



HAL
open science

Allergic and hypersensitivity conditions in non-specialist care: Flow diagrams to support clinical practice

Dermot Ryan, Bertine Flokstra-de Blok, Evangéline Clark, Clara Gaudin, Myriam Mamodaly, Janwillem Kocks, Jantina Lucia van Der Velde, Liz Angier, Kerstin Romberg, Radek Gawlik, et al.

► To cite this version:

Dermot Ryan, Bertine Flokstra-de Blok, Evangéline Clark, Clara Gaudin, Myriam Mamodaly, et al.. Allergic and hypersensitivity conditions in non-specialist care: Flow diagrams to support clinical practice. *Allergy*, 2022, <10.1111/all.15273>. <hal-03641107>

HAL Id: hal-03641107

<https://hal.umontpellier.fr/hal-03641107v1>

Submitted on 14 Apr 2022






HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons CC BY-NC 4.0 - Attribution - Non-commercial use - International License

Allergic and hypersensitivity conditions in non-specialist care: Flow diagrams to support clinical practice

Dermot Ryan¹  | Bertine M. J. Flokstra – de Blok^{2,3,4}  | Evangéline Clark⁵ | Clara Gaudin⁶ | Myriam Mamodaly⁵ | Janwillem Kocks^{2,7,8} | Jantina Lucia van der Velde^{3,9}  | Liz Angier¹⁰ | Kerstin Romberg^{11,12} | Radek Gawlik¹³ | Pascal Demoly^{5,14,15}  | Luciana Kase Tanno^{5,14,15} 

¹Usher Institute, University of Edinburgh, Edinburgh, UK

²General Practitioners Research Institute (GPRi), Groningen, The Netherlands

³University of Groningen, University Medical Center Groningen, GRIAC Research Institute, Groningen, The Netherlands

⁴Department of Pediatric Pulmonology and Pediatric Allergology, University of Groningen, University Medical Center Groningen, Beatrix Children's Hospital, Groningen, The Netherlands

⁵University Hospital of Montpellier, Montpellier, France

⁶University Hospital of Nantes, Nantes, France

⁷Observational and Pragmatic Research Institute, Singapore, Singapore

⁸University of Groningen, University Medical Center Groningen, GRIAC Research Institute, Groningen, The Netherlands

⁹Department of General Practice, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands

¹⁰Primary Care and Population Sciences, University of Southampton, Southampton, UK

¹¹Health Care Centre, Näsets Läkargrupp, Höllviken, Sweden

¹²Respiratory Medicine and Allergology, Clinical Sciences Lund, Lund University, Lund, Sweden

¹³Department of Internal Medicine, Allergology and Clinical Immunology, Silesian University of Medicine, Katowice, Poland

¹⁴IDESP, INSERM – University, Montpellier, France

¹⁵WHO Collaborating Centre on Scientific Classification Support, Montpellier, France

Correspondence

Dermot Ryan, Usher Institute, University of Edinburgh, Edinburgh, UK.
Email: dermotryan@doctors.org.uk

Funding information

The TF was sponsored by EAACI.

Abstract

Most patients presenting with allergies are first seen by primary care health professionals. The perceived knowledge gaps and educational needs were recently assessed in response to which the LOGOGRAM Task Force was established with the remit of constructing pragmatic flow diagrams for common allergic conditions in line with an earlier EAACI proposal to develop simplified pathways for the diagnosis and management of allergic diseases in primary care. To address the lack of accessible and pragmatic guidance, we designed flow diagrams for five major clinical allergy conditions: asthma, anaphylaxis, food allergy, drug allergy, and urticaria. Existing established allergy guidelines were collected and iteratively distilled to produce five pragmatic and

Abbreviations: A/H, allergic and hypersensitivity conditions; ADRs, adverse drug reactions; EAACI, European Academy of Allergy and Clinical Immunology; EAI/AAI, epinephrine/adrenalin auto-injector; FeNO, fractional exhaled nitric oxide; GINA, global Initiative for asthma; GPS, general practitioners; PEF, peak expiratory flow; SIgE, specific IgE; SIGN/BTS, Scottish Intercollegiate Guideline Network/British Thoracic Society.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2022 The Authors. *Allergy* published by European Academy of Allergy and Clinical Immunology and John Wiley & Sons Ltd.

accessible tools to aid diagnosis and management of these common allergic problems. Ultimately, they should now be validated prospectively in primary care settings.

KEYWORDS

allergy/hypersensitivity, diagnosis, flow-diagram, non-specialist care, primary care

1 | INTRODUCTION

In spite of the fact that allergy, in one of its many guises, is the reason for an estimated 6% of consultations, the primary care clinician has often received little or no training at either undergraduate or postgraduate level concerning this disease area.^{1,2} There is clearly a need to upskill healthcare professionals working in primary care.³ To date, there are two publications which have identified the core skills required for primary care practitioners with a further one for professions allied to health, but in general, there is no sign of these being implemented, although for the first time, allergy is included as part of the postgraduate curriculum for primary care in the United Kingdom.⁴⁻⁶

The making of a diagnosis, even if this is provisional until confirmed, is a critical step in patient management previously called for by European Academy of Allergy and Clinical Immunology (EAACI) "to develop simplified pathways for the diagnosis and management of allergic diseases in primary care."^{7,8} Diagnosis is a complex process, requiring an underlying level of relevant clinical knowledge, pattern recognition and interpretative skills to be successful.^{7,8} An incorrect diagnosis leads to inappropriate investigation and management decisions, which may cause patients harms and incur greater expense to the patient and to society.^{9,10}

The diagnostic process in allergy is further confounded by the presence of non-allergic diseases, from which it must be differentiated. For example, allergic asthma and non-allergic asthma¹¹ or IgE-mediated food allergy, non-IgE-mediated food allergy and non-immunologically mediated adverse reaction to foods.¹²

This is further seen with the recording of adverse drug reactions (ADRs), the vast majority of which are non-allergic in nature but which seem to be recorded, as allergic reactions.^{13,14}

There is an urgent need to bridge the gap between the situation in which we currently find ourselves and the time when primary care is equipped with the appropriate skills to diagnose allergy.^{3,15} The purpose of this EAACI task force was to distill existing allergy guidelines into simple, practical, accessible tools to aid diagnosis of common allergic problems encountered on a daily basis within primary care, while recognizing their applicability to other non-allergy specialist areas. We chose not to include rhinitis as this has been adequately addressed, incorporating simple flow diagrams developed by a multidisciplinary group, by the Allergic Rhinitis and its Impact on Asthma (ARIA) guideline.¹⁶

2 | METHODOLOGY



A pragmatic approach was taken to a pragmatic challenge. The core group decided the five topic areas which were to be included. The team was multidisciplinary consisting of two allergists, one respiratory/allergy specialist, one research scientist, four general practitioners (GP), and three PhD students (two going into primary care). Five subgroups were established, one for each of the topics: They developed the initial drafts which were reviewed and iteratively refined in a series of three face to face and four three-hour zoom sessions until the whole group reached agreement.

The five allergic and hypersensitivity conditions (A/H) we have chosen are as follows: Asthma, Anaphylaxis, Drug allergy, Food allergy, and Urticaria.

2.1 | Construction of the five logograms

A flow diagram was constructed for each of the five A/H consisting of schematic diagrams to cover different aspects of these conditions. The flow diagrams were designed using draw.io[®] with the intention of ultimately digitalizing the diagrams to enable presentation in electronically linked layers. Generally, most of the flow diagrams are available in one or two layers. More detail is available in additional layers which the GP will be able to access (when digitized) by clicking in the steps signaled by gray buttons or hover-boxes. The particular details available in the layers will depend on the characteristics of each condition. For the purpose of this paper, these data are attached as Appendices S1-S5, but it is hoped ultimately to have them available in an electronic format.

As A/H have overlapping aspects, the logograms may also be interlinked with the GP enabled to navigate to other relevant parts of the work taken as a whole. For instance, anaphylaxis is mainly

caused by drugs, food and *Hymenoptera* venom but may have urticaria as one of the manifestations and current uncontrolled asthma as risk factors. Where appropriate, hot links will be provided to rapidly access other logograms as indicated.

2.2 | Ethics and funding

No ethics committee approval was required for this work.

This work was funded by a Task Force grant from EAACI.

2.2.1 | Asthma

Current asthma guidelines are not instantly clear concerning diagnosis. Asthma, unlike many other disorders, does not have one clinically defining feature or measurement, being a syndrome.¹⁷ Diagnosis is very much like constructing a multidimensional jigsaw incorporating essential elements of history, physical examination, and investigation (bio-markers) including response to treatment. Breaking them down into probability categories (as suggested by the SIGN/BTS model¹⁸) aids the practitioner in choosing what investigations to perform and how to incorporate the results into the diagnostic process. We have drawn on GINA statement¹⁹ and BTS/SIGN guideline¹⁸ focusing on asthma diagnosis in general and not on the specific allergic asthma endotype.

