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## Research paper

# Developing clinical practice guidelines for the integration of Chinese medicine and biomedicine: A new process<sup>☆</sup>



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## ABSTRACT

**Introduction:** Despite the integration of Chinese medicine and biomedicine which has emerged in clinical practice worldwide, a comprehensive development process for clinical practice guidelines (CPG) has up to now been missing. A valid method for the rational use of predictions for herb-drug interaction is a biggest challenge in guideline development process.

**Methods:** This article summarises the development process by reviewing key literature from CPG developers. It focuses on key methods and challenges specific to CPGs for integration by using text mining and bioinformatics to provide a powerful adjunct to CPG development.

**Results:** The guideline development process identified, together with new approaches, incorporates evidence-based methodology and provides better decisions through analysis of uncertain herb-drug interaction.

**Conclusions:** This new process used three basic phases (preparation, development, and finalization) and seven steps providing a set of methodological principles for CPG development integrating Chinese medicine and biomedicine.

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## 1. Introduction

Chinese medicine (CM) is a widely practiced system of medicine in most of Asia [1], and is emerging as an accepted complementary approach to biomedical model of health care in many Western countries [2]. There are several convincing arguments for integration of these disparate systems of medicine. Integration is already helping patients with many chronic diseases [3,4], severe acute respiratory syndrome (SARS) [5], AIDS [6] and etc. Moreover, integration would be more economical for the health care system [7]. Even, integration would respond to the ever-increasing demand for complementary medicine and increased cultural sensitivity [8]. However, the confluence of biomedicine and CM presents many complex problems and opportunities for integration [9]. For example, it is quite common for a patient to seek herbal treatment while taking several prescription medications.

Reasonably enough, patients want to know about possible interactions and compatibility when taking prescription drugs and herbs simultaneously. In addition, timing of herbal formulas and drugs use is largely due to theoretical or known risks of interactions with herb-drug. Such specific questions, unfortunately, are often difficult (not impossible) to answer.

Because many patients receive both CM and biomedical treatments concurrently, there is a great need to develop clinical practice guidelines (CPGs) for rationally integrating assessment or treatment approaches from these two systems of medicine [10]. CPGs, important knowledge translation tools, are statements that include recommendations intended to optimize patient care that are informed by careful review of existing practice, and available published evidence on topic [11,12]. Although the goal of all CPGs is the same, to assist patients and practitioners in making care decisions. However, different organizations/groups use different methodologies to develop CPGs for different systems of medicine [13,14]. In biomedicine, the investigators always use strict evidence-based methodologies that follow accepted standards for developing CPGs [15]. Since 2004, the World Health Organization Regional Office for the Western Pacific (WHO/WPRO) has been in the process of developing international CPG for the use of traditional medicines [16]. Then, increasing CPGs for integration of

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CM and biomedicine (*hereinafter referred to as CPGs for integration*) have been developed in China [17,18]. The quality of these CPGs has remained suboptimal according to Appraisal of Guidelines for Research and Evaluation (AGREE) II Instrument evaluation [19,20], discussion of optimal integration therapy in CPGs has to remain open. Shortcomings in the guidelines process include the lack of 1) a special plan for CPG production, dissemination and implementation; 2) and a dedicated process to assess the needs of target users, answer specific questions such as possible herbs-drugs interactions, and the time of taking the herbs and ingesting the other drug or substances. To address these issues, our research group has committed to develop a new formal process for CPG of integration with the aid of interdisciplinary teams and experts. The present document summarises the main elements concepts of the guideline development methodology and key steps. It is anticipated that this progress will have a significant impact on the quality of care and clinical outcomes of individuals undergo integration treatment.

Our research group has committed to a CPG development progress that incorporates text mining and bioinformatics approaches that will help to produce valid CPGs while optimizing the use of limited resources. Ultimately, we hope that these changes will improve the clinical outcomes of individuals with integration therapies.

**2. Methods and results**

The following elements of classic parameter development process remain in the new process described in this document. The process includes three phases which are preparation phase, development phase and finalization phase.

