


Systematic review of methodology and reporting quality of global guidelines on fever in children

Chuan Zhang, MD^{a,b,c}, Lingli Zhang, MD^{a,b,c,*} , Liao Qiong, MD^{c,d}, Linan Zeng, MD^{a,b,c}, Di Wu, PhD^e, Fang Qin, PhD^e

Abstract

Objective: This study aimed to evaluate the global clinical practice guidelines on fever in children. We also aimed to select a guideline with good methodology and reporting quality to provide scientific reference for diagnosis and treatment of fever in children.

Methods: The Chinese and English databases Embase, PubMed, Cochrane library, China National Knowledge Infrastructure, Wanfang database, clinical guides, and the website of the Department of Public Health Administration were retrieved up to January 2020. The clinical practice guidelines on fever in children were included. The AGREE II instrument and Reporting Items for Practice Guidelines in Healthcare statement were used to evaluate the methodology and reporting quality of the guidelines.

Results: Eight clinical guidelines for fever in children were included. Methodological quality assessment showed that the recommendation level of ISP, South Africa, National Institute for Health and Care Excellence, China, and American College of Emergency Physicians were grade B (recommended with modification), while that of American Academy of Pediatrics, New South Wales, and South Australia was grade C recommendation (not recommended). No grade A recommendation guideline was found. The reporting quality from higher to lower was National Institute for Health and Care Excellence, the Chinese guideline, American College of Emergency Physicians, ISP, South Africa, New South Wales, South Australia, and American Academy of Pediatrics. The guideline recommendations were similar in various countries, but they were slightly different in various aspects, including body temperature measurement and the timing of drug administration.

Conclusion: There are limitations in the methodology and reporting quality of all eight global guidelines on fever in children. For future development of these guidelines, attention should be paid to improving applicability of the guidelines in terms of methodology. Additionally, the principles and explanations for formation of recommendations should be described, as well as the limitations of the reporting guideline in detail in terms of the reporting quality. Treatments of fever in children are similar in different countries, but there are still differences that require further research.

Abbreviations: AAP = American Academy of Pediatrics, ACEP = American College of Emergency Physicians, ICC = intraclass correlation coefficient, NICE = National Institute for Health and Care Excellence, RIGHT = Reporting Items for Practice Guidelines in Healthcare.

Keywords: AGREE II, clinical practice guideline, fever in children, reporting items for practice guidelines in healthcare statement

1. Introduction

Fever is one of the most common symptoms in children, accounting for an estimated one third of the reasons for pediatric

visits.^[1] Fever is a normal physiological response of the human body to diseases, but there is no evidence of a correlation between fever and the severity of the disease. However, because of the

Editor: Maya Saranathan.

This research was supported by Natural Science Foundation of China: Evidence-based Establishment of Chinese Essential Medicine List for Children: Developing the Methodology of Drug Varieties Selection (No.71704123) and Program for Yangtze River Scholars and Innovative Research Team in University (No. IRT0935).

The sponsor had no role other than to provide financial support.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

^aDepartment of Pharmacy, West China Second University Hospital, Sichuan University, Chengdu, China, ^bEvidence-Based Pharmacy Center, West China Second University Hospital, Sichuan University, Chengdu, China, ^cKey Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China, ^dDepartment of Pediatrics, West China Second University Hospital, Sichuan University, Chengdu, China, ^eWest China school of pharmacy, Sichuan University, Chengdu, China.

*Correspondence: Lingli Zhang, Department of Pharmacy, West China Second University Hospital, Sichuan University, Chengdu, China (e-mail: zhanglingli_2000@163.com).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Zhang C, Zhang L, Qiong L, Zeng L, Wu D, Qin F. Systematic review of methodology and reporting quality of global guidelines on fever in children. *Medicine* 2021;100:48(e28021).

Received: 20 April 2020 / Received in final form: 19 October 2021 / Accepted: 11 November 2021

<http://dx.doi.org/10.1097/MD.00000000000028021>

physical discomfort of fever in children, parents usually pay excessive attention and even panic, which lead to overtreatment and inappropriate treatments.^[2] A study conducted in the French population showed that the proportion of parents who correctly use physical cooling and drug therapy for fever is only 15% and 23%, respectively.^[3] Because of different understanding of fever in children, different pediatricians show great differences in the treatment of fever, and there are some problems, such as the improper use of antipyretic drugs.^[4]

Clinical practice guidelines can standardize management of fever by pediatricians.^[5] However, there are differences in the recommendations of clinical practice guidelines for fever in children, such as the definition of fever, measurement of body temperature, the choice of measurement tools, the timing of fever treatment, and treatment measures. These differences cause difficulties in proper clinical diagnosis and treatment. Therefore, evaluating the methodology and reporting quality of the guidelines based on evidence is required. Additionally, guidelines with good methodology and reporting quality should be selected to provide scientific reference for the diagnosis and treatment of fever in children.

2. Materials and methods

2.1. Search of guidelines

English and Chinese databases, guideline databases, and websites of the Department of Public Health Administration, Academy of Pediatrics, and the World Health Organization were searched up to January 2020, using keywords of fever, guideline, and children.

