



## Prevention and management of COVID-19 including Long COVID

*This document reflects the position of EUROCAM in prevention and management of COVID-19 including Long COVID. It covers susceptibility and resilience to COVID-19, preventive measures, individualized patient-centred treatment by Traditional Complementary and Integrative Medicine (TCIM) and research into its evidence base.*

### **Susceptibility to COVID-19**

In every epidemic some individuals become ill, and some may die, whereas others recover from illness and still others show no signs or symptoms of disease. These differences highlight a fundamental question of microbial pathogenesis: why are some individuals susceptible to infectious diseases while others who acquire the same microbe remain well?

The concept of susceptibility explains why the global pandemic of COVID-19 disease has had a disproportionate impact on patients living with chronic medical illness. Patients with underlying medical conditions are more likely to be hospitalised, need intensive care, require a ventilator to help them breathe, or die. Underlying conditions can be all kinds of chronic disease, use of alcohol or drugs, smoking, pregnancy, physical inactivity, overweight and obesity, mental health conditions such as depression or bipolar disorder, immunocompromised conditions.

In the first large-scale general population study on lifestyle risk factors (smoking, physical inactivity, obesity, and excessive alcohol intake) for COVID-19 using prospective cohort data with national registry linkage to hospitalisation<sup>1</sup>, the research team found a dose-dependent increase in risk of COVID-19 with less favourable lifestyle scores, such that participants in the most adverse category had 4-fold higher risk compared to people with the most optimal lifestyle. Unhealthy behaviours in combination accounted for up to 51% of the population attributable fraction of severe COVID-19. An unhealthy lifestyle synonymous with an elevated risk of non-communicable disease is also a risk factor for COVID-19 hospital admission. The research team argued that adopting simple lifestyle changes could lower the risk of severe infection.

Reducing susceptibility by building an effective immune system is a strategy needing attention<sup>2</sup>. The complex interrelationships between the immune system and a variety of

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<sup>1</sup> Hamer M et al. (2020). Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK. *Brain Behav Immun*, 87:184-187.

<sup>2</sup> Casadevall A, Pirofski L (2018). What Is a Host? Attributes of Individual Susceptibility. *Infect Immun*. 86(2): e00636-17.



lifestyle factors such as exercise, stress reduction, healthy nutrition, spending time in nature, positive inner attitudes, and well-being have already been demonstrated<sup>3,4,5,6,7,8</sup>.

### **General preventive measures**

Most emerging infectious diseases, and almost all known pandemics, are classified as zoonotic diseases (zoonoses)—that is, they involve microbial transmission among animals (wildlife or livestock) that ultimately “spills over” to humans. The rate at which novel microbes spill over and spread has risen in step with exponential increases in environmental and land use changes, disruption of wildlife habitats, global travel and trade, and increased human-animal contact. The One Health approach, which recognizes the connections among human, animal, and environmental health to better address health threats that include infectious diseases, is a particularly pertinent approach for pandemics, given their predominantly animal origins<sup>9</sup>.

When it comes to prevention, the burden of communicable disease has significantly and undeniably been reduced by vaccination. Vaccines are indeed an efficient health care measure to prevent infections, especially in people with compromised immune systems and chronic diseases. However, viruses, including the SARS-CoV-2-virus, constantly change through mutation to such a degree that first-generation vaccines tend to be less effective at preventing infection and serious illness. There are still many infectious diseases causing substantial morbidity especially in the older population, for which no vaccines are available so far. So, a broader perspective than vaccines alone is essential.

### **Resilience as a strategy for prevention**

Critical to health optimization in human beings is the development of psychological, physiological and metabolic resilience. Resilience is the capacity of an organism and other dynamic systems to adapt successfully to disturbances that threaten the viability, function, and development of that organism/system.

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<sup>3</sup> Kuo M. How might contact with nature promote human health? Promising mechanisms and a possible central pathway. *Front Psychol.* (2015) 6:1093. doi: 10.3389/fpsyg.2015.01093

<sup>4</sup> Black DS, Slavich GM. Mindfulness meditation and the immune system: a systematic review of randomized controlled trials. *Ann N Y Acad Sci.* (2016) 1373:13–24. doi: 10.1111/nyas.12998

<sup>5</sup> Pace TW, Negi LT, Adame DD, Cole SP, Sivilli TI, Brown TD, et al. Effect of compassion meditation on neuroendocrine, innate immune and behavioral responses to psychosocial stress. *Psychoneuroendocrinology.* (2009) 34:87–98. doi: 10.1016/j.psyneuen.2008.08.011

<sup>6</sup> Woods JA, Davis JM, Smith JA, Nieman DC. Exercise and cellular innate immune function. *Med Sci Sports Exerc.* (1999) 31:57–66. doi: 10.1097/00005768-199901000-00011

<sup>7</sup> Gershwin ME, German JB, Keen CL. *Nutrition and Immunology: Principles and Practice.* Berlin: Springer Science & Business Media (1999).

