r + I_u)S_u)^T$$

and $\mathcal{V}(I_r, I_u, E, Q)$ denotes all other flows within and out of the infected classes,

$$\mathcal{V} = \begin{bmatrix} -\mu f E - \theta \lambda Q + \eta_r I_r \\ -\mu(1 - f)E + \eta_u I_u \\ \mu E \\ \theta Q \end{bmatrix}.$$

Let $F = D\mathcal{F}$ and $V = D\mathcal{V}$ be the Jacobian matrices of the maps \mathcal{V} and \mathcal{F} , respectively, evaluated at the disease free equilibrium.

$$F = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ (1 - \sigma)\beta\varrho S_u(0) & (1 - \sigma)\beta S_u(0) & 0 & 0 \\ \sigma\beta\varrho S_u(0) & \sigma\beta S_u(0) & 0 & 0 \end{bmatrix} \quad \text{and} \quad V = \begin{bmatrix} \eta_r & 0 & -\mu f & -\theta \lambda \\ 0 & \eta_u & -\mu(1 - f) & 0 \\ 0 & 0 & \mu & 0 \\ 0 & 0 & 0 & \theta \end{bmatrix}.$$

A straightforward computation shows that

$$FV^{-1} = \begin{bmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ \frac{(1 - \sigma)\beta\varrho S_u(0)}{\frac{\eta_r}{\sigma\beta\varrho S_u(0)}} & \frac{(1 - \sigma)\beta S_u(0)}{\frac{\eta_u}{\sigma\beta S_u(0)}} & (1 - \sigma)f\frac{\beta\varrho S_u(0)}{\frac{\eta_r}{\sigma\beta\varrho S_u(0)}} + (1 - \sigma)(1 - f)\frac{\beta S_u(0)}{\eta_u} & (1 - \sigma)\lambda\frac{\beta\varrho S_u(0)}{\frac{\eta_r}{\sigma\beta\varrho S_u(0)}} \\ \frac{\sigma\beta\varrho S_u(0)}{\eta_r} & \frac{\sigma\beta S_u(0)}{\eta_u} & \sigma f\frac{\beta\varrho S_u(0)}{\eta_r} + \sigma(1 - f)\frac{\beta S_u(0)}{\eta_u} & \sigma\lambda\frac{\beta\varrho S_u(0)}{\eta_r} \end{bmatrix}$$

Following [34], the matrix FV^{-1} is well defined, and is the next generation matrix and \mathcal{R}_0 is the spectral radius of FV^{-1} .

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DECLARATION OF INTEREST

None.

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