



## Guidelines

## Recommendations and guidelines of integrative medicine for COVID-19 care: The APEC project outcome



Libin Jia <sup>a,\*</sup>, Michelle Beidelschies <sup>b</sup>, Joel M. Evans <sup>c</sup>, Richard C. Niemtow <sup>d</sup>, Songxuan Zhou Niemtow <sup>d</sup>, Jeffery A. Dusek <sup>e</sup>, Yufang Lin <sup>b</sup>, Charles Wu <sup>f</sup>, Yi-Chang Su <sup>g</sup>, C. Jason Wang <sup>h</sup>, Chien-Yu Lin <sup>i</sup>, Peristiwa Ridha Widhi Astana <sup>j</sup>, Danang Ardiyanto <sup>k</sup>, Rusmiyati Hardjoutomo <sup>l</sup>, Khwanchai Visithanon <sup>m</sup>, Jagravudh Puangkong <sup>m</sup>, Julalak Chokpaisarn <sup>n</sup>, Martha Villar Lopez <sup>o</sup>, Hiroshi Yotsuyanagi <sup>p</sup>, Myeong Soo Lee <sup>q</sup>, Hernan Jose Garcia Ramirez <sup>r</sup>, Cecilia Plaza Bobadilla <sup>s</sup>, Elizabeth Margarita Gonzalez Quinteros <sup>t</sup>, Monica Galanti de la Paz <sup>u</sup>, Cecilia C. Maramba-Lazarte <sup>v</sup>, APEC Health Working Group

<sup>a</sup> National Cancer Institute, USA

<sup>b</sup> Cleveland Clinic, USA

<sup>c</sup> The Center for Functional Medicine, USA

<sup>d</sup> The US Air Force Medical Corps, USA

<sup>e</sup> Connor Whole Health, USA

<sup>f</sup> Food and Drug Administration, USA

<sup>g</sup> Stanford University, USA

<sup>h</sup> National Research Institute of Chinese Medicine, Chinese Taipei

<sup>i</sup> Hsinchu MacKay Memorial Hospital, Chinese Taipei

<sup>j</sup> Sebelas Maret University of Surakarta, Indonesia

<sup>k</sup> Ministry of Health, Indonesia

<sup>l</sup> Public Health Management, Ministry of Health, Indonesia

<sup>m</sup> Department of Thai Traditional and Alternative Medicine, Thailand

<sup>n</sup> Prince of Songkla University, Thailand

<sup>o</sup> National University of San Marcos, Peru

<sup>p</sup> University of Tokyo, Japan

<sup>q</sup> Korea Institute of Oriental Medicine, Republic of Korea

<sup>r</sup> Complementary Care System, Mexico

<sup>s</sup> Academic Network of Integrative Medicine and Health, Chile

<sup>t</sup> Ministry of Health, Chile

<sup>u</sup> Academic University of Chile, Chile

<sup>v</sup> National Institutes of Health, Philippines

## ARTICLE INFO

## Keywords:

Integrative medicine  
COVID-19 care  
Guidelines

## ABSTRACT

This article - Recommendations and Guidelines of Integrative Medicine (IM) for COVID-19 Care - was one of the outcomes from an Asia-Pacific Economic Cooperation (APEC) Project (Integrative Medicine (IM) and COVID -19 Care) during the time between May 2022 and March 2023. With the efforts from care providers, researchers, health policy makers and healthcare administrative leaders among APEC economies, the purpose of this file was to provide comprehensive IM systems for COVID-19 care as recommendations and suggestive guidelines including care methods, tools, procedures, symptom conditions and targets selections, and points need to be considered during care applications. All cited COVID-19 care practices have confirmed their efficacy and usefulness either used alone or combined with conventional medicine. This article provides current useful medical information on IM for COVID-19 care which could benefit APEC economies and world health communities on their healthcare system.

\* Corresponding author at: National Cancer Institute, 9609 Medical Center Drive, 1W704, Rockville, MD 20850, USA.

E-mail address: [libinj@nih.gov](mailto:libinj@nih.gov) (L. Jia).

<https://doi.org/10.1016/j.imr.2024.101022>

Received 30 January 2024; Accepted 5 February 2024

Available online 7 February 2024

2213-4220/© 2024 Korea Institute of Oriental Medicine. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

## 1. Introduction

The end of 2019 brought forth the emergence of severe acute respiratory syndrome-related coronavirus (SARS-CoV-2), a novel coronavirus that triggered a pandemic affecting all populations across the world.<sup>1,2</sup> While various physical measures were implemented to contain the highly transmissible virus<sup>3,4</sup> and vaccines were rapidly developed to mitigate disease severity,<sup>5</sup> many still developed coronavirus disease 2019 (COVID-19). While most individuals with COVID-19 make a full recovery, there are a subset who die due to COVID-19 pneumonia or develop persisting symptoms several weeks after SARS-CoV-2 infection.<sup>6</sup> This complication is commonly referred to as post-acute sequelae of COVID-19 (PASC) or Long COVID.<sup>2,7</sup>

The severity of COVID-19 is linked to common nutrition and lifestyle-driven comorbidities, and the wide array of symptoms in COVID-19 and PASC require multimodal therapeutic interventions to address these complications.<sup>8</sup> Integrative Medicine (IM) is practicing medicine which selectively incorporates elements (such as nutrition and supplements, physical excises, mind-body interventions, acupuncture and acupressure, effective herbal medicine, life-style adjustment and psychotherapy) of complementary and alternative medicine into comprehensive treatment plans alongside conventional medicine. The IM which covers many fields including functional medicine (FM), traditional medicine (TM), folk medicine is one solution that incorporates evidence-based, multimodal interventions to treat the whole person.<sup>9</sup> As one field of IM, for example, FM looks upstream of a patient's signs, symptoms and diagnosis and considers the complex web of interactions within a patient's history, physiology, genetics, lifestyle and environment that contribute to their physical and mental functional status.<sup>10</sup> Implementing IM including FM, TM interventions may provide therapeutic benefits for preventing and/or managing COVID-19 and PASC which may help both developed and developing economies.

Therefore, a project proposal was submitted to the Asia-Pacific Economic Cooperation (APEC) in May 2021 by the economy of the United States, and co-sponsored by the APEC economies of Chinese Taipei, Indonesia and Thailand. Its purpose was to promote high quality, science-based, effective, safe and feasible IM applications and integrations with conventional medicine for COVID-19 care in the current pandemic situation. This first-of-its-kind project hosted a virtual APEC IM and COVID-19 Care Workshop and established Recommendations and Guidelines of IM for COVID-19 Care for all APEC economies and healthcare communities.

