


SEATTLE-based Research of Chinese Herbs for COVID-19 Study: A Whole Health Perspective on Chinese Herbal Medicine for Symptoms that may be Related to COVID-19

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Abstract

Introduction: East Asian Medicine (EAM) is a Whole System medicine that includes Chinese herbal medicine (CHM). Chinese herbal medicine has been utilized to reduce symptom burden in infectious disease, with notable theoretical reformulations during pandemics of the 3rd, 13th, and 17th centuries. Today, Licensed Acupuncturists trained in CHM have utilized it to treat symptoms and sequelae of COVID-19. However, little is known about its use or efficacy by the public and health practitioners. Understanding and evaluating whole medicine systems of healthcare is inherently complex; there is international consensus for a descriptive, pragmatic approach. We are conducting a feasibility pilot study using a prospective, pragmatic, observational design using Whole Health and Whole Person perspectives. The complexity of COVID-19 reflects the impact on multiple homeoregulatory systems and provides a unique opportunity to assess the impact of interventions such as EAM on whole health. Observation of these EAM encounters will provide valuable qualitative and quantitative data on the interface of an extant Whole System medicine with a novel complex illness as a precursor to a randomized clinical trial.

Methods: This ongoing study observes a CHM clinic offering telehealth consultations to a diverse patient population since April, 2020. Patients who report symptoms potentially related to COVID-19 disease are consented for standardized collection and analysis of demographic and clinical data from each clinical encounter.

Results: To date, 61 patients engaged in 195 consultations (mean 3.3) with 49 reporting symptom resolution sufficient to complete treatment, and 4 withdrawals. Just over half (62%) were female, with an average age of 45.7 years. A wide variety of CHM formulas and EAM dietary and lifestyle modifications were provided.

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Discussion: Adequate recruitment and retention suggest feasibility of the intervention and data collection. The rich dataset may facilitate the construction of Whole Health models of CHM's clinical impact, as well as integrative inquiry into CHM's effects on symptoms.

Keywords

Chinese herbal medicine, COVID-19, long haul COVID, post-acute COVID-19 Syndrome, pragmatic, telehealth, whole health

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Introduction

East Asian medicine (EAM) is a whole system of medicine that utilizes multiple therapeutic interventions (e.g., acupuncture, Chinese herbal medicine [CHM], individualized dietary and lifestyle self-care advice, gua sha, tui na, and moxibustion, exercise, among others). In the United States, EAM is practiced by Licensed Acupuncturists (LAc.), while the practice of CHM is restricted to those with specialized herbal medicine training.¹ East Asian medicine system therapies such as CHM and acupuncture are used to address a wide variety of symptoms, reflecting interrelated effects on neurological, endocrine, digestive, circulatory, muscular, and immune function; they are also used for wellness, health promotion, and disease prevention.²⁻⁶

Whole Systems Research⁷ is a phenomenological approach introduced early in the 21st century, diverging from the related concept of Complex Interventions Research.⁸ Whole Systems of medicine such as EAM, Ayurveda, European herbal medicine, and naturopathy may be studied as complex interventions within biomedical health care,⁹ but themselves apply a discrete body of knowledge and/or practice to the patient's goals of mental and physical health restoration, and do not necessarily require mediation by biomedical concepts. In studying whole systems, a pragmatic approach is indicated when evidence "further up the evidence pyramid" does not yet exist. In particular, a pragmatic design with dense measurement including the longitudinal collection of biopsychosocial data provides an opportunity to identify quantitative clinically important outcomes—that may occur in real-world treatment but be lost through protocolization for research.¹⁰

