COVID-19 Pandemic: End of emergency, but not end of challenge

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The World Health Organization (WHO) announced on Friday, May 5th, 2023 that *COVID-19 no longer constitutes a public health emergency of international concern (PHEIC)*, after 1191 consecutive days of emergency state. The WHO director-general made the decision based on the recommendation offered by the COVID-19 Emergency Committee.

In the International Health Regulation (IHR) 2005, there are three criteria for PHEIC: (1) an extraordinary event; (2) constitutes a public health risk through international spread of disease; and (3) requires a coordinated international response. Since IHR came into legal force in 2007, there has been so far seven public health emergencies, including the H1N1 influenza pandemic, Ebola, poliomyelitis, Zika, COVID-19, and monkeypox, all of which are caused by viral pathogens (Figure 1). Although not being the longest PHEIC, COVID-19 is undoubtedly the most influential, with more than 766 million confirmed cases and more than 6.9 million reported deaths to date, reshaping the world economy and health system.[1]

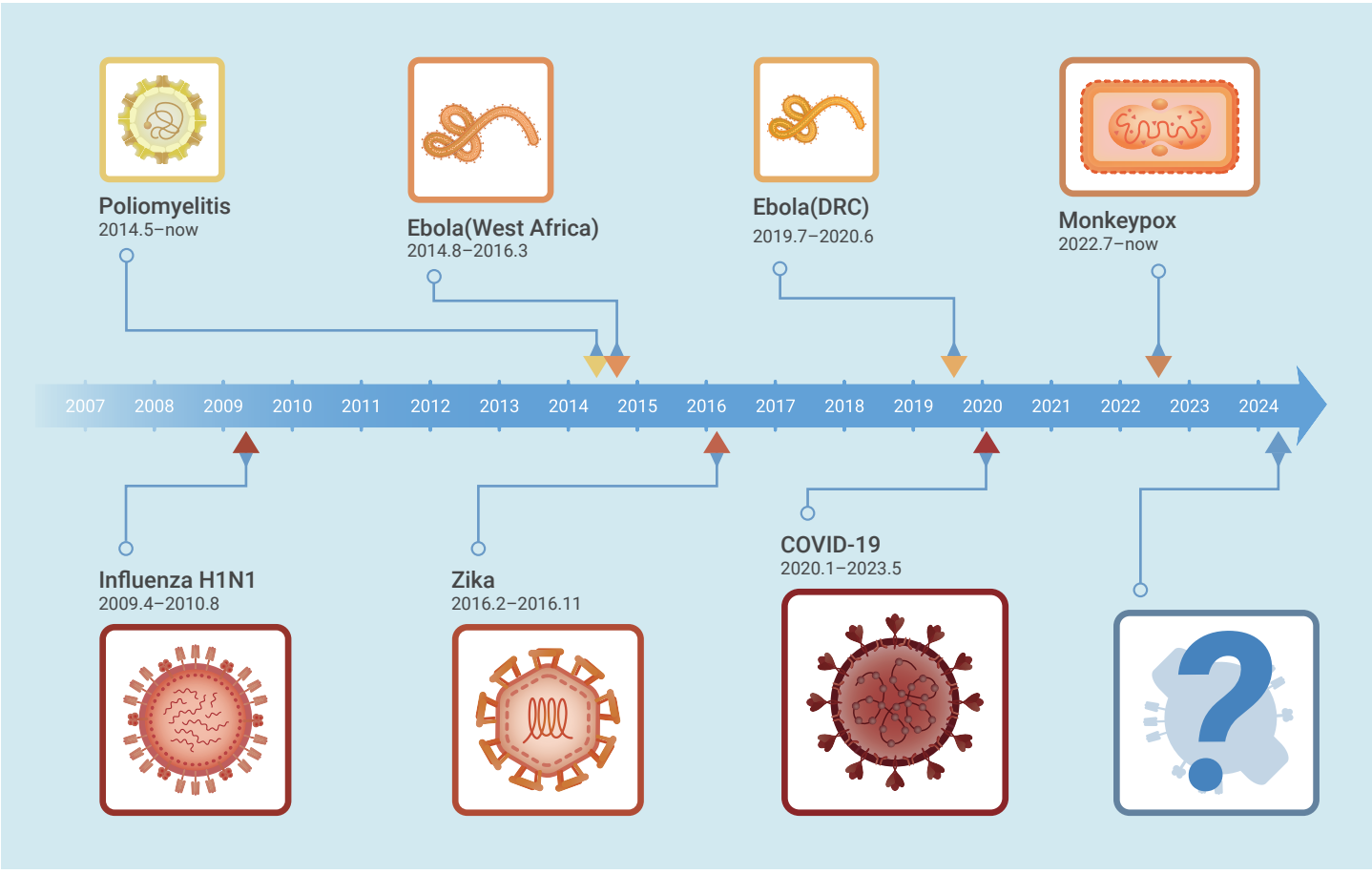

Figure 1. The seven public health emergencies of international concern (PHEIC) in history

