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Original Article

Research on Establishing a Core Outcome Set for Clinical Research of Traditional Chinese Medicine in Children with Abdominal Henoch-Schonlein Purpura

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Abstract ***Objective:*** This study aims to investigate and analyse the outcomes reported in clinical studies of abdominal Henoch-Schonlein purpura, and to establish the core outcome set (COS) for children with abdominal Henoch-Schonlein purpura (HSP). ***Methods:*** Following standard operating procedures for COS development, an systematic review was conducted to extract outcomes from the relevant clinical studies, then conducted two rounds of Delphi study, after that a consensus meeting was held to finalise COS. ***Results:*** A total of 6 outcomes were included in the final COS: the degree of abdominal pain, time to abdominal pain disappearance, and time to bloody stool disappearance, and the incidence of adverse reactions or complications. ***Conclusion:*** A COS comprising 6 outcomes for abdominal HSP has been established, providing a valuable reference for the selection of outcomes in future clinical trials in this area.

Key words *Children; Core outcome set; IgA vasculitis; Purpura*

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Background

Immunoglobulin A vasculitis (IgAV), commonly referred to Henoch-Schonlein purpura (HSP), is a type of non-thrombocytopenic small-vessel vasculitis and is the most common form of childhood systemic vasculitis (with an annual incidence ranging from 3-26.7 per 100,000, depending on the country).[1] The disease typically manifests with a palpable purpuric rash, gastrointestinal pain and bleeding,[2] kidney involvement, arthralgia, and/or arthritis.[3] Abdominal involvement is characterised by paroxysmal diffuse abdominal pain, often accompanied by gastrointestinal bleeding.[4] When gastrointestinal symptoms are typical, it is referred to as abdominal Henoch-Schonlein purpura (AHSP). The clinical efficacy and safety evaluation of medical interventions are typically based on the measurement and analysis of specific clinical outcomes.[5] However, studies have found that the outcomes used in clinical research are frequently inconsistent, nonstandard, or inessential, weakening the scientific and practical nature of research results and leading to research waste.[6,7] To address the multifaceted issues related to outcomes that are reported in clinical rials, experts in evidence-based medicine and clinical research

methodology have proposed strategies to establish core outcome set (COS). These sets represent an agreed-upon minimum standardised set of outcomes that should be measured assessed and reported in all trials focusing on a specific condition.[8-10] The development of a core outcome set for traditional Chinese medicine in abdominal Henoch-Schonlein purpura would minimise the heterogeneity of reported results and improve the methodological quality of clinical research in Traditional Chinese Medicine (TCM), which is important for international recognition.

Methods

We followed Core Outcome Measures in Effectiveness Trials (COMET) guidelines for this COS development study and reported on it by Core Outcome Set–Standards for Reporting.[11] The current report was drafted according to Core Outcome Set–Standards for Reporting guidelines, which include a systematic review, Delphi process, and consensus meeting. The production process of the core indicator set is shown in Figure 1.

Registration

This study was registered with Core Outcome Measures in Effectiveness Trials (https://www.comet-initiative.org/Studies/Details/1281) as Developing a Core Outcome Set of Traditional Chinese Medicine for abdominal Henoch-Schonlein purpura in Children.

Experts Committee

We have established an expert committee and a secretary group to support this study. The expert committee is composed of pediatricians, clinical epidemiologists, and experts in evidence-based medicine. The secretary group is composed of medical students.

In consideration of geographical balance, experts from various regions in China were invited. The expert committee to be included is as follows:

(1) Engaged in the following fields: TCM clinician specialising in children's abdominal Henoch-Schonlein purpura, and Western medicine clinician in paediatric gastroenterology, dermatology, and methodology.[12]

(2) Holds a senior professional title and has been practicing in clinical work in paediatrics for over 10 years.