Pre-Workshop activities aimed to identify experts in various APEC economies who utilize IM interventions for the prevention and management of COVID-19 by way of a literature review and utilized a survey to summarize best practice examples of IM for COVID-19 care in various APEC economies. The Workshop itself provided a forum to gather expertise from research, clinical care, prevention, and policy experts on IM care for COVID-19. This program provided a forum for the exchange of knowledge and experience, and to guide discussions around evidence-based strategies and policies related to IM for COVID-19 care.

## 2. Recommendations and guidelines of IM for COVID-19 care

The pre- and post-Workshop activities by various APEC economies informed the development of the Recommendations and Guidelines of IM for COVID-19 Care reported below.

### 2.1. The background and needs of IM for COVID-19 care

- Gap analysis
  - i. Available pharmacological interventions are specific for one aspect of COVID-19 pathophysiology. Therefore, patients may require polytherapy.
  - ii. Heterogenous presentation of COVID-19 and PASC make management difficult.

- Reasons for IM needed for COVID-19 care
  - i. Clear guidelines for the prevention and management of COVID-19 and PASC.
  - ii. Greater dialogue between IM including FM, TM and combination with conventional medicine providers and researchers who have experienced effective approaches and can help document experiences.
  - iii. Expansion of different medicine systems such as Traditional Chinese Medicine (TCM), Traditional Thai Medicine (TTM), Korean Medicine (KM), etc. interventions for the prevention and management of COVID-19 and PASC.

### 2.2. The evidence-based effective procedures, tools and systems of IM for COVID-19 care

Because COVID-19 and PASC share an underlying pathophysiology with various non-communicable diseases (e.g. heart disease, diabetes, asthma, etc.), non-pharmacological interventions known to prevent or manage these diseases may have biological plausibility for the management of COVID-19 and PASC, especially in the absence of rigorous, high-impact studies which are difficult in the face of a pandemic.

Interventions for the prevention and management of COVID-19 and PASC utilized by various APEC economies are summarized in [Table 1](#). The preventive strategy focuses on making people healthier while the management strategy focuses on improving immune system function to reduce symptoms, severity of acute illness and mortality, and reducing the long-term disability common in those with PASC.

### 2.3. How to effectively combine IM and conventional medicine for COVID-19 care

IM care models are intended to extend, not replace, current health-care models (e.g. pharmacological interventions). Integrative care incorporates alternative, evidence-based approaches for treatment including effective herbs, acupuncture/acupressure, or reiki. Functional medicine focuses upstream of reported symptoms to examine systemic imbalances. By eliminating what is in excess (e.g. stress, toxicants, etc.) and supplying what is deficient (e.g. Vitamin D, Omega-3, etc.), balance and ultimately optimal health can be restored. Functional medicine also incorporates an integrative approach within its therapeutic plans.

Working in collaboration with conventional medicine providers to support patients with COVID-19 and PASC is integral to their short-term, and long-term health. If patients are not responding to conventional treatments, based upon the severity of symptoms, patients should be referred to IM clinics to address nutrition and supplements, lifestyle adjustment, and stress management, and improve immune function and resilience. Such non-pharmacological interventions may ameliorate comorbid disease burden and reduce the cost of care; however, studies are warranted to demonstrate this claim.

### 2.4. The issues, challenges, and improvements of IM on COVID-19 care

Lack of rigorous studies (e.g. randomized, controlled clinical trials) to support the safety and efficacy of IM interventions for the management of COVID-19 and PASC.

Lack of dosing information for various IM interventions (e.g. botanicals, dietary supplements) for the management of COVID-19 and PASC.

The lack of uniform IM on COVID-19 care with protocolization across economies.

The recommendations for IM management of COVID-19 and PASC are first based on biologic plausibility rather than evidence. In a pandemic, time is of the essence. Therefore, providers acted based on the available literature with what they knew to optimize immune function, improve anti-viral function (based on key learnings of other viral infections), and what they knew about other coronaviruses and mechanisms of action.

**Table 1**  
Recommended IM/FM interventions for the Prevention and Treatment/Management of COVID-19 and PASC.

Integrative Intervention	Prevention	COVID-19					Mechanism/Outcome	Citations
		Asymptomatic	Mild	Moderate	Severe	PASC		
<b>Acupuncture/ Acupressure</b>			•	•			Suppresses inflammation, improves immunity, and regulates nervous system function. Resolves chest pressure and palpitations. Improves lung Qi and Yin deficiency. Improves Qi and blood stagnation and spleen Qi deficiency. Improves anosmia and ageusia.	Han et al. <sup>20</sup> Trager et al. <sup>21</sup> Williams and Moramarco <sup>22</sup> Hollifield et al. <sup>23</sup>
Electroacupuncture <i>plus</i> Octapolar or Static Magnet Qigong and acupressure								Niemtzow et al. <sup>24</sup>
<b>Mind-Body Interventions</b>			•	•			Improves lung function, pulmonary symptoms, and shortens length of hospital stay. Reduce stress, improve mental and physical health.	Liu et al. <sup>25</sup> Yang et al. <sup>26</sup> Buric et al. <sup>27</sup>
Yoga			•	•			Improves immunological profiles by strengthening cell-mediated immunity. Improves physical and physiological wellbeing and quality of life.	Basu-Ray et al. <sup>28</sup> Shah et al. <sup>29</sup>
<b>Herbal/Botanical Medicine</b>			•	•	•		Anti-viral activity Reduces inflammation. Reduces the proportion of critically ill patients.	Demeke et al. <sup>30</sup>
NRICM101 (TCM formula)	•		•	•			Reduces mortality rate.	Tsai et al. <sup>31</sup> Tseng et al. <sup>32</sup>
NRICM102 (TCM formula)					•			Tseng et al. <sup>32</sup> Wei et al. <sup>33</sup>
<i>Andrographis paniculata</i> <sup>a</sup>	•		•	•			Anti-inflammatory and immunomodulatory effects to prevent disease progression, reduce the chance of developing pneumonia and shortened viral shedding period.	Tanwattayanont et al. <sup>34</sup> Intharuksa et al. <sup>35</sup> Kligler et al. <sup>36</sup> Hu et al. <sup>37</sup> Department of Thai Traditional and Alternative Medicine <sup>17</sup> Juckmeta and Itharat <sup>38</sup>
Ya-Ha-Rak (TTM formula)	•		•	•			Reduces inflammation and pain.	Palo et al. <sup>39</sup> Singh et al. <sup>40</sup>
Ayurveda Rasayana	•		•	•			Improves immunogenicity and immunomodulation and support non-specific immunity. Reduces inflammation and pro-inflammatory cytokines.	Hartono et al. <sup>41</sup>
Curcumin and virgin coconut oil	•		•	•				
<b>Nutrition</b>							Prevents COVID-19 severity.	Kim et al. <sup>42</sup>
Plant-based diets or pescatarian diets	•							
Milpa diet (sustainable foods of Mexican origin)	•						Boosts the immune system.	Willet et al. <sup>43</sup>
<b>Dietary Supplements*</b>								
Probiotics	•		•	•			Ongoing studies are evaluating disease progression to severity and influence on symptoms. Antiviral actions by way of inhibition of viral entrance into host cells and stimulating innate immunity.	de Oliveira et al. <sup>44</sup> Alharbiet al. <sup>45</sup> Lebeer et al. <sup>46</sup> Biliavska et al. <sup>47</sup>