The EAM diagnosis and treatment of disease utilizes a whole systems health perspective by examining signs and symptoms across systems to culminate in a differential diagnosis encompassing the patient's overall presentation.¹¹ The CHM therapeutic intervention is characterized by the use of several herbal ingredients to comprise an herbal formula.¹² The individualized CHM formula generally comprises a guideline or core formula, indicated by the patient's presentation and resulting EAM differential diagnosis; the core formula may be modified by addition or subtraction of single herbs to address additional pathomechanisms or symptoms, or to prevent side effects.^{13,14} Core formula indications typically include a cluster of physical and psychoemotional symptoms along with

characteristic palpatory and observational findings including pulse speed and strength and tongue shape, color, and coating. Disease onset and course over time are also considered.¹³

For example, the CHM formula Xiao Chai Hu Tang (Minor Bupleurum Decoction) may be used with chronic or subacute symptoms such as a dry throat, bitter taste in the mouth, mild dizziness or vertigo, digestive upset, restlessness, and/or depressed mood. It is most characteristically administered during infectious disease with alternating fever and chills, or a prolonged or relapsing/remitting infectious disease course.¹⁵ Basic research on the formula has suggested antidepressive,¹⁶ hepatoprotective¹⁷ and anti-tumor¹⁸ effects, reduction of chemotherapy-induced diarrhea,¹⁹ and inhibition of multiple viruses including Hepatitis B and C,²⁰ rhinovirus, Epstein-Barr, and Influenza A.²¹ Chai Hu (Bupleurum), the formula's main ingredient, is widely used for antifebrile and immunomodulatory properties in Chinese poultry production.²² The formula's broad range of contemporary usage and apparent antiviral activity reflect both the promise and the challenge of translational research in CHM: it has been proposed as one of the formulas potentially useful for immunomodulation and symptom management in COVID-19 patients,²¹ but conventional research designs to date have not provided compelling evidence of its clinical efficacy in a biomedically defined population.²³

Chinese herbal medicine formulas such as Xiao Chai Hu Tang have been used to treat bacterial and viral infections for millennia.²⁴ Throughout human history, epidemics and plagues have swept through civilizations and affected every level of society with resulting shifts in political policies, scientific ideas, and group and personal religious beliefs.²⁵ Systems of medical knowledge, clinical, and practical, can grow during these times in response to the perturbation of a new epidemic context. In Chinese history, previous generations' medical theories and treatments were renegotiated and repurposed, even as completely new systems were developed.^{26,27} Famously, epidemics spawned three of the most influential and highly effective medical systems. These are the Shanghan Lun by Zhang Zhong-Jing in the 3–4th century CE, the Spleen-Stomach school of Li Dong-yuan in the 13th century, and the Warm Disease school led by Wu You-ke, Ye Tian-shi, and Wu Ju-tong of the 17th and 18th centuries, respectively.²⁶ Each of these physicians wrote treatises offering new styles of thought and new herbal remedies, while conserving elements

of existing systems and methods. These herbal traditions remain in use today, in clinics worldwide.

Prospective Whole Systems research on CHM in the United States faces considerable logistical challenges. When a natural substance is proposed for use as a drug in a clinical trial, an Investigational New Drug (IND) application is filed with the FDA. While the application²⁸ may not be onerous for a single compound in a conventional study, the number required for clinically appropriate individualized CHM treatment could be prohibitive if not carefully prepared. However, descriptive work, such as collecting information from patient charts, whether retrospective or prospective, can be conducted with oversight from an Institutional Review Board (IRB).

Our study team is conducting such a descriptive chart review of CHM treatment provided via telehealth for symptoms that may be related to COVID-19 via an EAM school located in the Pacific Northwest (Seattle Institute of EAM). Licensed acupuncturists with extensive experience writing individualized CHM prescriptions see patients via telehealth. Practitioners are able to use and modify any standard formula in Chinese medicine, as they would in regular clinical practice. Reliable tests for the Severe acute respiratory syndrome coronavirus 2 virus (SARS-CoV-2) were unavailable in this area early in the pandemic, and so we provided care to those whose symptoms resembled the Centers for Disease Control and Prevention (CDC) COVID-19 disease symptom list—which was changing weekly at the time—whether or not they had a positive test. We decided to collect observational, pragmatic data since an evidence basis for clinical impacts of CHM during pandemic viral outbreaks such as the novel coronavirus had not been established. Further, randomization to CHM plus usual care or usual care alone would be premature as foundational safety evidence is lacking, and thus unethical. It is for these reasons that the present study is pragmatic and observational in design. It is hoped that our work can inform the study design of future CHM efficacy research.

