Estimation of the number of preventable COVID-19 deaths in relation to the restrictive measures adopted in Europe

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Abstract

Introduction: In December 2019, a new coronavirus emerged in Wuhan, China, which has become a global health problem. **Objectives:** To estimate how many daily COVID-19 deaths per 100,000 population could have been avoided if each one of five restrictive measures had been implemented at the time the first case was diagnosed, and to estimate a multiple linear regression model predictive of the number of deaths per 100,000 population. **Methods:** A simple linear regression was performed between the days elapsed since the first COVID-19 diagnosed case, implementation of each one of the five restrictive measures carried out by the 39 European studied countries, the number of hospital beds per 1,000 population (independent variables) and the number of COVID-19 deaths per 100,000 population. **Results:** For each day elapsed from the first COVID-19 reported case to the adoption of restrictive measures, between 0.611 ($p = 0.004$) and 1.863 ($p = 0.000$) patients died per 100,000 population, depending on the implemented measure. **Conclusions:** Restrictive measures and social distancing, as well as promptness of their implementation, are necessary for achieving a decrease in COVID-19 infections and mortality.

KEY WORDS: COVID-19. Mortality. Public health. Virus. Prevention and control.

Estimación del número de fallecimientos evitables por COVID-19 en relación con las medidas restrictivas adoptadas en Europa

Resumen

Introducción: En diciembre de 2019 surgió un nuevo coronavirus en Wuhan, China, que se ha convertido en un problema de salud global. **Objetivo:** Estimar cuántos fallecimientos diarios atribuibles a COVID-19 por cada 100 000 habitantes se podrían haber evitado si se hubiese llevado a cabo cada una de las cinco medidas restrictivas al momento del diagnóstico del primer caso, así como estimar un modelo de regresión lineal múltiple predictivo del número de fallecimientos por cada 100 000 habitantes. **Métodos:** Se realizó un modelo de regresión lineal simple entre los días transcurridos desde el primer caso diagnosticado de COVID-19, la implantación de cada una de las cinco medidas llevadas a cabo por los 39 países europeos estudiados, el número de camas hospitalarias por 1000 habitantes (variables independientes) y el número de fallecimientos por COVID-19 por 100 000 habitantes. **Resultados:** Por cada día transcurrido desde el primer caso notificado de COVID-19 hasta la adopción de las medidas restrictivas, fallecieron entre 0.611 ($p = 0.004$) y 1.863 ($p = 0.000$) pacientes por cada 100 000 habitantes, dependiendo de la medida implementada. **Conclusiones:** Las medidas restrictivas y el distanciamiento social, así como la celeridad de su instauración, son necesarios para lograr el descenso del número de contagios de COVID-19 y su mortalidad.

PALABRAS CLAVE: COVID-19. Mortalidad. Salud pública. Virus. Prevención y control.

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Introduction

In December 2019, a new coronavirus emerged in Wuhan, China, which has become a global health problem:¹ SARS-CoV-2, belonging to the same family as SARS and MERS-CoV, all of them responsible for zoonotic infections, the first one, for COVID-19, and the third one, for Middle East respiratory syndrome.²

SARS-CoV-2 is a virus with a positive single-stranded RNA genome of approximately 30 kb, which has 74 to 99 % coincidence with the strands of the pangolin (*Manis javanica*) and horseshoe bat (*Rhinolophus sinicus*) coronaviruses.^{1,3-5} SARS-CoV-2 genome sequences are similar to those of SARS-CoV; however, there are certain differences such as the lack of the coding region for protein 8 in SARS-CoV-2, which might result in lower pathogenesis in comparison with SARS-CoV.⁶

SARS-CoV-2 transmission occurs from person to person through respiratory droplets, which are expelled when an infected person coughs or sneezes. Larger aerosols with higher contagious capacity can be generated in hospitals and closed spaces, where the virus persists for several hours, hence the need to restrict contact between people in order to prevent the spread of the virus.⁷

Objectives

- To estimate how many COVID-19-attributable daily deaths per 100,000 population could have been avoided if each one of the five restrictive measures established by European countries would have been adopted at the time the first case was diagnosed.
- To estimate a multiple linear regression model predictive of the number of COVID-19-attributable deaths per 100,000 population with regard to the five restrictive measures.