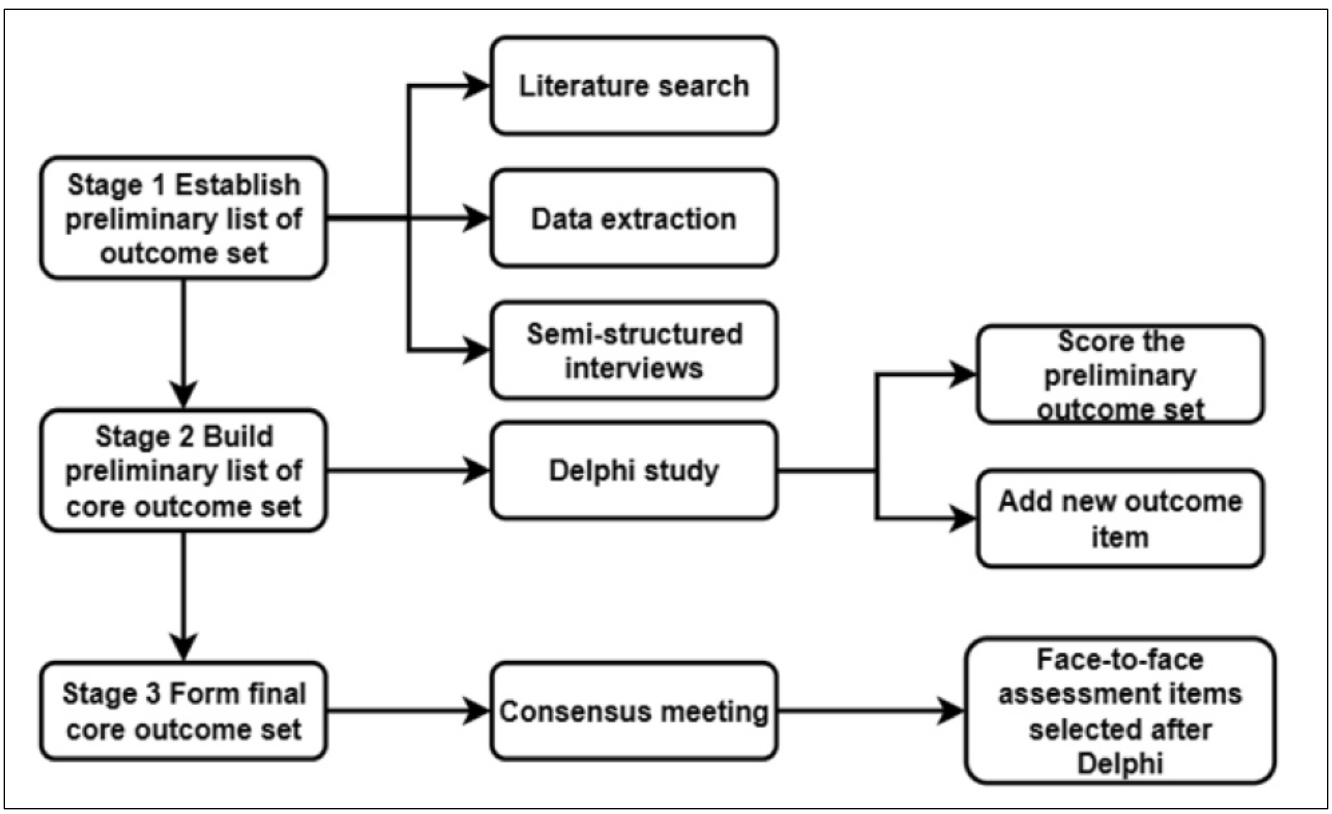

Figure 1 Flowchart illustrating the development of the COS.

(3) For those with COS research experience and who have published COS-related papers, their career is not limited to 10 years.

The secretary team collected and verified questionnaires, following the research process as planned. The expert committee facilitated the Delphi survey and will ultimately develop the final core outcome set in the consensus meeting.

Scope

The scope of the COS for abdominal Henoch-Schonlein purpura will be as follows:

(1) Health problems: meeting the diagnostic criteria of abdominal type or a combination of abdominal and cutaneous types, is classified as HSP (abdominal type) or HSP (abdominal type, cutaneous type), the abdominal Henoch-Schonlein purpura in the ICD-10 code is D69.009, which can be associated with cutaneous HSPD69.001;
(2) Target population: patients with abdominal Henoch-Schonlein purpura, aged 2-18 years.
(3) Intervention measures: mainly target at traditional Chinese medicine or integrate traditional and Western medicine (Western medicine can refer to universal outcomes).
(4) Research type: a clinical trial.

This COS is intended to serve as a standard for all clinical research on TCM focusing on the effectiveness and safety of interventions for abdominal Henoch-Schonlein purpura.

Systematic Review

To establish an preliminary outcomes and domains, we conducted a systematic review of outcomes reported in published trials from January 2010 to March 2020. This was done through a search strategy developed through discussion within the research group and by conducting searches across various databases including PubMed, EMBASE, the Cochrane Library, Web of Science, China Biomedical Literature Database, CNKI, VIP, and Wanfang database.

