Developing clinical questions and important outcomes for the clinical practice guideline for acupuncture and moxibustion for allergic rhinitis

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Research

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Abstract

Background

Acupuncture and moxibustion have been widely applied in treating allergic rhinitis (AR). However, there is a lack of evidence-based guidelines for acupuncture and moxibustion for AR, thus we started a project on developing an international clinical practice guideline (CPG) for acupuncture and moxibustion for AR (WFASRP202001-SC05) approved by the World Federation of Acupuncture-Moxibustion Societies (WFAS). This study aims to formulate the clinical questions and important outcomes for this guideline.

Methods

Based on the principle of the WFAS standardization committee, multiple methods including the International PICO question survey, Delphi survey, and consensus conference of guideline development group (GDG) were applied. International PICO questionnaires widely gathered the demands from the target population. Then GDG selected clinical questions and important outcomes for the guideline via a mixed method of Delphi survey and consensus conference.

Results

15 potential clinical questions and 10 sorts of outcomes were formulated under the supervision of a guideline steering group based on the analysis of 123 pieces of feedbacks from 17 countries of 5 continents. After 2 rounds of the Delphi survey, the consensus was reached in GDG that all of the potential questions were included. After 3 rounds of the Delphi survey, the consensus was reached that 9 of these outcomes were considered important outcomes.

Conclusion

15 clinical questions and 9 important outcomes were selected for the CPG for acupuncture and moxibustion for AR. Since there has not established a standard method in formulating the clinical questions and important outcomes for CPGs in acupuncture and moxibustion, this one will be a useful reference.

Background

Allergic rhinitis (AR) is one of the most common chronic diseases, with a prevalence of up to 40%[1]. Without efficient control, AR patients suffer high a risk of comorbidity with asthma[2] or other disorders of the immune system[3]. AR also seriously affects patients' life quality and increases the incidence of traffic accidents [4] and suicide [5].

Clinical evidence has accumulated that acupuncture and moxibustion were safe and efficient in treating allergic rhinitis (AR)[6–9]. Several clinical practice guidelines and consensus statements on allergic rhinitis recommend acupuncture-moxibustion therapy as a therapeutic adjunct[10–12]. However, the specific recommendation of acupuncture and moxibustion operation has not yet been given. Therefore, it is necessary to develop a clinical practice guideline (CPG) for acupuncture and moxibustion in treating AR. The CPG for acupuncture and moxibustion for allergic rhinitis approved by the China Association of Acupuncture and Moxibustion mainly served acupuncturists and relevant practitioners in China[13], whereas this guideline approved by the standardization working committee of WFAS (Project Number: WFASRP202001-SC05) will provide recommendations for practitioners around the world.

The establishment of clinical questions in the PICO (Patient, Intervention, Comparator, Outcome) framework is the key step in developing evidence-based CPG[14]. Ahead of the formulation of clinical question and important outcome of this guideline, we have designed an international PICO question survey for the target population[15] and set up the guideline steering group, the guideline draft group, and the guideline development group based on the regulation of the WFAS standardization committee. The objective of this study was to reach a consensus on the clinical questions and important outcomes for the CPG for acupuncture and moxibustion for allergic rhinitis.

Methods

The clinical questions and important outcomes were developed via three steps, referring to previous consensus studies[16, 17]. The following procedure was carried out: (1) International survey, analysis, and formulation of potential clinical question and outcome lists; (2) Delphi survey on importance rating of clinical questions and outcomes; (3) Consensus conference on the clinical questions and important outcomes for the CPG. The Delphi survey and consensus conference were applied as a mixed method for reaching the consensus (See Fig. 1). According to the scope of this international CPG for acupuncture and moxibustion for allergic rhinitis, the target population includes acupuncturists, TCM practitioners, otolaryngologists, teachers, and researchers in medical school. The applicable settings of this CPG are the acupuncture and moxibustion department in hospitals, clinics specialized in acupuncture and moxibustion, medical schools specializing in acupuncture and moxibustion, and research institutions related to acupuncture and moxibustion. Therefore, the international survey and consensus should reveal the demands of these target populations from different settings.

International survey on PICO clinical questions

To comprehensively reflect the demands on each aspect of clinical questions and outcomes, we have designed an online survey and send the questionnaire to the target populations from different countries. The questionnaire was also published in a journal for potential target populations to feedback[15]. For the feedback that could not formulate clinical questions in PICO format, we corresponded with the participant via telephone or email, explaining the PICO structure and asked them to fill the questionnaire again. We analyzed the most concerned foreground clinical questions and patients, interventions,

comparators, and outcomes related to the questions. The frequency or percentage of each element will be calculated and presented as statistical graphs. Then, the guideline draft group will formulate the potential clinical questions and outcomes lists based on the feedbacks under the supervision of the guideline steering group.

Delphi survey on importance rating of clinical questions and outcomes

Ahead of the consensus conference, we introduced the background knowledge and formulating process of the potential clinical questions and outcomes by PDF documents and asked the guideline development group (GDG) members to finish the first round of the Delphi survey online. For clinical questions and outcomes, GDG members were required to rate its importance, make comments if necessary (especially for the items that are strongly preferred or disagreed, comments were required), and choose familiarity (Ca) on the question as well as judgment basis (Cs). For clinical questions, the importance was rated by a 5 point Likert scale (very important = 5, important = 4, moderately important = 3, slightly important = 2, not important = 1)[18]. For outcomes, GRADE hierarchy rules (7 ~ 9 = critical, 4 ~ 6 = important, 1 ~ 3 = low important) were applied[14]. For each item, mean scores, coefficient of variation (CV = SD /($\bar{\chi}$), and authority coefficient (Cr=(Ca + Cs)/2) were calculated and displayed in statistical graphs.

Consensus conference on clinical questions and important outcomes

The process and results of the first step survey, as well as the formulation of potential clinical questions and outcomes, were introduced at the consensus conference online (via Tencent Cloud Meeting). Then, the result of 1st round Delphi survey was displayed anonymously, and each GDG member was required to express their opinion. Then there was a full discussion on the items with CV > 25%. After that, the 2nd round of the Delphi survey was carried out in the same way. For both clinical questions and outcomes, when the mean > 3 and CV ≤ 25%, the item was included; when the mean < 3 and CV > 25%, it was excluded; when CV > 25%, another round of Delphi survey was carried out. If the CV is still higher than 25% in the 3rd round survey, the item will be excluded[19].