*2.1. Development process*

To design an appropriate and acceptable process we reviewed international CPG development process, including handbooks, literatures on methodology and process for CPG development. The works of Scottish Intercollegiate Guidelines Network (SIGN) [21], National Institute for Health and Clinical Excellence (NICE) [22], World Health Organization (WHO)[23], The Guidelines International Network (GIN) [24], New Zealand Guidelines Group (NZGG)

[25] were reviewed. The methodologies developed by medical associations were also incorporated. In addition, the current situation and limitations of CPGs for CM/integration therapies were systemically analyzed, and the results were showed in our previous research [26,27]. Based on these works, a process including 3 basic stages was designed, including the preparation stage, the development stage and the finalization stage. Multiple methods were integrated into the process to cover the limitations of the current development of CPG for the integration of Chinese medicine and biomedicine. The flowchart of whole process is shown in Fig. 1.

*2.2. Preparation stage*

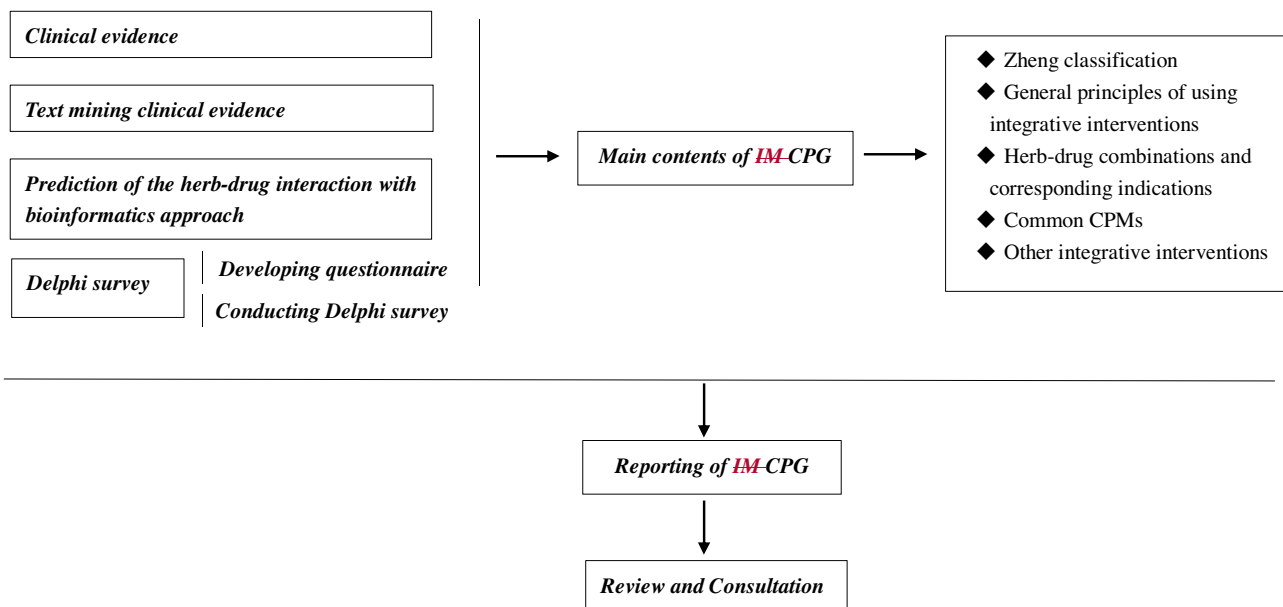
A multidisciplinary Guideline Development Committee (GDC) including the clinical experts, epidemiologists, clinical research methodology experts with evidence based medicine background, technical members with pharmaceutical, bioinformatics, toxicology background and relevant stakeholders should be included. The role of GDC is to provide administrative, publication, and logistical support to the guideline process.

