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Quality and consistency of clinical practice guidelines on the prevention of food allergy and atopic dermatitis: Systematic review protocol

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ABSTRACT

Background and aims: Allergy prevention strategies have gained significant traction as a means to attenuate the growing burden of allergic diseases over the past decade. As the evidence base for primary prevention of food allergy (FA) and atopic dermatitis (AD) is constantly advancing, clinical practice guideline (CPG) recommendations on interventions for FA and AD prevention vary in quality and consistency among professional organizations. We present a protocol for a systematic review of CPGs on primary prevention of FA and AD.

Methods: We will systematically review and appraise all CPGs addressing primary prevention of FA and AD and report our findings according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Electronic databases and manual website searches from January 2011 to March 2021 without language or geographical restrictions, and supplemented by author contact, will generate the list of potentially relevant CPGs to screen. Evaluation of the methodological quality, consistency, and global applicability of shortlisted CPGs will be performed by members of the Allergy Prevention Work Group of the World Allergy Organization (WAO) using the Appraisal of Guidelines for Research and Evaluation (AGREE) II and AGREE-REX (Recommendations EXcellence). instruments. Guideline contents, consistency, and quality of the recommendations will be summarised in tabular and narrative formats. We aim to present consolidated recommendations from international guidelines of the highest methodological quality and applicability, as determined by AGREE II and AGREE-REX.

Dissemination: This systematic review will provide a succinct overview of the quality and consistency of recommendations across all existing CPGs for FA and AD prevention, as well as crucial perspectives on applicability of individual recommendations in different geographical contexts.

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Results from this systematic review will be reported in a peer-reviewed journal. It will also inform a position statement by WAO to provide a practical framework to guide the development of future guidelines for allergy prevention worldwide.

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Keywords: Food allergy, Atopic dermatitis, Eczema, Primary prevention, Clinical practice guideline

BACKGROUND

Allergy is a longstanding area of intense interest for multiple stakeholders including families, clinicians, and policymakers.[1] Since the 1960s, the prevalence of asthma and allergies have been on a rise.[2,3] Although the prevalence of asthma may have approached a peak in most Westernised countries by the turn of the millennium,[4,5] food allergy (FA) has steadily increased in prevalence over recent decades.[6,31–34] One of the highest reported rates of FA was from a population-based cohort study involving 5276 Australian children, which showed an 11.0% prevalence of oral food challenge-confirmed FA in one-year-old Australian children.[7] Follow-up at 4 years revealed that 50% of this population-based cohort experienced symptoms of allergic diseases such as asthma and allergic rhinitis. In 2018, a population-based cross-sectional prevalence survey conducted in the United States, involving over 50 000 households, estimated that parent-reported IgE-mediated FA affected approximately 1 in 10 adults[8] and 1 in 12 children.[9] Food anaphylaxis, a major consequence to food allergic reactions, has also been rising in incidence across the decade.[10,11]

The rising prevalence of allergic diseases underscores the potential impact of effective allergy prevention strategies. Many international and regional scientific organizations have released consensus guidelines for allergy prevention strategies. Clinical practice guidelines (CPGs) are "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances".[25] CPGs often vary in terms of clinical focus, trustworthiness and intended end-users. They are also typically designed to be relevant to a specific population under the jurisdiction of the organization developing the guidelines and may not be applicable in locations other than where the CPG was developed.

As there are now a large number of clinical guidelines on allergic disease prevention from various scientific organizations around the world, it is important to systematically appraise the quality of these CPGs and their generalizability on a global perspective to better guide end-users. "Appraisal of Guidelines for Research and Evaluation (AGREE) II" is a widely validated international assessment tool that enables assessment of the methodological and reporting quality of CPGs. As the AGREE II instrument is limited in its ability to assess external applicability in different contexts, the newly launched "Appraisal of Guidelines Research and Evaluation–Recommendations Excellence (AGREE-REX)" tool serves as a complementary tool to evaluate the clinical credibility and global implementability of CPGs. A recently published systematic review (SR) compared recommendations from FA prevention guidelines and evaluated the methodological quality of CPGs using the AGREE II instrument.[35] Our proposed SR is different in that apart from evaluating the internal validity of CPGs, the external global applicability of the recommendations, ie, whether the CPG recommendations are credible and implementable across many different populations, will also be assessed by our appraisers. Seven appraisers, each representing different geographical regions of the world, will be invited to perform quality appraisals of the selected CPGs, unlike previous SR that included only two reviewers from a single country. The World Allergy Organization (WAO) Allergy Prevention Work Group consists of experienced allergists from across the globe, each having an

in-depth perspective of allergic disease epidemiology, healthcare infrastructure, and clinical practices in the country/region they represent. The Work Group is thus collectively uniquely positioned to evaluate the global applicability of existing CPGs. Our SR will also include non-English articles ensuring that views from non-English speaking regions will not be under-represented. In addition to the primary prevention of food allergy, interventions to prevent the onset of atopic dermatitis, which is often regarded as the first stage of the atopic march, will also be included. Overall, this systematic review will be the first to provide a critical appraisal of the current FA and AD prevention CPGs endorsed by scientific organizations with assessment of the quality and consistency of these recommendations and evaluation of their wider applicability.