Results

Participants in 1st step survey

There were 123 feedbacks of the international PICO question survey (30 from abroad and 93 from China) covered 17 countries from 5 continents, and the domestic participants were from 25 provinces respectively (Fig. 2a-b). Among all the participants, 81% were acupuncturists, 9% were physicians of Chinese medicine, 4% were medical school faculty, 3% were scientific researchers and 2% were Otolaryngologists (Fig. 2c). We also analyzed the years of working of the participants, finding that 24% of

them had working experience of equal or less than 5 years, 33% of them has worked for more than 5 but no more than 20 years, 43% have been working for more than 20 years.

Participants in the Delphi survey and consensus conference

The Delphi survey and consensus conference were carried out among GDG, which was comprised of experts in acupuncture and moxibustion, experts in evidence-based medicine, experts in otorhinolaryngology, experts in health economics, and allergic rhinitis patients (shown in Table 1). The GDG members are from six countries, where acupuncture is practical. The conflict of interest was required to declare ahead of the survey, and each member has signified the declaration of interest form.

Table 1
Guideline Development Group (GDG) members

Participant No.	Country (City)	Identity
1	China (Beijing)	Expert in acupuncture and moxibustion
2	China (Beijing)	Expert in acupuncture and moxibustion
3	China (Beijing)	Expert in acupuncture and moxibustion
4	China (Shijiazhuang)	Expert in acupuncture and moxibustion
5	China (Hefei)	Expert in acupuncture and moxibustion
6	China (Hongkong)	Expert in acupuncture and moxibustion
7	America (Virginia)	Expert in acupuncture and moxibustion
8	America (New York)	Expert in acupuncture and moxibustion
9	Australia (Sydney)	Expert in acupuncture and moxibustion
10	Japan (Tokyo)	Expert in acupuncture and moxibustion
11	Switzerland (Geneva)	Expert in acupuncture and moxibustion
12	China (Beijing)	Expert in otolaryngology
13	China (Beijing)	Expert in otolaryngology
14	Canada (Ottawa)	Expert in evidence-based medicine
15	China (Beijing)	Expert in evidence-based medicine
16	China (Beijing)	Expert in evidence-based medicine
17	China (Beijing)	Expert in health economics
18	China (Beijing)	Allergic rhinitis patient
19	China (Beijing)	Allergic rhinitis patient

1st step survey: PICO clinical question gathering

The most concerning clinical questions were first categorized into 3 types (**A**. *validation of effectiveness*; **B**. *optimal efficiency or non-inferiority*; **C**. *standardization or optimization of manipulation*.) Then the PICO elements were summarized respectively.

As shown in Fig. 3a, the *optimal efficiency or non-inferiority* related questions accounted for 43% (e.g., Compared with intranasal steroids spray only, could allergic rhinitis patients benefit more from the combination therapy of filiform needle therapy with intranasal corticosteroids? Compared with oral antihistamines, does moxibustion has an equal effect in treating seasonal allergic rhinitis?). The questions related to *validation of effectiveness* accounted for 36% (e.g., Compared with no treatment, could filiform needle therapy perform better in releasing perennial allergic rhinitis-related symptoms?). The questions related to *standardization or optimization of manipulation* accounted for 21% (e.g., Compared with 4 weeks filiform needle therapy, could 8 weeks treatment bring allergic rhinitis patients more benefit? Compared with filiform needle therapy, could the complementary of moxibustion enhance the therapeutic effect in moderate to severe allergic rhinitis patients?) The percentage of participant's concern on specific classifications of each PICO (Patient, Intervention, Comparator, Outcome) element were then calculated respectively.

For patient classification (shown in Fig. 3b), 22% of the participants focused on all types of allergic rhinitis patient, rather than a certain type, while 18% focused on seasonal AR, 17% on persistent AR, 14% on perennial AR, 8% on intermittent AR, 8% on moderate/severe AR, 12% on AR of different ages (e.g., AR in adult, AR in children, AR in the elder, etc.)

For intervention classification (shown in Fig. 3c), filiform needle therapy is the most concerned intervention (57%), following by moxibustion (15%), filiform needle therapy combining with moxibustion (8%), filiform needle therapy combining with medication (4%), acupoint catgut embedding (4%), electro-acupuncture (3%), auriculo-acupuncture (2%), filiform acupuncture combining with herbal therapy (2%), intradermal needle (2%), acupoint application (2%), sphenopalatine ganglion stimulation (1%), filiform needle therapy combining with cupping (1%), and fire needle (1%). Most of the combination therapies were related to the optimal efficiency questions to figure out whether the addition of other treatments could bring more benefit to AR patients.

For the comparator classification (shown in Fig. 3d), conventional treatments (including intranasal corticosteroids, intranasal and oral antihistamines, intranasal and oral decongestants, nasal saline, leukotriene receptor antagonists) was most frequently concerned (43%), followed by sham acupuncture or waitlist (36%), filiform needle therapy (17%), and moxibustion (5%). The conventional treatments usually occurred as the comparators of the optimal efficiency or non-inferiority related questions, and sham acupuncture or waitlist were correlated to effectiveness validating questions. For the questions related to *standardization or optimization of manipulation*, the control intervention might be filiform

needle therapy or moxibustion with different manipulation (e.g., fewer treating courses, lower treating frequency, without the addition of other therapies, etc.).

For the outcome classification (shown in Fig. 3e), most participants were concerned about several sorts of outcomes. Among these, symptom score was most concerned (92%), followed by disease control score (60%), medication score (43%), quality of life score (36%), patient satisfaction score (23%), adverse event rate (6%), clinical economic indicators (5%), laboratory immunological indicators (4%), Chinese medicine syndrome score (4%), and mental health score (2%).

According to the feedback from the target population, we draft 15 potential clinical questions and 10 sorts of outcomes for the Delphi study and consensus conference (shown in Table 2 and Table 3).

