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PII: S1876-3820(20)30389-9

DOI: <https://doi.org/10.1016/j.eujim.2020.101116>

Reference: EUJIM 101116

To appear in: *European Journal of Integrative Medicine*

Received Date: 16 March 2020

Revised Date: 1 April 2020

Accepted Date: 1 April 2020

Please cite this article as: { doi: <https://doi.org/>

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## Highlights of Traditional Chinese Medicine Frontline Expert Advice in the China National Guideline for COVID-19

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**Word count:** 3,605

### ABSTARCT

**Introduction:** The World Health Organization has declared the coronavirus disease (COVID-19) as a pandemic on 11 March 2020, after the number of confirmed cases outside China increased 13-fold. As the epicentre of the initial outbreak, China has been updating the National COVID-19 Diagnostic and Treatment Guideline with up-to-date information about the disease. To facilitate the implementation of integrative Chinese–Western Medicine in COVID-19

management, Traditional Chinese medicine (TCM) has been recommended in recent editions of the national guideline.

**Methods:** The national guideline summarised the opinions and frontline experience of medical experts across the country to provide by far the best management for COVID-19. We extracted the case definition and clinical classifications of COVID-19 in China along with relevant TCM treatments cited in the seventh edition of the guideline, with an intend to disseminate practical information to TCM practitioners and researchers around the world.

**Results:** We presented the most recent case definition, clinical classifications, and relevant TCM treatments of COVID-19 in accordance to recommendations of the Chinese guideline. TCM treatments are stratified into two groups based on patients' disease status. Four types of Chinese patent medicines are recommended for suspected COVID-19 cases. Several herbal formulae are recommended for confirmed COVID-19 cases according to their clinical classification and TCM pattern diagnoses. Two herbal formulae are also recommended for rehabilitation of recovering cases.

**Conclusion:** To control the waves of COVID-19 outbreak, countries must ensure the adherence of their citizens to local public health measures. Medical professionals should diagnose and treat patients according to up-to-date guidelines. Future evaluation of the outcomes of implementing TCM recommendations will strengthen the evidence base for COVID-19 management for the sake of public health and the internationalisation of TCM.

**Keywords:** Chinese Herbal Medicines; COVID-19; Guideline; Traditional Chinese Medicine

## 1. BACKGROUND

The coronavirus disease (COVID-19) unfolded in Wuhan, China, in December 2019 <sup>(1)</sup>. Without effective control measures, the disease has spread across the globe with more than one hundred countries reported confirmed cases <sup>(2)</sup>. Having realised that the number of new confirmed cases outside China has increased 13-folds, the World Health Organization finally decided to characterise COVID-19 as a pandemic on 11 March 2020 and requested member states to scale up their emergency response mechanisms <sup>(2)</sup>.

Being the epicentre of the initial outbreak, China developed and has been constantly updating its National COVID-19 Diagnostic and Treatment Guideline with up-to-date information about the aetiology, epidemiology, pathology, clinical features, diagnosis, and treatments of the disease. With strong support from the Chinese government <sup>(3)</sup>, Traditional Chinese Medicine (TCM), as a core component of the national healthcare system, has also been recommended in recent editions of the national guideline for the treatment of COVID-19. A month after the implementation of the guideline, Chinese officials reported that the preliminary outcome of the integrative Chinese–Western Medicine treatment approach appeared to be promising <sup>(4)</sup>. To disseminate practical information to TCM practitioners and researchers around the world, we extracted and present the case definition and clinical classifications of COVID-19 in China along with relevant TCM treatments cited in the seventh edition of the National COVID-19 Diagnostic and Treatment Guideline released on 3 March 2020 <sup>(5)</sup>.

TCM treatments recommended in the Chinese national guideline are stratified into two groups based on patients' disease status (*suspected COVID-19 case* or *confirmed COVID-19 case*). Four types of Chinese patent medicines are recommended for suspected COVID-19 cases according to their clinical features, while different herbal formulae are recommended for confirmed COVID-19 cases according to their clinical classification (*mild, moderate, severe, or critical*) and TCM pattern diagnosis. Two herbal formulae are also recommended for rehabilitation of recovering cases.

