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Inferring a cause-effect relationship between lockdown restrictions and COVID-19 pandemic trend during the first wave

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A R T I C L E  I N F O

Article history:
Received 23 January 2021
Revised 7 May 2021
Accepted 21 September 2021

Keywords:
COVID-19
SARS-CoV-2
Lockdown
Modelling
Health policy
Public health

A B S T R A C T

The large number of infected persons due to the COVID-19 pandemic and the need of hospital care for many of them induced the majority of world governments to implement lockdown measures. We developed an analytical model to evaluate the trend of the SARS-CoV-2 pandemic. This model was applied to the first four months of the epidemiological data of the most affected countries in Europe and Russia, in order to evaluate the effect of the lockdown on the epidemic curves during the first wave. According to our model, the difference between the beginning of the lockdown and the slope change of the curve representing the daily distribution of counts was: Germany and Spain 6 days, France 7 days, the United Kingdom 9 days, Italy 21 days, and Russia 30 days. On the basis of these results, we infer a possible cause-effect relationship between the lockdown imposed in countries taken into account and the curve representing the daily distribution of new cases. Lockdown measures imposed by governments slowed the spread of the pandemic and reduced the number of infected persons. In economic terms, the damage was considerable, with entire production sectors in crisis. On the other hand, the efforts and innovations implemented to produce vaccines and effective treatments against the pandemic could be applied also in other fields of public health.

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1. Introduction

The pandemic due to SARS-CoV-2 (or COVID-19) had the first diagnosed cases in the city of Wuhan (China) at the end of 2019 [1,2], followed by a rapid spread at a global level: initially in Asia, then in Europe, shortly after in the Americas, and more lately in Africa and Australia. Unlike the previous outbreaks occurred during the globalization era (SARS [3], MERS [4], and H1N1 [5]), COVID-19 is demonstrating a major spreading capacity. It is likely that an important role in spreading the virus is driven by the significant percentage of asymptomatic subjects, estimated to be greater than 15% of the total cases [6]. These subjects can unknowingly infect several other persons contributing to the diffusion of the epidemic.

As of 31 December 2020, the infected persons from COVID-19 in the world were 81.5 million [7]. Within the European Union, Italy was among the first countries dramatically stricken by the COVID-19 outbreak (until 31 December, confirmed cases are about 2.1 million), Spain (~1.9 million) had a similar trend to Italy until July, while France (~2.7 million) and Germany (~1.7 million) were the other countries most affected. The other most affected Euro-Asiatic and European countries were Russia (~3.1 million) and the United Kingdom (~2.5 million) [7]. Geographically, although Russia is a transcontinental nation, we considered to include it because of its proximity to European countries [8]. Since October 2020, a second wave hit primarily Europe, initially affecting Spain and France and shortly after with Germany (for the first time since the beginning of the pandemic experiencing a daily death level over 1,000 units [7]) and the UK affected (primarily due to the newly detected variant [9], supposedly meant to cause a much higher level of infections).

A significant percentage of patients with COVID-19 required hospital care during the first wave. In a study on 3,665 Chinese patients, the percentage of severe cases was of 25.5% [10]. The World Health Organization (WHO) reported that in Europe almost 40% of patients required hospital care and 5% intensive care [11]. The implications in terms of public health, workload in hospitals, and economic damage are worrisome.

Since there is no evidence to date of an effective treatment for SARS-CoV-2 and the first announcements of a successful vaccine date back only to November 2020 [12]. Therefore, the most pragmatic recommendation was to implement social distancing measures to minimise the contagion. Moreover, in order to contain the diffusion of the Coronavirus, the majority of world governments imposed lockdowns.

As a matter of fact, social distancing and limited movements are effective remedies to counter the spread of epidemics since ancient
times [13]. Two studies conducted in Wuhan [14] and Hong Kong [15] support this interpretation. An Italian study showed that implemented measures of containment were effective in reducing the increase of contagion while allowing more time for the national health system to increase the available number of beds in intensive care units, before the system reached its limits [16]. In economic terms, the damage was considerable [17], with entire production sectors in crisis, such as tourism and entertainment. On the other hand, social distancing gave the right push to launch policies aimed at the diffusion and innovation of digitization.

In epidemiology, fundamental data to study the evolution of outbreaks implies counting daily and cumulative number of cases. The daily distribution of cases is obtained from the number of new cases observed each day. The cumulative distribution of cases is available from the daily distribution summing the number of cases in a specific time interval from the first epidemic day to ith day considered.

