

Chinese herbal medicine and COVID-19: quality evaluation of clinical guidelines and expert consensus and analysis of key recommendations

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Abstract

Objective: To systematically review the clinical practice guidelines (CPGs) for the treatment of patients with coronavirus disease 2019 (COVID-19) using Chinese herbal medicine (CHM), assess the methodological quality as well as clinical credibility and implementability of specific recommendations, and summarize key recommendations.

Methods: As of April 2022, we conducted a comprehensive search on major electronic databases, guideline websites, academic society websites, and government websites to assess the methodological quality and clinical applicability of the included CPGs using the Appraisal of Guidelines for Research and Evaluation (AGREE) II tool and Evaluation-Recommendations EXcellence (AGREE-REX) instructions, respectively.

Results: The search yielded 61 CPGs, which were mostly published in 2020; moreover, 98.4% of the CPGs were published in China. Only five CPGs achieved a high-quality AGREE II rating; further, six CPGs could be directly recommended, with most of the CPGs still showing much room for improvement. CPGs had a low overall score in the AGREE-REX evaluation, with the domains of clinical applicability, values and preferences, and implementability being standardized in $21.80\% \pm 12.56\%$, $16.00\% \pm 11.81\%$, and $31.33\% \pm 14.55\%$ of the CPGs, respectively. Five high-quality CPGs mentioned 56 Chinese herbal formulas. Half of the recommendations had moderate or strong evidence level in the GRADE evaluation. The most frequently recommended herbal medicines were Lianhua Qingwen granule/capsule and Jinhua Qinggan granule; however, the strength of recommendation for each prescription varied across CPGs and populations.

Conclusions: The overall quality of current CPGs for COVID-19 for CHM still needs to be improved; moreover, the strength of the evidence remains to be standardized across CPGs.

Keywords: AGREE II, AGREE-REX, Chinese herbal formulations, COVID-19, Guideline, Quality evaluation

Graphical abstract: <http://links.lww.com/AHM/A34>.

Introduction

Since the first case was identified in December 2019, the coronavirus disease 2019 (COVID-19) has spread worldwide at a highly alarming rate. Accordingly, it has presented a global health emergency and a severe threat to human life and health. The World Health Organization (WHO) declared COVID-19 a Public

Health Emergency of International Concern, its highest level of alert for global public health, and one of the 10 emergencies the world is facing^[1-2]. During the COVID-19 pandemic, the strain has undergone several derivations, including the Alpha (Variant: B.1.1.7), Beta (Variant: B.1.351), Gamma, Zeta (Variant: P.1, P.2), Delta (Variant: B.1.617.2), C.37. (Variant: B.1.617.2), Lambda (Variant: C.37), Omicron (Variant: B.1.1.529), and Deltacron combination virus^[3]. As of June 2022, approximately 540.9 million people worldwide have been diagnosed with COVID-19, with cases in more than 200 countries, regions, or territories^[4].

Traditional Chinese medicine (TCM) is a medical science with a long history of thousands of years in the prevention and treatment of infectious diseases. COVID-19 symptoms include fever, cough, and fatigue^[5], which belong to the TCM category of “plague”. Studies have demonstrated the significant efficacy of Chinese herbal medicines (CHMs), including Qingfei Paidu Decoction^[6], Lianhua Qingwen capsule^[7-8], Jinhua Qinggan granule^[9], and Xuanfei Baidu Decoction^[10], concerning symptomatic relief in patients with COVID-19. Since the release of the diagnosis and treatment plan for pneumonia caused by novel coronavirus infection (trial version 3) by the National Health Commission of China, CHM-related treatment protocols have been recommended^[11]. Additionally, numerous provinces, cities, and autonomous regions have issued numerous expert consensus

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statements based on clinical practice guidelines (CPGs) that recommend the use of CHM^[12-14]. Furthermore, WHO clearly affirmed the effectiveness and safety of TCM in treating patients with COVID-19 in their report “*WHO Expert Meeting on Evaluation of Traditional Chinese Medicine in the Treatment of COVID-19*”, which encouraged WHO member states to consider TCM for COVID-19 treatment within their healthcare systems and regulatory frameworks^[15].

