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Review Article

Latest Effective Measures to Combat COVID-19: A Review

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Abstract

More and more people realize that implementation of preventive measures is the only option left to counteract the coronavirus disease 2019 (COVID-19) before specific antiviral drugs are developed. Hence, a number of behavioral, clinical and state interventions have been conducted by dozens of countries to stop or slow down the spread of the virus in the early stages of the epidemic. At present, with the evolution of COVID-19 pandemic getting worse, synthesizing and implementing all measures available are of paramount importance. However, some measures are still being controversial. We aimed to assist policymakers in decision making for better pandemic preparedness. We reviewed the literature that reported accumulated scientific experience to date and summarized the epidemic prevention and control measures in three aspects: control the source of infection, cut off the routes of transmission and protect the susceptible population. First of all, some new approaches were introduced to control the source of infection, such as implementing contact-tracing apps, nucleic acid mixed detection, repeated testing and the establishment of some specialized laboratories. Second, we need to take various measures to cut off all possible routes of transmission, especially persistently pay close attention to checking cold chain foods. Third, due to no valid vaccine has yet been developed, some measures that can cut development time of more conventional vaccines should be implemented or considered. By synthesizing the scientific experience in fighting the COVID-19 epidemic, we suggested the latest effective measures should be carried out concurrently from three aspects, so as to avoid making grim situation even worse.

Keywords: Effective measures; SARS-CoV-2; Cold chain; Routes of transmission; COVID-19

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), known as a member of the coronavirus family with a large, single-stranded, positive-sense RNA genome, is responsible for the pneumonia outbreak of coronavirus disease 2019 (COVID-19) (1). Approximately a third of people with COVID-19 infection remain asymptomatic (2), whilst a large proportion of patients usually show mild symptoms, including fever, cough and shortness of breath (3, 4). What's more, some patients progressed rapidly with acute respiratory distress syndrome and septic shock, which was eventually followed by multiple organ failure and death (4). With the accelerated spread of the disease, a total of 79 million cases and 1.7 million deaths have been reported globally as of 27 Dec 2020 (5). In this case, the current pandemic has created an un-

precedented impact on the public health and global economy in modern history.

In view of the urgency of the epidemic, many control measures are being introduced by nations around the world, including the implementation of strict quarantine measures, application of social distancing measures at schools and workplaces, lockdown of communities, intensive public education on personal hygiene such as frequent hand washing and wearing face masks, cancellation of large-scale events and even the issuance of flight bans to and from infected countries (6-8). However, some of these measures, such as general lockdown, proactive school closures and making it mandatory to wear masks in public places, have been widely debated in some countries (9-11).

Recently, as winter has begun in the Northern Hemisphere, COVID-19 outbreaks are getting worse, especially in regions that do not have the virus's spread under control (12). In Europe, the second wave of pandemic is under way. On 31st Dec 2020, the New Year's Eve, 55,892 coronavirus cases have been recorded in United Kingdom , marking the highest daily increase in coronavirus cases since the pandemic began (13). Meanwhile, prevalence had increased across all age groups compared with the previous round, and remained the highest in 18-24 yr olds (14). Many European countries such as England, France and Germany have already announced second national lockdowns (14, 15). According to data by the Centers for Disease Control and Prevention, the United States first crossed 200,000 new COVID-19 cases on the 3rd Dec 2020. Infections continued to climb to record levels, and on 30th Dec 2020, the nation recorded 230,337 new cases (16). Even in China, where pandemic has been controlled, the risk of outbreak increases. After a 2-month period without local transmission in China, new locally transmitted COVID-19 cases were confirmed in Xinjiang Uygur Autonomous Region, Beijing, Shenyang and four of China's largest port cities, Shanghai, Tianjin, Qingdao and Dalian (17-19). Therefore, in this review, we summed up accumulated scientific experience in fighting the COVID-19 epidemic and recommended latest measures to reduce outbreak risks, which will provide a powerful reference for epidemic control and the development of epidemic prevention measures.