*2.3. Developing stage*

The following steps describe the guideline development process from evidence selection to publication:

*2.3.1. Step 1: Searching, identifying and assessing clinical evidence*

A systematic search of clinical study on both diagnosis and therapeutics for relevant disease, especially the herb-drug combination therapy or other integrative interventions will be conducted. Eligibility criteria for identifying potentially relevant articles will be set up, including types of studies on CM diagnosis (Zheng classification), and integrated interventions. Once potential evidence is identified, the methodology used in each study will be assessed to ensure validity of study. Accepted tools will be used for assessing the methodological quality of different types of studies, like AMSTAR (Assessing the Methodological Quality of Systematic Reviews) [28] for systematic review (SR) or meta-analysis, the Cochrane Collaboration’s tool for assessing risk of bias [29] for randomized control trial (RCT), STROBE checklist for observational



**Fig. 1.** Process of Development of Clinical Practice Guidelines for integration of Chinese medicine and biomedicine.

studies [30] and CARE checklist [31] for case studies. Considering the characteristics of integrative therapies research, we recommend to use the evidence grading systems for CM established by Liu JP and his colleagues [32]. If related high quality CPGs either in CM or biomedicine have already developed, the core contents of CPGs, like diagnosis criteria in biomedicine and Zheng classification, could be extracted as an important reference in the new CPG for integration of Chinese medicine and biomedicine after careful assessment. The AGREE instrument [19,20] could be used to appraise the quality of CPGs.

### 2.3.2. Step 2: Exploring trends in integrative therapy topics via text mining

Since the clinical study evidence, as many paper described previously, is not strong, and also not enough for forming questionnaire for expert consensus in CPG development. We recommend exploring more data with text mining approach from all related clinical research literature in CPG development. Text mining process can be conducted in three domains according to the general contents of CPGs, including Zheng classification, herb-drug combinations and Chinese herbal proprietary medicines (CHPM). Using a data slicing algorithm based on the calculation of frequency is recommended, which has demonstrated in more details previously [32], to filter high frequency Zheng classification, related herb-drug combinations and commonly used CHPMs. After the rough results are obtained, the panel should review all the results based on the professional knowledge and delete the irrelevant items to correct the results. The results will be listed for further Delphi survey.

### 2.3.3. Step 3: Developing an appropriate questionnaire for Delphi survey

Based on the evidence and text mining results, all identified evidence and information derived from literature and text mining process will be listed as question items in the initial questionnaire. Each item will be provided with level of evidence and supporting data. To restrict number of items, the specific criteria to prioritize the items will be set by the GDC. The priority principle is defined as item with high level of evidence or supporting data. The contents of questionnaire will be based on the frame of diagnosis and treatments on integrative therapy, thus, items will be grouped under the following broad headings: commonly used Zheng classifications; the general principles of using integrative interventions; herb-drug combinations and corresponding indications; commonly used CHPMs and other integrative interventions. The initial questionnaire will be designed as a semi-structured questionnaire and open questions will be set to collect expert opinions.

### 2.3.4. Step 4: Conducting Delphi survey

Generally, a Delphi survey will be conducted, 3–5 rounds until the consensus is reached. In the first round, the experts will be invited to finish the questionnaire and add the follow contents: Zheng classifications, the general principles of using integrative interventions, herb-drug combinations and corresponding indications, CHPMs and other integrative interventions they commonly used in treatment of the relative disease. After much discussion of items, a revised questionnaire for the second round consultation is generated and subsequently disseminated to the experts who responded in the first round. Items are accepted as consensus directly when 80% of respondents reached agreement. Items receiving less than 20% will be removed. Items receiving between 20% and 80% agreement will be recruited to the next round consultation after the revisions. The third round of questionnaire is composed of the same questions which do not achieve consensus in previous consultation. Delphi rounds will be replicated until the

consensus is reached. The practitioners usually select from professionals working in the integrative medicine and the specific criteria of selecting experts will be settled based on Patient-Intervention-Comparison-Outcome (PICO) question of CPG for integration of Chinese medicine and biomedicine. The scale of a Delphi panel is recommended 10–18 experts [33].