(continued on next page)

Table 1 (continued)

Integrative Intervention	Prevention	COVID-19					Mechanism/Outcome	Citations
		Asymptomatic	Mild	Moderate	Severe	PASC		
Zinc <sup>a</sup>	•	•	•	•			Reduces severity of symptoms. Reduces duration of illness.	Prasad <sup>48</sup> Hulisz <sup>49</sup>
Arginine						•	Improves cell membrane and microvascular health.	Alexander et al. <sup>50</sup> Costa et al. <sup>51</sup> Mitchell et al. <sup>52</sup> Mills et al. <sup>53</sup> Park et al. <sup>54</sup> Zakay-Rones et al. <sup>55</sup>
Citrulline Elderberry <sup>a</sup>	•	•	•	•		•	Improves cell membrane and microvascular health. Reduces and improves symptoms. Reduces incidence and duration. Prevention of infection. Reduced duration of symptoms.	Bergman et al. <sup>58</sup> Martineau et al. <sup>59</sup> Alexander et al. <sup>50</sup> Biesalski et al. <sup>60</sup> Maggini et al. <sup>61</sup> Gombart et al. <sup>62</sup> Maggini et al. <sup>61</sup> Gombart <sup>62</sup>
Echinacea <sup>b</sup>	•						Reduces progression from colonization to illness. Reduces/resolves inflammation.	Sun et al. <sup>56</sup> Shah et al. <sup>57</sup>
Vitamin D <sup>b</sup>	•	•	•	•		•	Reduces symptom duration. Reduces mortality. Reduce incidence of illness associated with viral strains. Normalizes immune signatures and ensures gut health.	Martineau et al. <sup>59</sup> Alexander et al. <sup>50</sup> Biesalski et al. <sup>60</sup> Maggini et al. <sup>61</sup> Gombart et al. <sup>62</sup> Maggini et al. <sup>61</sup> Gombart <sup>62</sup>
Vitamin A <sup>a</sup>	•	•	•	•			Normalizes immune signatures and ensures gut health.	Maggini et al. <sup>61</sup> Gombart et al. <sup>62</sup> Gombart <sup>62</sup>
Vitamin B6	•	•	•	•		•	Improves immunity. Reduces mortality with sepsis.	Carr and Maggini <sup>63</sup> Schloss et al. <sup>64</sup> Fowler et al. <sup>65</sup>
Vitamin B12	•	•	•	•		•	Reduces inflammation. Improves immune system resilience. Reduces progression from colonization to illness. Reduces/resolves inflammation. Reduces the severity and duration of acute symptoms. Optimizes mitochondrial efficiency and reduces reactive oxygen species.	Maggini et al. <sup>61</sup> Gombart et al. <sup>62</sup> Aparicio-Trejo et al. <sup>66</sup>
Vitamin C <sup>c</sup>	•	•	•	•			Reduces/resolves inflammation. Optimizes mitochondrial efficiency and reduces reactive oxygen species.	Virmani et al. <sup>67</sup>
Vitamin E	•	•	•	•			Inhibits viral entry. Reduces symptoms.	Wu et al. <sup>68</sup> Qiu et al. <sup>69</sup> Kinker B et al. <sup>70</sup> Yin et al. <sup>71</sup>
N-Acetyl-Cysteine (NAC) <sup>d</sup>	•	•	•	•		•	Reduces inflammation. Improves immune system resilience.	Kunnumakkara et al. <sup>72</sup> Chainani-Wu <sup>73</sup> Furushima et al. <sup>74</sup> Menegazzi et al. <sup>75</sup> Lin et al. <sup>76</sup> Wang et al. <sup>77</sup>
Carnitine						•	Prevents infection. Reduces inflammation. Reduces inflammation. Primes innate immune function. Promotes viral eradication or inactivation.	
Quercetin <sup>d</sup>	•	•	•	•				
Curcumin <sup>f</sup>	•	•	•	•		•		
Epigallocatechin Gallate (EGCG) <sup>e</sup>	•	•	•	•				
Resveratrol <sup>f</sup>	•	•	•	•				
Berberine <sup>d</sup>	•	•	•	•				

(continued on next page)

Table 1 (continued)

