COVID-19 epidemic in Spain in the first wave: Estimation of the epidemic curve inferred from seroprevalence data and simulation of scenarios based on SEIR model

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ABSTRACT

The COVID-19 pandemic represents one of the most severe challenges in the recent history of public health. The aim of this study is to estimate the transmission rate parameter (β) and to predict the epidemic progression in Spain. We integrated data from Our World in Data. Our model considered a mean time from infection to death to be 24 days and the results of the seroprevalence survey in Spain. We calculated β using a SEIR model estimated by least squares. We also used a SEIR model to evaluate four scenarios: 1) model 1: no containment measures, 2) model 2: containment measures from the beginning of the epidemic, 3) model 3: mild measures since the 20th day, 4) model 4: strict containment measures since the 20th day. The estimated β parameter was 1.087. We calculated 41,210,330 infected people and 725,302 deaths in model 1; 165,036 infected people and 2,905 deaths in model 2;

4,640,400 infected people and 81,671 deaths in model 3; and, 62.012 infected people and 1,091 deaths in model 4. Peak of the epidemic varied from 69th day in model 1 to 216th day in model 4. Containment measures prevented a scenario with a significant increase in deaths and infected people. Our findings showed that, by stricter interventions such as quarantine and isolation could lead to reduce the potential peak number of COVID-19 cases and delay the time of peak infection.
Keywords: *public health, COVID-19, epidemiology, health policy*

1. INTRODUCTION

On December 31st, 2019, the Municipal Health Commission in Wuhan (Hubei province, China) reported 27 cases of pneumonia of unknown etiology that included seven serious cases, with common exposure to a seafood, fish and live animal wholesale market located in Wuhan city [1]. Onset of symptoms of the first case occurred on December 8th, 2019. On January 7th, 2020, Chinese authorities identified a new type of virus of the Coronaviridae family as the agent causing of the outbreak. Labelled afterwards as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), it is responsible for a disease called COVID-19 (Coronavirus Disease 2019).

Coronaviruses is a virus family causing infection in humans and in a variety of animals including birds and mammals, i.e. camels, cats, and bats. It is a zoonotic disease, which means that can be transmitted from animals to humans [2]. Human coronavirus infection (HCoV) can lead to clinical manifestations that range from the common cold with Winter seasonal pattern to other more serious ones such as those produced by Severe Acute Respiratory Syndrome (SARS) and the Middle East respiratory syndrome coronavirus (MERS-CoV) [3].

On March 11th, the WHO declared a global pandemic for COVID-19. From the beginning of this epidemic to the elaboration of this document, more than thirty million COVID-19 cases have been detected in the world. Out of this total, 640,040 cases have been detected in Spain according to data published by the Coordination Centre for Health Alerts and Emergencies of the Spanish Health Ministry [4]. So far, the gross fatality rate in Spain is 4.8% (30,495) [4] of reported cases, although it must be taken into account that these figures are subject to numerous reporting biases and different policies applied with diagnostic testing in each country [5].

Based on data accumulated so far in the European Union and United Kingdom, among confirmed cases 30% of people infected with COVID-19 required hospitalization and 4% were considered in critical condition, the latter defined as needing mechanical ventilation or any other criteria for intensive care unit (ICU) admission [5]. Along the same lines, in Spain, out of the first 18,609 cases with complete information, 43% required hospitalization and 3.9% were admitted to ICU [6]. An overall fatality rate of 14% (CI95% 3.9-32%) among hospitalized cases [7,8], and between 0.3% and 1% in the general population has been estimated through modelling [9].

Different public health strategies have been developed during this pandemic [10,11]. On Saturday 14 March 2020, the declaration of the state of alarm was published in the Spanish Official Gazette as a response to the public health crisis caused by COVID-19. The state of alarm was prolonged through the Royal Decree 476/2020 of 27 March, extending the state of alert declared by RD 463/2020 of 14 March. Assessing the impact of intervention strategies on the spread of COVID-19 and their consequences give valuable information to a better knowledge of the epidemiology of the infection and planning measures relating to future waves of COVID-19. This study aimed at estimating the transmission rate parameter (β) and to predict the epidemic progression taking into account four scenarios and incorporating the most recent COVID-19 epidemiological data from Spain.

2. DATA AND METHODS

Data sources

The information from the number of deaths per day from COVID-19, reported by Our World in Data from February 1st, 2020 to May 17th, 2020 was used.