Table 2
Potential clinical question list

Question No.	Details
1	Compared with no treatment, could allergic rhinitis patients benefit more from filiform needle therapy?
2	Compared with conventional treatments, could seasonal (or intermittent) allergic rhinitis patients benefit equally or more from filiform needle therapy?
3	Compared with conventional treatments, could perennial (or persistent) allergic rhinitis patients benefit equally or more from filiform needle therapy?
4	Compared with conventional treatments, could moderate-severe allergic rhinitis patients benefit equally or more from filiform needle therapy?
5	Compared with conventional treatments only, does the combination of filiform needle therapy increase the benefit of moderate-severe allergic rhinitis patients?
6	Compared with no treatment, could allergic rhinitis patients benefit more from moxibustion therapy?
7	Compared with conventional treatments, could seasonal (or intermittent) allergic rhinitis patients benefit equally or more from moxibustion therapy?
8	Compared with conventional treatments, could perennial (or persistent) allergic rhinitis patients benefit equally or more from moxibustion therapy?
9	Compared with conventional treatments, could moderate-severe allergic rhinitis patients benefit equally or more from moxibustion therapy?
10	Compared with conventional treatments only, does the combination of moxibustion therapy increase the benefit of moderate-severe allergic rhinitis patients?
11	Compared with filiform needle therapy or moxibustion therapy alone, does the combination of filiform needle therapy and moxibustion therapy increase the benefit for allergic rhinitis patients?
12	With the same treatment frequency, does a longer course of filiform needle therapy increase the benefit of allergic rhinitis patients?
13	With the same treatment course, does a higher frequency of filiform needle therapy increase the benefit for allergic rhinitis patients?
14	With the same treatment frequency, does a longer moxibustion therapy course increase the benefit for allergic rhinitis patients?
15	With the same treatment course, does a higher frequency of moxibustion therapy increase the benefit for allergic rhinitis patients?

Table 3
Outcome list

Outcome No.	Details
1	Symptom score (NOSE, CQ, TSS, TNSS, etc.)
2	Disease control score (VAS, RCAT, CARAT, RCSS, ARCT, etc.)
3	Quality of life score (RQLQ, RAPP, SF-36, etc.)
4	Mental health score (BDI, PHQ-2, etc.)
5	Medication score (RMS, MS, etc.)
6	Laboratory immunological indicators (IgE, IL-4, etc.)
7	Chinese medicine syndrome score
8	Adverse event rate
9	Clinical economic indicators (ICER, ICUR, etc.)
10	Patient satisfaction score

1st round of Delphi survey

Ahead of the consensus conference, a round of online Delphi survey was carried out to collect the GDG group's concerns on potential clinical questions and outcomes. All 19 GDG members submitted their choice and comment online. The result is shown in Fig. 4. According to our inclusion and exclusion criteria, all clinical questions were considered important (Fig. 4a), while the CV of the question 6, 14, 15 was higher than 25% (Fig. 4b). The authority coefficients of clinical questions were among 65.8–76.3% (Fig. 4c). For outcomes, all of the outcomes were considered important (Fig. 4d), while mental health score, laboratory immunological indicators, Chinese medicine syndrome score, and clinical economic indicators had high CV (Fig. 4e). The authority coefficients of outcomes were among 61.6–75.8% (Fig. 4f).

Consensus conference with Delphi survey

The GDG consensus conference on clinical questions and important outcomes was carried out online and all 19 GDG members attend the meeting. After the introduction of the preparation of this meeting (the members of the guideline drafting group, steering group, and GDG group; the WFAS approval of the project on developing the *clinical practice guideline for acupuncture and moxibustion for allergic rhinitis*; the result of the PICO question gathering; the definition and application of the potential clinical questions and outcomes; the result of 1st round Delphi survey and anonymous comments), each GDG member gave his/her ideas and discussed (especially for the items with high CV value).

For clinical questions, the discussion mainly focused on the question with high CV (6, 14, 15). These are questions focusing on the efficacy and application of moxibustion, and the difference in opinion was caused by the following aspects: (1) Moxibustion is not available in some foreign countries because of the smog during the treatment is not acceptable. (2) Moxibustion is less frequently used than filiform needle therapy in treating AR. (3) There was not enough evidence to support moxibustion's efficacy in AR treatment.

The discussion among GDG could be summarized as follows: (1) **Experts in acupuncture and moxibustion** from China recommend moxibustion therapy to be included in the guideline because it is frequently applied in AR treatment. The TCM syndromes and stages of AR are critical factors in acupuncture and moxibustion application, thus subgroup analysis on specified populations should be carried out for recommendation formulation. (2) **Experts in acupuncture and moxibustion** from America, Australia, Switzerland, Japan said that the low importance rating on moxibustion-related questions was mainly because of the limitation of moxibustion practice abroad. As the smog of moxibustion therapy could elicit the fire alarm system, it is not acceptable indoors without the special ventilation system. They suggested that the setting of moxibustion treatment, the quality of moxa, the specific type of moxibustion therapy should be articulated during the systematic review and recommendation formulation. (3) **Experts in otolaryngology** said that they doubted whether AR would get worse after moxibustion therapy because the moxa could be allergen itself. However, the Chinese medicine expert in otolaryngology said that the main allergen for seasonal AR is the pollen of mugwort in autumn [20, 21], while the mugwort leaves collected during April and June is the main component for moxa. From this aspect, the moxa would not worsen AR, but it remains controversial whether moxa smog could worsen AR symptoms. Therefore, the importance of moxibustion-related questions is less concerned. (4) **Experts in evidence-based medicine** said that there might not be enough high-quality evidence to support these clinical questions. However, these foreground questions are important during clinical practice. Therefore, the evidence-gathering process should cover all types of evidence, including randomized clinical trials, cohort studies, case-control studies, case series, and expert evidence[22]. (5) **Allergic rhinitis patient representatives** who have different types of western medication and acupuncture therapy previously. They felt that acupuncture could control the AR symptoms and enhance life quality in a longer period than other types of therapy, thus they preferred acupuncture therapy to other therapy. (6) **Expert in health economics** explained the economic consideration in clinical practice guidelines and emphasized its importance in weighing benefits and cost.

After a full discussion on clinical questions, a second round of the Delphi survey was launched and all GDG members finished the survey. The result was shown anonymously. According to the inclusion and exclusion criteria, all potential clinical questions were rated as important questions without obvious divergence (Fig. 5a-b), and the authority coefficient of each clinical question was above 70% (Fig. 5c). Therefore, the GDG reached a consensus to include the 15 clinical questions into the *clinical practice guideline for acupuncture and moxibustion for allergic rhinitis*.