In the Chinese guideline, healthcare professionals are encouraged to offer integrative Chinese–Western Medicine treatments for COVID-19 patients, regardless of their disease status and clinical classification, as soon as possible to achieve the best clinical outcome<sup>(5)</sup>. Those who would like to implement an integrative treatment approach may consult the conventional medicine section of the Chinese national guideline, which describe how the two types of the interventions maybe used in a coordinated manner<sup>(6)</sup>.

## 2. METHODS

We extracted the case definition and clinical classifications of COVID-19 in China along with relevant TCM treatments cited in the seventh edition of the guideline. The current translation is for educational and non-profit purposes. We have satisfied the conditions of fair use of open-source materials<sup>(7)</sup>. Since the guideline is an administrative document issued by The National Health Commission of the People's Republic of China, it is not necessary to obtain approval from Chinese officials according to the country's Copyright Law<sup>(8)</sup>.

## 3. RESULTS

### Case definition in China

#### *Suspected COVID-19 case*

To be classified as a suspected case in China, the patient should fulfil one of the following epidemiological risks criteria and two of the following clinical features:

- *Epidemiological risks criteria* – (1) travelled to or lived in Wuhan or other Chinese cities with confirmed cases in the last 14 days before symptom onset; (2) contacted with a confirmed case (tested positive for viral nucleic acid) in the last 14 days before symptom onset; (3) contacted with a person with fever or respiratory symptoms who travelled to or lived in Wuhan or other Chinese cities with confirmed cases in the last 14 days before symptom onset; or (4) cluster onset.
- *Clinical features* – (1) fever and/or respiratory symptoms; (2) radiological characteristics of COVID-19; or (3) normal or reduced total white blood cell count, or normal or reduced lymphocyte count in early-onset.

#### *Confirmed COVID-19 case*

To be classified as a confirmed case in China, the suspected case should fulfil one of the following pathological or serological criteria:

- (1) Test positive for SARS-CoV-2 nucleic acid in real-time rRT-PCR;
- (2) Viral genome sequencing reveals a high similarity to SARS-CoV-2; or
- (3) Test positive for serum SARS-CoV-2-specific IgM and IgG, serum SARS-CoV-2-specific IgG seroconversion, or a fourfold or greater rise in SARS-CoV-2-specific IgG titre between acute- and convalescent-phase sera.

### Clinical classifications in China

#### *Mild case*

- Mild clinical features without radiological characteristics of pneumonia.

*Moderate case*

- Fever and respiratory symptoms with radiological characteristics of pneumonia.

*Severe case*

- Fulfils one of the following: (1) tachypnoea with respiratory rate  $\geq 30$  breaths per minute; (2) resting peripheral capillary oxygen saturation  $\leq 93\%$ ; or (3) arterial oxygen partial pressure (PaO<sub>2</sub>) / fractional inspired oxygen (FiO<sub>2</sub>)  $\leq 300$ mmHg.

*Critical case*

- Fulfil one of the following: (1) respiratory failure and requires invasive mechanical ventilation; (2) shock; or (3) multiple organ failure and requires admission into intensive care unit.

**Traditional Chinese Medicine treatments***Suspected COVID-19 case*

*Clinical features 1* – Muscle fatigue accompanied with gastrointestinal discomfort

<sup>^</sup>\**Recommended Chinese patent medicine* –

- Huoxiang Zhengqi capsules
  - <sup>+</sup>Ingredients: Pogostemonis Herba, Glycyrrhizae Radix et Rhizoma Praeparata cum Melle, Atractylodis Macrocephalae Rhizoma, Pinelliae Rhizoma, Citri Reticulatae Pericarpium, Magnoliae Officinalis Cortex, Platycodonis Radix, Perillae Folium, Arecae Pericarpium, Poria, Angelicae Dahuricae Radix, Zingiberis Rhizoma Recens, and Jujubae Fructus

