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Coronavirus Pandemic

Nonpharmaceutical public health interventions to curb the COVID-19 pandemic: a narrative review

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Abstract

Nonpharmaceutical Interventions (NPI) consist of compulsory (isolation, quarantine, stay-at-home orders, banning public gatherings, nonessential business closures, school closures), and voluntary (social distancing, handwashing, respiratory etiquette, and universal mask wearing) measures. The aim of this narrative review is to evaluate the different forms of NPI and their effectiveness in combating the pandemic. Isolation can be indicated for symptomatic and asymptomatic infected people at home or at hospitals depending on the patient's clinical picture. Quarantine is a social distancing intervention in asymptomatic uninfected people who had contact with SARS-CoV-2 infected individuals. Stay-at-home orders refer to statewide mandates imposing nonessential business closures, prohibition of public events and gatherings, and travel restrictions. Studies have suggested that stay-at-home orders may be associated with a reduction in the incidence of COVID-19 in some countries. Mask wearing decreases the risk of COVID-19 in the community, especially when the surgical masks are used for vulnerable people. N-95 respirators protect health workers from COVID-19. NPI may be helpful to curb the COVID-19 pandemic while mass vaccination worldwide is not attainable, and the threat of SARS-COV-2 variants remain on the horizon.

Key words: SARS-CoV-2; COVID-19; Nonpharmaceutical Interventions.

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Introduction

Nonpharmaceutical public health interventions (NPI) can help curb the pandemic caused by SARS-CoV-2 until mass vaccination has been attained worldwide, and in the settling of the surge of SARS-CoV-2 variants of concern. NPI have been used in an attempt to tackle previous pandemics caused by contagious diseases, especially those inflicted by viral infection. NPI consist of compulsory (isolation, quarantine, stay-at-home orders, banning public gatherings, nonessential business closures, school closures), and voluntary (social distancing, handwashing, respiratory etiquette, and universal mask wearing) measures. In some countries, these measures are deployed via the public health authority's orders, and any non-compliance with such orders is penalized with fines or jail time [1].

Isolation refers to the confinement of an infected patient at home or in hospital. Quarantine refers to the confinement of those exposed to an infected patient, which may be completed at home or at community facilities, that may be especially designed for this purpose, or in public buildings readapted for this purpose.

Banning public gatherings refer, in general, to closure of bars, public entertainment venues, sporting events, and indoor gatherings. Maintaining a minimum distance of 1 m (3 ft) from one person to another has also been recommended. The efficacy of such measures remains largely unknown because they have not been tested in randomized trials. In addition, some interventions may indeed increase the risk of contagiousness [2], as is the case of quarantine in low and middle-income countries because of overcrowded living arrangements.

In the case of COVID-19, the effectiveness of NPI to overcome the pandemic is not entirely known because their use exceeds what studies during previous viral pandemics concluded, and because they have not been tested in randomized, controlled trials. In addition, some data are obtained from observational studies, but the study end-point varies from one study to another, and there are no studies whatsoever assessing specifically the efficacy of any particular type of NPI. Therefore, a formal metanalysis or a systematic review of medical literature regarding the role of NPI in curbing COVID-19 is unfeasible.

Accordingly, the aim of this narrative review is to search for evidence of NPI efficacy to curb the COVID-19 pandemic.

NPI in the context of COVID-19 pandemic

Isolation

Isolation of infected patients seems to be an effective containment strategy to fight COVID-19. Isolation can be done in community treatment centres which are temporary facilities especially prepared to combat the pandemic where patients receive daily medical care. Self-isolation at home, isolation in nurse care facilities, in hospitals, or in isolation camps (sports centre, health resorts, convention centres) can also be done [3].