Integrative Intervention	Prevention	COVID-19					Mechanism/Outcome	Citations
		Asymptomatic	Mild	Moderate	Severe	PASC		
Beta-glucans <sup>a</sup>	•	•	•	•			Regulates immunomodulation. Improves symptoms.	Volman et al. <sup>78</sup> Auinger et al. <sup>79</sup> De Marco Castro et al. <sup>80</sup>
Folate	•	•	•	•			Reduces inflammation. Improves immune system resilience.	Maggini et al. <sup>61</sup> Gombart et al. <sup>62</sup>
Iron	•	•	•	•			Reduces inflammation. Improves immune system resilience.	Maggini et al. <sup>61</sup> Gombart et al. <sup>62</sup>
Copper	•	•	•	•			Reduces inflammation. Improves immune system resilience.	Maggini et al. <sup>61</sup> Gombart et al. <sup>62</sup>
Omega-3 fatty acids						•	Reduces/resolves inflammation. Improves psychoneuro-immunity.	Yang et al. <sup>81</sup> Cagnina et al. <sup>82</sup>
Astragalus <sup>f</sup>	•	•	•	•			Primes innate immune function. Inhibits viral binding. Promotes viral eradication or inactivation.	McCulloch et al. <sup>83</sup> Zheng et al. <sup>84</sup> Polonikov <sup>85</sup>
Glutathione	•	•	•	•		•	Reduces/resolves inflammation. Optimizes mitochondrial efficiency. Reduces reactive oxygen species.	
Selenium	•	•	•	•			Reduces inflammation and oxidation. Improves immune system resilience.	Maggini et al. <sup>61</sup> Gombart et al. <sup>62</sup> Steinbrenner et al. <sup>86</sup> Alexander et al. <sup>50</sup>
Mushrooms <sup>d</sup>	•	•	•	•			Promotes viral eradication or inactivation. Modulation of innate immune response.	Dai et al. <sup>87</sup>
Nettles	•	•	•	•			Reduces viral replication.	Keyaerts et al. <sup>88</sup>
Leeks	•	•	•	•			Reduces viral replication.	Keyaerts et al. <sup>88</sup>
<b>Stress Resilience</b>	•	•	•	•	•	•	Reduces inflammation. Improves immune system resilience.	Buric et al. <sup>27</sup> Williams et al. <sup>89</sup> Woody et al. <sup>90</sup>
<b>Sleep Hygiene</b> 7 or more hours of sleep	•	•	•	•	•	•	Reduces infection risk. Optimizes vaccine efficacy.	Schmitz et al. <sup>91</sup> Richter et al. <sup>92</sup> Ibarra-Coronado et al. <sup>93</sup>
Melatonin		•	•	•		•	Reduces/resolves inflammation, and symptoms.	Zhang et al. <sup>94</sup> El-Missiry et al. <sup>95</sup> Favero et al. <sup>96</sup>
<b>Care Delivery Models</b> Shared medical appointments focused on nutrition and lifestyle Telemedicine	•	•	•	•	•	•	Improves functional status, COVID-related symptoms and global physical and mental health	Beidelschies et al. <sup>97</sup> Patels et al. <sup>98</sup> Der-Martirosian et al. <sup>99</sup> Ohannessian et al. <sup>100</sup> Narayanan et al. <sup>101</sup>

\*Additional references are available at: The Functional Medicine Approach to COVID-19: Virus-Specific Nutraceutical and Botanical Agents | The Institute for Functional Medicine (<https://www.ifm.org/news-insights/the-functional-medicine-approach-to-covid-19-virus-specific-nutraceutical-and-botanical-agents/>); Boosting Immunity: Functional Medicine Tips on Prevention & Optimizing Immune Function During the COVID-19 (Coronavirus) Outbreak | The Institute for Functional Medicine (<https://www.ifm.org/news-insights/boosting-immunity-functional-medicine-tips-prevention-immunity-boosting-covid-19-coronavirus-outbreak/>).

Strength of Evidence: a: Strong, b: Strong (for prevention) / Conditional (for treatment), c: Moderate (for sepsis treatment) / Conditional (for prevention), d: Limited, e: Limited (for prevention) / Conditional (for treatment), f: Conditional.

Conventional medicine providers may be reluctant to embrace IM approaches. Combined with patient uncertainty and panic, there was an opportunity for disingenuous advice filtered through technology/social media. This can complicate the evidence arena and tarnish the fields trying to be solution-oriented, evidence-based.

Nutrition and lifestyle-based interventions require extensive education by the provider and/or ancillary staff. In conventional medicine, the available time to deliver such recommendations is limited,<sup>11</sup> and providers are not always adequately trained.<sup>12</sup> However, many institutions have instituted education around the use of food as medicine.<sup>13</sup>

The ability to purchase healthy foods may be inaccessible or cost-prohibitive for many populations especially those disproportionately affected by COVID-19 and PASC.<sup>14</sup>

Patients experiencing PASC may feel misunderstood, unsupported, and frustrated. Therefore, access to longitudinal behavioral health/mental health support is warranted; however, this may have limited availability in certain populations.<sup>15</sup>

### 2.5. How to help developing APEC economies to use IM for COVID-19 care

IM including FM and TM can be used to extend the reach of existing healthcare systems to address comorbidities in communities where there is lack of access to medication. However, this requires collaboration with trained providers as well as education and guidance related to specific recommendations.

- Identification of trained providers:
  - i To identify an IM-trained provider across the United States, visit the Academy of Integrative Health and Medicine (AIHM): <https://aihmed.org/members/find-a-provider/>.
  - ii To identify a FM-trained provider across the world, visit The Institute for Functional Medicine (IFM): <https://www.ifm.org/find-a-practitioner/>.
- Education and guidance related to specific recommendations can be found here:
  - i. United States: The Institute for Functional Medicine. Available at <https://info.ifm.org/covid-19>.
  - ii. Thailand: “Traditional and Complementary Medicine Practice Guidelines in ASEAN: Thailand Section”.<sup>16</sup> “Guidelines of Thai Traditional and Alternative Medicine on the Prevention of the Spread of COVID-19”.<sup>17</sup> Clinical Practice Guidelines for diagnosis, treatment, and prevention of COVID-19 for Physicians and Health Professionals version 24 (11 July 2022). (in Thai).
  - iii. Mexico: “Homeopathic Medicine. Fundamentals, Evidence and Contributions to Health”.<sup>18</sup>
  - iv. Republic of Korea: “A Consensus Guideline of Herbal Medicine for Coronavirus Disease 2019”.<sup>19</sup>
  - v. Canada: The Canadian Integrative Medicine Association (CIMA). Available at <https://www.cimadoctors.ca/>.

### 2.6. The future development of IM on COVID-19 care

- Collaborate with various APEC economies on rigorous research studies to demonstrate efficacy.
- Focus on research efficiency for publication.
- Deliver quality publications to high-impact journals.
- Promote the widespread adoption of evidence-based strategies.
- Address underserved populations by increasing access to foods which can be used as medicine and developing cost-effective strategies for prevention.
- Promote the telehealth delivery of IM and FM interventions.
- Support healthcare workers who have disproportionately suffered from deleterious physical and psychological impacts of the COVID-19 pandemic (e.g. use of sonotherapy).

### 2.7. Suggestions on how APEC can do more on COVID-19 care

- Increase dialogue and connection, perhaps consider a consortium on COVID-19 care.
- Discuss and evaluate effective approaches and obstacles to implementation.
- Examine opportunities for deployment within various APEC economies and populations.