For each sort of outcome, there was an introduction on different indicators, including suitable population, construction validity, content validity, criteria validity, reliability, responsiveness and minimal clinically important difference (MCID), etc. [23] Then every GDG member gave their opinions on different types of outcome. The discussion mainly focused on 4 sorts of outcome with obvious divergence (mental health score, laboratory immunological indicators, Chinese medicine syndrome score, and clinical economic indicators), summarized as follow: (1) **Experts in acupuncture and moxibustion** considered all the outcomes important, among which symptom score that reflected nasal and non-nasal symptoms related to allergic rhinitis was the most important one. Disease control score, quality of life score, and medication score that reflects the severity of AR from other aspects were also frequently used in assessing treatment efficacy. However, the laboratory immunological indicators and clinical economic indicators were less commonly used in clinical trials on AR. (2) **Experts in otolaryngology** pointed out symptom score, disease control score, quality of life score, medication score as important outcomes. Meanwhile, they stressed the importance of mental status in related to AR, and introduced several scales to assess mental health in AR patients[24–27]. (3) **Experts in evidence-based medicine** suggested all related outcomes should be included to assess acupuncture and moxibustion in treating allergic rhinitis (efficacy, safety, clinical economic indicators, etc.). Different measurements belong to one sort of outcome could be synthesized via standardized mean difference (SMD) as lack of enough clinical evidence. Since this guideline is developed using GRADE system, outcomes related to safety and clinical economic indicators should be included. However, the laboratory immunological indicators are less important than other outcomes in clinical trials, for it is more commonly applied in mechanism studies rather than randomized clinical trials. The Chinese medicine syndrome score are less important, for there is lack of unified scales to Chinese medicine syndrome. (4) **Expert in health economics** pointed out that medication score, adverse event rate and clinical economic indicators were critical factors from the perspective of health economics. These factors determine benefits, harms and resource use of different treatment, so should be rated as important outcomes. (5) **Allergic rhinitis patient representatives** also mentioned the importance of symptom score, while they paid more attention on medication score, adverse event rate, clinical economic indicators and patient satisfaction score.

After a full discussion on outcomes, a second round of the Delphi survey was launched and all GDG members finished the survey. All outcomes were rated as important outcomes (Fig. 5d), while the laboratory immunological indicators and Chinese medicine score remained divergent (Fig. 5e). The authority coefficient of each outcome was above 70% except for the laboratory immunological indicators (Fig. 5f). Therefore, the second round of discussion on the two outcomes was carried out. For laboratory immunological indicators, GDG members who rated it highly believed this outcome could subjectively reveal the efficacy of acupuncture and moxibustion therapies on AR. However, GDG members who rated it lowly thought that there were a huge number of immunological indicators which make it unfeasible to synthesis these data. For the Chinese medicine syndrome score, GDG members who rated it highly believed that syndrome differentiation related to the treatment efficiency. Without this sort of outcome, there will be a lack of the characteristics of Chinese medicine. Whereas the GDG members who rated it lowly believed that the Chinese medicine syndrome score has not been used globally, and the Chinese

medicine syndrome of AR has not yet been unified. Chinese medicine syndrome score was developed based on AR symptoms, which could be comprehensively evaluated by symptom score, disease control score, and quality of life score. Therefore, the Chinese medicine syndrome score is redundant. Moreover, during the progression of AR, the syndrome might change spontaneously, which could not reflect the efficacy of treatment. After full discussion, a third round of the Delphi survey was carried out. Both outcomes were rated important (Fig. 6a), while the CV of Chinese medicine syndrome score is still higher than 25% (Fig. 6b), thus was excluded. The authority coefficients of both outcomes were above 70%. Therefore, the GDG reached a consensus of including 9 important outcomes in the *clinical practice guideline for acupuncture and moxibustion for allergic rhinitis*. Among these outcomes, symptom score rated as the most important one, followed by patient satisfaction score, disease control score, adverse event rate, quality of life score, medication score, clinical economic indicators, mental health score, and laboratory immunological indicators. In general, 15 clinical questions and 9 important outcomes were eventually included in the *clinical practice guideline for acupuncture and moxibustion for allergic rhinitis*.

Discussion

Since the clinical concerns from different target populations vary from each other, it is of priority to widely collect their most concerned PICO clinical questions. The scope of this guideline is to provide clinical practice recommendations for global acupuncturists, TCM practitioners, and relevant occupations. Therefore, the 1st step survey (international survey on PICO questions) covered participants from 17 countries of 5 different continents. As the majority of the potential users of this guideline will be Chinese acupuncturists, 81% of the participants in the 1st step survey were acupuncturists and 75% of the participants were from 25 different provinces of China. Other related occupations, such as physicians of Chinese medicine, otolaryngologists, medical school faculties, and scientific researchers who work on AR and acupuncture, were also included. Participants of different working experiences were all included to truly reflect the demands from the target population. After the 1st step survey, we extensively collected the most concerned clinical questions from the target population of this guideline and extracted each PICO element. Then, we summarized the most concerned clinical question into three types and analyzed the distribution of concern on each element. Eventually, under the instruction of the guideline steering committee, the guideline drafting group transferred the results of PICO question analysis into 15 clinical questions and 10 sorts of outcomes that could cover most of the target population's concerns.

The Guideline Development Group (GDG) plays a critical role in guideline formulation. Throughout the development of a clinical practice guideline, GDG members need to reach consensus in several key steps, among which consensus on review questions and important outcomes is the first step[28–30]. In this study, we constructed the GDG following the WFAS requirement[31]. Experts in acupuncture and moxibustion from different countries accounted for the majority of GDG. Experts in different fields (otolaryngology, evidence-based medicine, health economics) and AR patient representatives were also indispensable compositions. All GDG members have claimed their conflict of interest[32] and signed the Declaration of Interest Form of the WFAS standard expert committee.

After the generation of potential clinical questions and outcomes, the GDG reached a consensus on the clinical questions and important outcomes. Delphi Method, Consensus Conference, and the Nominal Group Technique are the most often applied strategies in clinical practice guideline development[33, 34]. In this study, we applied a mixed method of the Delphi survey and consensus conference. After the formulation of potential clinical questions and outcomes, the 1st round of the Delphi survey was carried out ahead of the consensus conference. Therefore, during the consensus conference, the distribution of importance rating and concerns on clinical questions and outcomes could be displayed anonymously, which makes the meeting more efficient in finding discordance and reach consensus. Then, the 1st round of discussion on the clinical questions was carried out, during which each GDG member share his/her opinions and expertise on the potential clinical questions. During the 2nd round of the Delphi survey, the coefficient of variation decreased while the authority coefficient increased, and the consensus was reached.

