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Different approaches to epidemic modeling – The Covid-19 case study

Davide Manca

PSE-Lab, Process Systems Engineering Laboratory, Dipartimento di Chimica, Materiali e Ingegneria Chimica “Giulio Natta”, Politecnico di Milano, Piazza Leonardo da Vinci 32, 20133 Milano, Italy
davide.manca@polimi.it

Abstract
The paper focuses on three different modeling approaches to describe the dynamic evolution of an epidemic. These models have been extensively tested in the field and applied to Italy, one of the countries that most suffered from Covid-19.

Keywords: Covid-19, pandemic, modeling, early-warning, vaccination policies.

1. Introduction
Covid-19 pandemic with its prolonged and iterated waves has caused emergencies at the hospital and political levels calling for responsible and prompt decisions. The “every day counts” saying is meaningful when one has to make choices and resolutions that have an impact on human lives. At the very beginning of Covid-19, there was no knowledge of the outbreak dynamics and rather simple questions about the expected allocation of resources for hospital wards and intensive care units (ICU) were difficult to answer. If one was able to answer those questions, the replies shocked both medical doctors and general managers of hospitals because the exponential growth of the pandemic phenomenon had never been experienced before in most continents of the world. The doubling time of infected, hospitalized, intubated, and dead individuals were unprecedented and often as short as two-three days.

Similar questions about the time evolution and intensity of the outbreaks were raised by local and central government representatives who were interested in making timely decisions to contain the spreading and relieve the pressure on all the organs responsible for the health and safety of citizens. Finally, the world of information focused most of its attention on the pandemic and on any news capable of predicting, quantifying, and assessing fragments of the whole framework. Mass media urged insistently on ever updated and critically analyzed pandemic data.

Most of the questions focused on what-if scenarios and resource allocation, pressure, and duration. The queries were first formulated for short-term horizons but quickly expanded towards medium- and long-term perspectives. The short-term horizon involved decisions for the allocation of hospital resources such as beds, wards, resuscitation personnel, and scarce material. The medium-term horizon called for decisions about non-pharmaceutical protective actions such as masks, swabs, social distancing, and lockdowns. These decisions had to find a balance between health/safety/treatment and economy/security/freedom of the population. Finally, both hospitals and governments called for a quantitative prediction of the pandemic on a long-term horizon to psychologically start seeing the light at the end of the tunnel (i.e. hope, perseverance, and resilience), to dynamically (re)allocate hospital means to elective medicine rather than...
emergency treatments, and to loosen the strict lockdown rules in favor of a progressive return to normality. In the meanwhile, there were new requests for a quantitative prediction of pandemic-related themes when the first wave came almost to an end but suddenly a second outbreak caught most of the countries unprepared. Afterward, there have been further pandemic waves and some nations have experienced the fourth and fifth waves with the onset of new virus variants. What it was deemed to be understood became suddenly new and unknown. The lessons learned were no more sufficient and a new call for quantifying the ever-changing and multifaceted pandemic became evident and compelling. In the meanwhile, the first vaccines were released. Initially, for several months, the doses were few and the fragile population was exposed to more infectious and lethal virus variants (e.g., alpha, beta, delta, omicron to cite the most circulated). The vaccination problem was hyper-constrained as several categories claimed the right to be vaccinated first and every government adopted different sanitary policies. These governments chose different criteria to vaccinate the population and to inject the vaccine with different time intervals between doses. There was a new call for understanding the optimal vaccination policy and finding a suitable compromise between population coverage in number and category to reduce both the overall pandemic risk and mortality, as well as achieve more robust sanitary and public force systems. The paper shows how the PSE community with its tools, algorithms, models, and methods can cover, analyze, and quantify the different topics and issues that were listed above.

2. Short-term pandemic models

At the very beginning of the Covid-19 outbreak, the hospital heads of resuscitation wards were overwhelmed by SARS-CoV-2. The most stringent resource in hospitals was ICU beds. Resuscitation heads had often to double and even increase three-, four-, five-folds the number of beds in a few days alongside the resources connected (e.g., air-breathing lines, respiratory devices, monitors, space allocation, dirty and clean areas/paths). Human resources were the determining step, which called for specialized ICU doctors and nurses. Indeed, these specialized operators can be neither increased nor hired in the characteristic time of an epidemic. It calls for years of planning and formation. Regarding the dynamics of Covid-19 ICU beds, they start from zero at the very beginning of an epidemic (or from a positive known value in case of subsequent waves) and they increase steadily up to a maximum value. In the following, the ICU wards begin emptying and they reach either a final null value at the end of the epidemic or a minimum nonzero plateau before a new outbreak triggers the inversion of deflation with a new inflation trend. Similar qualitative behavior occurs also for daily positives, hospitalized, healed, and dead. Conversely, the total cumulated values of those quantities are curves that are monotonically increasing and reach either temporary or permanent plateaus between two waves or at the end of the epidemic respectively. Manca et al. (2020) proposed three different curves that describe the inflation trend of a pandemic wave: the exponential, the logistic, and the Gompertz functions (Eq.s 1-3). The mathematical description of the exponential model is:

\[ y = a 10^{bt} \]  
\[ y = \frac{a}{1 + b \exp(-ct)} = \frac{a}{1 + b e^{-ct}} \]  
\[ y = a \exp(-b \exp(-ct)) = a e^{-be^{-ct}} \]
The adaptive parameters of Eq.s 1-3 can be evaluated through a nonlinear regression of real values that are periodically measured at both regional and national levels. For the sake of clarity, the logistic curve performs comparably and sometimes worse than the Gompertz model, which is the preferred one. Equally, the exponential model is very compact and effective at the very beginning of each outbreak but it soon overpredicts the epidemic dynamics. Hence, Gompertz is the most robust model and its analytical features allow also evaluating the inflection point, \( t_{\text{infl}} = \ln(b)/c \), and the halfway point, \( t_{\text{halfway}} = -\ln(\ln(2)/b)/c \). In addition, \( a \) is the asymptote of the dynamic inflation phenomenon. Once the plateau is reached, the curve starts decreasing and the reverse Gompertz function (Eq. 4) describes the deflation region:

\[
y = a \left( 1 - e^{-b e^{-c(t-t_0)}} \right)
\]  

(4)

Equally, the around-the-maximum period is well described by Eq. 5 which is an exponentially modified Gaussian (EMG) curve:

\[
y = 10^{at^2 + bt + c}
\]  

(5)

Figure 1 shows the typical dynamic behavior of both direct/reverse logistic and Gompertz functions, and the EMG curve for the ICU patients of Lombardy (the most populated region of Italy with over 10 million citizens) during the first pandemic wave.

**Figure 1: ICU patients in Lombardy and parametric models during the first Covid-19 wave.**

### 3. Medium-term pandemic models

Another family of epidemic models can describe the contagion dynamics on a medium-term horizon. These models are based on interconnected compartments that summarize the condition of individuals in a given population. The simplest compartmental model for
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an outbreak is the SIR model that is based on three compartments (susceptibles, infected, and removed) that describe the evolution of a population plagued by the epidemic. The population features \( N \) individuals, whose number is assumed constant (this hypothesis holds if \( N \) is sufficiently large and one assumes that the number of newborns equals that of fatalities and the prediction horizon is not too prolonged). Initially, \( N - 1 \) individuals are susceptible (i.e. they belong to the \( S \) compartment of those vulnerable to the virus) and one person is infected and belongs to the \( I \) compartment of those who can transmit the contagion with a reproduction number, \( \beta \). Once an infected individual either recovers or dies, they move to the \( R \) compartment, with a rate proportional to \( \gamma \). Eq. 6 summarizes the SIR model based on an ordinary differential system with suitable initial conditions:

\[
\begin{align*}
\frac{dS}{dt} &= -\beta \frac{I}{N} S \\
\frac{dI}{dt} &= \beta \frac{I}{N} S - \gamma I \\
\frac{dR}{dt} &= \gamma I
\end{align*}
\]  

(6)

The adaptive parameters of the model \( (\beta, \gamma) \) can be identified by a nonlinear regression that minimizes the distance between the real data and the model predictions. The continuing availability of periodically measured real data allows improving the quality of the model and better predicting the dynamics of the pandemic. The complexity of the SIR model can be increased (Giordano et al., 2020) by introducing further compartments (e.g., those infected but not yet contagious, those who died) or contributions (those who have recovered but may lose their immunity and move back to the susceptible compartment). The adaptive parameters may change in time according to virus mutations, improved capacity of treating the infection, and different behavior of the population induced by nonpharmaceutical measures such as lockdowns, curfews, and social distancing. For the sake of simplicity, Eq. 7 shows some modifications to the adaptive parameters that account for lockdown measures and modification of the healing rate. These modifications call for the evaluation of additional adaptive parameters that pave the way to further simulations of what-if scenarios in case of government decisions such as nonpharmaceutical interventions.

\[
\begin{align*}
\beta(t) &= \begin{cases} 
\beta_0, & t < t_{\text{lockdown}} \\
\beta_0 \exp\left(-\frac{t-t_{\text{lockdown}}}{\tau_\beta}\right) & \text{otherwise}
\end{cases} \\
\gamma(t) &= \gamma_0 + \frac{\gamma_1}{1 + \exp(-t + \tau_\gamma)}
\end{align*}
\]  

(7)

Compartmental models can be effective in predicting the expected dynamics of an epidemic. The so-called parametric runs allow quantifying the effect of different measures on the outcomes in terms of infected, recovered, and fatalities. Understanding the role played by adaptive parameters enhances the quality of decision-making aimed at prompt and effective resolutions for the health safety of citizens. Equally, compartmental models do not show a high degree of precision, rather they indicate the trend of the epidemic. However, their predictive capability usually increases towards the end of an outbreak once a good amount of real data allows refining the adaptive parameters.