Methods

An ecological study was designed in August 2020 involving 39 European countries. The inclusion criterion was having access to the data of all implemented measures that were included in the study. The date of first official COVID-19 diagnosis was established as the starting point⁸, and the number of days from its occurrence to the implementation of the following five measures was quantified:⁹

- Border closure.
- Closure of non-essential business.
- Closure of leisure and hospitality establishments.
- Prohibition of events and concentrations.
- Face-to-face classes suppression.

The rate of COVID-19 deaths per 100,000 population by June 20, 2020 was obtained for each one of the 39 countries,¹⁰ as well as the number of hospital beds per 1,000 population.^{11,12}

Statistical analysis

A simple linear regression model of the relationship between each one of the independent variables (days elapsed from the first case to border closure, days elapsed from the first case to the closure of non-essential business activities, days elapsed from the first case to the closure of leisure and hospitality establishments, days elapsed from the first case to the prohibition of events and concentrations, days elapsed from the first case to face-to-face classes suppression and number of hospital beds per 1000 population) and the dependent variable (rate of COVID-19 deaths per 100,000 population) was constructed in order to know the number of deaths per 100,000 population that could have been avoided each day if the restrictive measures would have been adopted at the time the first case was diagnosed.

On the other hand, a simple linear regression model of the relationship between the rate of COVID-19 deaths and the number of available hospital beds was generated, as well as a multiple linear regression predictive model between the number of deaths per 100,000 population (dependent variable) and the days elapsed from the first case to the prohibition of events and concentrations, given that the World Health Organization indicates that physical distancing and hand hygiene are the best preventive measures.¹³ This model was adjusted for the other independent variables, using the method of best model selection based on all equations. To select the final model, Mallows's Cp criterion was used, with the model with the lowest value being selected.

A level of significance with a p-value < 0.05 and a 95 % confidence index were considered. To externally assess the reliability of the model, prediction loss was evaluated using the shrinkage method, which consists of calculating the difference between the square of the multiple correlation coefficient of the model estimated in the derivation group (R^2) and the square of the simple correlation coefficient

between the predicted value with the estimated model in the derivation group and the dependent variable (Y), calculated in the validation group (r^2). A difference ≤ 0.1 was assumed to be acceptable. Analyses were carried out with the Stata program, version 15.

Results

Table 1 indicates the date the first official COVID-19 diagnosis took place on each one of the 39 analyzed European countries, the days elapsed until the implementation of each one of the five restrictive measures, the number of COVID-19 deaths per 100,000 population and the number of available hospital beds per 1,000 population.

Table 2 shows the b-coefficient obtained after the linear regression between the independent variable and each one of the dependent variables. Each b-coefficient expresses the number of daily deaths per 100,000 population that would have been avoided if each preventive measure would have been adopted on the day of the first COVID-19 diagnosis.

Table 3 describes the variables included in the predictive model, as well as their 95 % confidence intervals and p-value. Mallows's Cp value was 3.04, adjusted R^2 value was 0.538, and the prediction loss value (difference between R^2 and r^2 or shrinkage) was -1.209×10^{-8} .

Discussion

The purpose of this study was to estimate how many daily COVID-10 deaths per 100,000 population could have been prevented if each measure would have been taken at the time the first case was diagnosed. According to the results of this study, failure to adopt each one of the analyzed restrictive measures causes an increase of 0.611 to 0.929 deaths per 100,000 population for every 24 hours of delay in their implementation since the first case official diagnosis. This number of preventable deaths is statistically significant.

