Original Article

COVID-19 epidemic:
Comparison of three European countries with different outcome using Gompertz function method

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- Gompertz function
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ABSTRACT
BACKGROUND: COVID-19 has shocked the world and fully alerted scientific community against means to tackle the pandemic. The current work tries to assess the impact of COVID-19 in three European countries and evaluate the outcome using Gombertz function methods. **METHODS:** Daily mortality data were collected and analyzed from European Centre for Disease Prevention and Control for Greece, France, and Italy. **RESULTS:** The results show a good fit between the observed data and those obtained by the Gompertz function methods for the three countries. Using standardization methods for population incidence parameters for comparison, Greece, France, and Italy show substantial differences among disease dynamics regarding incidence and mortality rates as well as disease doubling times. **CONCLUSIONS:** The availability of daily epidemiological data about confirmed cases gives opportunities for research contributions through mathematical models, such as Gombertz, regarding comparison and analysis of COVID-19 dynamics and future trends among regions and countries.
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INTRODUCTION

The pandemic due to SARS-CoV-2 (severe acute respiratory syndrome coronavirus -2)and the corona virus disease 2019 (COVID-19)is associated -as this manuscript is prepared- with more than 580.000 deaths globally since its appearance and has shocked the world due to the extreme measures taken worldwide to contain it. Initiated from China and the province of Wuhan in late 2019 it spread worldwide with high morbidity and mortality impact, especially in European countries and USA and currently in South America. The WHO, on 31 January, declared the COVID-19 outbreak a public health emergency of international concern (PHEIC)[1]. The outcome of the still on-going pandemic is not clear with more than 10 million people diagnosed in 196 countries, possible reflecting only a fraction of the true number of infections due to differences in testing policy among countries[2]. Regarding Greece, the first confirmed case recorded at 28 February 2020 and subsequent cases reported in late February and early March. The first death recorded in 12 March and till today 3376 confirmed cases have been recorded with 191 deaths. This resulted in precautionary recommendations that escalated in restrictive lockdown measures on 23 March till 5 of May leading in a remarkable restriction in epidemic morbidity and mortality. However, that was not the case for other European countries, with the characteristic cost in human lives for Italy with more than 240.000 cases resulted I nearly 35.000 deaths, or France with 163.000 confirmed cases and approximately 30.000 deaths. The high incidence rates for Italy lead in total lockdown on 8 March whereas for France it was announced on March 16.

Apart of the quarantine and hygiene measures taken worldwide to contain the spreading of the disease, SARS-CoV2 awakened the scientific community in all medical associated scientific fields, in academia, industry, regulatory and hospital clinics. Efforts for development of successful tests, effective therapies, vaccine and supporting technologies are under progress and several clinical trials registered in WHO are ongoing till today[3]. The continuing research is aiming to provide means for treatment in the current cases but also to prevent recurrence of future disease waves worldwide. In this respect, a key point is the exploitation of epidemiological data regarding frequency measures that analyze the current dynamics of the pandemic, but most importantly, predict future scenarios. The availability of daily data regarding COVID-19 provide means for epidemiological scientists to create analyze and evaluate several scenarios.

Modelling epidemic is a widely accepted method to study its features and to evaluate reasonable epidemiological factors during the infectious disease outbreaks[4]. Important epidemiological parameters, during an outbreak like COVID-19 pandemic, include the final epidemic size, the duration and, some crucial time dimensions such as the turning time point and doubling time[5]. Several methods have been used to describe crucial dynamic dimensions of a pandemic. The Gompertz model was described by Gompertz in 1825 and was used to study the populations' growth. The development of an epidemic infectious diseases has similar characteristics to those of the growth of certain biological systems and populations. In this short report, population morbidity/mortality incidence parameters are presented for the three countries, (Greece, France, and Italy) and furthermore the Gompertz sigmoidal function is employed to analyze and compare the dynamic properties of the COVID-19 pandemic.

MATERIALS AND METHODS

Epidemiological data regarding the latest available public data on COVID-19 were retrieved from the European Centre for Disease Prevention and Control (ECDPC) regarding Greece, Italy and France[6]. The epidemiological data covered a period from February till June 10,2020. Data analysis was implemented through statistical software package Stata 14 (StataCorp. 2019. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP). The study used time series analysis and direct standardization methods for comparison of mortality incidence parameters. The estimation of the doubling time of the disease [doubling time refers to the length of time (days) required for the cumulative confirmed COVID-19 cases to double in size] was explored at three distinct time points: i) the beginning of the outbreak after the day in which cases reached 2 per 10^5 population for each country; ii) the week immediately prior the turning point of the epidemic curve and iii) the week 10 days after this. The Gompertz curve function was used to model the dynamics of the epidemic of the three countries. Generated fitted values were used to predict final epidemic size regarding the total mortality and confirmed cases. Moreover, using the first derivative of cumulative model we estimate the fitted values of the deaths and conformed cases per day to assess the time-dynamics of the outbreak such as the duration and the time turning-point.