## 3. Conclusions

This document was established during the time of the APEC Project – Integrative Medicine and COVID-19 Care, between May 2022 and March 2023. The purpose of this article is to provide a comprehensive IM system for COVID-19 care as recommendations and suggestive guidelines which cited care practices have confirmed their efficacy and usefulness either used alone or combined with conventional medicine. However, it has limitations on information collection, tools and care procedures development. Though it provides current useful information on IM for COVID-19 care, the readers need to be cautious when using IM tools, methods and procedures on their own care practices.

## Funding

This publication is one of the outcomes from APEC supported project (HWG 13 2021A, Integrative Medicine and COVID-19 Care). It was funded by APEC Support Fund/ASF: APEC Cooperation on Combating COVID-19 and Economic Recovery (CCER).

## Ethical statement

Not applicable.

## Data availability

The authors can provide the related data upon reasonable request.

## Declaration of competing interest

There is no conflict of interest from all authors.

## CRediT authorship contribution statement

**Libin Jia:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Funding acquisition, Supervision. **Michelle Beidelschies:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Joel M. Evans:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Richard C. Niemtow:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Songxuan Zhou Niemtow:** Methodology, Investigation. **Jeffery A. Dusek:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Charles Wu:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Yi-Chang Su:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **C. Jason Wang:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Chien-Yu Lin:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Peristiwa Ridha Widhi Astana:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Danang Ardiyanto:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Rusmiyati Hardjoutomo:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Khwanchai Visithanon:** Conceptualization, Methodology, Formal analysis, Investigation, Writing –

review & editing. **Jagravudh Puangkong:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Julalak Chokpaisarn:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Martha Villar Lopez:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Hiroshi Yotsuyanagi:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Myeong Soo Lee:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Hernan Jose Garcia Ramirez:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing. **Cecilia Plaza Bobadilla:** Methodology, Formal analysis, Investigation. **Elizabeth Margarita Gonzalez Quinteros:** Methodology, Formal analysis, Investigation. **Monica Galanti de la Paz:** Methodology, Formal analysis, Investigation. **Cecilia C. Maramba-Lazarte:** Methodology, Formal analysis, Investigation.

## Acknowledgement

We want to thank APEC Malaysia team for their review comments and Renee Wang for her contributions.