The Imperial College London showed that a combination of isolation of cases and voluntary quarantine for three months might prevent 31 % of deaths, in comparison with an epidemic without any control measures. Adding social distancing of people aged 70 years and older for four months would increase averted deaths to 49 %. The combination of isolation of cases, home quarantine, social distancing of the entire population, and closure of schools and

universities was considered to be the most effective combination to reduce the reproduction number to a value close to one.¹⁴

Although more comprehensive and stringent prevention and control measures are more effective for COVID-19 containment, at some point the incremental effect of adding another restrictive measure is only minimal and should be weighed against negative collateral effects, such as social and economic consequences for communities that have been subjected to the measures for long periods, which could also lead to an increased burden on health in general.¹⁵

For the control of the epidemic in Europe, some researchers defined three scenarios based on mathematical models that predict quite accurately the projection of the epidemic and the demand for health resources during the time of the exponential curve:¹⁶

- No mobility restrictions.
- Partial restrictions.
- Full restrictions that only allow essential services activity.

Based on these three scenarios, the impact of the epidemic evolution on the number of cases and of those who will require conventional hospitalization or admission to an intensive care unit is predicted. This also gives rise to the recommendation to apply these mobility restrictions according to the number of cases in the region, based on which two types of areas are defined:

- Type A area, with ≥ 100 cases per 100,000 population on last week, where establishing complete closure of activities for at least 15 to 21 days is recommended.
- Type B area, with < 100 cases per 100,000 population, where implementing partial confinement and reducing activities to 30 % and internal mobility to 25 % is recommended.

These measures should be accompanied by social distancing and diagnostic tests in cases where infection is suspected. Implementation of measures of this type has achieved a gradual reduction in the number of cases in three to four weeks.¹⁶

Assuming that strict distancing and confinement measures contribute to a decrease in the number of cases and, consequently, of deaths, the following steps should be directed at how to de-escalate the imposed restrictive measures. If due to the enormous social and economic costs of confinement the quarantine was prematurely terminated, there would be a return to the initial scenario where the epidemic exponentially spreads again.¹⁷

Table 1. Analyzed independent variables regarding the restrictive measures adopted in Europe

Country	Date of first diagnosed case	Deaths (per 100,000 population)**	Days between first case and border closure	Days between first case and closure of non-essential business activities	Days between first case and closure of hospitality and leisure establishments	Days between first case and prohibition of concentrations and events	Days between first case and face-to-face classes suspension	Hospital beds (per 1,000 population)
Albania	09/03/2020	1.54	6	4	4	-1*	-1*	2.9
Germany	27/01/2020	10.73	49	50	50	50	49	8.3
Armenia	01/03/2020	12.20	15	21	15	15	15	4.2
Austria	25/02/2020	7.80	15	20	20	14	20	7.6
Belgium	04/02/2020	84.89	45	43	39	35	39	6.2
Bulgaria	08/03/2020	2.95	4	5	5	5	5	6.8
Czech Republic	01/03/2020	3.16	1	13	13	9	10	6.5
Croatia	25/02/2020	2.62	18	23	23	15	20	5.6
Denmark	27/02/2020	10.38	16	20	15	15	18	2.5
Slovakia	06/03/2020	0.51	7	10	7	33	10	1.6
Slovenia	05/03/2020	5.27	5	11	11	11	11	4.6
Spain	01/02/2020	60.62	45	42	42	42	41	3
Estonia	27/02/2020	5.22	19	29	15	15	18	5
Finland	29/01/2020	5.93	48	Not closed	48	43	48	4.4
France	24/01/2020	44.29	53	51	51	41	52	6.5
Georgia	26/02/2020	0.38	17	22	22	24	5	2.6
Greece	26/02/2020	1.77	18	21	15	15	13	4.3
Hungary	04/03/2020	5.86	8	13	13	7	12	7
Ireland	29/02/2020	35.38	28	25	15	12	12	2.8
Iceland	28/02/2020	2.83	21	Not closed	25	17	17	3.2
Italy	31/01/2020	57.35	46	40	38	38	33	3.4
Latvia	02/03/2020	1.56	15	Not closed	23	11	11	5.8