Inclusion criteria: (1) Research type: a clinical trial; (2) Participation: Participants were meet the diagnostic criteria of HSP (abdominal type) or HSP (cutaneous types, abdominal type) of traditional Chinese medicine and /or Western medicine; Participants were under 18 years of age; (3) Design of experimental and control groups: The intervention measures for the experimental group and the control group are traditional Chinese medicine and / or integrated traditional Chinese and Western medicine, and the form of contrast is not limited; (4) Outcome: no limit on outcome indicators and follow-up time;

Exclusion criteria: (1) HSP of mixed type with abdominal gastrointestinal symptoms (ICD-10 code D69.006) and other organs and systems other than common five type were excluded; (2) The information of outcome indicators cannot be obtained.

Two reviewers independently screened citations and extracted data on study characteristics, outcomes, and measures (with a third author as arbiter if needed). The frequency of occurrence of each outcome measure in each study was recorded, and the reporting rate was calculated. We only extracted the outcome indicators included in the literature report, classified all indicators according to professional knowledge without duplicate removal, and drafted the preliminary list of outcomes and outcome domains.

Semi-structured Interviews

We extracted all outcome indicators and their corresponding fields, creating a comprehensive blueprint. Through iterative small-scale pre-interviews, we combined and refined the removal of certain outcome. This process culminated in the development of an interview outline, designed to be presented to participating experts for evaluation of its importance.

The target population was selected using purposive sampling, and the sample size was determined based on "information saturation". A questionnaire survey was conducted among Chinese and Western children's HSP clinical experts/researchers, focusing on interviews with clinical experts who specialise in Chinese medicine in treating children with AHSP.

Considering the varying professional titles of the interviewees and the diverse capacities of hospitals in providing medical care, education, and conducting medical research, we selected some clinicians from the departments of traditional Chinese medicine specialising in paediatrics, digestion, and dermatology. This group included directors, deputy directors, and attending doctors for the interviews.

Semi-structured interviews are conducted through a combination of online voice interviews and face-to-face interviews by qualified interviewers. Based on the interview outline prepared in advance, the interviewees, through qualitative semi-structured interviews, based on professional theoretical knowledge and clinical

experience, provided important outcomes regarding the clinical efficacy in AHSP clinical trials. They also shared relevant information about the measurement time points based on their professional theoretical knowledge and clinical experience. Establishing the preliminary outcome domain, lay the foundation for the design of the Delphi expert questionnaire.

Delphi Study

We formulate the expert questionnaires based on the preliminary outcomes, combined with the modification opinions and supplementary outcomes proposed during the interview. The survey will involve two rounds of surveys completed by a panel of participants to assess the importance of outcomes and select significant outcome for subsequent consensus meetings.

We invited experienced experts from various regions and medical institutions in China to participate in the questionnaire survey. The selection of experts is primarily based on database queries, telephone consultations, and industry recommendations. This includes abdominal HSP's clinical experts in traditional Chinese medicine and Western medicine, clinical researchers and other relevant professionals.

In the end, there were four Western medicine experts, one pharmacy expert, and 31 Chinese medicine experts joined.

First Round

The questionnaire is distributed online through the electronic questionnaire app and email. Responses were kept confidential and were not visible to each other.

Participants would be asked to score individual outcomes using the nine-point Likert scale: 1 to 3 indicate that the outcome is not important, 4 to 6 suggest it is important but not critical, and 7 to 9 indicate that the outcome is critical. This scale was created by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) working group and has been widely adopted by developers of core outcome sets. Additionally, participants were invited to suggest any outcome measures that they would consider relevant but are missing from the list of outcomes. Any additional outcomes would be considered by the research group and included in the scoring in the second round of Delphi.

When the first-round survey were completed, we collected questionnaires and conducted statistical analysis. A standardised definition will be applied to the results to identify core outcomes, as defined by the 70/15% consensus definition as advocated by the COMET initiative.[13] The criteria are as follows: (1) Consensus inclusion: ≥70% of the participants scored outcomes as 7-9, and <15% of the participants scored a outcome as 1-3. (2) Consensus exclusion: If 70% or more of the participants scored outcomes as 1-3, and less than 15% rated a outcome as 7-9. (3) No consensus: Values other than the above.[12]

At the end of the first round of Delphi, outcomes that achieve "Consensus in" would be included in the preliminary core outcome set and discussed in the subsequent consensus meeting. There is no need to repeat scoring in the second round of Delphi. Outcomes that achieved "Consensus out" will be excluded directly and will not be displayed repeatedly in the second round of questionnaire. Outcomes that achieved "No consensus" would form the questionnaire of the second round.

