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How equity is addressed in clinical practice guidelines: a content analysis

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1) Conceiving and designing this review: Chunhu SHI, Jinhui TIAN and Kehu YANG,

2) Searching, extracting data and analyzing the data: Chunhu SHI, Quan WANG and Kehu YANG,

3) Writing and amending manuscript: Chunhu SHI, Jinhui TIAN, Dan REN and Jennifer O'Neill

4) When disagreements happened, discussing with Kehu YANG and Jinhui TIAN.

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6) Important comments and english editing: Jennifer O'Neill

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Abstract

Background

Clinical practice guidelines (CPGs) assist practitioner and patient decisions for specific clinical circumstances. The number of CPGs has increased dramatically and has focused on the effectiveness and cost-effectiveness of interventions to balance benefits versus harms and cost. However, equity rarely is addressed in CPGs. Incorporating equity into guidelines presents methodological challenges.

Objectives

To review the methods for incorporating equity in CPGs.

Design

We electronically searched Medline, retrieved references and browsed guideline development organization websites to identify eligible papers which provide a checklist/framework/tools/recommendations on when, how and to what extent equity should be incorporated in CPGs. No assessment of quality was conducted. After study selection by two authors, general characteristics and checklists items/framework components from included studies were extracted. Based on the questions or items from checklists/frameworks (unit of analysis), content analysis was conducted to identify themes and questions/items were grouped into these themes.

Results

10 papers were included from 3405 citations. In total, a list of 87 questions/items was generated from 17 checklists/frameworks. After content analysis, questions were grouped into 8 themes: 'scope', 'searching', 'formulate recommendations', 'appraisal', 'monitor implementation', 'assess the quality of CPGs', 'reporting' and 'the process to develop CPGs'. Four included checklists covered more than five of these themes. We also summarized the process of guideline development.

Conclusion

For targeted population specific CPGs, 'scope', 'searching', 'formulate recommendations', 'appraisal', 'monitor implementation', 'assess the quality of CPGs', 'reporting' and 'the process to develop CPGs' should be addressed when including equity in CPGs under the guidance of a scientific guideline development manual.

Strengths and limitations of this study

- Methodological challenges are the barriers of incorporating equity into guidelines. For this topic, this study synthesizes some themes (e.g. 'scope', 'formulate recommendations', 'searching', 'appraisal', 'monitor implementation', 'assess the quality of CPGs', and 'reporting') and a developing process through a content analysis of eight papers.
- These findings allow the guideline panel to consider equity issues into guidelines and contribute methodologists to develop a methodological document in future.
- These findings provide some valuable guidance, however no statement on methodological issues in equity or new checklist is built.

Background

Health is defined by the World Health Organization (WHO) as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"[1]. However,

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health interventions may create differences in health outcomes across socioeconomic, demographic and geographic factors, described as health inequalities. When these differences are avoidable, unnecessary and unjust they are described as health inequities [2,3]. The WHO recognizes that reducing inequities in health is important since health is a fundamental human right [4]. Inequities in health and health care are well documented in relationship to social and economic factors, including Place of residence (e.g. rural, urban, inner city, Race/ethnicity/culture/language, Occupation, Gender/sex, Religion, Educational, Socioeconomic status and Social capital (e.g. availability of neighborhood support, social stigma, civic society) (PROGRESS) [5]. Equity issues have been shown to have negative effects on health status [6,7]. For example, as Wallace et al. [8] reported, the HIV epidemic's structure in the US was influenced by two such determinants, the link between geographic regions and the socioeconomic structure, function, and history of the regions. Another example is that low birth weight can be predicted by socioeconomic status, especially poverty. [9] From the Global Burden of Disease (GBD) Study in 2010, age-specific, sex-specific and regional heterogeneity were severely highlighted in disability-adjusted life years (DALYs), causes of death, and mortality [10-12].

Clinical practice guidelines, as defined by the Institute of Medicine, are 'systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.' [13] They are an increasingly familiar part of clinical practice and may provide concise guidance on which assessment programs to order, how to provide medical or surgical interventions, or other details of clinical practice [14]. Guideline development is becoming more evidence-based [15].

Regardless of the setting, there is potential for the CPG to introduce inequities. Differences in health outcomes across population groups are possible if equity is not considered in guideline development and CPGs and their recommendations may create or increase health inequities [16]. The inclusion of equity considerations in CPG development and implementation has become increasingly important [17,18]. However, incorporating equity into guidelines remains a challenge; the main barriers are methodological and conceptual limitations [17,19]. In this paper we aimed to review methods for including equity considerations in CPGs.

Present investigation

Eligibility criteria

We conducted this review to investigate methodological guidance for including equity in CPGs. Only methodological guidance, guidelines, and articles that described when, how and to what extent equity issues could be incorporated in CPGs were included in this review.

Information sources and search

Relevant studies were obtained from the following sources.

1) MEDLINE (1966 to Jan 2013) was electronically searched using an adapted version of the search strategy developed by Haase A et al. (2007) for the identification of clinical practice guidelines [20]: (recommendation[All Fields] OR "consensus"[MeSH Terms] OR "consensus"[All Fields] OR "guideline"[Publication Type] OR "guidelines as topic"[MeSH Terms] OR "guideline"[All Fields]) AND (equal* OR equal[All Fields] OR "Civil Rights"[Mesh] OR equity[All Fields] OR equit*) limited in "Humans and Title/Abstract";
2) Relevant studies were retrieved from reference lists of eligible articles;
3) In Jan 2013, we browsed guidelines development organizations' websites including: National Institute for Health and Clinical Excellence (NICE), New Zealand Guidelines Group, Scottish

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Intercollegiate Guidelines Network, Guideline International Network (G-I-N), CMA Infobase: Clinical Practice Guidelines, PUBGLE, Trip Database, and National Guideline Clearinghouse, etc.;

4) Online publications from the 'International Journal for Equity in Health' (from 2002 to Jan 2013) was hand-searched;
5) We also emailed SIGN, the New Zealand Guidelines Group and National Guideline Clearinghouse, etc. to access specific documents.

Study selection and data collection process

Authors CHS and QW independently screened titles and abstracts. The full text (if published) of all potentially relevant studies were retrieved and independently assessed for inclusion by QW and KHY. CHS and KHY carried out data extraction independently using a standard data extraction form (Appendix 1: Data extraction form). We planned to translate papers reported in non-English language journals (if any) before assessment. Where more than one publication on the same guidance existed, only the publication with the most complete data was included. Any further information or clarification required from the authors was requested by written or electronic correspondence and relevant data obtained in this manner were included in the review. Disagreements were resolved in consultation among the authors.

Data items

In this review, data items are the questions or items from all available instruments, checklists, critical appraisal tools and indices which were designed to guide the incorporation of equity issues into CPGs or assessing the quality of CPGs within equity issues. No data on participants (P), interventions (I), comparators (C), clinical outcomes (O) and study designs (S) was extracted.

Synthesis of results

In this review, written documents and phrases were the unit of analysis so that no quantitative data were analyzed by specific software. Using content analysis, authors CHS and JHT synthesized methodological themes and processes on how to address equity issues in guideline development. Content analysis is 'a research technique for making replicable and valid inferences from data to their context.' [21], which 'emphasizes the quantification of the 'what' that messages communicate, the 'who' (the source), the 'why' (the encoding process) and the consequences of 'effects' they have 'on whom'' [21], by which themes can be summarized from meaningful qualitative data. A simplified process was used in this review: identifying units of analysis (the items/questions), excluding irrelevant information and abstracting the phrase or words from each unit of analysis, labeling these concepts, grouping and creating themes to link the underlying concepts together in categories. (Appendix 2: The process of content analysis) No additional analysis was used in this review.

Results

Guidance selection

We retrieved 3370 citations from MEDLINE. After reviewing titles and abstracts, 3353 were excluded. 23 additional citations were identified from the combined search of guideline development organization websites, the International Journal for Equity in Health and emailing guideline development organizations. After reviewing titles and abstracts, 17 papers were excluded. The full text-versions of 23 papers were obtained in total. After screening their reference lists, an additional 12 citations met our eligibility criteria. In total, 35 potentially relevant full texts were screened, out of which 25 full-texts were excluded. The major reason for exclusion was that

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the papers did not focus on methods for addressing equity in CPGs. Finally, 8 papers (from 10 documents) [16-18,22-28] were included in this review (Figure 1: Selection process of included studies).

Study characteristics

The characteristics of the included studies are reported in the table of characteristics of included studies (Table 1).

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Table 1 Characteristics of the included papers

Ref	Study	Journal/Sources	Publication type	Definition of equity	Scope	Targeted users	Funding
16	Eslava-Schmalbach J 2011	Rev. salud publica	Review	Casas-Zamora JA 2004, Whitehead M. 1992	Why, How	unclear	No declaration
18	Dans AM 2007	Journal of Clinical Epidemiology	Article	Braveman 2003, Whitehead 1992	Assessment	CPGs users	Rockefeller Foundation, Norwegian Health Services Research Center
22	Oxman AD 2006	Health Research Policy and Systems	Review	Braveman 2003, Whitehead 1992	When, What, How	CPGs developers	WHO, Norwegian Knowledge Centre for the Health Services
23	Acosta N 2011	Rev. salud publica	Review	None provided	How	CPGs developers	No declaration
24, 25	NICE 2012 & NICE 2012	NICE	Guideline	None provided	How	CPGs developers	No declaration
17, 26	Aldrich R 2003 & NHMRC 2002	BMJ & NHMRC	Article & Guideline	None provided	How	CPGs developers	No declaration
27	Keuken DG 2008	Dissertation	Dissertation	None provided	How	unclear	Netherlands Organization for Health Research and Development
28	WHO 2012	WHO	Guideline	None provided	How	CPGs developers	No declaration

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We included four guidelines or handbooks published by National Institute for Health and Clinical Excellence (NICE), the National Health and Medical Research Council (Australia, NHMRC) and WHO [24-26,28]. Six guiding reviews or original articles [16-18,22,23,27] were identified from Medline.
Three reports [16,18,22] defined equity issues according to definitions from Braveman (2003) [29], Whitehead (1992) [2] or Casas-Zamora JA (2004) [30]. Others did not provide a definition. For the scope of included studies, Eslava-Schmalbach J (2011) [16] focused on why equity issues should be addressed in CPGs; Oxman AD (2006) [22] focused on when to address them and what content should be addressed; Dans AM (2007) [18] focused on how to assess the quality of CPGs including equity; and seven studies [16,17,22-28] focused on how to address equity in CPGs. For targeted users, Dans AM 2007 [18] provided guidance to CPG users; five studies [17,22-26,28] aimed to provide guidance to CPG developers; and Keuken DG (2008) [27] and Eslava-Schmalbach J (2011) [16] did not provide any details. Five studies [16,17,23-26,28] did not provide details of financial support.
Keuken DG (2007) [27] provided recommendations only related to sex-related factors in guideline development. NICE (2012) [24,25] provided population characteristics on equity issues, equality in guideline development, a checklist for scoping, a checklist for early guideline development and a checklist for formulating recommendations. Dans AM (2007) [18] provided an equity lens to assess the quality of guidelines within equity issues. Focusing on the WHO guidelines, Oxman AD (2006) [22] reviewed related articles to provide guidance to address equity in guidelines. Eslava-Schmalbach J (2011) [16] described why equity issues should be addressed in guidelines. Acosta N (2011) [23] provided simple guidance for including equity in guidelines; NHMRC (2002) [26] and Aldrich (2003) [17] provided indicators and search terms for socioeconomic position and a framework for using evidence on socioeconomic position in the development of clinical practice guidelines. Rather than focusing on equity issues in particular, the WHO (2012) [28] provided advice on equity issues in 'PICO question components' and 'evidence retrieval and synthesis' sections.

Synthesis of results

In total, 87 questions/items were collected. After content analysis, 8 themes were identified: 'scope', 'formulate recommendations', 'searching', 'appraisal', 'monitor implementation', 'assess the quality of CPGs', 'reporting' and 'the process to develop CPGs'. (see Table 2: Summary of finding; Figure 2: The process of including equity in CPGs; Appendix 3: Content analysis of individual studies)

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Table 2 Summary of findings

Studies	Themes							
	Scope	Searching	Formulate recommendations	Appraisal	Monitor implementation	Assess the quality of CPGs	The process to develop CPGs	Reporting
Eslava-Schmalbach J 2011 [16]	√						√	
Dans AM 2007 [18]	√		√	√	√	√		
Oxman AD2006 [22]	√			√	√			
Acosta N 2011 [23]	√			√	√			
NICE 2012 [24] & NICE 2012 [25]	√	√	√	√			√	
Aldrich R 2003 [17] & NHMRC 2003 [26]	√	√	√	√	√		√	
Keuken DG 2007 [27]	√	√	√	√	√		√	√
WHO 2012 [28]	√	√						

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Scope

All 8 papers [16-18,22-28] reported the 'scope' of their paper. These included why it is necessary to address equity (the differential effectiveness across groups, negative impact of guideline without equity considerations and improving overall effectiveness of guideline within equity) [16], the presence of differential effects across groups (when to address equity) [22], targeted population, PROGRESS framework (what are social determinants of health) [5], and the changes and comments for scope [24,25].

Searching

Four of the included papers [17,24-28] described the 'searching' theme, including searching relevant study designs, changing search strategies, the usage of terms/markers for equity, the appraisal of eligibility criteria for 'searching' and providing an equitable search strategy.

Formulate recommendations

Four papers [17,18,24-27] reported how to formulate recommendations or what should be considered when formulating recommendations, including the balance between harms and benefits, formulating equitable recommendations (such as considering barriers and facilitators of interventions, and mitigating negative effects that may produce inequities during the formulation of recommendations), how to advance recommendations and adjust recommendations.

Appraisal

Six papers [17,18,22-27] fulfilled the 'appraisal' theme, including the appraisal of scientific evidence, such as the appraisal of appropriate modifiers, study design, sample size, analysis methods, the applicability and relevance of evidence, influence of equity evidences, the quality of evidence, the necessity of evidence and making changes and evidence gaps, as well as the appraisal of recommendations, such as the relevance of recommendations, the impact of recommendations and the quality of development process.

Monitor implementation

Five papers [17,18,22,23,26,27] described the 'monitor implementation' theme, including what should be considered during implementation and how to monitor implementation including:minimizing barriers to implementation, informing adaptation and decision making in some specific settings, developing an equitable implementation strategy, changing the organizational structure, and monitor the effects of implementation. When no evidence was found, changing search strategies, scope and promotion strategies were reported.

Assess the quality of CPGs

Dans AM (2007) [18] reported how to 'assess the quality of CPGs', including whether recommendations considered priorities for disadvantaged populations and factors to explore differential effects across groups during the scoping stage. The authors suggest assessing whether there are differential effects from the intervention across groups and considering these when formulating recommendations as well as addressing barriers to implementation and the impact of the recommendations.

Others

Keuken DG (2007) [27] reported the knowledge needs for the various ways of reporting guidelines. The authors stated that CPGs should highlight gender, and CPG developers should balance advantages and disadvantages of different reporting methods. Eslava-Schmalbach J (2011) [16] focused on why equity issues should be considered during the scoping stage. NICE (2012) [24,25] highlighted the need for engagement with stakeholders during every stage of the development

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process.