2.2. Inclusion and exclusion criteria

Newly published clinical practice guidelines on fever in children (0–18 years old) were included, excluding repeated published guidelines, and including guidelines for fever caused by specific diseases, such as malaria and dengue fever in adults and children. The language was limited to Chinese and English.

2.3. Assessment of guidelines

2.3.1. Assessment of the methodology quality of the guideline using the appraisal of guidelines for research & evaluation II instrument. There are six domains of the AGREE II instrument^[6] as follows: scope and purpose, stakeholder involvement, rigor of development, clarity of presentation, applicability, and editorial independence, with a total of 23 items and one overall assessment item. The researchers scored each item according to the criteria, with a score of 7 indicating very consistent with the criteria and a score of 1 indicating very inconsistent. Assessment of the guidelines was carried out independently by two researchers (WD and ZC). Consensus needed to be discussed when the difference in scores was ≥ 2 . The score for the six domains was then calculated as follows: [(actual score of this domain – minimum possible score)/(maximum possible score – minimum possible score) $\times 100\%$]. According to the scores of each domain of this guideline, the degree of recommendation of the guideline was divided into three levels as follows: grade A (recommended) with a score of all six domains $\geq 60\%$; grade B (recommended after modification) with three to five domains with a score $\geq 60\%$; and grade C (not recommended) with \geq four domains with a score $\geq 60\%$.

2.3.2. Assessment of the reporting quality of guidelines using the reporting items for practice guidelines in health-care (RIGHT) statement. The RIGHT checklist^[7] includes seven domains as follows: basic information (items 1–4), background (items 5–9), evidence (items 10–12), recommendations (items 13–15), review and quality assurance (items 16 and 17), funding and declaration and management of interests (items 18 and 19), and other information (items 20 to 22). According to the consistency of each item, the researchers evaluated as yes (fully reported; the content of the item was comprehensive, detailed and met all RIGHT standards), no (unreported; this item did not report information in the RIGHT standard), or insufficient (insufficiently reported; this item had relevant content, but was not fully reported in accordance with the RIGHT standard). Evaluation of the guidelines was conducted independently by two researchers (WD and ZC) and consensus needed to be discussed when there were conflicting opinions.

2.4. Statistical analysis

Microsoft Excel was used to input the evaluation data and SPSS16.0 statistical software was used for data analysis. The intraclass correlation coefficient (ICC) was used to test the consistency of the evaluation results of the two researchers. An ICC value ≥ 0.75 represented good consistency, ≥ 0.4 and < 0.75 represented general consistency, and < 0.4 represented poor consistency.

Ethical approval was not necessary because the study did not involve patients, and the clinical practice guidelines were available online.

3. Results

3.1. Search results

A total of 474 reports were obtained, including 447 in English and 27 in Chinese. Eight guidelines on fever in children that met the inclusion criteria of this study were included. Flow diagram of guidelines selection process was in Figure 1.

3.2. Basic characteristics of the included guidelines

The eight guidelines were from the American Academy of Pediatrics (AAP),^[8] the American College of Emergency Physicians (ACEP),^[9] China,^[10] the Italian Pediatric Society,^[11] National Institute for Health and Care Excellence (NICE),^[12] South Africa,^[13] New South Wales, Australia,^[14] and South Australia.^[15] The included guidelines were published between 2010 and 2019, and were developed by academic committees or governments. Of these, four were evidence-based guidelines and six included detailed descriptions of evidence classification.

3.3. AGREE II assessment results

The ICC value of the two researchers was ≥ 0.75 and the evaluation results were consistent with each other. The results of the evaluation are shown in Table 1.

3.3.1. Scope and purpose. The average score of the domain of scope and purpose was 89%, with six guidelines that described clinical questions, the overall objective of the guideline, and to whom the guideline is meant to apply. The overall objective of the guideline was not clearly described in the Chinese guideline, while