As this guideline will be developed using the GRADE system[35], the GDG rated the importance of all sorts of outcomes and selected the important and critical outcomes accordingly. Ten sorts of outcome indicators were mentioned in this survey: symptom score, disease control score, quality of life score, mental health score, medication score, laboratory immunological indicators, Chinese medicine syndrome score, adverse event rate, clinical economic indicators, and patient satisfaction score. Among these, symptom score mainly focuses on the nasal and non-nasal symptom related to allergic rhinitis, including NOSE (Nasal Obstruction Symptom Evaluation) [36], CQ (Congestion Qualifier)[37], TSS (Total Symptom Scales)[38], TNSS (Total Nasal Symptom Score) [39], etc. Disease control scores include Visual analog scale (VAS)[40, 41], RCAT (Rhinitis Control Assessment Test)[42], CARAT (Control of Allergic Rhinitis and Asthma Test)[43, 44], RCSS (Rhinitis Control Scoring System)[45], ARCT (Allergic Rhinitis Control Test) [46], etc. There are various types of indicators to assess the quality of life of AR patients, such as RQLQ (Rhinoconjunctivitis Quality of Life Questionnaire)[47, 48], RAPP (RhinAsthma Patient Perspective)[49, 50], SF-36 (Medical Outcome Study Questionnaire Short Form 36 Health Survey)[51, 52], etc. The mental health score is another critical concern in AR management[26], scales such as BDI (Beck Depression Inventory)[24] and PHQ-2 (Patient Health Questionnaire-2)[53] have been mentioned. Medication score is commonly used to reflect the efficacy of complementary therapy, it could be described as RMS (Rescue Medication Score)[54, 55] or MS (Medication Score)[56]. Laboratory indicators are concerned for its validation of clinical efficacy and potential mechanisms, such as allergen-specific IgE, cytokines, and immune cells related to allergic rhinitis (concentration of IL-2, IL-4, IL-10, etc.), neuropeptides, etc.[57, 58] Chinese medicine syndrome score which reflects the changes of syndromes (such as the *lung deficiency and invasion of cold syndrome*, the *spleen qi deficiency syndrome*, the *kidney yang deficiency syndrome*, etc.) was also mentioned in the survey[59–61]. Concern on safety, economics, and patient preference, which could be indicated by adverse event/ side effect rate[62, 63], clinical economic indicators (such as incremental cost-effectiveness ratio, incremental cost-utility ratio, etc.)[64], and patient satisfaction score (using the Likert scale[65]), are important factors in the process from evidence to decision.

For the important outcomes, though all of them were rated as important or critical, there existed discordance on several items, and after three rounds of Delphi survey and discussion, 9 outcomes were

considered important for this guideline. They were ranked in order of priority, so it could be feasible to weigh the advantages and disadvantages during the formulation of recommendations. Among these, symptom score was considered the most important outcome since its wide application in AR assessment. Patient satisfaction score was the second priority since both patient representative and clinical practitioners attached importance to it. The coefficient of variation of 9 sorts of outcomes decreased during three rounds of the Delphi survey, which means the GDG gradually reached a consensus. However, the Chinese syndrome score remained highly divergent and was excluded. The increasing authority coefficient means the discussion and interpretation were comprehensive and effective.

Strengths and limitations

The strength of this study is the joint application of multi-methods (international PICO question survey, Delphi survey, and consensus conference). Previously, the items of the Delphi survey were developed based on systematic review and interview [66, 67], while we carried out an online clinical question survey among the global target population, using a semi-structured PICO questionnaire, which could help us to obtain the demands from the potential users and avoid the data-driven problems. After formulating the potential clinical question and outcome lists, 1st round of the Delphi survey was held ahead of the consensus conference to summarize the concerns from GDG. Therefore, the divergence and comments could be displayed anonymously at the conference to minimize the authoritative effect. Moreover, this made the consensus conference was more efficient, for the discussion could be more focusing on the divergence. During the conference, each GDG members were required to show their opinions which could represent the potential users, beneficiary, and methodologists. This enhanced the equality and representativeness in the discussion.

There are also several limitations in this study. Firstly, since lack of background knowledge of the PICO framework in clinical practitioners in acupuncture and moxibustion, the clinical question-gathering process was time-costing. For there were some feedbacks not in PICO form during the survey, we needed to contact the participants, interpret the PICO framework, and ask them to fill the questionnaire again. Secondly, although the Delphi voting results were displayed anonymously and all GDG members were required to share their views, dominant GDG numbers might impose their opinions upon more reticent colleagues. Therefore, the individual generation and round-robin fashion of NGT[68–70] might be referential for future improvement.

Conclusion

15 clinical questions and 9 important outcomes were selected by GDG for the *clinical practice guideline for acupuncture and moxibustion for allergic rhinitis*. Since this will be the first edition of WFAS CPG for acupuncture and moxibustion for Allergic Rhinitis, the clinical questions and important outcomes are universally applicable and reflect the most fundamental and urgent demands from global users. The joint application of multi-methods in this study could be useful for the relevant CPG studies.

Declarations

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Availability of data and materials

Details of data are available from the corresponding author upon request.

Ethics approval and consent to participate

All procedures were performed in accordance with the guidelines of World Federation of Acupuncture-Moxibustion Societies (Approval No. WFASRP202001-SC05).

Consent for publication

All the authors were concerned and agreed to publish before the submission.

Competing interests

The authors declare that there are no competing interests regarding the publication of this paper.

Authors' contribution

SD drafted the manuscript, JZ designed the study, SD, CY and SW collected and analyzed the data. SC, SG and WG revised the manuscript and gave suggestions. All authors have read and approved the final manuscript.