Estimation of model parameters

Taking into account the mean incubation period of the COVID-19 infection to be 7 days [11] and the mean duration from onset of symptoms to death to be 17 days [12], the mean time between infection and death to be 24 days was considered. Therefore, the new theoretical cases for each day have been estimated moving back daily deaths 24 days and using the Spain seroprevalence survey results, which estimated that 5% of population was affected by SARS-CoV2 [13].

Once estimated the daily theoretical cases of COVID-19 in Spain, the β value was calculated using a SEIR model estimated by least squares. The β parameter value with the smallest root mean squared error was choosen. This parameter represents the transmission rate, which means the probability of transmitting disease between a susceptible and an infectious individual. This model assumes that Exposed [E] population is asymptomatic but infectious, and [I] refers to the symptomatic and infectious population. The incubation rate, σ was described as the rate by which the exposed individual develops symptoms.

After calculating the value for β, different SEIR models were applied taking into account various scenarios:

- Model 1: SEIR model without containment measures.
- Model 2: SEIR model with containment measures from the beginning of the epidemic (since the confirmation of the first case in Spain).
- Model 3: SEIR model with some containment measures (stay at home, wash the hands well and often and keep the distance) since the 20th day of the epidemic.
- Model 4: SEIR model with strict containment measures (additional restrictions to mobility and work activity) since the 20th day of the epidemic.

We summarized our parameters in Table 1.

Data sources for our SEIR model

Table 1

Parameters	Notation	Values	References
Initial population size	N	47,100,396	Instituto Nacional de Estadística (www.ine.es)
Initial susceptible population	S	31	Estimated based on WorldData data and seroprevalence survey
Transmission rate	β_0	1.087	Estimated based on WorldData data and seroprevalence survey
Average duration of infection	γ^{-1}	5 days	Lin et al [14]
Average incubation period	σ^{-1}	7 days	Prem et al [11]
Public sense of risk based on known critical cases and deaths	D(t)	0.05*I(t)	Wu et al [24]
Intensity of responds	k	100	Lin et al [14]
Governmental action strength	α	(0, 0.5, 0.7)	Lin et al [14]

The SEIR model is a compartmental model for modeling how a disease spreads through a population. It is an acronym for Susceptible [S], Exposed or latent [E], Infected [I], Recovered or dead [R]. When a disease is introduced to a population, the people move from one of these classes (or compartments) to the next. We assume that latent [E] population is asymptomatic but infectious, and [I] refers to the symptomatic and infectious population.

SARS-CoV-2 was first confirmed to have spread to Spain on 31 January 2020 and we simulated until September 27, 2020 (in particular, t = (0, 240)). In the first model, the transmission rate remained constant in the period (in particular, β = 1.087). Thus, the model is formulated as follows:

$$\begin{cases} S'(t) = -\dfrac{\beta S(t)I(t)}{N}, \\ E'(t) = \dfrac{\beta S(t)I(t)}{N} - \sigma E(t), \\ I'(t) = \sigma E(t) - \gamma I(t), \\ R'(t) = \gamma I(t), \end{cases}$$

In the rest of the models, the transmission rate function formulated in Qianying Lin et al. (2020) was adopted, considering the effect of governmental action and individual actions (stay at home, wash the hands well and often and keep the distance). The containment measures applied from the 20th day of the epidemic for models 3 and 4 were simulated. Thus, our SEIR model is formulated as follows:

$$\begin{cases} S'(t) = -\dfrac{\beta(t)S(t)I(t)}{N}, \\ E'(t) = \dfrac{\beta(t)S(t)I(t)}{N} - \sigma E(t), \\ I'(t) = \sigma E(t) - \gamma I(t), \\ R'(t) = \gamma I(t), \end{cases}$$

where

$$\beta(t) = \beta_0 \left(1 - \alpha(t)\right) \left(1 - \frac{D}{N}\right)^k,$$

for model with containment measures from the beginning of the epidemic, and

$$\begin{cases} \beta_0, & si\ t < 20 \\ \beta(t) = \beta_0 \left(1 - \alpha(t)\right) \left(1 - \dfrac{D}{N}\right)^k, & si\ t \geq 20 \end{cases},$$

for models with mild containment measures and strict containment measures, respectively; where β_0 is the transmission rate without containment measures, α(t) (with values in the interval [0, 1]) represents the government actions, D(t) is the public feeling of risk as a consequence of the known critical cases and deaths, and k measures the intensity of the individual reactions.