Second Round

The process of the second round were the same as before. Participants who completed round 1 would be invited to complete round two. They would be informed of the mean, median, and range of importance scores for each outcome from the previous round. At the end of the Delphi study, all outcomes that achieved "Consensus in" constitute a preliminary COS, which would be taken forward to a face-to-face meeting for discussion. Agreement would be measured using defined consensus rules of outcome inclusion.[14]

Consensus Meeting

Both an offline and online venue hosted the consensus meeting. We further picked experts with more authority or in-depth understanding of the disease from among the experts who took part in the Delphi survey, and we invited them to attend a consensus meeting to vote on and discuss the outcome indicators found in the survey. Email invitations with a link to the online consensus meeting will be sent to those who are willing to join. Before the meeting, participants were provided with an agenda, objectives, and methods, and presented summary data from the systematic review and Delphi process. The contents of the consensus meeting covered five aspects: (1) Reporting the research backgrounds and methods; (2) Reporting the results of two rounds of the Delphi survey; (3) Putting forward the key points to be discussed; (4) Thoroughly discussing the core outcomes of the candidate, including the definition, measurement and importance; (5) Voting on the outcomes and achieving a

consensus through discussion to finalise the final COS.

After the consensus meeting, the preliminary core outcome set will be further clarified into three categories: A1 (outcomes that are critical and require reporting) and A2 (conditional reporting outcome: important but may not be reported due to lack of relevance or feasibility). The remaining outcome that entered the preliminary core outcome indicator set but did not reach a consensus on inclusion would be automatically classified as A3 (outcomes that are important can be reported as an option).

Experts were convened to discuss all indicators included in COS, covering their definitions, measurement methods, and significance. They also voted on the preliminary core outcome set and immediately compiled statistics on the voting results on the spot to clarify outcomes agreed upon by consensus. The consensus definition for inclusion in the COS is as follows: (1) A1 outcomes: at least 80% of respondents had to vote that the item should be included in the final COS. (2) A2 outcomes: at least 65% of respondents had to vote that the item should be included in final COS. (3) Outcomes that do not meet the above conditions are classified as A3.

Result

Systematic Review

A total of 89 studies were included in this study, including 86 randomised controlled studies and 3 cohort studies, all of which reported outcomes; seven reports were funded, but none reported conflict of interest declarations. Sixty-nine outcomes were extracted from 89 research. The details of the systematic review are as follows (Figure 2).

From the functional attributes of the outcomes, it is planned to categorise the preliminary outcome items by professional knowledge to seven outcome domains: Clinical symptoms and signs index, overall efficacy index, TCM syndrome-type efficacy scores, blood biochemical outcomes, safety outcomes (including adverse reactions and complications) and other outcomes.

Semi-structured Interviews

Based on the outcomes extracted from the literature, formed an interview outline containing 79 outcomes and 13 outcomes domains through pre-interview. We interviewed 10 clinicians, including five chief physicians,

