Asia-Pacific
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Recommendations and Guidelines of Integrative Medicine (IM) for COVID-19 Care

APEC Health Working Group

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Acronyms

APEC	Asia-Pacific Economic Cooperation
COVID-19	Coronavirus Disease 2019
CIMA	Canadian Integrative Medicine Association (CIMA)
EGCG	Epigallocatechin Gallate
FM	Functional Medicine
IM	Integrative Medicine
KM	Korean Medicine
PASC	Post-Acute Sequelae of COVID-19
SARS-CoV-2	Severe Acute Respiratory Syndrome-Related Coronavirus-2
SMA	Shared Medical Appointments
TCM	Traditional Chinese Medicine
TTM	Traditional Thai Medicine

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 (1, 2). While various physical measures were implemented to contain the highly transmissible virus (3, 4) and vaccines were rapidly developed to mitigate disease severity (5), 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 (6). This complication is commonly referred to as post-acute sequelae of COVID-19 (PASC) or Long COVID (2, 7).

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 (8). 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 (9). 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 (10). 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 Indonesia; Chinese Taipei; 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 establish 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.

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.

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. 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.

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

- IM care models are intended to extend, not replace, current healthcare 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.

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.

- 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 (11), and providers are not always adequately trained (12). However, many institutions have instituted education around the use of food as medicine (13).

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

- 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 (15).

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:
        - To identify an IM-trained provider across the United States, visit the Academy of Integrative Health and Medicine (AIHM): https://aihm.org/members/find-a-provider/.
        - 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:
        - **United States:** The Institute for Functional Medicine. Available at https://info.ifm.org/covid-19.
        - **Thailand:** "Traditional and Complementary Medicine Practice Guidelines in ASEAN: Thailand Section" (16).
          "Guidelines of Thai Traditional and Alternative Medicine on the Prevention of the Spread of COVID-19" (17).
          Clinical Practice Guidelines for diagnosis, treatment, and prevention of COVID-19 for Physicians and Health Professionals version 24 (11 July 2022), (in Thai).
        - **Mexico:** "Homeopathic Medicine. Fundamentals, Evidence and Contributions to Health" (18).
        - **Republic of Korea:** "A Consensus Guideline of Herbal Medicine for Coronavirus Disease 2019" (19).
        - **Canada:** The Canadian Integrative Medicine Association (CIMA). Available at https://www.cimadoctors.ca/.

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).

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.

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

		COVID-19						
Integrative Intervention	**Prevention**	**Asympto-matic**	**Mild**	**Moderate**	**Severe**	**PASC**	**Mechanism/ Outcome**	**Citations**
Acupuncture / Acupressure			✓	✓		✓	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.	Han Z *et al.* (20) Trager RJ *et al.* (21) Williams JE and Moramarco J (22) Hollifield M *et al.* (23)
Electro-acupuncture *plus* Octapolar Static Magnet						✓	Improves anosmia and ageusia.	Niemtzow *et al.* (24)
Qigong and Acupressure					✓		Improves lung function, pulmonary symptoms, and shortens length of hospital stay.	Liu ST *et al.* (25)
Mind-Body Interventions			✓	✓			Reduce stress, improve mental and physical health.	Yang HJ *et al.* (26) Buric I *et al.* (27)

