

# Analytical Performance, Quality of Life and Costs Related to Allergy Testing: Results from Two Systematic Literature Reviews

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## Introduction

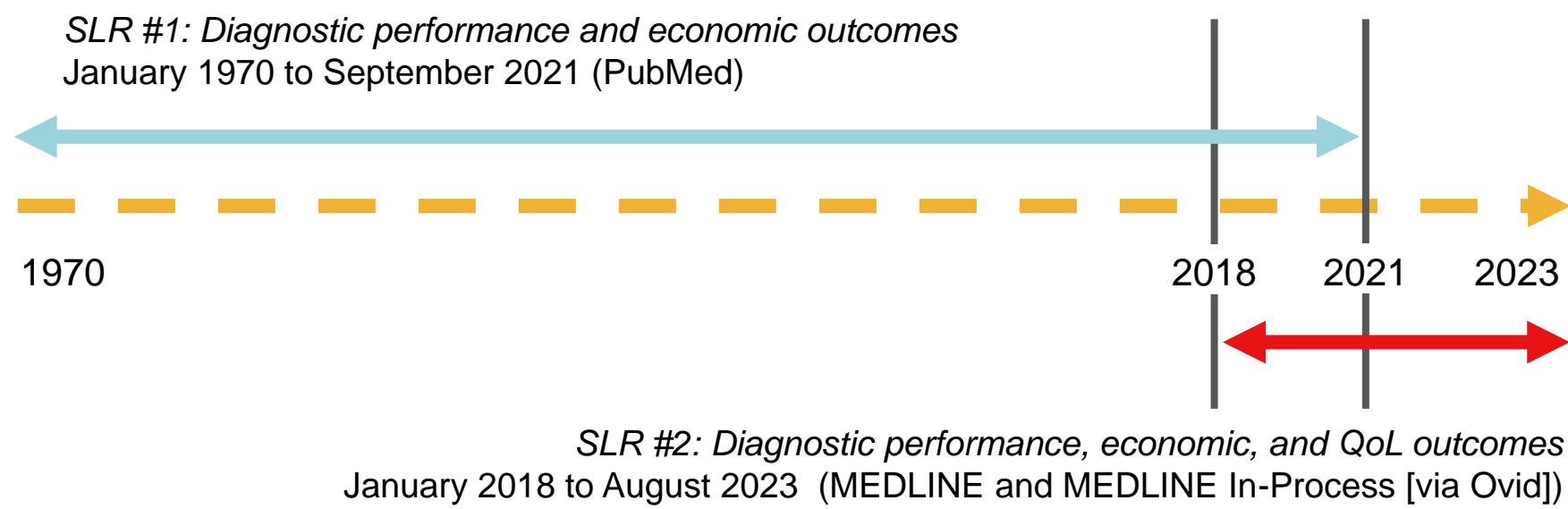
Many patients with allergies are misdiagnosed or undiagnosed, causing increased morbidity, reduced quality of life (QoL), and an economic burden on healthcare systems.<sup>1</sup> Skin-prick tests (SPT) and serum immunoglobulin E tests (slgE) are the main tools for aiding allergy diagnosis, and the diagnostic performance of these tests has been widely studied.<sup>2</sup> However, the impact of different allergy testing on costs, healthcare resource use (HCRU), and patient QoL remains underreported. Within slgE testing, there is also a gap in knowledge for the performance of testing with whole allergens compared to allergen components outside of food allergies.

The objective of this review was to assess the impact of allergy testing on QoL, costs, and HCRU, and to briefly compare the diagnostic performance of various allergy testing methods, with a focus on whole allergens versus allergen components.

