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The Worldwide Challenge of COVID-19 Patient Overload on Hospitals: A Modelling, Meta-Analysis-Based Study

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Abstract
Since a huge load of infected incoming people in the time of COVID-19 needs to be managed in medical facilities, estimation of the load extent of the outbreak and design of the facilities accordingly, can help the authorities to be equipped for such challenges. The basic reproduction number (R0) was obtained from a random-effects model in the meta-analysis procedure. The cumulative death numbers (CDN) were then estimated using the cubic curve estimations, which in turn, was based to estimate the required beds in each country. The shortages of beds were calculated from the difference between the available and required beds. Finally, a multiple barriers strategy was proposed according to epidemiological parameters to decrease patient overload during the outbreaks. The mean pooled R0 was found to be 3.04 (95%CI: 2.62-3.45). The correlation coefficients for the cubic curve estimations for different countries were 0.97-0.99. From hospital beds shortage standpoint, the results showed that Australia, South Korea, and Turkey are in a better position relative to other countries studied. However, Italy, Spain, France, the USA, and the UK will experience limitations if no action be taken to prevent COVID-19 from spreading. If the exponential growth of infection remains for the next weeks, the related authorities should consider much more hospital beds (as well as related supplementary equipment and medical-based staff) for COVID-19 infected cases. Although the considerable changes in the medical-based footprints can allocate the side effects of the challenge, it seems that we need to refine our frameworks to prevent or minimize, at least, the life losses.
Key words: COVID-19, Hospital beds, Critical care beds, Modelling, Meta-analysis.

Introduction

The quick and increasing worldwide spreading of a new coronavirus (COVID-19) has faced the world with another pandemic disease in thirty-one-century as declared by WHO [1]. Outbreaks especially new ones, can put the communities under significant social, economic, and life-related stresses [2,3]. There is a valuable, empirically right quote saying that what happens twice, happens thrice [4]. On the other hand, a coordinated global response is inevitably required to prepare health organizations to deal with this unprecedented challenge [5]. Therefore, a comprehensive recognition of the problem not only from extent but also from depth is of critical and priority importance. The recognition can be ranged from the origin, transmission routes, genomic structure, epidemiology of COVID-19, clinical features, diagnostic, treatment, prevention, follow-up, etc. [6].

Unfortunately, a huge load of potentially infected incoming people needs to be managed in the medical facilities that may have certain limitations on infrastructures [7], especially in countries with vulnerable health systems [8]. The medical structures are deeply suffering from the mathematical and epidemiological-based calculations of the outbreaks-originated challenges. Estimation of the load extent on the outbreaks, therefore, and (re) design of the facilities accordingly, can help the authorities to be equipped for the next challenges and to have maximum performance in such situations.

This study aims to explore and evaluate the problem extent imposed by COVID-19 in medical-based structures of 21 countries worldwide, to give some technical analyses in this framework, to present some solutions to deal with the challenges in the world. The authors hope that the results be useful to help prevent or minimize, at least, the loss of lives.

Materials and Methods

Study Framework

In this study, the shortage of hospital beds (as total and critical care beds (CCB)) was estimated in the COVID-19 epidemic situation for 21 countries in the world. For this, four consecutive stages were conducted as illustrated in Figure 1. At the first stage, R_0 was obtained from a meta-analysis procedure. The cumulative death number was then estimated for the probable peak of the infection in the next 40 days using a modeling approach, which in turn, was based to estimate the required beds in each country. The shortages of beds were then estimated for each country (available beds - required beds). A multiple barriers strategy was finally proposed according to epidemiological parameters for the avoidance of patient overload during the outbreaks.

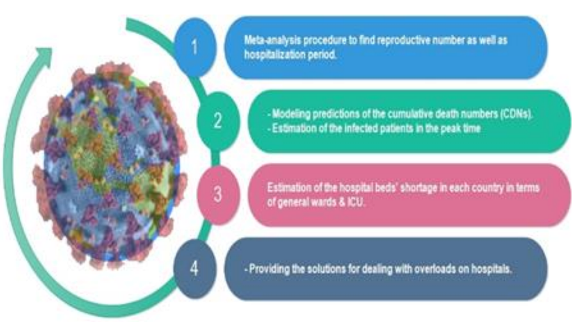


Figure 1. Working flow diagram of this study

Search strategy

The comprehensive literature searches were conducted according to PRISMA statement [9] (Figure 2) in PubMed, Scopus, and Web of Science in the title, abstract, or keywords from inception to April 7th, 2020 with no time restriction but in english by the MeSH and non-MeSH terms of ("COVID-19" OR "severe acute respiratory syndrome coronavirus 2" OR "2019 novel coronavirus" OR "2019-nCoV" OR "SARS-CoV-2") AND ("basic reproduction number" OR "basic Reproduction rate" OR "basic Reproduction number").