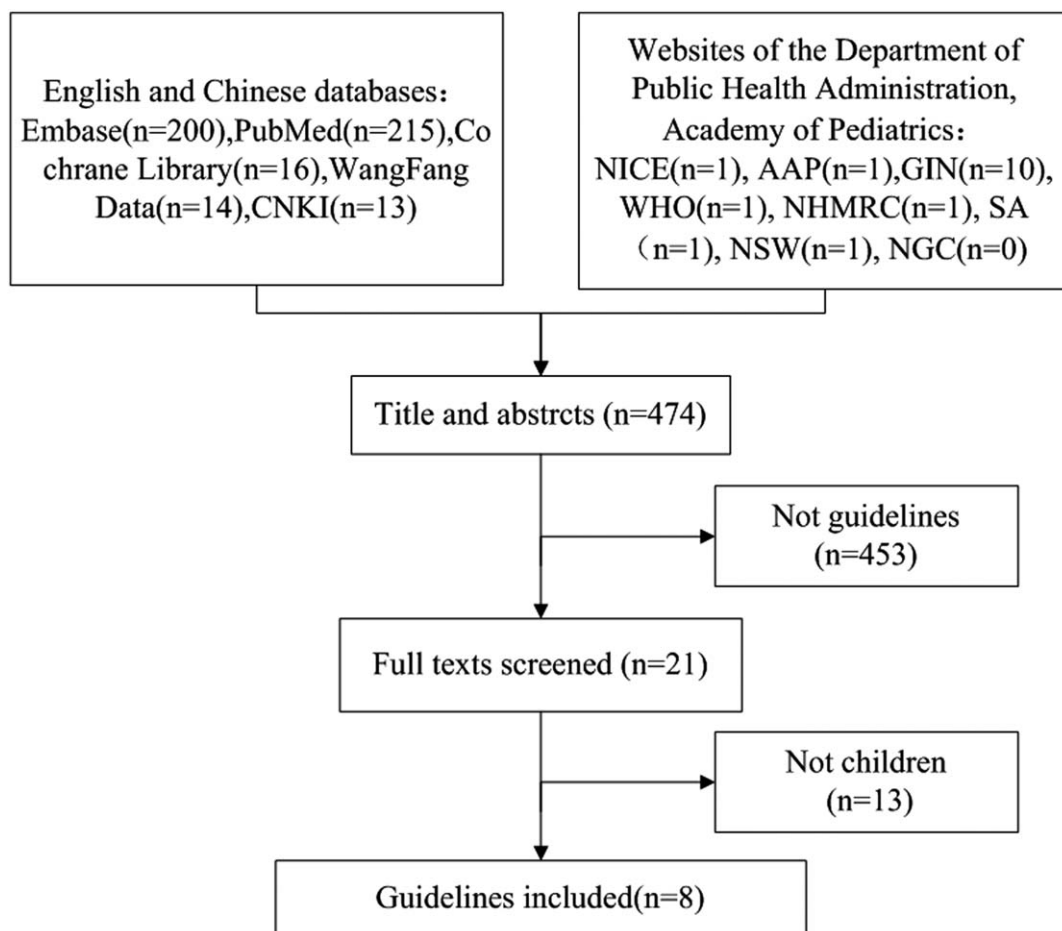


Figure 1. Flow diagram of guideline selection process.

the overall objective and clinical questions were not described in detail in the AAP guideline.

3.3.2. Stakeholder involvement. The average score of the domain of stakeholder involvement was 60%, and the ISP and Chinese guidelines scored the highest (75% for both guidelines). The AAP and South Australian guidelines scored low at 36% and 33%, respectively, because of their failure in describing the

guideline development group in detail and they did not consider the views of the target users, patients, and public. All guidelines described the target users, but in different degrees of detail.

3.3.3. Rigor of development. The average score of the domain of rigor of development was 53%. The NICE guideline described in detail the selection method of evidence, the strengths and limitations of each measure, the methods for formulating the

Table 1

AGREE II assessment results of the included guidelines.

Included guidelines	Scope and Purpose	Stakerhold and Involvement	Rigour of Development	Clarity of Presentation	Applicability	Editorial Independence	No. of domains with a score ≥60%	No. of domains with a score ≤30%	Recommended level
AAP	75	36	26	36	6	63	2	2	C
IPS	92	75	70	92	31	62	5	0	B
South African	92	50	28	86	31	88	3	1	B
NICE	97	81	92	94	73	58	5	0	B
New South Wales, Australia	94	56	27	81	23	25	2	3	C
South Australia	94	33	35	92	33	29	2	1	C
China	78	75	71	92	25	96	5	1	B
ACEP	89	75	76	78	29	42	4	1	B

AAP = American Academy of Pediatrics, ACEP = American College of Emergency Physicians, AGREEII = Appraisal of Guidelines for Research & Evaluation II, IPS = Italian Pediatric Society, NICE = National Institute for Health and Care Excellence.