The process of including equity in CPGs

Four papers [16,17,24-27] reported on 'the process of developing CPGs', and included the following common steps: identifying questions, development of search strategies, appraisal of scientific evidence, synthesizing the evidence, formulation of recommendations and writing the guideline documents. These results and our findings mentioned above, indicate that CPG development requires an integrated process, including the following themes: 'scope', 'search', 'appraising scientific evidence', 'synthesizing the evidence', 'formulating recommendations', 'appraising recommendations', 'monitoring implementation', 'assessing the quality of CPGs', and 'appropriate reporting the documents' stages. (Figure 2: The process of including equity in CPGs)

Discussion

Summary of evidence

We identified eight papers focusing on how to address equity issues in guidelines. Eight themes were identified, which included 'scope', 'formulate recommendations', 'searching', 'appraisal', 'monitor implementation', 'assess the quality of CPGs', 'the process to develop CPGs' and 'reporting'. From these included checklists/frameworks, we found a few open questions which provided suggestions rather than items with appraisal functions and recommended frameworks. Few guidance documents described how to assess the quality of CPGs which considered equity issues in their recommendations, the process to develop CPGs, or how to report a guideline with equity considerations. Dans AM (2007) [18], NHMRC (2003) [26], Keuken DG (2007) [27], Aldrich R (2003) [17] and NICE (2012) [24,25] covered more than five themes. We summarized a process to develop guidelines which consider equity issues according to our findings and previously described frameworks.

All included papers reported the 'scope' theme. When a guideline is developed, a description of why equity should be considered needs to be based on the differential effectiveness of interventions between subgroups. The PROGRESS framework is recommended for identifying potentially disadvantaged groups when describing the scope of the CPG [5]. Four papers [17,24-28] described the 'searching' theme, but, only NICE (2012) [24,25] suggested the consideration of study design; and NHMRC (2003) [26] & Aldrich R (2003) [17] provided search terms on equity issues. Identifying evidence including systematic reviews, clinical practice guidelines, randomized controlled trials and supplementary literature is essential for guideline development. The search strategy must be transparent and reproducible. The reporting of databases, time periods, key words, subject headings, language restrictions, gray literature, and eligibility criteria should be considered [31].

Before formulating recommendations, the quality of scientific evidence must be appraised by respective appraisal tools to variable evidence classifications. The relevance, applicability, impacts of evidence on equity needs and evidence gaps should be assessed. For quality of guidelines, the guideline panel should use the Appraisal of Guidelines Research & Evaluation (AGREE) instrument (which includes the following domains: explicit scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence [32]) to check whether equity issues have been considered appropriately. When evidence gaps exist, expert opinion or consensus is necessary to allow guideline developers to highlight future research needs [31]. NHMRC (2003) [26] & Aldrich R (2003) [17] provide strategies that can be used if no evidence is available, including changing the search strategy. For specific

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subgroup populations, guideline developers should counterpoise harms and benefits of interventions, consider barriers and facilitators of interventions, and adjust recommendations for specific settings. Furthermore, comments from relevant stakeholders and adaption are necessary. Only Dans AM (2007) provided an equity lens to appraise the quality of guideline with equity considerations. For the development of a guideline, we suggest that a well-designed handbook such as the 'WHO handbook for guideline development' [28], 'SIGN 50 A guideline developer's handbook' [33], 'Handbook on Clinical Practice Guidelines' [34] or NICE 'the guidelines manual 2012' [24] is utilized. The process of guideline development outlined in this paper will be more effective when used in combination with the handbooks mentioned above.

Limitations

With the comprehensive search strategy, only 8 papers (containing 87 questions or items) were included in this review. However, compared to previous reviews [23], our study includes a wider collection of handbooks and guidance documents. Although Acosta N (2011) included 20 studies (of which only three [18,22,26] were included in our review), [23] the authors only discussed equity in the development of clinical practice guidelines with a narrative literature review. We have extracted the methodological checklists/frameworks from the eligible studies. Content analysis was used because of its methodological characteristics and reliable measures to achieve trustworthiness [35]. However, a limitation of content analysis itself is that the likelihood of replicability for the analysis procedure is low [21].

Conclusions

By reviewing the existing guidance documents and guidelines, eight themes, 'scope', 'formulate recommendations', 'searching', 'appraisal', 'monitor implementation', 'assess the quality of CPGs', 'the process to develop CPGs' and 'reporting' were identified for guiding the incorporation of equity issues into clinical practice guidelines. Among existing checklists, Keuken DG (2007) [27] and NHMRC (2003) [26] covered most of these themes and have the greatest potential to be used as a tool for guiding equity considerations in guidelines. No grading systems or scoring criteria were found from existing checklists.

Contributors All authors contributed to the manuscript. CHS, JHT and KHY conceived and designed this review; CHS, QW and KHY searched extracted data and analyzed the data; CHS, JHT, DR and JO wrote and amended manuscript; we discussed with KHY and JHT when disagreements happened; JO did important comments and English editing.

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Data sharing statement No additional data available.

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Figure 1 Selection process of included studies

Figure 2: The process of including equity in CPGs

Appendix 1 Data extraction form

Appendix 2 The process of content analysis

Appendix 3 Content analysis of individual paper

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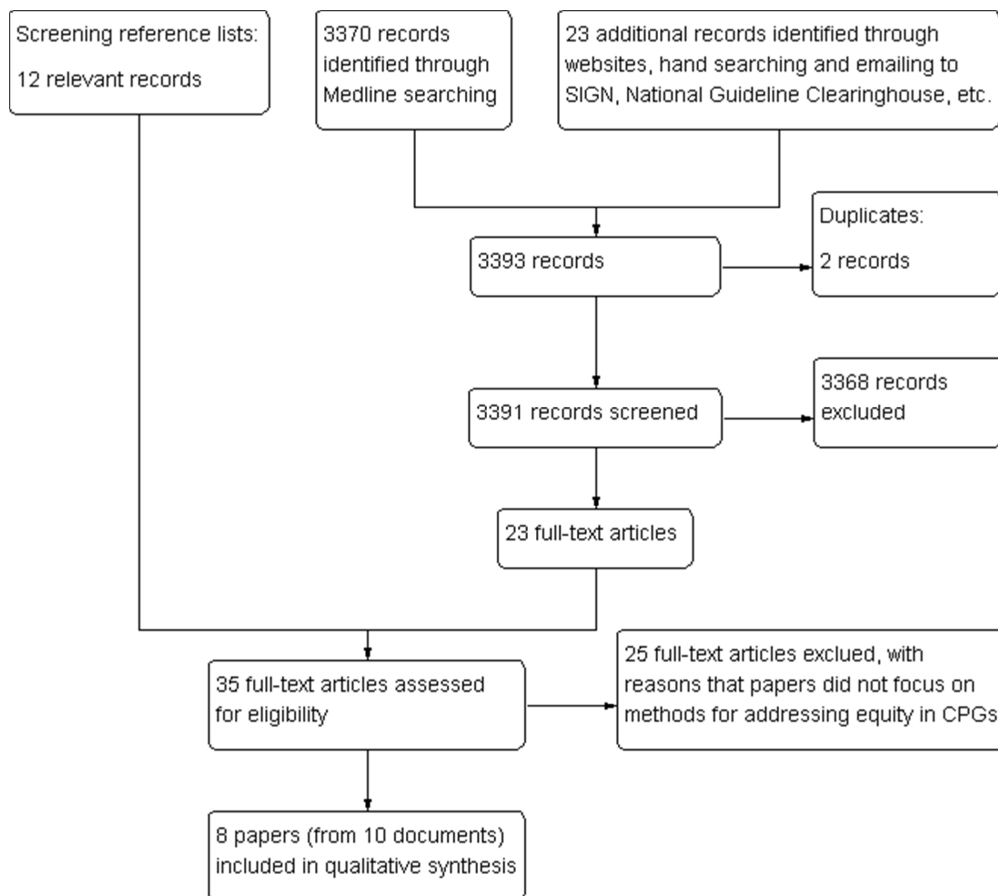

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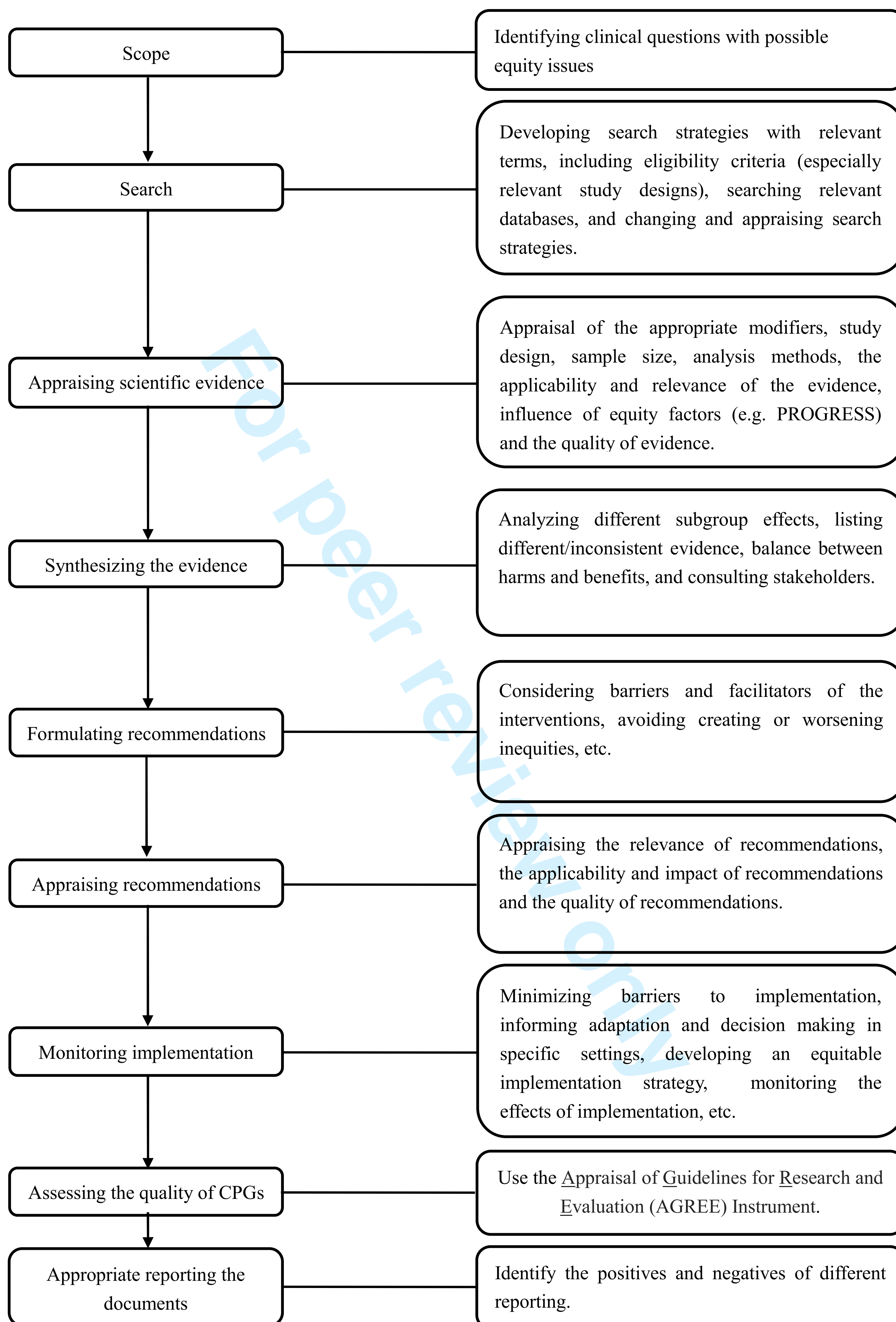
Figure 2: The process of including equity in CPGs



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Appendix 1 Data extraction form

ID	**Answers**
Date	__/__/__ (M/D/Y)
Reviewers	________________
Study details	**Descriptions**
Title	
First author	
Year of publication	
Journal's name	
Information type	Please specify:

Checklists or frameworks, etc for content analysis	
No.	**Checklists items/frameworks components**
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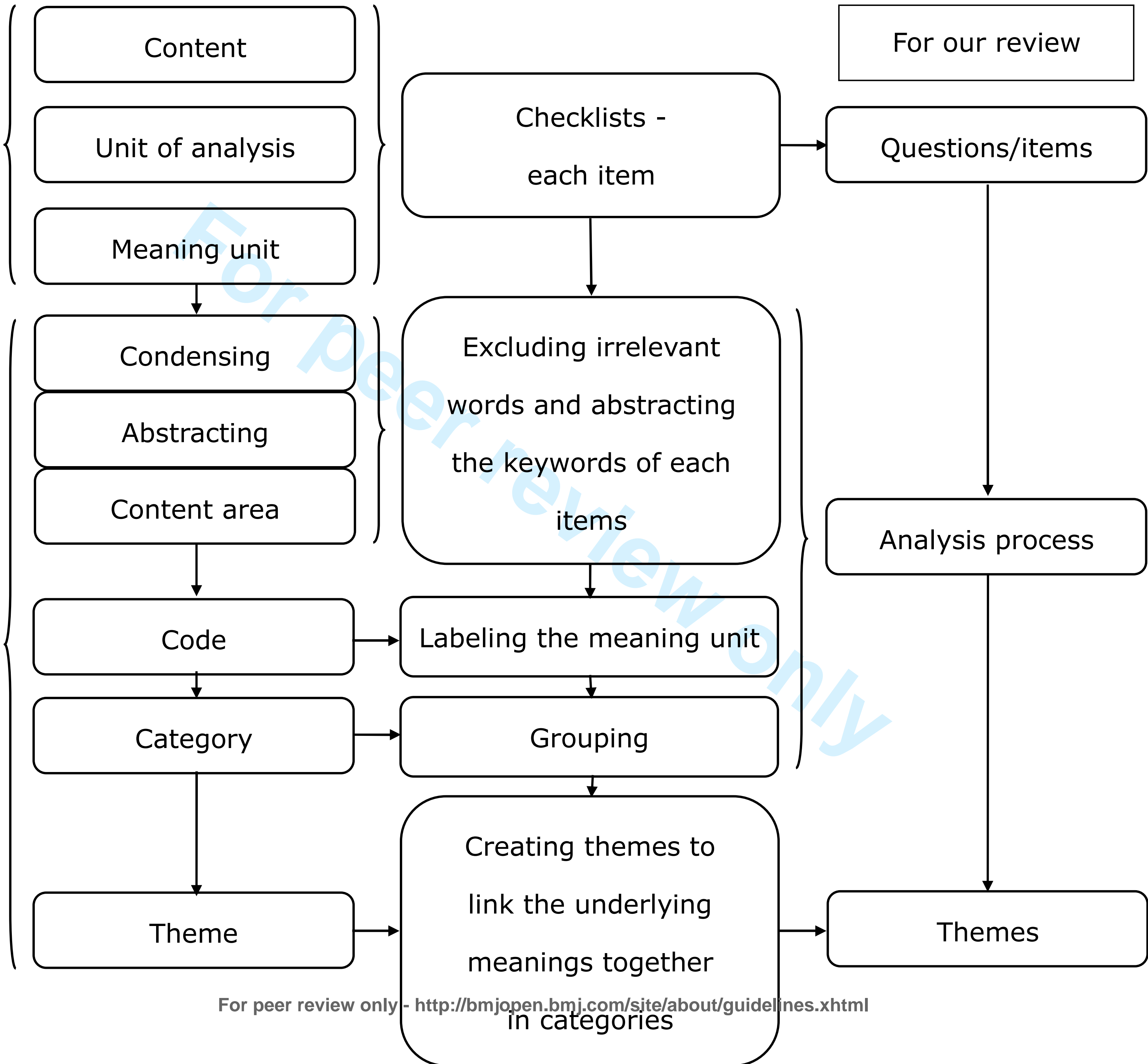
Appendix 2 The process of content analysis