This study was designed specifically with Whole Health principles in mind.²⁹ The Whole Health model emphasizes a personalized and proactive approach to healthcare that

empowers people to engage in self-care to improve their physical, mental, and emotional health during the pandemic. Participants were given individualized lifestyle, dietary, and self-care advice. The study was also designed with a Whole Person³⁰ perspective, and biopsychosocial data were collected across multiple body systems. In keeping with recent messaging from National Center for Complementary and Integrative Health (NCCIH), a whole person health perspective keeps an entire person in view or in mind—not focused solely on separate organs or body systems. This Whole Person Health viewpoint encourages the consideration of biological, behavioral, social, and environmental levels of intervention with the goals of promoting health and resilience while preventing diseases.³⁰ The purpose of this paper is to provide an overview of the SEATTLE-based Research of Chinese Herbs for Symptoms Possibly Related to COVID-19 (SEARCH) study with particular emphasis on Whole Health design principles and to provide some preliminary Whole Person outcomes.

Methods

Study design and setting

This single-site prospective, observational, pragmatic study investigates online telehealth encounters administered through the community clinic of the Seattle Institute of East Asian Medicine (SIEAM). The study began during the early months of the coronavirus disease 2019 (COVID-19) pandemic in the Pacific Northwest region of the United States and is ongoing. All enrolled participants are observed and followed up at regular intervals during their treatment course (see Table 1). Study review and oversight are provided by SIEAM's IRB (approved 04-04-20). The study was subsequently approved as exempt from review, due to no more than minimal risk, by the IRB of the University of Utah (IRB 0013148). We submitted our protocol to the FDA as a precautionary measure. The study Research Electronic Data Capture (REDCap) is hosted by the University of Utah. The study was registered on May 8, 2020, in the [ClinicalTrials.gov](https://clinicaltrials.gov) registry (Identifier: NCT04380870).

Table 1. Study Timeline.

	Day 1	Day 2	Day 3	Day 4-6	Day 7	Day 8-13	Day 14	Day 90	Day 180	Day 365
Screening	X									
Initial consult	X									
Follow up consult		X	X	PRN		PRN				
Patient Check in					X		X			
Follow up questionnaires								X	X	X

Note. PRN = when necessary.

Participants

All eligible participants are outpatients under the care of a biomedical primary care provider (PCP) who have experienced one or more symptoms identified in the CDC COVID-19 guidelines available at the time of enrollment, and who have tested positive for SARS-CoV-2 or are suspected of having COVID-19 disease. Participants have been consented to and enrolled in this ongoing study since May 2020. We are conducting the study according to the principles expressed in the Declaration of Helsinki.³¹ Written informed consent was obtained from the participants after being informed of all aspects relevant to the participant's decision to participate. Individual participants remain anonymous during and after data collection.

Inclusion criteria were: Patients presenting for care to SIEAM's clinic who in the last 28 days have experienced 1 or more of the possible COVID-19 symptoms identified in the most current CDC guidelines; these changed over the course of the study but included: Fever or chills, non-productive cough, dyspnea, myalgia, fatigue, headache, nausea or vomiting, diarrhea, new loss of taste or smell, sore throat, congestion or runny nose, normal or decreased leukocyte counts, and pneumonia; patients not exhibiting these symptoms but at a high risk of exposure are also eligible; patients must be 18 or more years old, and under the care of a PCP.

Exclusion criteria are: use of anticoagulants, immunosuppressants, antiseizure medications, or antipsychotic medications; active cancer treatment; medications with potential interaction with herbal medicine; unable to engage in telehealth consultations for any reason; pregnant; breastfeeding; unable to communicate in English; have an open legal case about their health; and at the discretion of the practitioner or screener for reasons related to safety concerns for the individual.