To evaluate the trend of the SARS-CoV-2 pandemic, we developed an analytical model based on a log-logistic growth function. The model was applied to epidemiological data of the most affected countries in Europe, for the purpose of evaluating the trends in order to find a possible cause-effect relationship between the lockdown and the daily distribution of new cases.

2. Materials and methods

2.1. Data source

Data for this study was extracted from the public database available through the European Union Open Data Portal [18]. Data consists of four variables related to the dates (day, month and year in complete and separated formats), daily diagnosed cases, cumulative number for 14 days of cases per 100,000 inhabitants, daily number of deaths, number of inhabitants for each country in 2019, and four variables related to country name and localization (country-territory name, geospatial linked data, country territory code, and continent explanation). The database was daily updated until 14 December 2020, after this date the update became weekly. Data used in our study was downloaded on 16 October 2020 and contained all records from 1 January 2020 onwards. The variables of interest were the following: complete date, daily diagnosed cases, daily deaths, number of inhabitants for each country in 2019, and country-territory name. The cumulative variables were obtained by collecting daily variables with in house developed software. We selected the European countries with the highest number of diagnosed cases until 1 June 2020, as reported by the European Centre for Disease Prevention and Control (an agency of the European Union) [19]. The selected countries were: France, Germany, Italy, Russia, Spain, and the United Kingdom.

2.2. Model design

Our model is based on a function like to cumulative log-logistic distribution [20,21]. This function was already used in our previous article on the forecast of COVID-19 in Italy [22]. For the current study, the model was implemented with first and second derivatives of a cumulative log-logistic function (hereafter C(t)). It is a time dependent function, with three free parameters: N, a, and b. C(t) is the cumulative number of cases on day t, N is the cumulative number of cases at the end of the time period considered, a and b are the parameters that govern the asymmetry and the growth rate of the curve (the model is reported in more details in the Appendix A.1). C(t) has an initial-exponential-phase until its point of inflection and successively a flatten saturation phase (asymptotic trend). In order to determine the parameters of the C(t) curve, we developed an algorithm in R environment (version 3.6.3) [23], based on the maximum statistical significance of α and b, according to their P-values, and varying N with step = 1000. The best-fit parameters were computed by the nls package, whereas the 95% confidence interval (hereafter CI) was computed by the nlsstools package. The first derivative of C(t) (hereafter C′(t)) is related to the distribution of daily cases, and its point of maximum is the estimated epidemic peak. The second derivative of C(t) (hereafter C′′(t)) can be interpreted as the slope of C(t). In particular, the point of maximum of C′′(t) indicates the start of the slowdown of growth rate (SGR) of the C(t) curve.

The cause-effect relationship between lockdowns declared in each country taken into consideration and the daily epidemic curves was evaluated by the difference (expressed in days) between the initial date of the lockdown and the date corresponding to SGR. The beginning of the epidemic in a country was defined considering the day on which the first case was diagnosed. In our model the time frame considered for all the countries was of 120 days (4 months), starting from the initial date of the outbreak. Within this period the epidemic peak for all countries considered was observed.

It is possible to infer an analogy between our model and the kinematics: for each time t, C(t) represents the total number of infected persons, C′(t) representing the infection speed, while C′′(t) represents the infection acceleration.

2.3. Statistical analysis

Statistical analysis for cumulative distributions was computed by t-statistics embedded in the nls package. For each free parameter of the distributions, we calculated the CI using the asymptotic method embedded in the nlsstools package. CI is the range of possible values for a parameter, based on a set of data. This range has an associated confidence level, usually fixed at 95%, indicating probability that the estimated interval will contain the true value of the parameter.

In order to verify the significance between the daily distributions of new cases and the C(t) curves, we computed the Kolmogorov-Smirnov two-sample test (hereafter KS). The KS statistic is a rank test. Therefore, it is a non-parametric test with a null hypothesis stating that the two distributions are the same. The statistical level of significance was fixed at 0.05.

3. Results

In Table 1 we reported the epidemiological characteristics of the countries considered, 120 days after the start of the epidemic. Spain was the country with the highest prevalence (51 confirmed cases per 10,000 inhabitants), France and Germany were the countries with the lowest prevalence (22 confirmed cases per 10,000 inhabitants). The highest fatality was recorded in Spain (20%), while the lowest fatality was observed in Russia (1%). In Table 1 we also report the rules adopted for each country to counter the spread of the epidemic. Generally, restrictions were enforced for mass gatherings and movements, with schools and workplaces closed (see Appendix A.2 for more details).