<sup>8</sup> Dinu M, Abbate R, Gensini GF, Casini A, Sofi F. Vegetarian, vegan diets and multiple health outcomes: a systematic review with meta-analysis of observational studies. *Crit Rev Food Sci Nutr.* (2017) 57:3640–9. doi: 10.1080/10408398.2016.1138447

<sup>9</sup> Daszak P et al (2021). Infectious Disease Threats: A Rebound To Resilience. *Health Affairs (Millwood)*, 40(2):204-211.

Patient resilience is, therefore, a critical strategy of prevention. It protects an individual from developing physical and emotional illness in the face of stress and other pathogenic factors. Within this context, it is essential to understand that integrative medicine interventions support the adaptive coping mechanisms of the host rather than addressing specific diseases and dealing with impersonal risk factors.

Traditional, Complementary and Integrative Medicine (TCIM) holds a substantial potential for building resilience and strengthening preventative resources through a variety of easily feasible, accessible, evidence-based preventive, and therapeutic options such as changing lifestyle and diet, using herbs, strengthening physical and mental resilience and reducing stress. TCIM approaches, such as Traditional Chinese/Indian/ European Medicine, homeopathy, yoga, mind-body medicine and dietary supplements can help in prevention and treatment of COVID-19<sup>10</sup>. They have been prescribed for COVID-19 patients and the general population with considerable usage prevalence.

### Long COVID

Long COVID, also known as Post COVID Syndrome, is defined as a variety of symptoms that continue after the clearance of acute COVID-19 infection, such as fatigue, cognitive impairment, dyspnea, headaches, cardiac problems, sleep disturbances, muscle or joint pain, depression and posttraumatic stress disorder.<sup>11</sup> Over 30% of individuals affected by COVID-19, including asymptomatic cases and approximately 80% of patients hospitalized for COVID-19 may experience Long COVID<sup>12</sup>.

One of the most puzzling aspects of the COVID-19 pandemic is understanding why some people who have short-term COVID later develop new symptoms. Or they may continue to have symptoms while also developing new ones. These Long COVID symptoms can vary a lot from person to person, which makes it hard to understand why some people are more likely to have Long COVID.

A systematic review<sup>13</sup> suggests a high degree of similarities between long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Long COVID and ME/CFS appear to have certain commonalities in their clinical features as well as pathophysiology. The pathogenesis of ME/CFS has been linked to multiple underlying processes including immune system dysregulation, hyperinflammatory state, oxidative stress, and autoimmunity. A particular phenotype of ME/CFS has been termed post-infectious fatigue syndrome, and it has been linked to acute viral infections such as Epstein–Barr virus (EBV) and human parvovirus (HPV)-B19.

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<sup>10</sup> Seifert G et al. (2020) The Relevance of Complementary and Integrative Medicine in the COVID-19 Pandemic: A Qualitative Review of the Literature. *Front. Med.* 7:587749

<sup>11</sup> Crook H et al (2021). Long Covid—mechanisms, risk factors, and management. *BMJ.* 2021:374.

<sup>12</sup> Ceban F (2022) Fatigue and cognitive impairment in Post-COVID-19 Syndrome: A systematic review and meta-analysis. *Brain Behav Immun.* 101: 93–135.

<sup>13</sup> Wong TL, Weizer DJ (2021). Long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) — A Systemic Review and Comparison of Clinical Presentation and Symptomatology. *Medicina*, 57,418.



A recent study about a multidisciplinary rehabilitation (MDR) program based both on physical and psychological reconditioning suggests that such a program can be effective, safe and feasible in reducing symptoms and improving physical fitness and psychological parameters in patients with Long COVID<sup>14</sup>.