RESULTS

Cumulative mortality incidence (per 10^5 population) among several European countries are shown in Figure 1. It is evident that European countries showed different trends that can be stratified in three groups of "low", "medium" and "high" cumulative incidence of mortality per 10^5 of population, with Belgium demonstrating thus far the poorest outcome and the highest incidence of mortality (84 deaths per 10^5 population).Greece demonstrate a "low" value (1.67 per 10^5 population)while Italy had a"high" mortality rate (58 per 10^5 population)and France grouped in "medium" mortality group (43 per 10^5 population) respectively.

Figures 2 (top panel) displays the cumulative number

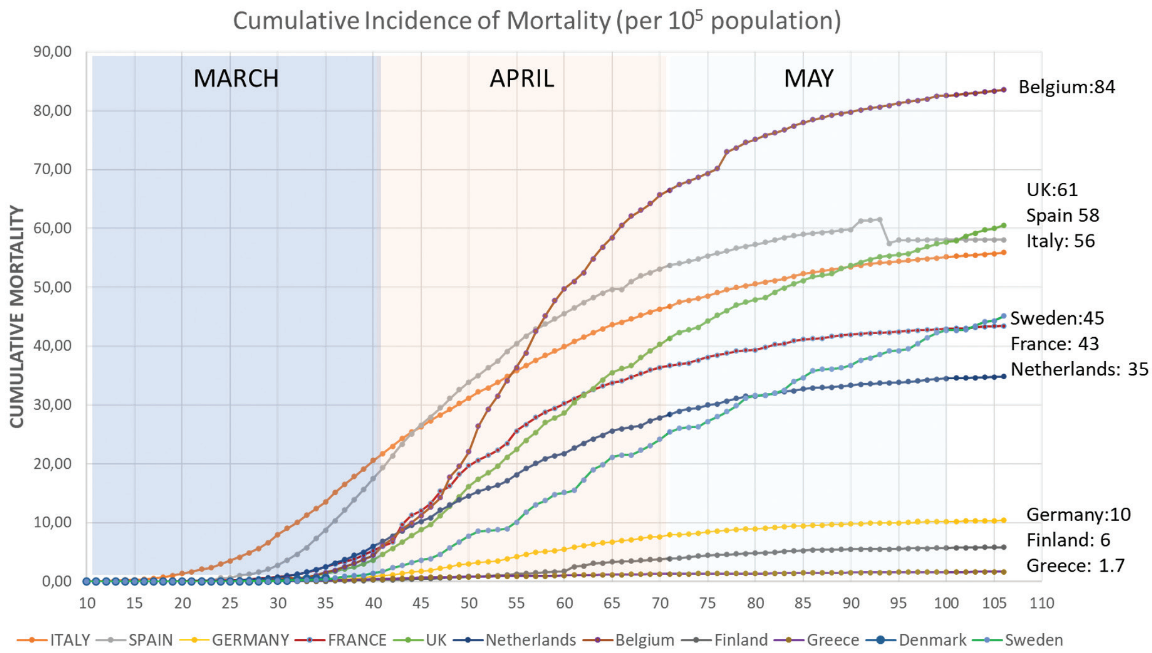

FIGURE 1. Cumulative incidence of mortality among several European countries till June 2020.