The inclusion criteria were studies reporting on R0 of COVID-19. All retrieved documents were screened based on titles and abstract, using the following exclusion criteria: irrelevant and non-report R0 and mean with standard deviation (± SD) or range or 95% CI, and insufficient data. Titles and abstracts were separately reviewed carefully by two expert researchers (MS and MF) to remove ineligible studies. The full text of the screened articles was then checked by the researchers for data extraction and quality assessment.

Data extraction & quality assessment

The required data was extracted using the predefined form as the mean of R0 with 95% CI or standard deviation (±SD or range), first author, and publication year, sample size, and geographical place. The quality of the studies was assessed using the case report guideline (CARE) [10], the Quality Appraisal of Case Series Studies Checklist the IHE [11], and the critical appraisal tool to assess the quality of cross-sectional studies (AXIS) [12]. The AXIS Case Series Studies Checklist, and CARE included 20, 20, and 13 items.

Statistical analysis

To calculate a mean effect size for each study, the data were quantitatively analyzed using comprehensive meta-analysis software (CMA; version 2.2.064). The pooled effect size was expressed as mean (95% confidence interval (CI)) using the random-effects model. Between studies' heterogeneity (χ^2) was estimated based

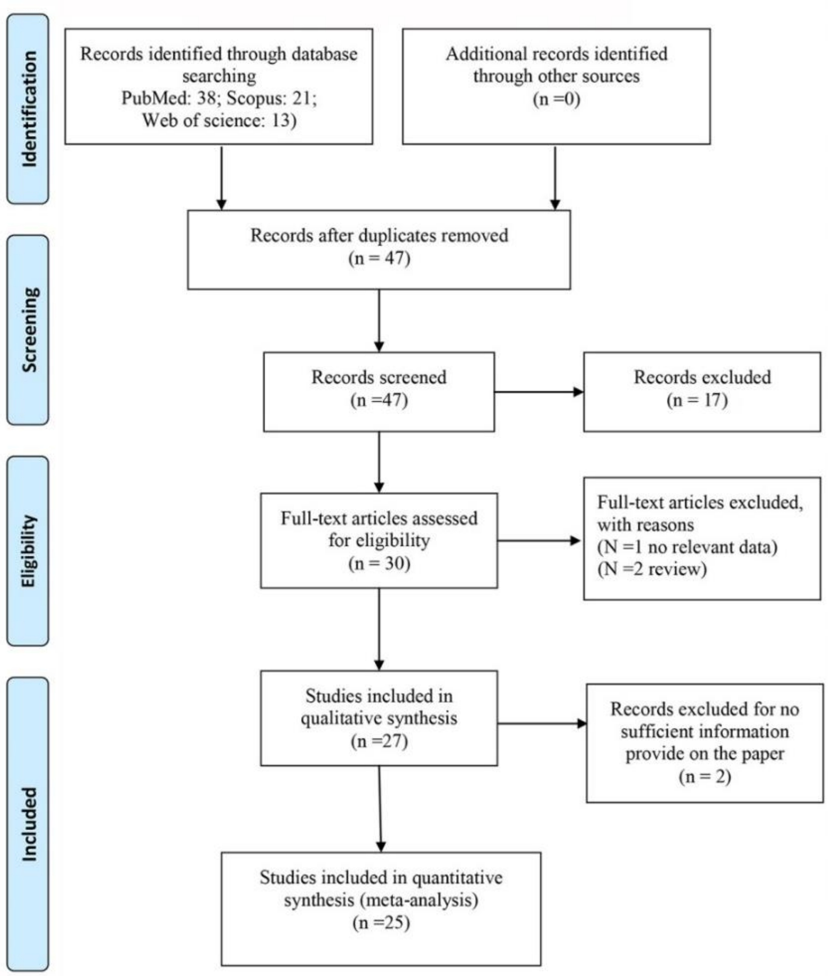


Figure 2. Flow diagram of the search strategy

on the Q-statistic I2 test. A subgroup analysis based on the place was performed to evaluate the possible sources of heterogeneity.