CPGs provide a valuable resource for guiding clinical practice^[16]. Notably, previous assessments of CPG quality have reported considerable variability and irregularity in the development of CPGs^[17-18]. During the last 2 years, CHM-related guidelines and expert consensus have emerged with several updated versions. However, given the limited periodicity of COVID-19 in clinical practice, it is difficult to establish high-quality CPGs within a short period. Moreover, current guidelines and expert consensus statements were developed using different people and processes probably without an adequate evidence base, which may not accurately inform clinical practice.

A critical review of CPGs can be used to systematically assess and summarize the current state of guidance on a clinical topic^[16], which may improve COVID-19 guidelines on administering herbal medicines. There are several tools for assessing the methodological quality of CPGs. Appraisal of Guidelines for Research and Evaluation (AGREE) II is the most widely used quality assessment tool and is effective for clinical and laboratory guidelines^[19]. However, AGREE II still cannot fully assess the specific recommendations in CPGs. The AGREE-Recommendation EXcellence (AGREE-REX) tool was introduced in 2019 to assess clinical credibility, reliability, and implementability, which allowed a further comprehensive evaluation of CPGs^[20].

We performed a comprehensive review, evaluation, and summary of the guidelines for treating COVID-19 in CHM. Specifically, we aimed to systematically search CHM-related CPGs for COVID-19, evaluate the methodological quality and clinical applicability of the included CPGs, and summarize the critical recommendations of high-quality parts.

Materials and methods

Search strategy and guideline eligibility

We conducted a systematic literature review to obtain guidelines and expert consensus statements on COVID-19 treatment with CHM from inception to April 2022. We conducted searches on PubMed, Embase, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang database, China Science and Technology Journal Database, and China Biology Medicine disc using a combination of subject headings (MeSH/Emtree) and keywords. Further, we comprehensively searched the Canadian Medical Association CPG Infobase, Guidelines International Network, National Guideline Clearinghouse, National Institute for Health and Clinical Excellence, New Zealand Guidelines Group, Registered Nurses Association of Ontario, Scottish Intercollegiate Guidelines Network, Patient Safety Network, WHO,

Chinese Association of Integrative Medicine, and Chinese Association of Chinese Medicine. Additionally, we critically reviewed literature published by government agencies at all levels as well as TCM committees and related organizations. The search terms mainly included “COVID-19” “SARS-CoV-2” “2019 Novel Coronavirus*” “Medicine, Chinese Traditional” “patent medicine” “integrated traditional Chinese and Western medicine” “Guideline*” “consensus” “recommendation*”. Supplementary Tables S1 and S2, <http://links.lww.com/AHM/A27> show the detailed search strategy described above and a complete list of literature sources.

Eligibility criteria

We included CPGs (including standard guidelines, rapid advice guidelines, and adaptation guidelines) that met the definition provided by the Institute of Medicine^[21]. Moreover, expert consensus statements and related documents were considered. Included CPGs and expert consensus mentioned recommendations regarding the use of CHM in patients with COVID-19 and were published after December 2019. If the CPGs were updated, only the latest version was included. Language types were limited to English and Chinese.

We excluded the following documents: unavailable papers, duplicate guidelines, translated versions of guides or explanatory documents, commentaries, editorials, notes, or case reports.

Screening and data extraction

The retrieved literature was imported into the web-based systematic review software, “Rayyan” for screening analysis. Two reviewers (Zheng QY and Xiong L) first independently performed title and abstract screening, followed by further full-text screening based on the inclusion criteria.

Two reviewers (Zheng QY and Huang HY) used a standard data extraction form to extract information and data from the included CPGs, including title, publication year, country, target population, development institutions, length, funding source, and update status. The extracted data were cross-checked; additionally, any disagreements were resolved through discussion or by a third reviewer (Luo XF).

Quality assessment

All quality domain scores for the included CPGs were assessed using the AGREE II and AGREE-REX tools. Four and five investigators independently performed assessments using AGREE II and AGREE-REX, respectively. The reviewers held prior discussions to develop appropriate assessment criteria based on the corresponding manuals and training tools.

