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A modelling of COVID-19 outbreak with a linear compartmental model

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Abstract. Our human community faces a pandemic, which has lead us to lockdown half of world inhabitants. We are so disarmed to deal with the coronavirus (SARS-CoV-2) that lockdown seems us the only countermeasure suitable to stop the pandemic, whatever the resulting economic cost could be. First publications focus on disease characteristics, on disease infectivity, on available treatments, on ICU medical care, on lockdown but not on medical countermeasure simulation. In order to fill this gap, we propose a flow model, which calculates by period the people in different disease stages and under medical treatments and which propagates flow of people between periods. We use a discrete representation of the SIR model over a horizon of six months. Cplex solver has been chosen as a simulator.

Keywords: Operational research for healthcare, compartmental models, linear programming, COVID-19 countermeasures.

1. Introduction

Our human community faces a pandemic, which has lead us to lockdown half of world inhabitants. We are very disarmed to deal with the coronavirus (SARS-CoV-2) and lockdown seems the only countermeasure suitable to stop the pandemic, whatever the resulting economic cost could be. First publications focus on disease characteristics (Cheng et al., 2020; Van der Werf and Peltekian, 2020; Wang et al., 2020), on disease infectivity (Liu Y. et al., 2020; Rocklöv et al, 2020; Yuan et al., 2020), on available first intention treatments (Chen et al., 2020; Gautret et al., 2020; HCSP, 2020), on ICU medical care (Azoulay et al., 2020, Darmon et al., 2020; Ministère de la Santé, 2020; Schultz et al., 2020) and on lockdown (Gram Pedersen and Meneghin, 2020; Rocklöv et al., 2020). We have not found papers dealing with COVID-19 simulation in order to evaluate and size medical countermeasures.

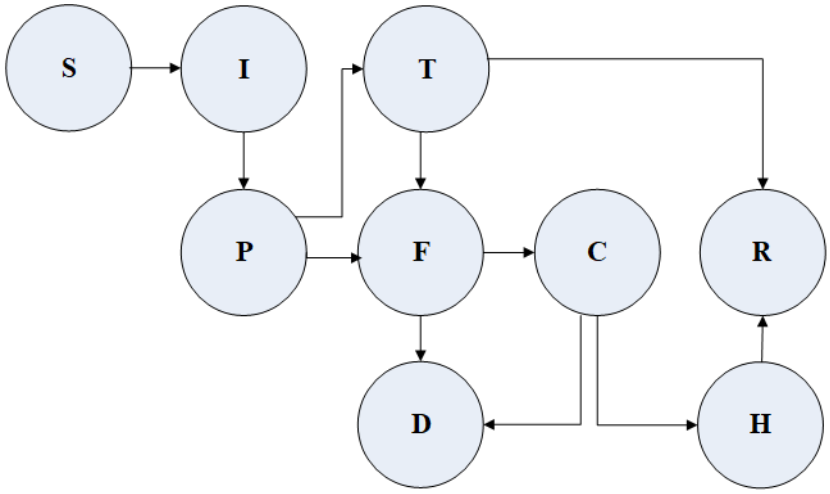
The SIR (Susceptible-Infectious-Recovered) model is known as a compartmental model in epidemiology. The SIR model, in the basic case, stratifies the population into three health status: susceptible to the disease (denoted by S), infected by the disease (denoted by I), and removed from the disease (denoted by R). In lot of literature cases, the infected people will be divided into several stages, such as (Latent i.e. without symptoms, Prodromal i.e. with symptoms and Fulminant i.e. severe/deteriorated state) (Guinet et al., 2018; Perra and Conçalves, 2015). In order to simulate an epidemic, we use it as a flow model, calculating by period the people in different disease stages and under medical treatments, and propagating flow of people between periods. We use a discrete representation of the SIR model over a horizon of daily periods. When the disease is not transmitted directly from person to person (such as a poisoning) or when the infection rate is constant over a whole population (seasonal flu), the SIR model can be linearized (Guinet et al., 2018; Liu M. et al., 2019). The transmission rate between S and I, is assumed constant and the propagation of flow from S to I can be a function of S only.

Perra and Gonçalves (2015) suggest to calculate roughly the propagation rate β from S to I according to the function taking into account demography such as λ = β * I where λ is the force of infection. This latter is equal to the probability to be infected multiply by the number of contacts. Knowing, the basic reproduction number R0 (Guerra et al., 2017) which is equal to the probability to be infected multiply by the number of contacts multiply by the duration of infectivity D, together with I the number of infected people, we can calculate the propagation rate β. The number of infected people supposes to know the symptomatic and asymptomatic cases.