The between-study variance of true effects was estimated using the tau-squared statistic. The publication bias was determined using Begg's funnel plots with the Egger's and Begg's tests. Furthermore, the subgroups were analyzed for sensitivity using leave-one-out sensitivity analysis. All related analyses were evaluated using p-values at a 95 % confidence limit.

Modelling predictions

In this study, the cumulative death numbers (CDNs) for 20 countries (Table 1 Appendix) were predicted to give a wider perspective on the management of COVID-19-dictated challenges by the government as well as local health authorities. The related data (e.g. the number of hospital beds between the years of 2017 and 2020) as well as COVID-19 information, were accessible from published papers and online database [13-15], Such prediction can show what will be happening soon, and therefore, can help the authorities to implement measures in hospital-based facilities and/or the control measures. Due to the fast and widespread, defense against COVID-19 reached the medical services of all countries, which imposes an unpredicted overload on the facilities. For this reason, the outbreak was evaluated for the next 40 days and the required number of hospital beds for each country was estimated at the peak time. For this, CDNs for each country (published daily by WHO [16]) were fitted into an exponential model, which in R0 was specified to be 2.78 from the above-mentioned meta-analysis procedure. The CDNs of each country for the next 40 days were predicted and based on the calculation of the required hospital beds in such peak conditions. Considering CDN, 2.3 % fatality rate of COVID-19 [17], and the fact that 30 % of the infected cases are admitted in the hospitals [18], the hospitalized patients as the number of cases admitted to general wards and critical care services were calculated. The shortage of hospital beds in both sections was estimated from the difference between the available beds and required beds.

Results and Discussion

Mata-analysis

The diagram of study selection (PRISMA) is illustrated in Figure 2. A total of 47 of 72 documents were screened for the systematic and meta-analysis of R0 with COVID-19, 17 studies were excluded after the title and abstract screening. After precise review of full texts, 27 studies [19-45] were eligible for inclusion, from which seven were excluded due to insufficient data. Finally, 25 studies were considered in the meta-analysis [20-32,34-45]. Detailed features of the included documents are displayed in Table 1 Appendix.

Heterogeneity for all analyses was significant (P<0001); the I^2 statistic for heterogeneity for R0 variable was 99.1%. The average score for the quality assessment of studies was found to be 0.75. Figure 3 illustrated the combined estimates for the mean R0. The random-effects model meta-analysis for 25 studies showed a significant R0 (3.04 day, 95% CI: 2.62 to 3.45). These pooled effects were not robust in the leave-one-out sensitivity analysis (Figure 3a) (P <0.001).

A subgroup analysis for R0 was conducted based on the geographical place. The mean R0 in the world (other countries except China) (mean= 3.48; 95% CI: 3.43 to 3.53; P <0.000) is higher than Wuhan city (mean= 3.02; 95% CI: 2.98 to 3.06; P <0.000) and China (except Wuhan) (mean= 2.70; 95% CI: 2.66 to 2.75; P <0.001). Detailed forest plots of the R0 are demonstrated in the supplementary file.

Publication Bias

Figure 3 b shows the funnel plot for the Meta-analysis of the mean R0 of COVID-19. The 25 studies related R0 (white spots) are symmetrically distributed around the mean pooled effect size. The R0 bias result was approved by Egger's linear regression test (intercept = 0.57; S.E. =3.69; 95% CI: -7.00 to 8.14; t=0.15; df =27; one-tailed and two-tailed P > 0.87). The Trim and Fill process showed no publication bias was found in the meta-analysis (black spot).

