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Original Article

Methodological proposals for developing trustworthy recommendations of integrative Chinese-Western medicine



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ABSTRACT

Background: To refine the methods of developing clinical practice guidelines (CPGs) for integrative Chinese-Western medicine (ICWM), promoting the formation of trustworthy, implementable recommendations that integrate the strengths of Chinese and Western medicine.

Methods: Using a nominal group technique (NGT) approach, a multidisciplinary expert panel was established. The panel identified key methodological issues in ICWM-CPG development through literature review and iterative discussions, and formulated methodological proposals to address these issues. The final set of proposals was achieved through consensus among the panel members.

Results: The collaborative effort resulted in the identification of five pivotal methodological issues and the subsequent establishment of 22 specific recommendations. These encompass strict adherence to renowned standards, such as those proposed by the Institute of Medicine (IOM) and Guidelines International Network (G-I-N), the employment of methodologies like the GRADE approach and RIGHT statement, the strategic constitution of a balanced development group, the adept identification of ICWM-focused clinical inquiries, the nuanced integration of diverse evidence sources, and the detailed crafting of transparent, implementable recommendations.

Conclusions: This study concentrates on the most crucial and prevalent methodological issues in ICWM-CPG development, proposing a series of recommendations. These suggestions result from a multidisciplinary expert consensus, aiming to provide methodological guidance for ICWM-CPG developers, building upon the current foundational methodologies.

1. Introduction

Integrative Chinese-Western Medicine (ICWM) is an evidence-based medical approach that combines the theories, knowledge, and practices of both traditional Chinese medicine and conventional Western medicine,^{1–3} has great potential in addressing various important health issues.^{4,5} A significant number of clinical practice guidelines (CPGs) for ICWM (ICWM-CPGs) exist to direct clinical practices. In 2023, three

prominent Chinese societies jointly issued 53 ICWM-CPGs.⁶ However, current ICWM-CPGs often face challenges such as lack of rigor, implementation difficulties, and poor adherence, similar to other CPG developments in China.⁷ The distinct nature of ICWM necessitates additional methodological considerations beyond those addressed in traditional guidelines,^{8–12} which provide essential guidance for standardizing the development process but may not fully account for the unique challenges posed by the distinct nature of ICWM.^{13,14} To address the

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critical and widespread methodological issues in current ICWM-CPG development, we aimed to provide proposals for establishing trustworthy recommendations, with the intention of offering reference for the development of ICWM-CPGs worldwide.

2. Methods

We employed a nominal group technique (NGT) approach to identify key methodological issues in ICWM-CPG development and to formulate related proposals.¹⁵ We began by assembling a multidisciplinary expert panel based on predefined selection criteria, which included expertise in evidence-based medicine, guideline methodology, ICWM, statistics, or nursing; participation in the development of at least 5 ICWM-CPGs; publication of ICWM-related research within the past 3 years; and interest in the study and willingness to participate voluntarily. The resulting panel consisted of 3 guideline methodologists, 2 statisticians, 2 ICWM experts, 2 nursing experts, and 5 evidence-based medicine researchers.

We conducted a literature search in the PubMed database using terms such as "clinical practice guideline," "integrative," "Chinese medicine," "recommendation," "current," "limitation," "barrier," and "challenge." Studies that investigated the status and challenges of ICWM-CPG development were included, and the methodological issues and suggestions raised in these studies were collected and summarized.

We shared the research objectives—to identify key methodological issues in ICWM-CPG development and to propose methods for establishing trustworthy recommendations—to all members and conducted six discussions from February 25, 2023, to July 30, 2023. In each discussion, members freely expressed their views on a central theme, while a researcher documented the discussions. The statement was finalized when no further comments were offered by any member.

3. Results

In the initial discussion, members identified 5 key methodological issues based on the literature review results and previous research experience:

- 1) Which fundamental methodological guidance should be referred to in the development of international trustworthy ICWM-CPG?
- 2) How can a multidisciplinary guideline development group be established to ensure that Chinese medicine and Western medicine are equally considered, favoring their coexistence and complementarity?
- 3) How to identify clinical questions with a focus on ICWM advantages?
- 4) What should be considered in selecting, assessing, and integrating the evidence?
- 5) How to form accurate, reliable, understandable, and implementable recommendations?

Over the course of five subsequent discussions, members conducted a detailed exploration of each issue, which ultimately led to the formulation of associated methodological proposals.

Box 1 summarizes the methodological issues that warrant particular attention for the developers of CWM-CPGs, beyond the classical CPG methodology guidance, along with targeted proposals aimed at facilitating their effective resolution.

Box 1. Methodological issues and recommendations for the development of trustworthy ICWM-CPGs

Methodological issue 1: Which fundamental methodological guidance should be referred to in the development of international trustworthy ICWM-CPGs?