## References

- World Health Organization (WHO). Coronavirus (COVID-19) Dashboard 2023 [Available from: <https://Covid19.who.int/>].
- Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol.* 2021;19(3):141–154.
- Li H, Yuan K, Sun YK, Zheng YB, Xu YY, Su SZ, et al. Efficacy and practice of facemask use in general population: a systematic review and meta-analysis. *Transl Psychiatry.* 2022;12(1):49.
- Jefferson T, Dooley L, Ferroni E, Al-Ansary LA, van Driel ML, Bawazeer GA, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. *Cochrane Database Syst Rev.* 2023;1(1):Cd006207.
- Graña C, Ghosn L, Evrenoglou T, Jarde A, Minozzi S, Bergman H, et al. Efficacy and safety of COVID-19 vaccines. *Cochrane Database Syst Rev.* 2022;12(12):Cd015477.
- Xie Y, Bowe B, Al-Aly Z. Burdens of post-acute sequelae of COVID-19 and severity of acute infection, demographics and health status. *Nat Commun.* 2021;12(1):6571.
- Proal AD, VanElzakker MB. Long COVID or post-acute sequelae of COVID-19 (PASC): an overview of biological factors that may contribute to persistent symptoms. *Front Microbiol.* 2021;12:698169.
- Seifert G, Jeitler M, Stange R, Michalsen A, Cramer H, Brinkhaus B, et al. The relevance of complementary and integrative medicine in the COVID-19 pandemic: a qualitative review of the literature. *Front Med.* 2020;7:587749 (Lausanne).
- National Institutes of Health (NIH). Complementary, Alternative, or Integrative Health: what's In a Name?: national Center for Complementary and Integrative Health 2023 [updated March, 13, 2023. Available from: <https://www.nccih.nih.gov/health/complementary-alternative-or-integrative-health-whats-in-a-name>.
- Bland J. Defining function in the functional medicine model. *Integr Med.* 2017;16(1):22–25 (Encinitas).
- Sara Berg M. How to give good nutrition advice when time is short. *Am Med Assoc.* 2019. [Available from: <https://www.ama-assn.org/delivering-care/public-health/how-give-good-nutrition-advice-when-time-short> .
- Cresci G, Beidelschies M, Tebo J, Hull A. Educating future physicians in nutritional science and practice: the time is now. *J Am Coll Nutr.* 2019;38(5):387–394.
- Downer S, Berkowitz SA, Harlan TS, Olstad DL, Mozaffarian D. Food is medicine: actions to integrate food and nutrition into healthcare. *BMJ.* 2020;369:m2482.
- Garba NA, Sacca L, Clarke RD, Bhoite P, Buschman J, Oller V, et al. Addressing food insecurity during the COVID-19 pandemic: intervention outcomes and lessons learned from a collaborative food delivery response in south Florida's underserved households. *Int J Environ Res Public Health.* 2022;19(13).
- Kola L, Kohrt BA, Hanlon C, Naslund JA, Sikander S, Balaji M, et al. COVID-19 mental health impact and responses in low-income and middle-income countries: reimagining global mental health. *Lancet Psychiatry.* 2021;8(6):535–550.
- Department of Thai traditional and alternative medicine. Traditional and complementary medicine practice guidelines in ASEAN: Thailand Section 2020.
- Department of Thai Traditional and Alternative Medicine. Guidelines of Thai traditional and alternative medicine on the prevention of the spread of COVID-192021. Available from: 2023 [https://tpd.dtam.moph.go.th/images/oic/E-Book/Covid\\_ver5\\_complete.pdf](https://tpd.dtam.moph.go.th/images/oic/E-Book/Covid_ver5_complete.pdf).
- Unidad de Análisis Económico. Homeopathic Medicine: fundamentals, Evidence and Contributions to Health2022. 2023 Available from: [https://www.gob.mx/cms/uploads/attachment/file/789857/Evidencias\\_homeopat\\_a\\_frente\\_al\\_COVID\\_19\\_En\\_ingl\\_s.pdf](https://www.gob.mx/cms/uploads/attachment/file/789857/Evidencias_homeopat_a_frente_al_COVID_19_En_ingl_s.pdf).
- Lee BJ, Lee JA, Kim KI, Choi JY, Jung HJ. A consensus guideline of herbal medicine for coronavirus disease 2019. *Integr Med Res.* 2020;9(3):100470.
- Han Z, Zhang Y, Wang P, Tang Q, Zhang K. Is acupuncture effective in the treatment of COVID-19 related symptoms? Based on bioinformatics/network topology strategy. *Brief Bioinform.* 2021;22(5).
- Trager RJ, Brewka EC, Kaiser CM, Patterson AJ, Dusek JA. Acupuncture in multidisciplinary treatment for post-COVID-19 syndrome. *Med Acupunct.* 2022;34(3):177–183.
- Williams JE, Moramarco J. The role of acupuncture for long COVID: mechanisms and models. *Med Acupunct.* 2022;34(3):159–166.
- Hollifield M, Coccoza K, Calloway T, Lai J, Caicedo B, Carrick K, et al. Improvement in long-COVID symptoms using acupuncture: a case study. *Med Acupunct.* 2022;34(3):172–176.
- Niemtzow R. and Niemtzw S.Z. Medical acupuncture: COVID "long haulers": treating long-term effects of COVID-19 syndrome. 2022.
- Liu ST, Zhan C, Ma YJ, Guo CY, Chen W, Fang XM, et al. Effect of qigong exercise and acupressure rehabilitation program on pulmonary function and respiratory symptoms in patients hospitalized with severe COVID-19: a randomized controlled trial. *Integr Med Res.* 2021;10(Suppl):100796.
- Yang HJ, Setou N, Koh E. Utilization of mind-body intervention for integrative health care of COVID-19 patients and survivors. *Int J Environ Res Public Health.* 2022;19(11).
- Buric I, Farias M, Jong J, Mee C, Brazil IA. What is the molecular signature of mind-body interventions? A systematic review of gene expression changes induced by meditation and related practices. *Front Immunol.* 2017;8:670.
- Basu-Ray I, Metri K, Khanra D, Revankar R, Chinnaiyan KM, Raghuram N, et al. A narrative review on yoga: a potential intervention for augmenting immunomodulation and mental health in COVID-19. *BMC Complement Med Ther.* 2022;22(1):191.
- Shah K, Adhikari C, Saha S, Saxena D. Yoga, immunity and COVID-19: a scoping review. *J Family Med Prim Care.* 2022;11(5):1683–1701.
- Demeke CA, Woldeyohanis AE, Kifle ZD. Herbal medicine use for the management of COVID-19: a review article. *Metabol Open.* 2021;12:100141.
- Tsai KC, Huang YC, Liaw CC, Tsai CI, Chiou CT, Lin CJ, et al. A traditional Chinese medicine formula NRICM101 to target COVID-19 through multiple pathways: a bedside-to-bench study. *Biomed Pharmacother.* 2021;133:111037.
- Tseng YH, Lin SJ, Hou SM, Wang CH, Cheng SP, Tseng KY, et al. Curbing COVID-19 progression and mortality with traditional Chinese medicine among hospitalized patients with COVID-19: a propensity score-matched analysis. *Pharmacol Res.* 2022;184:106412.
- Wei WC, Liaw CC, Tsai KC, Chiou CT, Tseng YH, Chiou WF, et al. Targeting spike protein-induced TLR/NET axis by COVID-19 therapeutic NRICM102 ameliorates pulmonary embolism and fibrosis. *Pharmacol Res.* 2022;184:106424.
- Tanwattayanont J, Piriyananusorn N, Sangsoi L, Boonsong B, Sunpaoa C, Tanamatayarat P, et al. Use of Andrographis paniculata (Burm.f.) Wall. ex Nees and risk of pneumonia in hospitalized patients with mild coronavirus disease 2019: a retrospective cohort study. *Front Med.* 2022;9:947373 (Lausanne).
- Intharuksa A, Arunotayanun W, Yooiin W, Sirisa-Ard P. A comprehensive review of andrographis paniculata (Burm. f.) Nees and its constituents as potential lead compounds for COVID-19 drug discovery. *Molecules.* 2022;27(14).
- Kligler B, Ulbricht C, Basch E, Kirkwood CD, Abrams TR, Miranda M, et al. Andrographis paniculata for the treatment of upper respiratory infection: a systematic review by the natural standard research collaboration. *Explore.* 2006;2(1):25–29 (NY).
- Hu XY, Wu RH, Logue M, Blondel C, Lai LYW, Stuart B, et al. Andrographis paniculata (Chuan Xin Lian) for symptomatic relief of acute respiratory tract infections in adults and children: a systematic review and meta-analysis. *PLoS ONE.* 2017;12(8):e0181780.
- Juckmeta T, Itharat A. Anti-inflammatory and antioxidant activities of Thai traditional medicine remedy called "Ya-Ha-Rak". *J Health Res.* 2012;26:205–210.
- Palo T, Thaworn A, Charoenkij P, Thamsersang O, Chotewuttakorn S, Triparara P, et al. The effects of Thai Herbal Ha-Rak formula on COX isoform expression in human umbilical vein endothelial cells induced by IL-1 $\beta$ . *Evid Based Complement Alternat Med.* 2017;2017:9383272.
- Singh RS, Singh A, Kaur H, Batra G, Sarma P, Kaur H, et al. Promising traditional Indian medicinal plants for the management of novel Coronavirus disease: a systematic review. *Phytother Res.* 2021;35(8):4456–4484.
- Hartono SB, Sari Y, Avicena A, Maryani SC, et al. The effect of Curcumin and virgin coconut oil towards cytokines Levels in COVID-19 patients at Universitas Sebelas Maret Hospital, Surakarta, Indonesia. *Pharmacogn J.* 2022;14(1):216–225.
- Kim H, Rebholz CM, Hegde S, LaFiura C, Raghavan M, Lloyd JF, et al. Plant-based diets, pescatarian diets and COVID-19 severity: a population-based case-control study in six countries. *BMJ Nutr Prev Health.* 2021;4(1):257–266.
- Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, et al. Food in the Anthropocene: the EAT–Lancet commission on healthy diets from sustainable food systems. *Lancet.* 2019;393(10170):447–492.
- de Oliveira GLV, Oliveira CNS, Pinzan CF, de Salis LVV, Cardoso CRB. Microbiota modulation of the gut-lung axis in COVID-19. *Front Immunol.* 2021;12:635471.
- Alharbi KS, Singh Y, Hassan Almalki W, Rawat S, Afzal O, Alfawaz Altamimi AS, et al. Gut microbiota disruption in COVID-19 or Post-COVID illness association with severity biomarkers: a possible role of Pre /Pro-biotics in manipulating microflora. *Chem Biol Interact.* 2022;358:109898.
- Lebeer S, Bron PA, Marco ML, Van Pijkeren JP, O'Connell Motherway M, Hill C, et al. Identification of probiotic effector molecules: present state and future perspectives. *Curr Opin Biotechnol.* 2018;49:217–223.
- Biliavska L, Pankivska Y, Povnitsa O, Zagorodnya S. Antiviral activity of exopolysaccharides produced by lactic acid bacteria of the genera *Pediococcus*, *Leuconostoc* and *Lactobacillus* against human adenovirus type 5. *Medicina.* 2019;55(9) (Kaunas).
- Prasad AS. Zinc is an antioxidant and anti-inflammatory agent: its role in human health. *Front Nutr.* 2014;1:14.
- Hulisz D. Efficacy of zinc against common cold viruses: an overview. *J Am Pharm Assoc.* 2003;44(5):594–603 2004.