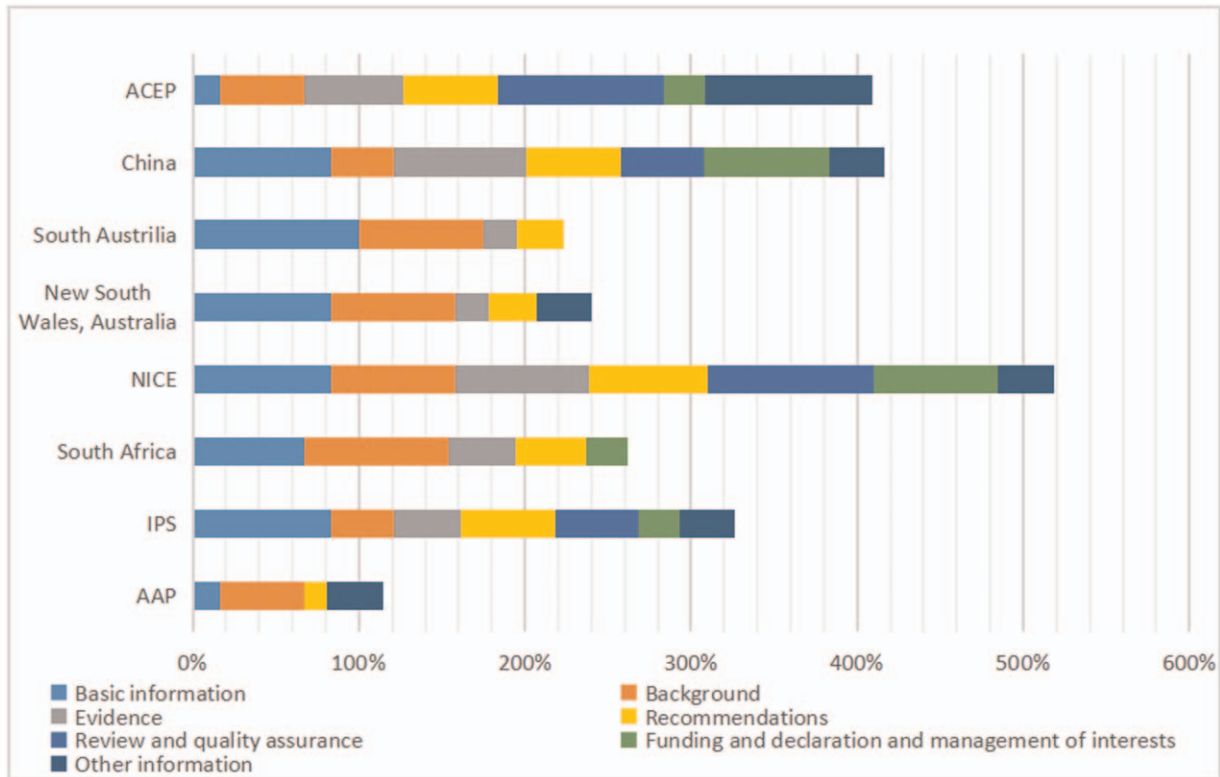


Figure 2. RIGHT assessment results.

recommendations, and the external expert review and update procedure of the guideline, with the highest score of 92%. The ISP guideline did not describe whether it was externally reviewed by experts before its publication. Four guidelines did not describe the evidence processing methods, and therefore, had low scores in this domain.

3.3.4. Clarity of presentation. The average score of the domain of clarity of presentation was 81%. All guidelines had specific and unambiguous recommendations. The ISP, NICE, South Australian, and Chinese guidelines scores were > 90% in this domain. AAP, New South Wales, and ACEP guidelines did not explicitly present different options for management of the condition or clinical question, and the main recommendations of the AAP guidelines were not clear.

3.3.5. Applicability. The average score of the domain of applicability was 31% and only the UK guideline had a score of $\geq 60\%$. None of the guidelines discussed in detail potential facilitators and barriers in applying the recommendations. The AAP, ACEP, ISP, and Chinese guidelines did not present the monitoring and/or auditing criteria of application of the guidelines. Only the UK guideline provided advice and/or tools on how the recommendations can be put into practice, and provided tools that can be downloaded free of charge on its website.

3.3.6. Editorial independence. The average score of the domain of editorial independence was 58%. The New South Wales and South Australian guidelines did not clearly address the competing interests of guideline development group members, and thus scored $\leq 30\%$. The Chinese and South African

guidelines described the competing interests of guideline development group members and clarified that the views of the funding body did not influence the content of the guideline. Therefore, these guidelines scored 96% and 88%, respectively.

3.4. RIGHT assessment results

The results of the seven domains are shown in Figure 2.

3.4.1. Basic information. South Australia had the highest full reporting rate which referred to the reporting of all items in this domain (100%), and the AAP and ACEP guidelines had the lowest full reporting rate (17%). The full reporting rates for title/subtitle were 87.5% (items 1a and 1c) and 62.5% (item 1b). The full reporting rates for executive summary, abbreviations and acronyms, and corresponding developer were 50% (item 2), 62.5% (item 3), and 50% (item 4), respectively.

3.4.2. Background. The South African guideline had the highest reporting rate of 88%, while the ISP and Chinese guidelines had the lowest reporting rate of 38%. The full reporting rate for a brief description of the health problem was 62.5% (item 5). The full reporting rates for the aim(s) of the guideline and specific objectives (item 6), the primary population(s) that is affected by the recommendation(s) (item 7a), the subgroups that have special consideration (item 7b), and the intended primary users of the guideline (item 8a) were 87.5%, 100%, 62.5%, and 100%, respectively. The full reporting rate for the setting(s) for which the guideline is intended was 50% (item 8b). None of the eight guidelines described in detail all contributors to development of the guidelines who were selected and their roles and responsibilities.

ties (item 9a). Only the South African and New South Wales guidelines reported in detail all individuals who were involved in developing the guidelines, including their title, role(s), and institutional affiliation(s) (item 9b).

3.4.3. Evidence. The full reporting rate of the AAP guidelines was 0, while those of the NICE and Chinese guidelines were the highest (80%). The NICE and Chinese guidelines fully reported on the key questions that were the basis for the recommendations in population, intervention, comparator, and outcome (item 10a), and the NICE, Chinese, and ACEP guidelines indicated how the outcomes were selected and sorted (item 10b). The South Australian guideline was based on existing systematic reviews (item 11a), but it did not adequately report references, how those reviews were identified and assessed, and whether they were updated (item 11b). Except for the AAP and South Australian guidelines, the other six guidelines described the approach used to assess the certainty of the body of evidence (item 12).