## Materials and methods

- Two systematic literature reviews (SLR) were conducted following guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement<sup>3</sup> and pre-defined protocols.
- The SLRs were performed as part of a wider program to identify data on diagnostic performance, economic outcomes, and the QoL impact (SLR #2 only) of allergy testing. (Figure 1)

Figure 1. Overview of SLR timelines according to publication date



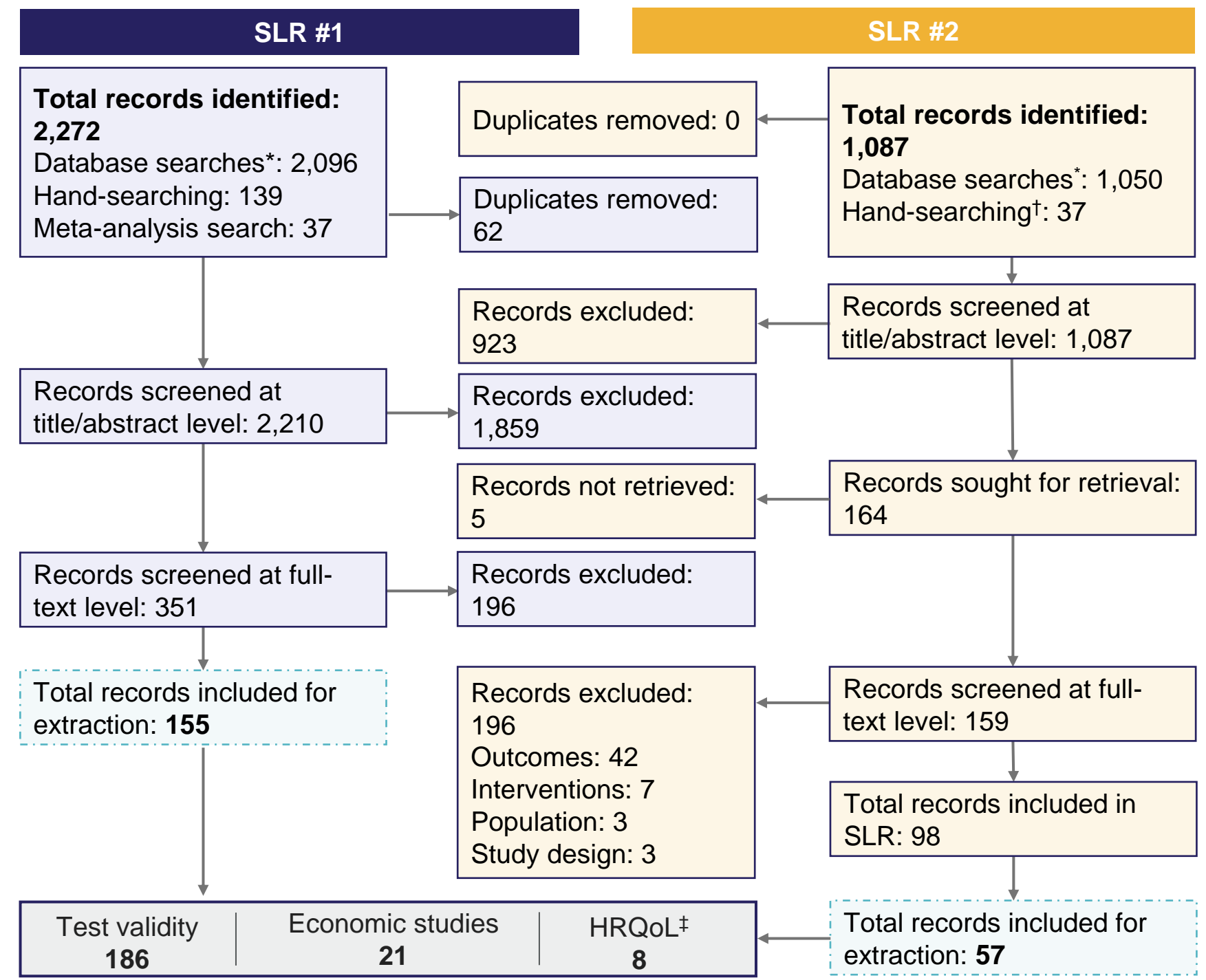
Abbreviations: QoL, quality of life; SLR, systematic literature review

- Supplementary searches of relevant conference proceedings from the American College of Allergy, Asthma, and Immunology, the American Academy of Allergy, Asthma and Immunology, and the European Academy of Allergy and Clinical Immunology were conducted for both SLRs.
- Additional systematic selection criteria were applied to studies evaluating test performance given the high volume of evidence identified: only studies published as full-text articles and including a sample size of least 100 were considered. No additional restrictions were applied to studies reporting QoL and economic data.
- Studies exclusively on patch tests, basophil activation tests, basophil histamine release, multiple antigen simultaneous testing, and eosinophil cationic protein tests were not considered.
- Literature screening was conducted by two reviewers, with a third reviewer resolving any discrepancies. Data extraction was performed by one reviewer and all entries were validated by a second reviewer.