Control the source of infection

Finding the source of infection is crucial for controlling the pandemic. First of all, in areas with severe epidemics, the community should implement quarantine or closure measures, for example, set up temperature checkpoints at entrance and exit, perform the identification and temperature measurement of each resident entering and leaving the community (20). When the body temperature is abnormal, people should go to the hospital for taking nucleic acid test, and only after the result is negative, they can enter the community. Second, nucleic acid tests should be performed regularly for high risk or vulnerable groups such as volunteers, medical staff, people >60 yr old or with diseases that affect their immune system. And then, while the Center for Disease Control and Prevention has identified the COVID-19 patients, their family members, colleagues, friends, and all people who coincide with the trajectories of diagnosed patients should be organized to take nucleic acid tests immediately. In addition, the research on transmission chain and subsequent efficient intervention play critical roles in preventing further deterioration of COVID-19. Based on this, some countries have launched or planned to implement contact-tracing apps like health code. In China, health code is a code based on color, which determines people's risk of exposure and freedom of movement based on factors like their state of health, travel history, and duration of time spent in risky areas. It is divided into green, yellow, red, and according to the actual situation of dynamic conversion. The green code represents that the user is healthy and can move freely. People with yellow code or red code may have a potential risk of infection and need to self-quarantine, and cannot be allowed to enter the public place (21). After 7-14 days of home isolation, and no abnormality, their codes will be changed to the green codes.

In order to improve the efficiency and accuracy of nucleic acid detection, some effective measures such as nucleic acid mixed detection, repeated testing and the establishment of some specialized laboratories need to be taken urgently. 1) Close contacts and patients in fever clinic should be tested for COVID-19 singly, but for people at low risk, we can give priority to nucleic acid mixed detection. Specifically, nine or ten individual samples are pooled for a single nucleic acid testing. At present, there are two different strategies for sample pooling. One approach is pooling swab samples during the collection process, and the other is pooling viral transport medium of the samples in the laboratory (22). Samples in positive pool need to be tested one by one to find out which sample caused the positive result and to screen the corresponding patient (23). Rapidly, we collected swabs for repeated testing and isolate close contacts. This pooled screening strategy ensures the testing sensitivity roughly equal to that before, meanwhile, it could save the reagents, increase overall testing capacity of the COVID-19 with limited resources (24), and in the end, facilitate detection of early community transmission and implement timely infection control measures. 2) The importance of repeated testing has been widely known since the nasopharyngeal specimens may miss some infections and the probability of the SARS-CoV-2 being present in the nasal-pharynx increases over time (25). In areas with outbreaks of COVID-19, large-scale population repeated testing is crucial. Julian Peto (26,27) et al had recommended universal weekly testing as the UK COVID-19 strategy, and we believe it could complement with alternating periods of lockdown and relaxation of restrictions in controlling epidemic and saving millions of lives. 3) The rapid establishment of some specialized laboratories has played a significant role in the prevention and control of the epidemic. For example, the gas film version of the "Fire Eye" laboratory, as the largest nucleic acid testing laboratory in China, has improved the efficiency of nucleic acid testing significantly (28).

Currently, there is no very effective treatment for patients with COVID-19. The WHO announced on Oct 16, 2020 that remdesivir, hydroxychloroquine have little or no effect on severe COVID-19 cases, and only dexamethasone is effective in treating pneumonia and inflammation of the lungs (29). Therefore, we need to actively take a variety of measures in clinical treatment. The government should mobilize national resources to meet the demand of the clinical treatment, including building new hospitals and sending medical experts and clinicians to the worst affected area. Some countries and areas, such as the UK, Australia, China, Saudi Arabia and South Carolina (30-33) have given COVID-19 patients free tests or treatment. We believed that it is necessary to provide subsidies to avoid people abandoning treatment and leading to more spread, particularly in countries that have reached critical stage. Meanwhile, official clinical guidelines would be developed and updated in time based on the experience from clinical practice. In order to promote more rational use of medical resources, we should take different measures for patients with different degrees of disease severity. Until now, asymptomatic infection tends to be identified among young people (<20 yr old) and its proportion among all confirmed cases widely differed (from 1.95% to 87.9%) (34). Isolation and close observation at home for 14 days after diagnosis are regarded as a better option for these asymptomatic infections (35), and recent findings indicated that testing during quarantine may reduce the length of isolation, decrease the physical and mental stress caused by long quarantines (36). "However, suspected and confirmed cases must be treated in isolated hospitals with effective isolation and protection conditions" (37). For symptomatic patients, close monitoring of vital signs and symptomatic support treatment, including the treatment of basic diseases, symptom relief, effective supportive treatment of internal organs and active treatment of complications, are important to improve the survival rate (38). For instance, patients with increased lung infiltration should be treated with selective M3 blockers to reduce pulmonary secretions and broad-spectrum antibiotics to prevent lung infections (39). For