2.2.2 | Anaphylaxis

Arguably, anaphylaxis is the most severe manifestation of allergic diseases, increasing in incidence and prevalence and resulting in poor quality of life with the risk of fatality. In primary care, one is rarely witness to an actual attack, but has to recognize from the history what has happened and what to do next to make the patient safe. Misdiagnosis can increase considerably the risk of death, thus referral to an allergy or respiratory specialist is key for risk stratification. We have drawn on the current EAACI guideline on anaphylaxis¹² which is currently being reviewed.²⁰ Only three percent of countries worldwide have an anaphylaxis guideline.²¹

2.2.3 | Food allergy

As much as 30% of the population believes that they have a food allergy,²²⁻²⁴ leading to a high level of requests to GPs for allergy testing (specific IgE [sIgE]). Differentiating IgE-mediated food allergy from non-IgE-mediated food allergy and non-immunologically mediated adverse reactions to foods is an essential skill, as well as identifying patients at higher risk of severe reactions and the interpretation of sIgE in relation to food allergy. All these skills need to be developed with confidence.^{25,26} We have drawn on the current EAACI guideline on food allergy and anaphylaxis.²⁶

2.2.4 | Drug allergy

Drug allergy is a small subset of Adverse Drug Reactions; there is a tendency, however, to classify all ADRs as allergic. Our intention is to facilitate the differentiation between allergic and non-allergic reactions so that patients are not inappropriately labelled, sometimes with negative consequences (e.g., misdiagnosis of penicillin allergy leading to inappropriate antibiotic prescription, resistant bacteria and increased morbidity and mortality²⁷). We have drawn on the ICON guideline²⁸ and a paper outlining the role of primary care in drug hypersensitivity.²⁹

2.2.5 | Urticaria

Urticaria is mistakenly believed by many to be an IgE-mediated type 1 hypersensitivity reaction (allergy) with the consequence that unnecessary investigations are performed which in turn provide results, which are open to misinterpretation with significant impact on the life of the patient.³⁰⁻³³ The frequently associated angioedema frequently leads to unscheduled visits, including emergency room visits. We have drawn on EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria.³⁴ This has been subsequently superseded by the 2021 update, which re-affirms our approach.³⁵

3 | RESULTS

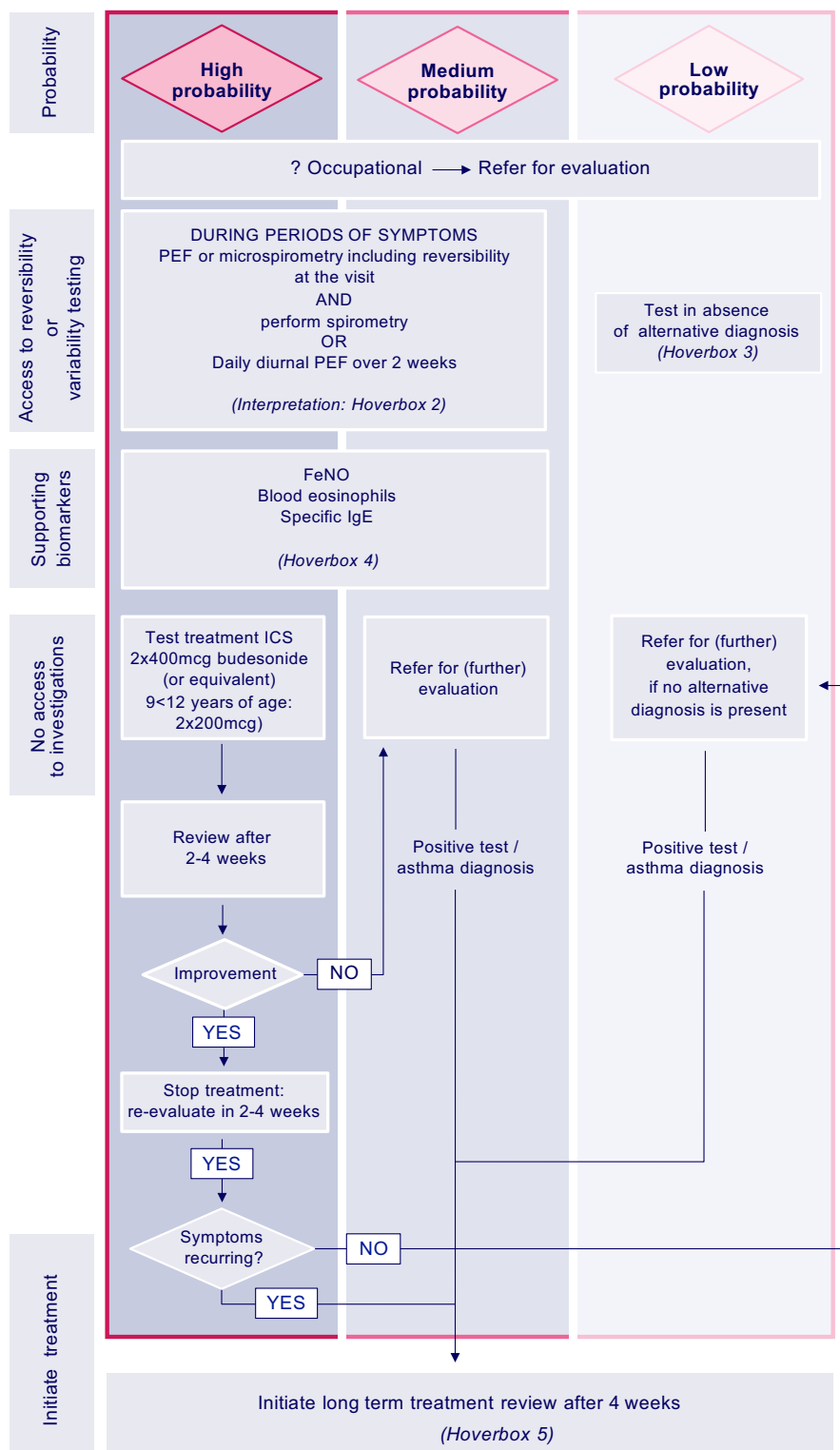
Note: Information pertaining to hover-boxes appears in the specific Appendices S1-S5 annex.

3.1 | Asthma

The asthma logogram consists of one schematic flow diagram comprising two steps: assessing probability based on clinical history and physical examination, (Figure 1); diagnosis depending on probability and availability of tests (Figure 2). As asthma is a long-term condition, there is no need to rush into the diagnosis of asthma. The diagnosis needs careful consideration, as long-standing, sometimes lifelong treatment is required. Although spirometry is an important element in the diagnosis of asthma, clinical suspicion, based on careful history taking, is the initial step in building the jigsaw. Many of the current guidelines are based upon the availability of spirometry. Unfortunately, spirometry and bronchodilator and/or hyperreactivity testing is not accessible everywhere. As an alternative, 2 weeks of peak-flow measurements can be considered.

In low probability cases based on the symptoms, history, and physical examination, alternative diagnoses (available by hovering over the gray buttons [hover box] Asthma Annex Appendix S1) should be considered before additional testing. Spirometry is always preferred as the next step, but based on the probability of asthma, initial treatment with inhaled corticosteroids (with or without fast

FIGURE 2 Diagnostic route based on probability AND availability of investigations



3.2 | Anaphylaxis

The anaphylaxis flow-diagram covers 2 main situations: 1) patient potentially experiencing anaphylaxis, (Figure 3) and 2) patient having possibly experienced anaphylaxis (Figure 4). In the first flow diagram, key symptoms are highlighted to support prompt identification and

treatment of anaphylaxis, followed by individualized emergency plan and recommendations regarding referral. The second flow diagram is focused on key aspects of the clinical history to support risk reduction and referral to the specialist for risk stratification. Additional details indicated by the hover-boxes are to be found in the Anaphylaxis annex Appendix S2.