Recommendation 1.1: Trustworthy ICWM-CPGs should meet the criteria of the IOM $\,$

Recommendation 1.2: The development processes of ICWM-CPGs might refer to the checklist of G-I-N

Recommendation 1.3: GRADE approach should be used to rate the certainty of evidence and the strength of recommendations

Recommendation 1.4: The reporting of ICWM-CPGs should refer to the RIGHT statement

Methodological issue 2: How can a multidisciplinary guideline development group be established to ensure that Chinese medicine and Western medicine are equally considered, favoring their coexistence and complementarity?

Recommendation 2.1: Appoint a pair of impartial chairpersons possessing professional qualifications in Chinese and Western medicine and effective leadership skills to supervise and facilitate team integration

Recommendation 2.2: Specify the responsibilities, selection criteria, and anticipated size for each panel

Recommendation 2.3: Establish an effective mechanism and formal procedure to facilitate close collaboration between clinical experts and methodologists

Recommendation 2.4: Utilize a structured timeline to delineate stage-specific objectives and responsibilities, and regularly review progress to enhance the efficiency of guideline development

Recommendation 2.5: Dynamic identify and manage potential conflicts of interest among team members comprehensively

Methodological Issue 3: How to identify clinical questions with a focus on ICWM advantages?

Recommendation 3.1: Utilize the PIPDS model to s structure and summarize specific advantages of ICWM

Recommendation 3.2: Collect and select clinical questions follow the process of interview, evidence review, and experts consensus which should involve both Chinese and Western medicine

Recommendation 3.3: Organize and categorize clinical questions from a disease-syndromes combination perspective.

Methodological issue 4: What should be considered in selecting, assessing, and integrating the evidence?

Recommendation 4.1: Incorporate outcomes reflecting the advantages of ICWM, in addition to patient-important outcomes

Recommendation 4.2: Find the relative advantages among the competing interventions via network meta-analysis method

Recommendation 4.3: Perform subgroup analyses and assess the credibility of subgroup effects to explore the efficacy discrepancy, thus supporting personalized treatment strategies

Recommendation 4.4: Consider expanding the review process and adopting a framework for evidence synthesis when incorporating multi-evidence

Methodological issue 5: How to form accurate, reliable, understandable, and implementable recommendations?

Recommendation 5.1: Utilize internationally recognized terminology and concepts

Recommendation 5.2: Integrate the diagnostic and therapeutic principles as well as the holistic perspective of Chinese medicine into the organization and composition of recommendations

Recommendation 5.3: Consider the practical implementation context of the interventions

Recommendation 5.4: Exercise caution when recommending pharmacological interventions, ensuring standardized preparation and qualifications.

Recommendation 5.5: Provide comprehensive, practical guidance for the implementation of recommended interventions, including precise methods of application, procedural steps for implementation, and pertinent considerations

Recommendation 5.6: Visualize the ICWM diagnostic and therapeutic processes to enhance clarity and organization of recommendations.

ICWM: integrative Chinese-Western medicine; CPG: clinical practice guideline; ICWM-CPG: clinical practice guideline for integrative Chinese-Western medicine; IOM: Institute of Medicine; G-I-N: Guidelines International Network.

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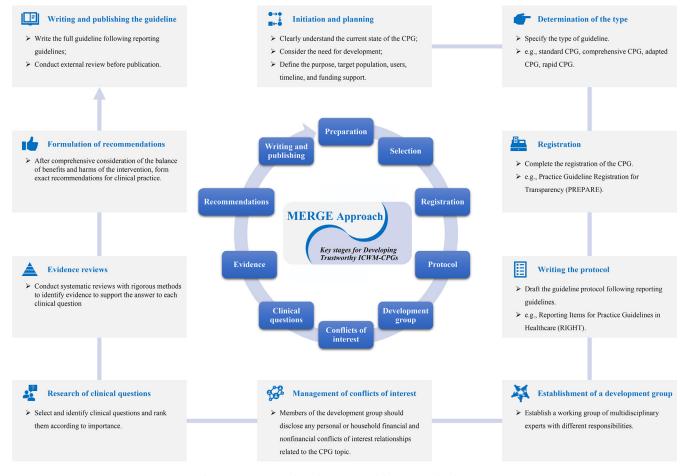


Fig. 1. Key stages in clinical practice guidelines (CPG) development.

3.1. Which fundamental methodological guidance should be referred to in the development of international trustworthy ICWM-CPG?