### 2.3.5. Step 5: Predicting the herb-drug interaction with bioinformatics approaches

One major characteristic of CPG for integration of Chinese medicine and biomedicine is its recommendations on using both CM herbs and drugs. Thus the recognition of potential herb-drug interactions would be an important issue in CPGs developing process. About twenty years ago, evidence for herb-drug interactions in humans was inconsistently reported through case studies. In the last ten years, scientific verification and applications beyond prescriptions have begun to be explored. It is possible to predict when herb/drugs interact by knowing their properties. For our purpose, research on predicting the herb-drug interaction with bioinformatics approaches will be conducted. A list of herb-drug combinations generated from the text mining process, literature evidence and expert's consensus will be used as candidates for evaluating their interaction effect by a systems pharmacology approach [28] including structure-, omics- and network-based systematic investigations. Mapping between the pharmacology network of herb-drug combination candidate and molecular network of a given disease will be conducted by using graph merge tool to calculate the efficacy index of the network. Centrality value distribution of best interaction between herbs and drugs in specific disease network, and on-target and off-target of intersection can be clearly presented. Corresponding three important parameters including Major Therapeutic Effect (MTE), Associated Therapeutic Effect (ATE) and Side Effect (SE) are defined for the evaluation of herb-drug interactions.

### 2.3.6. Step 6: Review and consultation process

In this step, formal consensus conference will be conducted. GDC members will review all the data and evidence formulated in the previous stages and make final decision on those data whether can be used to produce CPGs for integration. The conference will include background presentations to ground conversations on empirical information to facilitate cohesive discussion. Participants will be led in structured discussions. Care will be taken to ensure that all participants express views, that all ideas are discussed in-depth, and that assertive participants do not dominate the discussion. Points from the participants and decisions generated by conference and draft resolution will be recorded. The resolution will be circulated to all the participants in the consensus group. Revisions will be made on resolutions based on their responses. The process will replicate until consensus is reached. Every participant will be required to sign the resolution if the resolution accurately represented the decisions made during the meeting.

### 2.3.7. Step 7: Reporting of CPG for integration of Chinese medicine and biomedicine of CM and biomedicine

Reporting CPG in right way can promote the understanding of CPG and advance a transparent CPG's development process [34]. To ensure the transparency of the whole process, the key information of each step will be clearly described following a standardized report guideline. A proposed reporting checklist for CPG including 8 topics and 23 sub items is summarized in Table 1.

## 2.4. Finalization stage

In this stage, external review, dissemination, implementation and further updating of the CPG for integration of Chinese

**Table 1**  
Checklist for Reporting CPG for the integration of Chinese medicine and biomedicine.

Topic	Specified Items	Description
1. Title	1.1 Title	Provide an appropriate title including the specified disease's name using International Classification of Disease (ICD). Relevant CM disease should be noted in subheading.
	1.2 Subheading	
2. Introduction	2.1 Scope	Describe goal of the CPG with specific details concerning the targeted users, application of regions and countries, the key clinical questions. A brief description of development process should be Clearfield.
	2.2 Development Process	
3. Background	3.1 Epidemiological Details Natural History in WM	Describe epidemiological details (such as incidence, prevalence and risk factors), and natural history of the relevant diseases both in CM or WM, and the understanding of disease based on CM theory.
	3.2 Understanding of disease based on CM Theory	
4. Diagnostic criteria	4.1 Current Western medical diagnostic criteria	Describe Western diagnostic criteria, classification of CM pattern including symptoms and signs of each pattern, with the corresponding support data derived from text mining process, survey and literature evidence.
	4.2 CM patterns classification and diagnosis	
5. Integrative intervention	5.1 Basic principle of integration of interventions	A specific description of the relevant integrative interventions incorporates basic principle including corresponding indications, commonly use herb-drug combinations with support data and evidence, and others options of integrative intervention. Considering operability of IM CPG, detailed indications should be provide like when the Chinese medicines or western medicine can be stopped for further taking.
	5.2 Herbal-drug combinations	
	5.3 Others options of integrative Intervention	
	5.4 Indications for the withdrawal of herb-drug interactions	
6. Methods	6.1 Identified clinical evidence	Describe the basic information of the key steps in development process, including clinical evidence (search strategy, evaluation of the strengths and quality of evidence, grading of recommendations), text Mining process (basic method and results), predicting approaches (basic method and results), Delphi process (expert Selection, basic Information of survey and statistics), review and consultation process, implementation, and updating plan.
	6.2 Text mining process	
	6.3 Predicting approaches	
	6.4 Delphi process	
	6.5 Review and consultation process	
	6.6 Implementation	
	6.7 Updating	
7. References	–	Provide all the relevant inferences including literature used as evidence
8. Appendices	8.1 Working group membership	Working Group Membership, standardized table evidence and recommendation, vocabulary and others
	8.2 Grade of evidence and recommendation	
	8.3 Vocabulary	
	8.4 Others	