50. Alexander J, Tinkov A, Strand TA, Alehagen U, Skalny A, Aaseth J. Early nutritional interventions with zinc, selenium and vitamin D for raising anti-viral resistance against progressive COVID-19. *Nutrients*. 2020;12(8).
51. Costa G, Shushanof M, Bouskela E, Bottino D. Oral L-arginine (5g/day) for 14 days improves microcirculatory function in healthy young women and healthy and type 2 diabetes mellitus elderly women. *J Vasc Res*. 2022;59(1):24–33.
52. Mitchell WK, Phillips BE, Wilkinson DJ, Williams JP, Rankin D, Lund JN, et al. Supplementing essential amino acids with the nitric oxide precursor, L-arginine, enhances skeletal muscle perfusion without impacting anabolism in older men. *Clin Nutr*. 2017;36(6):1573–1579.
53. Mills CE, Khatri J, Maskell P, Odongel C, Webb AJ. It is rocket science - why dietary nitrate is hard to 'beet'! Part II: further mechanisms and therapeutic potential of the nitrate-nitrite-NO pathway. *Br J Clin Pharmacol*. 2017;83(1):140–151.
54. Park HY, Kim SW, Seo J, Jung YP, Kim H, Kim AJ, et al. Dietary arginine and citrulline supplements for cardiovascular health and athletic performance: a narrative review. *Nutrients*. 2023;15(5):1268.
55. Zakay-Rones Z, Thom E, Wollan T, Wadstein J. Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections. *J Int Med Res*. 2004;32(2):132–140.
56. Sun LZ, Currier NL, Miller SC. The American coneflower: a prophylactic role involving nonspecific immunity. *J Altern Complement Med*. 1999;5(5):437–446.
57. Shah SA, Sander S, White CM, Rinaldi M, Coleman CI. Evaluation of echinacea for the prevention and treatment of the common cold: a meta-analysis. *Lancet Infect Dis*. 2007;7(7):473–480.
58. Bergman P, Lindh AU, Björkhem-Bergman L, Lindh JD. Vitamin D and respiratory tract infections: a systematic review and meta-analysis of randomized controlled trials. *PLoS ONE*. 2013;8(6):e65835.
59. Martineau AR, Jolliffe DA, Hooper RL, Greenberg L, Aloia JF, Bergman P, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ*. 2017;356:i6583.
60. Biesalski HK, Nohr D. Importance of vitamin-A for lung function and development. *Mol Asp Med*. 2003;24(6):431–440.
61. Maggini S, Wintergerst ES, Beveridge S, Hornig DH. Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. *Br J Nutr*. 2007;98(1):S29–S35 Suppl.
62. Gombart AF, Pierre A, Maggini S. A review of micronutrients and the immune system-working in harmony to reduce the risk of infection. *Nutrients*. 2020;12(1).
63. Carr AC, Maggini S. Vitamin C and immune function. *Nutrients*. 2017;9(11).
64. Schloss J, Lauche R, Harnett J, Hannan N, Brown D, Greenfield T, et al. Efficacy and safety of vitamin C in the management of acute respiratory infection and disease: a rapid review. *Adv Integr Med*. 2020;7(4):187–191.
65. Fowler AA, Truweit JD, Hite RD, Morris PE, DeWilde C, Priday A, et al. Effect of vitamin C infusion on organ failure and biomarkers of inflammation and vascular injury in patients with sepsis and severe acute respiratory failure: the CITRIS-ALI randomized clinical trial. *JAMA*. 2019;322(13):1261–1270.
66. Aparicio-Trejo OE, Reyes-Fermin LM, Briones-Herrera A, Tapia E, León-Contreras JC, Hernández-Pando R, et al. Protective effects of N-acetyl-cysteine in mitochondria bioenergetics, oxidative stress, dynamics and S-glutathionylation alterations in acute kidney damage induced by folic acid. *Free Radic Biol Med*. 2019;130:379–396.
67. Virmani MA, Cirulli M. The role of L-carnitine in mitochondria, prevention of metabolic inflexibility and disease initiation. *Int J Mol Sci*. 2022;23(5).
68. Wu W, Li R, Li X, He J, Jiang S, Liu S, et al. Quercetin as an antiviral agent inhibits influenza A virus (IAV) entry. *Viruses*. 2015;8(1).
69. Qiu X, Kroeker A, He S, Kozak R, Audet J, Mbikay M, et al. Prophylactic efficacy of Quercetin 3- $\beta$ -O-D-Glucoside against ebola virus infection. *Antimicrob Agents Chemother*. 2016;60(9):5182–5188.
70. Caasu KB. Quercetin: a promising treatment for the common cold. *J Infect Dis Prev Med*. 2014;2(2).
71. Yin H, Guo Q, Li X, Tang T, Li C, Wang H, et al. Curcumin suppresses IL-1 $\beta$  secretion and prevents inflammation through inhibition of the NLRP3 inflammasome. *J Immunol*. 2018;200(8):2835–2846.
72. Kunnumakkara AB, Bordoloi D, Padmavathi G, Monisha J, Roy NK, Prasad S, et al. Curcumin, the golden nutraceutical: multitargeting for multiple chronic diseases. *Br J Pharmacol*. 2017;174(11):1325–1348.
73. Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: a component of tumeric (*Curcuma longa*). *J Altern Complement Med*. 2003;9(1):161–168.
74. Furushima D, Nishimura T, Takuma N, Iketani R, Mizuno T, Matsui Y, et al. Prevention of acute upper respiratory infections by consumption of catechins in healthcare workers: a randomized, placebo-controlled trial. *Nutrients*. 2019;12(1).
75. Menegazzi M, Campagnari R, Bertoldi M, Crupi R, Di Paola R, Cuzzocrea S. Protective effect of epigallocatechin-3-gallate (EGCG) in diseases with uncontrolled immune activation: could such a scenario be helpful to counteract COVID-19? *Int J Mol Sci*. 2020;21(14).