In Table 2 we summarized the dates of interest, the best-fit parameters of the C(t) functions, and the p-value related to the KS test for C(t) functions for the countries taken into consideration. The difference expressed in days between the initial date of the lockdown and the SGR was: Germany and Spain 6 days, France 7 days, the United Kingdom 9 days, Italy 21 days, and Russia 30 days. The a parameter for Germany and Spain resulted in a lower significance level. This can be observed in Fig. 1 as a lesser adaptation of the C(t) curves to the data of these two countries, when compared to the other countries. It is noteworthy to mention that the values
Table 1

Epidemiological characteristics 120 days after the beginning of the epidemic for the countries considered. In the last column, we report the social distancing and limited movements adopted to counter the spread of epidemics.

| Country | Population to 2019 (in million) | Date 120 days after the start of the epidemic | Cumulative number of cases | Cumulative number of deaths | Prevalence (cases per ten-thousand) | Fatality (deaths per cent) | Rules adopted |
|---------|---------------------------------|-----------------------------------------------|---------------------------|----------------------------|-------------------------------------|---------------------------|---------------|
| France  | 67.0                            | 23 May                                        | 144,566                   | 28,289                     | 22                                  | 20                        | RMG, SC, LM, NEWC, NCN |
| Germany | 83.0                            | 26 May                                        | 179,002                   | 8,302                      | 22                                  | 5                         | RMG, SC, LM, NEWC, NCN |
| Italy   | 60.4                            | 29 May                                        | 231,732                   | 33,142                     | 38                                  | 14                        | RMG, SC, LM, NEWC, NCN |
| Russia  | 145.9                           | 30 May                                        | 387,623                   | 4,375                      | 27                                  | 1                         | RMG, SC, LM, NEWC, LCN  |
| Spain   | 46.9                            | 30 May                                        | 239,228                   | 27,125                     | 51                                  | 11                        | RMG, SC, LM, NEWC     |
| United Kingdom | 66.6                | 30 May                                        | 252,863                   | 37,231                     | 38                                  | 15                        | RMG, SC, LM, NEWC     |

Note: Prevalence is the ratio between diagnosed cases and population. Fatality is the ratio between deaths and diagnosed cases.

§ Restriction on mass gathering (RMG); school closures (SC); limitation on movements (LM); non-essential workplace closures (NEWC); national (NCN) or local (LCN) curfew at night. More details and references on the lockdowns are reported in the Appendix A.2.

Table 2

Dates of interest and best-fit parameters of the $C(t)$ curves for the countries taken into consideration. The $P$-values in the last column are related to the Kolmogorov-Smirnov two-sample test, calculated for the $C(t)$ curves.

| First epidemic day (2020) | Date of the lockdown$^A$ | Date of the SGR | Number of days from lockdown to SGR | Date of the epidemic peak | $a$ (95% CI) | $b$ (95% CI) | $N \times 10^3$ (95% CI) $^A$ | P(KS) |
|--------------------------|--------------------------|-----------------|-----------------------------------|--------------------------|--------------|--------------|-------------------------------|-------|
| France                   | 25 Jan                   | 17 Mar          | 24 Mar (60) $^A$                  | 7                        | 5 Apr (72) $^A$ | 1.52 $\times 10^{13}$ (0.64, 2.40)** | -8.12 (-8.25, -7.99)** | 143 (138, 145) | 0.69 |
| Germany                  | 28 Jan                   | 17 Mar          | 23 Mar (56)                       | 6                        | 4 Apr (68)   | 1.02 $\times 10^{11}$ (0.27, 1.76)** | -7.59 (-7.76, -7.42)** | 177 (169, 179) | 0.59 |
| Italy                    | 31 Jan                   | 24 Feb          | 16 Mar (46)                       | 21                       | 31 Mar (61)  | 1.12 $\times 10^{11}$ (0.72, 1.52)** | -5.53 (-5.62, -5.49)** | 230 (222, 234) | 0.31 |
| Russia                   | 1 Feb                    | 28 Mar          | 27 Apr (87)                      | 30                       | 12 May (102) | 1.55 $\times 10^{11}$ (1.19, 1.91)** | -9.01 (-9.06, -8.96)** | 383 (340, 420) | 0.69 |
| Spain                    | 1 Feb                    | 14 Mar          | 20 Mar (49)                      | 6                        | 1 Apr (61)   | 2.94 $\times 10^{12}$ (0.76, 5.13)** | -6.92 (-7.10, -6.74)** | 237 (229, 240) | 0.31 |
| United Kingdom           | 1 Feb                    | 23 Mar          | 1 Apr (61)                       | 9                        | 19 Apr (79)  | 3.74 $\times 10^{11}$ (2.54, 4.94)** | -6.02 (-6.09, -5.95)** | 250 (230, 264) | 0.48 |

Note: $^A$ References on the lockdown dates are reported in the Appendix A.2.