severe cases of COVID-19, treatment with rehabilitation plasma could be considered if plasma of recovered patients is sufficient, and all patients presented with respiratory failure requiring mechanical ventilation immediately to prevent hypoxemia (37). Last but not least, there are no specific anti-SARS-CoV-2 drugs in the clinic and the crisis has deepened. To overcome it, all countries and research institutes should unite and commit to the development of effective drugs.

Cut off the routes of transmission

As one of the most important measures in the prevention and control of infectious diseases, cutting off the routes of transmission is to block the spread of the virus from infected patients to susceptible people. Up to now, most people have held that SARS-CoV-2 is primarily transmitted through respiratory droplets and contact routes. However, the possible transmission of aerosol, fecal-oral or food cold chain is non-negligible in view of the rapid global spread of COVID-19.

Recommendations on face masks vary across countries (11) and the data for the variety of masks in use by the public are messy, disparate and hastily assembled (40). Nevertheless, meta-analysis of case-control studies have suggested that wearing masks and wearing N95 masks are highly effective in preventing the spread of SARS (41), and it is also effective for SARS-CoV-2 from respiratory droplets. As for this, the use of face masks has become ubiquitous in many countries, especially Asian countries such as South Korea, China and Japan. At present, more than 100 countries require or even enforce people to cover their faces when they leave home as preventive action against COVID-19 (42). For other countries, given that public transport, cinemas, supermarkets and shops have been identified as high-risk environments for transmission, we believe that making face masks compulsory in these places will be a significant measure in the future.

Timely implementation of control strategies that keep social distance and reduce close contact has proven effective in delaying the rates of transmission (43, 44). The outdoor restriction measure would be enforced based on the severity of the epidemic. In the worst affected areas, the government could consider taking multiple methods, including city-wide lockdowns, the suspension of public transportation, domestic self-isolation or pause on the resumption of work and school (45).

Aerosols from highly infective subjects can effectively transmit SARS-CoV-2 in indoor environments (46). The virus can remain viable and infectious in aerosols for hours and on surfaces up to days in experimental study (47). Recently, the viral RNA can be detected in the air samples collected from intensive care units, computerized tomography rooms, outdoor of inpatient and outpatient buildings (48). Additionally, the isolation of infectious virus from stool samples has proven that SARS-CoV-2 could be transmitted via fecal-oral route (49, 50), although more researches are still needed because the majority of the data are from China. Previous studies have shown that SARS-CoV-2 is susceptible to standard disinfection methods though it can be highly stable in a favorable environment (51, 52). A variety of commonly used disinfectants, such as household bleach (1:49 or 1:99), chlorhexidine (0.05%), chloroxylenol (0.05%) and disinfecting solution (Dermo docyn), can reduce viral viability (51, 52). Consequently, on the one hand, it is necessary to provide cleaning supplies in public places, including bleach-based cleaning agents and disinfectants in sufficient quantities to facilitate regular cleaning. On the other hand, ventilation should be strengthened including both natural and mechanical ventilation (53). Besides, when handling the stools and other bodily fluids or disinfecting the environments of patients, strict precautions must be observed to avoid the generation of infectious aerosols (54).