The methodological quality of the recommended program was assessed using the AGREE II tool^[22], which comprises 23 items in six theoretical domains: (I) Scope and Purpose (Clauses 1–3), (II) Stakeholder Involvement (Clauses 4–6), (III) Rigor of Development (Clauses 7–14), (IV) Clarity of Presentation (Clauses 15–17), (V) Applicability (Clauses 18–21), and (VI)

Editorial independence (Clauses 22–23). Each item in a single domain is rated on a seven-point Likert scale ranging from one (did not meet criteria) to seven (fully met criteria). Reviewers scored each clause based on the AGREE II Manual^[22] and justified each clause by recording the page number (or paragraph number) and the specifics of the supporting information in the comments field. Subsequently, clauses with a score discrepancy of > 2 points were discussed and the reviewers reevaluated the score (either by modifying or keeping the original score). An assessment score of 60% in each domain indicated better compliance with the criteria. Guideline/consensus statements were considered to be of “low quality” if they scored <60% in two or more domains of AGREE II and <50% in domain 3; “moderate quality” if they scored ≥60% in three or more domains, except for domain 3; and “high quality” if they scored ≥60% in at least half of the six domains, including domain 3. Subsequently, the four reviewers’ scores were finalized and a composite score was calculated as described below. Each domain score was derived from the total score of each item in the standardized domain as follows: (score obtained – lowest possible score)/(highest possible score – lowest possible score) × 100%. A recommendation for each guideline was provided based on the overall score^[23] as follows: not recommended, <30%; recommended with modifications, 30% to 60%; and recommended, >60%^[23].

As a complement to the AGREE II tool, AGREE-REX comprises three theoretical domains: (I) clinical applicability (Clauses 1–3), (II) values and preferences (Clauses 4–7), and (III) implementability (Clauses 8–9). Consistent with AGREE II, all clauses were assessed

using a seven-point Likert scale (1 and 7 indicating low- and high-quality, respectively)^[20].

Statistical analysis

The total scores for each domain were expressed as a percentage of the maximum possible score for that domain. Therefore, the range of possible scores was 0 to 100%, which represented the worst and best possible ratings for each domain, respectively. Descriptive analyses were performed using estimators of central tendency and dispersion, including mean and standard deviation or median and interquartile ranges. We evaluated the inter-rater reliability of the two tools using an intraclass correlation coefficient (ICC) (two-way random mixed model). The ICC can measure the consistency of evaluation results across different raters^[24] and is classified as follows: ICC ≤ 0.4 (very poor); ICC ≥ 0.75 (excellent); 0.4 < ICC < 0.75 (moderate).

Results

Guideline identification and characteristics of included guidelines

Our search yielded 2,188 records. After the titles and abstracts were screened and duplicates were removed, 110 records were included in the full-text review. Among them, we excluded 12 old versions, 15 guideline interpretation documents, two repeated versions in different languages, 19 articles that were not guidelines or expert consensus, and one article that did not specifically mention herbal treatment options. Finally, we included 61 eligible CPGs in the quality evaluation (Figure 1).