In the global healthcare community, numerous organizations and individuals have issued over 100 systematic recommendations aimed at improving and standardizing the methods for developing CPGs.¹⁶ Notably, the Institute of Medicine (IOM) has pioneered the establishment of standards,¹² which are globally recognized as one of the most reputable methodological guidance for CPG development. Similarly, the Guidelines International Network (G-I-N) has developed a checklist outlining the detailed elements involved in CPG development.¹¹ Furthermore, guidance from organizations such as the World Health Organization (WHO),¹⁰ the Scottish Intercollegiate Guidelines Network (SIGN),⁹ and the National Institute for Health and Care Excellence (NICE) also offers valuable insights.⁸ These methods, proposed by organizations with extensive expertise and experience in CPG development, highlight the key stages including: (1) initiation and planning; (2) determination of the guideline type; (3) registration; (4) writing the protocol; (5) establishment of a development group; (6) management of conflicts of interest; (7) research of clinical questions; (8) evidence reviews; (9) formulation of recommendations; and (10) writing and publishing the guideline (Fig. 1). The standards we recommend are applicable to the development of CPGs in virtually any healthcare fields. Any specific consideration in ICWM-CPG development should be constrained by the framework of standard methods.

The process of transitioning from evidence to recommendations is at the core of developing trustworthy CPGs, and this holds especially true for ICWM, where the evidence and practice are complex. Employing a decision framework based on the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) method (Fig. 2),^{17,18} a mature system for evaluating certainty of evidence and strength of recommendation, significantly aids in this process.

Most CPGs predominantly present recommendations and their formulation process in written form. When reporting CPGs, adherence to the Reporting Items for Practice Guidelines in Healthcare (RIGHT) guidelines is essential to ensure transparency and enhance the dissemination of trustworthy guidelines.¹⁹

3.2. How can a multidisciplinary guideline development group be established to ensure that Chinese medicine and Western medicine are equally considered, favoring their coexistence and complementarity?

The success of ICWM-CPGs relies on assembling a proficient, diverse team with extensive knowledge and technical acumen.¹¹ Effective collaboration requires the integration of diverse perspectives from stakeholders across various disciplines, even if they initially lack an in-depth understanding of each other's specializations.

Initially, it is crucial to designate a pair of impartial chairpersons to direct and synchronize the group's endeavors. These chairpersons must be individuals endowed with professional credibility and strong leadership skills. They should also possess foresight to anticipate and address potential communication barriers that may arise among experts from different nationalities and diverse professional backgrounds, while ensuring the accuracy of the overall direction. The chairperson's responsibility is to ensure that every member contributes to the common goal and facilitate consensus-building. However, the chairpersons should not solely rely on long-term experience and outstanding expertise in a spe-

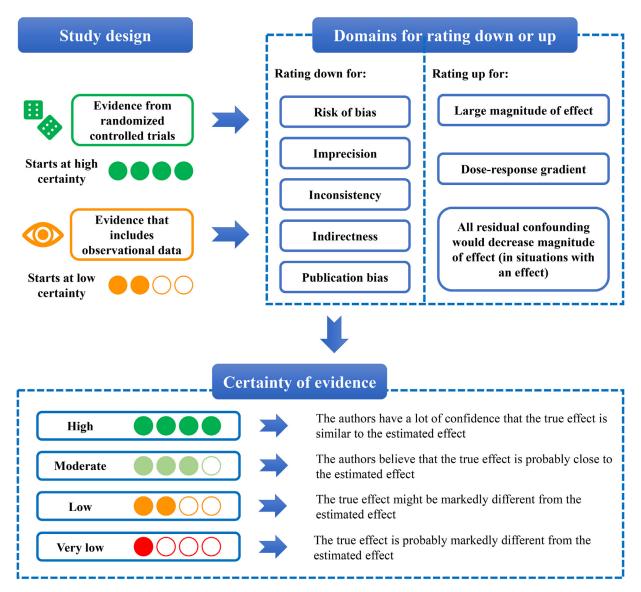


Fig. 2. The use of GRADE approach for assessing certainty of evidence and strength of recommendations in clinical practice guidelines (CPG) development.

cific medical field but should possess a balanced and comprehensive knowledge to mitigate any potential biases.

Regarding the development group's structure and magnitude, striking a balance is key. An excessively small group might overlook key stakeholders, while an overly large one could inflate costs and diminish efficiency. Although no definitive size is prescribed, we suggest a framework comprising a steering committee, chaired by 1-2 individuals, a secretariat manned by 2-3 personnel versed in evidence-based, clinical, and Chinese medicine, an evidence review panel of 6-10 researchers skilled in evidence-based medicine, and an expert panel of 20-30 multidisciplinary professionals. These professionals should possess a broad understanding of both Chinese and Western medicine to circumvent inefficiencies caused by overly compartmentalized expertise. Moreover, it is advisable to establish a review panel consisting of external stakeholders, including outside peers and experts, representatives of the sponsoring organization, and members of the public, to conduct a comprehensive review of the guidelines. The composition and responsibilities of development group for an ICWM-CPG is detailed in Table 1.

Considering that ICWM-CPG development is typically a long-term endeavor, employing a holistic structured timeline to oversee and spur the progress of various panels within the development group is essential for efficiency. This schedule should segment the overarching goal into staged objectives, assign clear responsibilities, and facilitate regular check-ins to promptly address any impediments.