Yoga			✓	✓			Improves immunological profiles by strengthening cell-mediated immunity. Improves physical and physiological wellbeing and quality of life.	Basu-Ray I *et al*. (28) Shah K *et al.* (29)
Herbal/Botanical Medicine			✓	✓	✓		Anti-viral activity Reduces inflammation.	Demeke CA *et al*. (30)
NRICM101 (TCM formula)		✓	✓	✓			Reduces the proportion of critically ill patients.	Tsai KC *et al*. (31) Tseng YE *et al*. (32)
NRICM102 (TCM formula)					✓		Reduces mortality rate.	Tseng YH et al. (32) Wei WC *et al.* (33)
Andrographis paniculata[a]		✓	✓	✓			Anti-inflammatory and immunomodulatory effects to prevent disease progression, reduce the chance of developing pneumonia and shortened viral shedding period.	Tanwettiyanont J *et al*. (34) Intharuksa A *et al*. (35) Kligler B *et al*. (36) Hu XY *et al*. (37) Department of Thai Traditional and Alternative Medicine (17)
Ya-Ha-Rak (TTM formula)		✓	✓	✓			Reduces inflammation and pain.	Juckmeta T and Itharat A (38) Palo T *et al*. (39)
Ayurveda Rasayana		✓	✓	✓			Improves immunogenicity and immunomodulation and support non-specific immunity.	Singh RS *et al.* (40)
Curcumin and virgin coconut oil		✓	✓	✓			Reduces inflammation and pro-inflammatory cytokines.	Hartono *et al*. (41)
Nutrition								
Plant-based diets or pescatarian diets		✓					Prevents COVID-19 severity.	Kim H *et al*. (42)
Milpa diet (sustainable foods of Mexican origin)		✓					Boosts the immune system.	Willet W *et al.* (43)

Dietary Supplements *								
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 G *et al*. (44) Alharbi KS *et al*. (45) Lebeer S *et al*. (46) Biliavska L *et al*. (47)
Zinc[a]	✓	✓	✓	✓			Reduces severity of symptoms. Reduces duration of illness.	Prasad A (48) Hulisz D (49) Alexander J *et al*. (50)
Arginine						✓	Improves cell membrane and microvascular health.	Costa G *et al*. (51) Mitchell WK *et al*. (52) Mills CE *et al*. (53)
Citrulline						✓	Improves cell membrane and microvascular health.	Park H *et al*. (54)
Elderberry[a]	✓	✓	✓	✓			Reduces and improves symptoms. Reduces incidence and duration.	Zakay-Rones Z *et al.* (55)
Echinacea[b]	✓						Prevention of infection. Reduced duration of symptoms.	Sun LZ *et al*. (56) Shah SA *et al*. (57)
Vitamin D[b]	✓	✓	✓	✓		✓	Reduces progression from colonization to illness. Reduces/resolves inflammation.	Bergman P *et al*. (58) Martineau AR *et al*. (59) Alexander J *et al*. (50)
Vitamin A[a]	✓	✓	✓	✓			Reduces symptom duration. Reduces mortality. Reduce incidence of illness associated with viral strains.	Biesalski HK *et al*. (60) Maggini S *et al*. (61) Gombart AF *et al*. (62)
Vitamin B6	✓	✓	✓	✓		✓	Normalizes immune signatures and ensures gut health.	Maggini S *et al*. (61) Gombart AF (62)
Vitamin B12	✓	✓	✓	✓		✓	Normalizes immune signatures and ensures gut health.	Maggini S *et al*. (61) Gombart AF *et al*. (62)

Vitamin C[c]	✓	✓	✓	✓			Improves immunity. Reduces mortality with sepsis.	Carr AC and Maggini S (63) Schloss J *et al*. (64) Fowler AA *et al*. (65)
Vitamin E	✓	✓	✓	✓			Reduces inflammation. Improves immune system resilience.	Maggini S *et al*. (61) Gombart AF *et al*. (62)
N-Acetyl-Cysteine (NAC)[d]	✓	✓	✓	✓		✓	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.	Aparicio-Trejo OE *et al*. (66)
Carnitine						✓	Reduces/resolves inflammation. Optimizes mitochondrial efficiency and reduces reactive oxygen species.	Virmani MA *et al*. (67)
Quercetin[d]	✓	✓	✓	✓			Inhibits viral entry. Reduces symptoms.	Wu W *et al*. (68) Qiu X *et al*. (69) Kinker B *et al*. (70)
Curcumin[f]	✓	✓	✓	✓		✓	Reduces inflammation. Improves immune system resilience.	Yin H *et al*. (71) Kunnumakkara AB *et al*. (72) Chainani-Wu N (73)
Epigallocate-chin Gallate (EGCG)[e]	✓	✓	✓	✓			Prevents infection. Reduces inflammation.	Furushima D *et al*. (74) Menegazzi M *et al*. (75)
Resveratrol[f]	✓	✓	✓	✓			Reduces inflammation.	Lin S *et al*. (76)
Berberine[d]	✓	✓	✓	✓			Primes innate immune function. Promotes viral eradication or inactivation.	Wang J *et al*. (77)
Beta-glucans[a]	✓	✓	✓	✓			Regulates immunomodulation. Improves symptoms.	Volman JJ *et al*. (78) Auinger A *et al*. (79)