3.4.4. Recommendations. The reporting rate of the AAP guideline was the lowest (14%) and that of the NICE guideline was the highest (71%). All eight guidelines provided clear, precise, and actionable recommendations (item 13a). Of these, the AAP, ISP, and ACEP guidelines did not provide separate recommendations for important subgroups (item 13b). Additionally, the AAP, South Australian, and New South Wales guidelines did not indicate the strength of recommendations and the certainty of the supporting evidence (item 13c). With regard to the rationale/explanation for recommendations, only the ISP and ACEP guidelines fully described whether values and preferences of the target population(s) were considered in the formulation of each recommendation (item 14a). The ISP, NICE, and Chinese guidelines described whether cost and resource implications were considered in the formulation of recommendations (item 14b). The eight guidelines did not fully describe other factors taken into consideration when formulating the recommendations, such as equity, feasibility, and acceptability (item 14c). The NICE and ACEP guidelines described the processes and approaches used by the guideline development group to make decisions, particularly the formulation of recommendations (item 15).

3.4.5. Review and quality assurance. The reporting rate of NICE and ACEP guidelines was 100% in the domain of review and quality assurance, while that of the AAP, South African, and South Australian guidelines was 0. The NICE and ACEP guidelines indicated whether the draft guideline underwent independent review (item 16). The ISP, NICE, ACEP, and Chinese guidelines fully indicated whether the guideline was subjected to a quality assurance process (item 17).

3.4.6. Funding, declaration, and management of interests. The NICE and Chinese guidelines had the highest reporting rates of 75%, while the New South Wales and South Australia guidelines had the lowest reporting rate of 0%. The ISP, NICE, ACEP, South African, and Chinese guidelines described the specific sources of funding for all stages of guideline development (item 18a). However, these guidelines did not describe the role of funder(s) in the different stages of guideline development and in the dissemination and implementation of the recommendations (item 18b). The NICE and Chinese guidelines fully described what types of conflicts (financial and nonfinancial) were relevant to guideline development (item 19a). These guidelines also

described how conflicts of interest were evaluated and managed, and how users of the guidelines can access the declarations (item 19b).

3.4.7. Other information. Except for the South Australian and South African guidelines, the other six guidelines described where the guideline, its appendices, and other related documents that can be accessed (item 20). Additionally, only the ACEP guideline fully described the gaps in the evidence and/or provided suggestions for future research (item 21) and limitations in the guideline development process (item 22).

3.5. Summary of recommendations

Table 2 shows comparison of similarities and differences of the eight guidelines in the target population, the definition of fever, body temperature measurement, physical and drug cooling, and antipyretic drugs. The definition of fever was consistent in different countries, and anal temperature was the gold standard. However, measurement of anal temperature is difficult in the clinic, and therefore, axillary temperature and ear temperature are suggested. The temperature measuring tools slightly varied in the different guidelines, and these included an electronic thermometer, mercury thermometer, and infrared ear thermometer. An electronic thermometer was recommended instead of a mercury thermometer in the Chinese guideline, but this was not mentioned in the other guidelines. The recommendation for physical cooling was consistent in different guidelines, which did not recommend too little or too much dressing and the use of an ethanol bath for cooling. The purpose of antipyretic and analgesic drugs is not to reduce body temperature, but to relieve the discomfort of children. Antipyretic drugs cannot prevent febrile seizures and cannot be regularly used to prevent a vaccination response.

Only the AAP and Chinese guidelines mentioned the specific timing of antipyretic drugs, while other guidelines recommended the timing and purpose of using antipyretic drugs to alleviate discomfort of children. Paracetamol and ibuprofen are first-line antipyretic drugs for children that were recommended by different guidelines, and mefenamic acid was also recommended in the South African guideline. The recommended ages for using paracetamol and ibuprofen were slightly different in different guidelines, and the dose, frequency, and maximum daily dose were essentially the same. Combined or alternate use of paracetamol and ibuprofen was not recommended.

4. Discussion

In this study, eight global guidelines on managing fever in children were obtained through systematic retrieval. Using the AGREE II instrument, the recommendation level of the ISP, South African, NICE, Chinese, and ACEP guidelines was assessed as grade B, and that of the AAP, New South, and South Australia guidelines was grade C. No grade A recommendation was found. Applicability was the lowest rated domain of the guidelines, except in the NICE guideline. Poor applicability is a common problem of international guidelines.^[16–18] The applicability of the guideline requires a large amount of investment of resources. The development group of the guideline should be fully aware of promotion and obstacles to implementation of the recommendations. Additionally, clinical implementation of the recommendations should be enhanced through pilot guidelines, economic

Table 2
Comparison of recommendations in the eight guidelines.