Throughout this evidence-based decision-making process, the pervasiveness of conflicts of interest must be meticulously managed, given the intricate potential for various interest relationships inherent in ICWM-CPG development compared to standard guidelines. Beyond monetary conflicts (personal income, research funding, etc.), participants should avoid unjustifiable biases against specific medical systems. Even within one system, divergent schools of thought may exist, necessitating recognition of participants' leanings. Furthermore, financial stakes like patent ownership for potential recommendations demand scrupulous scrutiny. Addressing conflicts of interest necessitates a systemic, evolving approach, extending through the guideline's formulation. All participants should disclose potential conflicts via a standardized declaration, aiming to document and address any conflicts proactively. Identified conflicts mandate decisive responses, ranging from public disclosure to participant dismissal when warranted.

3.3. How to identify clinical questions with a focus on ICWM advantages?

Clinical questions reflect crucial and pressing demands in clinical practice, providing a starting point for developing CPGs. Precisely defining the scope of clinical questions in ICWM-CPG enhances their speci-

Table 1

The composition and responsibilities of development group for ICWM-CPG.

Panels	Recommended number of members	Recruitment requirements	Major responsibilities
Steering committee	1–2	Individual(s) (1) possesses a moderate level of professional expertise and strong organizational and coordination leadership abilities; and (2) without specialization in any particular field of Chinese or Western medicine.	 (1) Initiating and planning the guideline; (2) coordinating the development of the guideline; (3) establishing other panels, and systematically managing conflicts of interest; (4) overseeing the process of guideline development; and (5) reviewing and approving the recommendations and the full text of the guideline.
Secretarial section	2-3	Individuals with backgrounds in EBM, clinical medicine, and Chinese medicine research.	 (1) Coordinating and organizing the work of other panels; (2) drafting the protocol; (3) organizing the research on the clinical questions; (4) organizing consensus meetings; (5) managing personnel and recording meetings throughout the entire guideline development process; (6) drafting the full text of the guideline and submitting it for publication; and (7) organizing the dissemination and promotion of the guideline.
Evidence review panel	6–10	Individuals with research expertise in EBM, Chinese medicine, and related fields.	(1) Systematically retrieving, evaluating, and synthesizing evidence, and grading the certainty of evidence; and (2) producing an evidence summary table and drafting recommendations based on the evidence reviews.
Consensus expert panel	20–30	(1) Professionals from multidisciplinary fields such as EBM, clinical medicine, Chinese medicine, ICWM, and health economics; and (2) with a minimum of 7–10 being conventional medicine professionals.	(1) Constructing clinical questions and selecting outcome indicators; (2) prioritizing the importance of clinical questions; (3) voting on and reaching consensus on recommendations; and (4) providing suggestions for revising and improving the full text of the guideline.
External review panel	5–10	External stakeholders, including outside peers and experts, representatives of the sponsoring organization, and members of the public.	(1) Reviewing the recommendations and the full text of the guideline; and (2) providing specific suggestions for revising and improving the guideline.

ICWM-CPG: clinical practice guidelines of integrative Chinese-Western medicine; EBM: EBM; ICWM: integrative Chinese-Western medicine.

ficity, focusing on the unique characteristics and benefits of ICWM, thereby enabling the effective utilization in practice. Simultaneously, it strengthens the guidance of ICWM-CPGs, thereby increasing their significance.

ICWM offers a multitude of notable advantages, including the provision of natural and less invasive treatments, enhancement of overall health and well-being, treatment of the individual rather than just the symptoms or disease, addressing the underlying causes of diseases, prioritizing individual needs, and increasing treatment effectiveness while managing disease and its associated symptoms, among other benefits. The specific advantages of ICWM could be structured and broken down into advantageous patient populations, advantageous interventions, advantageous parts, and advantageous disease-syndromes (PIPDS).² For instance, when compared to using standard care alone, the combination of LHQW granules (capsule) with standard care has shown significant benefits in reducing the conversion rate of severe cases, improving the effective rate, and enhancing the recovery rate of chest CT manifestations in patients with mild and moderate COVID-19.²⁰ By employing the PIPDS model, researchers could systematically identify advantageous patient populations, beneficial interventions like the incorporation of LHQW granules (capsules) alongside standard care, advantageous parts encompassing the management and recuperation of COVID-19, and beneficial disease-syndromes particularly in the context of mild and moderate COVID-19.

We recommend investigating these advantages through a comprehensive approach, which includes reviewing research evidence, considering the theories and practical experiences of Chinese medicine, consulting clinical experts in relevant fields, and interacting with patients who have firsthand experience with ICWM.