In the case of the Diamond Princess Cruise ship which has been infected by a single COVID-19 case, all passengers have been tested for the disease, so symptomatic cases and the asymptomatic cases are known (Mizumoto and Chowell, 2020, Rocklöv et al., 2020). However, the population living on the ship is more homogenous, compared to the more spatially variable population in Wuhan or in France. Thanks to Rocklöv et al. (2020), the basic reproduction number R0 of the disease is available. So β = (R0) / (D * I). The I number can be seen as a scale factor. Moreover, the passengers of the Diamond Princess Cruise ship have been lockdown on ship in order to stop the disease decreasing the number of people infected by infected people i.e. lowering the basic reproduction number R0.

2 An extension of the SIR model

2.1 The compartmental model



In the figure above, an individual appears first in the susceptible state (S). He goes to the infected state if he acquires the disease (I). If symptoms appear, he reaches the prodomal state (P). If treatments are available, he receives a first intention treatment in hospital (T). In absence of treatment or if the treatment fails, the patient goes to the fulminant state (F). Next, he can be admitted in an available intensive care bed (C). Finally, either he is healed (R) after a hospitalization stay in medicine (H), or he died (D).

2.2 The stages

- S for susceptible, i.e. patients who can be infected,
- I for infected, i.e. patients who have the covid-19 illness, for R0 = 4.8 i.e. without lockdown (Roques et al., 2020), R1=1.78 i.e. with lockdown (Rocklöv et al., 2020), D = 20 (Roques et al., 2020) and I = 621 (Mizumoto and Chowell, 2020), the transition rates from S to I are β0 = 4.8/(20*621) ≈ 0,0386% and β1 =

1.78/(20*621) ≈ 0,0143% respectively,

- P for prodomal, i.e. infected patients who develop symptoms within an average range of 6 days (Yuan et al., 2020), the transition rate from I to P is equal to 30% (Darmon et al., 2020; Mizumoto and Chowell, 2020; Rocklöv et al., 2020),
- T patients with the first-line treatment (antiviral, anti-inflammatory, antibiotic treatments) (Chen et al., 2020; Gautret et al., 2020; HCSP, 2020), i.e. prodomal patients treated as soon as symptoms appear and during 10 days (Darmon et al., 2020),
- F for fulminant, i.e. infected patients with acute respiratory distress which have been hospitalized in an emergency department and who wait for an intensive care bed thanks to mechanical ventilation ; prodomal patients turn into fulminant patient if untreated with first-line treatment ; failed patients with first-line treatment become fulminant with a rate equal to 21% (Santé Publique France, 2020; Chen et al., 2020; Gautret et al., 2020),
- C fulminant patients admitted to ICU cares during 14 days, i.e. fulminant patients who have found an ICU bed (Ministère de la Santé, 2020),
- H hospitalized patients from ICU during 10 other days of hospitalization or for a first line treatment (Ministère de la Santé, 2020),
- D for dead, i.e. fulminant patients who have not found an ICU bed (100%) (Annane et al., 2012) or dead in an ICU bed (37%) (Ministère de la Santé, 2020).
- R for recovered patient from the first line treatment and ICU stay.

3. A linear simulation model

3.1 Data

- Nbstat: number of patient states, 9 states have been defined (S for susceptible, I for infected, P for prodromal, T for cured with a first intension treatment, F for fulminant, C for hospitalized in ICU, H for hospitalized in medicine, R for healed, D for dead),
- Nper: number of periods in days (a horizon of 180 days is studied),
- Nepat: number of people susceptible to be infected i.e. the French population or AURA Region population,
- Irat: infection rate, i.e. percentage of susceptible people infected without lockdown i.e. 0,0386%,
- Icnf: infection rate, i.e. percentage of susceptible people infected with lockdown i.e. 0,0143%,
- Prat: prodromal rate, i.e. percent of people developing symptoms, 30%,
- Frat: failure rate of the first intention treatment, 21%,
- Crat: failure rate of ICU treatment, 37%,
- Drat: death rate, i.e. percent of people who died waiting ICU cares, 100%,
- Canti: cost for first intention treatment medication in a hospital per day, 1200€,
- Cicu: cost of patient admission in ICU, 2300€,
- Hlife: human life cost estimation regarding legal indemnity in France for a 65 old victim, i.e. 300 000€ according to ONIAM (https://www.oniam.fr/procedure-indemnisation/bareme-indemnisation) a human life cost allows us to avoid a multi-criteria optimization,
- Nbed: number of ICU beds which are available to receive sick people,
- Nmed: number of places which are available to receive sick people in medicine departments,
- CHdose: number of first intention treatments available,
- Cdet: period when the lockdown begins,
- Pdet: period when the epidemic is ended (seasonal characteristic),
- Alos: length of hospitalization in a medicine department for first intention treatment, i.e. 10 days,

- Ilos: length of hospitalization in ICU, i.e. 14 days,
- Hlos: length of hospitalization in a medicine department after ICU, i.e. 10 days
- Lin: length of incubation, i.e. 6 days.