## Results

In total, 449 studies were included across both SLRs and 212 were included for data extraction, the majority of which reported on diagnostic test performance (Figure 2).

Figure 2. PRISMA flow diagram

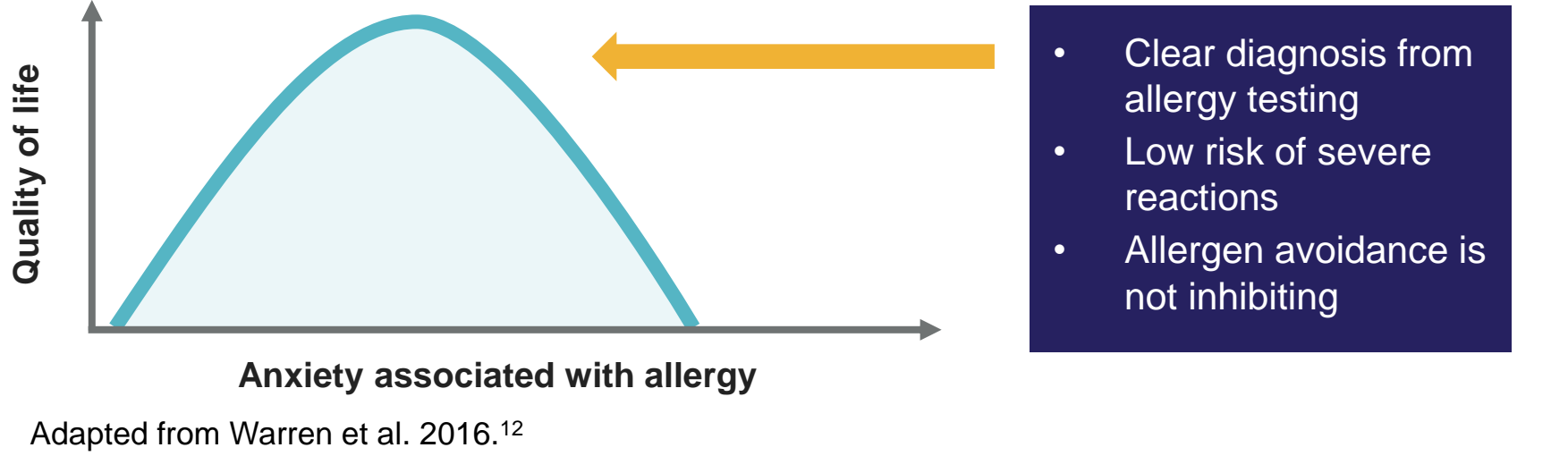


### Impact of allergy testing on QoL

Eight studies reported on the impact of allergy testing on QoL; three described the anxiety experienced by parents or caregivers of children undergoing allergy testing,<sup>4-6</sup> four reported on anaphylaxis rates,<sup>7-10</sup> and one estimated general QoL with a model.<sup>11</sup> (Figure 3)

- In three studies that investigated QoL associated with open food challenge (OFC), undergoing allergy testing alone had a positive impact on QoL regardless of outcome and led to reduced anxiety.<sup>4-6</sup>
- Two studies reported that a negative test result had a positive impact on QoL in parents and caregivers for children undergoing allergy testing.<sup>4,5</sup> However, one of these studies showed that three months after OFC, higher QoL values were reported among those with a positive diagnosis than those with a negative result.<sup>4</sup> This may be because of the opportunity to avoid allergens and thus reducing the frequency of exacerbations.