Patients potentially experiencing anaphylaxis

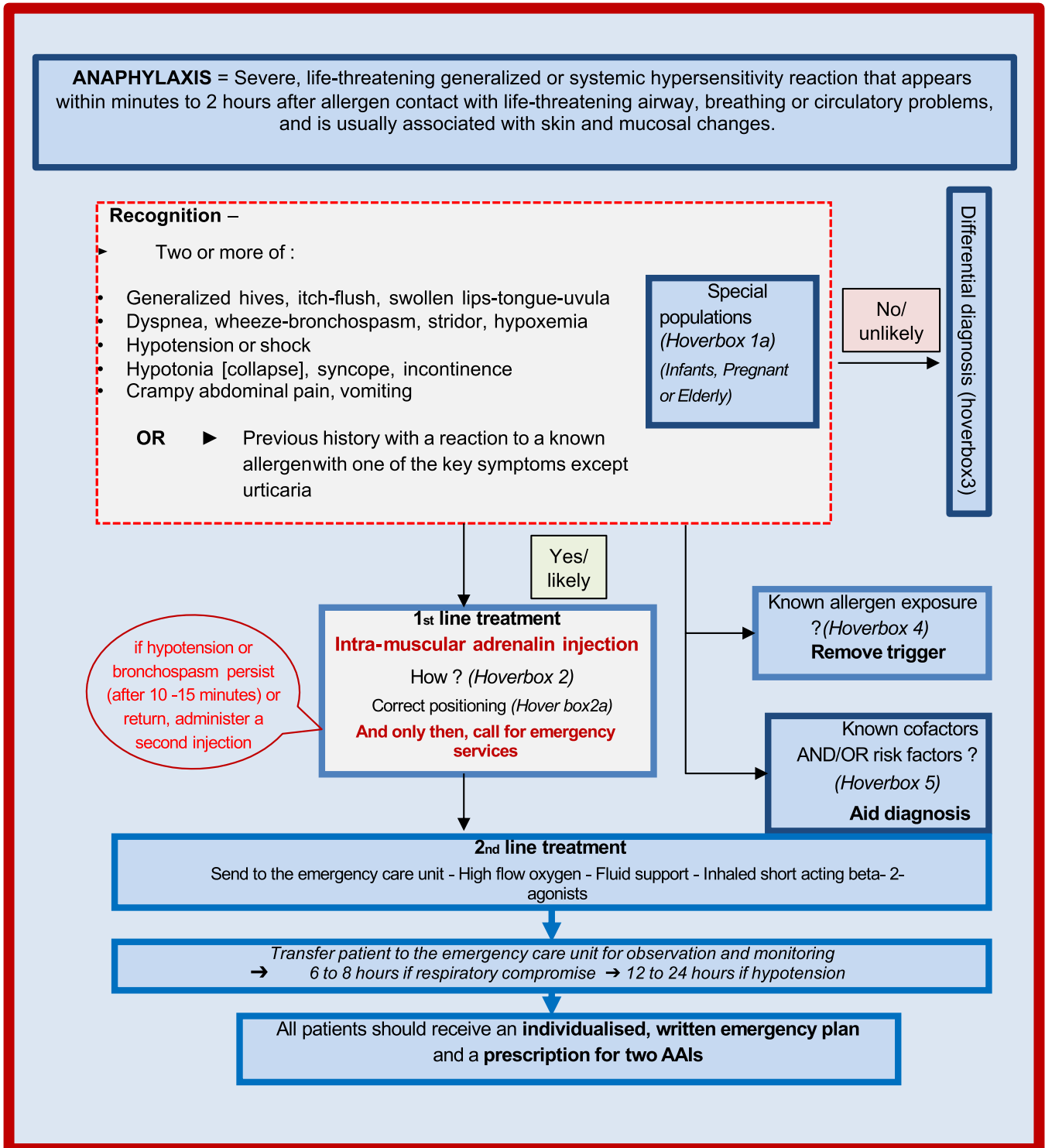


FIGURE 3 Patient potentially experiencing anaphylaxis

3.3 | Drug allergy

Drug allergies are a subset of all adverse drug reactions, as discussed above: three flow diagrams were created: 1) differentiation between

drug allergy/hypersensitivity and adverse drug reactions, (Figure 5) 2) addresses patients currently experiencing drug allergy/hypersensitivity reaction, (Figure 6) 3) addresses patients reporting a past history of possible drug allergy/hypersensitivity (Figure 7). More