In low-income countries, self-isolation is a problem because of limited space within the housing arrangements. In fact, it is almost impossible to isolate an infected person who lives in an overcrowded house [4]. In this context, the isolation could be done in isolation camps facilitated by governments, in health resorts, holiday camps, hotels, convention centres, and sport complexes. This has been successfully done, for example, in Mongolia [5]. Nevertheless, this still is an intangible measure since COVID-19 has become a disease of vulnerable people [4].

Isolation can also be indicated for asymptomatic infected people. The following example outlines the need for isolating asymptomatic SARS-CoV-2-infected people. During an outbreak associated with a religious cult, 303 patients were diagnosed with SARS-CoV-2 infection based on a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test. Of those, 193 (64%) were symptomatic, whereas the remaining 110 (36%) patients were asymptomatic on isolation. Of the asymptomatic patients, 21 (19%) developed symptoms consistent with COVID-19 during the isolation period, and the remaining 89 out of 110 (26%) were asymptomatic. Importantly, the viral load and the proportion of negative test conversion was similar between symptomatic (70%) and asymptomatic people (75%) 21 days following the initial diagnosis [6].

Although the isolation centres of symptomatic and asymptomatic patients are efficient in controlling the contagion, it is necessary to balance the risk posed by NPI in societies governed by authoritarian regimes and countries with a low human development index (HDI) with the benefits brought by NPI themselves, before having them introduced as a health measure.

Quarantine

Quarantine is a social distancing intervention in asymptomatic uninfected people who had contact with an individual with SARS-CoV-2. It is necessary because those who have had contact with other infected people, even though asymptomatic, may transmit the disease, or will be symptomatic within the next 14 days on average. However, the incidence of patients who tested positive during the quarantine period varies from one study to another.

One such study on 126 asymptomatic patients returning from Wuhan to Germany, has shown that only two (2%) patients developed COVID-19 during the quarantine period [7]. Another study reported data from 92 asymptomatic patients who had flown from Wuhan to Singapore; one patient (1%) tested positive, whereas others had inconclusive test result [8].

An outbreak that occurred in a call center in South Korea showed that among 1,146 employees, 97 (9%) developed SARS-CoV-2 infection; of these, 89 (92%) patients were symptomatic at the time of testing, 4 (4%) were pre-symptomatic (developed symptoms later on), and 4 (4%) were asymptomatic after 14 days of quarantine. About 225 households with confirmed cases were followed; COVID-19 was found in 34 (16%). Interestingly, no household of pre-symptomatic or asymptomatic patients developed COVID-19 in the follow-up days [9].

In low and middle-income countries, quarantined individuals who wear masks inside the house and practice self-distancing may decrease the probability of secondary attacks in other family members [10].

Stay-at-home orders

Stay-at-home orders refers to statewide mandates imposing nonessential business closures, prohibition of public events and gatherings, and travel restrictions [11]. Stay-at-home orders have been enacted in some parts of the world. Nevertheless, its efficacy to curb the pandemic is unknown. Some studies have suggested that stay-at-home orders may be associated with a reduction in the incidence of COVID-19 in some countries.

In the United States, the incidence of COVID-19 for 10,000 residents at 10, 20, and 30 days following a stay-at-home order was -0.51 ($p < 0.01$), -1.15 ($p = 0.02$), and -4.71 ($p = 0.02$), respectively, in a state that adopted this social intervention in comparison with another that did not. This suggests that stay-at-home order for the general population may be accompanied by a reduction of 217 cases per month of COVID-19 [12].

After a stay-at-home order in four states of the United States, the incidence of hospitalization due to COVID-19 was 64% less than projected, suggesting that the measure was effective in lowering the cumulative incidence of hospitalization. However, stay-at-home orders were enacted with other NPI. Furthermore, loss of health insurance observed in the same period may also have contributed for the decrease in hospitalization. Therefore, it is difficult to know how effective this order really was [13]. A reduction in the number of cases from 12% to 5% has also been observed in another study, thus slowing the case-doubling rate from 6 days to 14 days [11].

