Editorial

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Post COVID-19 burden: focus on the short-term condition

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The catastrophic pandemic of the coronavirus disease 2019 (COVID-19) has caused serious harm to human life and global social economy. As of June 13, 2022, there were more than 530 million confirmed cases of COVID-19 and over 6.3 million deaths[1]. During the past 2 years, global studies on prevention and therapies for COVID-19 have achieved a series of promising findings, including antiviral drugs (Remdesivir, Molnupiravir, Paxlovid) and monoclonal antibodies (Bamlanivimab and Etesevimab, Sotrovimab, Casirivimab and Imdevimab)[2]. World Health Organization (WHO) has validated 11 vaccines for the emergency use listing (EUL)[3]. As of June 13, 2022, more than 11.9 billion vaccine doses have been administered worldwide[1]. In China, integrated using of traditional Chinese medicine (TCM) and Western medicine is one of the highlights in fighting COVID-19. "Three formulations and three drugs" (Jinhua Qinggan granules, Lianhua Qingwen capsule, Xuebijing injection, and Qingfei Paidu decoction, Huashi Baidu decoction, Xuanfei Baidu decoction) have been approved by National Medical Products Administration (NMPA) as new drugs or adding indications for COVID-19[4]. The new drugs and vaccines had become effective weapons in the fight against the pandemic.

Post COVID-19 condition

A proportion of patients recovered from acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have ongoing, recurrent, or new symptoms which would persist for weeks, months, or longer. These post COVID-19 symptoms have become a new public health problem that needs to be concerned. The incidence of multi-organ complications ranged from 10% to 80% among COVID-19 survivors[5]. The most common symptoms were fatigue, dyspnea, cognitive impairment, various neuropsychiatric symptoms[5]. According to published research data, 13.3% COVID-19 patients would experience "post COVID-19 condition" for a month or longer after infection, and 2.5% would experience the condition that may last for three months or longer [6]. A cohort study including more than 13 million cases suggested that vaccination only reduced the risk of post COVID-19 condition by about 15%[7]. Since May 2020, a series of terms and definitions have been proposed to describe the symptoms of the post COVID-19 condition, such as "Long Covid" "Long Haulers" "Long-haul COVID" "Chronic COVID syndrome." However, different definition usually covered different phases after symptoms onset (Figure 1)[8–21]. In October 2021, WHO released a definition for post COVID-19 conditions as "three months from the onset of COVID-19 with symptoms that last for at least two months"[20]. The definition put forward by WHO is more focused on the prolonged consequences issues of COVID-19; however, it is not conducive to guiding early interventional studies in short-term conditions(STCs).

Short-term and long-term post COVID-19 conditions

According to the results of several cohort studies, patients who recovered from acute COVID-19 reported persistent symptoms after hospital discharge or negative nucleic acid. Short-term and long-term follow-up data have revealed the common post COVID-19 symptoms, mainly including fatigue, muscle pain, dyspnea, palpitations, chest pain, headache, insomnia, loss of smell, loss of taste, hair loss, *etc*[22–32]. For STCs, fatigue was the most frequently reported condition (12.8%–97.7%), followed by muscle pain (0.6%–62.9%), cough (8.5%–59.5%), and headache (3.4%–91.2%). Similarly, fatigue was more profound in long-term conditions (LTCs) than other symptoms like insomnia, chest pain, headache, and hair loss. Generally, fatigue, muscle pain, and headache were tracked at all follow-up stages with higher incidence. In China, fatigue, hair loss, and insomnia were the major symptoms in patients who recovered from COVID-19[30,32]. In contrast, dyspnea, fatigue, and loss of smell were the most frequently reported symptoms in some European countries (ie, the United Kingdom and Spain)[23,28]. In Africa

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and Southeast Asia, fatigue was also the most common persisting symptom of post COVID-19 conditions[22,24]. Studies in the United States suggested that more attention should be paid to respiratory symptoms (like cough and chest tightness), loss of taste, and the mental health in people with COVID-19[25,27]. (Figure 2).

Several published systematic reviews have shown that individuals hospitalized during acute COVID-19 infection had higher risk of post COVID-19 condition compared with non-hospitalized patients[33–34]. In different countries or regions, the prevalence rate of post COVID-19 conditions was reported highest in Asia, followed by Europe and the United States[34]. The incidence of post COVID-19 conditions is different in distinct regions, which might be related to the SARS-CoV-2 variant strain. For example, Omicron variant tended to