METHODS

Objectives

This paper sets out the protocol for a systematic literature review to support the position paper on primary prevention of FA and AD from the WAO Allergy Prevention Work Group. Specifically, we will explore the scope of CPGs (clinical orientation and purpose, complexity of presentation, and intended end-users) for FA and AD prevention, and examine the consistency and quality of CPG recommendations across guidelines: to present synthesized recommendations of guidelines assessed as being of highest methodological quality and to evaluate implementability of CPGs in different geographical settings.

Eligibility criteria

Studies will be eligible for inclusion in the review if they meet the following criteria:

- **Population:** Clinical Practice Guidelines (CPGs) that refer to primary prevention of FA and AD, regardless of the country of origin of the professional body developing the guidelines. These guidelines should focus on children (<18 years of age) and there will be no restriction on gender or ethnicity.
- **Interventions:** Any interventions to prevent the development of FA, including the prevention of any particular type of FA and AD. CPGs that include single or combined methods for the prevention of FA and AD will be included.
- **Comparators:** Not applicable as this review aims to evaluate CPGs
- **Outcomes:** To explore the scope of CPGs (clinical orientation and purpose, complexity of presentation, and intended end-users) for FA and AD prevention; to examine the consistency of CPG recommendations across guidelines; to examine the methodological quality of CPGs using the AGREE II instrument; [26] to evaluate implementability of CPGs in different geographical settings using the AGREE-REX instrument; [27] and to present synthesized recommendations of guidelines rated as being of highest methodological quality.
- **Timeframe & language:** The literature searches, including electronic databases and manual website searches, will be performed from January 2011 to March 2021 (Supplementary Material), and the search will be updated just before final publication. For CPGs with more than 1 version, only the most recent version will be included. There will be no limit on language or geographical location. Only CPGs endorsed by national or international scientific societies will be included. We will use external resources to extract relevant information from the included non–English-language articles. If such resources are not available, we will contact external translation services to extract relevant information from and/or acquire translations of source documents.

In the initial abstract screening phase, CPG studies will be excluded if they are:

- intended solely for allergic rhinitis and asthma or
- only targeted at the adult population
- not endorsed by national or international scientific societies, such as those developed only by individual hospitals.

In the subsequent full-text review phase, CPG studies will be excluded if they are:

- not intended for primary prevention of FA and AD

- only refer to the diagnosis and treatment of FA and AD
- randomized controlled trials, nonrandomized, controlled prospective clinical trials, long-term follow-up studies (eg. open-label follow-up studies), prospective observational studies (eg, phase 4 studies) and systematic reviews (including meta-analyses). Only CPGs will be included in this review and not individual RCTs.

Information sources

Eight bibliographic databases will be searched by a methodologist (MS).

- MEDLINE and MEDLINE In-Process (using PubMed platform)
- Embase (using Elsevier Platform)
- CINAHL
- ISI Web of Science (Thomson Web of Knowledge)
- WHOLIS (World Health Organization Library Information System)
- PAHO (Pan American Health Organization database)
- Science Citation Index and Social Sciences Citation Index
- TRIP Database

An extensive website search of all prominent professional allergy society websites will be performed manually to identify relevant CPGs on FA and AD prevention. The website search strategy has been included in appendix 1.

The search strategy is developed with input from methodologists working in partnership with clinicians (all authors).

STUDY RECORDS

Data management

Literature search results will be downloaded into an Endnote database and exported into Excel, and duplicates and superseded CPGs were eliminated. The review process will include the following steps: abstract screening phase and a subsequent full-text review phase. This will be followed by consecutive stages of data extraction, methodological quality evaluation by AGREE II, applicability evaluation by AGREE-REX and data synthesis.

Selection process

Titles and abstracts of studies identified from the electronic databases and the internet searches will first be reviewed by 2 researchers (ASYL, EHT), independently and in parallel, according to the predetermined inclusion and exclusion criteria set out in this protocol. The reviewers will receive training prior to the selection procedure. Full-text copies of all studies identified as potentially relevant will be obtained and their eligibility for inclusion assessed by the same pair of reviewers, independently and in parallel. Studies that do not fulfill the inclusion criteria will be excluded. Any discrepancies will be resolved by consensus, and if necessary, arbitration by a third reviewer (GWKW).

Data extraction process

Data will be extracted from full-text versions of all shortlisted CPGs. Two reviewers from the Work Group will independently extract and reassess the level of evidence from the included studies. The data extracted will include guideline characteristics such as title and year of publication, name and location of publishing organization, range of topic(s) addressed, intended patient population, evidence base, and study quality-assessment items. FA and/or AD prevention-specific recommendations from each CPG will be extracted and grouped into subcategories: recommendations that target pregnant women, lactating mothers, infants, children and adults, and multi-pronged recommendations targeting mother and infant simultaneously. The system used to determine the strength of recommendations and underlying quality of evidence will be summarised.