Social Distancing

The fact that SARS-CoV-2 is transmissible from person to person, mainly by droplets [14], and more rarely by airborne viral particles [15], has led policymakers to suggest that people should keep a distance from one another. However, which distance should keep people apart is still debatable. A recent metanalysis has apparently filled this gap. Chu *et al*. performed a metanalysis on 7 longitudinal cohort studies enrolling 577 patients; they found that a distance of 1 meter between people was associated with a relative risk of 0.30 in comparison to no distance at all among people. Moreover, the authors observe that a distance of 2 meters was even better than the distance of 1 meter between people [16].

Prohibition of gatherings with more than 10 people

Gatherings of more than 10 people have been associated with the spread of COVID-19. In a scientific meeting involving 14 people who shared a room of 70 m² for 9.5 hours without any NPI, one symptomatic patient tested positive for SARS-CoV-2 one day after the meeting ended. This index patient spread the disease to 11 other people who had attended the meeting [17]. A choir practice has also shown that, among 61 participants, one was symptomatic, and transmitted the disease to 53 other patients. The same has occurred in a call centre in which 97 (8.5%) of workers were infected following the observation of one case of COVID-19 [9].

Mass religious gatherings pose an even higher risk to the population. In Malaysia, an international religious ceremony with 19,000 people was responsible for 5,000 new cases of COVID-19. After returning to their country of origin, these people spread the disease to at least 6 other countries [18]. To avoid such problem, the Lunar New Year in Mongolia was cancelled before the first case of COVID-19 [5].

Despite limited evidence, this NPI has been largely popular. A nationwide survey conducted in the United States has shown that about 85% of interviewed people in Los Angeles, New York and in the country as whole agree with such recommendations. This acceptance, however, was higher in retired rather than unemployed people, and in older than younger people. Nonessential workers adhered less than essential workers to this order [19].

Nonessential business closures

Nonessential business closures, as far as we know, have never been studied without other concomitant NPIs. Therefore, its impact on COVID-19 control is not entirely clear. Nonessential business closures usually refer to entertainment venues (theatres, cinemas, bars, restaurants, dancing clubs) being closed. It has been implemented to promote social distancing and diminish overcrowded gatherings. In the United States, about 67% of people agree with not dining in a restaurant as a means to protect themselves from SARS-CoV-2 [19]. In Mongolia, nonessential business closures were ordered as soon as the first laboratory confirmed case was observed [5].

School and college closures

School closures as a means to mitigate the impact of COVID-19 pandemic is a matter of considerable debate. School closures seem to have a positive impact on a viral epidemic when the virus has low transmissibility, and attacks more children than adults, as is the case with the influenza virus; the opposite has settled for SARS-CoV-2. In fact, the prevalence of SARS-CoV-2 infection in children (< 18 years) is low, approaching 0.65% [20]. In addition, in Taiwan, the COVID-19 pandemic was curbed without closing schools probably because the transmission rate in children in a classroom has a R_0 less than 1 [21]. Furthermore, a systematic review has shown that closing schools did not have any positive impact on COVID-19 mitigation as well as in any other coronavirus epidemic [22].

On the other hand, almost half of the children can be asymptomatic (22% of cases) or pre-symptomatic (20% of cases). In addition, pre-symptomatic children have a shorter duration of the average incubation period (2.5 days) than adults do. Furthermore, the mean viral shedding period in children is longer (17.6 days) than observed in adults. Therefore, the time of closure and reopening schools will continue to be a matter of debate [23].

Closing schools is not devoid of unbearable consequences. School closures lead to a USD 2.5 trillion loss in future earnings and may have caused a 19% reduction in working hours of health workers [24]. This is a big problem because a 15% reduction of health care workers has been associated with a marked increase in COVID-19 mortality [21]. Besides, grandparents may have to take care of children if the parents cannot; consequently, a rise of COVID-19 might be anticipated in this high-risk population, as had happened in Italy early in the pandemic. Furthermore, in many countries, school is a provider of meals and nutrition; school closures, therefore, may be associated with children malnutrition [24]. Finally, school closures can aggravate social iniquities. Therefore, the benefits of school closures should outweigh the problems associated with them.