Modelling predictions

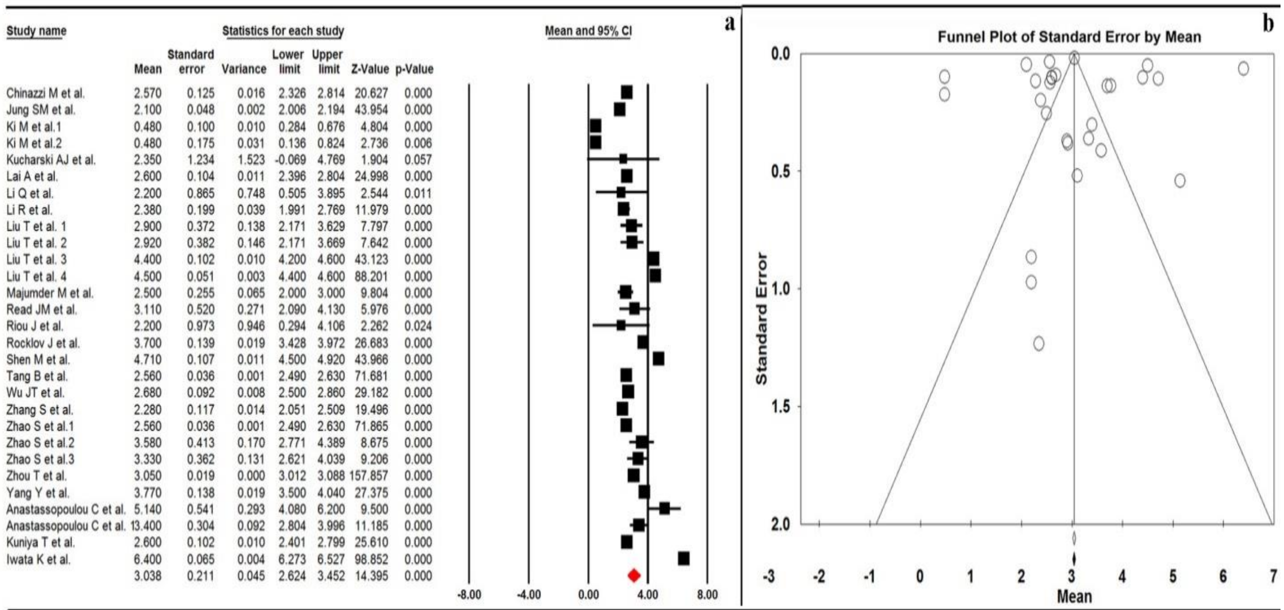
The cubic curve estimation results showed that without taking any more measures, CDNs will increase in the future days, exponentially for all countries, except China. The correlation coefficient for the estimations was ranged from 0.97 to 0.99 as can be seen in Figure 4. With the good fitness of data with the model, we can estimate hospital beds shortages (except for China, whose trend has been returned) based on the predicted CDNs.

Hospital beds shortage

When an infection is restrained mainly in the medical frontier, equipping the medical system with sufficient facilities is of crucial importance. In this situation, estimating the maximum number of the required beds (as total and CCB) will present an accurate perspective to the medical or health related authorities.

For this reason, a comprehensive analysis was conducted to estimate the maximum number of patients who need to be hospitalized in either general wards or ICU. The results of this study showed that Australia, Germany, Switzerland, Denmark, Portugal, South Korea, Norway, Austria, China, and Turkey are in a better position relative to other countries studied, respectively. However, the other countries will experience hospital beds shortage if no action be taken to prevent COVID-19 from spreading (Figure 4).

From the CCB bed requirements point of view, all countries except Australia, South Korea,



Study name	Mean	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Chinazzi M et al.	2.570	0.125	0.016	2.326	2.814	20.627	0.000
Jung SM et al.	2.100	0.048	0.002	2.006	2.194	43.954	0.000
Ki M et al.1	0.480	0.100	0.010	0.284	0.676	4.804	0.000
Ki M et al.2	0.480	0.175	0.031	0.136	0.824	2.736	0.006
Kucharski AJ et al.	2.350	1.234	1.523	-0.069	4.769	1.904	0.057
Lai A et al.	2.600	0.104	0.011	2.396	2.804	24.998	0.000
Li Q et al.	2.200	0.865	0.748	0.505	3.895	2.544	0.011
Li R et al.	2.380	0.199	0.039	1.991	2.769	11.979	0.000
Liu T et al. 1	2.900	0.372	0.138	2.171	3.629	7.797	0.000
Liu T et al. 2	2.920	0.382	0.146	2.171	3.669	7.642	0.000
Liu T et al. 3	4.400	0.102	0.010	4.200	4.600	43.123	0.000
Liu T et al. 4	4.500	0.051	0.003	4.400	4.600	88.201	0.000
Majumder M et al.	2.500	0.255	0.065	2.000	3.000	9.804	0.000
Read JM et al.	3.110	0.520	0.271	2.090	4.130	5.976	0.000
Riou J et al.	2.200	0.973	0.946	0.294	4.106	2.262	0.024
Rocklov J et al.	3.700	0.139	0.019	3.428	3.972	26.683	0.000
Shen M et al.	4.710	0.107	0.011	4.500	4.920	43.966	0.000
Tang B et al.	2.560	0.036	0.001	2.490	2.630	71.681	0.000
Wu JT et al.	2.680	0.092	0.008	2.500	2.860	29.182	0.000
Zhang S et al.	2.280	0.117	0.014	2.051	2.509	19.496	0.000
Zhao S et al.1	2.560	0.036	0.001	2.490	2.630	71.865	0.000
Zhao S et al.2	3.580	0.413	0.170	2.771	4.389	8.675	0.000
Zhao S et al.3	3.330	0.362	0.131	2.621	4.039	9.206	0.000
Zhou T et al.	3.050	0.019	0.000	3.012	3.088	157.857	0.000
Yang Y et al.	3.770	0.138	0.019	3.500	4.040	27.375	0.000
Anastassopoulou C et al.	5.140	0.541	0.293	4.080	6.200	9.500	0.000
Anastassopoulou C et al.	13.400	0.304	0.092	2.804	3.996	11.185	0.000
Kuniya T et al.	2.600	0.102	0.010	2.401	2.799	25.610	0.000
Iwata K et al.	6.400	0.065	0.004	6.273	6.527	98.852	0.000
	3.038	0.211	0.045	2.624	3.452	14.395	0.000