Under the naive scenario (model 1), the governmental action strength α = 0 and intensity of individual reactions k = 0 was assumed. The model with containment measures from the beginning of the epidemic and mild containment measures, α = 0.5 and α = 0.4 respectively, and k = 100. The model with strict containment measures was considering stricter government containment measures with α = 0.7 and K = 100. Lin et al. used K = 1117.3, but a higher value was considered because the political reality and social environment in China are different than in the Western world [14].

The estimated number of deaths from COVID-19 in Spain during the first 21 weeks of 2020 was 43,945 deaths [15]. Considering that in Spain approximately 2,500,000 inhabitants were infected [13], the case fatality rate (CFR) estimated was 1.76%.

3. RESULTS

The study estimated the basic reproduction number to be $R_0 = \frac{\beta_0}{\gamma} = 5.435$. The basic reproductive number is derived by assuming that the mean infectious period is 5 days, and the transmission rate is 1.087, which was estimated with a SEIR model. If the average R0 in the population was greater than 1, the infection will spread exponentially. If R0 is less than 1, the infection will spread only slowly, and it will eventually die out. The highest value of R0, the fastest an epidemic will progress. The basic reproduction number may vary across locations because contact rates among people may differ due to differences in population density and cultural differences [16].

Summary of predictions from four scenarios of containment measures against COVID-19 disease in Spain

Table 2

T= 82 days	No containment measures	Containment measures from the beginning of the epidemic (α=0.5)	Mild containment measures (α=0.4)	Strict containment measures (α=0.7)	Scenario based on reality
Case fatality rate	1.8%	1.8%	1.8%	1.8%	1.8%
Population without recovery	6035730	57863	1668610	12124	485498
Total infected population	41210330	165036	4640400	62012	2508658

Total population recovered or death	35174600	107173	2971790	49888	2023160
Total death population	725302	2905	81671	1091	44152
Population not affected	813362	46810900	39047300	47017500	43794700
Total recovered population	34449298	104268	2890119	48796	1979008
Max. Simultaneous infected population	9352370	57863	1668610	12124	485498
Max. New daily infections	2160730	16862	468500	2915	112030
Max. New daily recoveries	1872300	10973	318600	2370	95440
R0 (basic reproduction number)	5,435	5,435	5,435	5,435	5,435

Four different models according to control measures for containing the pandemic in Spain were considered. Table 2 summarizes these models. Model 1 implied no containment measures. In this scenario 41,210,330 infected people (with an estimated peak of 2,160,730 people infected per day) and 725,302 people could have died were estimated. In the second model, with containment measures from the beginning of the epidemic (since the confirmation of the first case in Spain), there was an estimated 165,036 infected people, with a peak of 16,862 infected patients per day. In model 3 and 4, the impact of containment measures to control the epidemic were studied on day 25 after the first reported COVID-19-related case. The third model considered a scenario with mild containment measures (stay at home, wash the hands well and often and keep the distance). This model estimated 4,640,400 infected people and 81,671 deaths. The estimated peak of new cases was 468,500 people per day. Finally, 62,012 infected people and 1,091 deaths were expected in the model 4 (strict containment measures including restrictions to mobility and work activity since the 20th day of the epidemic). The report of cumulative active infections up to May 17 for Spain was examined onto our predicted model and the peak of new daily infections reached 112,030 cases was found.

Estimated theoretical cases

Figure 1

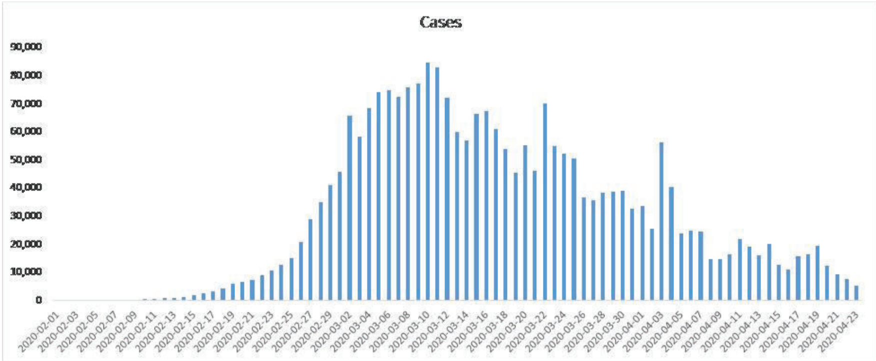

Figure 1 shows the data on the number of daily reported theoretical cases, which indicate that the peak of the epidemic was reached on March 10, 2020.