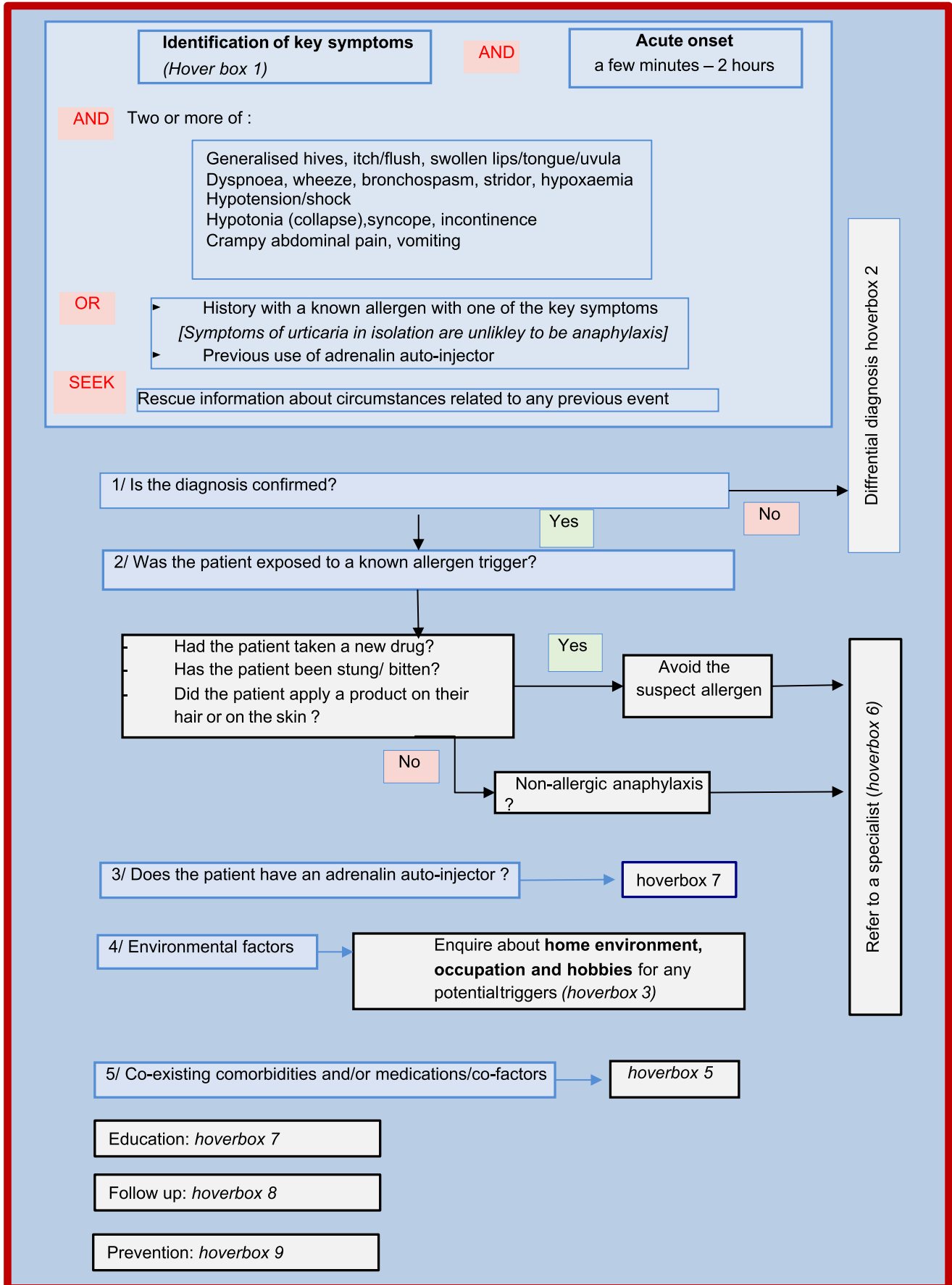


FIGURE 4 Patient having possibly experienced anaphylaxis

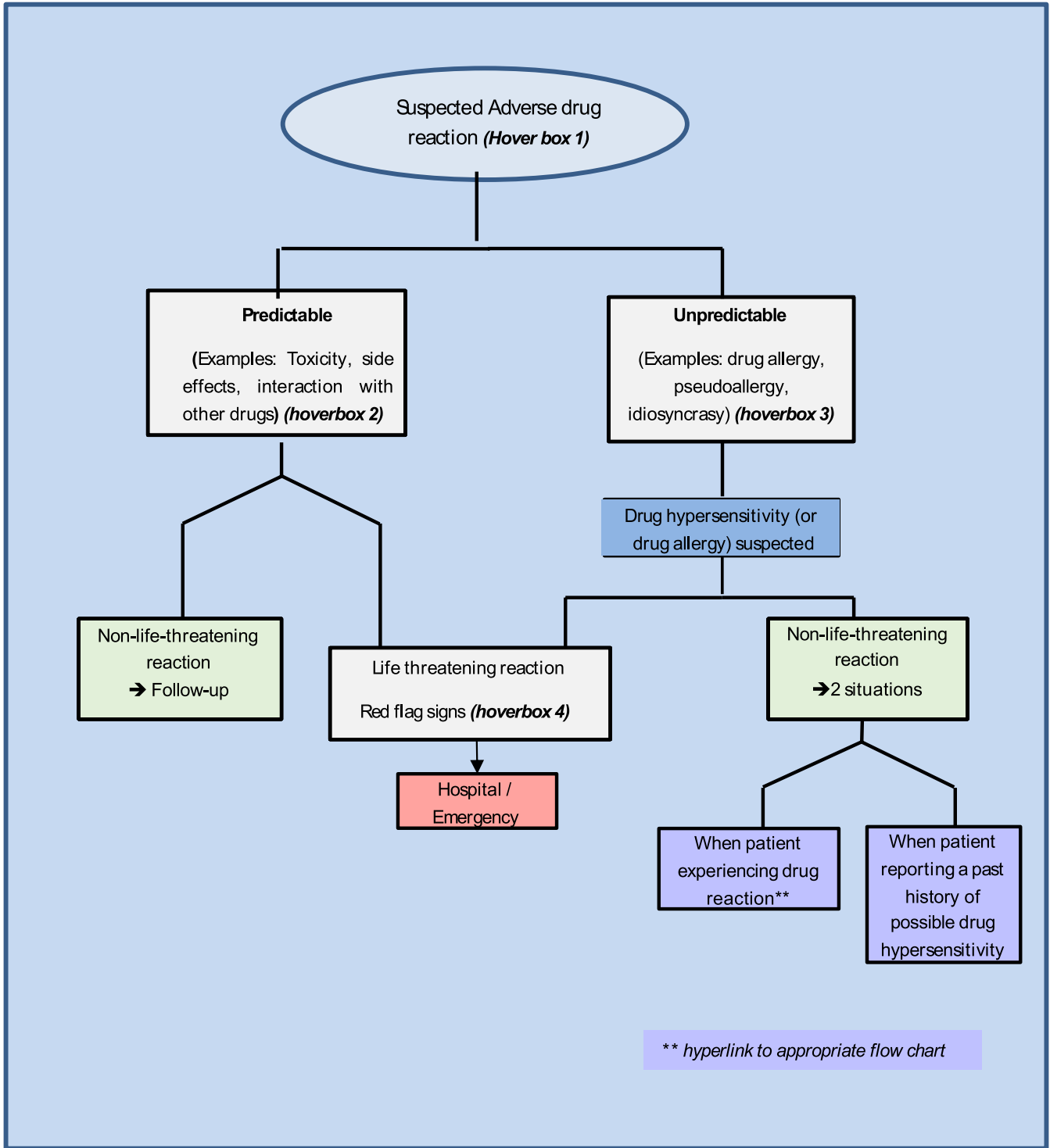


FIGURE 5 Differentiation between drug allergy/hypersensitivity and adverse drug reactions

information, linked to the 3 flow diagrams is indicated by the gray buttons, available in the Appendix S3 drug allergy annex.

3.4 | Food allergy

The food allergy logogram focusses on IgE-mediated food allergy and consists of two schematic flow diagrams aiming at: 1) differentiating

food allergy from other food related problems, (Figure 8) 2) determining the likelihood of food allergy (Figure 9). The first flow diagram inquires about exposure to typical foods and typical symptoms related to food allergy to differentiate "maybe food allergy" from "less likely food allergy." A list of typical foods and typical symptoms related to food allergy is available behind the corresponding gray buttons which is available in the Appendices S1–S5 annex. In addition, by inquiring about systemic reactions, "maybe food allergy" is differentiated from