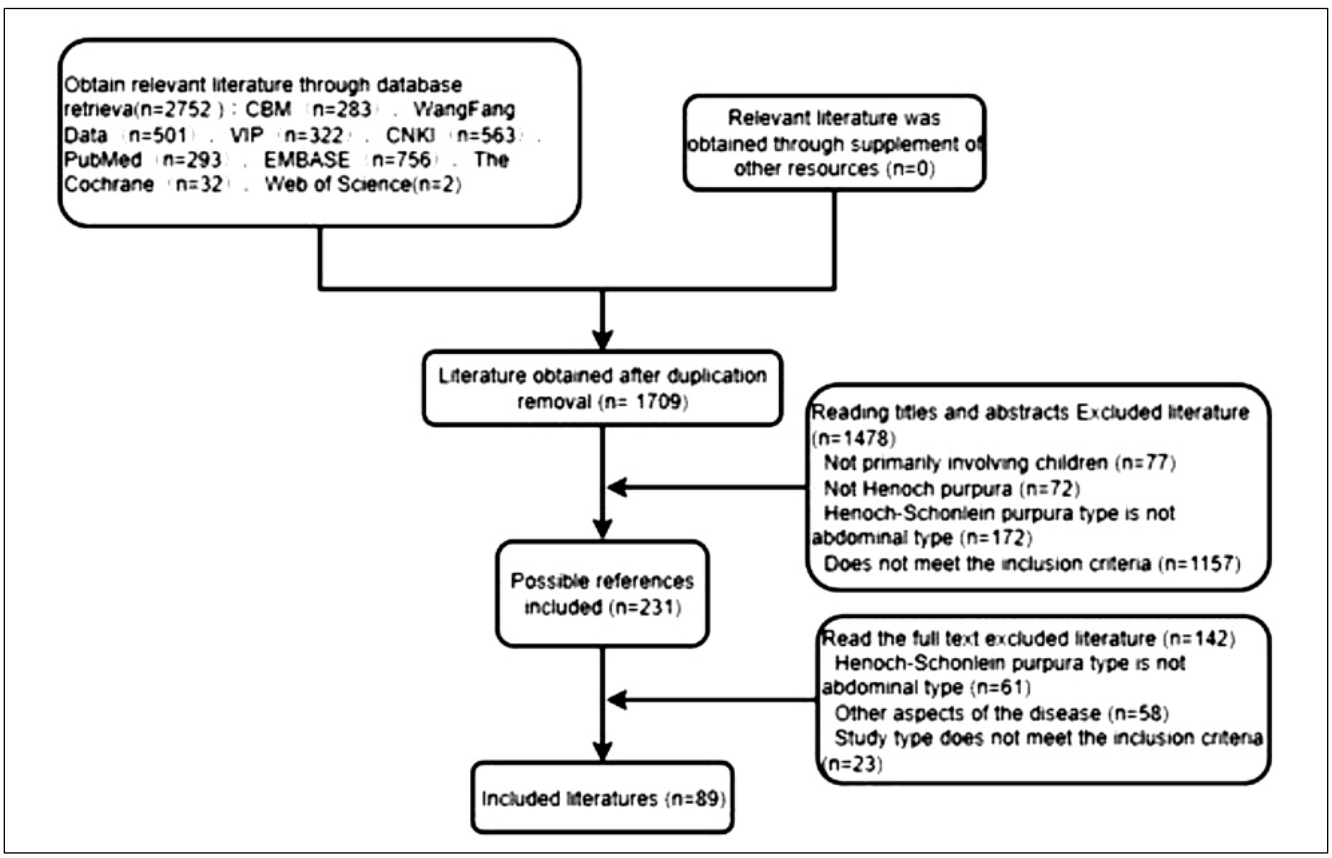

Figure 2 Flowchart of literature screening.

three deputy chief physicians, and two attending physicians, all from Beijing Children's Hospital. After experts added and deleted the outcome in the interview outline, for example, experts in traditional Chinese medicine suggested adding biochemical indicators, coagulation functions, other indicator fields, and a series of outcome indicators, a total of 33 outcomes were added, and 17 outcomes were deleted. Finally, a preliminary outcome list containing 95 outcomes and 10 outcomes fields was formed. Because the individual outcome indicators supplemented by individual experts did not reach the approval of most experts, they were not included in the preparation of the Delphi expert questionnaire. Therefore, there were 92 outcomes and 10 outcomes domains that finally entered the Delphi expert questionnaire.

Delphi Study

We selected 42 experts from 20 hospitals across the country representing 12 disciplines and distributed 36 online questionnaires. Among them were four Western medicine experts, one pharmacologist, the remaining 31 experts specialise in Chinese medicine. In the first round, 36 questionnaires were collected, with a positivity rate of 86%. There are 20 indicators scoring 7 to 9 points. The average scores for each outcome indicator are detailed in Table 1.

Of the 92 preliminary outcomes presented to the Delphi panel in round 1, we found that 14 had met the criteria of consensus. Therefore, they were included in the preliminary list of core outcome set after this round. No outcomes were excluded after round one.

In round two of the Delphi process, the remaining 78 outcomes were once again presented to the panelists from round one, 36 questionnaires were submitted to 36 experts who participated in the first round, 35 were returned, and the percentage of experts in favor was 97.22%. By the end of this round, an additional 4 outcomes had reached consensus. Therefore, a total of 18 outcomes were selected for the preliminary core outcome indicator set for discussion of a consensus meeting (Table 2).

During the two rounds of Delphi, a total of 17 additional outcomes were identified, including Rash (Range and degree of rash, The severity and color of the rash, Skin rash on face), Digestive system (Fasting time, Helicobacter pylori-positive, Degree of repair of digestive tract mucosa (such as gastrointestinal congestion and oedema, bleeding point, erosion, ulcer range, location, etc.)), Overall efficacy (The incidence rate of abdominal HSP, Diet recovery, Selection of hormone varieties, initial daily dose, initial use time, and hormone reduction, Glucocorticoid reduction time, Degree of malnutrition in children, The number of cases of concurrent Henoch-Schonlein purpura nephritis), Biochemical indicators (Prealbumin, transferrin, retinol, Anti-streptococcal haemolytic (ASO) concentration), Cellular immune index(Autoantibody related tests, Cell factor), Security (Liver and kidney function).

These indicators were discussed together at the expert consensus meeting.