*Clinical features 2* – Muscle fatigue accompanied with fever

<sup>^</sup>\**Recommended Chinese patent medicines* –

- Jinhua Qinggan granules
  - <sup>+</sup>Ingredients: Lonicerae Japonicae Flos, Gypsum Fibrosum, Ephedrae Herba Praeparata cum Melle, Armeniaca Semen Amarum, Scutellariae Radix, Forsythiae Fructus, Fritillariae Thunbergii Bulbus, Anemarrhenae Rhizoma, Arctii Fructus, Artemisiae Annuae Herba, Menthae Haplocalycis Herba, and Glycyrrhizae Radix et Rhizoma
- Lianhua Qingwen capsules
  - <sup>+</sup>Ingredients: Forsythiae Fructus, Lonicerae Japonicae Flos, Ephedrae Herba Praeparata cum Melle, Armeniaca Semen Amarum, Gypsum Fibrosum, Isatidis Radix, Dryopteridis Crassirhizomatis Rhizoma, Houttuyniae Herba, Pogostemonis Herba, Rhei Radix et Rhizoma, Rhodiola Crenulatae Radix et Rhizoma, Menthae Haplocalycis Herba, and Glycyrrhizae Radix et Rhizoma.
- Shufeng Jiedu capsules
  - <sup>+</sup>Ingredients: Polygoni Cuspidati Rhizoma et Radix, Forsythiae Fructus, Isatidis Radix, Bupleuri Radix, Patriniae Herba, Verbenae Herba, Phragmitis Rhizoma, and Glycyrrhizae Radix et Rhizoma.

<sup>^</sup> *The recommended Chinese patent medicine should only be used under instruction of a qualified TCM clinician.*

<sup>\*</sup>*The recommended Chinese patent medicines are registered in China. If they are not available outside China, they may be offered to patients in the form of herbal decoction.*

<sup>+</sup>*No endangered animal species is included.*

*Confirmed COVID-19 case*

- Qingfei Paidu Decoction
  - *Application* – Based on the clinical observations made by clinicians across different regions, this is a basic Chinese herbal medicine formula applies to mild cases, moderate cases, and severe cases. It may also apply to critical cases, depending on the condition of individual patients. Where appropriate, medical professionals may choose to prescribe other formulae introduced in the subsequent sections of this article, based on the TCM diagnosis of patients.
  - <sup>+</sup>@*Basic formula* – Ephedrae Herba 9g, Glycyrrhizae Radix et Rhizoma Praeparata cum Melle 6g, Armeniacae Semen Amarum 9g, Gypsum Fibrosum 15–30g (decoct first), Cinnamomi Ramulus 9g, Alismatis Rhizoma 9g, Polyporus 9g, Atractylodis Macrocephalae Rhizoma 9g, Poria 15g, Bupleuri Radix 16g, Scutellariae Radix 6g, Pinelliae Rhizoma Praeparatum cum Zingibere et Alumine 9g, Zingiberis Rhizoma Recens 9g, Asteris Radix et Rhizoma 9g, Farfarae Flos 9g, Belamcandae Rhizoma 9g, Asari Radix et Rhizoma 6g, Dioscoreae Rhizoma 12g, Aurantii Fructus Immaturus 6g, Citri Reticulatae Pericarpium 6g, and Pogostemonis Herba 9g.
  - *Method of usage* – Decoct the above medicinals with water. One decoction per day in two doses. Consume one warm dose every morning and evening, 40 minutes after meals. Three decoctions per treatment course. When possible, consume a half bowl of rice soup after each dose. Patients with a dry tongue and fluid-humour depletion may consume one bowl of rice soup. Start another course when the patient has his or her symptoms improved but is not yet cured. The formula of the second course may be amended as appropriate when the patient has other conditions or comorbidities. Stop the medication when the patient presents with no symptoms.
- Treatment strategies for mild cases based on differential Chinese medicine diagnosis
  - (1) Cold-dampness obstructing the lung
    - *Clinical features* – Fever, muscle fatigue, muscle pain, coughing, expectoration of sputum, chest discomfort, shortness of breath, loss of appetite, nausea, vomiting, and ungratifying defecation. Pale tongue with teeth-marked, or pale red tongue. White, thick and curdy tongue fur, or white and slimy tongue fur. Soggy or slippery pulse.
    - <sup>+</sup>@*Recommended formula* – Ephedrae Herba 6g, Gypsum Fibrosum 15g, Armeniacae Semen Amarum 9g, Notopterygii Rhizoma et Radix 15g, Descurainiae Semen & Lepidii Semen 15g, Dryopteridis Crassirhizomatis Rhizoma 9g, #Pheretima (Earthworm; *not endangered*) 15g, Cynanchi Paniculati Radix et Rhizoma 15g, Pogostemonis Herba 15g, Eupatorii Herba 9g, Atractylodis Rhizoma 15g, Poria 45g, Atractylodis Macrocephalae Rhizoma 30g, Crataegi Fructus Tostum 9g, Hordei Fructus Germinatus Tostum 9g, Massa Medicata Fermentata Tostum 9g, Magnoliae Officinalis Cortex 15g, Arecae Semen Tostum 9g, Tsaoko Fructus Tostum 9g, and Zingiberis Rhizoma Recens 15g.
    - *Method of usage* – Decoct the above medicinals with 600ml of water. One decoction per day in three doses. Consume one dose every morning, noon, and evening, before meals.
  - (2) Dampness-heat in the lung
    - *Clinical features* – Mild fever or no fever, slight aversion to cold, muscle fatigue, heaviness in the head and body, muscle pain, dry coughing with small amounts of sputum, sore throat, dry mouth without a desire to drink, chest discomfort, absence of sweating or difficulty in sweating, loss of appetite, nausea, vomiting, and watery