Treatment

All CHM consultations are delivered online via telehealth by LAcS with extensive experience in CHM. Patients are followed through the natural course of their EAM consultation sessions and treatment. LAcS determine CHM formula recommendations, which generally consisted of a guideline core formula with addition or subtraction of single herbs, according to the patient's presentation and resulting EAM syndrome diagnosis. Chinese herbal medicine is dispensed in three possible forms including pills, loose herbs which are cooked and decocted into a tea, or granules that are added to hot water and consumed as a tea. Selection of herb form is made by the patient, with LAc advice, according to their needs and living circumstances. We dispense CHM from the school and employ no-contact herb pick up and/or delivery by mail to ensure participant safety.

Participants are enrolled at a first screening appointment to gather baseline information and check inclusion and exclusion criteria. The initial consult is then scheduled for the same or subsequent day. Telehealth visits last up to 30 minutes,

during which the LAc consults with the participant regarding their symptoms, inspects their tongue (surface and underneath), and determines the patient's EAM differential diagnosis and CHM formula recommendation, as well as consulting the patient on what form, and mode of delivery or pickup best suits their situation. In keeping with a Whole Health perspective of patient empowerment, individualized lifestyle advice was provided to each patient during the telehealth visit. Advice included suggestions of what to eat and avoid eating, type and duration of physical activity, how long to rest, and at what frequency to take their CHM and the dosage. Finally, before the CHM formula is filled, a simultaneous cross-reference of drug/herb interactions is conducted using the TRC Natural Medicines Database³² at each CHM consultation.

LAcS determine the frequency and interval of CHM consults according to each participant's presentation. Between consults, each participant is followed up by email or phone at a standardized 24 and 48 hours after each consult, and then at 3, 6, and 12 months after baseline (Table 1). Participants were encouraged to consult with their PCP as needed at their own discretion, while the protocol also allows for the participants with concerning symptoms to be referred back to their PCP or emergency care at LAc discretion.

Data collection and storage

Our study team met several times each week in February and March 2020 to come to a consensus on what data fields would be collected from the patient charts. We aimed to include data that would be informative for EAM practitioners, medical providers, nurse practitioners, and health professionals, as well as health scientists. The chosen fields include biological data (e.g., blood test results) and participants' psychological, cognitive, and social reports. We also collect signs and symptoms from a EAM point of view, and the clinician's self-reported diagnostic reasoning. Data from these chosen fields are entered into a REDCap database designed for this study. SIEAM graduate students were trained to cull the participant's charts for the necessary data and enter it into REDCap. In addition, students involved in the study meet regularly with SIEAM scientists overseeing data collection to discuss challenges and work out solutions.

Outcomes

Outcomes are categorized as quantitative and qualitative. Quantitative outcomes are the number of participants enrolled biweekly, exposure status, comorbidities, change in symptom severity, concurrent medications, frequency of CHM differential diagnosis, frequency of base formula used, adverse events, and patient acceptability. Qualitative outcomes are emergent themes from the analysis of clinical reasoning text. This paper reports intermediate data on key outcomes related to the Whole Health and Whole Person paradigm outcome

approach. Several forthcoming manuscripts will report on all quantitative and qualitative outcomes.

Investigational new drug applications (IND)

Concurrent with our work outlined above, we are gathering documentation to support a regulatory filing with the Food and Drug Administration (FDA). This documentation is a necessary next step to conducting future prospective controlled research in CHM, and we are following the successful model used by other researchers.³³ We first received from our expert herbalist collaborators at SIEAM a list of the 60 most necessary single herbs to reduce symptom burden associated with COVID-19; these single herbs are also the constituents of the main guideline formulas used. Next, we developed a

database to place herb information into the required categories: pharmacology, toxicology, interactions with biomedical drugs, and previous human research. With help from advanced pharmacy students, we searched HerbMed Pro, Natural Medicine, PubMed, Chinese Traditional Herb Database, and the textbooks *Chinese Herbal Medicine: Materia Medica*³⁴ and *Formulas & Strategies*.¹⁵ During the research, systematic reviews and meta-analysis resources were primarily considered. The primary targets included COVID-, viral infection-, and influenza-related articles as well.