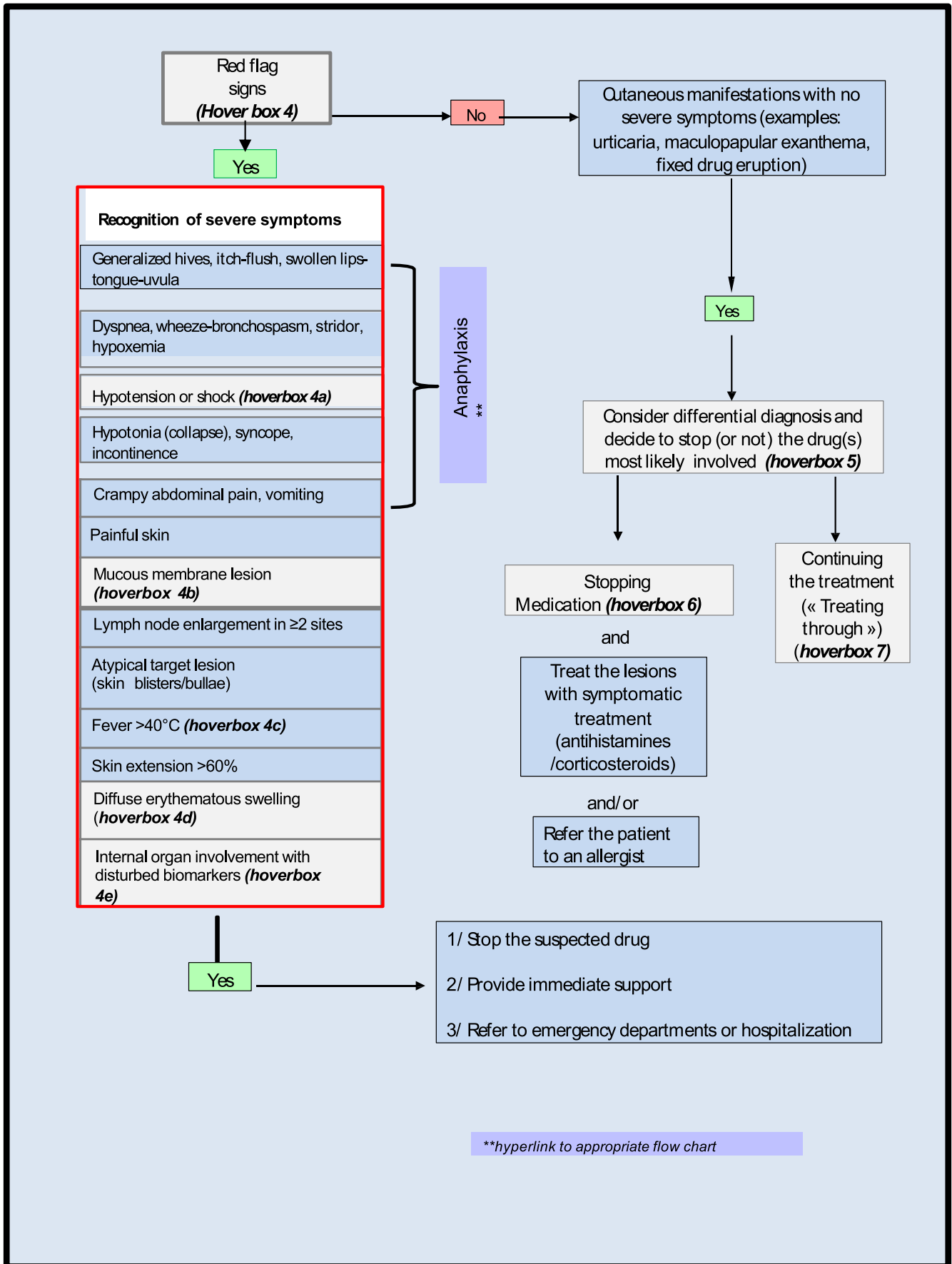


FIGURE 6 Patient experiencing a drug reaction

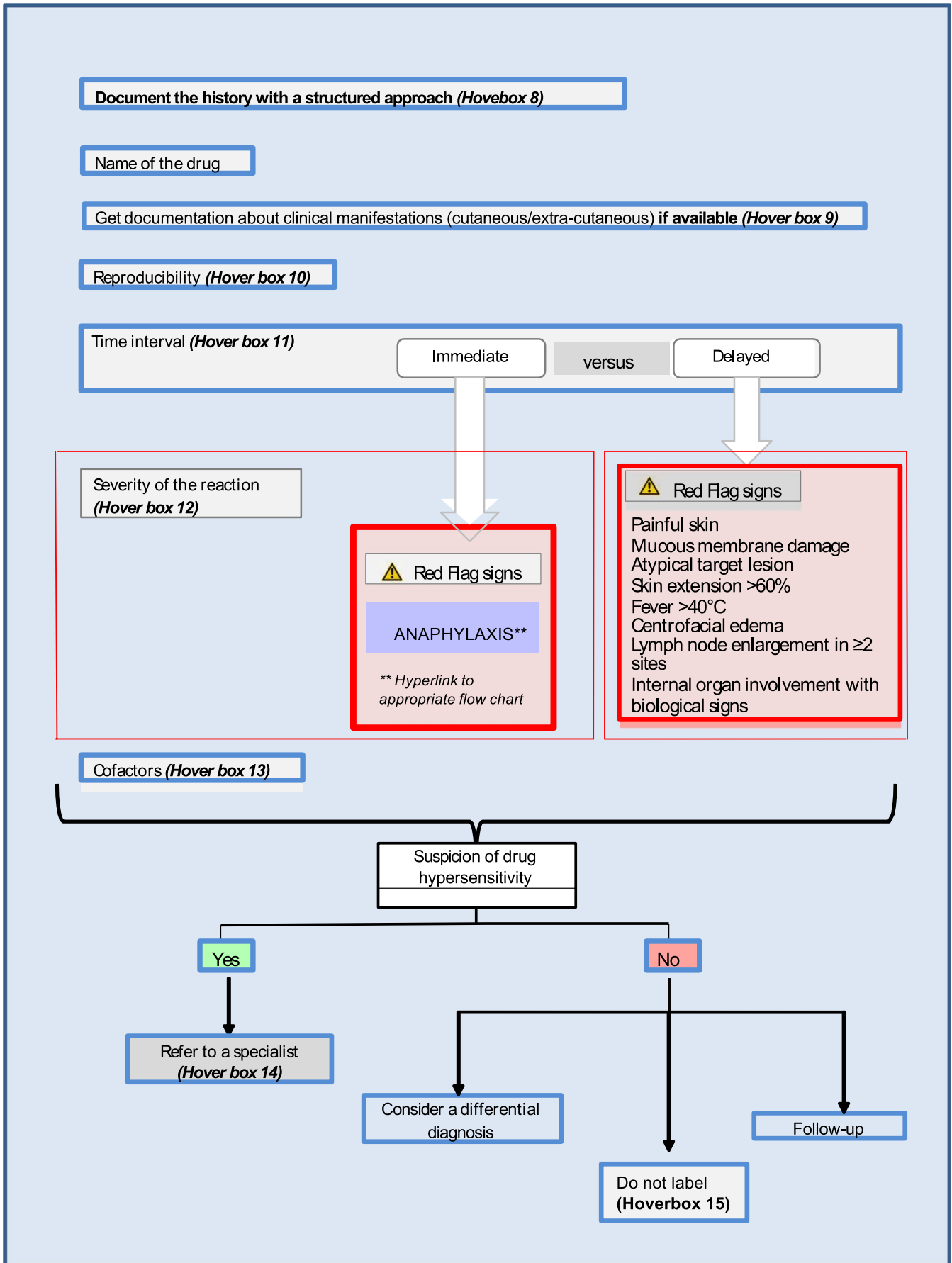


FIGURE 7 Patient reporting a past history of drug hypersensitivity

Differentiating food allergy from other food related problems

Click on the grey buttons for more information.

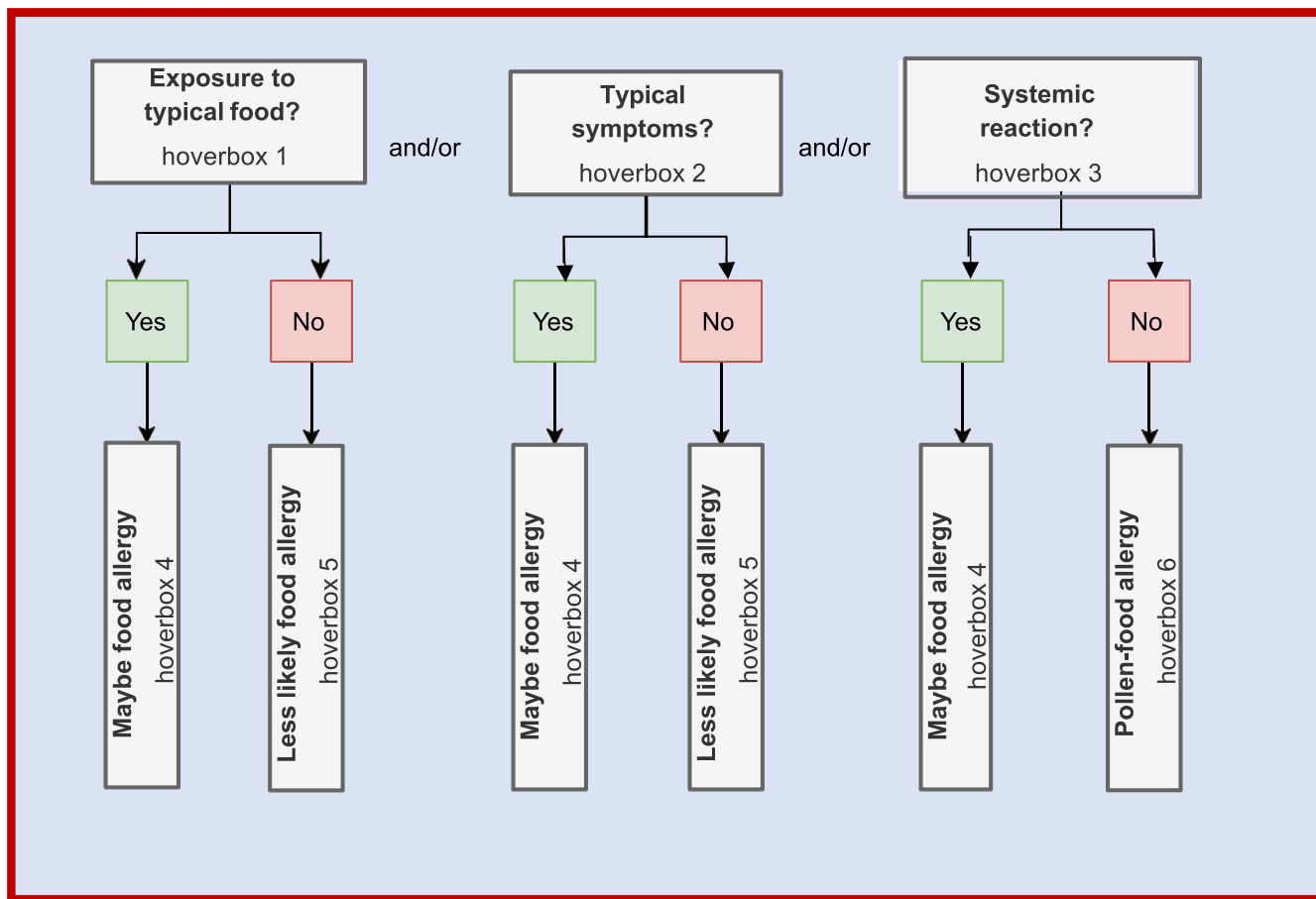


FIGURE 8 Differentiating food allergy from other food related problems

“pollen-food allergy,” as the latter usually causes mild symptoms and patients do not need to be referred to a specialist. In the second flow diagram, “maybe food allergy” is further divided into “high likelihood of food allergy” and “low likelihood of food allergy,” based on five factors: time between ingestion of food and start of reaction, eliciting amount, reproducibility, environment, and specific IgE for the suspected food. The greater the number of “green factors” present, the higher the likelihood of food allergy. The more “red factors” are present, the lower the likelihood of food allergy. Based on the likelihood of food allergy recommendations for referral and management are provided. Further information is provided in the hover-boxes in the Food allergy annex, Appendix S4.

3.5 | Urticaria

The urticaria logogram consists of 2 flow diagrams addressing acute urticaria (Figure 10) and chronic urticaria (Figure 11). The first flow-diagram, supports the recognition and treatment of

acute urticaria, excluding potential differential diagnosis or association with red flag signs, which would require immediate management (link to anaphylaxis). The second flow diagram support referral to a specialist. More details are provided in the gray buttons or hover-boxes in the Appendix S5 urticaria annex to support the previous information.

