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## Diagnosing and managing common food allergies: a systematic review

Schneider Chafen JJ, Newberry SJ, Riedl MA, Bravata DM, Maglione M, Suttorp MJ, Sundaram V, Paige NM, Towfigh A, Hulley BJ, Shekelle PG

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### CRD summary

This review concluded that best practices for management and prevention of food allergies were greatly hindered by a lack of uniformity of criteria for making a diagnosis. Given the limited quality of the studies and heterogeneity among studies, the authors' conclusions seem appropriate, but interpretation should take into account potential for review bias.

### Authors' objectives

To assess the prevalence, diagnosis, management and prevention of food allergies.

### Searching

PubMed, Cochrane Database of Systematic Reviews, DARE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched between 1988 and September 2009 for articles in English. Search terms were reported. The World Allergy Organisation Journal was searched between 1988 and February 2009. Other potentially relevant articles were identified through searching references and contacting experts (this could yield studies from outside the search period).

### Study selection

Prospective studies that assessed diagnostic tests and used food challenge as a criterion standard in a defined population were eligible for inclusion. Studies needed to report sufficient data to calculate sensitivity and specificity. Randomised and non-randomised controlled trials of management and prevention of food allergies were eligible. In food allergies where anaphylaxis was common (such as shellfish, fish and peanuts), cohort studies with more than 100 participants were eligible for inclusion.

Included diagnostic studies were of children aged one month to 14.3 years (where reported). Studies compared diagnostic tests (serum food-specific immunoglobulin E (IgE), skin prick test or atopy patch test) with a food challenge reference test. Most studies of management compared an intervention (elimination diets, immunotherapy, food substitutions or alterations, medical or pharmacologic therapies, probiotics and education) with a control. Foods evaluated were cow's milk, hen's eggs, peanut/tree nut, shellfish/fish and other. Studies of prevalence and prevention were included in the review, but the findings are not reported here.

Two reviewers independently screened titles and abstracts for inclusion. Discrepancies were resolved by discussion.

### Assessment of study quality

Diagnostic studies were assessed using QUADAS criteria. Randomised controlled trials (RCTs) of management were assessed using the Jadad scale. Observational studies on management of allergies were initially considered to be of poor quality, but were then rated as good quality if there was a high level of follow-up ( $\geq 90\%$ ), large sample size ( $> 500$  patients) and attempted to reduce bias through study design or statistical analysis.

The authors did not state how many reviewers performed the validity assessment.

### Data extraction

For diagnostic studies, sensitivities and specificities were extracted to calculate the summary receiver operator characteristic (ROC) curves, weighted by sample size, and 95% confidence intervals (CIs).

It was unclear how many reviewers were involved in data extraction, but discrepancies were resolved through discussion or by referral to a third reviewer.

### Methods of synthesis

For diagnostic studies, summary ROC curves (area under the curve, AUC) and 95% CIs were calculated for all food allergies and separately for cow's milk allergy and hen's egg allergy. Separate analyses were performed for studies using skin prick and serum food-specific IgE tests. There were insufficient studies to calculate summary ROC curves for atopy patch test studies for peanut/tree nut or fish/shellfish allergies.

Pooling of results for management studies was not possible; findings were presented as a narrative synthesis.

## Results of the review

### Diagnostic studies (18 prospective studies, n=2,806):

Sample sizes ranged between 34 and 495 children. Study quality was reported to be fair; between 11 and 18 studies met 10 of the 12 QUADAS criteria.

There were no statistically significant differences between skin prick tests compared with food challenge (AUC 0.87, 95% CI 0.81 to 0.93; 13 studies) or serum food-specific IgE tests compared with food challenge (AUC 0.84, 95% CI 0.78 to 0.91; 11 studies) for all food allergies.

There were no statistically significant differences for cow's milk allergy (AUC 0.84, 95% CI: 0.75 to 0.92; eight skin prick test studies and AUC 0.78, 95% CI 0.70 to 0.86; nine serum food-specific IgE test studies) and hen's egg allergy (AUC 0.87, 95% CI 0.76 to 0.97; five skin prick test studies and AUC 0.85, 95% CI 0.62 to 1.09; five serum food-specific IGE test studies).

### Management studies (25 studies, n=2,006):

Sample sizes ranged between 12 and 567. Overall, studies were reported to be of fair quality (seven good, 12 fair and six poor).

Studies of oral or subcutaneous immunotherapy reported some improvement on desensitisation compared with controls, but there was insufficient evidence on tolerance and safety (five studies). There was insufficient evidence from studies on food substitutions (three studies) or alterations (five studies) to make definitive conclusions. There was evidence that medical or pharmacologic therapies can improve management of allergies (five studies). One study each assessed elimination diets and low allergen diets and reported improvements in allergies compared with controls. One study reported reduced nut reactions after education. Two studies reported no improvement on outcomes in infants who received probiotics.

## Authors' conclusions

Conclusions about best practices for management and prevention of food allergies were greatly hindered by a lack of uniformity of criteria for making a diagnosis.

## CRD commentary

The review question was broad and was supported by appropriate inclusion criteria for study design and broad criteria for intervention, comparator, participants and outcomes. The literature search was adequate, but as articles were restricted to English it was possible that language bias may have been introduced. Previously published criteria were used to assess study quality, which was described as fair for both diagnostic and management studies. The authors undertook screening and data extraction in duplicate; it was not clear whether this was true for validity assessment, which meant that reviewer error and bias could not be ruled out. No formal tests of statistical heterogeneity were reported, but where heterogeneity was deemed to be present a narrative synthesis was appropriate. The authors acknowledged limitations with the included studies, such as their quality and heterogeneity in definitions of food allergy. The authors acknowledged that they did not formally evaluate for publication bias. There were few details reported on participants in the management studies. Only a small number of studies were included for some comparisons. Given the limitations with the available evidence, the authors' conclusions seem appropriate, but interpretation should take into account potential limitations with the review process.

## Implications of the review for practice and research

**Practice:** The authors stated that there was a need for standard criteria to define a food allergy and a set of evidence-based guidelines from which to make a diagnosis.

**Research:** The authors stated that there was a need for greater rigour in the design, execution and reporting of food allergy studies. There was a need for more controlled studies that assessed elimination diets in patients with non-anaphylactic food allergy symptoms.

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