Figure 3A, B. The forest and funnel plot of R_0 for COVID-19

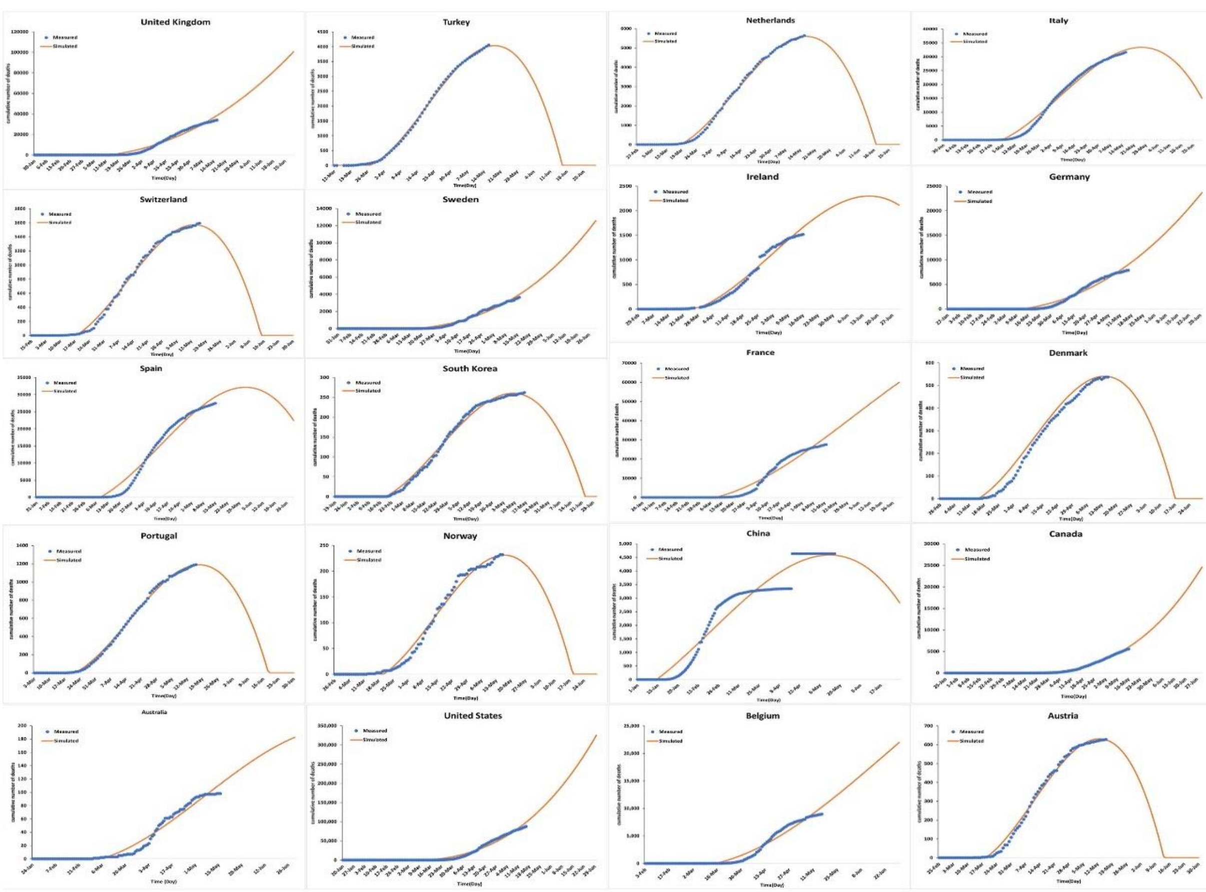


Figure 4. Observed and predicted CDNs in the studied countries using a cubic curve estimation