4 | DISCUSSION

In this study, we describe the development of 5 flow diagrams designed to assist primary care physicians (and other non-allergy specialists) manage patients with symptoms suggestive of Allergy/Hypersensitivity reactions. The strengths of this study are that for each logogram we followed the same methodology, having in mind not only the background knowledge on the topics including the guidelines previously published but also the necessity for logograms to be easily accessible, intuitive, and usable within the time restrictions of a high primary care workload. Although GPs are active and

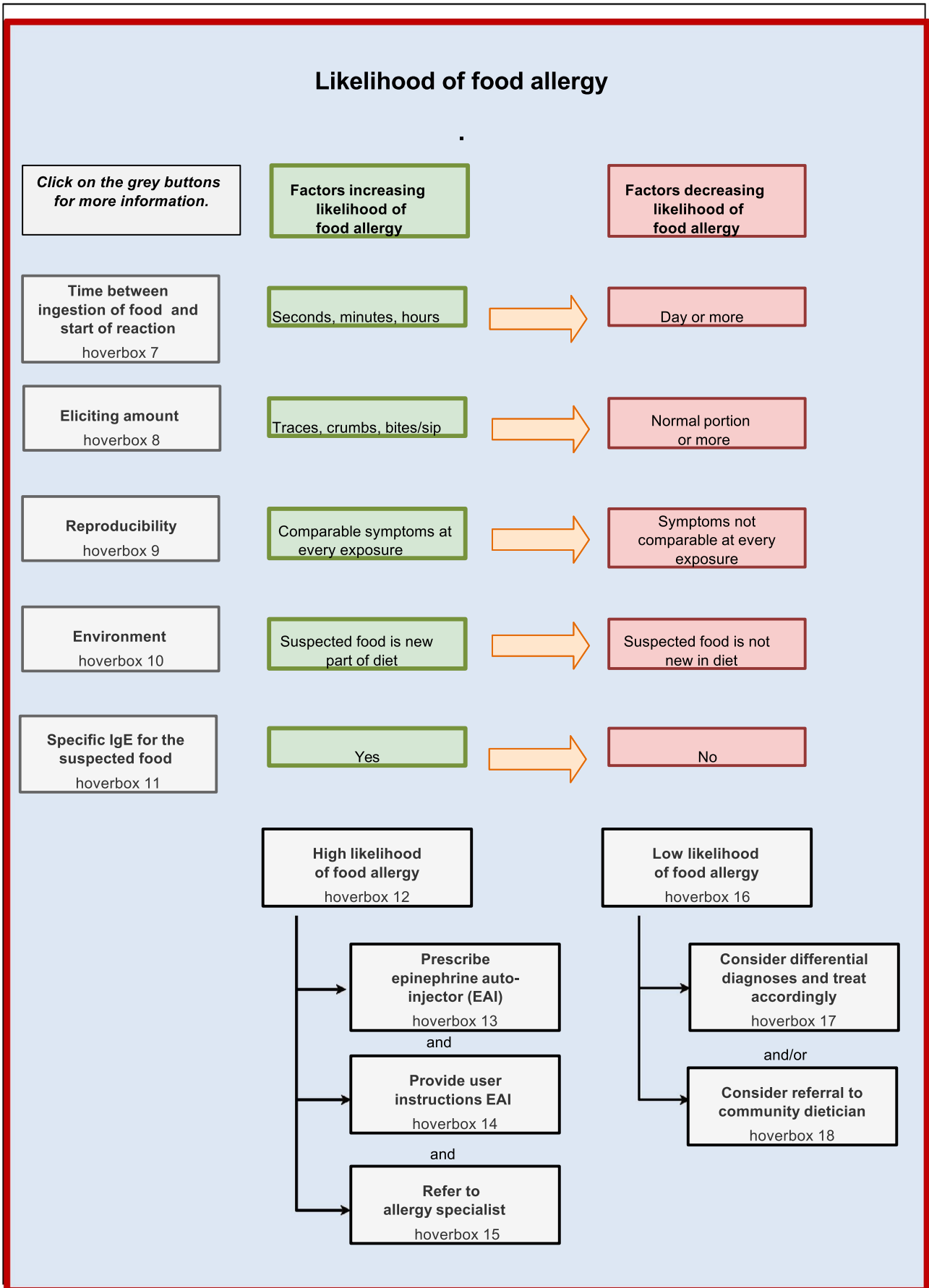


FIGURE 9 Likelihood of food allergy

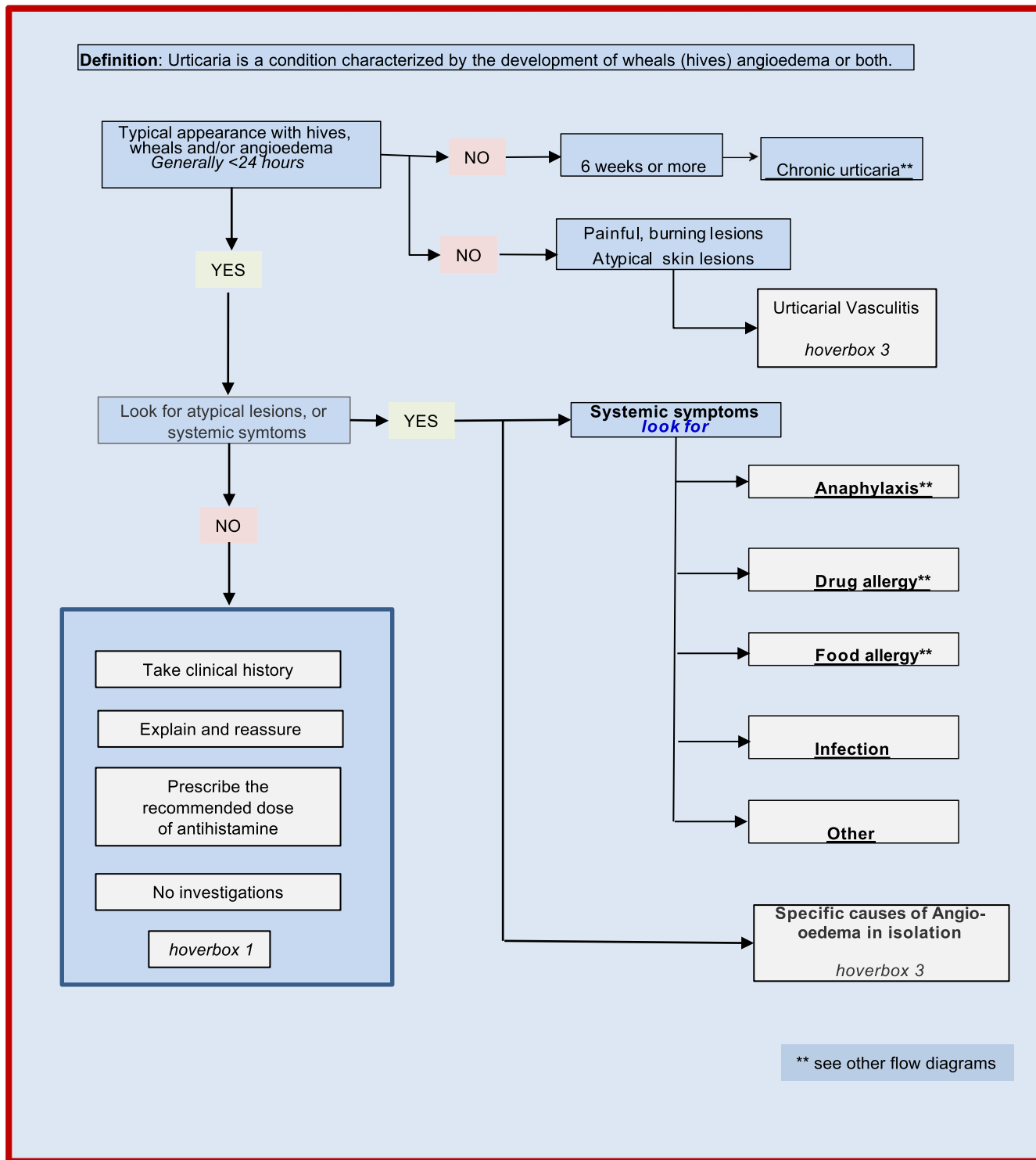


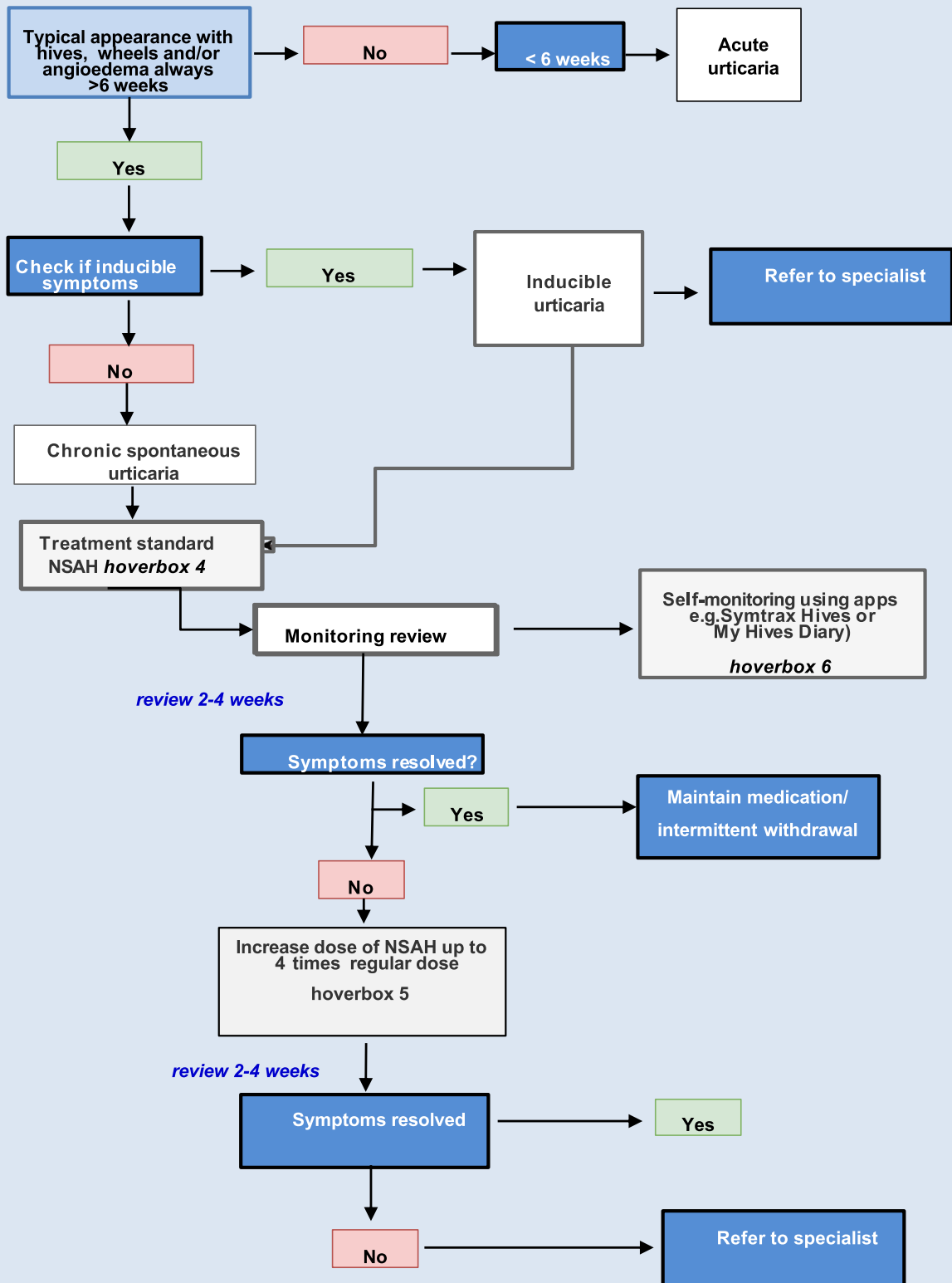
FIGURE 10 Diagnosis of acute urticaria

play a key role globally, in both high- and middle-/low-income countries, in the delivery of health care, their specific needs are not met by guidelines and to a great extent, written by specialists.

The logograms were developed by the task force members from different European countries. This collaboration provided rich international information from different healthcare systems enabling the logograms to be suitable for use in different European countries,

recognizing that clinical practice and availability of resources may differ. For example, referring a patient who experienced anaphylaxis to a specialist will soon be obligated by law in France, but in Sweden, GPs with a special interest in allergy are trained to perform the risk-assessment for anaphylaxis in primary care. Another example is the availability of epinephrine auto-injectors (EAI). In most European countries, EAIs are reimbursed by insurance companies. However,

Approx. 8% of those with acute urticaria develop chronic urticaria



NSAH: Non-sedating anti-histamine

FIGURE 11 Diagnosis of chronic urticaria

in Poland, EAls are not reimbursed, and in Romania, EAls are even not available. Although these logograms have been developed in Europe, in the future, these logograms could also be used in other parts of the world, taking into account the possible differences in healthcare systems and resources that may exist between countries. In addition to targeting improvements in diagnosis and management of allergic diseases in primary care, the tools also aim to reduce the burden on specialist allergy services by enabling GPs to diagnose and treat mild and moderate allergies, referring only severe and/or atypical cases to secondary care and therefore enabling GP to access essential decisions rapidly without unnecessary referrals to specialist allergy services.

This work is not without limitations: The lack of knowledge and confidence in managing allergy in primary care has previously been highlighted in other EAACI position statements with a commitment by EAACI to address these deficits. The authors acknowledge that the current work would benefit from prospective validation in primary care. The flow diagrams, in common with the guidelines from which they are derived, will not give 100% certainty concerning diagnosis but that nirvana has yet to be attained by any diagnostic process. While reducing uncertainty, some uncertainty still remains, a situation with which GPs deal with every day of their working lives.³⁶