								De Marco Castro E *et al.* (80)
Folate	✓	✓	✓	✓			Reduces inflammation. Improves immune system resilience.	Maggini S *et al.* (61) Gombart AF *et al.* (62)
Iron	✓	✓	✓	✓			Reduces inflammation. Improves immune system resilience.	Maggini S *et al.* (61) Gombart AF *et al.* (62)
Copper	✓	✓	✓	✓			Reduces inflammation. Improves immune system resilience.	Maggini S *et al.* (61) Gombart AF *et al.* (62)
Omega-3 fatty acids						✓	Reduces/resolves inflammation. Improves psychoneuro-immunity.	Yang CP *et al.* (81) Cagnina RE *et al.* (82)
Astragalus[f]	✓	✓	✓	✓			Primes innate immune function. Inhibits viral binding. Promotes viral eradication or inactivation.	McCulloch M *et al.* (83) Zheng Y *et al.* (84)
Glutathione	✓	✓	✓	✓		✓	Reduces/resolves inflammation. Optimizes mitochondrial efficiency. Reduces reactive oxygen species.	Polonikov A (85)
Selenium	✓	✓	✓	✓			Reduces inflammation and oxidation. Improves immune system resilience.	Maggini S *et al.* (61) Gombart AF *et al.* (62) Steinbrenner H *et al.* (86) Alexander J *et al.* (50)
Mushrooms[d]	✓	✓	✓	✓			Promotes viral eradication or inactivation. Modulation of innate immune response.	Dai X *et al.* (87)
Nettles	✓	✓	✓	✓			Reduces viral replication.	Keyaerts E *et al.* (88)
Leeks	✓	✓	✓	✓			Reduces viral replication.	Keyaerts E *et al.* (88)

Stress Resilience	✓	✓	✓	✓	✓	✓	Reduces inflammation. Improves immune system resilience.	Buric I *et al.* (27) Williams DP *et al.* (89) Woody A *et al.* (90)
Sleep Hygiene								
7 or more hours of sleep	✓	✓	✓	✓	✓	✓	Reduces infection risk. Optimizes vaccine efficacy.	Schmitz NCM *et al.*(91) Richter K *et al.* (92) Ibarra-Coronado EG *et al.* (93)
Melatonin[f]		✓	✓	✓		✓	Reduces/resolves inflammation, and symptoms.	Zhang R *et al.* (94) El-Missiry MA *et al.* (95) Favero G *et al.* (96)
Care Delivery Models								
Shared medical appointments (SMA) focused on nutrition and lifestyle						✓	Improves functional status, COVID-related symptoms and global physical and mental health	Beidelschies M *et al.* (97) Patels S *et al.* (98)
Telemedicine	✓	✓	✓	✓	✓	✓		Der-Martirosian C *et al.* (99) Ohannessian R *et al.* (100) Narayanan S *et al.* (101)

*Additional references are available at:
The Functional Medicine Approach to COVID-19: Virus-Specific Nutraceutical and Botanical Agents | The Institute for Functional Medicine (ifm.org)
Boosting Immunity: Functional Medicine Tips on Prevention & Optimizing Immune Function During the COVID-19 (Coronavirus) Outbreak | The Institute for Functional Medicine (ifm.org)

[a]Strength of Evidence: Strong
[b]Strength of Evidence: Strong (for prevention); Conditional (for treatment)
[c]Strength of Evidence: Moderate (for sepsis treatment); Conditional (for prevention)
[d]Strength of Evidence: Limited
[e]Strength of Evidence: Limited (for prevention); Conditional (for treatment)
[f]Strength of Evidence: Conditional

This document was established during the time of this APEC Project – Integrative Medicine and COVID -19 Care between May 2022 – March 2023. The purpose of this file 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.

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