3.2 Variables

- EVs(p): Number of persons who evolve to state s = {S,I,P,T,F,C,H,D,R} during period p.

3.3 Objective Function

$$Minimize\ (Z) = \sum_{p=1}^{Nper} EVD(p) * Hlife + \sum_{p=1}^{Nper} EVC(p) * Cicu * Ilos + \sum_{p=1}^{Nper} EVT(p) * Canti * Alos + \sum_{p=1}^{Nper} EVH(p) * Canti * Hlos \quad (1)$$

3.4 Constraints

$$EVS(1) = Nepat \quad (2)$$
$$EVS(p) = EVS(p-1) * (1 - Irat) \quad p = 2, \dots, Cdet - 1 \quad (2bis)$$
$$EVS(p) = EVS(p-1) * (1 - Icnf) \quad p = Cdet, \dots, Pdet \quad (2ter)$$
$$EVS(p) = 0 \quad p = Pdet + 1, \dots, Nper \quad (2quar)$$

People can be infected from the first period to the ending period of the epidemic (state S).

$$EVI(p) = 0 \quad p = 1, \dots, Lin \quad (3)$$
$$EVI(p) = EVS(p - lin) * Irat \quad p = Lin + 1, \dots, Cdet - 1 \quad (3bis)$$
$$EVI(p) = EVS(p - lin) * Icnf \quad p = Cdet, \dots, Nper \quad (3ter)$$

People in contact are infected and are symptomatic or asymptomatic after Lin days of incubation (state I). Infection rates depend on countermeasures.

$$EVP(p) = 0 \quad p = 1, \dots, Lin \quad (4)$$
$$EVP(p) = EVI(p-1) * Prat - EVT(p-1) \quad p = Lin + 1, \dots, Nper \quad (4bis)$$

Only a part of people develops symptoms (state P). First intention treatments are administrated as soon as symptoms appear (state T).

$$EVT(p) = 0 \quad p = 1, \dots, Lin \quad (5)$$
$$\sum_{p=Lin}^{Nper} EVT(p) \leq CHdose \quad (5bis)$$

The number of first intention treatments is limited.

$$EVF(p) = 0 \quad p = 1, \dots, Lin \quad (6)$$
$$EVF(p) = EVF(p-1) * (1 - Drat) + EVP(p-1) - EVC(p-1) \quad p = Lin + 1, \dots, Lin + Alos \quad (6bis)$$
$$EVFp = EVF(p-1) * (1 - Drat) + EVP(p-1) - EVC(p-1) + EVT(p-1) * Frat \quad p = Lin + Alos + 1, \dots, Nper \quad (6ter)$$

After Lin days of incubation and without treatment, patients wait for hospitalization in ICU units (state F), part of them are admitted (state C) and part of them begin to die. Failed patients with first-line treatment also become fulminant.

$$EVC(p) = 0 \quad p = 1, \dots, Lin \quad (7)$$
$$\sum_{q=p}^{p+Ilos-1} EVC(q) \leq Nbed \quad p = 1, \dots, Nper - Ilos + 1 \quad (7bis)$$
The number of ICU beds is limited for each period. Patients admitted in ICU from period p to (p+ILos-1) will occupy a bed for the Ilos periods, related to the length of stay. Beds' capacities must be verified for each Ilos value.

$$EVH(p) = 0 \quad p = 1, \dots, Lin + Ilos - 1 \quad (8)$$
$$EVH(p + Ilos) = EVC(p) * (1 - Crat) \quad p = Lin, \dots, Nper - Ilos \quad (8bis)$$
Medicine care stay follows ICU stay in the hospital (state H) Ilos periods later.

$$\sum_{q=p}^{p+Hlos-1} EVH(q) + \sum_{q=p}^{P+Alos-1} EVT(q) \leq Nmed \quad p = Lin, \dots, Nper - Max[Hlos, Alos] + 1 \quad (9)$$
The number of medicine places is limited and they are used for a defined length of stay. We calculate the number of patients from period p to period (p+Hlos-1) or (P+Alos).

$$EVD(p) = 0 \quad p = 1, \dots, Lin \quad (10)$$
$$EVD(p) = EVF(p-1) * Drat + EVC(p-1) * Crat \quad p = Lin, \dots, Nper \quad (10bis)$$
Non-treated people and failed ICU patients die (state D).