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Appendix 3 Content analysis of individual paper

Eslava-Schmalbach J 2011 [16]

Items	Categories	Coding	Themes
1. Differential effectiveness by social groups of interventions could diminish final effectiveness of CPG in the General Social Security and Health System (GSSHS);	The negative impact of differential effectiveness across groups	Reasons for addressing equity in guideline	Scope
2. To not consider geographical, ethnic, socioeconomic, cultural and access diversity issues within the CPG could have a potential negative impacts of the CPG;	The negative impact regardless of equity issues	Why to address equity into guideline	Scope
3. Overall effectiveness of GPC could be better if equity issues are included in the quality verification checklist of the guideline questions;	Better effectiveness of guideline when equity is included	Why to address equity into guideline	Scope
4. Incorporating equity issues in the process of developing CPG could be cost effective, because improve overall effectiveness of CPG.	Improving overall effectiveness of guideline	Why to address equity into guideline	Scope

Note: This article discussed why equity issues should be addressed into guidelines

Dans AM 2007 [18] The equity lens

Items	Categories	Coding	Themes
1. Do the public health recommendations in the guidelines address a priority problem for disadvantaged populations?	Priorities for disadvantaged populations	Equity issues	Scope
2. Is there a reason to anticipate different effects of intervention in disadvantaged and privileged populations?	Factors to explore differential effects across groups	Equity issues	Scope
3. Are the effects of the intervention valued differently by disadvantaged compared with privileged populations?	Differential effects from evidences across groups	Formulating recommendation, appraisal of the scientific evidence	Appraisal, formulating recommendations
4. Is specific attention given to minimizing barriers to implementation in disadvantaged populations?	Minimizing barriers to implementation	Implementation	Implementation
5. Do plans for assessing the impact of the recommendations include disadvantaged populations?	Assessing the impact of recommendations	Appraisal of recommendation	Appraisal

Note: Providing some examples on how to address equity into guideline.
This article provided a lens to assess the quality of guideline which addressed equity issues.

Oxman AD 2006 [22]

Items	Categories	Coding	Themes

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1. When and how should inequities be addressed in systematic reviews that are used as background documents for recommendations? The following question should routinely be considered: are there plausible reasons for anticipating differential relative effects across disadvantaged and advantaged populations? If there are plausible reasons for anticipating differential effects, additional evidence should be included in a review to inform judgments about the likelihood of differential effects.	Differential effects across groups is indicated to address equity	When to address equity	Scope
2. What questions about equity should routinely be addressed by those making recommendations on behalf of WHO? (the following additional questions should routinely be considered)	Equity issues	Equity issues	Scope
How likely is it that the results of available research are applicable to disadvantaged populations and settings?	Assessing applicability of available evidence	Appraisal of scientific evidence	Appraisal, scope
How likely are differences in baseline risk that would result in differential absolute effects across disadvantaged and advantaged populations?	Assessing effects of baseline risk across groups	appraisal the difference between groups	Appraisal, scope
How likely is it that there are important differences in trade-offs between the expected benefits and harms across disadvantaged and advantaged populations?	Assessing the balance between benefits and harms across groups	Appraisal the needs of evidences	Appraisal, scope
Are there different implications for disadvantaged and advantaged populations, or implications for addressing inequities?	Assessing the needs of evidence implications	Appraisal the needs of evidences	Appraisal, scope
3. What context specific information is needed to inform adaptation and decision making in a specific setting with regard to impacts on equity?	Informing adaptation and decision making		
Those making recommendations on behalf of WHO should routinely consider and offer advice about the importance of the following types of context specific data that might be needed to inform adaptation and decision making in a specific setting: Effect modifiers for disadvantaged populations and for the likelihood of differential effects; Baseline risk in relationship to social and economic status; Utilization and access to care in relationship to social and economic status; Costs in relationship to social and economic status; Ethics and laws that may impact on	Effect modifiers, baseline risk, access to interventions, costs, ethics and availability of resources should be used to inform adaptation	Implementation of guidelines in specific setting	Implementation

strategies for addressing inequities; Availability of resources to address inequities.			
4. What implementation strategies are likely be needed to ensure that recommendations are implemented equitably?	Equitable implementation strategy	Implementation	Implementation
Organizational changes are likely to be important to address inequities. While it may only be possible to consider these in relationship to specific settings, consideration should be given to how best to provide support for identifying and addressing needs for organizational changes. In countries with pervasive inequities institutional, cultural and political changes may first be needed.	Organizational changes		
Appropriate indicators of social and economic status should be used to monitor the effects of implementing recommendations on disadvantaged populations and on changes in social and economic status.	Monitor the effects of implementation		
5. What 'maps' are available of the different dimensions of inequity locally?	Appraisal of local setting inequities	Implementation	Implementation
Note			
Acosta N 2011 [23]			
Items	Categories	Coding	Themes
1. Target population involvement during all phases of designing, implementing and evaluating CPG;	Equity is necessary to all phases of the development process	Appraisal of the quality of development process	Appraisal
2. "Cultural capacity" seen as being necessary in CPGs' "cultural translation" for interventions to have less disparity regarding their application and results;	Cultural capacity is necessary for guideline	Equity issues	Scope
3. Considering psycho-social factors which could affect implementing CPG;	Psycho-social factors, facilitators of implementation	Equity issues, implementation	Scope, implementation
4. Considering system inequities so that any health intervention would also confront risks and obstacles to health care due to socioeconomic status.	Socioeconomic status	Equity issues	Scope
Note			
NICE 2012 [24, 25]			
Items	Categories	Coding	Themes
The protected characteristics; Equality in guideline development			

The protected characteristics are: age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex, sexual orientation, marriage and civil partnership, socio-economic, other	Population characteristics on equity issues	Equity issues	Scope
Checklist for scoping			
1. What are the potential equality or discrimination issues linked to the guideline topic?	Equity issues	Equity issues	Scope
Are there inequalities in prevalence, risk factors or impact - or in use or benefit - related to the topic or intervention?	Equity in prevalence or risk factors	Equity issues	Scope
Is the condition more common, or is its severity greater, in people from a specific group or with a particular disability?	Prevalence of equity condition	Equity issues	Scope
Is there a risk of discrimination?	Equitable scoping	Equitable scoping	Scope
Do comments from stakeholders highlight the potential for direct or indirect discrimination, or for promoting equality?	Comments on equity issues	Comments for scoping	Scope
2. Should any changes be made to the scope?	Considering factors on changes in scope	Changes on scope	Scope
Consider the degree of relevance to equality, and the proportionate response in relation to this. The greater the relevance of a function t equality, the greater the regard that should be paid to equality issues.	Considering relevance of equity to change scope		
Consider the views of stakeholders.	Considering comments from stakeholders		
Summarize any changes made at this stage.	Summarize changes		
Identify any information gaps that have been identified.	Identify evidence gaps		
3. As it currently stands, is the scope discriminatory?	Considering some factors on scoping	Equitable scoping	Scope
Have groups who need special consideration been identified?	Identify potential special groups		
Are there any exclusions?	Exclusion criteria		
If there are exclusions, are the reasons legitimate, and is the exclusion proportionate?	Equitable and appropriate exclusion		
4. Should any further information be identified and assessed?	Identifying and assessing further information	Consulting comments in scoping stage	Scope
Have important stakeholders been omitted from or not responded to the consultation process?	Consulting stakeholders' comments		
Consider specific questions for stakeholders (for example, at the scoping workshop).	Consulting stakeholders' comments		
Summarize the action to be taken.	Taking action		
5. Is there anything specific that should be done to ensure that the guideline development group (GDG) will have	Considering other specific questions	Specific questions in scoping stage	Scope

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relevant information to consider equalities issues when developing guidance?			
Action to address this needs only to be proportionate.	Appropriate action		
Consider specific questions for stakeholders.	Consider specific questions for stakeholders		
Consider relevant bodies to consult.	Consulting relevant bodies		
Checklist for early guideline development			
1. How relevant is the evidence to eliminating discrimination, advancing equality and fostering good relations?	Relevance of evidence	Appraisal of scientific evidence	Appraisal
2. Do the review questions reflect the scope? Do they identify issues affecting specific groups?	Effectiveness of clinical questions	Appraisal of effects on scoping	Appraisal
3. Was the search strategy comprehensive? Consider a range of study of types for addressing the review questions (such as qualitative studies).	Comprehensive search strategy (appropriate study design)	Appraisal of search strategy	Appraisal, searching
4. Were particular issues identified during consultation on the scope? Consider amending the search strategy in the light of comments.	Considering comments to change search strategy to collect necessary evidence	Appraisal of the necessary on evidence and making changes	Appraisal
5. Were the evidence review criteria inclusive? Check that criteria do not inappropriately exclude studies on specific groups.	Appropriate and inclusive criteria of eligibility studies	Appraisal of eligible criteria	Appraisal, searching
6. What is the state of the evidence base? Where are the evidence gaps?	Evidence gaps and evidence state	Appraisal of evidence gaps	Appraisal
Checklist for formulating recommendations			
General questions			
1. How relevant are the recommendations to discrimination and equality? Which recommendations are likely to be most relevant?	Relevance of recommendations to equity	Appraisal the relevance of recommendations	Appraisal
2. Where evidence is unavailable to assess a potential issue, could this be reflected in recommendations for future research?	Addressing the case where evidence is unavailable	Appraisal of evidence gaps	Appraisal
Questions to consider to avoid discrimination include:			
Summarizing the following questions:	Access of interventions, barriers and facilitators of interventions, and appraisal of the access to avoid inequity during formulating recommendations	Formulating equitable recommendations	Formulating recommendations
1. Does access to the intervention depend on membership of	Access to the intervention and specific group		

a specific group?			
2. Do any criteria make it easier or more difficult in practice for people in a specific group to gain access to the intervention?	Barriers and facilitators of the access of interventions		
3. Does the way in which people would be assessed for whether or not they receive the intervention make it easier or more difficult for people in a specific group to gain access to it?	Assessing the barriers and facilitators of the access of interventions		
4. Does any part of the recommendation make it plausible that a person's age, disability, gender reassignment, pregnancy and maternity, marriage or civil partnership, race (including ethnic or national origins, color or nationality), religion or belief (including lack of belief), sex, sexual orientation or socioeconomic status could affect their access to an intervention? If so, what steps could be taken to address this?	Effects of equity on access to interventions		
5. Does any recommendation refer to age? If so, is age a good indicator of either risk or benefit from treatment and is the reason for the reference explained?	Effects of age on recommendations		
6. Do comments from stakeholders highlight areas of possible discrimination or ways of avoiding it?	Comments		
Questions to consider to advance equality of opportunity include:			
Summarizing the following questions:	Assessing and advancing the effectiveness and availability of recommendations, and access to interventions	Appraisal and advancing recommendations	Appraisal, formulating recommendations
1. Could the recommendations advance equality for people in a specific group, either through access to the intervention or by means of the intervention? Have stakeholders identified particular opportunities?	Advancing equity		
2. Could the recommendations be reformulated to make implementation more acceptable to, or appropriate for, people in a specific group?	Change of recommendations		
3. Would more favorable treatment of any kind help disabled people to gain access to the intervention on the same basis as people without that disability? What additional measures would achieve this?	Equitable access to interventions		
4. Do comments from stakeholders highlight opportunities	Comments		

for advancing equality?			
Questions to consider to foster good relations include:			
1. Is there an opportunity to tackle prejudice? 2. Is there an opportunity to promote understanding? 3. Do comments from stakeholders highlight the need for tackling prejudice or promoting understanding?	Foster relations of recommendations with equity	Adjusting recommendations	Formulating recommendations

Note: Describing a process of development: topic scoping, assessing the evidence, draft guideline, final guideline.
Providing some examples on how to addressing equity into guidelines

Aldrich 2003 [17], NHMRC 2002 [26]

Items	Categories	Coding	Themes
SEP refers to the components of economic and social well-being in a societal context. It is a concept that includes both: resource-based measures such as income and educational qualifications; and prestige-based measures such as an individual's rank or status in a social hierarchy, for example the prestige associated with certain occupations.	Definitions of SEP	Equity issues	Scope
Table 2: Markers and search terms for socioeconomic position	Providing some markers and search terms for socioeconomic position	Search terms	Search
Socioeconomic status as an effect modifier in RCTs	Assessing the impact of SEP and health in RCTs.	Appraisal scientific evidence	Appraisal
Problems in extrapolation of RCTs to disadvantaged populations. "Randomized controlled trials frequently use homogeneous population samples and analyze the effects of simple, single interventions. Factors associated with consent, inclusion and exclusion are not always randomly distributed."	Baseline characteristics and eligibility criteria in evidence body	Targeted population	Scope
Assessing the quality of evidence on SEP. 'evidence exists on the various relationships between SEP and health in epidemiological, cohort, cross-sectional, observational, and qualitative studies.'	Assessing the quality of evidence	Appraisal of scientific evidence	Appraisal
Literature review on the relationship between socioeconomic position and health and clinical practice guidelines. 'Guideline developers explicitly acknowledge evidence of the relationship between SEP and health and then use that evidence to shape and develop guidelines and associated	Showing evidence on why equity should be addressed into guideline	Necessary of equity	Scope

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recommendations for the broad population.'

A framework for using evidence on socioeconomic position in the development of clinical practice guidelines

Summarizing the following items	Framework	Framework	Process
Step 1: Identify the health decisions required.			
The health decision could be any type, from individual treatment decisions to the formulation of guidelines for whole communities. In the context of CPG development, there may be many decisions at different points in the diagnosis/ treatment pathway for a single guideline.	Clinical decisions required	Equity issues	Scope
Step 2: Search the literature for evidence that, due to SEP, population subgroups may experience barriers to and/or have limited capacity or opportunities to achieve equal health gains.			
The literature should be searched using markers of SEP, the condition or disease of interest, and the required health decision to identify population sub-groups which may experience barriers, limited capacity or opportunities to achieve the same health gains as other sub-groups or populations.	Searching evidence on equity	Equitable searching	Searching
Step 3: Search the literature to identify interventions that address barriers and/or opportunities to achieving equal health gains			
Literature describing interventions that attempt to address barriers to achieving equal health gains across sub-groups should be identified.	Searching and assessing equitable evidence on application	Appraisal of applications and searching evidences	Searching, appraisal
Step 4: Synthesize evidence from Steps 2 and 3 and current clinical best practice evidence to develop recommendations			
Develop recommendations in order to achieve health gains in terms of mortality, morbidity, survival, well-being and equity.	Formulating equitable recommendations	Formulating recommendations	Formulating recommendations
Other			
What to do when there is no evidence: broadening the search strategy; broadening the search scope; applying generic principles to promote health equity	Change searching strategies, scope, and promotion strategies, when no evidence was found	Searching and implementation	Searching, implementation
Note: Providing a process of guideline development			
Providing some examples and case study on how to develop guideline.			