Results of four SEIR models depeding on containment measures for 240 days

Figure 2

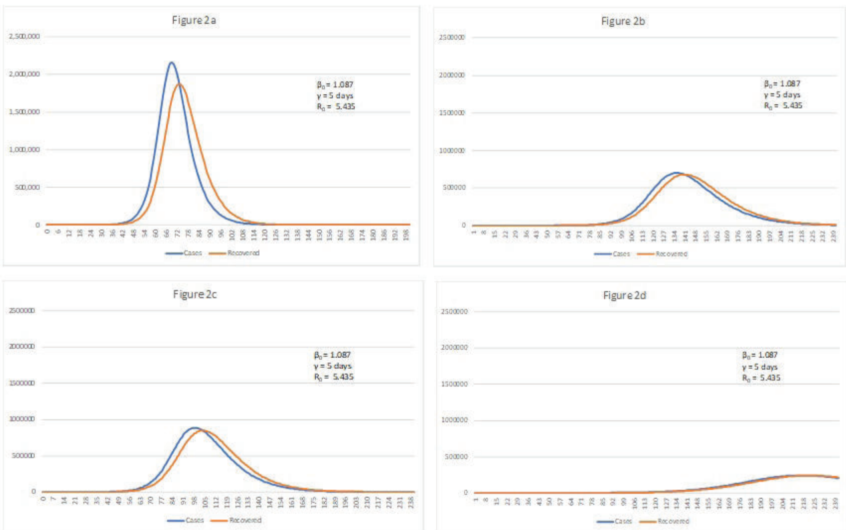

Figure 2a shows the first scenario where the epidemic would have peaked by 69th day (in this scenario using a period of 240 days,), although this scenario would imply a peak of 2,160,730 new daily infections. Figure 2b presents results from the second model. The maximum new daily infections would have been 702,050 and the epidemic would have peaked after 135 days. In this scenario, measure would have been implemented from the beginning of the epidemic (first infection detected in Spain). Figure 2c shows a third model with mild restrictions from day 82 after first case detected. The epidemic in this model would have reached by 99th day and the peak of new daily infections would have been 887,250. A scenario based on strict control measures would have reached the peak of the epidemic on day 216, but would have involved a maximum number of daily infections of 244,140 (Figure 2d).

Cases accumulated by scenarios according to SEIR model

Table 3

Time	Date	No containment measures	Containment measures from the beginning of the epidemic	Mild containment measures	Strict containment measures	Scenario based on reality
1	2020-02-01	4	4	4	4	31
2	2020-02-02	8	8	8	8	72
3	2020-02-03	13	12	13	13	128
4	2020-02-04	19	16	19	19	202
5	2020-02-05	25	20	25	25	302
6	2020-02-06	34	25	34	34	436
7	2020-02-07	44	30	44	44	615
8	2020-02-08	57	35	57	57	854
9	2020-02-09	72	42	72	72	1,176
10	2020-02-10	92	48	92	92	1,606
11	2020-02-11	117	56	117	117	2,183
12	2020-02-12	148	65	148	148	2,957
13	2020-02-13	187	74	187	187	3,993
14	2020-02-14	236	85	236	236	5,381
15	2020-02-15	297	97	297	297	7,242
16	2020-02-16	373	110	373	373	9,735
17	2020-02-17	469	124	469	469	13,075
18	2020-02-18	588	141	588	588	17,552
19	2020-02-19	737	159	737	737	23,550
20	2020-02-20	923	179	923	923	30,269
21	2020-02-21	1,157	202	1,141	1,129	37,793
22	2020-02-22	1,448	227	1,381	1,333	46,748
23	2020-02-23	1,813	255	1,652	1,538	57,403
24	2020-02-24	2,269	287	1,958	1,748	70,083
25	2020-02-25	2,840	322	2,307	1,965	85,172
26	2020-02-26	3,553	361	2,705	2,189	106,155
27	2020-02-27	4,446	404	3,159	2,422	135,083
28	2020-02-28	5,562	453	3,679	2,665	170,262
29	2020-02-29	6,957	507	4,274	2,919	211,512
30	2020-03-01	8,702	567	4,955	3,184	257,405
31	2020-03-02	10,885	634	5,734	3,461	323,297
32	2020-03-03	13,614	709	6,625	3,752	381,780
33	2020-03-04	17,026	793	7,646	4,056	450,440
34	2020-03-05	21,293	886	8,814	4,374	524,726
35	2020-03-06	26,628	989	10,151	4,707	599,547
36	2020-03-07	33,298	1,105	11,681	5,056	672,047