$^A$ Values are related to 120 days after the start of the epidemic. CI of $N$ are calculated by CI of $a$ and $b$.

$^A$ In parenthesis we report the number of days since the start of the epidemic.

$^A P < 0.01$, $^{**} P < 0.001$

$^A$ Date of local lockdown. National lockdown was declared in Germany on 23 March, in Italy on 9 March, and in Russia on 30 March.

![Fig. 1](image-url)

Fig. 1. Cumulative distributions of observed cases and $C(t)$ curves obtained by the model. The dot and dash line indicates the end exponential phase of $C(t)$.

of the $N$ parameter were in agreement with the observed cumulative counts after 120 days from the begging of the outbreak, as reported in Table 1.

Fig. 1 shows the cumulative distributions of the diagnosed cases and the fitted $C(t)$ curves obtained by our model ($P$ of the fit parameters < 0.01). When observing the curves, it is clear that France, Germany, Spain, and Italy were in a more advanced phase of the outbreak at the end of the period considered. The point and dash lines indicate the points of inflection of $C(t)$, corresponding to the end of the exponential phase. These points were obtained from the maximums of $C(t)$.

Fig. 2 reports the daily distributions of the diagnosed cases and the $C(t)$ curves. It is worth noting that Russia and the United Kingdom had the epidemic peak for a few weeks. Starting from the
beginning of the epidemic, Italy and Spain reached their peak in 61 days, Germany in 68 days, France in 72 days, the United Kingdom in 79 days, and Russia in 102 days. The KS test provided significant results for all the countries considered ($P = 0.69$ for France and Russia; $P = 0.59$ for Germany; $P = 0.48$ for the United Kingdom; $P = 0.31$ for Italy and Spain). Therefore, observed and modelled daily data can be considered as descending from a same distribution. The point and dash lines indicate the points of inflection of $C(t)$, corresponding to its SGR.

The $C'(t)$ curves are shown in the Fig. 1 of the Appendix A.3. For countries towards the end of the epidemic, these curves first have a maximum, next they cross zero, then they have a minimum, finally they asymptotically tend to zero. The maximum of $C'(t)$ indicates the point of inflection of $C(t)$, that is the SGR.

4. Discussion

The $C(t)$ function used to fit the cumulative distribution of cases has a pattern with an initial exponential phase and a final slow saturation phase, which resulted in matching closely with observed data of all countries taken into consideration. In fact, the model provided statistically significant $C(t)$ curves ($P < 0.01$) for the countries toward the end of the outbreak (France, Germany, Italy, and Spain) and for those that had the epidemic peak for a few weeks (Russia and the United Kingdom). The good adaptation of the function to data is due to the particular parameterization adopted. On the other hand, beyond the application reported in this study, it was successfully used as a forecast model of COVID-19 in Italy [22].

As expected, also the $C'(t)$ functions resulted statistically significant. The ascending phase of the epidemic was faster in Italy and Spain, and this feature could explain the dramatic health emergency occurred during the first months of the outbreak. It is also interesting to note that in all countries the epidemic peak was reached from 12 to 18 days after SGR.

The growth rate of the function $C(t)$ increases up to the inflection point and then decreases, as can be deduced from the trend of the $C'(t)$ curves. It is reasonable to suppose that this variation, i.e. the SGR, was due to people’s behaviour to avoid contagion and lockdown imposed by governments. In fact, had no measures been taken to slowdown the spread of the Coronavirus, the diffusion of the epidemic would have increased until herd immunity would be achieved.

As the mean time of the SARS-CoV-2 disease incubation was estimated in about 5 days [24,25], we could reasonably infer that the observation of a time greater than 5 days between lockdown and SGR can be interpreted as a cause-effect relationship. As a matter of fact, a time interval less than to 5 days is too short to consider the lockdown as main effect of the SGR, because it is also necessary to add few days to the mean incubation period in order to consider a delay for the diagnoses and the updating of data. In light of these clarifications, for all countries considered we can infer a cause-effect relationship between lockdown and SGR. In particular, for Germany, France, and Spain, there was indeed a major contribution thanks to the different behaviour citizens had to limit contagion. On the other hand, just considering the dates of national lockdowns, only Germany has a no compatible time interval with a cause and effect connection. As a matter of fact, governments issued early advice about going out only for essential needs, avoiding crowded places, wearing face masks, washing hands frequently.