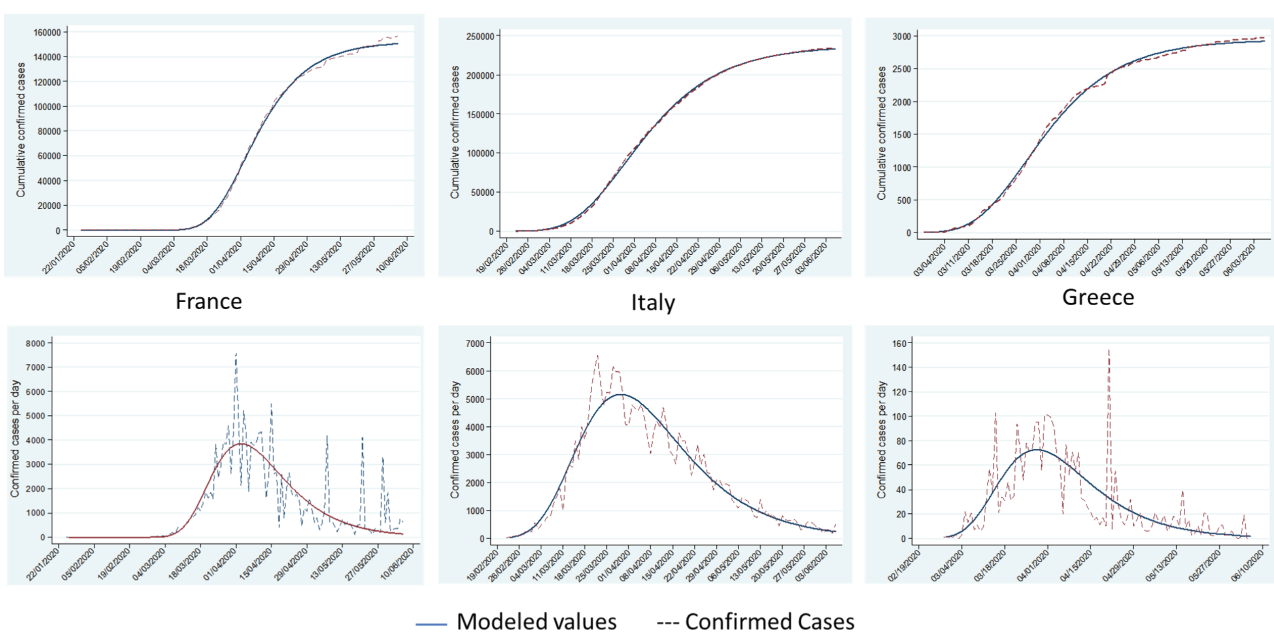

FIGURE 2. Cumulative and daily incidence of cases (per 10^5 population) between Greece, Italy and France (observed and modeled).

of observed infected persons against elapsed time (in day) as well as the daily cases (lower panel)to their fitted values, by country. An exceptionally good fit between observed and modelled data is noticed with r^2: 0.995 for Greece, r^2: 0.9914 for France and r^2: 0.9984 for Italy. The residuals of the fit were low and random(data not shown). Overall, the cumulative number of diagnosed positive cases is particularly large among the population of France and Italy and exceptionally low for Greece. From Figure 2, it is also revealed that the cumulative is flatting,after 84, 96 and 124 days for Greece, Italy, and France, respectively, which is suggesting for these countries that currently epidemic is in retreat. The modeled daily variation of the confirmed cases calculated as the first derivative of the Gompertz curve (which also showed good fit with the actual cases for all 3 countries, Figure 2, lower panel). The daily distribution of the confirmed cases demonstrates a positively skewed bell-shaped curve common for COVID-19 epidemic. However, it is clear that daily distribution of confirmed cases in Greece is flattened and scaled between 0-160 while this not the case for both Italy and France in which the daily number of diagnosed cases scaled between 0-7000.

The doubling time of mortality during the months of lockdown is represented for all three countries in Figure 3. Disease doubling time for Greece at the initiation of the epidemic is predicted approximately in 3.6 days while for Italy and France is 2.2 and 2.3 days respectively (Figure 3). As the epidemic progressed, the week just before the turning time-point, doubling time took longer for the cumulative incidence in all 3 countries, 8.9 days for Greece, 6.6 for Italy, and 5.6 days for France. Finally, a significant increase in the doubling time of mortality was observed during the de-escalated period of the epidemic curve, 59.8, 22.1 and 25.7 for Greece, Italy, and France, respectively. It is evident that for all three cases till March the doubling time remained low whereas in April had tripled and increased tenfold in the last month, indicating a sharp slowdown in the epidemic and a sharp drop in its dynamic which is now in its final slowdown as it is also estimated from the modeled curves (Figure 3).