The National Institute for Health Research (NIHR) in the UK suggested that people experiencing long COVID may exhibit different syndromes<sup>15</sup>, such as post-intensive care syndrome (equivalent to the acute post-COVID phase), post-viral fatigue syndrome (if fatigue is the predominant post-COVID symptom), permanent organ damage (an underlying mechanism explaining long-term symptoms), and long-term COVID syndrome (equivalent to long and persistent post-COVID phases) based on the premise that post-COVID symptoms range in intensity and duration and are not linear or sequential.

The USA National Institute of Health RECOVER Initiative aims to understand how people recover from a COVID infection, and why some people do not fully recover and develop Long COVID. In addition, to study pathogenesis over time and possible relation to other organ dysfunction/disorders, and to identify interventions to treat, prevent and recover from Long COVID.

## Research

Since the beginning of the Coronavirus disease 2019 (COVID-19) pandemic, various complementary and alternative medicine approaches have been used in clinical practice. The WHO COVID-19 Research Database includes 6,800 publications on Traditional Medicine, of which 1,412 randomised clinical trials, 1,404 controlled clinical trials.<sup>16</sup> The Virtual Health Library TCIM Americas, established by a collaboration of Latin American and Caribbean centre on health sciences information and PAHO (Pan American Health Organisation) includes 127 reviews on the contributions of TCIM in the context of COVID-19<sup>17</sup>.

Lack of government trust in non-conventional medicine prevented many nations (most of the developed economies) to adopt TM interventions, despite demand from population and lack of viable conventional choices.

The most important element for inclusion of TCIM in COVID-19 management has been government buy-in, leading to early or strategized policies and decisions., primarily in China and India.

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<sup>14</sup> Compagno S et al. (2022). Physical and psychological reconditioning in long COVID syndrome: Results of an out-of-hospital exercise and psychological - based rehabilitation program. *Int J Cardiol Heart Vasc*; 41:101080.

<sup>15</sup> Fernández-de-Las-Peñas C et al (2021). Defining Post-COVID Symptoms (Post-Acute COVID, Long COVID, Persistent Post-COVID): An Integrative Classification. *Int J Environ Res Public Health*, 18(5):2621

<sup>16</sup> <https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/> [accessed 22 July 2022]

<sup>17</sup> <https://mtci.bvsalud.org/en/evidence-map/> [accessed 22 July 2022]

### *China's governmental policy*

Traditional Chinese medicine (TCM) has a long history of preventing and controlling infectious diseases, and it has widely been used in the treatment of COVID-19 in China. The National Health Commission for People's Republic of China published the "Guidance for Corona Virus Disease 2019 – Prevention, Control, Diagnosis and Management" incorporating Traditional Chinese Medicine (TCM) interventions for mild, moderate, severe and critical stages of the disease, specifying the TCM diagnostic criteria in each stage and specifying medicines for it. A year later this publication was followed up by "Diagnosis and Treatment Protocol for Novel Corona Virus Pneumonia." Reports suggest that these interventions were used very effectively and appropriately in China's COVID management policies.

In 15 RCTs comparing Western biomedicine alone vs Western biomedicine plus TCM using RCTs showed that additional Chinese medication reduced the rate of progression to severe Covid-19, accelerated symptom recovery, and improved post-infectious lung function, while not increasing the risk of adverse events compared with conventional Western medication alone.

Systematic review of 16 retrospective cohort studies with 1645 valid confirmed COVID-19 patients, comparing patients receiving TCM medicines in addition to Western biomedicine, with patients received biomedical treatment alone. The outcomes assessed in three aspects, that is, overall indicator, symptoms indicator and blood indicator, showed that the integrated treatment group had better treatment outcomes compared with the stand-alone biomedical treatment, and reduced the mortality rate.

In addition, numerous case reports were published with promising results.

WHO is seriously studying the experience and evidence from different countries that had used traditional and complementary medicine products, practice, practitioners in their COVID-19 pandemic response. At the WHO Expert Meeting on Evaluation of Traditional Chinese Medicine in the Treatment of COVID-19 on 28 Feb – 2 Mar 2022, some key findings were presented as follows:

- The experts agreed that the evidence evaluation reports applied appropriate and rigorous methodology to determine the current level of clinical evidence and safety of the studied TCM interventions used in the trials.
- For mild-to-moderate cases, there is encouraging evidence that the studied TCMs, when administered as add-on interventions to conventional treatment, may shorten the time for viral clearance, resolution of clinical symptoms and length of hospital stay when compared to conventional treatment alone.
- The studied TCM interventions given in addition to conventional treatment were well tolerated and have a safety profile that is comparable to that of conventional treatment alone.
- There is encouraging evidence that early application of TCM may result in better clinical outcomes for patients with mild-to-moderate COVID-19.