Consensus Meeting

Sixteen experts who are regarded as reasonably authoritative, possess a thorough understanding of AHSP, and are prepared to take part in the vote and debate were invited to the consensus meeting out of the 36 experts who completed the Delphi survey. This group included one Western medicine expert, one pharmacy expert, and 10 Chinese medicine experts. Six outcomes were meeting the consensus inclusion criteria (Table 3), and the remaining 12 outcome indicators were automatically included in A3. After expert discussion, there are four outcomes were finally identified as A1 (Outcomes that are critical and require reporting): the degree of abdominal pain, time to abdominal pain disappearance, and time to bloody stool disappearance, and safety, such as the incidence of adverse reactions or complications (like intestinal obstruction or intussusception). Two other outcomes included in A2 (Conditional reporting outcome) were the improvement of lower intestinal wall oedema by abdominal ultrasonography, and TCM syndrome type efficacy score.

Discussion

This study followed established COMET methods for COS development. We used systematic review methods and conducted qualitative interviews with the clinicians to compile a comprehensive list of potential outcomes. Robust consensus-building (Delphi and consensus meeting) methods were then used to establish 6 outcomes for inclusion in the final core outcome set.[15] The outcomes are relevant for children and are appropriate for all cases of abdominal Henoch-Schonlein purpura. It is anticipated that the outcomes will be used in future clinical and research studies, and reviews, and for helping to develop future guidelines for abdominal Henoch-Schonlein purpura.[16]

In the previous systematic review, we found that the

Table 1 Score of the importance of outcome items in different outcome domains

Outcome domain	7-9 points	4-6 points	1-3 points
Rash	Rash recurrence rate	Time of rash resolution The time when the rash began to subside Time of complete resolution of the rash 2-week rash resolution rate Angioneurotic oedema	
Digestive system	Time for gastrointestinal symptoms to turn negative Degree of abdominal pain Abdominal pain relief Time to abdominal pain disappearance Abdominal pain duration/abdominal pain disappearance time Vomiting duration/Vomiting disappearance time Time of haematemesis disappearance Blood stool disappearance time Remission time of bloody stool Improvement of intestinal wall oedema under abdominal ultrasound Complications such as intestinal obstruction and intussusception The recurrence rate of gastrointestinal symptoms	Time of vomiting relief Remission time of haematemesis Time of fecal occult blood turning negative Cases of gastrointestinal mucosa repair Comparison of ascites before and after treatment Comparison of abdominal lymph node enlargement before and after treatment	
Overall efficacy	Effective Recurrence rate Glucocorticoid dosage (mg/kg) Duration of glucocorticoid therapy	Hospitalisation days	
Therapeutic effect of TCM syndrome type	Efficacy score of TCM syndrome types		
Biochemical index		Electrolyte (potassium ion, sodium ion, chloride ion), Albumin, Total blood protein, Serum urea nitrogen Serum creatinine, Uric acid, cholesterol, Blood fat, Serum triglyceride, ALT, AST, Serum cystatin, Endogenous creatinine clearance, Urine amylase, Serum amylase, Serum lipase, Blood sugar Blood calcium	
Blood routine index	C-reactive protein	Red blood cell, Haemoglobin, Haematocrit, Mean corpuscular volume, Mean haemoglobin, Mean haemoglobin concentration, Red blood cell distribution width, Reticulocyte count, White blood cell count, Percentage of neutrophils, Lymphocyte percentage, Monocyte percentage Neutrophil count, Lymphocyte count, Monocyte count, platelet, Average platelet distribution width, ESR	
Coagulation function	D-Dimer	Coagulation time, Bleeding time, Prothrombin activity PTA, Plasma thromboplastin time PT, Activated partial thromboplastin time APTT, Antithrombin AT, Fibrinogen FIB, Fibrin degradation product FDP	
Humoral immunity index		LgA, lgD, lgE, IgG, lgM, complement, γ-interferon, Cold globulin experiment, Immune complex	
Cellular immune index		CD3+ (total T lymphocytes), CD3+CD4+ (Th cells), CD3+CD8+ (Ts cells), Th /Ts cell ratio, CD19+ (B lymphocyte), CD16+CD56+ (NK cells)	
Safety		Adverse drug reactions	

outcomes extracted from the literature were heterogeneous and numerous. Some outcomes had repetitive meanings or unclear definitions, reflecting the heterogeneity of outcomes for abdominal Henoch-Schonlein purpura. Although a common vasculitis in pediatric practice, well-designed controlled studies are lacking.[17] This is partially due to the usual self-limiting nature of the disease.[18,19] Therefore, the significant heterogeneity among outcomes measured and reported is a common issue across all trials.[20] When outcome heterogeneity arises, it hampers the ability to compare the effectiveness of interventions across trials and to combine trial results (such as in a meta-analysis). This leads to significant inefficiencies in research and contributes to research waste, ultimately creating barriers to greater evidence-based practice.