Figure 3. Impact of correct allergy diagnosis on anxiety and QoL



One study investigated the occurrence of anaphylaxis during OFC, which can result in severe and potentially life-threatening reactions; anaphylactic reactions increased with allergen sensitization, as measured via SPT and slgE testing.<sup>8</sup>

- Studies have also mentioned the challenges of reporting anaphylaxis rates since events may be underreported by patients, caregivers, or healthcare providers.<sup>9,10,13</sup> Events occurring during allergy testing were more likely to be acknowledged and reported.

### Impact of allergy testing on economic outcomes

One study reported on HCRU,<sup>14</sup> 13 on costs,<sup>5,14-25</sup> and seven were economic evaluations associated with allergy testing.<sup>18,26-31</sup> slgE testing and SPT were associated with lower costs (slgE range: €12.00<sup>23</sup> to €16.88<sup>15</sup>; SPT range: €25.29<sup>15</sup> to €48.00<sup>5</sup>); OFCs were considerably more expensive (range: €160.00<sup>23</sup> to €1,231.00<sup>15</sup>).

In two studies, in vitro allergy testing reduced the overall long-term costs of allergies by reducing the use of unnecessary medication and other related expenses, and by preventing hospitalizations.<sup>19,25</sup> (Table 1)

Table 1. Impact of in vitro allergy testing on per-patient allergy costs

Study (Setting)	No Testing	Testing
Zethraeus 2010 (Italy) <sup>25</sup>	€802	€560
Mascialino 2019 (Sweden) <sup>19</sup>	SEK 3,440	slgE: SEK 2,400; OFC: SEK 11,000

Abbreviations: OFC, oral food challenge; SEK, Swedish krona; slgE, serum immunoglobulin E

From the included economic evaluations, four reported slgE testing to be cost-effective, in terms of test performance, compared to food challenges.<sup>26-28,31</sup> One study found that early peanut introduction (EPI) was most effective in preventing peanut allergy when compared to EPI plus screening (SPT and slgE).<sup>29</sup> Lastly, modified quantitative testing was more cost-effective than in vitro methods in a US-based model.<sup>18</sup> (Table 2) The main cost drivers included subsequent medication use, hospitalizations, laboratory costs, and outpatient resource use.<sup>18,30,31</sup>

Table 2. Economic evaluation outcomes

Test	Economic Evaluation
<b>Index:</b> Multiplex slgE <sup>26,28</sup> <b>Reference:</b> DBPCFC or OFC	<ul style="list-style-type: none"><li>Multiplex slgE is cost effective and cost saving compared with DBPCFC in children with suspected peanut allergy.</li><li>DBPCFC was noted as time-consuming, costly, and may induce severe reactions.</li></ul>
<b>Index:</b> SPT <sup>27</sup> <b>Reference:</b> DBPCFC, MA	<ul style="list-style-type: none"><li>In patients with suspected peanut allergies, MA increased QALYs and reduced costs compared with DBPCFC and SPT.</li></ul>
<b>Index:</b> Early peanut introduction + SPT or IgE <sup>29</sup> <b>Reference:</b> Early peanut introduction + no screening	<ul style="list-style-type: none"><li>A no-screening approach for early peanut introduction prevented more peanut allergy cases and reduced total healthcare costs compared with screening (SPT and slgE).</li><li>QALYs and rate of allergic reactions were similar between early introduction strategies (i.e., testing/no-testing).</li><li>slgE and SPT resulted in fewer cases of peanut allergy prevented, as those with sensitization beyond cut-off levels would be considered allergic and not offered OFC.</li></ul>
<b>Index:</b> slgE <sup>30</sup> <b>Reference:</b> No testing	<ul style="list-style-type: none"><li>In England, slgE testing in school children with asthma could result in &gt;£105 million in cost savings over 5 years through reduced hospitalizations.</li></ul>
<b>Index:</b> Multiplex slgE + SPT <sup>31</sup> <b>Reference:</b> SPT	<ul style="list-style-type: none"><li>In patients with pollen sensitization, multiplex slgE + SPT reduced the need for allergen-specific immunotherapy compared with SPT alone, thus reducing costs.</li></ul>
<b>Index:</b> MQT* <sup>18</sup> <b>Reference:</b> Intradermal dilution testing, in vitro testing	<ul style="list-style-type: none"><li>At a high prevalence of allergic rhinitis, MQT was less costly than in-vitro testing and intradermal testing.</li><li>MQT was more cost effective than in-vitro testing alone and in combination with intradermal testing.</li><li>The model was sensitive to changes in prevalence, costs and the sensitivity and specificity of testing methodologies.</li></ul>