- stool or ungratifying defecation. Pale red tongue. White, thick and slimy tongue fur, or yellow and thin tongue fur. Slippery and rapid pulse, or soggy pulse.
- <sup>+</sup>@*Recommended formula* – Arecae Semen 10g, Tsaoko Fructus 10g, Magnoliae Officinalis Cortex 10g, Anemarrhenae Rhizoma 10g, Scutellariae Radix 10g, Bupleuri Radix 10g, Paeoniae Radix Rubra 10g, Forsythiae Fructus 15g, Artemisiae Annuae Herba 10g (decoct later), Atractylodis Rhizoma 10g, Isatidis Folium 10g, and Glycyrrhizae Radix et Rhizoma 5g.
  - *Method of usage* – Decoct the above medicinals with 400ml of water. One decoction per day in two doses. Consume one decoction every morning and evening.
- Treatment strategies for moderate cases based on differential Chinese medicine diagnosis
    - (1) Dampness toxin obstructing the lung
      - *Clinical features* – Fever, coughing with small amounts of sputum or coughing with yellow sputum, chest discomfort, shortness of breath, abdominal distension, and constipation. Dark red and enlarged tongue. Yellow and slimy tongue fur, or yellow and dry tongue fur. Slippery and rapid pulse, or string-like and soggy pulse.
      - <sup>+</sup>@*Recommended formula* – Ephedrae Herba 6g, Armeniacae Semen Amarum 15g, Gypsum Fibrosum 30g, Coicis Semen 30g, Atractylodis Rhizoma 10g, Pogostemonis Herba 15g, Artemisiae Annuae Herba 12g, Polygoni Cuspidati Rhizoma et Radix 20g, Verbenae Herba 30g, Phragmitis Rhizoma 30g, Descurainiae Semen & Lepidii Semen 15g, Citri Grandis Exocarpium 15g, and Glycyrrhizae Radix et Rhizoma 10g.
      - *Method of usage* – Decoct the above medicinals with 400ml of water. One decoction per day in two doses. Consume one decoction every morning and evening.
    - (2) Cold-dampness obstructing the lung
      - *Clinical features* – Mild or no fever, feeling of feverishness, dry coughing with small amounts of sputum, fatigue, chest discomfort, stomach discomfort, nausea, and watery stool. Pale or pale red tongue. White tongue fur, or white and slimy tongue fur. Soggy pulse.
      - <sup>+</sup>@*Recommended formula* – Atractylodis Rhizoma 15g, Citri Reticulatae Pericarpium 10g, Magnoliae Officinalis Cortex 10g, Pogostemonis Herba 10g, Tsaoko Fructus 6g, Ephedrae Herba 6g, Notopterygii Rhizoma et Radix 10g, Zingiberis Rhizoma Recens 10g, and Arecae Semen 10g.
      - *Method of usage* – Decoct the above medicinals with 400ml of water. One decoction per day in two doses. Consume one decoction every morning and evening.
  - Treatment strategies for severe cases based on differential Chinese medicine diagnosis
    - (1) Epidemic toxin obstructing the lung
      - *Clinical features* – Fever, flushed face, coughing with small amounts of sticky yellow sputum or with blood, panting, shortness of breath, fatigue, dry mouth with bitter taste and sticky feeling in the mouth, loss of appetite, nausea, ungratifying defecation, reddish urine with reduced amount. Red tongue. Yellow and slimy tongue fur. Slippery and rapid pulse.
      - <sup>+</sup>@*Recommended formula (Huashi Baidu Decoction)* – Ephedrae Herba 6g, Armeniacae Semen Amarum 9g, Gypsum Fibrosum 15g, Glycyrrhizae Radix et Rhizoma 3g, Pogostemonis Herba 10g (decoct later), Magnoliae Officinalis Cortex 10g, Atractylodis Rhizoma 15g, Tsaoko Fructus 10g, Pinelliae Rhizoma Praeparatum 9g, Poria 15g, Rhei Radix et Rhizoma 5g (decoct later), Astragali