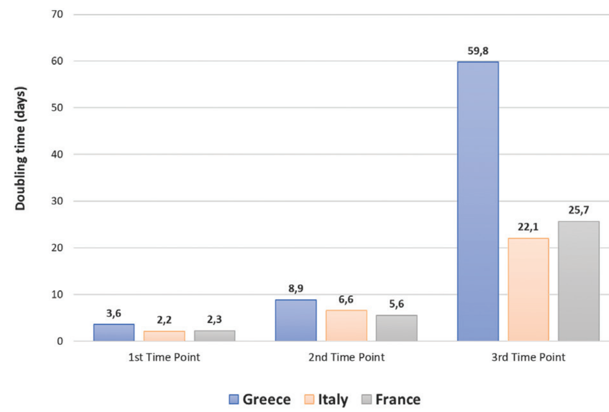

FIGURE 3. Disease doubling time in three different time points.

The corresponding Gompertz curve and the data of total deaths (cumulative mortality) are shown in Figure 4 (top panel) for all 3 countries. Significant differences in the trend of the case fatality rates (CFR) till June 6 are calculated, and were approximately 5.9% for Greece, for Italy around 14.4%, and for France at 18.8%. A decline in the death rate is observed for Greece after the first week of April while for the Italy and France the decline delayed one week more beginning after April 8th and 15th respectively. Figure 4 also shows the daily deaths observed and modeled. A steady increased rate is observed with a characteristic peak at April 3 for France and April 5 for Greece whereas for Italy it is observed around April 10.

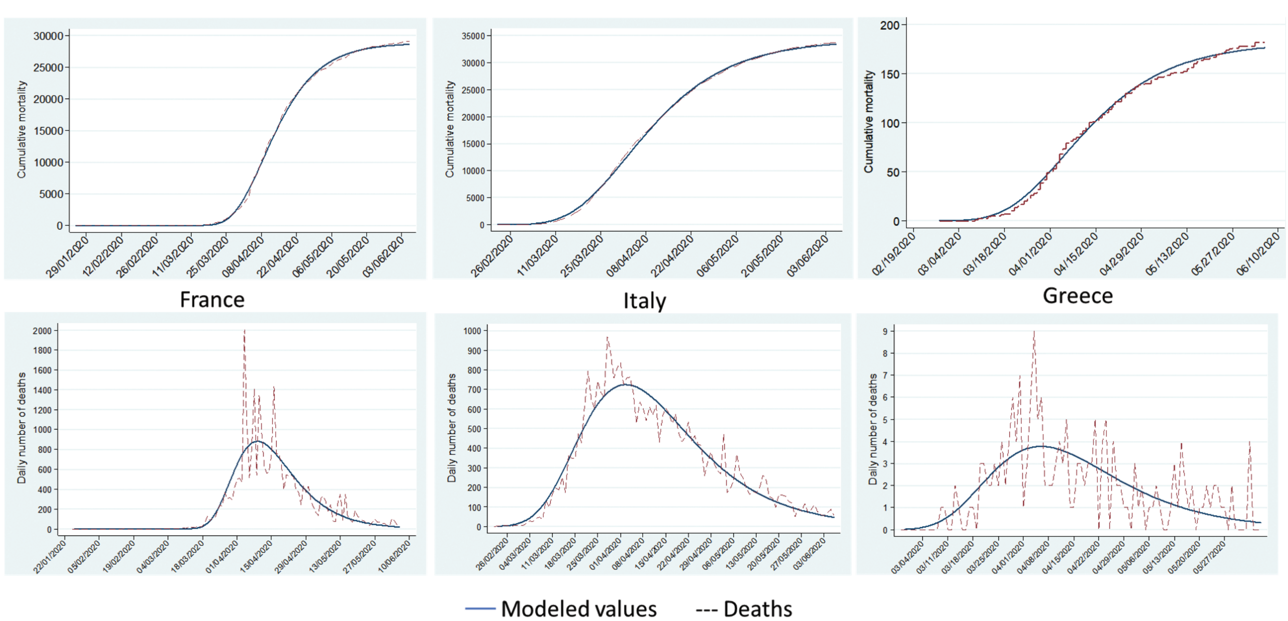

FIGURE 4. Cumulative and daily incidence of deaths between Greece, Italy, and France (observed and modeled).