3.4. What should be considered in selecting, assessing, and integrating the evidence?

Critics have long pointed out the absence of critical evidence reviews in integrative medicine, which is a direct reflection of the reliability of ICWM-CPGs.^{21–24} As a comprehensive medical system that integrates different medical systems, guidelines developed from an ICWM perspective must uphold critical thinking and pursue high-quality evidence reviews, while also considering the unique characteristics.²⁵

Firstly, it is crucial to select appropriate outcomes based on specific advantages and evaluation objectives. For instance, in the treatment of patients with mild to moderate COVID-19, the coadministration of Chinese and western medicine could enhance overall efficacy.²⁰ Therefore, developers should focus on assessing whether intervention of Western medicine combined with Chinese medicine, compared to sole Western medicine intervention, yields significant clinical advantages. Another example is in the case of breast cancer patients undergoing conventional treatments like chemotherapy, where the integration of Chinese medicine shows potential in symptom management and prognosis enhancement.²⁶ In such cases, developers should consider outcomes such as the reduction of complications and the mitigation of adverse reactions.

In addressing specific issues, ICWM intervention could encompass either standalone Chinese medicine or Western medicine interventions, or a combination of both. The guiding principle for recommending these interventions in ICWM-CPGs is "appropriate emphasis on either Chinese or Western medicine, depending on the situation," advocating for the endorsement of the optimal intervention regardless of its origin.²⁷ Original studies often struggle to furnish direct comparative evidence for various Chinese and Western medicine interventions and combined interventions. Utilizing network meta-analysis (NMA) proves to be an effective approach to construct indirect comparisons and generate reliable evidence, assisting developers in determining the best intervention.²⁸ Indeed, it is crucial to emphasize the consideration of decision thresholds to assess the magnitude of effects, and to base judgments regarding differences in intervention effects on the presence of clinical minimal important differences rather than relying solely on statistical significance when comparing interventions.^{29,30}

Furthermore, Chinese medicine emphasizes personalized treatment approaches.² Implementing subgroup analyses or regression analyses designed based on the Specific Advantages Identified through the Pattern Identification, Pathogenesis, Drug, and Syndrome (PIPDS) model is a viable method to investigate the efficacy differences of ICWM interventions under different circumstances. Tools such as the instrument to assess the credibility of effect modification analyses (ICEMAN) can aid in evaluating the credibility of subgroup effects, thus providing evidence to support personalized ICWM intervention strategies.³¹

Subbiah posits that if all evidence is likened to an iceberg, the classical evidence pyramid predominantly encompasses the visible tip, while a multitude of evidence types remain submerged. Chinese medicine boasts a long history of application and possesses a wealth of practical experiences and original theories. The key to harnessing the advantages of ICWM lies in identifying valuable components from this wealth and judiciously integrating them into decision-making processes.³²

3.5. How to form accurate, reliable, understandable, and implementable recommendations?

The medical systems of Chinese and Western medicine have originated from vastly different practices, resulting in distinct medical frameworks.³³ When formulating recommendations within ICWM-CPGs, it is essential to utilize globally accepted terminology and classification standards to reduce potential comprehension obstacles. Relevant reference standards include the classification and codes of diseases and patterns of traditional Chinese medicine,³⁴ the Clinic terminology of traditional Chinese medical diagnosis and treatment,³⁵ and the WHO international standard terminologies on traditional Chinese medicine,³⁶

ICWM interventions may concurrently possess multiple PIPDS advantages, implying that one intervention can potentially address various identical needs of users or multifaceted requirements of a single user. Therefore, the organization of recommendations should ideally be based on a tailored design, considering the unique characteristics of traditional Chinese medicine, such as the concept of combining syndrome differentiation and holistic perspective, to fully leverage the advantages of ICWM interventions. For instance, acupuncture may effectively alleviate anxiety, depression, post-treatment fatigue, and pain among breast cancer survivors simultaneously.³⁷ Recommending acupuncture for breast cancer survivors experiencing the multiple symptoms can reduce costs and prevent redundant treatments.

Furthermore, the formulation of recommendations must consider the target implementation environment. Certain interventions from Chinese or Western medicine may not be covered by health insurance or even approved in specific countries or regions.³⁸ In addition to regulatory and financial constraints, the scarcity of professional medical institutions equipped to administer these integrative interventions may also pose a significant barrier to their feasibility.³⁹ Issuing recommendations devoid of considerations for such practical limitations would not only be futile but could also incite controversy.⁴⁰ Similarly, the acceptability of ICWM, its cultural foundation, and the institutional readiness to professionally administer and monitor such treatments should be rigorously assessed in relation to the target implementation environment.

In recommending pharmacological interventions that incorporate Chinese medicinal components, it is imperative to ascertain that the medicinal products are derived from standardized preparation processes and have attained the requisite credentialing. Concurrently, elucidating the potential interaction risks inherent in the combined usage of these traditional medications with Western pharmaceuticals is essential.^{41,42} It is of paramount importance to explicitly declare the safety evidence associated with these traditional medicaments and to meticulously disclose the disparities in adverse events between monotherapy and combined therapy modalities. This degree of transparency not only fortifies trust in the recommendations but also furnishes practitioners and patients with the critical information necessary for informed decisionmaking processes.