Radix 10g, Descurainiae Semen & Lepidii Semen 10g, and Paeoniae Radix Rubra 10g.

- *Method of usage* – Decoct the above medicinals with 100–200ml of water. One to two decoction(s) with two to four doses per day. Oral administration or feeding via nasogastric tube.

(2) Blazing of both qi and nutrient

- *Clinical features* – High fever, agitation, thirsty, panting, shortness of breath, delirium, loss of consciousness, blurred vision, purpura, hematemesis, nasal bleeding, and convulsion. Crimson tongue. Less or no tongue fur. Sunken and fine pulse, or floating, big and rapid pulse.
- <sup>+</sup>@*Recommended formula* – Gypsum Fibrosum 30–60g (decoct first), Anemarrhenae Rhizoma 30g, Rehmanniae Radix 30–60g, <sup>#</sup>Bubali Cornu (buffalo horn; *not endangered*) 30g (decoct first), Paeoniae Radix Rubra 30g, Scrophulariae Radix 30g, Forsythiae Fructus 15g, Moutan Cortex 15g, Coptidis Rhizoma 6g, Lophatheri Herba 12g, Descurainiae Semen & Lepidii Semen 15g, and Glycyrrhizae Radix et Rhizoma 6g.
- *Method of usage* – Decoct the above medicinals with 100–200ml of water. One to two decoction(s) with two to four doses per day. Oral administration or feeding via nasogastric tube.

- Treatment strategy for critical cases

(1) Internal block and external collapse

- *Clinical features* – Difficulty in breathing, panting after slight movement (may require invasive mechanical ventilation), convulsion, agitation, sweating, and cold extremities. Dark purple tongue. Thick and slimy tongue fur, or dry tongue fur. Floating and big pulse without root.
- <sup>+</sup>@*Recommended formula* – Ginseng Radix et Rhizoma 15g, Aconiti Lateralis Radix Praeparata 10g (decoct first), and Corni Fructus 15g, along with Suhexiang pills or Angong Niu Huang pills. May prescribe Rhei Radix et Rhizoma 5–10g to patients with invasive mechanical ventilation having abdominal distension or constipation. May prescribe Rhei Radix et Rhizoma 5–10g and Natrii Sulfas to 5–10g with sedatives and muscle relaxants when ventilator-patient dyssynchrony occurs.
- *Method of usage* – Depends on the condition of the patient, as well as consensus between Chinese and conventional medicine clinicians.

- Treatment strategies for patients in the recovery period based on differential Chinese medicine diagnosis

(1) Lung-spleen qi deficiency

- *Clinical features* – Shortness of breath, fatigue, loss of appetite, nausea, vomiting, stomach fullness, difficulty in defecation, and watery stool. Pale and enlarged tongue. White and slimy tongue fur.
- <sup>+</sup>@*Recommended formula* – Pinelliae Rhizoma Praeparatum 9g, Citri Reticulatae Pericarpium 10g, Codonopsis Radix 15g, Astragali Radix Praeparata cum Melle 30g, Atractylodis Macrocephalae Rhizoma Tostum 10g, Poria 15g, Pogostemonis Herba 10g, Amomi Fructus 6g (decoct after), and Glycyrrhizae Radix et Rhizoma 6g.
- *Method of usage* – Decoct the above medicinals with 400ml of water. One decoction per day in two doses. Consume one dose every morning and evening.