Norway, Austria, China and Turkey will be challenged to manage patients in intensive care units, respectively (Figure 4). Therefore, if the growth of infection remains for the next few weeks, the relative authorities should consider more and more hospital beds for patients in both general wards and intensive care units, along with the related supplementary instruments (e.g. ventilators) as well as the medical-based staffs [7]. Otherwise, a considerable number of unnecessary fatalities will become unavoidable. All the calculated values are presented in Supplementary file.

Overflowing of these units with the patients may also lead to selective treatment of them, which in turn, increases fatality rate, even from the estimated values [46]. In such a situation, moreover, the medical staff will face complicated conditions in which their life can endanger them as well. Besides, a medical-based solving of an outbreak treatment has huge economic and social negative consequences [47]. Therefore, drawing up the basic and essential strategies for relocation of the fighting borders from treatment to prevention line seems to be necessary. The spread of COVID-19 can be alleviated not only by early diagnosis, isolation, and quick treatment [48] but also by the employment of a robust procedure to trace contacts [8]. The current analysis showed that medical-based structures in the mentioned countries need to be changed dramatically so that the footprints can respond to a peak load of patients in complicated situations such as epidemics. Therefore, it seems that we need to refine our frameworks to prevent or minimize, at least, the life losses. It may mean redesigning the global health architecture of the response to epidemics [49]. All in all, the countries need to improve their emergency preparedness plans to support their nations against such sudden outbreaks as is going to occur in the next few weeks. For this reason, an epidemiological-based strategy is discussed in the following section.

Pursuing a multiple barriers strategy to decrease the overload on hospitals

To improve the first line of defense, instead of the last one (i.e. hospitals), we need to take some control strategies to limit transmission of the viral agent of COVID-19 [50]. These approaches are time-honored methods, which in multiple barriers strategy (MBS) can be considered as illustrated in Figure 5. MBS can be comprised of barrier precautions (e.g. masks, gloves, and handwashing), quarantine, case isolation, movement restrictions, which have received relatively limited attention from the authorities in the emergence of COVID-19. Fortunately, introducing the epidemiological parameters into the MBS, enable health sectors to undertake appropriate control measures quantitively, although in a non-linear way [51]. The parameter of R0 implies the average number of secondary infections produced by a first infected case. In $R0 < 1$, the infection will not be transmitted, whereas in $R0 > 1$ the number of infected cases multiplies and an epidemic may occur [52]. Therefore, without considering population heterogeneity and temporal development, the R0 value of 2.78 for COVID-19 clearly shows its high probability to be spread. The value of R0 is calculated as:

$$R0 = D \times c \times \beta$$

Where D is the duration of infectiousness, c is the number of contacts of an infected case with the suspected cases per time; β is the probability of transmission in each mentioned contact. It is obvious that decrease of R0 strongly depends on attempts to reduce 1) β (including personal health-related measures such as face masks, gloves, handwashing), 2) c (e.g. quarantine, case isolation, movement restrictions), and 3) D (e.g. fast diagnostic, isolation, and antimicrobial therapy) [53] as illustrated in Figure 5. Providing personal protective equipment (parameter β) such as face mask, gloves, handwashing liquids along with accurate training can assure contact precautions and prevent the nations from spreading the illness.