Our diagnostic uncertainties should be shared with the patient as we work with them to manage their problems.³⁷

Our flow diagrams are designed to be developed to be digitized and used within a consultation. There is much information available through the gray buttons and "hover-boxes." Incorporating all of these in a written paper defeats the purpose of providing immediacy but would be available at a click of the button in the Appendices S1–S5 annexes.

Our flow diagrams are untested, although this is a common feature of guidelines: The very limited literature in this area to date suggests that such initiatives are successful.^{38–42} Such testing should not be confined to diagnostic confirmation but on the wider impacts on the patient⁴¹ and the healthcare system.⁴²

It is hoped that this work will be widely disseminated and in particular that it will be digitalized to provide instant access. Digitalization will permit easy access to the underlying rationale and supporting information as required. We have constructed the flow diagrams with Appendices S1–S5 annexes and hover-boxes with a view to accelerating this process.

5 | CONCLUSION

We have distilled a multiplicity of current guidelines, largely developed by allergy specialists, and adapted them to be clear, concise comprehensible and accessible to primary care and other non-allergy clinicians in a pragmatic flow-diagram format.

ACKNOWLEDGEMENTS

We thank EAACI for their support.

CONFLICT OF INTEREST

DR: Has received remuneration for educational initiatives or speaker fees from: Chiesi, Viatrix, GSK, AZ, Trudell, Regeneron, Novartis. PD: Has received remuneration for board and/or speaker bureau from Chiesi, IQVIA, Ménarini, Sanofi, Regeneron, AstraZeneca, Bausch & Lomb, ThermoFisher Scientific, Mylan, Novartis. KR: received remuneration for educational initiatives or speaker fees from: AstraZeneca, ALK, Boehringer Ingelheim, Chiesi, GSK, Mylan, Mundipharma and Novartis. JK: reports grants, personal fees and non-financial support from AstraZeneca, grants, personal fees and non-financial support from Boehringer Ingelheim, grants and personal fees from Chiesi, grants, personal fees and non-financial support from GSK, non-financial support from Mundi Pharma, grants and personal fees from Teva, personal fees from MSD, personal fees from COVIS Pharma, grants from Valneva outside the submitted work; and Janwillem Kocks holds <5% shares of Lothar Medtec GmbH and 72.5% of shares in the General Practitioners Research Institute. BFB: was employed by General Practitioners Research Institute (GPRI) at the time of the study. In the past 3 years (2019–2021), GPRI conducted investigator- and sponsor-initiated research funded by non-commercial organizations, academic institutes, and pharmaceutical companies (including AstraZeneca, Boehringer Ingelheim, Chiesi, GSK, Mundipharma, Novartis, and Teva). All other authors declare no COI.


CONSENT FOR PUBLICATION

All the authors consented for publication.