$$EVR(p) = 0 \quad p = 1, \dots, Lin \quad (11)$$
$$EVR(p) = EVI(p-1) * (1 - Prat) \quad p = Lin + 1, \dots, Lin + Alos \quad (11bis)$$
$$EVR(p) = EVI(p-1) * (1 - Prat) + EVT(p - Alos) * (1 - Frat) \quad p = Lin + Alos + 1, \dots, Lin + Min(Alos, Hlos) + Ilos \quad (11ter)$$
$$EVR(p) = EVI(p-1) * (1 - Prat) + EVT(p - Alos) * (1 - Frat) + EVC(p - Ilos - Hlos) * (1 - Crat) \quad p = Lin + Min(Alos, Hlos) + Ilos + 1, \dots, Nper \quad (11quar)$$
Recovered people are asymptomatic people plus cured patients with first line or ICU treatment (state R).

4. Results

We study the period from the February 23 to May 23, i.e. a horizon of 90 days. The population lockdown begins on March 17, i.e. on day 22. Problems are solved with Cplex (https://www.ibm.com/search?lang=en&cc=us&q=Cplex). Model parameters are defined in an Excel sheet (see Figure 1) and results are written in another Excel sheet. Lockdown countermeasures compared with efficient first line treatments are simulated.

Studied population:	65000000		End of infection period:	90
Reference of infected population for R0:	621		Lockdown start period:	22
Strength of infection without lockdown:	0,24		Number of beds available in Intensive Care Units:	15000
Strength of infection with lockdown:	0,09		Number of beds available in Hospital:	150000
Prodromal rate:	0,30			
Therapeutic failure rate under treatment	0,21		Incubation time:	5
Case fatality rate with resuscitation:	0,37		Duration of first-line therapeutic treatment:	10
Case fatality rate without resuscitation:	1,00		Length of stay in Intensive Care Unit:	14
			Length of stay in medicine:	10
Compensation cost for death:	300 000 €			
Hospitalization cost in Intensive Care Unit:	2 300 €		Number of antibiotic or antiviral treatments available…:	1000000
Hospitalization cost in medicine:	1 200 €			
Cost of antibiotic or antiviral treatment:	1 200 €			

Figure 1: Excel sheet for CPEX model parameters

Scenarios for France (65 Millions of inhabitants)	Number of infected people	Number of people on treatment	Number of people in ICU	Number of deaths	Number of healings	Medical and compensation costs in K€
With lockdown (Frat = 0,21)	1 065 949	319 785	60 054	29 320	1 036 629	15 021 423
With lockdown and efficient first line treatment (Frat = 0,05)	1 065 949	319 785	15 989	5 916	1 060 033	6 247 955
Without lockdown (Cdet = Pdet)	2 115 408	634 622	93 406	74 425	2 040 983	33 656 811
Without lockdown and with efficient first line treatment	2 115 408	634 622	31 731	11 741	2 103 667	12 399 250

Table 1: Scenario Results for France

Scenarios for AURA Region (8 Millions of inhabitants)	Number of infected people	Number of people on treatment	Number of people in ICU	Number of deaths	Number of healings	Medical and compensation costs in K€
With lockdown (Frat = 0,21)	131 194	39 358	8 265	3 058	128 136	1 718 360
With lockdown and efficient first line treatment (Frat = 0,05)	131 194	39 358	1 968	728	130 466	768 979
Without lockdown (Frat = 0,21)	260 358	78 107	16 403	6 069	254 289	3 410 136
Without lockdown (F and efficient first line treatment rat = 0,05)	260 358	78 107	3 905	1 445	258 913	1 526 061

Table 2: Scenario Results for AURA Region

Regarding victims, our results approximate quite well the reality (28 367 deaths on May 24 for France and 2 702 deaths on May 14 for AuRA Region), which has been very globally approximated (see Tables 1 and 2). An efficient first line treatment seems to be the best countermeasure to fight the pandemic of COVID-19 decreasing drastically the number of dead peoples i.e. by 5. Furthermore, lockdown of inhabitants is also a simple and good countermeasure to reduce by 2 the number of epidemic victims. Regarding the use of intensive care beds, an efficient first line treatment is the most powerful countermeasure to reduce by 3 the medical resource intensity.

The computation times are around 3 seconds for each scenario. The Cplex model is available on demand.

5. Conclusion

We have studied the health countermeasure chosen by half of countries over the world to face the COVID-19 pandemic. Population lockdown seems to be the most powerful action in the absence of an efficient treatment such as a viral treatment or vaccine. In France, population lockdown has not had exactly the same impact for the whole country and the AURA Region. In the case of a second pandemic wave, dedicated lockdowns per Regions could be more suitable.

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