ICWM pharmacological interventions may have various versions with different formulations and dosage forms. On the other hand, some non-pharmacological interventions, such as Tai Chi and meditation, are typically self-administered by users without the necessity of visiting specialized treatment facilities. Hence, recommendations within ICWM-CPGs should furnish a comprehensive and detailed standard operating procedure to guide the utilization of interventions.

After formulating recommendations, it is highly advisable for developers to employ graphical representations to vividly illustrate the diagnostic and treatment processes of ICWM. This approach not only aids in the concise summarization and systematic listing of recommendations, but also effectively organizes recommended practices into a coherent sequence, providing a logical framework. Simultaneously, it enhances readability while intuitively emphasizing the distinctive characteristics of ICWM. Of paramount importance, it assists users in achieving a comprehensive grasp and understanding of ICWM, thereby facilitating more precise decision-making regarding diagnostic and treatment strategies.

4. Discussion

With the rapid progression of ICWM and the emergence of pertinent evidence, the absence of trustworthy ICWM-CPGs can lead to significant inefficiencies in resource allocation and hinder the development of highquality clinical practices. Building on generic CPG development methodologies proposed by organizations such as WHO, G-I-N, and GRADE, the working group considered the unique aspects of ICWM-CPG development and developed targeted methodological proposals that address key issues, such as integrating diverse disciplinary perspectives from Chinese and Western medicine, identifying clinical questions to leverage ICWM advantages, and using appropriate methods in evidence synthesis (Box 1).

One of the main challenges in developing reliable ICWM-CPGs is the limited high-quality evidence in this field. ICWM, by its intrinsic nature, amalgamates an array of therapeutic modalities derived from both Chinese and Western medicine. Traditional RCTs frequently encounter difficulties in accommodating the multifaceted and individualized aspects inherent in ICWM.⁴³ To surmount this challenge, it is imperative for researchers to explore innovative research designs, encompassing pragmatic trials and real-world evidence, which are better equipped to accommodate the intricacies of ICWM interventions.⁴⁴ Pragmatic trials offer a degree of flexibility in intervention delivery that aligns harmoniously with the personalized character of ICWM. Real-world evidence, derived from routine clinical practice, contributes invaluable insights into the functioning of ICWM across diverse patient cohorts. These nonconventional research designs serve as complementary mechanisms to the traditional RCTs, presenting a more comprehensive perspective on the efficacy and safety profile of ICWM interventions.⁴⁵

ICWM focuses on holistic patient care, which requires a shift towards patient-centered outcomes in guideline recommendations. While traditional clinical trials often focus on surrogate endpoints or biomedical markers, ICWM aims to improve overall well-being.⁴⁶ Therefore, patient-reported outcomes, such as quality of life, symptom improvement, and patient satisfaction, should be prioritized. Active involvement of patients in the development of ICWM-CPGs assumes pivotal importance. Their perspectives proffer invaluable insights into the outcome parameters of utmost significance to them, as well as their perception of the benefits and risks entailed by integrative therapeutic approaches.⁴⁷ The inclusion of patient representatives in guideline committees serves to ensure recommendations are in alignment with patient values and preferences. ICWM's profound cultural underpinnings give rise to intricate ethical considerations. These considerations pertain to variations in informed consent practices, disclosure of treatment modalities, and considerations of patient autonomy within diverse cultural contexts. Developers must navigate these cultural nuances while adhering to ethical principles that uphold individual choices. To foster greater cultural sensitivity, cross-cultural training for healthcare professionals involved in ICWM is imperative.

In conclusion, the development of trustworthy ICWM-CPGs stands as a multifaceted challenge that demands innovative research methodologies, a recalibration towards patient-centric outcomes, heightened cultural awareness, and a heightened focus on education and training. By addressing these imperatives, ICWM can offer an evidence-based, patient-centered therapeutic paradigm that respects cultural diversity and upholds ethical imperatives.

Declaration of competing interest

The authors declare that no competing interests exist.

CRediT authorship contribution statement

Honghao Lai: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. Mingyao Sun: Investigation. Bei Pan: Investigation. Baojin Han: Investigation. Tingting Lu: Investigation. Lei Fang: Methodology, Writing – review & editing. Jie Liu: Methodology, Writing – review & editing. Long Ge: Writing – review & editing, Supervision.

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Ethical statement

Not applicable.

Data availability

Not applicable.