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Figures

Fig. 1

Figure 1

Procedure of formulating clinical questions and important outcomes

Fig. 2

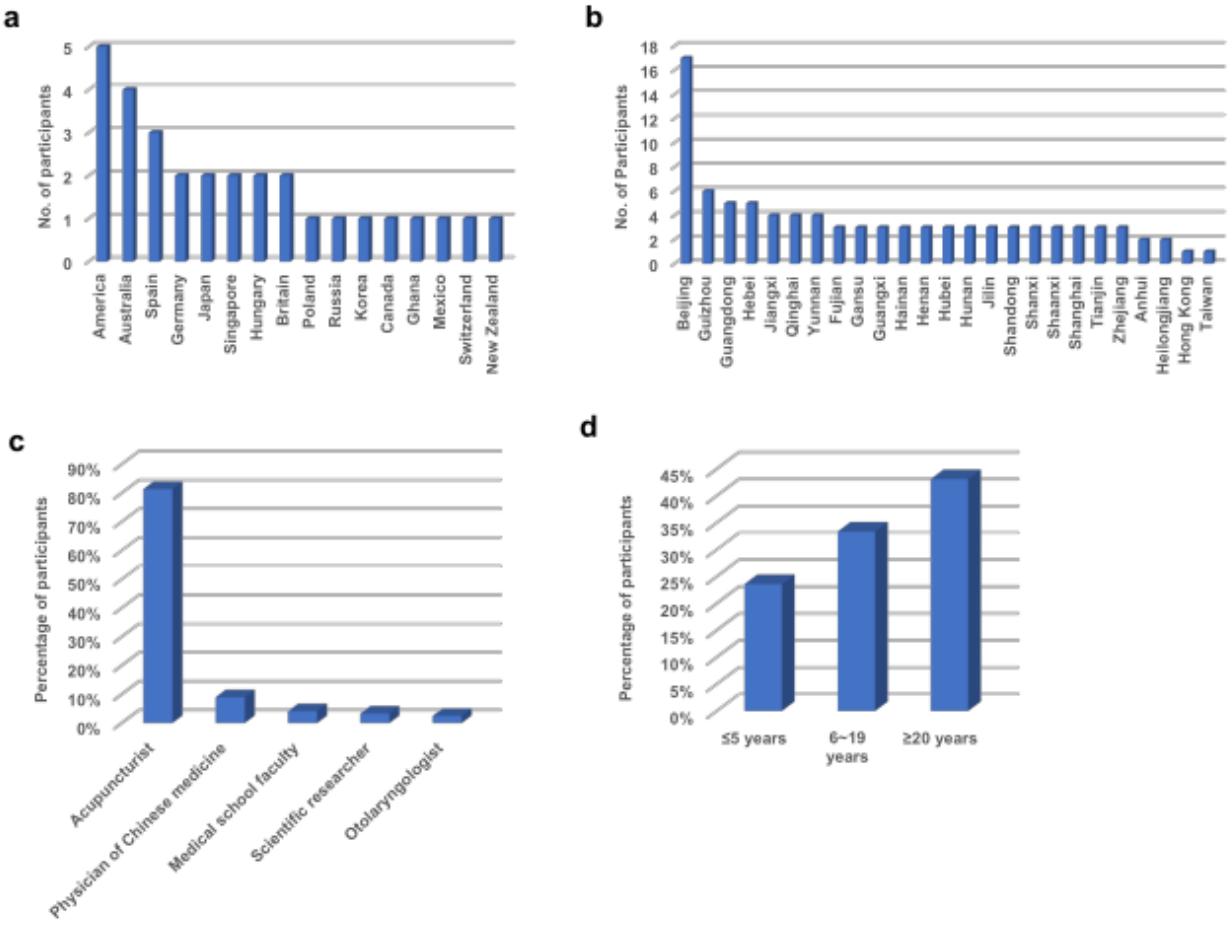

Figure 2

Information of participants in the first step survey. a distribution of participants abroad; b distribution of domestic participants; c distribution of participants' occupation; d distribution of participants' working experience.