In general, the rules adopted to counter the spread of the epidemic were similar in the countries considered. In fact, the laws enacted by governments had as a common denominator the objective of keeping the citizens at home. However, some differences among countries were observed. France, Germany and Italy approved a national curfew during the night. In the United Kingdom, some universities adopted a blended model that mixed remote and in-person teaching. Likewise, the Italian government implemented the hardest lockdown, with restrictions also on physical activities outdoors. However, in this country remote working was largely implemented, as well in France, Germany, Spain, and in the United Kingdom. Also wearing masks when travelling by public transport was a generalised measurement to contain the COVID-19 outbreak. In general, public transport was reduced. As a matter of fact, business related activities and school attendance do not necessarily imply an extensive or exclusive use of public transport. Another social distancing measure was physical distancing (at least one meter). Considering these restrictions, the low population density in Siberia may have played a role in the epidemic spread in Russia.
Generally, the closing of schools and workplaces were drastic decisions, but necessary to contain the pandemic. This led to well-known consequences for student learning and an economic negative impact. Unfortunately, after the first epidemic wave, such rules were adopted again, at a national or local level, to contain the new COVID-19 outbreaks.

A limitation of our method is represented by its non-applicability to data with an irregular trend. For an example, a new spread of COVID-19 after the lockdown - caused by the general public resuming behaviour which was common prior to the Coronavirus outburst - makes the trend of the curves not regular, therefore not making the model adaptable to data. This limitation could be solved applying the model on temporal intervals of the counts with a regular trend. Other limitations to our method are related to counts and updating of data. As a matter of fact, since there were many undetected asymptomatic individuals, the number of infected people may have been underestimated. We also consider as a limitation the Russians of Asian ethnicity, who could help explain the differences observed between Russia and the other countries. Moreover, the untimely updating of counts could have had an impact on the trend of the functions. The purpose of this study was to develop a generalised model of the pandemic caused by COVID-19, with the aim of obtaining useful information on the effectiveness of the containment measures taken. To note, that our method is able to determine the slope change in a completely analytical mode, without a priori assumptions. On the contrary, the Interrupted Time Series Regression [26] is a method used for the same purpose in studies of public health, which requires empirical choices [27]. Our model showed a good adaptation to observed data of the most affected countries in Europe, but it can be used with data of other countries.

Lockdowns imposed by governments were useful to decrease the number of people infected and to slowdown the spread of the virus. Several studies reported that social distancing can be useful to mitigate Coronavirus transmission [14–16]. In addition, a study based on simulations reported the efficacy of the social distancing in conjunction with testing and contact tracing of all suspected cases [28]. On the other hand, to support the effectiveness of lockdowns, it is possible to detect the remarkable increase of new cases observed about one month after the end of most stringent measures of the lockdown in May, which took place in all countries except for the United Kingdom (see the references on the lockdowns in the Appendix A.2). As a consequence of the implemented health policies, all the countries considered, except Russia, succeeded about to cancel the new infections approximately five months after the outbreak began (see Fig. 1 in the Appendix A.4, where daily counts are showed until 31 December 2020). Unfortunately, the result on the counts reduction was not maintained in these countries. It is likely that the resumption of infections was caused by several factors, such as a superficial approach to infection control, which allowed unrestricted movements of citizens both within and across different countries; the general public increasingly did not keep on respecting governmental guidelines to prevent and reduce the spread of the disease; the end of summer, with increasingly more indoor activities and higher risk exchanges.

Because of the abovementioned factors, infection levels started to increase again at the end of August, forcing governments to adopt further restrictive measures and ultimately new lockdowns. Many countries [29] implemented both health and non-health measures [30], with a broad spectrum of implications largely beyond the healthcare context and not always based on evidence of the actual documented effects of interventions. Going forward, governmental policies should also consider significant investments in public health promotion, structural long lasting technological interventions and economic sustainment measures to mitigate the effects of social distancing and the disruption of entire sectors of the economy.

Better transparency and communication for the implemented policies is essential [17], both for the prevention of the disease spread but also in order to make sure measures being rolled out or planned for the short and long term are well received and followed through by all the stakeholders involved, in all levels of society across nations.