37	2020-03-08	41,637	1,234	13,432	5,421	747,851
38	2020-03-09	52,059	1,378	15,436	5,804	824,994
39	2020-03-10	65,086	1,538	17,729	6,205	909,815
40	2020-03-11	81,364	1,716	20,354	6,624	993,030
41	2020-03-12	101,701	1,915	23,357	7,064	1,065,262
42	2020-03-13	127,103	2,137	26,794	7,524	1,125,440
43	2020-03-14	158,820	2,385	30,727	8,007	1,182,315
44	2020-03-15	198,406	2,661	35,227	8,512	1,248,655
45	2020-03-16	247,788	2,968	40,375	9,041	1,316,244
46	2020-03-17	309,353	3,311	46,265	9,595	1,377,226
47	2020-03-18	386,045	3,693	53,002	10,175	1,431,244
48	2020-03-19	481,485	4,119	60,708	10,782	1,476,780
49	2020-03-20	600,116	4,594	69,521	11,419	1,532,047
50	2020-03-21	747,346	5,123	79,599	12,085	1,578,208
51	2020-03-22	929,729	5,713	91,122	12,783	1,648,476
52	2020-03-23	1,155,136	6,371	104,295	13,514	1,703,565
53	2020-03-24	1,432,922	7,104	119,351	14,279	1,755,797
54	2020-03-25	1,774,059	7,921	136,555	15,081	1,806,244
55	2020-03-26	2,191,210	8,832	156,209	15,921	1,842,851
56	2020-03-27	2,698,640	9,848	178,657	16,800	1,878,476
57	2020-03-28	3,312,040	10,980	204,284	17,721	1,916,869
58	2020-03-29	4,047,950	12,241	233,533	18,686	1,955,708
59	2020-03-30	4,922,980	13,648	266,900	19,696	1,994,994
60	2020-03-31	5,952,500	15,215	304,945	20,753	2,027,762
61	2020-04-01	7,149,140	16,962	348,305	21,861	2,061,512
62	2020-04-02	8,520,800	18,910	397,687	23,021	2,087,226
63	2020-04-03	10,068,690	21,080	453,890	24,236	2,087,226
64	2020-04-04	11,785,770	23,499	517,805	25,508	2,143,655
65	2020-04-05	13,655,660	26,196	590,424	26,841	2,184,101
66	2020-04-06	15,652,820	29,200	672,849	28,236	2,208,030
67	2020-04-07	17,743,890	32,549	766,294	29,697	2,233,119
68	2020-04-08	19,890,110	36,280	872,099	31,227	2,257,762
69	2020-04-09	22,050,840	40,438	991,721	32,829	2,272,405
70	2020-04-10	24,186,610	45,071	1,126,747	34,507	2,287,047
71	2020-04-11	26,261,850	50,234	1,278,883	36,264	2,303,565
72	2020-04-12	28,247,670	55,985	1,449,950	38,104	2,325,351
73	2020-04-13	30,121,970	62,393	1,641,869	40,031	2,344,369
74	2020-04-14	31,870,000	69,531	1,856,661	42,048	2,360,530
75	2020-04-15	33,483,600	77,482	2,096,382	44,161	2,380,797
76	2020-04-16	34,960,170	86,338	2,363,132	46,373	2,393,565
77	2020-04-17	36,301,410	96,200	2,659,000	48,689	2,404,547
78	2020-04-18	37,512,390	107,183	2,986,000	51,114	2,420,262
79	2020-04-19	38,600,070	119,410	3,346,030	53,654	2,436,690
80	2020-04-20	39,572,850	133,023	3,740,830	56,313	2,456,065
81	2020-04-21	40,439,840	148,175	4,171,900	56,314	2,468,387
82	2020-04-22	41,210,330	165,036	4,640,400	56,316	2,477,672
83	2020-04-23	41,893,330	183,798	4,640,465	56,318	2,485,440
84	2020-04-24	42,497,620	204,668	4,640,532	56,320	2,490,708

Table 3 shows the accumulated cases estimated to four scenarios, and the theoretical accumulated cases that were estimated with the mortality data provided by Our World in Data and the seroprevalence survey. The results show the sensitivity analysis of the SEIR models, and they indicate that on day 82 of the epidemic Spain reaches 2,500,000 cases, which coincides with the seroprevalence survey.