A population-based longitudinal study carried out in 50 states of the United States assessing the impact of non-college schools closing on clinical course of COVID-19 has showed a reduction of 62% in cumulative incidence, and a reduction of 58% in mortality after adjustment for other non-pharmaceutical interventions (stay-at-home orders, nonessential business closure, and prohibition of gathering with more 10 people). States that enacted closing schools earlier in the pandemic benefited more than those that enacted closing schools later. Based on these findings, it was estimated that 137 million cases of COVID-19 were prevented over a 26-day-period, and 40,600 deaths were precluded over a 16-day-period [25]. However, the contribution of closing schools in comparison with non-pharmacological interventions has not been determined in that study.

Therefore, reopening schools is largely desirable provided that the benefit outweighs potential risks. Children appear to have been less infected than adults. In addition, when infected, children develop less severe disease than adults. However, children can transmit the disease to adults. Therefore, a proper balance is needed before schools can reopen. In this sense, the best way to reopen schools is to maintain a low transmission rate of COVID-19 in the community. In fact, countries that have a low transmission rate of the pandemic have opened primary schools with nonpharmacological measures to contain the virus without any additional burden on the community [26].

Reopening colleges during a pandemic is a colossal task. On the one hand, it is necessary to consider the financial implications because many schools are private and need economic input. On the other hand, it is a priority to guarantee the students' health and safety. As far as colleges are concerned, Paltiel *et al.* have developed an analytic model to simulate a safe college return. Along with other well-recognized nonpharmacological measures to curb the pandemic, testing students every 2 days would allow a safe return to the campus [27]. However, testing every 2 days might not be feasible in practice.

Another model emphasizes that testing every 15 days is reasonable, if other nonpharmacological measures are taken, such as social distancing, wearing universal mask, contact tracing, self-quarantining, proper cleaning, physical barriers in areas of high traffic, improved ventilation, limiting the number of visitors, and isolation of diseased students [28].

Universal mask wearing

Wearing of masks has been recommended to protect people from being infected by SARS-CoV-2 and to control the spread of the virus from infected people. This universal mask wearing may be particularly useful to protect people from transmission by asymptomatic people with SARS-CoV-2 in a hospital setting, especially health workers [29]. Nonetheless, wearing masks may be important to prevent SARS-CoV-2 infection in the community as well, especially in vulnerable people and those in quarantine [30]. However, the type of mask to be used is still a matter of debate.

A recent metanalysis [16] has shown that face masks – N95 respirators, medical mask, or cotton mask- are associated with 34% relative risk of coronavirus infection, suggesting a 66% reduction in favor of mask wearing. The use of N95 masks were associated with a greater reduction versus no mask using (RR = 0.04). This was not surprising since N95 respirators are associated with a 95% reduction in small droplets inhalation, whereas surgical masks reduce droplet inhalation by up to only 30% [31]. In contrast, a metanalysis of four randomized control trials has shown that the performance of surgical masks is similar to that seen with N95 masks to preclude viral infection, including those by coronaviruses or influenza, in health care workers. The authors suggested that N95 masks should be for aerosol-generating procedure [32].

A study performed on health workers showed a 22% reduction in infection following universal (health workers and patients) mask wearing orders [3]. However, N95 masks may not be recommended for general public use. In fact, only about 12% of 714 contactors of infected patients passed a visual fit mask test [34]. Since the commonest mask misuse was leaving a space between the mask and the wearer's skin,

it is conceivable that the common public using these masks are, indeed, at higher risk of SARS-CoV-2 infection.