Fig. 3

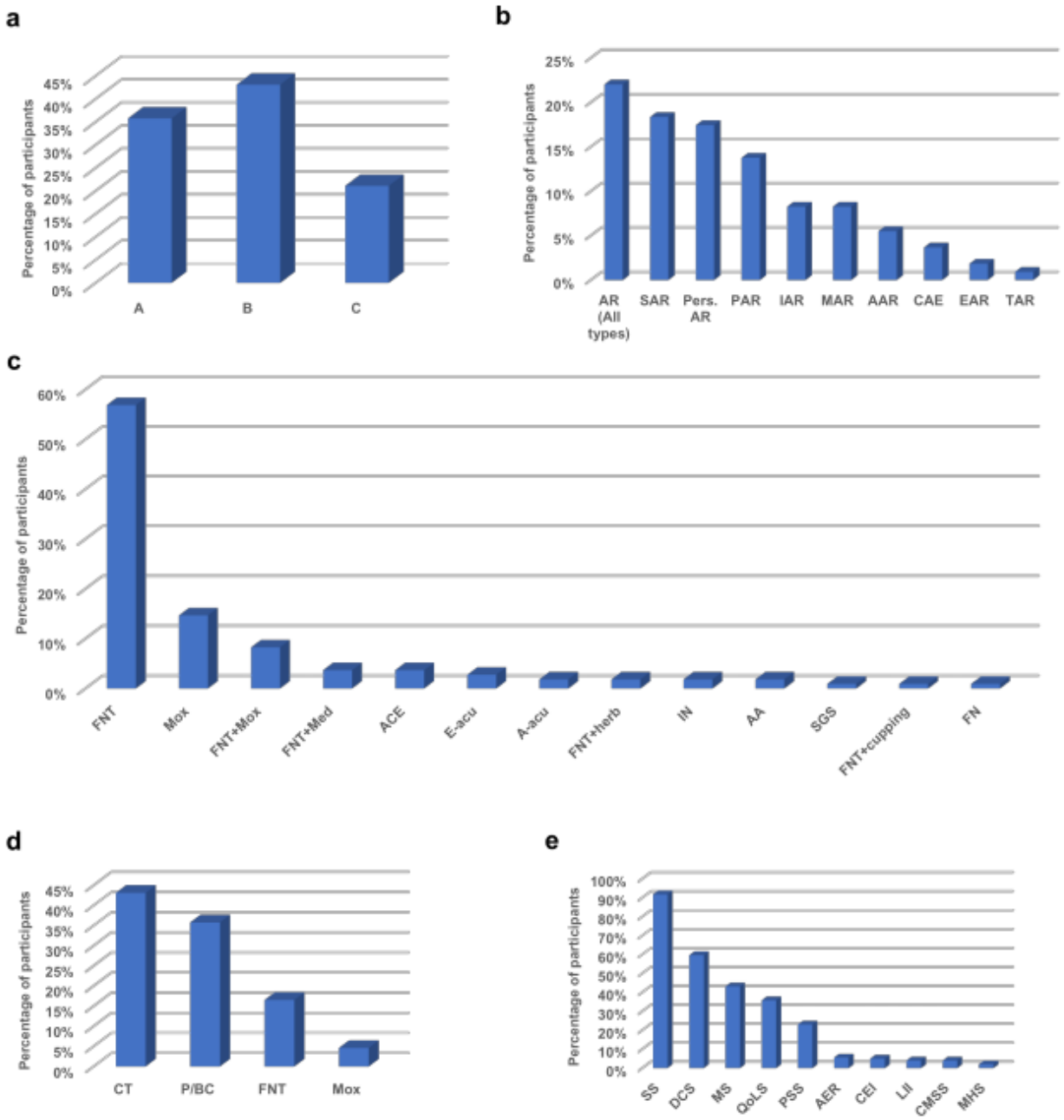

Figure 3

PICO elements summary of the 1st step survey. a Clinical question classification; b Participant's concern on patients; c Participant's concern on interventions; d Participant's concern on comparations; e Participant's concern on outcomes. AR (all types of AR), SAR (seasonal AR), PAR (perennial AR), Pers. AR (persistent AR), IAR (intermittent AR), MAR (moderate-to-severe allergic rhinitis), AAR (adult AR), CAR (child AR), EAR (elder AR), TAR (teenager AR), FNT (filiform needle therapy), Mox (moxibustion), Med

(medication), ACE (acupoint catgut embedding), E-acu (electro-acupuncture), A-acu (auriculo-acupuncture), IN (intradermal needle), AA (acupoint application), SGS (sphenopalatine ganglion stimulation), FN (fire needle), CT (conventional treatments); P/BC (placebo or blank control), SS (symptom score), DCS (disease control score), MS (medication score), Quality of life score (QoLS), PSS (patient satisfaction score), AER (adverse event rate), CEI (clinical economic indicators), LII (laboratory immunological indicators), CMSS (Chinese medicine syndrome score), MHS (mental health score).

Fig. 4

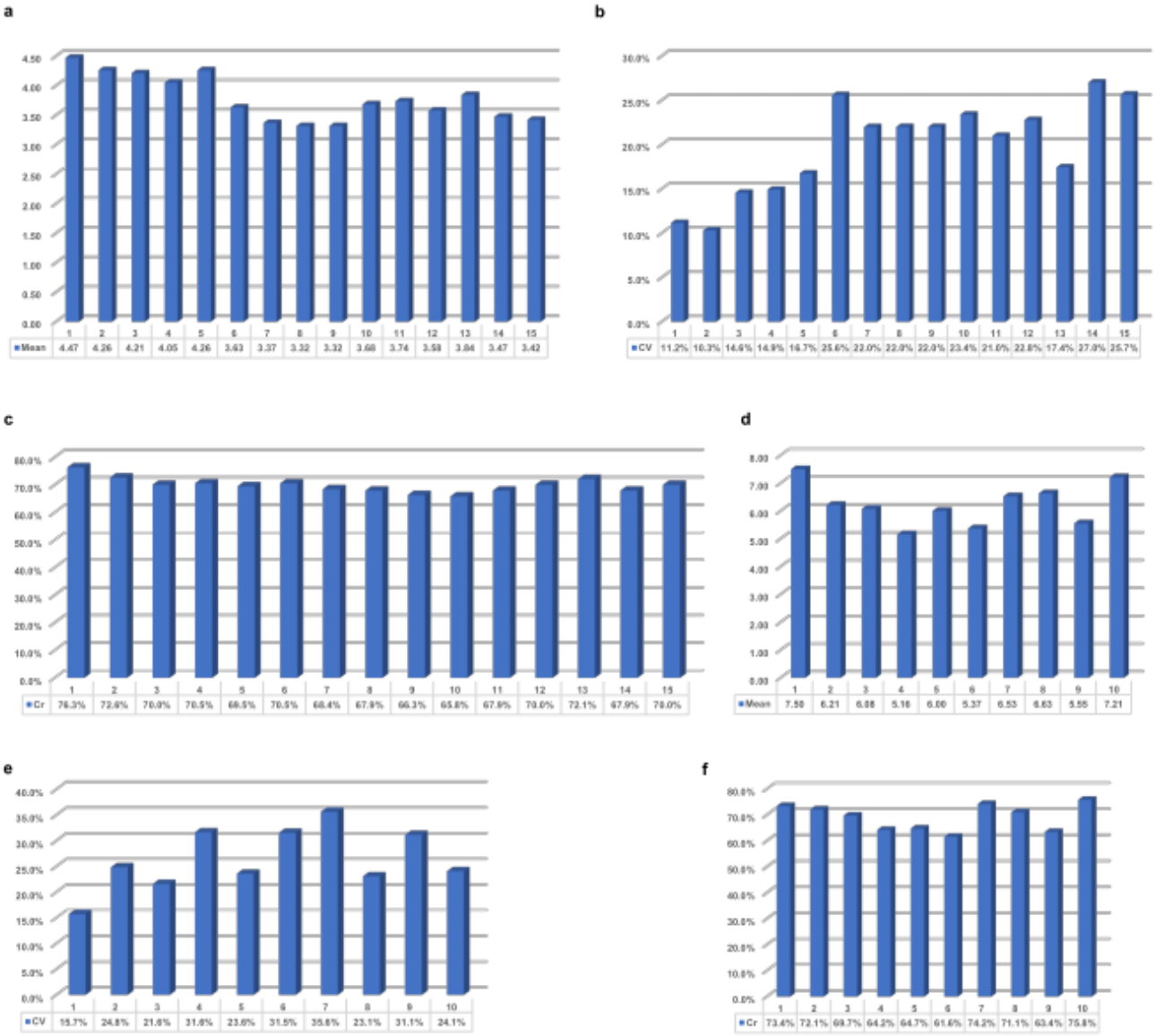

Figure 4

Results of 1st round Delphi survey. a Importance rating of clinical questions; b CV of clinical question rating; c Cr of clinical questions; d Importance rating of outcomes; e CV of outcome rating; f Cr of outcomes.