(Continued)

Table 1. Analyzed independent variables regarding the restrictive measures adopted in Europe (Continued)

Country	Date of first diagnosed case	Deaths (per 100,000 population)**	Days between first case and border closure	Days between first case and closure of non-essential business activities	Days between first case and closure of hospitality and leisure establishments	Days between first case and prohibition of concentrations and events	Days between first case and face-to-face classes suspension	Hospital beds (per 1,000 population)
Lithuania	28/02/2020	2.72	17	17	17	13	13	7.3
Luxemburg	29/02/2020	18.1	Partial closure	16	16	18	16	4.8
North Macedonia	26/02/2020	11.86	16	Partial closure	17	13	13	4.4
Moldova	08/03/2020	13.54	9	17	5	5	3	5.8
Montenegro	17/03/2020	1.45	-4*	-4*	-4*	-4*	-4*	-4*
Norway	26/02/2020	4.67	19	Not closed	15	15	15	3.9
The Netherlands	27/02/2020	35.45	19	25	17	14	14	4.7
Poland	04/03/2020	3.58	11	27	9	6	8	6.5
Portugal	02/03/2020	14.92	14	17	17	10	14	3.4
United Kingdom	31/01/2020	64.27	Not closed	52	49	17	49	2.8
Romania	26/02/2020	7.82	15	20	20	11	14	6.3
Russia	31/01/2020	5.67	59	57	57	57	57	8.2
Serbia	06/03/2020	3.75	6	12	5	6	10	5.7
Sweden	31/01/2020	50.30	48	Not closed	Not closed	58	46	2.6
Switzerland	25/02/2020	22.97	21	20	20	3	20	4.7
Turkey	11/03/2020	6.04	3	10	5	5	5	2.7
Ukraine	03/03/2020	2.29	13	14	9	9	9	8.8

*Days elapsed between closure or suspension and first case diagnosis, since the measures were adopted before the first case.

**By June 23, 2020.

Table 2. b-coefficients of the simple linear regression between each independent variable and the dependent variable (COVID-19-attributable deaths per 100,000 population)

Independent variable	b-coefficient	95 % CI		p
		Lower limit	Upper limit	
Days between first diagnosed case and border closure	0.780	0.446	1.114	0.000*
Days between first diagnosed case and closure of non-essential businesses	0.929	0.512	1.347	0.000*
Days between first diagnosed case and closure of leisure and hospitality establishments	0.739	0.350	1.127	0.000*
Days between first diagnosed case and prohibition of events and concentrations	0.611	0.208	1.015	0.004*
Days between first diagnosed case and face-to-face classes suspension	0.786	0.427	1.145	0.000*
Hospital beds per 1,000 population	-2.348	-6.072	1.376	0.209

*Statistically significant value.

Table 3. Coefficients of the variables of the estimated model of preventable COVID-19 deaths and restrictive measures

Independent variable included/model constant	b-coefficient	95 % CI		P
		Lower limit	Upper limit	
Constant	12.527	-3.229	27.886	0.111
Days between first diagnosed case and prohibition of events and concentrations	-0.672	-1.429	0.079	0.080
Days between first diagnosed case and border closure	1.421	0.672	2.175	0.001*
Hospital beds per 1,000 population	-3.016	-5.820	-0.192	0.037*

*Statistically significant value.

Conclusions

An adequate healthcare system, well-trained professionals and adequate restrictive and social distancing measures are essential for reducing the number of COVID-19 infections, as well as their mortality rates. The earlier the restrictive measures are implemented,

the lower the number of deaths due to SARS-CoV-2 infection will be.

Conflict of interests

The authors declare that they have no conflicts of interest.

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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