ORCID

Dermot Ryan  <https://orcid.org/0000-0002-4115-7376>

Bertine M. J. Flokstra - de Blok  <https://orcid.org/0000-0001-5356-764X>

Jantina Lucia van der Velde  <https://orcid.org/0000-0002-6681-9436>

Pascal Demoly  <https://orcid.org/0000-0001-7827-7964>

Luciana Kase Tanno  <https://orcid.org/0000-0003-3236-1225>

REFERENCES

- Gupta R, Sheikh A, Strachan DP, Anderson HR. Burden of allergic disease in the UK: secondary analyses of national databases. *Clin Exp Allergy J Br Soc Allergy Clin Immunol*. 2004;34(4):520–526.
- Shehata Y, Ross M, Sheikh A. Undergraduate allergy teaching in a UK medical school: mapping and assessment of an undergraduate curriculum. *Prim Care Respir J J Gen Pract Airw Group*. 2006;15(3):173–178.
- Ryan D, Angier E, Gomez M, et al. Results of an allergy educational needs questionnaire for primary care. *Allergy*. 2017;72(7):1123–1128.
- Potter PC, Warner JO, Pawankar R, et al. Recommendations for competency in allergy training for undergraduates qualifying as medical practitioners: a position paper of the world allergy organization. *World Allergy Organ J*. 2009;2(8):150–154.
- Michaelis LJ, Skypala LJ, Gardner J, Sheikh A, Fox AT, Holloway JA. Upskilling healthcare professionals to manage clinical allergy. *Clin Exp Allergy J Br Soc Allergy Clin Immunol*. 2019;49(12):1534–1540.
- Curriculum-topic-guides-300819.pdf [Internet]. <https://www.rcgp.org.uk/-/media/Files/GP-training-and-exams/Curriculum>

- 2019/Curriculum-Topic-Guides-300819.ashx?la=en. Accessed November 7, 2020.
7. Hampton JR, Harrison MJ, Mitchell JR, Prichard JS, Seymour C. Relative contributions of history-taking, physical examination, and laboratory investigation to diagnosis and management of medical outpatients. *Br Med J*. 1975;2(5969):486-489.
 8. Jutel M, Papadopoulos NG, Gronlund H, et al. Recommendations for the allergy management in the primary care. *Allergy*. 2014;69(6):708-718.
 9. Donner-Banzhoff N, Seidel J, Sikeler AM, et al. The phenomenology of the diagnostic process: a primary care-based survey. *Med Decis Mak Int J Soc Med Decis Mak*. 2017;37(1):27-34.
 10. Rosborough K, Keller C, Jung J, et al. A retrospective audit of chronic urticaria in the Irish paediatric population. *Arch Dis Child*. 2019;104(Suppl 3):A213.
 11. Virchow JC. Diagnostic challenges of adult asthma. *Curr Opin Pulm Med*. 2016;22(1):38-45.
 12. Muraro A, Roberts G, Worm M, et al. Anaphylaxis: guidelines from the European academy of allergy and clinical immunology. *Allergy*. 2014;69(8):1026-1045.
 13. Fernando B, Morrison Z, Kalra D, Cresswell K, Sheikh A. Approaches to recording drug allergies in electronic health records: qualitative study. *PLoS One*. 2014;9(4):e93047.
 14. Foreman C, Smith WB, Caughey GE, Shakib S. Categorization of adverse drug reactions in electronic health records. *Pharmacol Res Perspect*. 2020;8(2):e00550.
 15. Wallengren J. Identification of core competencies for primary care of allergy patients using a modified Delphi technique. *BMC Med Educ*. 2011;11:12.
 16. Bousquet J, Schönemann HJ, Togias A, et al. Next-generation allergic rhinitis and its impact on asthma (ARIA) guidelines for allergic rhinitis based on grading of recommendations assessment, development and evaluation (GRADE) and real-world evidence. *J Allergy Clin Immunol*. 2020;145(1):70-80.e3.
 17. Borish L, Culp JA. Asthma: a syndrome composed of heterogeneous diseases. *Ann Allergy Asthma Immunol*. 2008;101(1):1-9.
 18. Scottish Intercollegiate Guideline Network (SIGN) / British Thoracic Society (BTS). British guideline on the management of asthma 2019. www.sign.ac.uk/sign-158-british-guideline-on-the-management-of-asthma.html. Accessed 10 May 2020.
 19. GINA-2019-main-report-June-2019-wms.pdf [Internet]. <https://ginasthma.org/wp-content/uploads/2019/06/GINA-2019-main-report-June-2019-wms.pdf>. Accessed 10 May 2020.
 20. de Silva D, Roberts G, Worm M, Muraro A, EAACI Food Allergy and Anaphylaxis Guidelines Group. EAACI anaphylaxis guidelines: systematic review protocol. *Clin Transl Allergy*. 2020;10:14.
 21. Sheikh A, Sheikh Z, Roberts G, Muraro A, Dhimi S, Sheikh A. National clinical practice guidelines for food allergy and anaphylaxis: an international assessment. *Clin Transl Allergy*. 2017;7:23.
 22. Nwaru BI, Hickstein L, Panesar SS, et al. The epidemiology of food allergy in Europe: a systematic review and meta-analysis. *Allergy*. 2014;69(1):62-75.
 23. Lyons SA, Burney PGJ, Ballmer-Weber BK, et al. Food allergy in adults: substantial variation in prevalence and causative foods across Europe. *J Allergy Clin Immunol Pract*. 2019;7(6):1920-1928.e11.
 24. Lyons SA, Clausen M, Knulst AC, et al. Prevalence of food sensitization and food allergy in children across Europe. *J Allergy Clin Immunol Pract*. 2020;8(8):2736-2746.e9.
 25. Gupta RS, Springston EE, Kim JS, et al. Food allergy knowledge, attitudes, and beliefs of primary care physicians. *Pediatrics*. 2010;125(1):126-132.
 26. Muraro A, Werfel T, Hoffmann-Sommergruber K, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy*. 2014;69(8):1008-1025.
 27. Sacco KA, Bates A, Brigham TJ, Imam JS, Burton MC. Clinical outcomes following inpatient penicillin allergy testing: a systematic review and meta-analysis. *Allergy*. 2017;72(9):1288-1296.
 28. Demoly P, Adkinson NF, Brockow K, et al. International consensus on drug allergy. *Allergy*. 2014;69(4):420-437.
 29. Doña I, Caubet JC, Brockow K, et al. An EAACI task force report: recognising the potential of the primary care physician in the diagnosis and management of drug hypersensitivity. *Clin Transl Allergy*. 2018;8:16.
 30. Thomsen SF, Pritzler EC, Anderson CD, et al. Chronic urticaria in the real-life clinical practice setting in Sweden, Norway and Denmark: baseline results from the non-interventional multicentre AWARE study. *J Eur Acad Dermatol Venereol JEADV*. 2017;31(6):1048-1055.
 31. Guillet G, Bécherel P-A, Pralong P, et al. The burden of chronic urticaria: French baseline data from the international real-life AWARE study. *Eur J Dermatol EJD*. 2019;29(1):49-54.
 32. Savic S, Leeman L, El-Shanawany T, et al. Chronic urticaria in the real-life clinical practice setting in the UK: results from the noninterventional multicentre AWARE study. *Clin Exp Dermatol*. 2020;45(8):1003-1010.
 33. Maurer M, Raap U, Staubach P, et al. Antihistamine-resistant chronic spontaneous urticaria: 1-year data from the AWARE study. *Clin Exp Allergy J Br Soc Allergy Clin Immunol*. 2019;49(5):655-662.
 34. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. *Allergy*. 2018;73(7):1393-1414.
 35. Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy*. 2021;77(3):734-766.
 36. Alam R, Cheraghi-Sohi S, Panagioti M, Esmail A, Campbell S, Panagopoulou E. Managing diagnostic uncertainty in primary care: a systematic critical review. *BMC Fam Pract*. 2017;18(1):79.
 37. Simpkin AL, Schwartzstein RM. Tolerating uncertainty - the next medical revolution? *N Engl J Med*. 2016;375(18):1713-1715.
 38. Flokstra-de Blok BM, van der Molen T, Christoffers WA, et al. Development of an allergy management support system in primary care. *J Asthma Allergy*. 2017;10:57-65.
 39. Flokstra-de Blok BMJ, Brakel TM, Wubs M, et al. The feasibility of an allergy management support system (AMSS) for IgE-mediated allergy in primary care. *Clin Transl Allergy*. 2018;8:18.
 40. Levy ML, Walker S, Woods A, Sheikh A. Service evaluation of a UK primary care-based allergy clinic: quality improvement report. *Prim Care Respir J J Gen Pract Airw Group*. 2009;18(4):313-319.
 41. Smith HE, Wade J, Frew AJ. What proportion of adult allergy referrals to secondary care could be dealt with in primary care by a GP with special interest? *Clin Transl Allergy*. 2015;6:3.
 42. Jones RB, Hewson P, Kaminski ER. Referrals to a regional allergy clinic - an eleven year audit. *BMC Public Health*. 2010;10:790.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Ryan D, Flokstra - de Blok BMJ, Clark E, et al. Allergic and hypersensitivity conditions in non-specialist care: Flow diagrams to support clinical practice. *Allergy*. 2022;00:1-16. doi:[10.1111/all.15273](https://doi.org/10.1111/all.15273)