Medical masks are recommended for vulnerable people (> 60 years of age and with underlying comorbidities) and for infected patients. Non-medical mask is recommended for people in public settings, on public transportation, and when a close contact can be anticipated (cashiers, servers etc) [35]. Notably, medical masks with ties have a higher (71%) performance in filtering particles than medical mask with ear loops (38%) [36]. However, evidence to support such recommendations in the setting of COVID-19 is limited. Moreover, a randomized trial carried out in the setting of influenza-like illness has shown that non-medical masks (cotton mask) are associated with higher level (RR=13: CI 1.69 to 100) of influenza-like disease in comparison with the use of surgical mask [37]. Therefore, the recommendation for cloth mask use should be received with caution; it should not be recommended for health workers and preferably not for vulnerable people.

The reuse of N95 masks is not recommended but has been accepted in the setting of availability curtailment of these respirators, especially for health workers. However, if reused, 3 to 5 shifts or an average 12 hours of use may be accepted. However, dome-shaped N95 mask should be worn instead of N-95 duckbill masks because the latter has a failure rate three times higher in comparison with the former [38]. Furthermore, expired N95 masks or sterilized N95 still maintain their filter capacity > 95%; therefore, in case of limitations in availability of masks, such masks may continue to be used with similar efficiency [36].

Face touching is believed to be an important way to start a COVID-19 infection. Masks may prevent droplets or airborne virus particles from entering through the nose, mouth, and eyes. A study compared the face touching behavior before and during pandemic; a marked decrease in this behavior was observed in many countries, mainly in those where mask wearing was mandatory [39].

Since symptomatic or asymptomatic people can transmit SARS-CoV-2, shared workplace offices should enforce the wearing of masks, frequent handwashing, and keeping the office space as ventilated as possible. People with coughing symptoms should not share offices. By following these practices, the risk of being infected by an asymptomatic person is lowered. Another possibility for increasing protection is the use of face shields.

It has been shown that wearing face shields along with masks is associated with a 66% reduction in the infection rate of SARS-CoV-2 [16]. A study carried out on community health workers who used alcohol hand rub, surgical masks, gloves, and shoe covers routinely during the work (counselling asymptomatic family contacts of patients who had tested positive for SARS-CoV-2) showed a decrease from 19% to 0% of COVID-19 following the introduction of face shields as personal protection equipment [40].

Interestingly, a country that has eliminated the pandemic has not used masking orders as part of the repertoire of nonpharmacological interventions to curb COVID-19 pandemic [41]. This underscores that fact that several NPI need to be deployed altogether.

Deployment of NPI

At this time, little is known about the efficacy of NPI to curb COVID-19 pandemic. It has now become clear that a combination of NPIs seems to be better than each measure in isolation, although evidence-based support for NPI is scanty. Cordon sanitaire, traffic restriction, social distancing measures, isolation, centralized quarantine, and mask wearing were deployed in Wuhan, the city in which the pandemic originated, 23 days after the beginning of the pandemic. The number of cases was 162.6 per million before NPI deployment and dropped to 77.9 per million about 23 days after NPI, and 17.2 per million thereafter. The reproductive number was 3.82 before NPI implementation, < 1.0 about 13 days after NPI implementation, and < 0.3 about 34 days after NPI implementation [42].

Specifically, the association of intra city public transport ban, closed entertainment venues, and public gathering banning were responsible for the marked decrease in the incidence of the disease, from estimated 744,000 cases to confirmed 29,839 cases [43]. A study performed in the United States enrolling 19,164 patients showed a marked decrease in the incidence of positive molecular tests for SARS-CoV-2 (from 17.85 to 3.8%, and from 14.3% to 9.8%) in two states. Such a decrease paralleled enacted measures of social distancing, namely shutting down bars and restaurants, banning social gatherings, and stay-at-home orders [44].

Implementing NPI depends on several social characteristics, and is not devoid of potential social disruption. Engaging people in such social interventions is crucial to the point that the community has “voice in all interventions” that have been planned [1]. One important aspect is the literacy level of the people who will follow the social restrictions so that

they are able to understand the benefit of such restrictions. The best example of this is Mongolia, a country with a low income but high literacy indicators, which was able to overcome the pandemic [5].