medicine and biomedicine needs to be completed before finalizing the whole development process. External review process will be conducted once the CPG has been drafted to ensure it is representative of the comprehensive perspectives of related professionals. Experts from integrative medicine hospitals except GDG committee members are invited for evaluating the quality of the development process, and the CPG will be applied in hospitals to assess its applicability. The GDC has responsibility to design the implementation plan to ensure appropriate use of CPG in integrative medicine hospitals. And in order to update CPG in time, the GDC has responsibility to collect signals that need for updating as new evidence or consensus arises. Emerging evidence or consensus will be reviewed by all members of the GDC whether it can potentially affect current clinical management strategies. Once new evidence or consensus necessitates changing contents of CPG, the revision of CPG for integration of Chinese medicine and biomedicine will be conducted.

Totally, this process is a living document that will be updated as the new CPG development process is tested. The process used to develop specific CPGs for integration will be described upon their publication. Because of continuous improvement and innovation, the process used may not necessarily match what is described in this paper.

### 3. Discussion

Over the past two decades, the development process for CPGs has become increasingly rigorous, in accordance with rapidly evolving principles. Today, 'guidelines/formal process for guidelines' have reached new heights, generating the imperative for changes in CPG development process. The increasing complexity of CPGs for integration of Chinese medicine and biomedicine has required an extensive revision of development processes and methods. The present article has summarized the basic methodological principles and tools that will be applied in the future production of all CPGs for integration.

An investigation which evaluated eleven CM/integration treatment CPGs suggested that most of CPGs did not clearly describe how the CPGs had been developed and in some of CPGs the key steps were missing. Lack of appropriate process leads low adherence to the general process in development of these CPG. In this progress, we incorporated many widely adopted tools such as AGREE into the CPG development process. These tools could improve the quality and validity of CPGs, and facilitate subsequent implementation efforts. Insufficient evidence is another problem in CM CPG [10] and it is become more outstanding in CPG for integration of Chinese medicine and biomedicine of CM and biomedicine [7,8]. In addition to establishing an improved CPG development process through traditional tools, we have prioritized the development of CPGs through new methods. Accordingly, we have proposed a new process of CPG for integration of Chinese medicine and biomedicine with two methods, to proceed as follows:

1 Prediction of the drug-herb interaction with a bioinformatics approach. This method is dependent on information extracted from published validation data to obtain the interaction between the combinational herb-drug candidates in the disease. Historically, herbs and drugs have been two very different treatment modalities which have rarely, if ever, been used together. The line that separates herbs and drugs, however, has been blurred in recent decades with the increased accessibility to the lay public. It is not uncommon for one patient to take multiple drugs and herbs concurrently. It becomes very difficult to predict whether the combination of drugs-herbs will lead to unwanted side-effects and/or interactions. It is imprudent to assume that there will be no interactions in CPGs for integration. And, it is just as unwise to abandon integration treatment simply for the fear of possible interactions. The solution to this situation is in the understanding of drugs-herbs interactions. With understanding of these mechanisms with systems pharmacology approaches, one can recognize potential interactions and take proper actions to prevent their occurrence. The results of

prediction process will be used as a kind of supporting data resource for developing CPG for integration of Chinese medicine and biomedicine.