Results

At the time of publication, we have consented 61 subjects and entered data from 57 of these into the REDCap database.

Table 2. Study Demographics.

Demographics	Details (n = 57)
Sex	Female = 35 (62%); Male = 22 (38%)
Age	Average = 45.73 years (Range 25–69)
Race	Caucasian = 33 Native American/Alaska Native = 1 Hispanic = 1 Black or African-American = 1 Unknown = 21
Ethnicity	Non-Hispanic = 30 Hispanic = 5 Not disclosed = 22
Treatments	Total = 195 Average = 3.31 per participant Range (1–9)
Long Hauler	N = 10

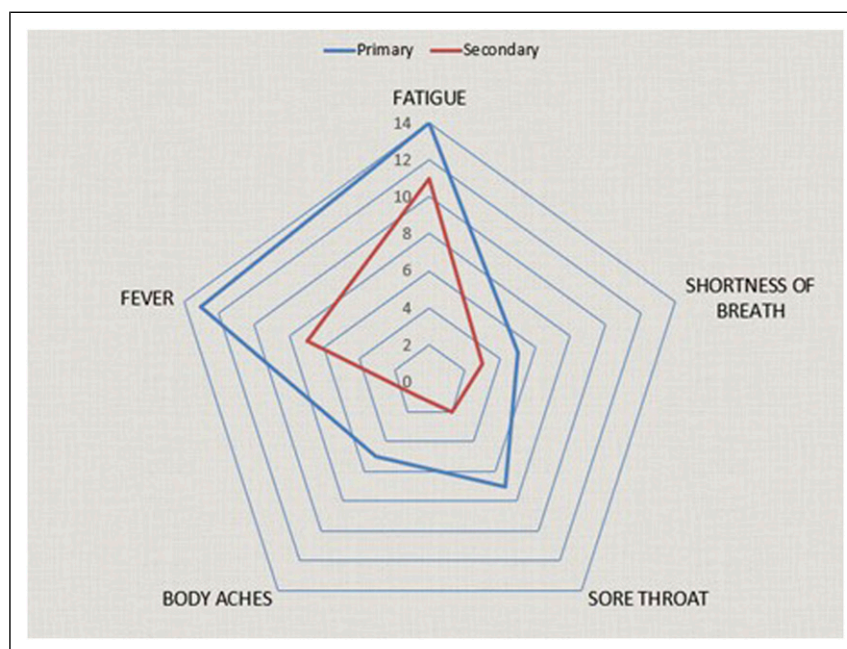


Figure 1. Primary and secondary complaints at baseline.

While our results are preliminary, they do support the feasibility of collecting whole health and whole person outcomes across multiple systems. To date, we have a predominantly female sample of an average age of 45.73 years (range 25–69 years). This sample is also predominantly Caucasian and non-Hispanic, and an average of 3 treatments per participant was received (range 1–9). Participants reported that the reason for the initial visit was prevention (1.6%), treatment (54.5%), or sequelae (43.9%). Please refer to [Table 2](#) for demographic data.

Baseline primary and secondary complaints

The most frequent primary and secondary complaints at baseline were fatigue (combined primary and secondary complaints: 25 of 61 participants), fever (20 of 61 participants), body aches (5 of 61 participants), sore throat (9 of 61 participants), and shortness of breath (8 of 61 participants). Please refer to [Figure 1](#).