## (2) Dual deficiency of qi and yin

- *Clinical features* – Muscle fatigue, shortness of breath, dry mouth, thirsty, palpitation, profuse sweating, loss of appetite, mild or no fever, and dry coughing with small amounts of sputum. Dry tongue. Fine or vacuous pulse.
- <sup>+</sup><sup>@</sup>*Recommended formula* – Adenophorae Radix 10g, Glehniae Radix 10g, Ophiopogonis Radix 15g, Panacis Quinquefolii Radix 6g, Schisandrae Chinensis Fructus 6g, Gypsum Fibrosum 15g, Lophatheri Herba 10g, Mori Folium 10g, Phragmitis Rhizoma 15g, Salviae Miltiorrhizae Radix et Rhizoma 15g, and Glycyrrhizae Radix et Rhizoma 6g.
- *Method of usage* – Decoct the above medicinals with 400ml of water. One decoction per day in two doses. Consume one dose every morning and evening.

<sup>@</sup>*The name of herbal medicines are stated in accordance to the Pharmacopoeia of the People's Republic of China 2015* <sup>(9)</sup>.

<sup>+</sup>*No endangered animal species is included.*

<sup>#</sup>*These are animal products and may not be available outside China.*

#### 4. DISCUSSION

##### Rigorous evaluation of Traditional Chinese Medicine as an epidemic response

The integrative Chinese–Western Medicine treatment approach has been widely implemented in China. For instance, up to 67% of confirmed cases in Zhejiang province received TCM interventions, in conjunction to conventional treatment <sup>(10)</sup>. The Chinese official reported that this has yielded promising outcomes, with 23 confirmed cases in Wuhan discharged from hospital after receiving integrative medicine treatment <sup>(11)</sup>. Considering the urgency of treating an increasing number of patients in some countries and jurisdictions, TCM clinicians suggested that the practical application of Chinese herbal medicine should be given priority <sup>(12)</sup>. It seems to be impossible to conduct a rigorous evaluation of its efficacy and effectiveness in the midst of an epidemic.

Individuals sceptical of TCM posed a serious doubt to this suggestion, criticising that the Chinese government is battling against the COVID-19 with “politicalised pseudoscience” <sup>(13)</sup>. However, the Ebola experience demonstrated the feasibility of rigorously evaluating therapeutic measures during an epidemic <sup>(14)</sup>, and the evaluation of Chinese herbal medicine for COVID-19 is by no means an exception. Indeed, in the case of COVID-19 where experimental infection could not be used to facilitate the conduct of randomised trials, the current outbreak provides the only opportunity for evaluating the efficacy of Chinese herbal medicine. It is now the prime time to start randomised trials as the peak of the epidemic has passed in China <sup>(15)</sup>, and the healthcare system has more capacity to plan for evaluation. In fact, on 3 February 2020, the Ministry of Science and Technology has launched a clinical research programme on integrative medicine treatment for COVID-19, in which COVID-19 treatment centres in Hubei, Beijing, Tianjin, Hebei and Guangdong will participate <sup>(16)</sup>.

The launching of this programme represents an important step towards researching integrative treatment. However, divergent views on what constitute the most promising investigational TCM intervention seem to challenge the coordinated effort. Despite the prompt development of a national guideline, only four provinces, namely Shanxi, Anhui, Fujian and Qinghai, have adopted it, and Beijing, Tianjin and Xinjiang implemented its revised version <sup>(17)</sup>. Shanghai, Henan and Chongqing decided to develop their own Chinese herbal medicine treatment scheme

<sup>(17)</sup>. The National Administration of Traditional Chinese Medicine initiated another clinical research programme in Shanxi, Shaanxi, Hebei and Heilongjiang, investigating a single Chinese herbal formula intended for different stages of the disease <sup>(18)</sup>.