Keuken DG 2007 [27]	Recommendation for focusing on sex-related factors in guideline development		
Items	Categories	Coding	Themes
Formulation of initial key questions (and sub questions)			
Guideline developers should make an assessment to determine if there are any plausible reasons for anticipating differential	Considering differential relative effects across gender	Social determinants of target population	Scope

relative effects for both sexes. If so, make sure that the key questions are formulated clearly to facilitate a review of the literature.			
Development of search strategies			
Guideline developers should make sure that search strategies are capable of detecting evidence (both direct and indirect) that supports or refutes any hypothesized differential effects.	Importance of an equitable search strategy	Search strategy	Search strategy
Appraisal of scientific evidence			
Guideline developers should determine whether the studies they review are well designed.	Well designed studies	Assessing study design	Appraisal
Guideline developers should determine whether the study population is stratified and whether it is sufficiently large for an analysis of differential effects on the basis of sex.	Large sample size for analysis across gender	Appraising sample size	Appraisal
Guideline developers should determine whether the relevant subgroup analyses have been carried out correctly (in key studies).	Correctly subgroup analysis	Appraising analysis methods	Appraisal
Guideline developers should determine whether sex is a modifier for the research outcome.	Sex as a modifier	Detecting modifiers	Appraisal
Formulation of recommendations for the guideline			
Where appropriate, guideline developers may consider how likely it is that the results of published research are applicable to both men and women when formulating recommendations.	Applicability of study results	Applicability of evidence	Appraisal of scientific evidence
Where appropriate, guideline developers may consider how likely it is that differences in baseline risk would result in differential absolute effects when formulating recommendations.	Influences across baseline risk on absolute effects	Influence of equity evidences	Appraisal of scientific evidence
Where appropriate, guideline developers may consider how likely it is that there are important differences in trade-offs between any anticipated harmful and beneficial effects when formulating recommendations.	Balance between harms and benefits	Balance between harms and benefits	Formulate recommendations
Where appropriate, guideline developers may consider whether any of these considerations warrant the use of different recommendations when formulating recommendations.	Warrant on the usage of different recommendations	Equitable usage of recommendations	Monitor implementation
Other (For composition of the guideline document)			
Guideline developers should have prior knowledge of the various ways in which sex-related factors can be represented	Knowledge of the various ways on reporting guidelines	Variable reporting	Reporting

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in guidelines: when evidence has been found; if differences were expected but no evidence was found; if no information is available.			
Selected sex-related factors may be mentioned in various subsections of the document: throughout the text; in specific paragraphs; in a subsection on special populations; in footnotes.	Highlighting the gender factor	Reporting	Reporting
It is useful to reflect on the advantages and disadvantages of each option before drafting the guideline.	Trade-offs between advantages and disadvantages of different reporting.	Assessing equitable reporting	Reporting
Note: Describing a process of development: formulation of initial key questions (and sub questions); development of search strategies; appraisal of scientific evidence; formulation of recommendations for the guideline; composition of the guideline document.			

WHO 2012 [28]

Items	Categories	Coding	Themes
Who is targeted by the action being recommended? (1) How can they be best described? What are the relevant demographic factors? Please consider age groups, sex, ethnicity, social identities, behavioral characteristics, etc. (2) What is the setting? For example, hospitals, communities, schools. (3) Are there any subgroups that might need to be considered? (4) Are there groups or subgroups that should be excluded?	Population characteristics (including equity issues), subgroup and exclusion criteria	Equity issues	Scope
'Figure 6.1 Evidence retrieval decision diagram' provided a process on how to identify relevant systematic review, including social and educational policies and practices (the Campbell Collaboration). Eligibility studies from low- and middle-income countries and regional databases are highlighted in 'Search strategies' section.	Searching relevant studies to equity	Searching	Searching
Note: Providing some examples on how to address equity issues into guidelines. Providing a process of developing questions: Step 1: Generate initial list of questions; Step 2: Draft PICO questions; Step 3: List relevant outcomes; Step 4: Comment and revise; Step 5: Rate outcomes; Step 6: Prioritize questions			

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Text S1 - Checklist of items to include when reporting a systematic review or meta-analysis

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2，3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3，4

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Section/topic	#	Checklist item	Reported on page #
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3， 4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	No. Unnecessary
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	No. Unnecessary
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	4
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	No. Unnecessary
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	No. Unnecessary
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	4， 5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	No. Unnecessary
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	No. Unnecessary
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and	5， 6

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Section/topic	#	Checklist item	Reported on page #
		measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	No. Unnecessary
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	No. Unnecessary
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	6，7
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	7，8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	8

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How equity is addressed in clinical practice guidelines: a content analysis

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How equity is addressed in clinical practice guidelines: a content analysis

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2) Searching, extracting data and analyzing the data: Chunhu SHI, Quan WANG and Kehu YANG,

3) Writing, amending and revising manuscript: Chunhu SHI, Jinhui TIAN, Dan REN, Jennifer Petkovic and Yang Yang,

4) When disagreements happened, discussing with Kehu YANG and Jinhui TIAN.

5) Final approval of manuscript: Chunhu SHI, Jinhui TIAN, Quan WANG, Dan REN, Jennifer Petkovic, Kehu YANG and Yang Yang,

6) Important comments and English editing: Jennifer Petkovic and Yang Yang

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Abstract

Objectives

Considering equity into guidelines presents methodological challenges. This study aims to qualitatively synthesize the methods for incorporating equity in CPGs.

Setting

Content analysis of methodological publications.

Eligibility criteria for selecting studies

Methodological publications were included if they provided checklists/frameworks on when, how and to what extent equity should be incorporated in CPGs.

Data sources

We electronically searched Medline, retrieved references, and browsed guideline development organization websites from inception to Jan 2013. After study selection by two authors, general characteristics and checklists items/framework components from included studies were extracted. Based on the questions or items from checklists/frameworks (unit of analysis), content analysis was conducted to identify themes and questions/items were grouped into these themes.

Primary outcomes

The primary outcomes were methodological themes and processes on how to address equity issues in guideline development.

Results

8 studies with 10 publications were included from 3405 citations. In total, a list of 87 questions/items was generated from 17 checklists/frameworks. After content analysis, questions were grouped into 8 themes ("scoping questions", "searching relevant evidence", "appraising evidence and recommendations", "formulating recommendations", "monitoring implementation", "providing a flow chart to include equity in CPGs", and "others: reporting of guidelines and comments from stakeholders" for CPG developers and "assessing the quality of CPGs" for CPG users). Four included studies covered more than five of these themes. We also summarized the process of guideline development based on the themes mentioned above.

Conclusion

For disadvantaged population-specific CPGs, eight important methodological issues identified in this review should be considered when including equity in CPGs under the guidance of a scientific guideline development manual.

Strengths and limitations of this study

- Methodological challenges are the barriers of incorporating equity into guidelines. For this topic, this study synthesizes some themes ("scoping questions", "searching relevant evidence", "appraising evidence and recommendations", "formulating recommendations", "monitoring implementation", "providing a flow chart to include equity in CPGs", and "others: reporting of guidelines and comments from stakeholders" for CPG developers and "assessing the quality of CPGs" for CPG users) and a developing process through a content analysis of eight studies.
- These findings allow the guideline panel to consider equity issues into guidelines and contribute methodologists to develop a methodological document in future.
- These findings provide some valuable guidance, however no statement on methodological issues in equity or new checklist is built.

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Background

Health is defined by the World Health Organization (WHO) as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"[1]. Health outcomes can be influenced by inaccessibility to health interventions for certain population groups, such as the poor and because of unequal distribution of medical resources. When differences in health outcomes across socioeconomic, demographic and geographic factors are avoidable, unnecessary and unjust they are described as health inequities [2,3]. The WHO recognizes that inequities in health should be reduced since health is a fundamental human right [4] and, in 2005,set up the Commision on Social Determinants of Health to collect, collate, and synthesize evidence on inequities and to make recommendations for action to address them [5].

Inequities in health and health care are well documented in relation to social and economic factors, according to the actronym PROGRESS-Plus, including Place of residence, Race/ethnicity/culture/language, Occupation, Gender/sex, Religion, Education, Socioeconomic status and Social capital [6] and additional factors related to personal characteristic, features of relationships, and time-dependent characteristics (captured by "Plus")[7]. Equity issues have been shown to have negative effects on health status [8-13]. For example, as Wallace et al. [14] reported, the HIV epidemics structure in the US was influenced by two such determinants, the link between geographic regions and the socioeconomic structure, function, and history of the regions.

Clinical practice guidelines, as defined by the Institute of Medicine, are 'systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.' [15] They are an increasingly familiar part of clinical practice and may provide concise guidance on which assessment programs to order, how to provide medical or surgical interventions, or other details of clinical practice [16]. Guideline development is becoming more evidence-based [17]. CPGs advocate that the most effective therapies are recommended as suggested by the evidence, however, the most effective intervention may not be available to all groups within a population. For example, a new therapy may be effective, but CPG developers need to consider whether it is available (and sufficiently cost-effective) for disadvantaged populations [18].

Therefore, CPG developers should discuss whether recommendations can ensure equitable provision of health care for the disadvantaged. Regardless of the setting, there is potential for the CPG to introduce inequities. Differences in health outcomes across population groups are possible if equity is not considered in guideline development. CPGs and their recommendations have the potential to create or increase health inequities [19]. The inclusion of equity considerations in CPG development and implementation has become increasingly important [20, 21]. For example, to balance the effective versus efficiency dilemma of CPGs, the National Health Service (NHS) recommends the development of guiding principles to support the pursuit of equity in health care [22]. However, incorporating equity into guidelines remains a challenge; the main barriers are methodological and conceptual limitations [20, 23]. We aimed to review methods for including equity considerations in CPGs in this paper.

Present investigation

Eligibility criteria

We conducted this review to investigate methodological guidance for including equity in CPGs. Only methodological guidance, guidelines, and articles that described when, how and to what extent equity issues could be incorporated in CPGs were included in this review. Types of eligible

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studies included: guidelines for incorporating equity into CPGs, empirical literature discussing equity-specific methodological issues of CPG development, quantitative or qualitative literature reviews that identify equity-specific methodological elements of CPG development.

Information sources and search

Relevant studies were obtained from the following sources.

1) MEDLINE (1966 to Jan 2013) was electronically searched using an adapted version of the search strategy developed by Haase A et al. (2007) for the identification of clinical practice guidelines [24]: (recommendation[All Fields] OR "consensus"[MeSH Terms] OR "consensus"[All Fields] OR "guideline"[Publication Type] OR "guidelines as topic"[MeSH Terms] OR "guideline"[All Fields]) AND (equal* OR equal[All Fields] OR "Civil Rights"[Mesh] OR equity[All Fields] OR equit*) limited in "Humans and Title/Abstract";
2) Relevant studies were retrieved from reference lists of eligible articles;
3) In Jan 2013, we browsed guideline development organizations' websites including: National Institute for Health and Clinical Excellence (NICE), New Zealand Guidelines Group, Scottish Intercollegiate Guidelines Network (SIGN), Guideline International Network (G-I-N), CMA Infobase: Clinical Practice Guidelines, PUBGLE, Trip Database, and National Guideline Clearinghouse, etc.;
4) Online publications from the 'International Journal for Equity in Health' (from 2002 to Jan 2013) was hand-searched;
5) We also emailed SIGN, the New Zealand Guidelines Group and National Guideline Clearinghouse, etc. to access specific documents.

Study selection and data collection process

Authors CHS and QW independently screened titles and abstracts. The full text (if published) of all potentially relevant studies were retrieved and independently assessed for inclusion by QW and KHY. CHS and KHY carried out data extraction independently using a standard data extraction form (Appendix 1: Data extraction form). We planned to translate papers reported in non-English language journals (if any) before assessment. Where more than one publication on the same guidance existed, only the publication with the most complete data was included. Any further information or clarification required from the authors was requested by written or electronic correspondence and relevant data obtained in this manner were included in the review. Disagreements were resolved in consultation with co-authors.

Data items

In this review, data items are the questions or items from all available instruments, checklists, critical appraisal tools and indices which were designed to guide the incorporation of equity issues into CPGs or assessing the quality of equity considerations within CPGs. No data on participants, interventions, comparators, clinical outcomes and study designs was extracted.

Synthesis of results

Written phrases were the unit of analysis and therefore no quantitative data were analyzed by specific software. Using content analysis, authors CHS and JHT synthesized methodological themes and processes on how to address equity issues in guideline development. Content analysis is 'a research technique for making replicable and valid inferences from data to their context.' [25], which 'emphasizes the quantification of the 'what' that messages communicate, the 'who' (the source), the 'why' (the encoding process) and the consequences of 'effects' they have 'on whom'' [25], by which themes can be summarized from meaningful qualitative data. A simplified process

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was used in this review: identifying units of analysis (the items/questions), excluding irrelevant information, abstracting the phrase or words from each unit of analysis, labeling these concepts, grouping them, and creating themes to link the underlying concepts together in categories. (Appendix 2: The process of content analysis) No additional analysis was used in this review.

Results

Guidance selection

We retrieved 3370 citations from MEDLINE and 23 additional citations from the guideline development organization websites, the International Journal for Equity in Health and emailing guideline development organizations. After removing duplicates and reviewing titles and abstracts, 3368 citations were excluded. By reviewing reference lists of the remaining 23 full-text articles, we obtained 12 relevant citations. In total, 35 potentially relevant full texts were screened, out of which 25 full-texts were excluded. The main reason for exclusion was that the focus of the papers was not on methods for addressing equity in CPGs. Finally, 8 studies with 10 publications [19-21,26-32] were included in this review (Figure 1: Selection process of included studies).

Study characteristics

Six studies [19-21,26,27,31]were retrieved from Medline, and four [28-30,32] were identified from guideline development organizations' websites. Only three studies [19,21,26] defined equity issues according to different definitions[2,33,34]. Included studies focused on different methodological topics related to equity including why [19], when [26], what [26] and how [19,20,26-32] CPG developers should address equity issues in CPGs, and how to assess the quality of CPGs, including equity,[21] for CPG users. Five studies (from 7 publications) [19,20,27-30,32] did not provide details of financial support. The characteristics of the included studies are provided in the Table 1.

In terms of relevant information extracted and analyzed, Keuken DG (2007) [31] provided "Recommendation for focusing on sex-related factors in guideline development"; NICE (2012) [28,29] provided "The protected characteristics", "Equality in guideline development ", a "Checklist for scoping", a "Checklist for early guideline development" and a "Checklist for formulating recommendations"; Dans AM (2007) [21] provided "The equity lens" to assess the quality of guidelines including equity issues; targeting at on the WHO guidelines mainly, Oxman AD (2006) [26] reviewed related articles to provide guidance to address equity in guidelines; Eslava-Schmalbach J (2011) [19] described why equity issues should be addressed in guidelines; Acosta N (2011) [27] provided simple guidance for including equity in guidelines; Aldrich (2003) [20] and NHMRC (2002) [30] provided indicators and search terms for socioeconomic factors and a framework for using evidence on socioeconomic factors in the development of clinical practice guidelines; rather than focusing on equity issues in particular, the WHO (2012) [32] provided advice on equity issues in its "PICO question components" and "evidence retrieval and synthesis" sections.