Some have viewed the termination of PHEIC as the end of the pandemic or even the end of the disease, and therefore start celebration. Indeed, effective anti-viral medications and clinical management plans against SARS-CoV-2 have been developed in the past three years. High population-immunity has formed by infection and vaccination. The infectious disease surveillance system has been established. All of these achievements contribute to the decline of the number of confirmed new cases, deaths, and admission to intensive care unit.

Yet is it really the end of the pandemic? No. Actually, COVID-19 is an international disease, and the challenge by COVID-19 still remains.

To begin with, SARS-CoV-2 continues to evolve into more infectious and highly immune-escaping mutants, such as the Omicron variant, which is more inclined to escape from the immunity established by prior infection, and protection from previous SARS-CoV-2 infection is low.[2] There are increasing repeated infection by SARS-CoV-2, especially when the immune memory from previous infection or vaccination wane over time. Repeated infection may increase the risks of death, hospitalization and sequelae in multiple organ systems, and the incidence of these adverse outcomes also increase with times of repeated infection.[3] In fact, it is predicted that COVID-19 will co-exist with us and may evolve into seasonal epidemics, similar to influenza. The efficacy of current anti-viral treatment agents against future mutants is also unknown, with the escape of the latest mutant from most available

monoclonal antibodies being the best example. Continuous effort shall be paid to develop novel and broad-spectrum treatment reagents.

Long COVID is another noteworthy issue of concern. It is defined as symptoms lasting for more than 3 months from the onset of COVID-19 with no alternative explanations. It is reported that about 73% people have at least 1 persistent symptom after the acute phase of infection.[4] Further, an post-acute sequela may still exist in about 55% COVID-19 survivors even 2 years after discharge.[5] As the number of infections increases, there will be more individuals with a range of symptoms relevant to Long COVID, which has a huge impact on work and life. Many of these population cannot go back to work, causing the short of workforce. Unfortunately, even today, there is still no clear mechanism to this sequela revealed, let alone the methods to diagnose it accurately and treat it effectively. It is critical to improve the capabilities of early diagnosis and treatment to Long COVID.

With the transition into long-term COVID-19 management, special attention should be paid to the population at increased risk of developing severe COVID-19, especially the immuno-suppressed patients. The optimal course of anti-viral medication or vaccination scheme is unknown. In clinical practice, we have observed some patients with B cell deficiency who experience prolonged COVID-19. How to provide treatment for this group of patients is also an outstanding issue, but there is little experience for us to refer to. Other immunodeficient population, such as AIDS patients, patients with malignancy, dialysis, long term bedridden, and other conditions should also be given special attention to. Better treatment for severe COVID-19 is also urgently needed.

What can we do in the future? The end of PHEIC actually suggests the transition into long-term management of the disease. According to WHO, a PHEIC is usually serious, sudden and unusual. As COVID-19 has been epidemic for more than 3 years, its destructive effect is not as huge as it broke out three years ago. COVID-19 is no longer an extraordinary event according to WHO, but it is still in pandemic, and the public health risk that it brings still exist. International response should be coordinated at all time.

The public health emergency caused by COVID-19 may come to an end, but the challenge it brings still remains as SARS-CoV-2 does not disappear. As mutants appear continuously and high-risk group are easy to develop into severe COVID-19, the study on COVID-19 should not be suspended. When COVID-19 is no longer as severe as before, and become a seasonal epidemic like influenza, we should never quit searching for new therapeutic methods, more effective vaccines and strategies to deal with severe COVID-19 and Long COVID. Whether COVID-19 belongs to PHEIC is a binary event. However, the actual situation can be complicated, and cannot be described by only one concept. It is wise to develop corresponding measures based on the actual situation.

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DECLARATION OF INTERESTS

The authors declare no competing interests.