

ImmunoCAP® ISAC and Microtest for multiplex allergen testing in people with difficult to manage allergic disease: a systematic review and cost analysis

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Scientific summary

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Scientific summary

Background

Multiplex allergen tests are molecular diagnostic tests, in the form of a glass slide, which can simultaneously test for the presence of multiple antibodies in blood samples (up to 51 allergen sources). Multiplex allergen testing is likely to be used in secondary care settings or specialist tertiary care centres, as an addition to allergen challenge testing and in addition to, or in place of, single immunoglobulin E (IgE) antibody testing. Multiplex tests may be useful for investigating people with difficult to manage allergic disease: people who are allergic to two or more allergens and/or have allergies to unknown sources. In the UK it is estimated that 10 million patients have two or more allergies.

Objectives

The overall aim of this project was to summarise the evidence available to inform estimates of the clinical effectiveness and cost-effectiveness of adding multiplex allergen testing to the investigation of people with difficult to manage allergic disease, in secondary or tertiary UK care settings. We defined the following research objectives to address this aim:

1. To assess the effects on clinical outcomes (e.g. allergy symptoms, incidence of acute exacerbations) of adding multiplex allergen testing to the investigation of people with difficult to manage allergic disease.
2. To assess the effects on treatment (e.g. restriction diets, immunotherapy, number of allergen challenge tests required) of adding multiplex allergen testing to the investigation of people with difficult to manage allergic disease.
3. To assess the accuracy of multiplex allergen testing in predicting clinical reactivity and to investigate whether or not multiplex allergen testing can provide diagnostic information additional to that provided by current standard care in the UK [clinical history, skin prick tests (SPTs), single IgE testing].
4. To assess the cost-effectiveness of adding multiplex allergen testing to the investigation of people difficult to manage allergic disease in secondary or tertiary care settings.

Methods

Assessment of clinical effectiveness

Fifteen databases, including MEDLINE (via OvidSp), MEDLINE In-Process Citations, MEDLINE Daily Update, PubMed (National Library of Medicine), EMBASE, Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment (HTA) database, Science Citation Index (SCI), Conference Proceedings Citation Index-Science (CPCI-S), BIOSIS Previews, Latin American and Caribbean Health Sciences Literature (LILACS), National Institute for Health Research (NIHR) HTA programme, and the US Food and Drug Administration (FDA), were searched from 2005 to April 2015 for terms relating to ImmunoCAP®, Microtest (Microtest Matrices Ltd, London, UK) or allergy microarray tests. Additional searching was performed for grey literature, three trial registries and seven conference proceedings. Risk of bias was assessed using QUADAS-2, The Critical Appraisal Skills Programme (CASP) cohort risk-of-bias tool, or a review-specific tool designed by the authors, as appropriate. Search results were screened for relevance independently by two reviewers. Studies were included if they were of adults or children with allergy who received a multiplex allergen test [ImmunoCAP® Immuno Solid-phase Allergen Chip (ISAC) Thermo Fisher Scientific/Phadia AB, Uppsala, Sweden, or Microtest] in comparison with standard pathways of care. Full text inclusion assessment, data extraction and quality assessment were conducted by one reviewer and checked by a second. Results were summarised narratively.

Assessment of cost-effectiveness

MEDLINE, MEDLINE In-Process and Daily Update, EMBASE, EconLit, IDEAS via Research Papers in Economics and NHS Economic Evaluation Database were searched for full cost-effectiveness analysis of multiplex allergen testing from 2005 to May 2015. Included studies are appraised using a quality checklist based on Drummond (Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods For The Economic Evaluation Of Health Care Programmes*. 3rd edn. Oxford: Oxford University Press; 2005).

Owing to a lack of data on the clinical effectiveness of multiplex allergen testing, no long-term cost-effectiveness model was developed. A conceptual model structure was developed, literature on utility scores was reviewed, and cost analyses were performed to examine the short-term costs of various possible diagnostic pathways.

Results

Clinical effectiveness

A total of 8619 records were identified from searching and screened for inclusion. Fifteen studies were included in the review. No studies were identified of people with difficult to manage allergic disease in the UK. All studies evaluated versions of ImmunoCAP ISAC: none was identified for Microtest. ImmunoCAP ISAC 112 is the most recent version of the ImmunoCAP ISAC array (the number refers to the number of tests per array). None of the included studies was classified as having a low risk of bias.

No studies were identified which investigated clinical outcomes.