References

- Li Q, Luo X, Li L, et al. Toward better translation of clinical research evidence into rapid recommendations for traditional Chinese medicine interventions: A methodological framework. *Integr Med Res.* 2022;11(3):100841. doi:10.1016/j.imr.2022.100841.
- Wang WJ, Zhang T. Integration of traditional Chinese medicine and Western medicine in the era of precision medicine. J Integr Med. 2017;15(1):1–7. doi:10.1016/S2095-4964(17)60314-5.
- Chan KW, Chow TY, Yu KY, et al. Effectiveness of Integrative Chinese-Western Medicine for Chronic Kidney Disease and Diabetes: A Retrospective Cohort Study. *Am J Chin Med.* 2022;50(2):371–388. doi:10.1142/S0192415X2250015X.
- Chao J, Dai Y, Verpoorte R, et al. Major achievements of evidence-based traditional Chinese medicine in treating major diseases. *Biochem Pharmacol.* 2017;139:94–104. doi:10.1016/j.bcp.2017.06.123.
- Dai YJ, Wan SY, Gong SS, Liu JC, Li F, Kou JP. Recent advances of traditional Chinese medicine on the prevention and treatment of COVID-19. *Chin J Nat Med.* 2020;18(12):881–889. doi:10.1016/S1875-5364(20)60031-0.
- Announcement by the Chinese Association of Integrative Medicine, the Chinese Association of Chinese Medicine, and the Chinese Medical Association on the Joint Release of 52 Integrative Chinese and Western Medicine Diagnosis and Treatment Plans. Accessed April 23, 2024. http://www.caim.org.cn/info_content.jsp?id=10322
- Chen Y, Wang C, Shang H, Yang K, Norris SL. Clinical practice guidelines in China. BMJ. 2018;360:j5158. doi:10.1136/bmj.j5158.
- Introduction | Developing NICE guidelines: the manual | Guidance | NICE. Published October 31, 2014. Accessed April 24, 2024. https://www.nice.org.uk/ process/pmg20/chapter/introduction
- SIGN 50: a guideline developer. SIGN. Accessed. April 24, 2024. https://testing36. scot.nhs.uk.
- 10. WHO handbook for guideline development, 2nd Ed.. Accessed April 24, 2024. https://www.who.int/publications-detail-redirect/9789241548960
- Qaseem A, Forland F, Macbeth F, et al. Guidelines International Network: toward international standards for clinical practice guidelines. Ann Intern Med. 2012;156(7):525–531. doi:10.7326/0003-4819-156-7-201204030-00009.
- Graham R, Mancher M, Miller Wolman D, Greenfield S, Steinberg E. Clinical Practice Guidelines We Can Trust. Institute of Medicine (US) committee on standards for developing trustworthy clinical practice guidelines. National Academies Press (US); 2011 Accessed April 24, 2024 http://www.ncbi.nlm.nih.gov/books/NBK209539/.
- Yu X, Wu S, Zhang J, et al. Developing TCM clinical practice guidelines: a comparison between traditional Chinese medicine and western medicine. *Integrative Med Res.* 2023;12(2):100952. doi:10.1016/j.imr.2023.100952.