Fig. 5

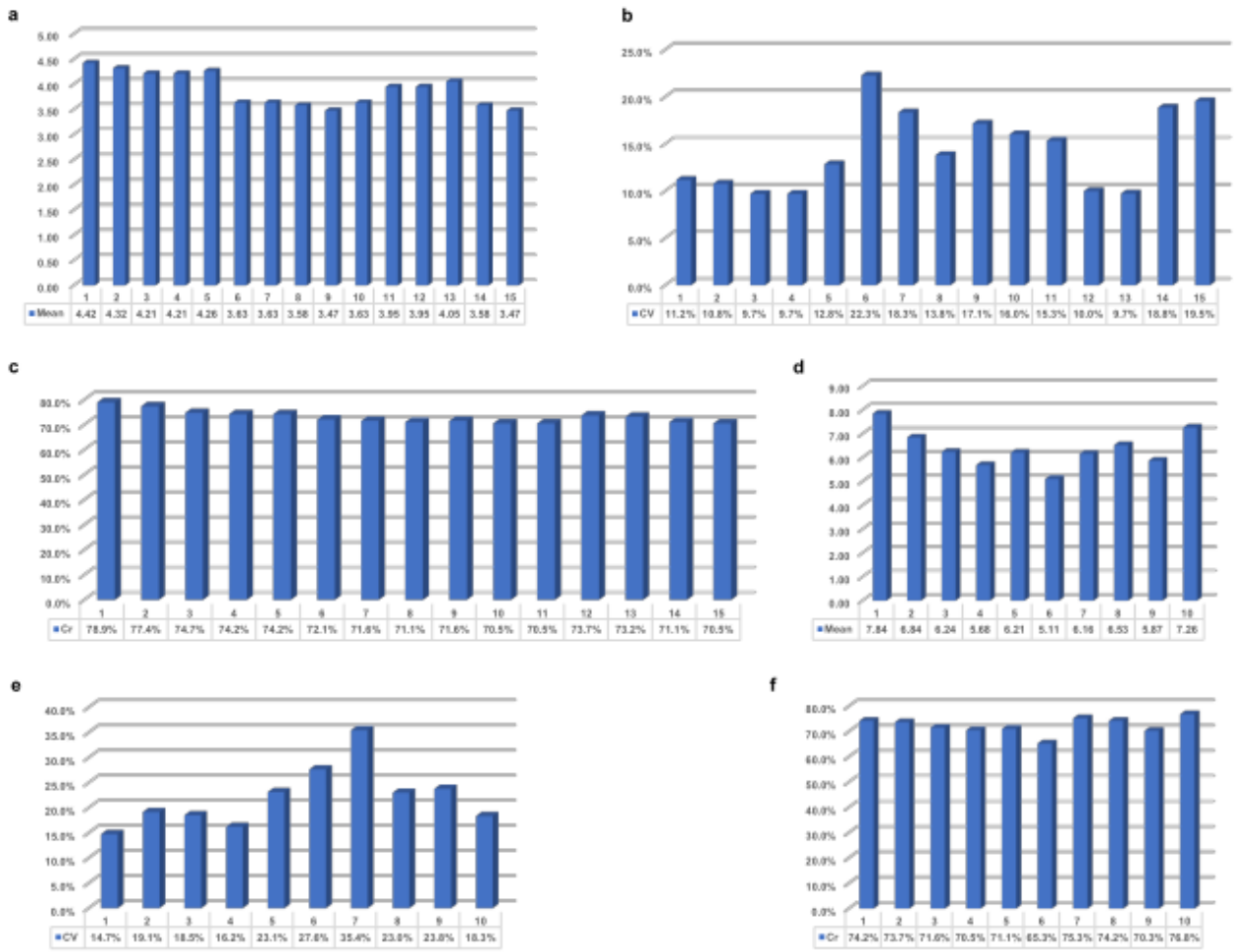

Figure 5

Results of 2nd round Delphi survey. a Importance rating of clinical questions; b CV of clinical question rating; c Cr of clinical questions; d Importance rating of outcomes; e CV of outcome rating; f Cr of

outcomes.

Fig. 6

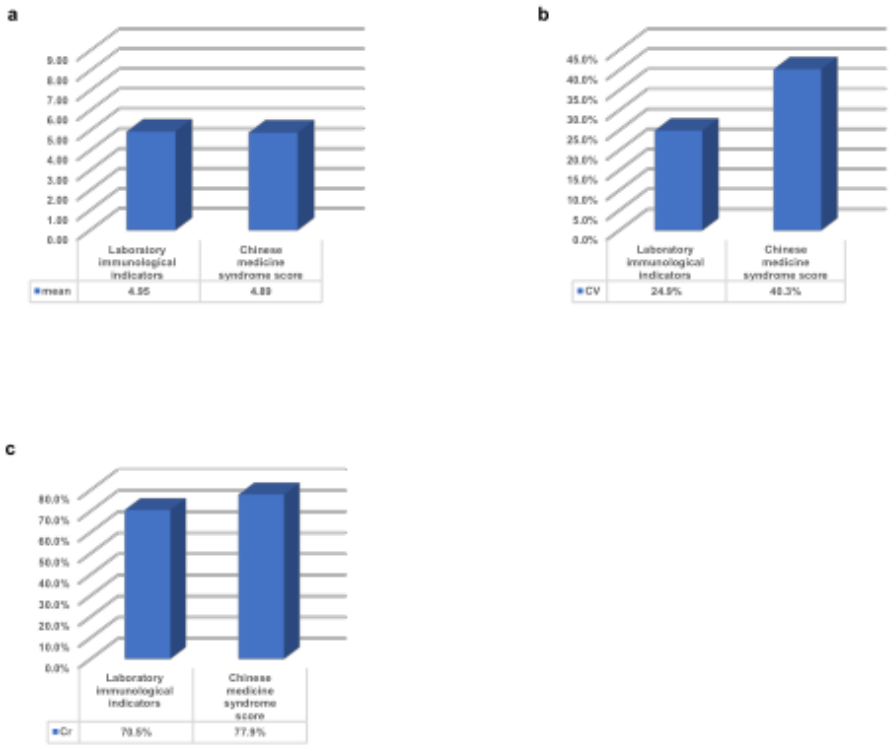

Figure 6

Results of 3rd round Delphi survey. a Importance rating of outcomes; b CV of clinical question rating; c Cr of clinical questions