We chose an online Delphi method because it allowed for the participation of clinicians and researchers from multiple sites across different areas. This strategy also enabled the purposeful selection of a panel to ensure representation of a variety of stakeholders from different areas and healthcare systems, including both professionals and patients.[20] The use of the anonymous Questionnaire Star software also helped minimise social pressures when it came to voting. This enabled the study to involve a high level of expert participation, enhancing the accuracy of the data and results while reducing bias. Since the Delphi survey was disseminated via email and an online questionnaire, it was easy to access to ascertain the total number of individuals approached and, consequently, the proportion who participated. Also, although reminders for

Table 2 Preliminary core outcome set formed after two rounds of Delphi

Outcome domain	Outcome indicator
Rash	Rash recurrence rate
Digestive system	Time for gastrointestinal symptoms to turn negative Degree of abdominal pain Abdominal pain relief Time for abdominal pain to subside Abdominal pain duration/abdominal pain disappearance time Time of haematemesis disappearance Blood stool disappearance time Remission time of bloody stool The recurrence rate of gastrointestinal symptoms Improvement of intestinal wall oedema under abdominal ultrasonography Complications such as intestinal obstruction and intussusception
Overall efficacy	Efficiency Recurrence rate Glucocorticoid dosage (mg/kg) Duration of glucocorticoid therapy
Therapeutic effects of TCM syndrome types	Efficacy score of TCM syndrome types
Blood routine index	D-Dimer

Table 3 The final core outcome set of AHSP

Category	Outcome
A1 (Outcomes that are critical and require reporting)	The degree of abdominal pain Time to abdominal pain disappearance Time to bloody stool disappearance Safety, such as the incidence of adverse reactions or complications (like intestinal obstruction or intussusception)
A2 (Conditional reporting outcome)	The improvement of lower intestinal wall oedema by abdominal ultrasonography TCM syndrome type efficacy score

completion were circulated, not all participants who took part in round one participated in round two.[21]

During the expert consensus meeting, there were varying opinions among the experts regarding individual outcomes with higher scores in the Delphi questionnaire, such as the improvement of lower intestinal wall oedema by abdominal ultrasonography. Although ultrasound is economical and easy to operate, it is a relatively subjective examination and greatly influenced by the patient's condition, ultrasound equipment, and operator. Therefore, it was included in A2 (conditional reporting outcome). We recommend that authors consider the study context and participant when interpreting this outcome. There is a need for future research to determine the best methods to operationalise these outcomes.[22] In particular, relevant outcomes of traditional Chinese medicine, such as the TCM syndrome type efficacy score, can be used when conducting a clinical trial related to traditional Chinese medicine intervention.

Selecting a COS is only part of the process of standardising outcomes.[15] How each outcome should be defined and measured plays a fundamental role in ensuring that future pooling of data is possible.[23-25] Defining these outcomes will require an initial systematic review of reported definitions, followed by a consensus process. The responses in Delphi suggested that establishing a consensus process for utilising these outcomes would be highly complex and challenging; nevertheless, the outcomes identified during the process are expected to be of interest to researchers and other stakeholders. To date, there is no consensus on the optimal method for defining and quantifying the outcome measures included in this core outcome set. Also, there is no evidence or consensus to date on what time points are the most beneficial time points for measurement. Most intervention trials do not utilise validated measurement instruments to report outcome measures.[26] The next phase will be to determine how to measure the selected outcome measures in the final core outcome set by conducting a systematic review to identify the available outcome measurement instruments are available for the outcome measures included in this core outcome set.[27] Methodology for developing of core outcome sets is evolving, and we acknowledge that our COS will need regular updates as new outcomes and metrics are developed over time.

Limitations

This study did not utilise a more comprehensive mixed methods approach, which would have involved conducting patient interviews alongside our systematic review, to determine outcomes for incorporation in the Delphi round of the core outcome set development process.[6,26] However, this was mitigated by including them in semi-structured interviews and by extracting outcomes during the systematic review. Additionally, Delphi round one participants were enabled to suggest additional outcomes for consideration. It could be confirmed by a recent study that outcomes obtained from patient interviews do not directly influence the final core outcome set because they coincide with the outcomes presented after round one of the Delphi process.[28] Besides, there is guidance that recommends maximising the response rate from a variety of groups.[29] In addition, it is important to strike the right balance between the feasibility of using the COS and obtaining sufficient depth of information to distinguish between outcomes of interest.