Quality assessment strategy

The AGREE II instrument will be used to critically appraise the methodological rigour and to report the quality of included guidelines.[26] The AGREE II consists of 23 items organised into the following 6 domains: scope and purpose (3 items), stakeholder involvement (3 items), rigour of development (8 items), clarity of presentation (3 items), applicability (4 items) and editorial independence (2 items). Appraisers will also

provide an overall assessment on the quality of the CPGs and whether the CPGs will be recommended for use. Assessment will be conducted independently at the "My AGREE Plus" platform.

AGREE-REX, is a complementary tool which will be used to evaluate the credibility and applicability of the CPG recommendations. The AGREE-REX instrument comprises of 3 domains with 9 items including clinical applicability (domain 1), values and preferences (domain 2) and implementability (domain 3) and 1 overall quality assessment item that must be considered to ensure that guideline recommendations are clinically credible and implementable.[27] Each of the 24 items in AGREE II and 9 items in AGREE-REX will be scored on a seven-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). Each of the domain scores will be calculated independently by summing up all the scores of the individual items in a domain, as well as by scaling the total as a percentage of the maximum possible score for that domain, rather than aggregating into a single quality score. Domain scores will be calculated as (obtained score–minimum possible score)/(maximum possible score–minimum possible score). The minimum possible score is calculated as 1 × (number of items) × (number of appraisers). The maximum possible score will be calculated as 7 × (number of items) × (number of appraisers). CPGs with domain 1 (scope and purpose), 3 (rigour of development) scoring >70% in AGREE II will be considered of acceptable quality.

Quality assessment of all included CPGs will be independently performed by seven appraisers in the Work Group, each representing a different geographical region (South & Southeast Asia, East Asia, North America, South America, South-eastern Europe, West-northern Europe, and Africa) using the AGREE II and AGREE-REX instruments.[27,28] Each appraiser will answer questions regarding their assessment of the applicability of each guideline's recommendations in the reviewers' own geographical context. Before these scores are summed and calculated, the independent appraisers will be required to reach a consensus on any AGREE II and AGREE-REX item scores on quality assessment that are more than 2 points apart on the 7-point scale.

Data synthesis

A descriptive table will be produced to summarise the recommendations from all included CPGs and a narrative summary of the contents, consistency, and quality of CPG recommendations will be produced. Regular discussions will be held among the group of reviewers to achieve consensus on data extraction and presentation. Continuous nonparametric and parametric variables will be presented as median and interquartile range or mean and standard deviation, respectively. One-way ANOVA (Analysis of Variance) tests will be used to examine mean differences in the AGREE-REX item scores as a function of the CPG characteristics such as the type of authoring organization and country of development. Correlation between the individual domains and between the AGREE-REX and AGREE II domain scores will be calculated. A 2-tailed $P < .05$ will be considered as statistically significant. We then aim to present consolidated recommendations from international guidelines that are of the highest methodological quality and clinical implementability, as determined by scores of >70% in domains 1 and 3 of AGREE II and domain 3 (implementability) of AGREE-REX.

REGISTRATION, ETHICS, AND REPORTING

This review has been registered with the International Prospective Register of Systematic Reviews (PROSPERO): https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=265689 - (PROSPERO Registration Number CRD42021265689). Any amendment to the protocol together with a full explanation will be documented on the PROSPERO site simultaneously. We plan to report results from this systematic review in a peer-reviewed journal. These results will be used to inform the position paper on primary prevention of FA and AD from the WAO Allergy Prevention Work Group.

Ethical approval is not required for systematic reviews. Each author's potential conflicts of interest will be disclosed. The PRISMA checklist will be used to guide the reporting of the systematic review: http://www.prisma-statement.org/.[29,30]

CONCLUSION

The position paper from the WAO Allergy Prevention Work Group will provide a succinct overview of CPGs for FA and AD prevention. It will also provide an evaluation of the consistency between guidelines, summary of key recommendations with the highest quality evidence, and a commentary on applicability of individual recommendations in different geographical contexts, and it will highlight recommendations where consideration should be given to the local context. It will also highlight gaps in the current published literature and provide a practical framework to guide the development of future guidelines for allergy prevention.

Abbreviations

AD: Atopic dermatitis; AGREE-II: Appraisal of Guidelines for Research and Evaluation - II; AGREE-REX: Appraisal of Guidelines for Research and Evaluation–Recommendations Excellence (AGREE-REX); CPG: Clinical Practice Guideline; FA: Food allergy; ISAAC: International Study of Asthma and Allergies in Childhood; LEAP: Learning Early About Peanut Allergy; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO: Prospective Register of Systematic Reviews; SR: Systematic review; WAO: World Allergy Organization

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Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Authors' contributions

ASYL and EHT developed an initial draft for refinement by GWKW. All authors have made substantial contributions to conception and design of this paper, further refinements of the manuscript and given final approval of the version to be published.

Ethics approval

Ethical approval is not required for this systematic review. However, each author's potential conflicts of interest have been disclosed.

Authors' consent for publication

All authors have given their consent for publication in WAO Journal.

Declaration of competing interest

The authors declare that they have no competing interests.

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2022.100679.

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