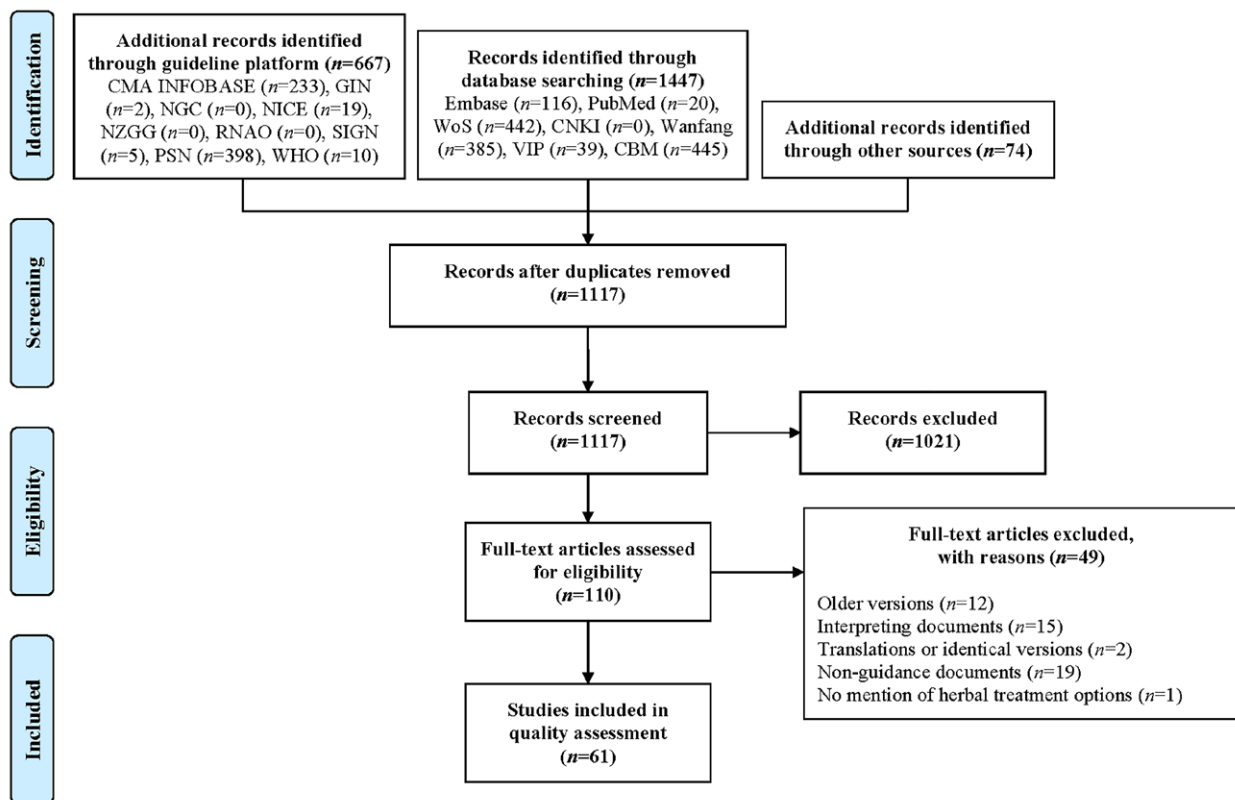


Figure 1. Literature screening flowchart.

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Supplementary Table S3, <http://links.lww.com/AHM/A27> shows a general overview of the basic information of the included CPGs. There were 44, 5 and 12 guidelines and expert consensus statements published in 2020, 2021, and 2022 respectively. Almost all included CPGs were published in China (98.4%), with only one guideline being published in South Korea^[25]. Most CPGs were reported by multi-institutional and inter-organizational collaborations; further, they targeted the general public; susceptible populations; suspected COVID-19 cases; and asymptomatic, confirmed, and post-hospital recovery patients. Most CPGs were published in journals; further, 25 CPGs were only published on the official websites of various levels of government or health commissions. Twelve CPGs indicated receiving financial support; however, most CPGs (78.7%) did not report on financial sponsorship. Additionally, 31 CPGs were updated versions of previous guidelines or expert consensus statements, while the rest lacked updated versions.

Consistency of evaluation results

The four researchers agreed well on the quality evaluation of the CPGs based on AGREE II. Except for one CPG with moderate agreement (ICC = 0.73, 95% CI 0.55–0.86), the other CPGs were assessed with the excellent agreement (ICC ≥ 0.80). The five investigators evaluated the CPGs' based on the AGREE-REX tool with good agreement. A few CPGs (23%) showed moderate agreement, while the remaining showed excellent consistency. Supplementary Table S4, <http://links.lww.com/AHM/A27> shows the assessment stability results for all CPGs.

AGREE II

The average standardization percentages of the 61 CPGs in the six domains were as follows: Scope and Purpose (66.4%), Stakeholder Involvement (30.4%), Rigor of Development (16.1%), Clarity of Presentation (77.4%), Applicability (25.0%), and Editorial independence (14.0%), with an overall moderate-to-low score. Based on our criteria, there were only five high-quality CPGs^[26–30], nine moderate-quality CPGs^[25,31–38], and 47 low-quality CPGs^[12–14,39–82]. Regarding the recommendation level, six CPGs were directly recommended, 50 were recommended after modification, and five could not be sufficiently recommended. Supplementary Table S5, <http://links.lww.com/AHM/A27> and Figure 2 show the evaluation results of each CPG.

Scope and purpose

This domain is related to the primary purpose and target population of the CPGs. The scores for this domain ranged from 27.8% to 100%. There were 37 guidelines or recommendations (60.7%) with a score >60%, which succinctly stated the health content and expected outcomes; moreover, they clearly stated the scope of application for the target population or provided the definition and diagnosis of the disease in the CPGs. The evidence-based guideline^[29] produced by the School of Public Health of Lanzhou University had the highest

score in this domain (100%), while the COVID-19 prevention and treatment protocol issued by the Health Commission of Inner Mongolia Autonomous Region^[57] showed the lowest score (27.8%).