	AAP	ACEP	IPS	South African	NICE	New South Wales, Australia	South Australia	China
Target population	Nr	≤2 yr old	nr	nr	<5 yr old	<5 yr old	<3yr old	<5 yr old
Definition of fever	Nr	Anal temperature ≥38°C	nr	Body temperature ≥38°C	Increased body temperature exceeds the upper limit of normal body temperature fluctuations during 1 d	Anal temperature ≥38°C	Anal temperature ≥38°C, axillary temperature or Eardrum temperature ≥37.5°C	Anal temperature ≥38°C or axillary temperature ≥37.5°C
Temperature measurement	Nr	Nr	<4 wk: electronic ampit thermometer ≥4 wk: Electronic ampit thermometer or infrared ear (skin) thermometer	Infrared eardrum thermometer or axillary temperature, measuring mouth temperature and anal temperature is not recommended	<4 wk: electronic ampit thermometer 4 wk-5 yr old: 1. electronic ampit thermometer 2. Axillary chemical point thermometer 3. Infrared eardrum thermometer	Anal temperature, measuring mouth temperature, anal temperature and ear temperature is not recommended	Anal temperature is the gold standard, ear temperature is the most correlated with anal temperature, and axillary temperature is the least correlated	Digital thermometer
Physical defences								
Should not be worn too little or tightly	Nr	nr	Nr	✓	✓	✓	nr	Nr
Using the ethanol scrubbing method to cool down is not recommended	✓	nr	✓	nr	Nr	✓	nr	✓
Using warm sponges to handle fever is not recommended	✓	nr	✓	✓	✓	✓	nr	✓
The purpose of antipyretic analgesics	✓	nr	✓	✓	✓	✓	✓	Nr
The purpose of antipyretics is to relieve discomfort in children with fever	✓	nr	✓	✓	✓	✓	✓	Nr
The purpose of antipyretics is not to lower body temperature	✓	nr	✓	✓	✓	✓	nr	Nr
The response to antipyretic and analgesics is unable to determine the severity of the disease	Nr	nr	✓	✓	✓	✓	nr	✓
Antipyretics do not prevent fever and convulsions	✓	nr	✓	✓	✓	nr	✓	✓
Antipyretics cannot be used to prevent vaccine responses	✓	nr	✓	✓	Nr	nr	nr	Nr
The use of antipyretic and analgesic								
When to use antipyretic drugs	>38.3°C	nr	Nr	nr	Nr	nr	nr	≥2 mo, anal temperature ≥39.0°C (Mouth temperature 38.5°C, axillary temperature 38.2°C) or discomfort and depression due to fever
Recommended drugs	Paracetamol and ibuprofen	nr	Paracetamol and ibuprofen	Paracetamol, ibuprofen and metenamic acid	Paracetamol and ibuprofen	Paracetamol and ibuprofen	Paracetamol and ibuprofen	Paracetamol and ibuprofen
Age at which paracetamol can be used	Born	nr	Born	3 mo	Nr	Born	3 mo	2 mo
Oral dose of paracetamol (mg/kg/ dose)	10-15	nr	10-15	15	Nr	15	15	10
Minimum interval between two doses of paracetamol	4 h	nr	4-6 h	4-6 h	Nr	4 h	4-6 h	6 h
Maximum daily dose of paracetamol	90 mg/kg	nr	Nr	90 mg/kg, 4g in total	Nr	nr	90 mg/kg	6 mo
Age at which ibuprofen can be used	6 mo	nr	Nr	3 mo	Nr	6 mo	3 mo	6 mo
Dose of ibuprofen (mg/kg/dose)	10	nr	10	10	Nr	10	5-10	10
Minimum interval between two doses of ibuprofen	6 h	nr	6-8h	6h	Nr	6h	6-8h	6-8h
Maximum daily dose of ibuprofen	40 mg/kg	nr	Nr	40 mg/kg	Nr	nr	nr	Nr
The combined use of paracetamol and ibuprofen is not recommended	×	nr	✓	✓	✓	nr	✓	✓
Alternate use of paracetamol or ibuprofen is not recommended	×	nr	✓	✓	×	✓	✓	✓
Ibuprofen is not recommended	✓	nr	✓	Cautious	Nr	nr	Cautious	Nr
Ibuprofen seems not to exacerbate asthma symptoms	✓	nr	✓	Not asthma caused by NSAIDS	Nr	nr	Nr	Nr
Paracetamol seems not to exacerbate asthma symptoms	✓	nr	✓	Not asthma caused by NSAIDS	✓	nr	nr	Nr

✓ agree; × disagree; nr, not reported.
AAP = American Academy of Pediatrics, ACEP = American College of Emergency Physicians, IPS = Italian Pediatric Society, NICE = National Institute for Health and Care Excellence, NSAIDS = Non-Steroidal Antiinflammatory Drugs.

assessment, training education, and patient's education.^[19] The NICE guideline is a good reference for other guidelines in terms of applicability. To promote application, the UK guideline published relevant information on the official website of the guideline, including comprehensive information, such as guideline appendices, updated information, resources and applications, and relevant evidence. Nevertheless, studies have shown that the compliance of doctors on measurement recommendations for vital signs of febrile children in the NICE guideline is still lower than 50%.^[20] How to bridge the gap between clinical practice and clinical guidelines is an important aspect of updating the guidelines.^[21-22] The rigor of development of the AAP, New South Wales, South Australian, and South African guidelines is problematic. Furthermore, the methods for searching evidence and formulating the recommendations have not been clearly described, as well as whether the guideline has been externally reviewed by experts before its publication. After the draft of the Chinese guideline was completed, it was fully studied and reviewed by pediatric doctors and nurses from 25 hospitals.