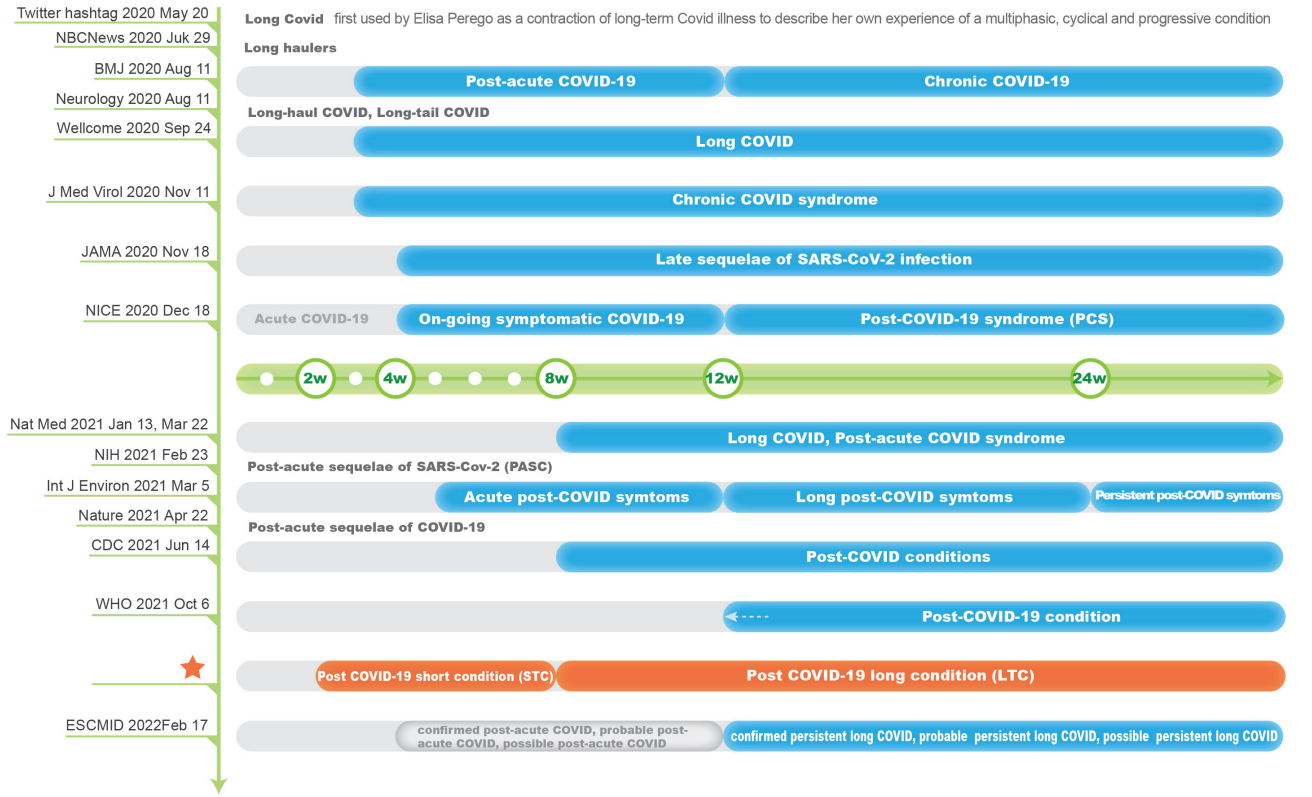

Figure 1. Timeline of definitions for post COVID-19 condition. 2 w, 4 w, 8 w, 12 w, and 24 w refer to 2 weeks, 4 weeks, 8 weeks, 12 weeks, and 24 weeks after acute infection with SARS-CoV-2. COVID-19: coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. ☆After the omicron outbreak in Tianjin from early January 2022, the authors proposed definition of STC and LTC.