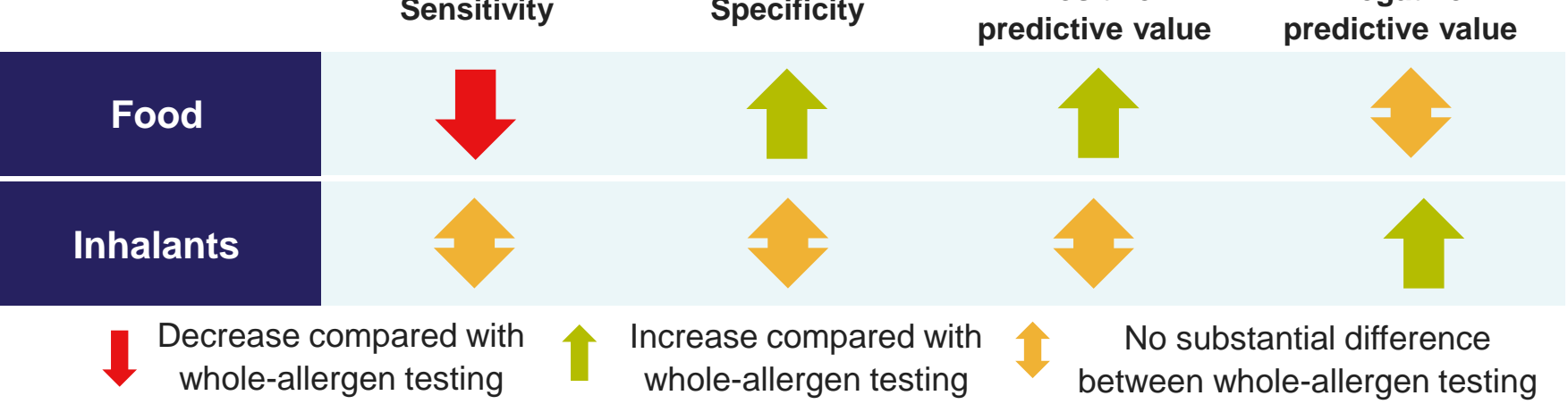
\*A combination of skin prick and intradermal testing  
Abbreviations: DBPCFC, double-blind placebo-controlled food challenge; IgE, immunoglobulin E; MA, molecular allergology; MQT, modified quantitative testing; OFC, oral food challenge; QALY, quality-adjusted life year; slgE, serum immunoglobulin E; SPT, skin-prick test

### Summary of diagnostic test performance for allergen component testing

Studies showed varying sensitivity and specificity in diagnostic tests. SPT was generally associated with high sensitivity and specificity but showed lower accuracy in food allergen testing compared with other allergens. There was a strong correlation between sensitivity/specificity and test cut-off values for both SPT and slgE, with decreased sensitivity and increased specificity with higher test cut-off values.

Allergen component testing appeared to be more likely to correctly rule out a diagnosis in patients without an allergy than showing a positive test result in patients with an allergy. The performance of allergen component diagnostics compared with whole-allergen testing varied between food and inhalant allergens. (Figure 4)

Figure 4. Allergen component testing compared with whole-allergen testing methodologies



## Conclusions

- Patients given definite allergy diagnoses experienced improved QoL over time compared with those without a diagnosis, likely because of the ability to avoid allergens where possible.
- Costs and HCRU varied across diagnostic tests, but allergy testing drove economic benefits through decreased inappropriate use of medications and related expenses.
- Test performance varied across methodologies; however, identifying precise and cost-effective testing techniques are essential to optimize diagnostic pathways and aid in informed decision-making.

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## Disclosures

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