Analyzing how governmental policies may be facing at times divergent reactions by the general public, with different levels of acceptance or rejection across countries (North-South divide [29]) is essential to better understand the determinants of such diversities, so that adaptive health and non-health related policies may be implemented with success.

At a global level, an important role in the evolution of the pandemic could be played by Coronavirus mutations [31]. A genomic study showed that a SARS-CoV-2 variant carrying the Spike protein amino acid change D614G seems to be the prevalent form in the global pandemic, with a higher degree of infectious capacity [32]. A SARS-CoV-2 variant (called 202012/01), sequenced in the United Kingdom on December 2020, seems associated to an increase of new cases in this country. Preliminary results on this virus mutation shown no statistically significant difference in hospitalisation and in the likelihood of reinfection between variant cases and comparator group [9].

5. Conclusions

The pandemic due to the SARS-CoV-2 virus is breaking down like a tsunami on a large part of the world population from early 2020. The implications in terms of public health, workload in hospitals, and economic damage were worrisome. Since there is no evidence of effective treatment regimens and successful vaccines have been available on December 2020, the majority of world governments declared a lockdown.

We developed an analytical model of COVID-19 pandemic so that we could follow the evolution of the cumulative and daily counts of diagnoses cases in the most affected countries in Europe (France, Germany, Italy, Russia, Spain, and the United Kingdom). We applied our model to data of the first four months of the pandemic in relation to this situation of an increase of infections post-lockdown. Indeed, in all countries taken into consideration, the initial date of the outbreak occurred between late January and early February. Therefore, we studied the trend of the epidemic until late May or early June, that is until a few weeks after the resumption of some activities stopped with the lockdown. Our model, tested on data of the countries taken into consideration, resulted to be matching appropriately with the observed distributions. In particular, we were able to determine the time interval between the beginning of the lockdown and the slope change in the curve representing the daily distribution of cases. For all countries considered, this time interval resulted to be greater than the mean time to manifest symptoms of the Coronavirus disease. Through the proposed model, we obtained the epidemic peak dates, then the duration of the ascending and descending phase for each countries. Based on these considerations, our method could be useful in public health to understand the various steps of the evolution of the epidemic, also for different countries with respect those considered.

Currently, a second wave is taking place in Europe, with daily counts greater than the observed peaks during the first wave. The signs of a new increase in the number of infections should be a warning to governments and citizens to continue enforcing behaviours aimed at containing the spread of the pandemic, until herd immunity can be achieved through effective vaccines or medical treatments mitigating the effects of the disease.
The lockdowns imposed by governments due to the dramatic health emergency generated by the Coronavirus disease are creating considerable damage to the world economy. At the same time, efforts made globally to find effective vaccines and targeted treatments have led to important results in less than a year. Favourable phase 3 trial outputs were published in December 2020 [33,34] while other vaccine candidates are scheduled for completion within 2021 [35,36]. During the first and second quarter of 2021 mass vaccination campaigns will play an important role in reducing the spread of the disease. Health policies will be fundamental to restarting the economy, by securing the strategic sectors of the states, such as health, and education. Moreover, thanks to successful clinical research finalized during the Covid-19 pandemic [36,37] we can expect new effective vaccines and more targeted medical treatments, such as monoclonal antibodies, also for other diseases. In such critical context, the best health policy to be implemented should be aiming at transforming challenges into opportunities.

Since global control of the SARS-CoV-2 pandemic is challenging, not only the appropriate governmental policies will be needed to eradicate the disease, but also the individual behavior of all parties involved, including the general public and not only the healthcare professionals.

The World Health Organization has included "vaccine hesitancy" among the 10 threats to Global Health [38]. The lack of trust in vaccines and mistrust towards the various stakeholders in the supply chain (in particular drug companies and governments) are some of the main reasons behind the reluctance towards vaccines and this can be a critical challenge in stopping COVID-19.

We should not take for granted the promotion of the importance of vaccination, which can change a lot depending on the countries, socio-economic contexts, religious affiliation, and changes in government policies [39]. Immunization programs should not be confined to insiders alone. Communication should also be simplified and disseminated through different channels with "tone of voice" suited to the context. In addition, schools, companies, public administrations, transport services and many other realities should be systematically included, through information and promotion of vaccination programs beyond purely health contexts and far beyond simple measures dedicated to public health.

Declaration of Competing Interest

None.

Acknowledgments

The author thanks Dr. Alessandro Gallo for providing medical writing support, specifically for manuscript copyediting, performing literature search and verification of references.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.healthpol.2021.09.008.

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