Stakeholder involvement

This domain is related to the extent to which CPGs are developed to meet the user practice environment and whether they adequately account for the perspectives of their target users. The scores for this domain ranged from 0% to 88.9%. Only 12 CPGs (19.7%) had a score >60% and they generally did not consider requirements related to this domain well. The guideline on treating severe COVID-19 with integrated traditional Chinese and Western medicine published by the Zhejiang University of Traditional Chinese Medicine^[28] received the highest

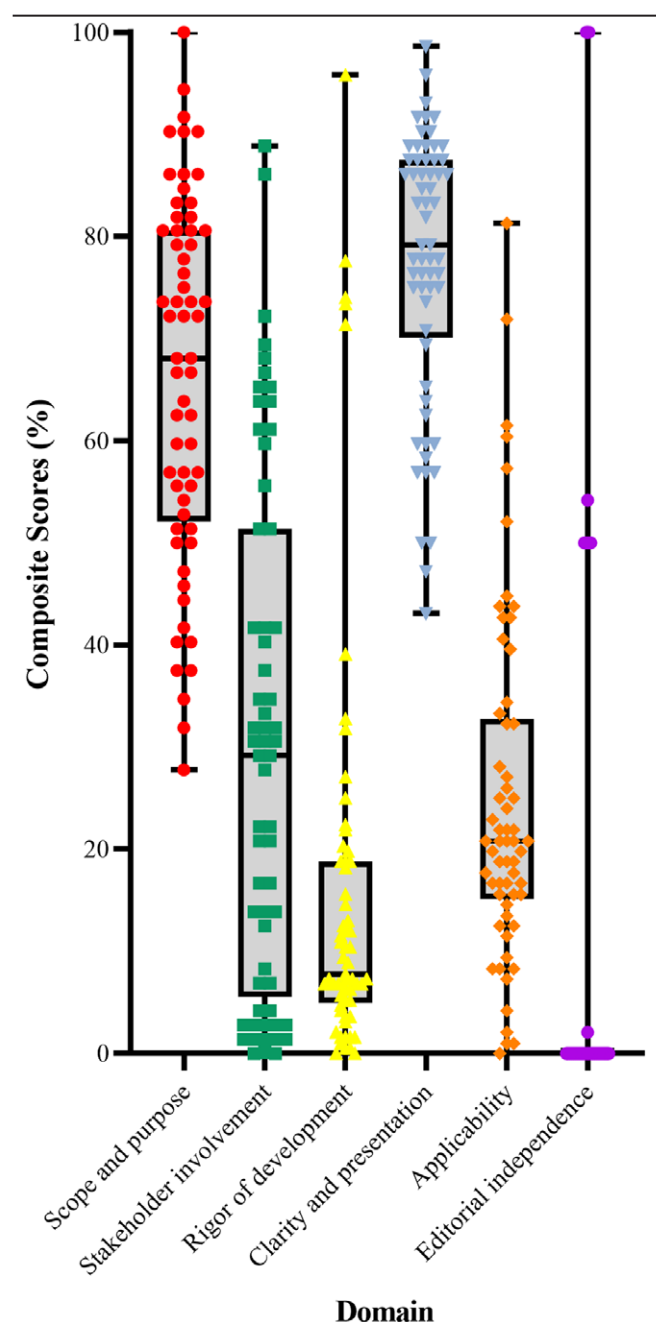


Figure 2. Box plots: AGREE II standardized domain scores.

score (88.9%). Contrastingly, the prevention and treatment protocols issued by the Health Commissions of Gansu^[80] and Inner Mongolia Autonomous Regions^[57] had the lowest scores (0%).

Rigor of development

This domain focuses on the methodology of guideline development. The scores for this domain ranged from 0% to 95.8%. Only five CPGs (8.2%) had scores >60%, with most of them lacking systematic searches, lacking details regarding their external reviews and updates, and failing to sufficiently consider the potential side effects and associated risks of the recommended protocols. The evidence-based guideline by the School of Public Health of Lanzhou University^[29] had the highest score (95.8%) while the prevention and treatment protocols issued by the Gansu^[80] and Heilongjiang Health Commission^[75] had the lowest score (0%).

Clarity and presentation

This domain focuses on the presentation and clarity of the CPGs. The scores for this domain ranged from 43.1% to 98.6%. Fifty CPGs had scores >60%. The evidence-based guideline by the School of Public Health of Lanzhou University^[29] received the highest score (98.6%), while the prevention and treatment protocol issued by the Health Commission of Xinjiang Uygur Autonomous Region^[69] had the lowest score (43.1%).