- 2 Text mining method. Text mining has been widely used in medical research and been introduced into CM research for quickly identified potential information. The aim of text mining method is used for collecting high frequency Zheng classifications, herb-drug combinations and CPMs reported in clinical studies, which imply that they are well known by practitioners in some extent. We consider this high frequency information as a kind of supporting data for forming CPGs for integration of CM and biomedicine.

#### 4. Conclusion

Our research group has committed to a CPG development progress that incorporates text mining and bioinformatics approaches that will help to produce valid CPGs for integration of CM and biomedicine while optimizing the use of limited resources. Ultimately, we hope that these changes will improve the clinical outcomes of individuals with integration therapies.

#### 5. Conflicts of interest

No competing financial interests exist.

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#### References

- [1] D. Normile, Asian medicine: the new face of traditional Chinese medicine, *Science* 299 (5604) (2003) 188–190.
- [2] G. Dobos, I. Tao, The model of western integrative medicine: the role of Chinese medicine, *Chin. J. Integr. Med.* 17 (1) (2011) 11–20.
- [3] L. Director J, L. Li J, M. Zhang, et al., Chinese herbal medicines for type 2 diabetes mellitus, *Cochrane Database Syst. Rev.* 115 (3) (2004).
- [4] J. Wang, X. Xiong, G. Yang, Y. Zhang, Y. Liu, Y. Zhang, Z. Zhang, J. Li, X. Yang, Chinese herbal medicine qi ju di huang wan for the treatment of essential hypertension: a systematic review of randomized controlled trials, *Evid.-Based Complement. Altern. Med.: eCAM* 2013 (3) (2013) 243–243.
- [5] X. Liu, M. Zhang, L. He, et al., Chinese herbs combined with Western medicine for severe acute respiratory syndrome (SARS), *Cochrane Database Syst. Rev.* 10 (10) (2012) CD004882–CD004882.
- [6] W. Zou, Y. Liu, J. Wang, et al., Traditional Chinese herbal medicines for treating HIV infections and AIDS, *Evid.-Based Complement. Altern. Med.* 2012 (4) (2012) 277–293.
- [7] XUHAOU, The integration of traditional Chinese medicine and Western medicine, *Eur. Rev.* 11 (2) (2003) 225–235.
- [8] J. Cai, Integration of traditional Chinese medicine with Western medicine—right or wrong? *Soc. Sci. Med.* 27 (5) (1988) 521–529.
- [9] J.H. Qu, B. Liu, Z.Q. Zhang, et al., Capturing the opportunities to initiate an in-depth integration of traditional Chinese medicine and western medicine, *Front. Med.* 8 (3) (2014) 268–271.
- [10] Aiping Lu, Keji Chen, Improving clinical practice guideline development in integration of traditional Chinese medicine and western medicine, *Chin. J. Integr. Med.* 21 (3) (2015) 163–165.
- [11] C. Black, S. Peterson, J. Mansfield, et al., Using population-based data to enhance clinical practice guideline development, *Med. Care* 37 (6 Suppl) (1999) 254–263.
- [12] R.M. Rosenfeld, R.N. Shiffman, Clinical practice guideline development manual: a quality-driven approach for translating evidence into action, *Otolaryngol. Head Neck Surg.* 140 (140) (2009) 1–43.
- [13] H.W. Cho, E.H. Hwang, B. Lim, et al., How current Clinical Practice Guidelines for low back pain reflect Traditional Medicine in East Asian Countries: a systematic review of Clinical Practice Guidelines and systematic reviews, *PLoS One* 9 (2) (2014) e88027.
- [14] Y. Motoo, I. Arai, I. Hyodo, et al., Current status of Kampo (Japanese herbal) medicines in Japanese clinical practice guidelines, *Complement. Ther. Med.* 17 (3) (2009) 147–154.