Standard, transparent, and clear reporting of the methodology and recommendations of guidelines not only improve the quality of the guideline, but also facilitate the dissemination and implementation of the guideline.^[7] In this study, the RIGHT statement was used to assess the reporting quality of guidelines on fever in children. Our results from the RIGHT statement were almost consistent with those assessed by the AGREE II instrument, which suggested that there was a certain correlation between the methodological quality and the reporting quality. The assessment items of these two tools have their own focus, but both include the scope and purpose of the guidelines, the evidence and recommendations in the development of the guidelines, and funding and conflicts of interest. Because the RIGHT statement is the reporting standard and focuses more on reporting of information on the guideline development process, the applicability of the guideline has not been evaluated.

It is challenging to develop unbiased, independent, transparent, and rigorous guidelines.^[23] Those challenges do not only exist in technical aspects, but can also be the result of a lack of awareness of conflicts of interest and insufficient and ineffective management in the guideline development process. How to deal with conflicts of interest and sources of funding in clinical practice guidelines are persistent and difficult issues. Of the eight guidelines, only two fully described what types of conflicts were relevant to guideline development. It is important that submitting conflict of interest statements according to the RIGHT Statement at the time of publishing their guideline.

Studies have shown that misuse of antipyretic drugs is a common problem in fever in children.^[24] Our study showed that only the AAP and Chinese guidelines clearly described the timing of antipyretic drugs, while the other guidelines indicated the use of antipyretic drugs when fever causes discomfort in children. A study conducted in Italy showed that, using the same guideline, pediatricians with different clinical experience, such as community pediatricians, hospital pediatricians, and junior pediatricians, had different timing of using antipyretic drugs.^[25] However, in this previous study, more than 60% of doctors used antipyretic drugs at 38.5°C, and 10% of resident pediatricians, 13% of community pediatricians, and 22% of pediatricians used 38°C as the timing for antipyretic drugs. Ibuprofen has a similar antipyretic effect and safety to that of paracetamol. However, considering the effects of ibuprofen on

the kidneys, the Italian guideline does not recommend ibuprofen for children with dehydration, varicella, and Kawasaki disease. All guidelines do not recommend a combination of the two antipyretic drugs. The AAP and NICE guidelines recommend that alternative use of antipyretic drugs be considered when fever continues or is still feverish before the next medication. A meta-analysis showed an increase in the proportion of children who did not have fever after 6 hours of alternate use of antipyretic drugs.^[26] However, this was of little clinical significance and could lead to dose errors. Therefore, alternate use of antipyretic drugs was not recommended by the authors of this meta-analysis.

The results of our study are consistent with those of the assessment of guidelines on fever in children using the AGREE tool by Chiappini in 2017.^[27] However, in our study, the RIGHT statement was included to assess the reporting quality of the guidelines. Additionally, more guidelines were included in our study, such as the Chinese guideline, and updated guidelines were used, such as the NICE 2019 guideline.

This study has the following limitations. Guidelines on fever caused by identified specific diseases were not included. Therefore, our results may not be applicable to all febrile children. Additionally, the language was limited to Chinese and English, and guidelines published in other languages may have been omitted.

5. Conclusion

There are limitations in the methodology and reporting quality of all eight global guidelines on fever in children. For future development of these guidelines, attention should be paid to improving applicability of the guidelines in terms of methodology. Additionally, the principles and explanations for formation of recommendations should be described, as well as the limitations of the reporting guideline in detail in terms of the reporting quality. Treatments of fever in children are similar in different countries, but there are still differences that require further research.

Author contributions

LLZ and CZ conceived the study and acquired funding. DW, and CZ had full access to all data in the study, and take responsibility for the integrity of the data and the accuracy of the analyses. LLZ, CZ, and QL designed the study. LNZ and QL developed and tested the data collection forms. CZ drafted the manuscript. LLZ and QL reviewed the manuscript. All authors critically revised the manuscript and approved the final version. LLZ act as guarantors.

Conceptualization: Chuan Zhang, Lingli Zhang, Liao Qiong.

Data curation: Chuan Zhang, Di Wu, fang qin.

Formal analysis: Chuan Zhang, Linan Zeng, Di Wu.

Funding acquisition: Chuan Zhang, Lingli Zhang.

Investigation: Chuan Zhang, Liao Qiong.

Methodology: Chuan Zhang, Liao Qiong, Linan Zeng.

Project administration: Chuan Zhang.

Resources: Chuan Zhang.

Software: Linan Zeng.

Supervision: Lingli Zhang, Liao Qiong.

Validation: Liao Qiong.

Writing – original draft: Chuan Zhang, Lingli Zhang, Di Wu.

Writing – review & editing: fang qin.