- Despite inherent limitations, the results from the selected RCTs justify further investments in clinical trials to evaluate the potential benefits of selected TCMs in the management of COVID-19.

### *India's governmental policy*

The Ministry of AYUSH in India is responsible for the policies, planning, budget, implementation, regulation, and governance of all aspects related to AYUSH medical systems. AYUSH is the acronym of the medical systems that are being practised in India such as Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homeopathy. The Ministry issued several guidelines:

- on how citizens can protect themselves from COVID-19 and how to stay healthy, communicated to all Chief Secretaries of States/Union territories.
- on self-care by preventive health measures and boosting immunity with special reference to respiratory health
- for uniform management of COVID 19 pandemic for registered practitioners of respective system of AYUSH vetted by the Interdisciplinary AYUSH Research and Development Task Force of Ministry of AYUSH.
- that were circulated in public domain for the benefit of more than 700,000 registered AYUSH practitioners to help in the management of COVID 19 pandemic uniformly
- on Long COVID after incorporating AYUSH measures

In addition, they utilized AYUSH hospitals & colleges as COVID wards as Quarantine, isolation & Treatment Centre and instituting more than 150 scientific studies to generate evidence for AYUSH intervention

Several kinds of clinical research studies were performed: prophylactic studies (46) , treatment studies (49), observational studies (11), and others (17). Additionally 24 pre-clinical/experimental studies. They were all based on robust clinical design by Inter disciplinary AYUSH Research and Development Task Force on COVID 19 comprising of scientists, pulmonologists, epidemiologists, and AYUSH experts from reputed institutions. The studies showed very promising outcomes in prophylactic use as well as in management of mild to moderate COVID 19.

### *Research into treatment of COVID Long*

Due to the high degree of similarities between long COVID and Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), practitioners of TCIM base the treatment of Long COVID patients on the results obtained in ME/CFS patients.

A systematic review including 26 randomized controlled trials (RCTs) and in total 3,273 participants studied the following treatment modalities: mind-body medicine, distant healing, massage, tuina and tai chi, homeopathy, ginseng, and dietary supplementation. Studies of qigong, massage and tuina were demonstrated to have positive effects<sup>18</sup>.

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<sup>18</sup> Terje Alraek et al. (2011). Complementary and alternative medicine for patients with chronic fatigue syndrome: A systematic review. BMC Complement Altern Med. 2011; 11: 87.



Another systematic review including 31 randomized controlled trials (RCTs) and in total 2,255 participants studied acupuncture and moxibustion. The authors concluded that acupuncture is more effective than Chinese herbal medicine, western medicine and sham-acupuncture<sup>19</sup>.

## Conclusion

When it comes to prevention, health systems need to change their focus from responding to health threats towards achieving a healthy and resilient population. How the population responds to infections is, to a large extent, determined by the health status of the population. The implementation of medical modalities that improve patient resilience is crucial at this time.

More research must be aimed at exploring the role of resilience, i.e., the effects of diet, food production, exercise, age, psychological stress, and other factors that affect the immune response, both in animals and in humans. Health education, high-quality nutrition, and a healthy environment are fundamentals.

Medicine should have a broader scope, moving from a conditions-focused approach to include medical modalities which improve health and resilience.

It is essential to use all resources to fight a pandemic, including Traditional, Complementary and Integrative Medicine, with adequate evidence of safety, efficacy, and quality. Traditional, Complementary and Integrative Medicine offers interesting therapeutic options for preventing and treating viral infections such as COVID-19. A focus on TCIM will open new horizons in terms of improving the health and resilience of the population on a global scale. More research in this area is warranted.

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EUROCAM is an independent non-profit and non-governmental European umbrella organisation, representing patients, medical doctors, practitioners, and veterinarians, in the sector of Traditional, Complementary, and Integrative Medicine (TCIM), aimed at promoting the contribution of TCIM to better health in Europe.

EUROCAM runs the secretariat of the MEP Interest Group on Integrative Medicine & Health and is accredited as a non-state actor to the WHO Regional Office for Europe.

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<sup>19</sup> Taiwu Wang et al (2017) Acupuncture and moxibustion for chronic fatigue syndrome in Traditional Chinese medicine: a systematic review and meta-analysis. BMC Complement Altern Med. 2017; 17: 163.