- [15] R. Grol, Successes and failures in the implementation of evidence-based guidelines for clinical practice, *Med. Care* 39 (Suppl. 2 (8)) (2001) 46–54.
- [16] World Health Organization, WHO Traditional Medicine Strategy: 2014–2023, World Health Organization, 2013.
- [17] K.J. Chen, Current status and problems in developing clinical guidelines for Chinese medicine and integrative medicine, *J. Chin. Integr. Med.* 7 (4) (2009) 301–305.
- [18] W.X. Liang, Problems-solving strategies in clinical treatment guideline for traditional Chinese medicine and integrative medicine, *Zhong xi yi jie he xue bao = J. Chin. Integr. Med.* 6 (1) (2008) 1–4.
- [19] Y. Yuwen, X. Han, N. Shi, et al., Appraisal of clinical practice guidelines for the management of rheumatoid arthritis in traditional Chinese medicine using the AGREE II instrument: a systematic review, *Eur. J. Integr. Med.* 6 (2) (2014) 176–185.
- [20] Z. et al. Wei Deng Le Li Wang, Using AGREE II to evaluate the quality of traditional medicine clinical practice guidelines in China, *J. Evid.-Based Med.* (2016).
- [21] SIGN 50: A Guideline Developer's Handbook. Scottish Intercollegiate Guidelines Network, 2001.
- [22] NICE, Process and Methods Guides: The Guidelines Manual, (2012).
- [23] WHO, Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: a World Health Organization Guideline, *Diabetes Res. Clin. Pract.* 103 (3) (2014) 341–363.
- [24] A. Qaseem, F. Forland, F. Macbeth, et al., Guidelines International Network: toward international standards for clinical practice guidelines, *Ann. Intern. Med.* 156 (7) (2012) 525–531.
- [25] S. Ansari, A. Rashidian, Guidelines for guidelines: are they up to the task? A comparative assessment of clinical practice guideline development handbooks, *PLoS One* 7 (11) (2012) 847–849 (3).
- [26] Y. Yuwen, N.N. Shi, L.Y. Wang, et al., Development of clinical practice guidelines in 11 common diseases with Chinese medicine interventions in China, *Chin. J. Integr. Med.* 18 (2) (2012) 112–119.
- [27] N. Shi, L.L. Zhong, X. Han, et al., Enhanced evidence-based Chinese medicine clinical practice guidelines in Hong Kong: a study protocol for three common diseases, *Evid.-Based Complement. Altern. Med.* 2015 (2015) 1–7.
- [28] B.J. Shea, J.M. Grimshaw, G.A. Wells, et al., Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews, *BMC Med. Res. Methodol.* 7 (2) (2007) 1–7.
- [29] J.P.T. Higgins, S. Green, *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0, The Cochrane Collaboration, 2011, 2016. <http://handbook.cochrane.org/>.
- [30] M. Malta, L.O. Cardoso, F.I. Bastos, et al., STROBE initiative: guidelines on reporting observational studies, *Revista De Saúde Pública* 44 (3) (2010) 559–565.
- [31] R.H. Savel, E.B. Goldstein, M.A. Gropper, Critical care checklists, the Keystone Project, and the Office for Human Research Protections: a case for streamlining the approval process in quality-improvement research, *Crit. Care Med.* 37 (2) (2010) 725–728.
- [32] G. Zheng, H. Guo, Y. Guo, et al., Two Dimensions Data Slicing Algorithm, a New Approach in Mining Rules of Literature in Traditional Chinese Medicine// Emerging Research in Artificial Intelligence and Computational Intelligence, Springer, Berlin, Heidelberg, 2011, pp. 161–174.
- [33] C.P. Ferri, M. Prince, C. Brayne, et al., Global prevalence of dementia: a Delphi consensus study, *Lancet* 366 (9503) (2005) 2112–2117.
- [34] P. Shekelle, S. Woolf, J.M. Grimshaw, et al., Developing clinical practice guidelines: reviewing, reporting, and publishing guidelines; updating guidelines; and the emerging issues of enhancing guideline implementability and accounting for comorbid conditions in guideline development, *Implement. Sci.* 7 (4) (2012) 1–7.