Level of recovery

At the time of publication, 49 of 57 participants showed symptom reduction sufficient to conclude the intervention. Three participants are still in progress and are receiving CHM treatment. One participant reported an incomplete recovery and was referred for in-person acupuncture once it was safely available. One participant was lost to follow-up; one participant dropped out of the study due to a cancer diagnosis unrelated to the study; two participants discontinued treatment.

Whole health outcomes

Additional self-care recommendations were often offered by the practitioners. That these varied across the sample is evidence that practitioners are individualizing self-care to consider each participant, their presentation and stage of illness, and context. For example, some patients were advised to take it easy:

Suggests taking 2 weeks away from his meditation practice. Emphasizes the importance of taking a break to reset and note what effect the practice is having, particularly when reserves are depleted.

If possible, refrain from returning to work to give the body rest. Relapse of [symptoms] can happen with early exertion. The school will be writing a letter explaining [patient's] situation for her to bring to work, since she is not fit to return yet.

While others were encouraged to engage in moderate movement:

Advised walking around in a local park particularly on warm days regular and consistent exercise. 15 mins of bike riding or moving body, whatever works.

Suggestions also included getting more or better-quality sleep, dietary advice such as more regular meals and/or easy to digest foods, and use of tools such as an air purifier or neti pot.

Whole person health data collection

We successfully collected data across biopsychosocial domains. Please refer to [Table 3](#) for a list of variables.

Table 3. Whole person health variables.

Biological	
Bloodwork reported	COVID-19 test
Tongue assessment	Quality of tongue coat, tongue body, vasculature underneath the tongue
Physical history	Lung, heart, diabetes, digestion, headache, eye issues, eye pain, tinnitus, hearing loss, ear pressure, odd ear sensation, pain, nocturia, frequent daytime urination, stool, constipation, diarrhea, acid reflux, bloating, belching, stomach pain, hunger, abdominal distention, thirst, fall asleep easily, wake at night (and time), fall back asleep, enough sleep, feel refreshed in the morning, energy level
	If female: menstruating regularly, last menstrual period
COVID-19-specific	If exposed, date of exposure; doing anything to stay well; self-described COVID-19 symptoms; fever, chills, shaking, dizziness, paralysis, sweat, fatigue, sore throat, cough, shortness of breath, tight chest, ability to take a deep breath, arrhythmia, diarrhea, abdominal pain, nausea, taste, smell, skin issues
	Have you received a vaccine, which brand, how did you qualify, side effects from vaccine, if declined—thoughts about why you've chosen not to have the vaccine
Psychological	
	Anxiety, depression, perceived stress, overall are you feeling better, worse or about the same
Social/Behavioral	
	Social support and social network number
	Have you contacted your PCP; gone to the hospital
	I wear a mask when I am away from home, I socially distance, I limit the number of individuals that I am in the same room with

Feasibility

To date, we have been able to enroll participants (n = 61 at the time of publication), extract patient chart data, and populate REDCap (n = 57). We were able to populate 167 symptom and herbal formula and ingredient fields for Clinic Visits in REDCap and collect data across biological, physical, psychological, cognitive, and social domains.

Acceptability

Participants reported high adherence to taking the CHM as prescribed; we had 2 of 61 participants withdraw from the study. Positive feedback was provided to clinicians and the study coordinator. Students and faculty reported positive learning opportunities and experiences.

Safety

Serious adverse events (AEs) and minor AEs were tracked and documented. To date, no SAEs or AEs occurred. One person reported side effects of sweating (which is often a desired effect in the case of treating infectious diseases) and one person reported impaired sleep after one telehealth consult.