Synthesis of results

In total, 87 questions/items were collected. After content analysis, eight themes (seven for CPG developers, one for CPG users) were identified as following (see Appendix 3 Content analysis of the individual study). Then based on them, we outlined an integrated CPG development process for developers, including seven steps in total (see Figure 2 Overview of clinical practice guidelines development process (for CPG developers)).

For CPG developers:

Scoping questions

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Seven studies [19,20,26-32] reported the development of CPGs should include "Scoping questions" by which CPG developers could consider the reasons for addressing equity in their CPG (i.e. differential effectiveness across groups, negative impact of guideline without equity considerations, and improving overall effectiveness of guideline within equity) [19], the scenario and timing when equity should be addressed (example.g. the presence of differential effects across groups) [26], targeted populations, social determinants of health specified by PROGRESS or PROGRESS-Plus frameworks [6,7], and the changes and comments from stakeholders for the proposed question [28,29].

Searching relevant evidence

Four of the included studies [20,28-32] (six publications) described the 'Searching relevant evidence' theme, including appropriate study designs, changing search strategies when necessary, using terms/markers for equity, and appraising the eligibility criteria.

Appraising evidence and recommendations

Five studies [20,26-31] with seven publications fulfilled the "Appraising evidence and recommendations" theme, including the appraisal of scientific evidence, such as the appraisal of appropriate modifiers, study design, sample size, analysis methods, the applicability and relevance of evidence, influence of equity evidences, the quality of evidence, the necessity of evidence and making changes and evidence gaps, as well as the appraisal of recommendations, such as the relevance of recommendations, the impact of recommendations and the quality of development process.

Formulating recommendations

Three studies [20,28-31] with five publications provided guidance for how CPG developers should formulate recommendations to address equity issues as well as the elements that should be considered when synthesizing the evidence and formulating recommendations, including analyzing different subgroup effects, listing different/inconsistent evidence, balancing harms and benefits for disadvantaged populations, formulating equitable recommendations (such as considering barriers and facilitators of interventions for disadvantaged populations, and mitigating negative effects that may produce inequities during the formulation of recommendations), and how to advance recommendations and adjust recommendations.

Monitoring implementation

Four studies [20,26,27,30,31] with five publications described the "Monitoring implementation" theme. These studies included guidance on what should be considered during the implementation of CPGs and how to monitor implementation. Guidance suggested that CPG developers should minimize barriers to implementation, inform adaptation and decision-making in some specific settings, develop an equitable implementation strategy, change the organizational structure, and monitor the effects of implementation. When no evidence is available, CPG developers should change search strategies, scope of the questions, and promotion strategies.

Providing a flow chart to include equity in CPGs

Four studies [19,20,28-31] were included in the "Providing a flow chart to include equity in CPGs" theme. These included following common steps: identifying questions, developing search strategies, appraising scientific evidence, synthesizing the evidence, formulating recommendations and writing the guideline documents. Almost all of the elements in this theme were captured by the other themes except "Synthesizing the evidence". This additional element suggests that CPG developers should analyze subgroup effects, describe different/inconsistent evidence, balance

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harms and benefits, and consult comments from stakeholders.

Others: reporting of guidelines and comments from stakeholders

Keuken DG (2007) [31] reported the knowledge needs for the various ways of reporting guidelines. The authors stated that CPGs developers should balance advantages and disadvantages of different reporting methods. NICE (2012) [28,29] highlighted the need for engagement with stakeholders during every stage of the development process.

For the CPGs users:

Assessing the quality of CPGs

Dans AM (2007) [21] reported how CPG users can assess the quality of CPGs. This study includes limited guidance, including whether recommendations considered priorities for disadvantaged populations, and factors to explore differential effects across groups during the scoping stage. The authors suggest CPG users assess whether differential effects of the intervention across groups are valued, consider these when implementing the recommendations in practice, and address barriers to implementation, and the impact of the recommendations.

Discussion

Summary of evidence

We identified eight studies with 10 publications focusing on how to address equity issues in guidelines. Using different definitions of health equity the eight guiding studies may result in the difference of identifying the same conditions related to equity. Few studies provided methodological guidance to help CPG users identify important information on equity. After qualitative analysis, eight themes were identified, which included “scoping questions”, “searching relevant evidence”, “appraising evidence”, “formulating recommendations”, “monitoring implementation” , “providing a flow chart to include equity in CPGs”, and “others: reporting of guidelines and comments from stakeholders” for CPG developers and “assessing the quality of CPGs” for CPG users. Most of the included studies provided CPG developers or users with open-ended questions in checklists/frameworks rather than with a tool (with examples) to judge why, what, when, and how equity issues should be addressed. Few guidance publications described how to assess the quality of CPGs which considered equity issues in their recommendations, the process for developing CPGs, or how to report equity considerations. NHMRC (2003) [30], Keuken DG (2007) [31], Aldrich R (2003) [20] and NICE (2012) [28,29] covered more than five themes.

All included studies reported the “scoping questions” theme. When a guideline is developed, a rational for equity considerations should be described based on the differential effectiveness of interventions between subgroups. The PROGRESS and PROGRESS-Plus acronyms are recommended for identifying potentially disadvantaged groups when describing the scope of the CPG [6]. Four studies [20,28-32] described the “searching relevant evidence” theme, but, only NICE (2012) [28,29] suggested the consideration of study design. NHMRC (2003) [30] & Aldrich R (2003) [20] provided search terms on equity issues. Identifying evidence including systematic reviews, clinical practice guidelines, randomized controlled trials and supplementary literature is essential for CPG development. The search strategy must be transparent and reproducible. The reporting of databases, time periods, key words, subject headings, language restrictions, gray literature, and eligibility criteria should be considered [35].

Before formulating recommendations, the quality of scientific evidence must be appraised by appropriate appraisal tools. The relevance, applicability, impact of evidence on equity and

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evidence gaps should be assessed. Equity-specific CPG developers should focus on important questions, for example whether CPGs gave priority to the disadvantaged, how the applicability of the CPG and its evidence for disadvantaged populations was assessed, and whether implementation and monitoring strategies will detect effects for the most disadvantaged [36]. When evidence gaps exist, expert opinion or consensus is necessary to allow CPG developers to highlight future research needs [35]. NHMRC (2003) [30] & Aldrich R (2003) [20] provide strategies that can be used when there is a lack of evidence. For specific population subgroups, guideline developers should counterpoise harms and benefits of interventions, consider barriers and facilitators of interventions, and adjust recommendations for specific settings. Only Dans AM (2007) provided an equity lens to appraise the quality of a CPG with equity considerations. For the development of a CPG, we suggest that a well-designed handbook such as the “WHO handbook for guideline development” [32], “SIGN 50 A guideline developer’s handbook” [37], “Handbook on Clinical Practice Guidelines” [38] or NICE “the guidelines manual 2012” [28] is utilized. The process of CPG development (Figure 2) outlined in this paper will be more effective when used in combination with the handbooks mentioned above.

Limitations

With the comprehensive search strategy, only 8 studies (containing 87 questions or items) were included in this review. However, compared to previous reviews [27], our study includes a wider collection of handbooks and guidance documents. Although Acosta N (2011) included 20 studies (of which only three [21,26,30] were included in our review), [27] the authors only discussed equity in the development of CPGs with a narrative literature review. We extracted the methodological checklists/frameworks from the eligible studies and conducted content analysis. Content analysis was used because of its methodological characteristics and reliable measures to achieve trustworthiness[39]. However, a limitation of content analysis is that the likelihood of replicability for the analysis procedure is low [25].

Conclusions

By reviewing the existing guidance documents and guidelines, eight themes (i.e. “scoping questions”, “searching relevant evidence”, “appraising evidence and recommendations”, “formulating recommendations”, “monitoring implementation”, “providing a flow chart to include equity in CPGs”, and “others: reporting of guidelines and comments from stakeholders” for CPGs developers and “assessing the quality of CPGs” for CPGs users) were identified for guiding the incorporation of equity issues into clinical practice guidelines. Among existing checklists, Keuken DG (2007) [31] and NHMRC (2003) [30] covered most of these themes and have the greatest potential to be used as a tool for guiding equity considerations in guidelines. No grading systems or scoring criteria were found from existing checklists.

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Contributorship:

1) Conceiving and designing this review: Chunhu SHI, Jinhui TIAN and Kehu YANG, 2) Searching, extracting data and analyzing the data: Chunhu SHI, Quan WANG and Kehu YANG,

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3) Writing, amending and revising manuscript: Chunhu SHI, Jinhui TIAN, Dan REN, Jennifer Petkovic and Yang Yang,
4) When disagreements happened, discussing with Kehu YANG and Jinhui TIAN.
5) Final approval of manuscript: Chunhu SHI, Jinhui TIAN, Quan WANG, Dan REN, Jennifer Petkovic, Kehu YANG and Yang Yang,
6) Important comments and English editing: Jennifer Petkovic and Yang Yang

Data sharing: No additional data available.

FIGURE LEGENDS

Figure 1 Selection process of included studies

Figure 2 Overview of clinical practice guidelines development process (for CPGs developers)

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Table 1 Characteristics of the included studies

Study	Journal/Sources	Publication type	Definition of equity	Scope	Targeted users	Funding
Eslava-Schmalbach J 2011 [19]	Rev. salud publica	Review	Casas-Zamora JA 2004, Whitehead M. 1992	Why, How	CPGs developers*	No declaration
Dans AM 2007 [21]	Journal of Clinical Epidemiology	Article	Braveman 2003, Whitehead 1992	Assessing the quality of CPGs	CPGs users	Rockefeller Foundation, Norwegian Health Services Research Center
Oxman AD 2006 [26]	Health Research Policy and Systems	Review	Braveman 2003, Whitehead 1992	When, What, How	CPGs developers	WHO, Norwegian Knowledge Centre for the Health Services
Acosta N 2011 [27]	Rev. salud publica	Review	None provided	How	CPGs developers	No declaration
NICE 2012 [28] & NICE 2012 [29]	NICE	Guideline	None provided	How	CPGs developers	No declaration
Aldrich R 2003 [20] & NHMRC 2002 [30]	BMJ & NHMRC	Article & Guideline	None provided	How	CPGs developers	No declaration
Keuken DG 2008 [31]	Dissertation	Dissertation	None provided	How	CPGs developers*	Netherlands Organization for Health Research and Development
WHO 2012 [32]	WHO	Guideline	None provided	How	CPGs developers	No declaration

Note: * indicates that original studies did not report their targeted users by themselves and authors of this study specified them to be CPGs developers.

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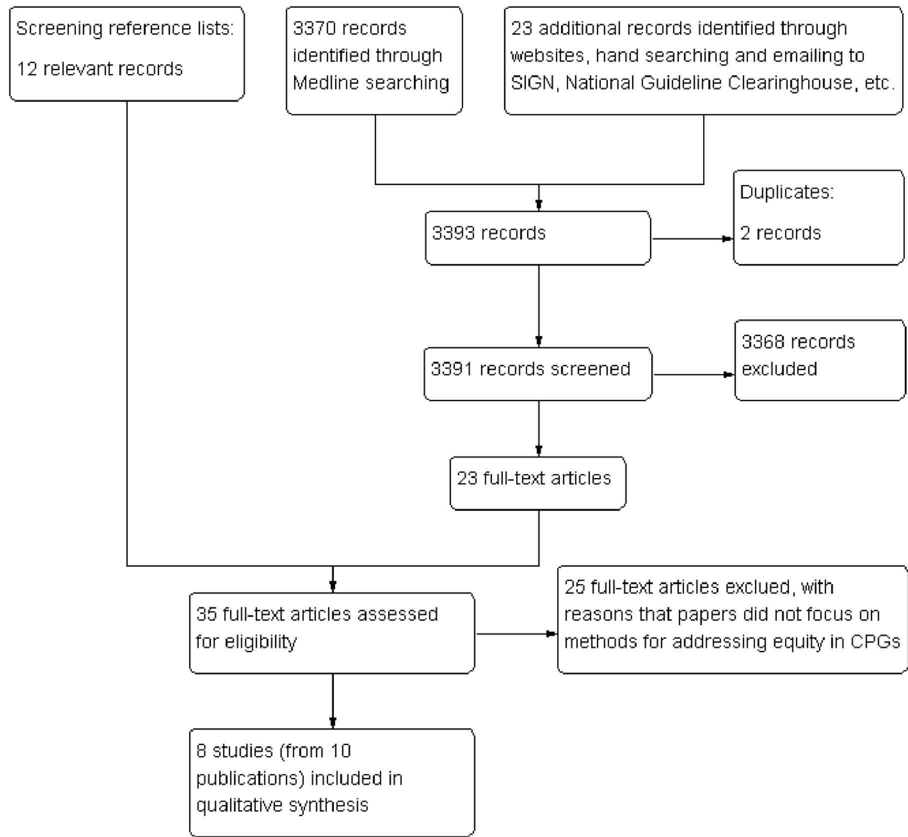

Figure 1 Selection process of included studies
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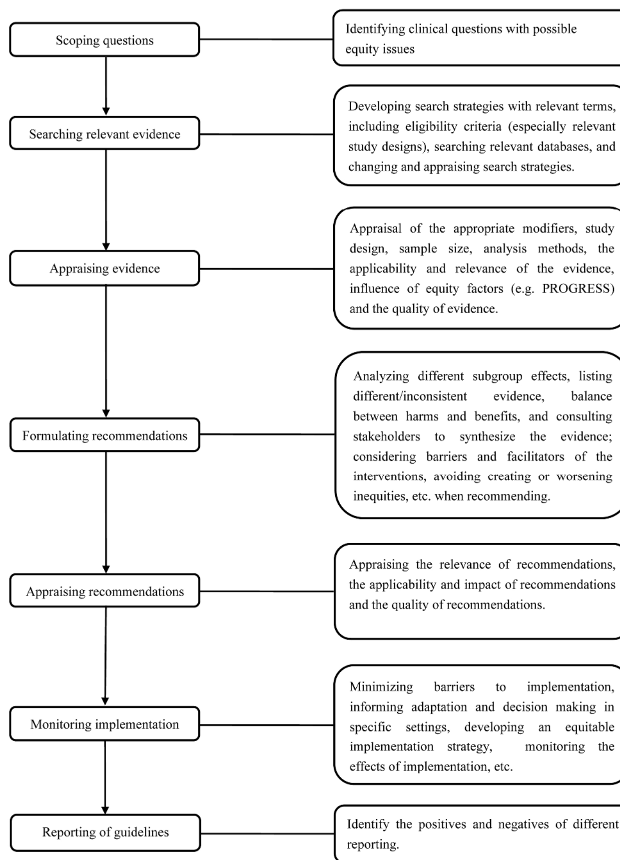

Figure 2 Overview of clinical practice guidelines development process (for CPGs developers)
210x330mm (300 x 300 DPI)

Appendix 1 Data extraction form

ID	**Answers**
Date	__/__/__ (M/D/Y)
Reviewers	____________________
Study details	**Descriptions**
Title	
First author	
Year of publication	
Journal's name	
Information type	Please specify:

Checklists or frameworks, etc for content analysis	
No.	**Checklists items/frameworks components**
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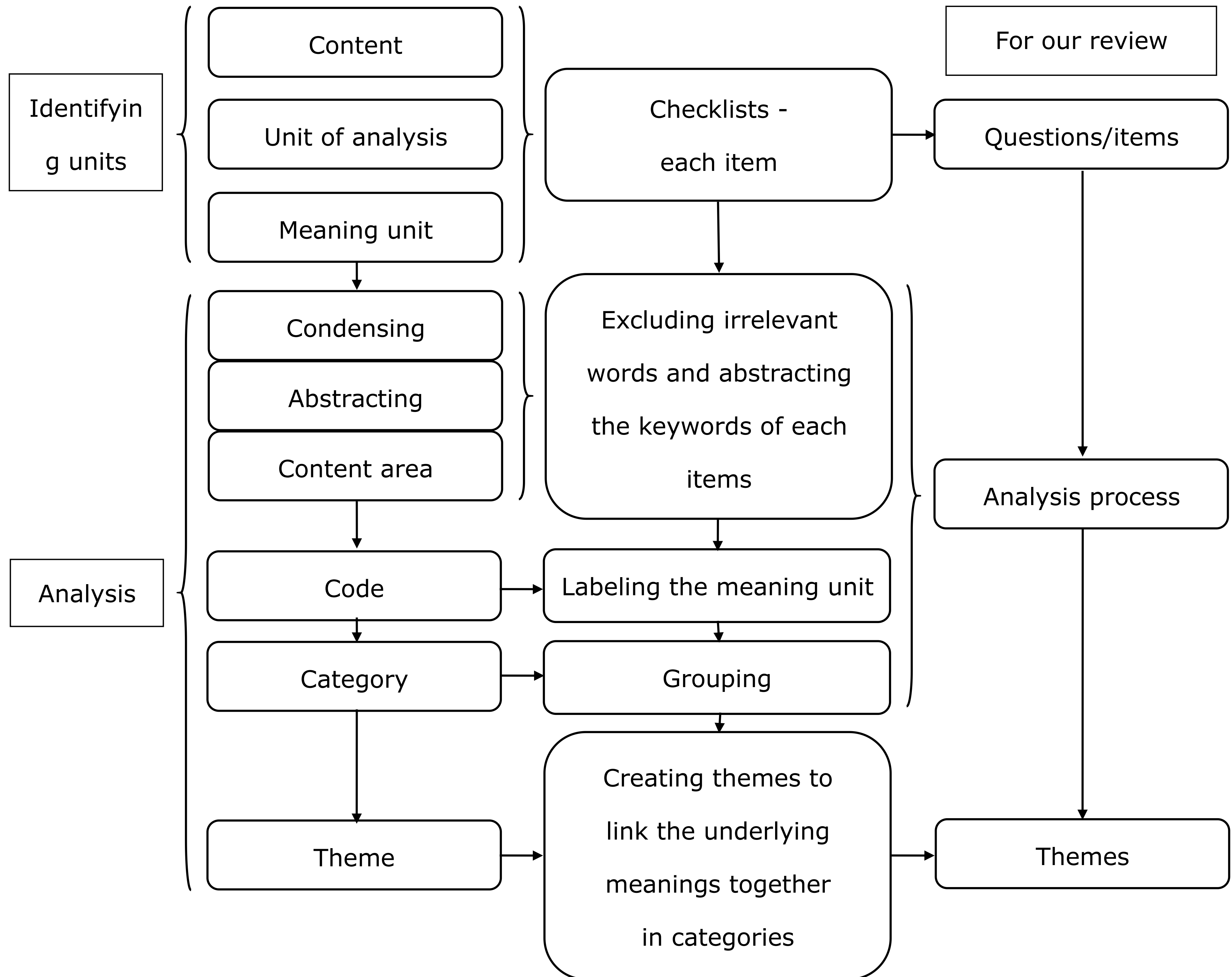
Appendix 2 The process of content analysis



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Appendix 3 Content analysis of the individual study

Eslava-Schmalbach J 2011 [16]			
Items	Categories	Coding	Themes
1. Differential effectiveness by social groups of interventions could diminish final effectiveness of CPG in the General Social Security and Health System (GSSHS);	The negative impact of differential effectiveness across groups	Reasons for addressing equity in guideline	Scoping questions
2. To not consider geographical, ethnic, socioeconomic, cultural and access diversity issues within the CPG could have a potential negative impacts of the CPG;	The negative impact regardless of equity issues	Why to address equity into guideline	Scoping questions
3. Overall effectiveness of GPC could be better if equity issues are included in the quality verification checklist of the guideline questions;	Better effectiveness of guideline when equity is included	Why to address equity into guideline	Scoping questions
4. Incorporating equity issues in the process of developing CPG could be cost effective, because improve overall effectiveness of CPG.	Improving overall effectiveness of guideline	Why to address equity into guideline	Scoping questions
Note: This article discussed why equity issues should be addressed into guidelines			

Dans AM 2007 [18]	The equity lens		
Items	Categories	Coding	Themes
1. Do the public health recommendations in the guidelines address a priority problem for disadvantaged populations?	Priorities for disadvantaged populations	Equity issues	Scoping questions
2. Is there a reason to anticipate different effects of intervention in disadvantaged and privileged populations?	Factors to explore differential effects across groups	Equity issues	Scoping questions
3. Are the effects of the intervention valued differently by disadvantaged compared with privileged populations?	Differential effects from evidences across groups	Appraising recommendation, appraisal of the scientific evidence	Appraising evidence and recommendations
4. Is specific attention given to minimizing barriers to implementation in disadvantaged populations?	Minimizing barriers to implementation	Implementation	Appraising implementation
5. Do plans for assessing the impact of the recommendations include disadvantaged populations?	Assessing the impact of recommendations	Appraisal of recommendation	Appraising evidence and recommendations
Note: This article provided a lens to assess the quality of guideline which addressed equity issues.			

Oxman AD 2006 [22]			
Items	Categories	Coding	Themes
1. When and how should inequities be addressed in systematic	Differential effects across groups is indicated to	When to address equity	Scoping questions

reviews that are used as background documents for recommendations? The following question should routinely be considered: are there plausible reasons for anticipating differential relative effects across disadvantaged and advantaged populations? If there are plausible reasons for anticipating differential effects, additional evidence should be included in a review to inform judgments about the likelihood of differential effects.	address equity		
2. What questions about equity should routinely be addressed by those making recommendations on behalf of WHO? (the following additional questions should routinely be considered)	Equity issues	Equity issues	Scoping questions
How likely is it that the results of available research are applicable to disadvantaged populations and settings?	Assessing applicability of available evidence	Appraisal of scientific evidence	Appraising evidence and recommendations, scoping questions
How likely are differences in baseline risk that would result in differential absolute effects across disadvantaged and advantaged populations?	Assessing effects of baseline risk across groups	appraisal the difference between groups	Appraising evidence and recommendations, scoping questions
How likely is it that there are important differences in trade-offs between the expected benefits and harms across disadvantaged and advantaged populations?	Assessing the balance between benefits and harms across groups	Appraisal the needs of evidences	Appraising evidence and recommendations, scoping questions
Are there different implications for disadvantaged and advantaged populations, or implications for addressing inequities?	Assessing the needs of evidence implications	Appraisal the needs of evidences	Appraising evidence and recommendations, scoping questions
3. What context specific information is needed to inform adaptation and decision making in a specific setting with regard to impacts on equity?	Informing adaptation and decision making		
Those making recommendations on behalf of WHO should routinely consider and offer advice about the importance of the following types of context specific data that might be needed to inform adaptation and decision making in a specific setting: Effect modifiers for disadvantaged populations and for the likelihood of differential effects; Baseline risk in relationship to social and economic status; Utilization and access to care in relationship to social and economic status; Costs in relationship to social and economic status; Ethics and laws that may impact on	Effect modifiers, baseline risk, access to interventions, costs, ethics and availability of resources should be used to inform adaptation	Implementation of guidelines in specific setting	Monitoring implementation

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strategies for addressing inequities; Availability of resources to address inequities.			
4. What implementation strategies are likely be needed to ensure that recommendations are implemented equitably?	Equitable implementation strategy	Implementation	Monitoring implementation
Organizational changes are likely to be important to address inequities. While it may only be possible to consider these in relationship to specific settings, consideration should be given to how best to provide support for identifying and addressing needs for organizational changes. In countries with pervasive inequities institutional, cultural and political changes may first be needed.	Organizational changes		
Appropriate indicators of social and economic status should be used to monitor the effects of implementing recommendations on disadvantaged populations and on changes in social and economic status.	Monitor the effects of implementation		
5. What 'maps' are available of the different dimensions of inequity locally?	Appraisal of local setting inequities	Implementation	Monitoring implementation
Note			

Acosta N 2011 [23]			
Items	Categories	Coding	Themes
1. Target population involvement during all phases of designing, implementing and evaluating CPG;	Equity is necessary to all phases of the development process	Appraisal of the quality of development process	Appraising evidence and recommendations
2. “Cultural capacity” seen as being necessary in CPGs’ “cultural translation” for interventions to have less disparity regarding their application and results;	Cultural capacity is necessary for guideline	Equity issues	Scoping questions
3. Considering psycho-social factors which could affect implementing CPG;	Psycho-social factors, facilitators of implementation	Equity issues, implementation	Scoping questions, monitoring implementation
4. Considering system inequities so that any health intervention would also confront risks and obstacles to health care due to socioeconomic status.	Socioeconomic status	Equity issues	Scoping questions
Note			

NICE 2012 [24, 25]			
Items	Categories	Coding	Themes

The protected characteristics; Equality in guideline development			
The protected characteristics are: age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex, sexual orientation, marriage and civil partnership, socio-economic, other	Population characteristics on equity issues	Equity issues	Scoping questions
Checklist for scoping			
1. What are the potential equality or discrimination issues linked to the guideline topic?	Equity issues	Equity issues	Scoping questions
Are there inequalities in prevalence, risk factors or impact - or in use or benefit - related to the topic or intervention?	Equity in prevalence or risk factors	Equity issues	Scoping questions
Is the condition more common, or is its severity greater, in people from a specific group or with a particular disability?	Prevalence of equity condition	Equity issues	Scoping questions
Is there a risk of discrimination?	Equitable scoping	Equitable scoping	Scoping questions
Do comments from stakeholders highlight the potential for direct or indirect discrimination, or for promoting equality?	Comments on equity issues	Comments for scoping	Scoping questions, others: comments from stakeholders
2. Should any changes be made to the scope?	Considering factors on changes in scope	Changes on scope	Scoping questions, others: comments from stakeholders
Consider the degree of relevance to equality, and the proportionate response in relation to this. The greater the relevance of a function t equality, the greater the regard that should be paid to equality issues.	Considering relevance of equity to change scope		
Consider the views of stakeholders.	Considering comments from stakeholders		
Summarize any changes made at this stage.	Summarize changes		
Identify any information gaps that have been identified.	Identify evidence gaps		
3. As it currently stands, is the scope discriminatory?	Considering some factors on scoping	Equitable scoping	Scoping questions
Have groups who need special consideration been identified?	Identify potential special groups		
Are there any exclusions?	Exclusion criteria		
If there are exclusions, are the reasons legitimate, and is the exclusion proportionate?	Equitable and appropriate exclusion		
4. Should any further information be identified and assessed?	Identifying and assessing further information	Consulting comments in scoping stage	Scoping questions, others: comments from stakeholders
Have important stakeholders been omitted from or not responded to the consultation process?	Consulting stakeholders' comments		
Consider specific questions for stakeholders (for example, at the scoping workshop).	Consulting stakeholders' comments		
Summarize the action to be taken.	Taking action		

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5. Is there anything specific that should be done to ensure that the guideline development group (GDG) will have relevant information to consider equalities issues when developing guidance? Action to address this needs only to be proportionate. Consider specific questions for stakeholders. Consider relevant bodies to consult.	Considering other specific questions Appropriate action Consider specific questions for stakeholders Consulting relevant bodies	Specific questions in scoping stage	Scoping questions, others: comments from stakeholders
Checklist for early guideline development			
1. How relevant is the evidence to eliminating discrimination, advancing equality and fostering good relations?	Relevance of evidence	Appraisal of scientific evidence	Appraising evidence and recommendations
2. Do the review questions reflect the scope? Do they identify issues affecting specific groups?	Effectiveness of clinical questions	Appraisal of effects on scoping	Appraising evidence and recommendations
3. Was the search strategy comprehensive? Consider a range of study of types for addressing the review questions (such as qualitative studies).	Comprehensive search strategy (appropriate study design)	Appraisal of search strategy	Appraising evidence and recommendations, searching relevant evidence
4. Were particular issues identified during consultation on the scope? Consider amending the search strategy in the light of comments.	Considering comments to change search strategy to collect necessary evidence	Appraisal of the necessary on evidence and making changes	Appraising evidence and recommendations
5. Were the evidence review criteria inclusive? Check that criteria do not inappropriately exclude studies on specific groups.	Appropriate and inclusive criteria of eligibility studies	Appraisal of eligible criteria	Appraising evidence and recommendations, searching relevant evidence
6. What is the state of the evidence base? Where are the evidence gaps?	Evidence gaps and evidence state	Appraisal of evidence gaps	Appraising evidence and recommendations
Checklist for formulating recommendations			
General questions			
1. How relevant are the recommendations to discrimination and equality? Which recommendations are likely to be most relevant?	Relevance of recommendations to equity	Appraisal the relevance of recommendations	Appraising evidence and recommendations
2. Where evidence is unavailable to assess a potential issue, could this be reflected in recommendations for future research?	Addressing the case where evidence is unavailable	Appraisal of evidence gaps	Appraising evidence and recommendations
Questions to consider to avoid discrimination include:			
Summarizing the following questions:	Access of interventions, barriers and facilitators	Formulating equitable	Formulating

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	of interventions, and appraisal of the access to avoid inequity during formulating recommendations	recommendations	recommendations, others: comments from stakeholders
1. Does access to the intervention depend on membership of a specific group?	Access to the intervention and specific group		
2. Do any criteria make it easier or more difficult in practice for people in a specific group to gain access to the intervention?	Barriers and facilitators of the access of interventions		
3. Does the way in which people would be assessed for whether or not they receive the intervention make it easier or more difficult for people in a specific group to gain access to it?	Assessing the barriers and facilitators of the access of interventions		
4. Does any part of the recommendation make it plausible that a person's age, disability, gender reassignment, pregnancy and maternity, marriage or civil partnership, race (including ethnic or national origins, color or nationality), religion or belief (including lack of belief), sex, sexual orientation or socioeconomic status could affect their access to an intervention? If so, what steps could be taken to address this?	Effects of equity on access to interventions		
5. Does any recommendation refer to age? If so, is age a good indicator of either risk or benefit from treatment and is the reason for the reference explained?	Effects of age on recommendations		
6. Do comments from stakeholders highlight areas of possible discrimination or ways of avoiding it?	Comments		
Questions to consider to advance equality of opportunity include:			
Summarizing the following questions:	Assessing and advancing the effectiveness and availability of recommendations, and access to interventions	Appraisal and advancing recommendations	Appraising evidence and recommendations, formulating recommendations, comments from stakeholders
1. Could the recommendations advance equality for people in a specific group, either through access to the intervention or by means of the intervention? Have stakeholders identified particular opportunities?	Advancing equity		
2. Could the recommendations be reformulated to make	Change of recommendations		