Applicability

This domain addresses the consideration of CPGs with respect to the applicability of the recommendations. The scores for this domain ranged from 0% to 81.3%. Only four CPGs had scores >60%. The evidence-based guidelines by the School of Public Health of Lanzhou University^[29] had the highest score (81.3%), while the prevention and treatment protocols issued by the Inner Mongolia Autonomous Region Health Commission^[57] did not take this aspect into account. Generally, the guidelines and expert consensus statements were not well considered with respect to impediments to guideline implementation, resource consumption, and audit criteria.

Editorial independence

The domain focuses on potential conflicts of interest for funders and experts. The scores for this domain

ranged from 0% to 81.3%. Only four CPGs had scores >60% and they entirely interpreted the content of this domain. In contrast, most CPGs provided by the regional Health Commission barely asserted the conflict of interest between the sponsoring organization and guideline development group.

AGREE-REX

The percentages of 61 CPGs standardized in the three domains were as follows: (1) 21.8% ± 12.6% (Clinical applicability), (2) 16.0% ± 11.8% (Values and preferences), and (3) 31.3% ± 14.6% (Implementability), with generally moderate-to-low scores. Figure 3 shows the specific domain scores and distribution.

Clinical applicability

This domain involves whether the CPG development is evidence-based and the extent to which the recommendations apply to the target users. The scores for this domain ranged from 2.0% to 81.0%. The evidence-based guideline by the School of Public Health of Lanzhou University^[29] showed the highest score (81.0%), with most CPGs showing significant flaws in this domain.

Values and preferences

This domain focuses on whether the preferences of intended users, patients, policy/policymakers, and guideline developers were considered in guideline development. The scores for this domain ranged from 0.0% to 68.0%. The evidence-based guideline by the School of Public Health of Lanzhou University^[29] showed the highest score (68%). Most CPGs did not consider the values and preferences of the target population. Moreover, they did not provide a specific description of the consensus formation process by the guideline developers.

Implementability

This domain involves the implementability of recommendations for patients and healthcare systems. The scores for this domain ranged from 0.0% to 82.0%. The evidence-based guideline by the School of Public Health of Lanzhou University^[29] had the highest score (82%). Most TCM recommendations did not consider the specificity of the elaborated regional application as well as the possible resource and cost issues in implementation.

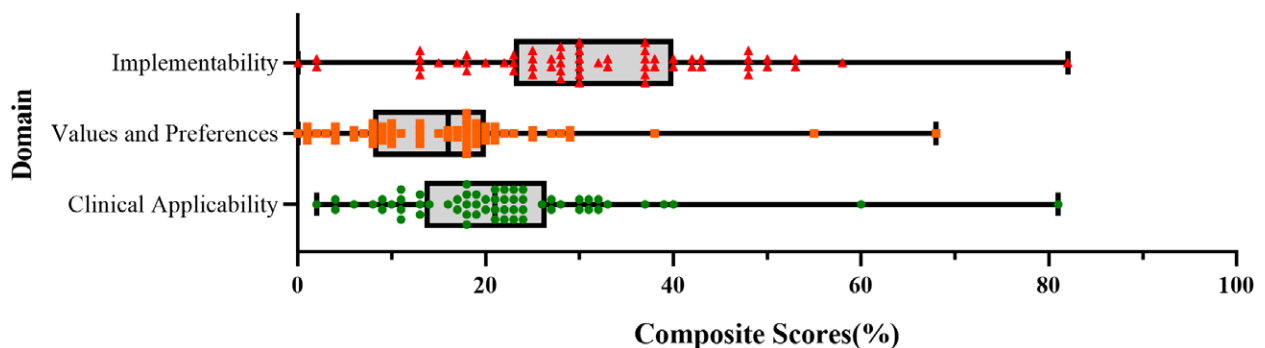


Figure 3. Box plots: AGREE-REX standardized domain scores.