Two studies ($n = 97$) investigated the use of ImmunoCAP ISAC to guide decisions on the discontinuation of restrictive diets in children with food allergies. Both studies reported that the results from ImmunoCAP ISAC were used to reintroduce foods, but details were unclear.

Two studies ($n = 373$) assessed clinicians' views on whether or not ImmunoCAP ISAC provided information useful in the management of patients. Clinicians judged that ImmunoCAP ISAC 103 provided new information useful in the management of the patient in 91–95% of cases. Added value was defined as the ability to discriminate allergens that were cross-immunoreactive rather than those that were responsible for sensitisation, or the ability to impact upon accuracy of diagnosis or allergen-specific immunotherapy (SIT) prescription that was not possible using standard diagnostic work-up.

Two studies ($n = 459$) investigated the effect on SIT prescriptions of adding ImmunoCAP ISAC testing to the standard diagnostic work-up of people with respiratory allergy. Clinicians judged that for 27–54% of patients changes were made to SIT prescriptions after ImmunoCAP ISAC 103 or ImmunoCAP ISAC 96 testing.

Two studies ($n = 428$) investigated the effect on diagnostic classification of adding ImmunoCAP ISAC 103 testing to the standard diagnostic work-up of people with allergic disease. In one study of idiopathic anaphylaxis, the addition of ImmunoCAP ISAC 103 led to the identification of new sensitisations with strong associations with anaphylaxis in 20% of participants, and in 32% additional sensitisations were identified which were not associated with anaphylaxis. A second study found that the addition of ImmunoCAP ISAC 103 testing resulted in increases in the numbers of people classified as 'polysensitised with suspected cross-reactivity' and the number of people diagnosed with both inhalant and food allergies, as well as facilitating a diagnosis for eight previously unclassifiable patients.

One study ($n = 9$) assessed the relationship between change in IgE levels (measured by ImmunoCAP) before and after a 3-year course of SIT, and the clinicians' evaluation of the benefit of SIT. The median specific IgE levels decreased and this change correlated with clinical benefit of SIT. Single tests for specific IgE measurements did not show a decrease.

Eight studies investigated diagnostic accuracy; none was conducted in people with difficult to manage allergic disease. ImmunoCAP ISAC 112 was not investigated; however, ImmunoCAP ISAC 103, 89, 50 out of 51 were investigated. The diagnostic performance of ImmunoCAP ISAC in comparison with either single IgE or SPT varied considerably between studies, according to the allergens investigated and the way in which ISAC testing was applied. In general, individual components of ImmunoCAP ISAC tended to have high specificity, but low sensitivity, relative to whole-allergen single IgE tests or SPTs for the prediction of allergic response. The studies did not provide any information on the specificity of the whole ImmunoCAP ISAC panel.

Assessment of cost-effectiveness

Four economic analyses and 14 health-related quality of life studies were included in the literature review. The systematic review component of this assessment found no data on the clinical consequences of adding multiplex allergen testing to current clinical practice; therefore, a long-term economic model to inform health policy decision-making was not possible. Therefore, the assessment aimed to inform research decisions and support future model-based economic evaluations.

All cost-effectiveness studies showed an increased effectiveness when using ImmunoCAP ISAC and the majority showed cost savings when using ImmunoCAP ISAC. The methods and assumptions used were largely unclear and the credibility of the assessments was questionable; therefore, these findings should be interpreted with extreme caution.

The evidence on utility values for allergic conditions in the UK population was limited.

Test costs for ImmunoCAP ISAC and Microtest were estimated to be £219.51 and £156.85, respectively. For SPT, single IgE and the food challenge test these were £62.29, £136.37 and £570.00, respectively. A speculative analysis indicated that multiplex allergen testing would have to result in a substantial reduction of the proportions of patients receiving single IgE testing and food challenge tests in order to be cost-saving in the short term. Analyses to compare the effect of replacing single IgE with multiplex testing were difficult to perform because of lack of information regarding where the multiplex test would sit in the care pathway.

Conclusions

No recommendations for service provision can be made based on the analyses included in this report. The clinical effectiveness and cost-effectiveness of using multiplex allergen testing in the investigation of people with difficult to manage allergic disease have yet to be adequately investigated. It is suggested that a consensus-based protocol for the use of multiplex allergen testing be developed. The clinical effectiveness and cost-effectiveness of the proposed protocol should then be assessed by comparing long-term clinical and quality of life outcomes and resource use in patients managed using the protocol with those managed using a standard diagnostic pathway.

Study registration

This study is registered as PROSPERO CRD42015019739.

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