While several re-emergent outbreaks linked to contaminated food sources (55) and studies showed that low-temperature could significantly prolong the persistence of SARS-CoV-2 (52,56), food safety should be given more attention. However, we always focus on restricting travels and social isolation measures, few restrictions exist on the freight of consumer goods. Hence, as

the potential vectors in virus transmission, frozen and refrigerated foods are still been widely overlooked. Since the inspections started, SARS-CoV-2 RNA contaminations in imported frozen food have been reported many times in China (57), and on Oct 18th, Chinese Center for Disease Control and Prevention isolated living coronavirus on a package of frozen food in Qingdao (58). Therefore, in addition to some simple precautions, special measures must be conducted to mitigate risks associated with food cold chain, e.g., testing food industry personnel regularly (59), requiring them to wear face coverings and gloves, sanitizing working environments adequately, and others. For consumers, they should handle food with caution and make sure the foods from cold chain are cooked thoroughly.

Protect the susceptible population

In order to protect the susceptible population from COVID-19, safe and effective vaccines are urgently needed. Nowadays, numerous research institutes and companies develop vaccine candidates targeting this novel disease, and almost 200 vaccines for COVID-19 are in clinical and preclinical testing (60). As the epidemic intensifies, some measures that can cut development time of more conventional vaccines have been implemented or considered. For example, on the one hand, we may test several vaccines simultaneously in an adaptive trial design using a single, shared control group, on the other hand, use of next-generation sequencing and reverse genetics would compress the timeline during epidemics (61). Additionally, for platforms with experience in humans, the clinical trials could be able to proceed in parallel with preclinical stages (62). A proposal presently is gaining traction: inject people with an experimental vaccine and then deliberately infect them (63). However, based on the ethical complexity and unknown risks, we believed that it must be considered or implemented with more caution. In addition, new variant of SARS-CoV-2 has been identified and may be associated with a surge of cases in southern England (64). Although there's no evidence to suggest this mutation makes the vaccine useless, we believe all types of these new mutations are noteworthy in the vaccine development.

Recently, several COVID-19 vaccines have been approved in Dec 2020. On Dec. 3rd, Britain became the first to approve the shot of Pfizer/BioNTech COVID-19 mRNA vaccine for emergency use, followed by many countries such as Canada, United States and European Union. Then, Moderna COVID-19 mRNA vaccine got authorization in Canada and United States (65). Latest, the UK's medicines regulator has approved the Oxford and AstraZeneca adenovirus vaccine, which is easier to distribute to care homes and other locations than the Pfizer vaccine (66). Immediately, mass vaccination programs have been started all over the world. While these vaccines had already been shown to be highly effective, their side effects also aroused people's attention. For example, at least eight people who received the Pfizer/BioNTech vaccine suffered severe allergy-like reactions in 2 weeks. Similar news has already created anxiety (67). Therefore, given the severity of the epidemic, we should get vaccinated as soon as possible, but more data are also urgently needed to provide a much more granular picture of vaccines' side effects and safety profiles.

Considering current shortages, the preliminarily effective vaccine should be preferentially allocated to high-risk groups with severe morbidity and mortality in the distribution strategy (68), such as the elderly, frontline healthcare workers, those involved in essential industries and people who will go to severely affected areas.

Conclusion

The rapid spread of COVID-19 is still a major threat to global public health and economic development. By synthesizing the measures that have already taken effect, we suggested that the control of COVID-19 can be carried out from three aspects: control the source of infection, cut off the routes of transmission and protect the susceptible population, so as to make the epidemic control more thorough and stricter. First

of all, some latest approaches such as implementing contact-tracing apps, nucleic acid mixed detection, repeated testing and the establishment of some specialized laboratories need to be taken urgently to track the source of the infection timely. Second, we should insist on wearing masks and providing cleaning supplies in public places. Meanwhile, special measures could be conducted to mitigate risks associated with food cold chain. Third, to protect the susceptible population from COVID-19, effective vaccines must be preferentially allocated to high-risk groups, and its side effects should be given more attention. Given the impending second wave of the pandemic, policymakers could consider putting these latest effective measures into practice to avoid making grim situation even worse.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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