To seize the opportunity of conducting quality research, establishing a national coalition of stakeholders across these initiatives is urgently needed. A multi-disciplinary team would be the key to success; it should consist of members who have expertise in COVID-19, TCM, clinical research methodology, as well as ethics and regulations, and those who are patient representatives. Additional research investment in terms of resources and personnel will enable the immediate systematic collection of data on outcomes which could later be shared across centres in a coordinated manner. Such data are expected to provide an insight as to how TCM interventions impact prognosis. Besides, they will help identify which promising Chinese herbal medications should be prioritised for further assessment in randomised trials. Since Chinese herbal medicine has already been widely prescribed across the nation, an efficacy-driven approach could be adopted, focusing on phase II or III randomised trials.

In the midst of the epidemic, a trial design should be practical yet reliable, aiming to quickly generate interpretable efficacy and short-term safety results. A rigorous randomised trial conducted in a transparent manner would help in clearly determining the worthiness of the current national policy on the use of Chinese herbal medicine.

## **Conclusion**

The World Health Organization has characterised COVID-19 as a pandemic. Whenever possible, healthcare professionals may diagnose and treat patients with reference to the most recent guidelines on COVID-19. More importantly, the global community must endeavour to ensure the adherence of public health measures, such as the recommendations from Public Health England who have strongly encouraged their citizens to stay at home unless they have legitimate reasons, to stay two metres away from each other, and to wash hands frequently for 20 seconds using soap and water <sup>(19)</sup>. We hope that future evaluation of the outcomes of implementing TCM recommendations will strengthen the evidence base for COVID-19 management not only for the sake of public health but also for the promotion of TCM status in the world.

## **CRedit Author Statement**

**Leonard TF Ho:** Writing - Original Draft, Writing - Review & Editing, Methodology

**Karina KH Chan:** Writing - Original Draft

**Vincent CH Chung:** Methodology, Supervision, Writing - Review & Editing

**Ting Hung Leung:** Conceptualisation

### **Conflict of Interest**

A conflicting interest exists when professional judgement concerning a primary interest (such as patient's welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It may arise for the authors when they have financial interest that may influence their interpretation of their results or those of others. Examples of potential conflicts of interest include employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

## **Author Contributions**

*Leonard TF Ho* – Writing - Original Draft, Writing - Review & Editing, Methodology

*Karina KH Chan* – Writing - Original Draft

*Vincent CH Chung* – Methodology, Supervision, Writing - Review & Editing

*Ting Hung Leung* – Conceptualisation

### **Declaration of Competing Interest**

Dr Vincent CH Chung is a member of the editorial board for the European Journal of Integrative Medicine. The remaining authors declare that there are no conflicts of interest regarding the publication of this paper.

### **Financial support**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

### **Acknowledgements**

Dr Vincent CH Chung is a Visiting Associate Professor of the Bachelor of Science in Biomedical Sciences & Bachelor of Medicine (Chinese Medicine) Programme, School of Biological Science, Nanyang Technological University, Singapore at the time of writing this manuscript.

### **References**

1. World Health Organization. Coronavirus disease (COVID-19) outbreak Geneva: World Health Organization; 2020 [cited 2020 Mar 11]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.
2. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Geneva: World Health Organization; 2020.
3. National Administration of Traditional Chinese Medicine. The Party Group of the National Administration of Traditional Chinese Medicine conveyed the spirit of the key instructions of general secretary Xi Jinping and the request of Premier Li Keqiang to study the prevention and control of novel coronavirus pneumonia (*Chinese*). China: National Administration of Traditional Chinese Medicine; 2020 [cited 2020 Mar 11]. Available from: <http://bgs.satcm.gov.cn/gongzuodongtai/2020-01-21/12465.html>.
4. The State Council of the People's Republic of China. Traditional Chinese medicine used to treat 85% of COVID-19 patients. China: The State Council of the People's Republic of China; 2020 [cited 2020 Mar 11]. Available from: [http://english.www.gov.cn/news/videos/202002/26/content\\_WS5e55d0c8c6d0c201c2cbcf7b.html](http://english.www.gov.cn/news/videos/202002/26/content_WS5e55d0c8c6d0c201c2cbcf7b.html).
5. National Administration of Traditional Chinese Medicine. Notice on the promulgation of the National COVID-19 Diagnostic and Treatment Guideline (Provisional Version 7) (*Chinese*). China: National Administration of Traditional Chinese Medicine; 2020 [cited 2020 Mar 11]. Available from: <http://bgs.satcm.gov.cn/zhengcewenjian/2020-03-04/13594.html>.
6. Chinese Society of Cardiology. Chinese Clinical Guidance For COVID-19 Pneumonia Diagnosis and Treatment. China: Chinese Society of Cardiology; 2020 [cited 2020 Mar 24]. Available from: <http://kjfy.meetingchina.org/msite/news/show/cn/3337.html>.
7. United States Copyright Office. More Information on Fair Use. Washington, D.C.: United States Copyright Office; 2020 [cited 2020 Mar 31]. Available from: <https://www.copyright.gov/fair-use/more-info.html>.
8. National Copyright Administration of the People's Republic of China. Copyright Law of the People's Republic of China (*Chinese*). China: National Copyright Administration of