DISCUSSION

Epidemiological and mathematical models are utilized today to describe and forecast progress of COVID-19 epidemic that could assist in decision making policies to contain the spreading of the disease[7,8]. The implementation of Gombertz, or other logistic models have well-describe the epidemic progress, forecasting that COVID-19 will be in decay, in the countries that was first initiated[9] as a result of the impact of containment and quarantine measures in the epidemic spread of COVID-19[10,11]. Moreover based on the confirmed cases and considering that healthcare policies for containment will stay put, Gombertz and logistic models can be utilized to predict the overall impact of the epidemic during its progression[12]. Utilizing available scientific data from ECDPC, this work tried using Gombertz function to describe the differences observed in Greece, Italy, and France. While, for Italy and France, prior studies tried to assess epidemic data such as infection, recovery, and mortality rates[13], for Greece thus far the implementation of epidemiological models such as Gompertz function methods, to our best knowledge, has not been reported. The precise measurement of the above outbreak parameters helps to understand not only the temporal pattern but also to estimate crucial dynamic features of an outbreak. Moreover, the instantaneous prediction of the epidemic size and growth is important factors especially if it achieved early. This information during an ongoing epidemic -such as COVID-19- could be extremely valuable for prevention and epidemic control[14]. Overall, in this work the utilization of Gombertz curve function allowed to model the dynamics of COVID-19 in the three countries and describe the differences that were observed regarding the incidence and mortality rates that places them in three different categories of "low", "medium", and "high" impact regarding COVID-19 epidemic crisis.

Countries in Europe are lifting restrictive measures in an effort, to return to normalcy thus it is important to assess the dynamics of the COVID-19 pandemic. Under current conditions, analysis of data thus far propose that pandemic wave is near its end. This does not presuppose that its evolution cannot be different from the changes that take place in relation to the end of quarantine measures. Since Europe became the focus of the pandemic wave, generally it followed the time sequence and duration that was initially experienced in China. Regarding its intensity, Greece showed a lower incidence rate compared to other European countries such as Italy or France which suffered from high the attack rates resulted in high mortality and morbidity. This can be attributed to several factors such as lockdown and quarantine actions timely taken and complied from citizens, environmental factors geographical conditions that favor isolation or regional distancing (e.g. islands in Greece vs continental regions in other countries) and other factors all of which will be under investigation in the upcoming years from the scientific community.

CONFLICT OF INTEREST

None.

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ΠΕΡΙΛΗΨΗ

Επιδημία COVID-19: Σύγκριση τριών ευρωπαϊκών χωρών με διαφορετικά αποτελέσματα χρησιμοποιώντας τη συνάρτηση Gombertz

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Πλαίσιο: *Ο COVID-19 έχει συγκλονίσει τον κόσμο και έχει ενεργοποιήσει την επιστημονική κοινότητα για την εξεύρεση μέσων για την αντιμετώπιση της πανδημίας. Η τρέχουσα εργασία προσπαθεί να αξιολογήσει τον αντίκτυπο του COVID-19 σε τρεις ευρωπαϊκές χώρες και να αξιολογήσει το αποτέλεσμα χρησιμοποιώ-*

ντας τα μοντέλα της συνάρτησης Gombertz. ***Μέθοδοι:*** *Συλλέχθηκαν και αναλύθηκαν καθημερινά επιδημιολογικά δεδομένα θνησιμότητας από το Ευρωπαϊκό Κέντρο Πρόληψης και Ελέγχου Νόσων για την Ελλάδα, τη Γαλλία και την Ιταλία.* ***Αποτελέσματα:*** *Τα αποτελέσματα δείχνουν ότι ταιριάζουν μεταξύ των παρατηρούμενων δεδομένων και εκείνων που μοντελοποιούνται μέσω της συνάρτησης Gompertz για τις τρεις χώρες. Χρησιμοποιώντας μεθόδους για τα μέτρα συχνότητας της επιδημιολογικής πορείας της COVID-19 στον πληθυσμό, η Ελλάδα, η Γαλλία και η Ιταλία δείχνουν σημαντικές διαφορές μεταξύ της δυναμικής της νόσου όσον αφορά τα ποσοστά επίπτωσης και θνησιμότητας καθώς και τους χρόνους διπλασιασμού των ασθενειών.* ***Συμπεράσματα:*** *Η διαθεσιμότητα καθημερινών επιδημιολογικών δεδομένων σχετικά με επιβεβαιωμένα κρούσματα της νόσου δίνει ευκαιρίες για ερευνητικές συνεισφορές μέσω μαθηματικών μοντέλων, όπως μέσω της συνάρτησης Gombertz, σχετικά με τη σύγκριση και ανάλυση της δυναμικής του COVID-19 και των μελλοντικών τάσεων εξέλιξης της επιδημίας μεταξύ περιοχών και χωρών.*

Πνεύμων 2020, 33(2):1-6.

Λέξεις - Κλειδιά: *Covid-19, Κορονοϊός, συνάρτηση Gompertz, δυναμικότητα εξέλιξης νοσημάτων*

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