76. Lin SC, Ho CT, Chuo WH, Li S, Wang TT, Lin CC. Effective inhibition of MERS-CoV infection by resveratrol. *BMC Infect Dis*. 2017;17(1):144.
77. Wang J, Wang L, Lou GH, Zeng HR, Hu J, Huang QW, et al. Coptidis Rhizoma: a comprehensive review of its traditional uses, botany, phytochemistry, pharmacology and toxicology. *Pharm Biol*. 2019;57(1):193–225.
78. Volman JJ, Ramakers JD, Plat J. Dietary modulation of immune function by beta-glucans. *Physiol Behav*. 2008;94(2):276–284.
79. Auinger A, Riede L, Bothe G, Busch R, Gruenewald J. Yeast (1,3)-(1,6)-beta-glucan helps to maintain the body's defence against pathogens: a double-blind, randomized, placebo-controlled, multicentric study in healthy subjects. *Eur J Nutr*. 2013;52(8):1913–1918.
80. De Marco Castro E, Calder PC, Roche HM.  $\beta$ -1,3/1,6-Glucans and immunity: state of the art and future directions. *Mol Nutr Food Res*. 2021;65(1):e1901071.
81. Yang CP, Chang CM, Yang CC, Pariante CM, Su KP. Long COVID and long chain fatty acids (LCFAs): psychoneuroimmunity implication of omega-3 LCFAs in delayed consequences of COVID-19. *Brain Behav Immun*. 2022;103:19–27.
82. Cagnina RE, Duvall MG, Nijmeh J, Levy BD. Specialized pro-resolving mediators in respiratory diseases. *Curr Opin Clin Nutr Metab Care*. 2022;25(2):67–74.
83. McCulloch M, Broffman M, Gao J, Colford JM. Chinese herbal medicine and interferon in the treatment of chronic hepatitis B: a meta-analysis of randomized, controlled trials. *Am J Public Health*. 2002;92(10):1619–1628.
84. Zheng Y, Ren W, Zhang L, Zhang Y, Liu D, Liu Y. A review of the pharmacological action of astragalus polysaccharide. *Front Pharmacol*. 2020;11:349.
85. Polonikov A. Endogenous deficiency of glutathione as the most likely cause of serious manifestations and death in COVID-19 patients. *ACS Infect Dis*. 2020;6(7):1558–1562.
86. Steinbrenner H, Al-Quraishy S, Dkhal MA, Wunderlich F, Sies H. Dietary selenium in adjunct therapy of viral and bacterial infections. *Adv Nutr*. 2015;6(1):73–82.
87. Ji Dai X, Stanilka JM, Rowe CA, Esteves EA, Nieves C, Spaiser SJ, et al. Consuming Lentinula edodes (Shiitake) mushrooms daily improves human immunity: a randomized dietary intervention in healthy young adults. *J Am Coll Nutr*. 2015;34(6):478–487.
88. Keyaerts E, Vijgen L, Pannecouque C, Van Damme E, Peumans W, Egberink H, et al. Plant lectins are potent inhibitors of coronaviruses by interfering with two targets in the viral replication cycle. *Antiviral Res*. 2007;75(3):179–187.
89. Williams DP, Koehnig J, Carnevali L, Sgoifo A, Jarczok MN, Sternberg EM, et al. Heart rate variability and inflammation: a meta-analysis of human studies. *Brain Behav Immun*. 2019;80:219–226.
90. Woody A, Figueroa WS, Benencia F, Zoccola PM. Stress-induced parasympathetic control and its association with inflammatory reactivity. *Psychosom Med*. 2017;79(3):306–310.
91. Schmitz NCM, van der Werf YD, Lammers-van der Holst HM. The importance of sleep and circadian rhythms for vaccination success and susceptibility to viral infections. *Clocks Sleep*. 2022;4(1):66–79.
92. Richter K, Kellner S, Hillemecher T, Golubnitschaja O. Sleep quality and COVID-19 outcomes: the evidence-based lessons in the framework of predictive, preventive and personalised (3P) medicine. *EPMA J*. 2021;12(2):221–241.
93. Ibarra-Coronado EG, Pantaleón-Martínez AM, Velázquez-Moctezuma J, Próspero-García O, Méndez-Díaz M, Pérez-Tapia M, et al. The bidirectional relationship between sleep and immunity against infections. *J Immunol Res*. 2015;2015:678164.
94. Zhang R, Wang X, Ni L, Di X, Ma B, Niu S, et al. COVID-19: melatonin as a potential adjuvant treatment. *Life Sci*. 2020;250:117583.
95. El-Missiry MA, El-Missiry ZMA, Othman AI. Melatonin is a potential adjuvant to improve clinical outcomes in individuals with obesity and diabetes with coexistence of Covid-19. *Eur J Pharmacol*. 2020;882:173329.
96. Favero G, Franceschetti L, Bonomini F, Rodella LF, Rezzani R. Melatonin as an anti-inflammatory agent modulating inflammasome activation. *Int J Endocrinol*. 2017;2017:1835195.
97. Beidelschies M, Alejandro-Rodriguez M, Guo N, Postan A, Jones T, Bradley E, et al. Patient outcomes and costs associated with functional medicine-based care in a shared versus individual setting for patients with chronic conditions: a retrospective cohort study. *BMJ Open*. 2021;11(4):e048294.
98. Patel S, GK BE, Beidelschies M. Evaluation of a functional medicine-based SMA for the management of post-COVID syndrome. *Int Congr Integr Med*. 2022.
99. Der-Martirosian C, Shin M, Upham ML, Douglas JH, Zeliadt SB, Taylor SL. Telehealth complementary and integrative health therapies during COVID-19 at the U.S. department of veterans affairs. *Telemed J E Health*. 2022.
100. Ohannessian R, Duong TA, Odone A JMIR Public Health Surveill; 2020:e18810.
101. Narayanan S, Lopez G, Liu W, Cohen A, Cohen L. The use of mobile-technologies to deliver integrative medicine during and beyond the COVID-19 world pandemic. *Glob Adv Health Med*. 2020;9:2164956120977437.