CHM Formulas dispensed

The guideline herbal formulas prescribed two or more times thus far are, listed in order of frequency: Xiao chai hu tang (Minor Bupleurum Decoction), Zhi sou san (Stop Coughing Powder), Gui zhi tang (Cinnamon Twig Decoction), Xiang fu xuan fu hua tang (Cyperus and Inula Decoction), Huo xiang zheng qi san (Patchouli/Agastache Powder to Rectify the Qi), Liu jun zi tang (Six Gentlemen Decoction), Wen dan tang (Warm Gallbladder Decoction), Sheng mai san (Generate the Pulse Powder), Ban xia hou pou tang (Pinellia and Magnolia Bark Decoction), Huo po xia ling tang (Patchouli/Agastache, Mangliolia Bark, Pinellia, and Poria Decoction), San ren tang (Three Nut Decoction), Hao qin qing dan tang (Sweet Wormwood and Scutellaria Decoction to Clear the Gallbladder), Er chen tang (Two Aged Decoction), Ban xia xie xin tang (Pinellia Decoction to Drain the Epigastrium), Bei mu gua lou san (Fritillaria and Trichosanthes Powder), Ma zi ren wan (Hemp Seed Pill), and Li zhong wan (Regulate the Middle Pill).

The form in which the herbs were dispensed was based on patient preference as well as clinician recommendations. Thus far in this study, the majority of CHM formulas were filled in granular form (roughly 75% of formulas), and loose herbs (roughly 25%), followed by pills (less than 1%).

IND Sub-study

As of this time we have completed collecting the necessary data fields for an FDA application for 60 individual herbs. We

are currently organizing the application for submission to the FDA.

Discussion

To date, most of our sample of predominantly female, midlife, Caucasian participants have shown clinical improvement in their symptoms sufficient to conclude treatment (49 of 57 participants). The most frequent baseline complaints were fever and fatigue. Whole Person health data were collected across biopsychosocial domains, while elements Whole Health treatment including individualized self-care and lifestyle advice were explored. The study has been feasible to conduct, as we delivered an intervention that utilized multiple ways in which herbs are dispensed: loose herbs, granules, and pills. The study maintained a truly pragmatic design and it has been feasible to retain a high percentage of participants. Participants were adherent to their CHM regimen and we observed a high level of compliance. Safety data were collected and no serious or minor AEs were reported; two participants reported side effects of the CHM. A variety of CHM formulas were dispensed, each customized based on the patient's symptom presentation as the CHM intervention was individualized. We have collected data on 60 individual herbs and will soon submit this information to the FDA requesting oversight for prospective work.

Most research in the medical and psychological fields to date has followed a "disease-focused" approach to health. Although there is growing research on the components and outcomes of well-being, very few studies have focused on traditional approaches and associated whole health practices that can be used as interventions to encourage optimal health.³⁵ In China, where CHM research and practice is routinely integrated with biomedical care, studies published to date addressing the current pandemic have also largely focused on addressing COVID-19 disease^{36,37} and the biological mechanisms underlying its most dangerous presentations.^{38,39} Feasibility of such research in the United States is necessarily constrained by multiple safety, regulatory, logistical, and cultural considerations appropriate to CHM's low level of integration with mainstream health care and paucity of Western clinical research. However, US practitioners do report use of CHM for prevention and to address acute and post-acute symptom burden in patients with suspected COVID-19.²⁷ This gap between research and extant practice constitutes both an opportunity and an imperative for prospective observational research that can ground emerging information, from basic and clinical research conducted in other countries, in the context of patients' lived experience. Insights gleaned from such practice-based research can benefit clinicians qualitatively while informing choice of intervention and quantitative outcome measures for future efficacy research.

One of the limitations of efficacy research on EAM has been the lack of well-defined biopsychosocial mechanisms. Using a Whole Health Model can address this deficit by encouraging the measurement of changes in well-being and linking those with psychosocial factors in a manner supported by Engel's biopsychosocial model⁴⁰ in which health science needs to: 1) account for both biochemical factors and expression of illness, 2) relate biomedical factors to both behavioral and psychosocial data as these are how most patients report clinical phenomena, 3) look at how psychosocial factors alter susceptibility and the course of an illness, 4) take into account psychosocial factors that determine when a patient defines themselves as a patient, and 5) address both biomedical healing as well as return to well-being. The Veterans Administration Whole Health²⁹ model underscores that the development of salutogenesis to be a partnership between the patient, their self-care, the community, and care team. The NCCIH current strategic plan⁴¹ also seeks to support research on the whole person and particularly achieving a better understanding of health promotion programs as they are studied in real-world settings, such as our SEARCH project.