Another important factor is empathy of the leaders towards the community. This has been exemplified in the case of New Zealand, another country that has also overcome the pandemic, in which the Prime Minister invited the community to work "as a team of 5 million people" [41]. The role played by the media is also paramount; its work should be reassuring to the people. Instead, great emphasis on the daily numbers of death or new cases may be detrimental, as people may neglect the risk of the disease [1]. Unfortunately, this is what has happened in Brazil.

A crucial point to be highlighted is the rise of misinformation on social media, which might lead to myths about the COVID-19 pandemic, and false impressions regarding this illness based on fake news [45]. For example, it is cumbersome to see fake news concerning the erroneous concept of the side effects of wearing masks that are publicized online, thus falsely encouraging people not to wear masks [46]. However, Vraga and Bode have studied fake news in the setting of COVID-19 and have fortunately shown that a correct information passed forward by reputable entities (like the World Health Organization, WHO, for example) may reduce misconceptions about COVID-19 prevention by 11%, thus counteracting the criminal misinformation against mask wearing to curb the pandemic [47]. Furthermore, it is reassuring to learn that people with critical thinking and who are knowledgeable about COVID-19 are less likely to remember false information when exposed to fake news in comparison to those without such characteristics [45]. Therefore, education is by far the best way to counteract fake news regarding NPI to curb the pandemic.

It must be pointed out that implementation of NPI, especially in the absence of social protection, depends heavily on the maintenance of familial income for living expenses. Economic recession associated with NPI to mitigate the impact of COVID-19 may be cumbersome, especially in low and middle-income countries. For example, a previous economic recession in Brazil, before the COVID-19-induced pandemic, caused 31,415 additional deaths secondary to cardiovascular disease or neoplasia [48].

Moreover, the number of suicides associated with NPI in the setting of COVID-19 is expected to cause an excess of 9,570 deaths worldwide [49]. Finally, lockdown and stay-at-home orders could cause more child deaths than COVID-19 [50]. Besides the adverse economic impact, unemployment can be associated with social violence. Social distancing measures have been associated with physical and emotional distress, and sexual abuse. In fact, a 25% increase in the sexual abuse cases have been observed in cities placed in lockdown [51].

Another important consequence of NPI is related to its impact on the management and treatment of cardiovascular diseases during the pandemic. A survey carried out in emergency departments of hospitals in Germany has shown a decrease in emergency admissions for heart failure by 22 to 28%, and for cardiac arrhythmias by 15 to 27% [52]. A marked decrease (about 15%) in hospitalizations for heart failure have also been observed; this decline is higher in heart failure with reduced left ventricular ejection fraction (about 66%), but also occurs in patients with heart failure with preserved ejection fraction (about 27%) [53]. Finally, the incidence of new-onset heart failure has also decreased by 30% [54]. The impact of such findings on morbidity or patient's excess mortality is unknown.

The same situation can also be observed regarding the incidence of acute myocardial infarction during the pandemic. The number of patients hospitalized for acute myocardial infarction dropped from 1,051 (4.1 per 100,000 persons-weeks) before the pandemic, to 61 (2.1 per 100,000 persons-week) during the pandemic. This decrease in the incidence of acute myocardial infarction was similar in patients with ST-elevation and non -ST-elevation myocardial infarction [55].

Another group that is severely threatened by COVID-19 is that of patients with neoplasia, who either may have not had access to oncological treatment or had their treatment postponed because of the risks of COVID-19. About 1% of patients with COVID-19 have concomitant cancer, which doubles the case-fatality of patients with both conditions. Furthermore, about 30% of hospitalized patients for cancer treatment developed SARS-CoV-2 during hospital stay, but only 1% of patients with cancer have been hospitalized for regular treatment [56]. It has been recommended that the treatment of patients with active cancer should be continued with medical oncology, surgical oncology, or radiation oncology whenever possible at the discretion of the attending physician [57].