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Summary of key suggestions in the recommendation CPGs

Supplementary Table S6, <http://links.lww.com/AHM/A27> summarizes the key recommendations of the five high-quality CPGs on herbal prescriptions for COVID-19 treatment. Among them, three and two CPGs were published in 2020 and 2021, respectively. The mentioned 56 herbal remedies in the recommendations, with about half of the recommendations receiving a moderate or higher evidence level and a strong recommendation in the GRADE evaluation. The recommendations of some CPGs were differentiated according to population age groups. Among them, Lianhua Qingwen granule/capsule received the most recommendations and was mentioned in eight CPGs. It is widely used to treat patients with mild and moderately severe COVID-19, including during nutritional support, symptomatic treatment, and antiviral/antibacterial treatment. Further, it is effective for symptoms, including fever or high fever, chills, muscle aches, nasal congestion and runny nose, cough, headache, dry sore throat, red tongue, and yellow or greasy moss. Jinhua Qinggan granule was recommended in seven CPGs. Additionally, it is widely used for all patients with COVID-19, especially for rehabilitating patients with fever, fatigue, cough, and severe illness. Qingfei Paidu Formulas were mentioned in six CPGs for use alone or in combination therapies to treat all patients with COVID-19. Xuanfei Baidu Formulas, Huashi Baidu Formulas, and Xuebijing injection have been widely recommended and applied. However, the recommendations for similar prescriptions varied across different CPGs and populations; moreover, many recommendations involved a combination with Western medicine.

Discussion

The rapid global spread of COVID-19 has affected social life and development. Since the end of 2019, there have been clinical studies on COVID-19; further, CPGs recommendations for appropriate treatment and rehabilitation have been issued. Consistent with the diagnosis and treatment guidelines of COVID-19 in China, TCM programs have been applied for the prevention, diagnosis, treatment, prognosis, and rehabilitation of all patients with COVID-19. Specific curative effects have been reported; additionally, CPGs have mentioned CHM treatment programs.

We systematically evaluated the methodological and reporting quality of 61 CPGs for COVID-19 treatment with CHM and analyzed the main recommendations. Most CPGs showed low methodological quality, with only five CPGs being rated as high quality using AGREE II and most CPGs (77.01%) were rated as low quality. Further, most CPGs could not receive a direct recommendation based on the ratings. Specifically, the included CPGs did not report the three AGREE-REX dimensions in a systematic and standardized manner. The main recommended CHM formulas were Lianhua Qingwen granule/capsule, Jinhua Qinggan granule, Qingfei Paidu decoction, Xuanfei Baidu decoction, Huashi Baidu decoction, and Xuebijing injection.

Most (60) CPGs were published in China with one being published in South Korea; further, most CPGs

were published in 2020, with relatively few being published in 2021 and 2022. Many research programs were conducted by Health Commissions of various provinces and cities, which often referred to the national overall diagnosis and treatment plan and formulate local-specific opinions according to local characteristics. In China, the large-scale epidemic mainly prevailed in 2020, with subsequent epidemic prevention and control measures mainly targeting the prevention of imported cases from abroad. Subsequently, the epidemic spread in China has scattered across multiple regions with intermittent and sudden spreads, which may influence the motivation of updating COVID-19 prevention and control programs in different regions.

In our study, the average scores of the six domains were 66.40%, 30.40%, 16.14%, 77.41%, 24.95%, and 14.0% for scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence, respectively. Compared with Li's report in 2020^[11], an improvement in the overall quality level of CPGs was observed. However, there remains room for improvement. Overall, most CPGs had low methodological and reporting quality. Specifically, there were low overall scores for domain 3 (Rigor of development), domain 5 (Applicability), and domain 6 (Editorial independence). Most prevention and treatment guidelines were developed without an evidence-based approach, so human experience should be incorporated into the use of specific prescriptions; further, most protocols did not report the potential side effects and risks related to the use of TCM formulas alone or in combination with Western and Chinese medicine. Other recommendations did not provide supporting evidence for specific recommendations. Since some governments undertook the total cost of patients with COVID-19, many CPGs did not consider cost-effectiveness, which may impede their dissemination and application.

The production process of Chinese medicine guidelines and expert consensus statements should be more rigorous and standardized. Before developing guidelines and expert consensus, target user groups and application targets should be clarified, which was not done in many CPGs. Only three CPGs^[27–28,38] mentioned that the views and choices of the target population were considered in the designation process, which was an essential aspect of CPG production. Moreover, the included CPGs relatively failed to describe the possibility and steps of the recommendation formation, external review scheme, and future updates. As appropriate, CPGs should disclose potential conflicts of interest of panel members and the impact of sponsorship. Future CHM-related CPGs regarding COVID-19 treatment should include more methodological experts among the panel members to improve the design and overall quality. Combined Western and Chinese medicine protocols have demonstrated significant efficacy in treating patients with COVID-19 and should be recommended more often in CPGs. There were no studies on the quality of reporting on CHM-related CPGs for treating COVID-19 based on the AGREE-REX tool. CPGs on herbal recommendations generally have low quality. Currently, the evidence composition of CHM recommendations