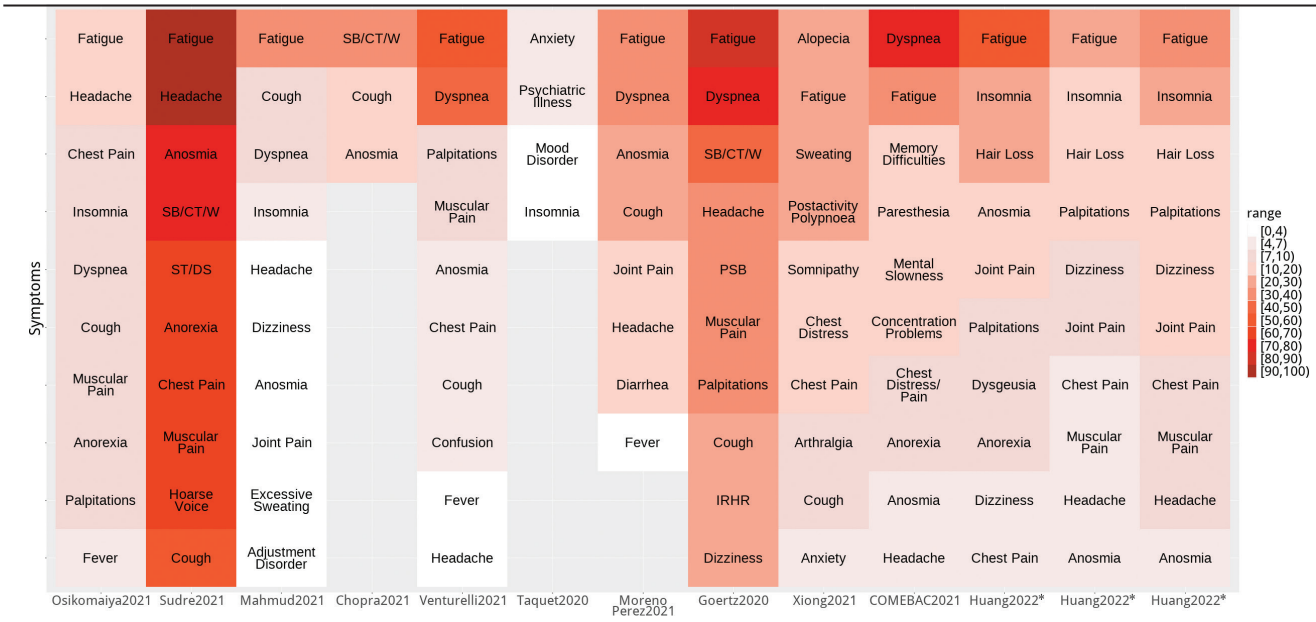

Figure 2. Top 10 symptoms of post COVID-19 cohort studies. ST/DS: sore throat or difficult on swallow; SB/CT/W: shortness of breath/chest tightness/wheezing; PSB: pain between shoulder blades; IRHR: increased resting heart rate. *Huang 2022: Select data at 6, 12, and 24 months.

cause less acute symptoms than the Delta variant[34–36]. According to other studies, the incidence of post COVID-19 conditions showed a decline at the early stage of the extended follow-up, while it showed an upward trend after 60 and 90 days in the follow-up [33,34].

Worldwide researches had highlighted the global public problem of post COVID-19 conditions. More attention should be paid to dealing with the problem. In April 2020, we put forward the principle of "early recovery, comprehensive recovery, self-recovery" to provide better post COVID-19 therapeutic guidance for maintaining health. In January 2022, we proposed the concepts of STC (less than 3 months from the onset of COVID-19) and LTC (after 3 months from the onset of COVID-19) for post COVID-19 management. It is necessary to find to interventions for STC, which can improve patients' life quality and decrease LTC.

Interventions for post COVID-19 STC

A study has demonstrated various mechanisms of post COVID-19 conditions, including viral persistence, immune dysregulation, and autoimmunity[37]. However, there was still a lack of specific drugs[38]. In China, TCM has shown its unique advantages and played a primary role in preventing, treating, and rehabilitating COVID-19.

In terms of rehabilitation, the *COVID-19 Diagnosis and Treatment Protocol* issued by the National Health Commission of China has adhered to the principle of early rehabilitation care of patients. Timely rehabilitation training and treatment are suggested for respiratory and physical functions, psychological disorders, for improving physical ability, constitution, and immunity to the greatest extent[39]. Since the first edition of *Guidelines for Integrated Traditional Chinese and Western Medicine rehabilitation during COVID-19 Recovery* was launched in April 2020[40], multiple guidelines have been published in China featuring the integration of TCM with Western medicine[41–44].

TCM can effectively relieve STC in patients. A randomized controlled trial (RCT) that recruited 388 discharged patients with COVID-19 showed that Qingjin Yiqi granules can improve the STC, in the improved scores of the modified Medical Research Council scale (mMRC) and the Borg scale[45]. An RCT including 131 convalescent patients showed the evidence that Bufei Huoxue capsule improved the attenuation of pneumonia lesions on chest computed tomography (CT) , 6-minute walk distance, and fatigue assessment inventory (FAI) scale[46]. An RCT with 200 cases showed a result that Shumian capsule can improve the STC, such as insomnia, anxiety, and depression[47]. A cohort study also verified the effects of TCM in improving the attenuation of pneumonia lesions on chest CT[48]. Based on current evidence, comprehensive treatment of TCM can effectively improve STC fatigue, shortness of breath, insomnia, *etc*.

Mostly, the STC can be reversed and cured under timely treatment. We proposed the concept of STC and aimed to promote earlier management of post COVID-19 conditions. Holistic and comprehensive approaches, such as herbal medicine, Chinese patent medicine, acupuncture and exercise are proved to be effective, safe and accessible for reducing post COVID-19 sequelae and improving the quality of patient's life. Multidisciplinary and international cooperation researches are warranted to strengthen relevant standards and provide more high quality clinical evidence. We hope integrated interventions for post COVID-19 conditions internationally agreed upon can be adopted worldwide.

Conflict of interest statement

Junhua Zhang and Boli Zhang are editorial board members of this journal.Xinyao Jin is an editorial office member and was excluded from the editorial process and publication decisions of this manuscript. Other authors declare no conflicts of interest.

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Author contributions

Boli Zhang, Junhua Zhang, and Qingquan Liu conceived and designed the article. Bo Pang, Xinyao Jin, Zhe Chen, and Wentai Pang drafted the article. Fengwen Yang provided a critical version of the manuscript. All authors contributed to the revision of the manuscript and approved the final manuscript.

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