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implementation more acceptable to, or appropriate for, people in a specific group?			
3. Would more favorable treatment of any kind help disabled people to gain access to the intervention on the same basis as people without that disability? What additional measures would achieve this?	Equitable access to interventions		
4. Do comments from stakeholders highlight opportunities for advancing equality?	Comments		
Questions to consider to foster good relations include:			
1. Is there an opportunity to tackle prejudice? 2. Is there an opportunity to promote understanding? 3. Do comments from stakeholders highlight the need for tackling prejudice or promoting understanding?	Foster relations of recommendations with equity	Adjusting recommendations	Formulating recommendations, comments from stakeholders
Note: Describing a process of development: topic scoping, assessing the evidence, draft guideline, final guideline. Providing some examples on how to addressing equity into guidelines			

Aldrich 2003 [17], NHMRC 2002 [26]			
Items	Categories	Coding	Themes
SEP refers to the components of economic and social well-being in a societal context. It is a concept that includes both: resource-based measures such as income and educational qualifications; and prestige-based measures such as an individual's rank or status in a social hierarchy, for example the prestige associated with certain occupations.	Definitions of SEP	Equity issues	Scoping questions
Table 2: Markers and search terms for socioeconomic position	Providing some markers and search terms for socioeconomic position	Search terms	Searching relevant evidence
Socioeconomic status as an effect modifier in RCTs	Assessing the impact of SEP and health in RCTs.	Appraisal scientific evidence	Appraising evidence and recommendations
Problems in extrapolation of RCTs to disadvantaged populations. "Randomized controlled trials frequently use homogeneous population samples and analyze the effects of simple, single interventions. Factors associated with consent, inclusion and exclusion are not always randomly distributed."	Baseline characteristics and eligibility criteria in evidence body	Targeted population	Scoping questions
Assessing the quality of evidence on SEP. 'evidence exists on the various relationships between SEP and health in epidemiological, cohort, cross-sectional, observational, and	Assessing the quality of evidence	Appraisal of scientific evidence	Appraising evidence and recommendations

qualitative studies.'			
Literature review on the relationship between socioeconomic position and health and clinical practice guidelines. 'Guideline developers explicitly acknowledge evidence of the relationship between SEP and health and then use that evidence to shape and develop guidelines and associated recommendations for the broad population.'	Showing evidence on why equity should be addressed into guideline	Necessary of equity	Scoping questions
A framework for using evidence on socioeconomic position in the development of clinical practice guidelines			
Summarizing the following items	Framework	Framework	Process
Step 1: Identify the health decisions required.			
The health decision could be any type, from individual treatment decisions to the formulation of guidelines for whole communities. In the context of CPG development, there may be many decisions at different points in the diagnosis/ treatment pathway for a single guideline.	Clinical decisions required	Equity issues	Scoping questions
Step 2: Search the literature for evidence that, due to SEP, population subgroups may experience barriers to and/or have limited capacity or opportunities to achieve equal health gains.			
The literature should be searched using markers of SEP, the condition or disease of interest, and the required health decision to identify population sub-groups which may experience barriers, limited capacity or opportunities to achieve the same health gains as other sub-groups or populations.	Searching evidence on equity	Equitable searching	Searching relevant evidence
Step 3: Search the literature to identify interventions that address barriers and/or opportunities to achieving equal health gains			
Literature describing interventions that attempt to address barriers to achieving equal health gains across sub-groups should be identified.	Searching and assessing equitable evidence on application	Appraisal of applications and searching evidences	Searching relevant evidence, appraising evidence and recommendations
Step 4: Synthesize evidence from Steps 2 and 3 and current clinical best practice evidence to develop recommendations			
Develop recommendations in order to achieve health gains in terms of mortality, morbidity, survival, well-being and equity.	Formulating equitable recommendations	Formulating recommendations	Formulating recommendations
Other			
What to do when there is no evidence: broadening the search strategy; broadening the search scope; applying generic principles to promote health equity	Change searching strategies, scope, and promotion strategies, when no evidence was found	Searching and implementation	Searching relevant evidence, monitoring implementation
Note: Providing a process of guideline development Providing some examples and case study on how to develop guideline.			

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Keuken DG 2007 [27]	Recommendation for focusing on sex-related factors in guideline development		
Items	Categories	Coding	Themes
Formulation of initial key questions (and sub questions)			
Guideline developers should make an assessment to determine if there are any plausible reasons for anticipating differential relative effects for both sexes. If so, make sure that the key questions are formulated clearly to facilitate a review of the literature.	Considering differential relative effects across gender	Social determinants of target population	Scoping questions
Development of search strategies			
Guideline developers should make sure that search strategies are capable of detecting evidence (both direct and indirect) that supports or refutes any hypothesized differential effects.	Importance of an equitable search strategy	Search strategy	Searching relevant evidence
Appraisal of scientific evidence			
Guideline developers should determine whether the studies they review are well designed.	Well designed studies	Assessing study design	Appraising evidence and recommendations
Guideline developers should determine whether the study population is stratified and whether it is sufficiently large for an analysis of differential effects on the basis of sex.	Large sample size for analysis across gender	Appraising sample size	Appraising evidence and recommendations
Guideline developers should determine whether the relevant subgroup analyses have been carried out correctly (in key studies).	Correctly subgroup analysis	Appraising analysis methods	Appraising evidence and recommendations
Guideline developers should determine whether sex is a modifier for the research outcome.	Sex as a modifier	Detecting modifiers	Appraising evidence and recommendations
Formulation of recommendations for the guideline			
Where appropriate, guideline developers may consider how likely it is that the results of published research are applicable to both men and women when formulating recommendations.	Applicability of study results	Applicability of evidence	Appraising evidence and recommendations
Where appropriate, guideline developers may consider how likely it is that differences in baseline risk would result in differential absolute effects when formulating recommendations.	Influences across baseline risk on absolute effects	Influence of equity evidences	Appraising evidence and recommendations
Where appropriate, guideline developers may consider how likely it is that there are important differences in trade-offs between any anticipated harmful and beneficial effects when formulating recommendations.	Balance between harms and benefits	Balance between harms and benefits	Formulating recommendations
Where appropriate, guideline developers may consider	Warrant on the usage of different	Equitable usage of	Monitoring

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whether any of these considerations warrant the use of different recommendations when formulating recommendations.	recommendations	recommendations	implementation
Other (For composition of the guideline document)			
Guideline developers should have prior knowledge of the various ways in which sex-related factors can be represented in guidelines: when evidence has been found; if differences were expected but no evidence was found; if no information is available.	Knowledge of the various ways on reporting guidelines	Variable reporting	Others: reporting of guidelines
Selected sex-related factors may be mentioned in various subsections of the document: throughout the text; in specific paragraphs; in a subsection on special populations; in footnotes.	Highlighting the gender factor	Reporting	Others: reporting of guidelines
It is useful to reflect on the advantages and disadvantages of each option before drafting the guideline.	Trade-offs between advantages and disadvantages of different reporting.	Assessing equitable reporting	Others: reporting of guidelines
Note: Describing a process of development: formulation of initial key questions (and sub questions); development of search strategies; appraisal of scientific evidence; formulation of recommendations for the guideline; composition of the guideline document.			

WHO 2012 [28]

Items	Categories	Coding	Themes
Who is targeted by the action being recommended? (1) How can they be best described? What are the relevant demographic factors? Please consider age groups, sex, ethnicity, social identities, behavioral characteristics, etc. (2) What is the setting? For example, hospitals, communities, schools. (3) Are there any subgroups that might need to be considered? (4) Are there groups or subgroups that should be excluded?	Population characteristics (including equity issues), subgroup and exclusion criteria	Equity issues	Scoping questions
'Figure 6.1 Evidence retrieval decision diagram' provided a process on how to identify relevant systematic review, including social and educational policies and practices (the Campbell Collaboration). Eligibility studies from low- and middle-income countries and regional databases are highlighted in 'Search strategies' section.	Searching relevant studies to equity	Searching	Searching relevant evidence

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Note: Providing some examples on how to address equity issues into guidelines.

Providing a process of developing questions: Step 1: Generate initial list of questions; Step 2: Draft PICO questions; Step 3: List relevant outcomes; Step 4: Comment and revise; Step 5: Rate outcomes; Step 6: Prioritize questions

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How equity is addressed in clinical practice guidelines: a content analysis

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2) Searching, extracting data and analyzing the data: Chunhu SHI, Quan WANG and Kehu YANG,

3) Writing, amending and revising manuscript: Chunhu SHI, Jinhui TIAN, Dan REN, Jennifer Petkovic and Yang Yang,

4) When disagreements happened, discussing with Kehu YANG and Jinhui TIAN.

5) Final approval of manuscript: Chunhu SHI, Jinhui TIAN, Quan WANG, Dan REN, Jennifer Petkovic, Kehu YANG and Yang Yang,

6) Important comments and English editing: Jennifer Petkovic and Yang Yang

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Abstract

~~**Background**~~

~~Clinical practice guidelines (CPGs) assist practitioner and patient decisions for specific clinical circumstances. The number of CPGs has increased dramatically and have focused on the effectiveness and cost-effectiveness of interventions to balance benefits versus harms and cost. However, equity rarely is addressed in CPGs. Incorporating equity into guidelines presents methodological challenges.~~

Objectives

Considering equity into guidelines presents methodological challenges. This study aims to qualitatively synthesize~~To review~~ the methods for incorporating equity in CPGs.

Setting

Content analysis of methodological publications.

Eligibility criteria for selecting studies

Methodological publications were included if they

~~**Design**~~

~~We electronically searched Medline, retrieved references, and browsed guideline development organization websites to identify eligible papers which~~ provide checklists/frameworks~~/tools/recommendations~~ on when, how and to what extent equity should be incorporated in CPGs.

Data sources

We electronically searched Medline, retrieved references, and browsed guideline development organization websites from inception to Jan 2013. ~~No assessment of quality was conducted.~~ After study selection by two authors, general characteristics and checklists items/framework components from included studies were extracted. Based on the questions or items from checklists/frameworks (unit of analysis), content analysis was conducted to identify themes and questions/items were grouped into these themes.

Primary outcomes

The primary outcomes were methodological themes and processes on how to address equity issues in guideline development.

Results

~~Ten~~8 studies with 10 publications~~papers~~ were included from 3405 citations. In total, a list of 87 questions/items was generated from 17 checklists/frameworks. After content analysis, questions were grouped into 8 themes (“scoping questions”, “searching relevant evidence”, “appraising evidence and recommendations”, “formulating recommendations”, “monitoring implementation”, “providing a flow chart to include equity in CPGs”, and “others: reporting of guidelines and comments from stakeholders” for CPG developers and “assessing the quality of CPGs” for CPG users). Four included studies covered more than five of these themes. We also summarized the process of guideline development based on the themes mentioned above.

Conclusion

For disadvantaged population-specific CPGs, eight important methodological issues identified in this review should be considered when including equity in CPGs under the guidance of a scientific guideline development manual.

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Strengths and limitations of this study

- Methodological challenges are the barriers of incorporating equity into guidelines. For this topic, this study synthesizes some themes ("scoping questions", "searching relevant evidence", "appraising evidence and recommendations", "formulating recommendations", "monitoring implementation", "providing a flow chart to include equity in CPGs", and "others: reporting of guidelines and comments from stakeholders" for CPG developers and "assessing the quality of CPGs" for CPG users) and a developing process through a content analysis of eight studies.
- These findings allow the guideline panel to consider equity issues into guidelines and contribute methodologists to develop a methodological document in future.

These findings provide some valuable guidance, however no statement on methodological issues in equity or new checklist is built.

Background

Health is defined by the World Health Organization (WHO) as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"[1]. Health outcomes can be influenced by inaccessibility to health interventions for certain population groups, such as the poor and because of unequal distribution of medical resources. When differences in health outcomes across socioeconomic, demographic and geographic factors are avoidable, unnecessary and unjust they are described as health inequities [2,3]. The WHO recognizes that inequities in health should be reduced since health is a fundamental human right [4] and, in 2005,set up the Commision on Social Determinants of Health to collect, collate, and synthesize evidence on inequities and to make recommendations for action to address them [5].

Inequities in health and health care are well documented in relation to social and economic factors, according to the actronym PROGRESS-Plus, including Place of residence, Race/ethnicity/culture/language, Occupation, Gender/sex, Religion, Education, Socioeconomic status and Social capital [6] and additional factors related to personal characteristic, features of relationships, and time-dependent characteristics (captured by "Plus")[7]. Equity issues have been shown to have negative effects on health status [8-13]. For example, as Wallace et al. [14] reported, the HIV epidemics structure in the US was influenced by two such determinants, the link between geographic regions and the socioeconomic structure, function, and history of the regions.

Clinical practice guidelines, as defined by the Institute of Medicine, are 'systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.' [15] They are an increasingly familiar part of clinical practice and may provide concise guidance on which assessment programs to order, how to provide medical or surgical interventions, or other details of clinical practice [16]. Guideline development is becoming more evidence-based [17]. CPGs advocate that the most effective therapies are recommended as suggested by the evidence, however, the most effective intervention may not be available to all groups within a population. For example, a new therapy may be effective, but CPG developers need to consider whether it is available (and sufficiently cost-effective) for disadvantaged populations [18].

Therefore, CPG developers should discuss whether recommendations can ensure equitable provision of health care for the disadvantaged. Regardless of the setting, there is potential for the CPG to introduce inequities. Differences in health outcomes across population groups are possible

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3 if equity is not considered in guideline development. CPGs and their recommendations have the
4 potential to create or increase health inequities [19]. The inclusion of equity considerations in CPG
5 development and implementation has become increasingly important [20, 21]. For example, to
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7 balance the effective versus efficiency dilemma of CPGs, the National Health Service (NHS)
8 recommends the development of guiding principles to support the pursuit of equity in health care
9 [22]. However, incorporating equity into guidelines remains a challenge; the main barriers are
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11 methodological and conceptual limitations [20, 23]. We aimed to review methods for including
12 equity considerations in CPGs in this paper.

13 **Present investigation**

14 **Eligibility criteria**

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16 We conducted this review to investigate methodological guidance for including equity in CPGs.
17 Only methodological guidance, guidelines, and articles that described when, how and to what
18 extent equity issues could be incorporated in CPGs were included in this review. Types of eligible
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20 studies included: guidelines for incorporating equity into CPGs, empirical literature discussing
21 equity-specific methodological issues of CPG development, quantitative or qualitative literature
22 reviews that identify equity-specific methodological elements of CPG development.