Face-to-face approaches allow for more extensive discussions but are constrained by limited due to COVID-19, resulting in a restricted number of participants in the face-to-face meetings. We found that online experts may be influenced by various factors such as region, environment, and equipment. The participation rate is generally slightly lower than that of offline experts, and they are unable to actively express their suggestions on the topic of discussion. However, through the statistics of the voting results of the consensus meeting, we believe that this limitation was significantly mitigated by the high agreement in the online panel of participants in consultation round.[30]

The respondents and included literature in this study were primarily based on clinical experts and trials of traditional Chinese medicine. The number of Western medicine experts is relatively small. The best approach would be to conduct interviews and Delphi processes with both Western medicine and traditional Chinese medicine practitioners. Contrasting their different COS opinions through the process so as to come up with a standard that is useful for the aim of TCM clinical trials in abdominal Henoch-Schonlein purpura. An extension of this work would be to repeat the process including a higher or more balanced proportion of participants from Western medicine participants, to determine whether the choice of outcomes changes.

Future iterations of the COS are expected and encouraged to enhance its utility. Future work may specifically address some of the sampling limitations in our study (e.g., a broader range of providers and international representation) or may focus on refining the

domains (e.g., evaluating applicability across different diagnoses or interventions).[31]

COS Applying Advice

We believe the COS should be utilised by future trialists as the minimum set of outcomes that should be collected in an HSP trial. Importantly, this COS represents a crucial step towards enhancing and advancing much-needed evidence synthesis in this specific disease area[32,33] It is challenging task to include all COS outcomes in an individual clinical trial. And the outcomes that have not been included in COS are also of great clinical significance. We need to have a more accurate understanding of the different categories in COS for abdominal HSP. The four outcomes of A1 are critical and require reporting in a clinical trial. The other two outcomes of A2 are conditional reporting outcome, and it is important but may not be reported due to lack of relevance or feasibility. Furthermore, when clinical trial focus on traditional Chinese medicine or when researchers have the conditions to perform abdominal ultrasound for intestinal wall oedema, the above outcomes are required to be reported.

Conclusion

In summary, we developed a Delphi expert questionnaire by summarising relevant literature and semi-structured interview results in the early stage. Subsequently, we held an expert consensus meeting based on the Delphi questionnaire results. Through this process, we identified a total set of 6 core outcomes and recommend that these outcomes be minimally measured in clinical trail assessing abdominal Henoch-Schonlein purpura in children. It will depend on the study population, the study design, and the intervention being assessed to determine which outcomes are appropriate to include.

List of consensus experts who participated in COS construction (in alphabetical order by pinyin of last name)

Ai Jun (Guangxi University of Chinese Medicine), Chang Ke (Hospital of Chengdu University of Traditional Chinese Medicine), Cui Xia (The Third Affiliated Hospital of Beijing University of Chinese Medicine, Feng Xiaochun (The Affiliated Hospital of Changchun University of Traditional Chinese Medicine), Hao Jing (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), He Qiang (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Huang Jing (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Hu Yan (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Li Min (Beijing Hospital of Traditional Chinese Medicine, Capital Medical University), Liu Chang (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Liu Yali (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Liu Jing (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Li Xin (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Peng Xiaoxia (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Qin Yanhong (Affiliated Hospital of Shanxi University of Chinese Medicine), Sun Liping (The Affiliated Hospital to Changchun University of Chinese Medicine), Wang Wenge (Air Force Medical Center, PLA), Wang Meng Qing (The First Hospital of Hunan University of Chinese Medicine), Wang Junhong (Dongzhimen Hospital, Beijing University of Chinese Medicine), Wu Liqun (East Hospital of Beijing University of Chinese Medicine), Wu Xianwei (Gansu Provincial People's Hospital), Xiao Heyin (Wangjing Hospital of China Academy of Chinese Medical Sciences), Xue Zheng（Shanghai Municipal Hospital of Traditional Chinese Medicine), Xu Jiaosheng (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Yang Yan (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Yang Yang (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Yuan Bin (Affiliated Hospital of Nanjing University of Chinese Medicine), Yu Changhe (Dongzhimen Hospital, Beijing University of Chinese Medicine), Yu Feihong (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Yu Jian (Children's Hospital of Fudan University), Zhang Baoqing (Affiliated Hospital of Shandong University of Traditional Chinese Medicine), Zhang Jing (Beijing Children's Hospital, Capital Medical University, National Center for Children's Health), Zhai Wensheng (The First Affiliated Hospital of Henan University of

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Conflict of Interest

All authors have disclosed no conflicts of interest.

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