

Correspondence and Replies

The added value of reporting likelihood ratios to laboratory test results in allergy and clinical immunology



To the Editor:

It was with much interest that we have read the article by Abrams et al¹ on using the Bayesian approach in reporting laboratory test results in allergy diagnostics. In their report, the authors make a case to include likelihood ratios (LRs) in the reports of laboratory tests, an idea we fully support.

Reporting LRs allows one to estimate the posttest probability for disease based on the pretest probability and the LR. Even if the pretest probability is not exactly known, the LR gives the physician a feeling (approximation) about how much the test result will change the probability for disease. In addition, it could increase the impact of laboratory diagnostics on health care.

In contrast to the classical dichotomous way of reporting test results based on a single cutoff, reporting LRs expresses the diagnostic value of a distinct test result or test result interval. For example, the relationship between the specific IgE antibody level and the chance for allergic disease can be expressed by continuous test result-specific LRs, as shown by Nalin et al² for peanut, or by test result interval-specific LRs, as shown by Van Hoeyveld et al³ for inhalant allergens (grass pollen and birch pollen with recombinant allergens). Based on the latter study,³ our clinical laboratory includes the test result interval-specific LR for ImmunoCAP (Thermo Fisher, Uppsala, Sweden) results of grass pollen, rPhl p 1.5, birch pollen, and rBet v 1 on the laboratory report (Table I). As expected, LRs increased when specific IgE antibody levels increased, providing more diagnostic accuracy. Values between 0.7 and 3.5 kU/L significantly affect posttest probability (LRs between 6.3 and infinity [$+\infty$]), but values exceeding 3.5 kU/L strongly suggest clinically relevant allergy (LR = $+\infty$) for these allergens.³ Also in other areas of clinical immunology, LRs are informative. There is substantial evidence that for many autoantibodies, the higher the autoantibody level, the higher the LR, and consequently, the probability for disease.⁴ This was shown for antinuclear antibodies, antineutrophil cytoplasm antibodies (ANCA), and tissue transglutaminase (reviewed in Fierz et al⁴). The 2017 revised international consensus on ANCA testing also advised reporting test result (interval)-specific LRs for proteinase-3 ANCA and myeloperoxidase ANCA.⁵

Finally, LRs express the clinical value of a test result independent of the unit used by the assay. This is especially useful for autoantibody tests for which good reference materials are unavailable and different units are applied by the manufacturers. It was shown that LRs harmonize ANCA⁶ and antinuclear antibody⁷ testing across assays.

Adding LRs to laboratory reports adds value to the field of allergy and clinical immunology. These reports can be supplemented with a graphical representation of posttest probability as a function of pretest probability and the laboratory result (eg, for a specific IgE result^{2,3}). Therefore, in agreement with Abrams et al,¹ we encourage further research in this area.

Xavier Bossuyt, MD, PhD^{a,b}
Glynis Frans, PhD^a

^aDepartment of Microbiology, Immunology, and Transplantation, KU Leuven, Leuven, Belgium

^bDepartment of Laboratory Medicine, University Hospitals Leuven, Leuven, Belgium. Conflicts of interest: The authors declare that they have no relevant conflicts of interest. Received for publication January 11, 2022; Revised January 27, 2022; accepted for publication February 22, 2022.

Corresponding author: Xavier Bossuyt, MD, PhD, Department of Laboratory Medicine, University Hospitals Leuven, Herestraat 49, B-3000 Leuven, Belgium. E-mail: xavier.bossuyt@uzleuven.be.

REFERENCES

1. Abrams EM, Chan ES, Portnoy J. Evolving interpretation of screening and diagnostic tests in allergy. *J Allergy Clin Immunol Pract* 2021;9:4183-91.
2. Nalin UG, Shroba J, Pandya A, Portnoy J. Diagnosis of peanut allergy using continuous likelihood ratios. *Ann Allergy Asthma Immunol* 2020;125:680-5.
3. Van Hoeyveld E, Nickmans S, Ceuppens JL, Bossuyt X. Defining thresholds of specific IgE levels to grass pollen and birch pollen allergens improves clinical interpretation. *Clin Chim Acta* 2015;450:46-50.
4. Fierz W, Bossuyt X. Likelihood ratio approach and clinical interpretation of laboratory tests. *Front Immunol* 2021;12:65262.
5. Bossuyt X, Cohen Tervaert JW, Arimura Y, Blockmans D, Flores-Suárez LF, Guillemin L, et al. Position paper: revised 2017 international consensus on testing of ANCAs in granulomatosis with polyangiitis and microscopic polyangiitis. *Nat Rev Rheumatol* 2017;13:683-92.
6. Bossuyt X, Damoiseaux J, Rasmussen N, van Paassen P, Hellmich B, Baslund B, et al. Harmonization of antineutrophil cytoplasmic antibodies (ANCA) testing by reporting test result-specific likelihood ratios: position paper. *Clin Chem Lab Med* 2020;59:e35-9.
7. Bossuyt X, Claessens J, Belmondo T, De Langhe E, Westhovens R, Poesen K, et al. Harmonization of clinical interpretation of antinuclear antibody test results by solid phase assay and by indirect immunofluorescence through likelihood ratios. *Autoimmun Rev* 2019;18:102386.

<https://doi.org/10.1016/j.jaip.2022.02.041>

TABLE I. Likelihood ratios (95% CIs) for allergy to grass pollen and birch pollen natural extracts and recombinant allergens for specific IgE test result intervals

Allergen	ImmunoCAP	< 0.1 kU/L	0.1-0.35 kU/L	0.35-0.7 kU/L	0.7-3.5 kU/L	>3.5-17.5 kU/L
Grass pollen mixture	gx3	0.00	0.22 (0.07-0.75)	1.19 (0.35-4.03)	$+\infty$	$+\infty$
rPhl p 1.5	g213	0.02 (0.004-0.06)	0.4 (0.11-1.44)	3.6 (0.73-17.44)	$+\infty$	$+\infty$
Birch pollen	t3	0	0.1 (0.01-0.75)	4.22 (0.44-40.09)	6.33 (2.19-18.24)	$+\infty$
rBet v 1	t215	0.03 (0.01-0.08)	1.41 (0.36-5.52)	1.41 (0.20-9.85)	$+\infty$	$+\infty$

Reproduced from Van Hoeyveld et al,³ with permission of the publisher (Elsevier).