References

- [1] Crocetti M, Moghbeli N, Serwint J. Fever phobia revisited: have parental misconceptions about fever changed in 20 years. *Pediatrics* 2001; 107:1241–6.
- [2] Boivin JM, Weber F, Fay R, et al. Management of paediatric fever: is parents' skill appropriate? *Arch Pediatr* 2007;14:322–9.
- [3] Bertille N, Fournier-Charrière E, Pons G, et al. Managing fever in children: a national survey of parents' knowledge and practices in France. *PLoS One* 2013;8:e83469.
- [4] Chiappini E, Principi N, Longhi R, et al. Management of fever in children: summary of the Italian Pediatric Society guidelines. *Clin Ther* 2009;31:1826–43.
- [5] Chiappini E, D'Elia S, Mazzantini R, et al. Adherence among Italian paediatricians to the Italian guidelines for the management of fever in children: a cross sectional survey. *BMC Pediatr* 2013;13:210–6.
- [6] Brouwers MC, Kerkvliet K, Spithoff K. AGREE Next Steps Consortium The AGREE reporting checklist: a tool to improve reporting of clinical practice guidelines. *BMJ* 2016;352:i1152.
- [7] Chen Y, Yang K, Marušić A, et al. A reporting tool for practice guidelines in health care: the RIGHT statement. *Ann Intern Med* 2017;166: 128–32.
- [8] Sullivan JE, Farrar HC. Section on clinical pharmacology and therapeutics, Committee on Drugs, fever and antipyretic use in children. *Pediatrics* 2011;127:580–7.
- [9] Mace Sharon E, Gemme Seth R, Valente Jonathan H, et al. Clinical policy for well-appearing infants and children younger than 2 years of age presenting to the emergency department with fever. *Ann Emerg Med* 2016;67:625–39.
- [10] Shuanghong Luo, Min Shu, Yang Wen, et al. Evidence-based guidelines for the diagnosis and management of certain problems in acute fever of unknown etiology in children aged 0 to 5 years in China (standard version). *CJEBP* 2016;11:81–96.
- [11] Elena C, Elisabetta V, Giulia R, et al. 2016 update of the Italian pediatric society guidelines for management of fever in children. *Pediatr* 2017;180:177–83.
- [12] NICE Guideline Updates Team (UK) Fever in under 5s: assessment and initial management. London: National Institute for Health and Care Excellence (UK); 2019. 11. www.nice.org.uk/guidance/.
- [13] Green Robin, Jeena Prakash, Kotze Shane, et al. Management of acute fever in children: guideline for community healthcare providers and pharmacists. *Suid-Afrikaanse tydskrif vir geneeskunde* 2013;103: 948–54.
- [14] New South Wales (NSW) Kids and Families. Children and Infants with fever – Acute management. 2010; 10. www.health.nsw.gov.au/policies/pd/2010/PD2010_063.html
- [15] South Australian Paediatric Practice Guidelines. Fever without a focus in infants and children excluding the newborn, 2013.
- [16] O'Donoghue KJM, Reed RD, Knight SR, et al. Systematic review of clinical practice guidelines in kidney transplantation. *BJS Open* 2017;1:97–105.
- [17] Tong A, Chapman JR, Wong G, et al. Screening and follow-up of living kidney donors: a systematic review of clinical practice guidelines. *Transplantation* 2011;92:962–72.
- [18] O'Donoghue KJM, Reed RD, Knight SR, et al. Critical appraisal of international clinical practice guidelines in kidney transplantation using the appraisal of guidelines for research and education II tool: a systematic review. *Transplantation* 2018;102:1419–39.
- [19] Brouwers MC, Kho ME, Browman GP, et al. AGREE next steps consortium. AGREE II: advancing guideline development, reporting and evaluation in healthcare. *Can Med Assoc J* 2010;182:E839–842.
- [20] Van de Maat J, Jonkman H, van de Voort E, et al. Measuring vital signs in children with fever at the emergency department: an observational study on adherence to the NICE recommendations in Europe. *European Journal of Pediatrics* 2020;179:191–200.
- [21] Donald E. Casey Jr. Why don't physicians (and patients) consistently follow clinical practice guidelines? *JAMA Intern Med* 2013;173:1581–3.
- [22] Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? a framework for improvement. *JAMA* 1999;282:1458–65.
- [23] Akl EA, El-Hachem P, Abou-Haidar H, et al. Considering intellectual, in addition to financial, conflicts of interest proved important in a clinical practice guideline: a descriptive study. *J Clin Epidemiol* 2014;67:1222–8.
- [24] Lubrano R, Paoli S, Bonci M, et al. Acetaminophen administration in pediatric age: an observational prospective cross-sectional study. *Ital J Pediatr* 2016;42:20.
- [25] Bettinelli A1, Provero MC, Cogliati F, et al. Symptomatic fever management among 3 different groups of pediatricians in Northern Lombardy (Italy): results of an explorative cross-sectional survey. *Ital J Pediatr* 2013;39:51.
- [26] Catherine A Pierce, Bryan Voss. Efficacy and safety of ibuprofen and acetaminophen in children and adults: a meta-analysis and qualitative review. *Ann Pharmacother* 2010;44:489–506.
- [27] Chiappini E, Bortone B, Galli L, et al. Guidelines for the symptomatic management of fever in children: systematic review of the literature and quality appraisal with AGREE II. *BMJ Open* 2017;7:e015404.