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24 **Information sources and search**

25 Relevant studies were obtained from the following sources.

26 1) MEDLINE (1966 to Jan 2013) was electronically searched using an adapted version of the
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28 search strategy developed by Haase A et al. (2007) for the identification of clinical practice
29 guidelines [24]: (recommendation[All Fields] OR "consensus"[MeSH Terms] OR
30 "consensus"[All Fields] OR "guideline"[Publication Type] OR "guidelines as topic"[MeSH
31 Terms] OR "guideline"[All Fields]) AND (equal* OR equal[All Fields] OR "Civil
32 Rights"[Mesh] OR equity[All Fields] OR equit*) limited in "Humans and Title/Abstract";
33
34 2) Relevant studies were retrieved from reference lists of eligible articles;
35 3) In Jan 2013, we browsed guideline development organizations' websites including: National
36 Institute for Health and Clinical Excellence (NICE), New Zealand Guidelines Group, Scottish
37
38 Intercollegiate Guidelines Network (SIGN), Guideline International Network (G-I-N), CMA
39 Infobase: Clinical Practice Guidelines, PUBGLE, Trip Database, and National Guideline
40 Clearinghouse, etc.;
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42 4) Online publications from the 'International Journal for Equity in Health' (from 2002 to Jan
43 2013) was hand-searched;
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45 5) We also emailed SIGN, the New Zealand Guidelines Group and National Guideline
46 Clearinghouse, etc. to access specific documents.

47 **Study selection and data collection process**

48 Authors CHS and QW independently screened titles and abstracts. The full text (if published) of
49 all potentially relevant studies were retrieved and independently assessed for inclusion by QW and
50
51 KHY. CHS and KHY carried out data extraction independently using a standard data extraction
52 form (Appendix 1: Data extraction form). We planned to translate papers reported in non-English
53 language journals (if any) before assessment. Where more than one publication on the same
54
55 guidance existed, only the publication with the most complete data was included. Any further
56 information or clarification required from the authors was requested by written or electronic
57 correspondence and relevant data obtained in this manner were included in the review.
58 Disagreements were resolved in consultation with co-authors.
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Data items

In this review, data items are the questions or items from all available instruments, checklists, critical appraisal tools and indices which were designed to guide the incorporation of equity issues into CPGs or assessing the quality of equity considerations within CPGs. No data on participants, interventions, comparators, clinical outcomes and study designs was extracted.

Synthesis of results

Written phrases were the unit of analysis and therefore no quantitative data were analyzed by specific software. Using content analysis, authors CHS and JHT synthesized methodological themes and processes on how to address equity issues in guideline development. Content analysis is ‘a research technique for making replicable and valid inferences from data to their context.’ [25], which ‘emphasizes the quantification of the ‘what’ that messages communicate, the ‘who’ (the source), the ‘why’ (the encoding process) and the consequences of ‘effects’ they have ‘on whom’’ [25], by which themes can be summarized from meaningful qualitative data. A simplified process was used in this review: identifying units of analysis (the items/questions), excluding irrelevant information, abstracting the phrase or words from each unit of analysis, labeling these concepts, grouping them, and creating themes to link the underlying concepts together in categories. (Appendix 2: The process of content analysis) No additional analysis was used in this review.

Results

Guidance selection

We retrieved 3370 citations from MEDLINE and 23 additional citations from the guideline development organization websites, the International Journal for Equity in Health and emailing guideline development organizations. After removing duplicates and reviewing titles and abstracts, 3368 citations were excluded. By reviewing reference lists of the remaining 23 full-text articles, we obtained 12 relevant citations. In total, 35 potentially relevant full texts were screened, out of which 25 full-texts were excluded. The main reason for exclusion was that the focus of the papers was not on methods for addressing equity in CPGs. Finally, 8 ~~papers~~studies with 10 publications~~(from 10 documents)~~ [19-21,26-32] were included in this review (Figure 1: Selection process of included studies).

Study characteristics

Six studies~~papers~~ [19-21,26,27,31] were retrieved from Medline, and four [28-30,32] were identified from guideline development organizations’ websites. Only three studies [19,21,26] defined equity issues according to different definitions[2,33,34]. Included studies focused on different methodological topics related to equity including why [19], when [26], what [26] and how [19,20,26-32] CPG developers should address equity issues in CPGs, and how to assess the quality of CPGs, including equity,[21] for CPG users. Five studies (from 7 publications~~papers~~) [19,20,27-30,32] did not provide details of financial support. The characteristics of the included studies are provided in the Table 1.

In terms of relevant information extracted and analyzed, Keuken DG (2007) [31] provided “Recommendation for focusing on sex-related factors in guideline development”; NICE (2012) [28,29] provided “The protected characteristics”, “Equality in guideline development ”, a “Checklist for scoping”, a “Checklist for early guideline development” and a “Checklist for formulating recommendations”; Dans AM (2007) [21] provided “The equity lens” to assess the quality of guidelines including equity issues; targeting at on the WHO guidelines mainly, Oxman AD (2006) [26] reviewed related articles to provide guidance to address equity in guidelines; Eslava-Schmalbach J (2011) [19] described why equity issues should be addressed in guidelines;

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3 Acosta N (2011) [27] provided simple guidance for including equity in guidelines; Aldrich (2003)
4 [20] and NHMRC (2002) [30] provided indicators and search terms for socioeconomic factors and a
5 framework for using evidence on socioeconomic factors in the development of clinical practice
6 guidelines; rather than focusing on equity issues in particular, the WHO (2012) [32] provided
7 advice on equity issues in its "PICO question components" and "—'evidence retrieval and
8 synthesis" 'sections.

Synthesis of results

In total, 87 questions/items were collected. After content analysis, eight themes (seven for CPG developers, one for CPG users) were identified as following (see Appendix 3 Content analysis of the individual study). Then based on them, we outlined an integrated CPG development process for developers, including seven steps in total (see Figure 2 Overview of clinical practice guidelines development process (for CPG developers)).:

For CPG developers:

Scoping questions

Seven studiespapers [19,20,26-32] reported the development of CPGs should include "Scoping questions" by which CPG developers could consider the reasons for addressing equity in their CPG (i.e. differential effectiveness across groups, negative impact of guideline without equity considerations, and improving overall effectiveness of guideline within equity) [19], the scenario and timing when equity should be addressed (example.g. the presence of differential effects across groups) [26], targeted populations, social determinants of health specified by PROGRESS or PROGRESS-Plus frameworks [6,7], and the changes and comments from stakeholders for the proposed question [28,29].

Searching relevant evidence

Four of the included studies [20,28-32] (six publications) described the 'Searching relevant evidence' theme, including appropriate study designs, changing search strategies when necessary, using terms/markers for equity, and appraising the eligibility criteria..

Appraising evidence and recommendations

Five papersstudies [20,26-31] with seven documents checklists/frameworkspublications fulfilled the "Appraising evidence and recommendations" theme, including the appraisal of scientific evidence, such as the appraisal of appropriate modifiers, study design, sample size, analysis methods, the applicability and relevance of evidence, influence of equity evidences, the quality of evidence, the necessity of evidence and making changes and evidence gaps, as well as the appraisal of recommendations, such as the relevance of recommendations, the impact of recommendations and the quality of development process.

Formulating recommendations

Three papersstudies [20,28-31] with five checklists/frameworkspublications provided guidance for how CPG developers should formulate recommendations to address equity issues as well as the elements that should be considered when synthesizing the evidence and formulating recommendations, including analyzing different subgroup effects, listing different/inconsistent evidence, balancing harms and benefits for disadvantaged populations, formulating equitable recommendations (such as considering barriers and facilitators of interventions for disadvantaged populations, and mitigating negative effects that may produce inequities during the formulation of recommendations), and how to advance recommendations and adjust recommendations.

Monitoring implementation

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Four papersstudies [20,26,27,30,31] with five documentschecklists/frameworkspublications described the "Monitoring implementation" theme. These papersstudies included guidance on what should be considered during the implementation of CPGs and how to monitor implementation. Guidance suggested that CPG developers should minimize barriers to implementation, inform adaptation and decision-making in some specific settings, develop an equitable implementation strategy, change the organizational structure, and monitor the effects of implementation. When no evidence is available, CPG developers should change search strategies, scope of the questions, and promotion strategies.

Providing a flow chart to include equity in CPGs

Four papersstudies [19,20,28-31] were included in the "Providing a flow chart to include equity in CPGs" theme. These included following common steps: identifying questions, developing search strategies, appraising scientific evidence, synthesizing the evidence, formulating recommendations and writing the guideline documents. Almost all of the elements in this theme were captured by the other themes except "Synthesizing the evidence". This additional element suggests that CPG developers should analyze subgroup effects, describe different/inconsistent evidence, balance harms and benefits, and consult comments from stakeholders.

Others: reporting of guidelines and comments from stakeholders

Keuken DG (2007) [31] reported the knowledge needs for the various ways of reporting guidelines. The authors stated that CPGs developers should balance advantages and disadvantages of different reporting methods. NICE (2012) [28,29] highlighted the need for engagement with stakeholders during every stage of the development process.

For the CPGs users:

Assessing the quality of CPGs

Dans AM (2007) [21] reported how CPG users can assess the quality of CPGs. This paperstudy includes limited guidance, including whether recommendations considered priorities for disadvantaged populations, and factors to explore differential effects across groups during the scoping stage. The authors suggest CPG users assess whether differential effects of the intervention across groups are valued, consider these when implementing the recommendations in practice, and address barriers to implementation, and the impact of the recommendations.

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Discussion

Summary of evidence

We identified eight papersstudies with 10 publications focusing on how to address equity issues in guidelines. Using different definitions of health equity the eight guiding studies may result in the difference of identifying the same conditions related to equity. Few studies provided methodological guidance to help CPG users identify important information on equity. After qualitative analysis, eight themes were identified, which included "scoping questions", "searching relevant evidence", "appraising evidence", "formulating recommendations", "monitoring implementation" , "providing a flow chart to include equity in CPGs", and "others: reporting of guidelines and comments from stakeholders" for CPG developers and "assessing the quality of CPGs" for CPG users. Most of the included studies provided CPG developers or users with open-ended questions in checklists/frameworks rather than with a tool (with examples) to judge why, what, when, and how equity issues should be addressed. Few guidance

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~~document~~publicationss described how to assess the quality of CPGs which considered equity issues in their recommendations, the process for developing CPGs, or how to report equity considerations. NHMRC (2003) [30], Keuken DG (2007) [31], Aldrich R (2003) [20] and NICE (2012) [28,29] covered more than five themes.

All included ~~papers~~studies reported the "scoping questions" theme. When a guideline is developed, a rational for equity considerations should be described based on the differential effectiveness of interventions between subgroups. The PROGRESS and PROGRESS-Plus acronyms are recommended for identifying potentially disadvantaged groups when describing the scope of the CPG [6]. Four ~~paper~~studiess [20,28-32] described the "searching relevant evidence" theme, but, only NICE (2012) [28,29] suggested the consideration of study design. NHMRC (2003) [30] & Aldrich R (2003) [20] provided search terms on equity issues. Identifying evidence including systematic reviews, clinical practice guidelines, randomized controlled trials and supplementary literature is essential for CPG development. The search strategy must be transparent and reproducible. The reporting of databases, time periods, key words, subject headings, language restrictions, gray literature, and eligibility criteria should be considered [35].

Before formulating recommendations, the quality of scientific evidence must be appraised by appropriate appraisal tools. The relevance, applicability, impact of evidence on equity and evidence gaps should be assessed. Equity-specific CPG developers should focus on important questions, for example whether CPGs gave priority to the disadvantaged, how the applicability of the CPG and its evidence for disadvantaged populations was assessed, and whether implementation and monitoring strategies will detect effects for the most disadvantaged [36]. When evidence gaps exist, expert opinion or consensus is necessary to allow CPG developers to highlight future research needs [35]. NHMRC (2003) [30] & Aldrich R (2003) [20] provide strategies that can be used when there is a lack of evidence. For specific population subgroups, guideline developers should counterpoise harms and benefits of interventions, consider barriers and facilitators of interventions, and adjust recommendations for specific settings. Only Dans AM (2007) provided an equity lens to appraise the quality of a CPG with equity considerations. For the development of a CPG, we suggest that a well-designed handbook such as the "WHO handbook for guideline development" [32], "SIGN 50 A guideline developer's handbook" [37], "Handbook on Clinical Practice Guidelines" [38] or NICE "the guidelines manual 2012" [28] is utilized. The process of CPG development (Figure 2) outlined in this paper will be more effective when used in combination with the handbooks mentioned above.

Limitations

With the comprehensive search strategy, only 8 ~~papers~~studies (containing 87 questions or items) were included in this review. However, compared to previous reviews [27], our study includes a wider collection of handbooks and guidance documents. Although Acosta N (2011) included 20 studies (of which only three [21,26,30] were included in our review), [27] the authors only discussed equity in the development of CPGs with a narrative literature review. We extracted the methodological checklists/frameworks from the eligible studies and conducted content analysis. Content analysis was used because of its methodological characteristics and reliable measures to achieve trustworthiness[39]. However, a limitation of content analysis is that the likelihood of replicability for the analysis procedure is low [25].

Conclusions

By reviewing the existing guidance documents and guidelines, eight themes (i.e. "scoping

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questions", "searching relevant evidence", "appraising evidence and recommendations", "formulating recommendations", "monitoring implementation", "providing a flow chart to include equity in CPGs", and "others: reporting of guidelines and comments from stakeholders" for CPGs developers and "assessing the quality of CPGs" for CPGs users) were identified for guiding the incorporation of equity issues into clinical practice guidelines. Among existing checklists, Keuken DG (2007) [31] and NHMRC (2003) [30] covered most of these themes and have the greatest potential to be used as a tool for guiding equity considerations in guidelines. No grading systems or scoring criteria were found from existing checklists.

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Figure 1 Selection process of included studies

Figure 2 Overview of clinical practice guidelines development process (for CPGs developers)

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Table 1 Characteristics of the included ~~papers~~studies

Study	Journal/Sources	Publication type	Definition of equity	Scope	Targeted users	Funding
Eslava-Schmalbach J 2011 [19]	Rev. salud publica	Review	Casas-Zamora JA 2004, Whitehead M. 1992	Why, How	CPGs developers*	No declaration
Dans AM 2007 [21]	Journal of Clinical Epidemiology	Article	Braveman 2003, Whitehead 1992	Assessing the quality of CPGs	CPGs users	Rockefeller Foundation, Norwegian Health Services Research Center
Oxman AD 2006 [26]	Health Research Policy and Systems	Review	Braveman 2003, Whitehead 1992	When, What, How	CPGs developers	WHO, Norwegian Knowledge Centre for the Health Services
Acosta N 2011 [27]	Rev. salud publica	Review	None provided	How	CPGs developers	No declaration
NICE 2012 [28] & NICE 2012 [29]	NICE	Guideline	None provided	How	CPGs developers	No declaration
Aldrich R 2003 [20] & NHMRC 2002 [30]	BMJ & NHMRC	Article & Guideline	None provided	How	CPGs developers	No declaration
Keuken DG 2008 [31]	Dissertation	Dissertation	None provided	How	CPGs developers*	Netherlands Organization for Health Research and Development
WHO 2012 [32]	WHO	Guideline	None provided	How	CPGs developers	No declaration

Note: * indicates that original studies did not report their targeted users by themselves and authors of this study specified them to be CPGs developers.

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Text S1 - Checklist of items to include when reporting a systematic review or meta-analysis

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	No
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4

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Section/topic	#	Checklist item	Reported on page #
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	No. Unnecessary
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	No. Unnecessary
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	No. Unnecessary
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	No. Unnecessary
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	No. Unnecessary
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	No. Unnecessary
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and	5， 6, 7

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Section/topic	#	Checklist item	Reported on page #
		measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	No. Unnecessary
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	No. Unnecessary
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers).	7, 8
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	8

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