is relatively limited; moreover, the relevant supporting evidence in CPGs has been inadequately described, which impeded the provision of high-quality recommendations. Nonetheless, CPGs can often provide recommendations regarding targeted CHM prescriptions for people at different infection stages. Consistent with the AGREE II results, the included CPGs showed low scores with respect to whether patient/population values and preferences were considered. Most CPGs were based on regional adaptations and did not sufficiently address their promotion and dissemination considerations as well as the resources and costs related to the implementation of recommendations. Our findings could inform the development of future CPGs and subsequent updates to current CPGs.

Most provinces, cities, and autonomous prefectures referred to national guidelines with respect to local characteristics when developing local prevention and treatment protocols. However, their production process overlooked numerous details, including the description of all relevant professionals involved in CPG development, which relatively affected the standardization and authority of the CPGs. Generally, the rating and report quality level of the CPGs and expert consensus statements were relatively low; accordingly, the standardization degree should be improved. Most expert consensus statements did not elaborate on the process of consensus formation and did not provide sufficient supporting evidence for the production process. Overall, CPGs and expert consensus statements had a relatively weak evidence base for specific TCM recommendations since they mostly relied on randomized clinical trials, with some not even citing relevant evidence. After the identified high-quality recommendations were integrated, the mainly recommended formulas were Lianhua Qingwen granule/capsule, Jinhua Qinggan granule, and Qingfei Paidu decoction. However, the strengths of recommendation for the same prescription varied across the CPGs. This could be attributed to differences in the target populations and application scenarios as well as differences in judgments regarding the same situation among expert groups. High-quality recommendations were often based on evidence from studies with high evidence levels, which was missing for several CPGs.

We must realize that in the early stages of a raging epidemic, expert consensus-based recommendations were already the highest level of available evidence. During emergencies, many guidance documents may not be produced according to the normative process of guidelines. Today, the situation has improved, and many guidelines and expert consensus should be conducted based on a standardized format to increase rigour. High-quality original studies are warranted to inform future high-quality CPGs and allow more uniform recommendations. Additionally, given the unique cultural background of TCM, the description of the disease signs relatively differed from mainstream descriptions, which may limit the widespread recognition and promotion of TCM. Although WHO has recognized the effectiveness of CHM in treating COVID-19, it has been insufficiently studied in other countries and ethnic groups.

Accordingly, there remains a long way with respect to the worldwide promotion of CHM.

Limitations

This study has several limitations. First, we only included CPGs published in Chinese and English. Although most CHM studies were published in these languages, there remains the potential for language bias. Second, there were challenges in contacting the relevant institutions to validate issues regarding the lack of description of issues related to the AGREE II domains. Admittedly, the CPG development process is often more rigorous than the description may indicate. Further, assessing the quality of CPG development and reporting using the AGREE II and AGREE-REX tools is subjective. It may not fully apply to the assessment of expert consensus or therapeutic schedule. Finally, although multiple researchers independently assessed the included CPGs and used ICC scores to check their consistency and reliability, potential biases may have remained.

Conclusions

The overall quality of TCM formulas for COVID-19 related CPGs was low, with inadequate consideration of key stakeholders' involvement, rigour of formulation, resource investment, and regional applicability. The recommended regimens were broadly similar across CPGs, yet the strength of evidence for recommendations varied significantly, and there is still a long way to go before TCM goes worldwide.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

Qingyong Zheng and Xiaofeng Luo conceived the manuscript idea. Qingyong Zheng and Ya Gao drafted the manuscript. Qingyong Zheng, Lu Xiong, Hengyi Huang, and Xiaofeng Luo filtered the articles and performed data extraction. Qingyong Zheng, Guoyuan OuYang, Junfen Li, and Wulayin-Saimire evaluated CPGs based on the AGREE II tool. Qingyong Zheng, Hengyi Huang, Jingjing Yang, Yu Zhang, and Xiaopeng Wang evaluated CPGs based on the AGREE-REX tool. Qingyong Zheng analyzed the data and completed the graphs. Xiaofeng Luo provided a critical version of the manuscript. All authors contributed to the revision of the manuscript and approved the final manuscript.

Ethical approval of studies and informed consent

Not applicable.

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