the People's Republic of China; 2020 [cited 2020 Mar 31]. Available from:

<http://www.ncac.gov.cn/chinacopyright/contents/479/17542.html>.

9. Chinese Pharmacopoeia Commission. The Pharmacopoeia of the People's Republic of China 2015. China: Chinese Pharmacopoeia Commission; 2015.

10. World Federation of Chinese Medicine Societies. Coverage Rate of TCM Treatment for Respiratory Illness Caused by the Novel Coronavirus Up to 67% in Zhejiang. China: World Federation of Chinese Medicine Societies; 2020 [cited 2020 Mar 26]. Available from: <http://en.wfcms.org/Englishpage/detatils.jsp?id=4136>.

11. National Administration of Traditional Chinese Medicine. Twenty-three COVID-19 infected patients in Wuhan are discharged from hospital after integrative Chinese–western medicine treatment (*Chinese*). China: National Administration of Traditional Chinese Medicine; 2020 [cited 2020 Mar 26]. Available from:

<http://www.satcm.gov.cn/hudongjiaoliu/guanfangweixin/2020-02-07/12872.html>.

12. China Business Journal. Guangdong Food and Drug Administration plans to include “Pneumonia No.1” into urgent examination, but experts say its applicability on mild cases needs to be discussed (*Chinese*). China: China Business Journal; 2020 [cited 2020 Mar 26]. Available from: [http://www.cb.com.cn/index/show/zj\\_m/cv/cv13476401260](http://www.cb.com.cn/index/show/zj_m/cv/cv13476401260).

13. Palmar J. Chinese Media Is Selling Snake Oil to Fight the Wuhan Virus. Washington, D.C.: Foreign Policy; 2020 [cited 2020 Feb 27]. Available from: <https://foreignpolicy.com/2020/02/03/tcm-shuanghuanglian-pseudoscience-chinese-media-is-selling-snake-oil-to-fight-the-wuhan-virus/>.

14. The PREVAIL II Writing Group for the Multi-National PREVAIL II Study Team. A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection. *N Engl J Med*. 2016;375(15):1448-56.

15. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *The Lancet*. 2020;395(10225):689-97.

16. World Federation of Chinese Medicine Societies. Clinical research on the prevention and treatment of new coronavirus with integrated Chinese and Western medicine officially launched. China: World Federation of Chinese Medicine Societies; 2020 [cited 2020 Mar 26]. Available from: <http://en.wfcms.org/Englishpage/detatils.jsp?id=4133>.

17. World Federation of Chinese Medicine Societies. Traditional Chinese Medicine Treatment for Pneumonia Caused by the Novel Coronavirus (2019-nCoV) Progressing Orderly. China: World Federation of Chinese Medicine Societies; 2020 [cited 2020 Mar 26]. Available from: <http://en.wfcms.org/wfcms/Englishpage/NoPicdetatils.jsp?id=4111>.

18. National Administration of Traditional Chinese Medicine. Progress in the search for potentially effective Chinese herbal medicine formula for COVID-19 (*Chinese*). China: National Administration of Traditional Chinese Medicine; 2020 [cited 2020 Mar 26]. Available from: <http://bgs.satcm.gov.cn/gongzuodongtai/2020-02-06/12866.html>.

19. The Government of the United Kingdom. Coronavirus (COVID-19): what you need to do. London: The Government of the United Kingdom; 2020 [cited 2020 Mar 24]. Available from: <https://www.gov.uk/coronavirus>.