4. DISCUSSION

A modified SEIR compartmental model accounting for infection from undiagnosed individuals and four scenarios of control measures was implemented. Also, the hypothetical evolution of the COVID-19 disease in Spain under these four scenarios was evaluated. The most important findings of this work can be summarized as follows: 1) our SEIR model estimated that implementing strict containment measures 82 days after the first case in Spain could have had a relevant impact on the disease spread, 2) The real situation of infection in Spain seems to be in an intermediate scenario between our models with moderate measures and strict measures against the disease. The main purpose of this study was to provide an evaluation of the lessons learned from the first wave of the pandemic and to understand new tools able to support the policymakers decision about the action to minimize the impact of the disease in the future.

The simulation scenarios were adjusted according to the population of Spain for a 240-day epidemic evolution. Our models simulated the conditions where COVID-19 is spreading in a closed population of 47,100,396 people, with and without the effect of governmental action and individual actions (stay at home, wash the hands well and often and keep the distance). Every model suggest that Spain would have reached the peak of the epidemic at different times, delaying the peak with serious and early measures. The findings are comparable with other previous studies as the Wuhan study, where analyzed the epidemics trend of COVID-19 in China and they found that under strong suppression of "lockdown Hubei" the epidemic of COVID-19 in China would achieve peak by late February and decline by the ed of April 2020.REF [17,18]. A recent study using a mathematical model named SEMCR estimated that the optimal timing of interventions differs between suppression and mitigation strategies, as well as depending on the definition of optimal. The study showed that immediate suppression taken in Wuhan significantly reduced the total exposed and infectious populations, and its success required efficient government initiatives and effective collaborative governance for mobilizing of corporate resources to provide essential goods. Also, in London, it was possible to take a hybrid intervention of suppression and mitigation for every 2 or 3 weeks over a longer period to balance the total infections and economic loss [19].

This study found that the R_0 value is equal to 5.44, which means that, in Spain, on average, each infected person is capable of infecting 5.44 people. According to a study published in Emerging Infectious Diseases [20], the median R_0 value was estimated to be 5.7 during the coronavirus disease outbreak in China. Therefore, when a virus is more infectious, a higher percentage of people would need to have immunity to stop the spread.

The SEIR models simulated with different scenarios showed that serious measures taken before March 14 contributed to a considerable reduction of COVID-19 cases. The growth of cases could have been substantially greater if the Government of Spain had not decreed a state of alarm or implemented any containment measure. Given the rapid rate of spread as seen in outbreaks in Europe and the United States, the entire human population is potentially susceptible to SARS-COV-2 infection. Therefore, containment measures as strict lockdown or identification of cases by testing can help prevent further transmission of the virus. Countries, such as the United States, Brazil or Mexico, did not adopt effective mitigation measures (introducing control measures early, strict lockdown measures or identification of cases) and have not managed to stop the transmission. Countries are adopting different ways to contain the SARS-COV-2 spread but there is no one-size-fits-all approach.

This kind of analysis can be useful to face a second wave of the SARS-COV-2 infection [21,22]. In Spain, some researchers called for an independent and impartial evaluation as part of process to be prepared for the next steps [23]. The key point in the interpretation of the findings is to define clearly a model with strict containment measures. The study has limitations, such as: there is not enough information on the immunity of recovered persons, so the model did not consider the transition from the recovered category to the exposed category; the model did not consider the number of tests performed or hospitalizations; and the model did not distinguish between asymptomatic and symptomatic people. However, these models allow a better estimation of the parameters once that the epidemiological curve has decreased, and mortality data have been used to estimate the theoretical cases in Spain. Since the underestimation in the count of cases is greater than that of deaths. It would also be convenient to analyze the epidemic by regions of Spain and to control where the outbreaks are detected so to adapt containment measures to specific regions.

In conclusion, the well-mixed SEIR compartmental model was developed to know the transmission patterns, estimating the effect of control measures in the COVID-19 epidemic, and to evaluate the model´s parameters. The findings showed that, by stricter interventions such as quarantine and isolation could lead to reduce the potential peak number of COVID-19 cases and delay the time of peak infection. Also, the results can facilitate the interpretation of intervention strategies to certain countries in light of its multiple natures and capabilities. And the findings could be useful to help to future analyses and supporting the policymakers' decisions on the minimization of the COVID-19 disease impact.

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