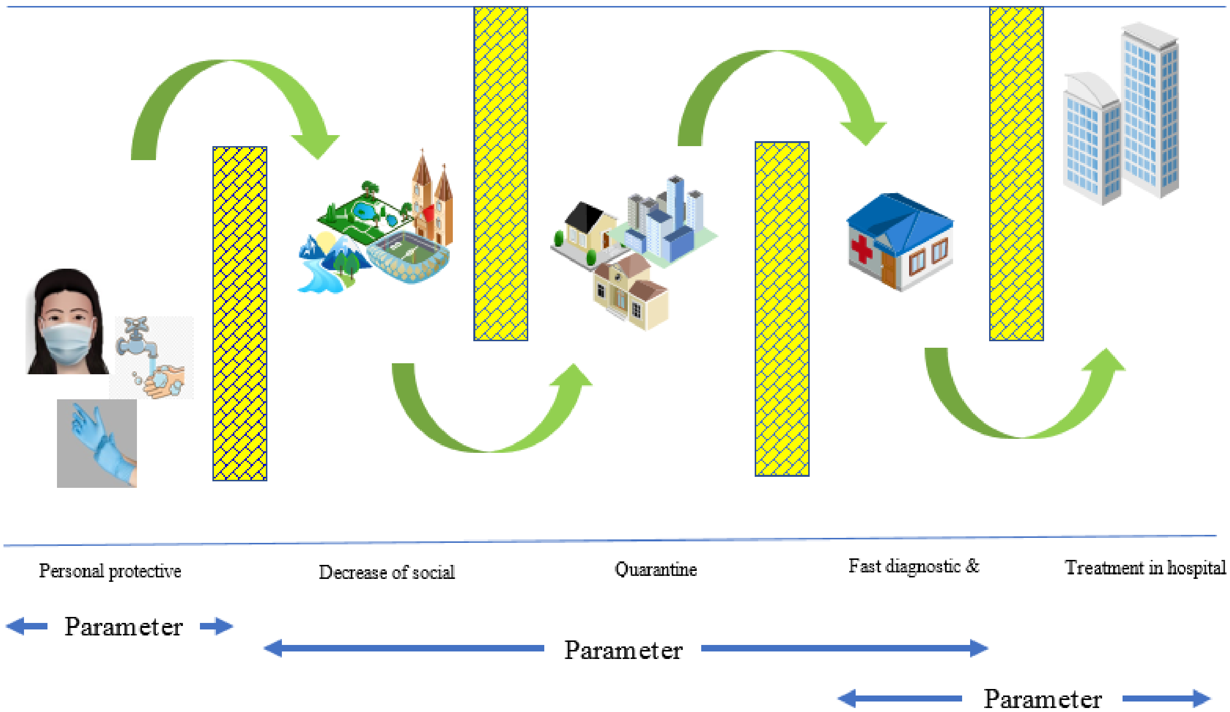


Figure 5. A multiple barriers strategy for decreasing the overload on hospitals according to the epidemiological factors

As a c-independent factor, quarantine plays a significant role in decreasing R0, because it can prevent transmission of the infection through incubating cases as well as reduce the time from onset of symptoms to admission in hospitals [54, 55]. The latter seems to be vital in conditions in which transmission occurs before symptom onset. Serial interval implies the duration of time between the onset of symptoms in a primary case and a secondary case [56]. Since the serial interval of COVID-19 (4-4.1 days) is less than the incubation period (4.4-5.4 days), a considerable proportion of second transmission will occur before illness onset [57]. This shows that quarantine is a critical option in decreasing the overload on hospitals.

The final way to decrease R0 by reducing the D value by fast diagnostic of the disease (reducing the time of infection to appearances of symptom), fast isolation, and fast hospitalization. Owning to in large incubation period, in the case of COVID-19 only the last approaches (i.e. prompt isolation and hospitalization) can be employed. Considering the relatively low generation time for COVID-19 (8.4 days) [58], the time to take action is crucial. Otherwise, we should fight in the final boundaries (i.e. hospitals) as occurred.

Therefore, it seems that in the exposure of the new outbreaks, such as COVID-19, the governments should enforce to high quality and quantity hospital-based facilities (e.g. beds, staffs, and equipment) or take the control measures. In conclusion, this study emphasis taking time-honored control measures in epidemic rather than focusing on the medical based treatment of the illness. However, understanding the epidemiological parameters for each illness quantitatively and qualitatively is vital to taking appropriate strategies. This study has some notable limitations which should be considered in the results' interpretation. First, the available hospital beds of the countries were from different years which should be updated by the authorities with new information and considered for an accurate estimation for each country. Second, the R0 considered in this study was adopted from homogeneous assumption-based studies. Since Covid-19 shows considerable heterogeneity in different aspects, it would affect on under or over estimation of the results. Finding an accurate R0, accordingly is of great importance.

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Footnotes

Authors' Contribution: MS, MF and EB conceived of the manuscript; MS, MF, and MA contributed to data collection; MS and MA contributed to data analysis and interpretation, and MS and MF drafted the document. All authors agree with the contents presented in this work.

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