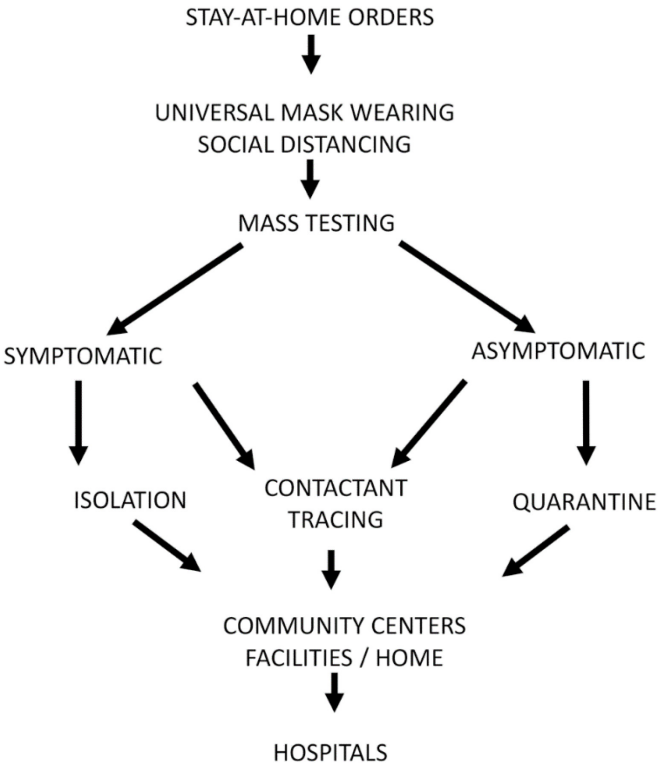
This holds particularly true for patients with early-stage cancer on curative chemotherapy since the benefit of treatment outweighs the risk of being infected with COVID-19 in infusion centers [58]. Since the delay of cancer treatment increases mortality, as observed

specifically in cases of breast cancer [56], postponing treatment is a priori not justifiable; rather, it requires a balanced decision by the attending physician considering the pros and cons.

It is important also to consider the apparent decrease in cancer incidence. A comparison between the incidence of six types of neoplasia (breast, colorectal, lung, pancreatic, gastric, and oesophageal) before and during the COVID-19 period has shown a marked decrease in the diagnosis of such neoplasia, varying from 25% in pancreatic cancer to 52% in breast cancer, thus confirming the negative impact of COVID-19 on patients with cancer. This reduced cancer incidence may be related to unemployment [56], which, in turn, may be secondary to the adoption of NPI in an attempt to curb COVID-19, ultimately being responsible for a projected 34,000 additional deaths [59].

It should be remembered that the possibility of a second wave of SARS-CoV-2 following NPI deployment remains, especially when universal testing and contact tracing have not been performed simultaneously. A model estimating R_0 in the mainland China has suggested that, following a lockdown, when the R_0 is > 1 again, the number of cases will increase exponentially, which is projected to be even worse than the first wave of infection, in terms of infected case numbers [60]. Figure 1 illustrates our suggested approach to deploy NPI.

Figure 1. Suggestion of deployment of Nonpharmaceutical Interventions to curb the COVID-19 pandemic.



Conclusions

It should be pointed out that only NPI deployment will probably not have a sustainable effect on curbing the pandemic. Universal mass testing, isolation or quarantine of asymptomatic and/or symptomatic infected people in community centres, not in overcrowded living arrangements, and close tracing of contacts have been successfully deployed in countries that have overcome the pandemic along with some types of NPI [61,62]. Therefore, correct investment on measures that are effective in curbing COVID-19 for a given country, with minimal social disruption is the best we can do while mass vaccination worldwide is not attainable, and the threat of SARS-CoV-2 variants are still on the horizon.

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