A challenge of conducting Whole Person health-informed studies is collecting information at different levels and conducting analyses as biopsychosocial models are still being developed. Fortunately, EAM uses a Whole Person health model by the NCCIH definition, while also providing its own clinically supported mechanisms that we can test with rigorous science. That is, our SEARCH whole person-informed data can help build complex models using extant EAM theory on how the levels interact, theory that can guide analyses informed by EAM. In short, EAM is Whole Person Focused and complex, supporting the use of Complexity Science tools in analysis.^{42,43}

One strength of our design is how efficiently the data collection aspect fit into extant patient care processes at the school clinic. We did not interrupt the regular, individualized procedures of faculty practitioners at SIEAM, and this allows us to collect data that is inherently generalizable because it is naturalistic. While our resulting data set is complex, this study design has less risk of study artifact biases. We implemented a study process that provided the opportunity for the whole school—faculty, administration, and students—could participate. This allowed for new learning experiences as faculty and students had the opportunity to learn about the research process. Students gained direct experience of real-world, novel research on CHM, filling formulas, creative problem-solving, and data entry. We have learned lessons along the way. For example, students initially followed up with participants at 24 and 48 hours. We quickly realized that faculty had to do this instead because of the seriousness of COVID-19 disease. The 48-hour follow-up was most important; we employed a quicker re-evaluation than may have been done typically. Again, this was due to the seriousness and the quickly changing clinical presentation of COVID-19.

This study has several limitations. First, naturalistic design can allow for multiple types of bias. Selection bias

is a threat to validity as subjects self-select to join this study. Our uncontrolled investigation is also vulnerable to bias, including competing explanations for effects such as attention placebo. Second, our lack of ability to recruit led to slow enrollment and a small (but growing) sample. Third, the majority of participants in our study took CHM in either granule or loose forms. Prior research has demonstrated lower compliance with granules and loose herb forms and indicated that participants preferred pills or tinctures.⁴⁴ Future work is needed to evaluate further feasibility and acceptability of granule and loose herbs among larger samples of participants. Fourth, this study was designed to be a feasibility pilot study as a precursor to a randomized controlled trial. As such, conclusions about the effectiveness of CHM for treating COVID related symptoms are limited. We are currently in the process of obtaining IND approval for $n = 60$ herbs for a randomized controlled trial. Fifth, COVID tests were not available in the early part of the pandemic, particularly in the city in which this study was conducted, thus we could not require a positive COVID test as there were not tests to be had. Sixth, pulse assessment was not conducted during this telehealth study as clinicians could not come into direct contact with patients due to safety regarding the pandemic. The pulse is an important diagnostic tool used to determine the differential diagnosis and resulting CHM formula. However, our study reflects real-world circumstances that typify pandemic conditions where reliance of the other approaches to diagnosis become central to how treatments are undertaken.

Looking ahead, research employing Whole Health and Whole Person-informed studies are needed. Whole Health designs would include the provision of personalized and proactive healthcare that empowers participants to engage in self-care to improve their physical, mental, and emotional health. Participants would be given individualized lifestyle, dietary, and self-care advice. Whole Person-informed³⁰ research design would collect biopsychosocial data across multiple body systems and would consider the intervention as multicomponent (biological, behavioral, social, and environmental levels of an intervention). For example, large datasets including biopsychosocial variables and increased computing power enables nonlinear analyses of complex change over time. This would allow the conduct of analyses to determine which symptoms cluster together in an attractor—when there is “stuckness,”⁴⁵ as well as to determine when symptoms change and improve together. In order to build on the present pragmatic and observational study, future work is needed to rigorously test CHM efficacy in a randomized controlled trial.

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