- guang Chen Z, H Luo, Xu S, Yang Y, chuan Wang S. Study on the methodology of developing evidence-based clinical practice guidelines of Chinese medicine. *Chin J Integr Med.* 2015;21(11):874–880. doi:10.1007/s11655-014-1896-1.
- Manera K, Hanson CS, Gutman T, Tong A. Consensus Methods: Nominal Group Technique. In: Liamputtong P, ed. Handbook of Research Methods in Health Social Sciences. Singapore: Springer; 2019:737–750. doi:10.1007/978-981-10-5251-4_100.
- Kredo T, Bernhardsson S, Machingaidze S, et al. Guide to clinical practice guidelines: the current state of play. *Int J Qual Health Care*. 2016;28(1):122–128. doi:10.1093/intqhc/mzv115.
- Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol*. 2011;64(4):383–394. doi:10.1016/j.jclinepi.2010.04.026.
- Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ*. 2008;336(7652):1049–1051. doi:10.1136/bmj.39493.646875.AE.
- Chen Y, Yang K, Marušic A, et al. A reporting tool for practice guidelines in health care: the RIGHT statement. Ann Intern Med. 2017;166(2):128–132. doi:10.7326/M16-1565.
- Ge L, Zhu H, Wang Q, et al. Integrating Chinese and western medicine for COVID-19: a living evidence-based guideline (version 1). *J Evid Based Med.* 2021;14(4):313–332. doi:10.1111/jebm.12444.
- Gorski DH, Novella SP. Clinical trials of integrative medicine: testing whether magic works? Trends Mol Med. 2014;20(9):473–476. doi:10.1016/j.molmed.2014.06.007.
- Power M, Hopayian K. Exposing the evidence gap for complementary and alternative medicine to be integrated into science-based medicine. *J R Soc Med.* 2011;104(4):155– 161. doi:10.1258/jrsm.2011.100271.
- McCartney M. The scam of integrative medicine. BMJ. 2011;343:d4446. doi:10.1136/bmj.d4446.
- MacPherson H, Peters D, Zollman C. Closing the evidence gap in integrative medicine. BMJ. 2009;339:b3335. doi:10.1136/bmj.b3335.
- Djulbegovic B, Guyatt GH. Progress in evidence-based medicine: a quarter century on. Lancet. 2017;390(10092):415–423. doi:10.1016/S0140-6736(16)31592-6.
- Fan L, Strasser-Weippl K, Li JJ, et al. Breast cancer in China. Lancet Oncol. 2014;15(7):e279–e289. doi:10.1016/S1470-2045(13)70567-9.
- Zhao F, Yang Z, Wang N, Jin K, Luo Y. Traditional Chinese Medicine and Western Medicine Share Similar Philosophical Approaches to Fight COVID-19. *Aging Dis.* 2021;12(5):1162–1168. doi:10.14336/AD.2021.0512.
- Tian J, Gao Y, Zhang J, et al. Progress and challenges of network meta-analysis. J Evid Based Med. 2021;14(3):218–231. doi:10.1111/jebm.12443.
- Brignardello-Petersen R, Florez ID, Izcovich A, et al. GRADE approach to drawing conclusions from a network meta-analysis using a minimally contextualised framework. *BMJ*. 2020;371:m3900. doi:10.1136/bmj.m3900.
- Brignardello-Petersen R, Izcovich A, Rochwerg B, et al. GRADE approach to drawing conclusions from a network meta-analysis using a partially contextualised framework. *BMJ*. 2020;371:m3907. doi:10.1136/bmj.m3907.
- Schandelmaier S, Briel M, Varadhan R, et al. Development of the Instrument to assess the Credibility of Effect Modification Analyses (ICEMAN) in randomized controlled trials and meta-analyses. CMAJ. 2020;192(32):E901–E906. doi:10.1503/cmaj.200077.
- Subbiah V. The next generation of evidence-based medicine. Nat Med. 2023;29(1):49– 58. doi:10.1038/s41591-022-02160-z.
- Tang JL, Liu BY, Ma KW. Traditional Chinese medicine. Lancet. 2008;372(9654):1938–1940. doi:10.1016/S0140-6736(08)61354-9.
- Classification and codes of diseases and patterns of traditional Chinese medicine. Accessed April 24, 2024. http://www.natcm.gov.cn/yizhengsi/zhengcewenjian/ 2020-11-23/18461.html
- Clinic terminology of traditional Chinese medical diagnosis and treatment. Accessed April 24, 2024. http://www.natcm.gov.cn/yizhengsi/zhengcewenjian/ 2020-11-23/18461.html
- WHO international standard terminologies on traditional Chinese medicine. Accessed April 24, 2024. https://www.who.int/publications-detail-redirect/ 9789240042322
- Greenlee H, DuPont-Reyes MJ, Balneaves LG, et al. Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. *CA Cancer J Clin.* 2017;67(3):194–232. doi:10.3322/caac.21397.
- You L, Liang K, An R, Wang X. The path towards FDA approval: A challenging journey for Traditional Chinese Medicine. *Pharmacol Res.* 2022;182:106314. doi:10.1016/j.phrs.2022.106314.
- Cassidy CE, Harrison MB, Godfrey C, et al. Use and effects of implementation strategies for practice guidelines in nursing: a systematic review. *Implement Sci.* 2021;16(1):102. doi:10.1186/s13012-021-01165-5.
- 40. Chan WV, Pearson TA, Bennett GC, et al. ACC/AHA special report: clinical practice guideline implementation strategies: a summary of systematic reviews by the NHLBI implementation science work group: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. *Circulation*. 2017;135(9):e122–e137. doi:10.1161/CIR.000000000000481.
- Luo H, Chen H, Liu C, et al. The key issues and development strategy of Chinese Classical Formulas pharmaceutical preparations. *Chin Med.* 2021;16(1):70. doi:10.1186/s13020-021-00483-6.
- Fan TP, Deal G, Koo HL, et al. Future development of global regulations of Chinese herbal products. J Ethnopharmacol. 2012;140(3):568–586. doi:10.1016/j.jep.2012.02.029.
- Jones DS, Podolsky SH. The history and fate of the gold standard. Lancet. 2015;385(9977):1502–1503. doi:10.1016/S0140-6736(15)60742-5.
- Zuidgeest MGP, Goetz I, Groenwold RHH, et al. Series: Pragmatic trials and real world evidence: Paper 1. Introduction. J Clin Epidemiol. 2017;88:7–13. doi:10.1016/j.jclinepi.2016.12.023.

- 45. Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The
- Loudon K, Ireweek S, Sullivan F, Donnan P, Inorpe KE, Zwarenstein M. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ*. 2015;350:h2147. doi:10.1136/bmj.h2147.
 Luo Y, Wang CZ, Hesse-Fong J, Lin JG, Yuan CS. Application of Chinese medicine in acute and critical medical conditions. *Am J Chin Med*. 2019;47(6):1223–1235. doi:10.1142/S0192415X19500629.
- McGoon MD, Ferrari P, Armstrong I, et al. The importance of patient perspectives in pulmonary hypertension. *Eur Respir J.* 2019;53(1):1801919. doi:10.1183/13993003.01919-2018.