A further differential equation can account for the vaccination of the population, which for most of the industrialized countries started in the middle of the second/third Covid-19 pandemic wave: \( \frac{dV}{dt} = V_\circ M \). The first differential equation of system (6) must be modified accordingly to account for the individuals that once vaccinated are assumed not to be susceptible anymore and therefore neither recover nor die but move directly to the \( V \) compartment: \( \frac{dS}{dt} = -\beta S \cdot I / N - V_d M \). \( V_d \) is the vaccination rate and \( M \) is the
fraction of individuals who were not infected and are vaccinated. $V_d$ is a dynamic input value that measures the capacity of the system (either regional or national) to daily inject the vaccine and decrease (after one or two doses) the number of susceptible individuals (Figure 2). Again, the model can be improved by removing some oversimplifications and accounting for reinfections and partial protection from infection as a function of the number of doses and vaccine maker. Parametric runs can quantify the effect of increasing the rate of vaccination and population coverage by computing the number of saved lives.

Figure 2: SIRDV model based on susceptible, infected, recovered, dead, and vaccinated compartments. The immune diagram collects both recovered and vaccinated individuals. Italy, third Covid-19 wave.

4. **Long term predictions**

Equations (2-5) can be extrapolated to long-term horizons to determine when the asymptotic condition for a maximum or minimum plateau is reached. Equally, it is possible to determine the time taken to reach and overtake a given threshold for both the inflation and deflation phases. These last bits of information are valuable when hospital managers have to either prepare for emergencies (during the inflation period) or progressively allocate resources to return to elective medicine (during the deflation period). Likewise, Equation (6) allows evaluating the asymptotic condition for rather long integration times. However, the user should be aware of the risks connected to the extrapolation of long-term models that depend heavily on adaptive parameters.

5. **Alternative vaccination policies**

In the case of a vaccination campaign against an epidemic, initially, the available doses are limited and a suitable vaccination policy should be chosen and implemented. The most effective indicator to account for is the number of fatalities. If the decision-makers try to minimize the fatalities toll then the pressure on the limiting resources of hospitals such as ICU beds and Covid-19 wards gets relieved and both medical doctors and nurses can cure the patients more efficiently, which results in a synergistic reduction of mortality. In the case of Italy, the first available doses (January 2021) were reasonably administered
to high-priority categories (such as hospital operators, health doctors, and fragile subjects). Nonetheless, it is well-known that Covid-19 mortality follows a monotonically increasing curve with age. In Italy, almost 99% of the officially documented 133,000+ victims of Covid-19 (as of November 2021) were people aged 50 and older. Unfortunately, the following doses did not strictly respect a reverse-order of age policy aimed at minimizing the fatalities. There were some diversions to lower priority categories that, thanks to their health status and age, were less exposed to either serious or fatal consequences (e.g., school and university personnel, armed forces, lawyers, scientific informants, social workers, customs and airport personnel, and funeral home staff).

An in silico vaccination simulator can quantify the difference between real fatalities and what might happen if an alternative vaccination procedure were adopted. That simulator relies on the immunization degree after injection (Creech et al., 2021) and the death distribution curve, which both allow assessing the expected number of saved lives. After having covered the high-priority categories, if one implements a rigid approach to vaccination based on the reverse order of age ranges (i.e. the elderly first, the young last) every dose can be injected to individuals in the following decreasing sequence of 90+, 80-89, 70-79, 60-69, 50-59, 40-49, 30-39, 20-29, and 12-19 years old. The rate of injected doses is available daily and the optimal reallocation of doses allows evaluating the number of lives that would be saved. In addition, the simulator can solve what-if scenarios such as what would happen if (i) the daily delivered doses increased by some percent, or (ii) the vaccination campaign to the elderly were anticipated of a few days, or (iii) some doses were diverted from lower priority categories to the elderly, or (iv) the interval between first and second dose were increased or decreased. Table 1 reports some results of different vaccination policies on the expected number of saved lives.

Table 1: Saved lives in Italy by alternative vaccination policies. Rows report the expected saved lives under the hypothesis of administering the same amount (100%) or 10% and 20% more daily doses than those injected in reality. The columns report the calculated saved lives under the three hypotheses of 0, 10, and 20 days anticipation with respect to reality (which started on 18-Feb-2021). The numbers in brackets quantify the increase over the basic case study of 18-Feb at 100% administrations. The assessment was carried out at the end of May 2021.

| Saved lives – ITALY | Start on 18-Feb-2021 | Start 10 days before | Start 20 days before |
|---------------------|----------------------|----------------------|----------------------|
| 100% of the real administrations | 3969 | 4465 (+12.50%) | 5317 (+33.96%) |
| 110% of the real administrations | 4905 (+23.58%) | 5414 (+36.41%) | 6311 (+59.01%) |
| 120% of the real administrations | 5712 (+43.92%) | 6245 (+57.34%) | 7083 (+78.46%) |

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