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REFERENCES

1. Buhl R, Humbert M, Bjermer L, et al. Severe eosinophilic asthma: a roadmap to consensus. *Eur Respir J*. 2017;49:1700634.
2. Chupp GL, Bradford ES, Albers FC, et al. Efficacy of mepolizumab add-on therapy on health-related quality of life and markers of asthma control in severe eosinophilic asthma (MUSCA): a randomised, double-blind, placebo-controlled, parallel-group, multicentre, phase 3b trial. *Lancet Respir Med*. 2017;5:390-400.
3. Zimmermann SC, Tonga KO, Thamrin C. Dismantling airway disease with the use of new pulmonary function indices. *Eur Respir Rev*. 2019;28(151):180122.
4. Cavalcanti JV, Lopes AJ, Jansen JM, Melo PL. Detection of changes in respiratory mechanics due to increasing degrees of airway obstruction in asthma by the forced oscillation technique. *Respir Med*. 2006;100:2207-2219.
5. Shirai T, Mori K, Mikamo M, et al. Respiratory mechanics and peripheral airway inflammation and dysfunction in asthma. *Clin Exp Allergy*. 2013;43:521-526.
6. Kelly VJ, Sands SA, Harris RS, et al. Respiratory system reactance is an independent determinant of asthma control. *J Appl Physiol*. 1985;2013(115):1360-1369.
7. Matsuno O, Komori C, Hang Y, Matsumoto T, Minamoto S. Effectiveness of omalizumab in a patient with severe asthma, low serum IgE level, and lack of sensitized allergens induced by oral steroid therapy: the usefulness of impulse oscillation for assessment of omalizumab therapy. *J Asthma*. 2012;49:839-842.
8. Oostveen E, MacLeod D, Lorino H, et al. The forced oscillation technique in clinical practice: methodology, recommendations and future developments. *Eur Respir J*. 2003;22(6):1026-1041.
9. Farah CS, Badal T, Reed N, et al. Mepolizumab improves small airway function in severe eosinophilic asthma. *Respir Med*. 2019;148:49-53.
10. Chapman KR, Albers FC, Chipps B, et al. The clinical benefit of mepolizumab replacing omalizumab in uncontrolled severe eosinophilic asthma. *Allergy*. 2019;74(9):1716-1726.
11. Gunsoy NB, Cockle SM, Yancey SW, et al. Evaluation of potential continuation rules for mepolizumab treatment of severe eosinophilic asthma. *J Allergy Clin Immunol Pract*. 2018;6(3):874-882.

SUPPORTING INFORMATION

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DOI: 10.1111/all.13951

Diagnostic testing for penicillin allergy: A survey of practices and cost perceptions

To the Editor,

Having a penicillin allergy label associates with worse healthcare outcomes and increased treatment costs.[1-3] However, whether penicillin allergy testing is cost-saving remains unclear, particularly as there is heterogeneity in the practice of such testing.[4]

Therefore, we developed an online questionnaire to assess the practice and cost perceptions of diagnostic tests used in penicillin allergy evaluation. Regarding cost perceptions, we asked respondents to estimate material, personnel, and facilities costs of performing each assessed diagnostic test. We also asked for estimates on the total paid amounts for each performed test (ie, perceived reimbursements by the State, insurance companies, or patients). Respondents provided a level of confidence (low, medium, or high) for each reported cost estimate. This questionnaire targeted drug allergy experts in Europe—we contacted European Network of Drug Allergy members by email, as well as first, last, and/or corresponding authors of publications in the field of drug allergy (our search was limited to publications of the last 10 years). Survey respondents were re-contacted to confirm outlier values.

To provide a broader comparison, we also contacted North American authors in the field of drug allergy, sending the same email to the Adverse Reactions to Drugs, Biologicals and Latex Committee of the AAAAI. In addition, we also (a) performed a comprehensive literature search in MEDLINE, Scopus, and Web of Science for publications assessing the costs of penicillin allergy tests, and (b) performed two cost assessments of material and personnel costs for skin tests and drug provocation tests (DPT)—one in a Portuguese private Allergy Unit and another in a Portuguese public hospital Unit.

All reported costs were converted into Euro (€) using the three-month average of June-August 2018. We performed descriptive analyses of data by standard methods. In addition, we identified factors associated with higher or lower reported cost estimates for each test by performing linear regressions with the log-transformation of summed reported costs as the dependent variable; multiple linear regression models were selected based on their AIC. Variables with missing data were excluded from regression models if missing values represented >5% of all responses; in the remaining cases, missing data were replaced by values determined by multivariate imputation by chained equations methods. We developed a Shiny-based online app to allow for interactive exploration of our results (Appendix S1 accessible at http://penallergy.med.up.pt).

TABLE 1 Description of the practice of penicillin allergy diagnosis tests reported by European and North American respondents (n = 51)

	Skin prick test	Intradermal test	Patch test	Specific IgE	Drug provocation test
Experience in performing the test/procedure—n (%)	48 (94.1)	47 (92.2)	31 (60.8)	34 (66.7)	48 (94.1)
Europe	42 (95.5)	41 (93.2)	29 (65.9)	33 (75.0)	41 (93.2)
North America	6 (85.7)	6 (85.7)	2 (28.6)	1 (14.3)	7 (100)
Percentage of patients with penicillin allergy label receiving the test/procedure—median (IQR)	75 (75)	80 (65)	15 (33)	30 (81)	80 (45)
Europe	85 (65)	80 (60)	20 (35)	30 (85)	80 (45)
North America	20 (58)	30 (53)	5 (0)	70[a]	98 (8)
Number of tests/procedures performed per patient—median (IQR)	5 (3)	5 (6)	3 (2)	3 (2)	3 (2)[b]
Europe	5 (3)	5 (6)	4 (3)	3 (2)	4 (2)[b]
North America	5 (1)	4 (5)	3 (0)	2[a]	2 (0.5)[b]
Number of drugs/determinants tested—median (IQR)	4 (2)	4 (3)	3 (2)	3 (2)	-
Europe	4 (3)	4 (2)	3 (2)	3 (1)	-
North America	4 (2)	4 (4)	5 (1)	2[a]	-
Aminopenicillin testing—n (%)	46 (95.8)	43 (91.5)	30 (88.2)	28 (90.3)	-
Europe	41 (97.6)	39 (95.1)	29 (87.9)	27 (93.1)	-
North America	5 (83.3)	4 (66.7)	1 (100)	1 (50.0)	-
Cephalosporin testing—n (%)	20 (41.7)	21 (44.7)	9 (26.5)	9 (26.5)	-
Europe	19 (45.2)	19 (46.3)	9 (27.3)	9 (27.3)	-
North America	1 (16.7)	2 (33.3)	0	0	-
Minutes required to perform each test/procedure—median (IQR)	45 (35)	45 (75)	40 (30)	180 (180)	300 (240)
Europe	45 (30)	60 (90)	40 (30)	180 (180)	300 (180)
North America	20 (30)	20 (34)	45 (15)	600[a]	120 (60)
Setting where the test/procedure is performed—n (%)					
Outpatient	31 (64.6)	27 (57.4)	24 (77.4)/24 (77.4)[c]	28 (82.4)[d]	20 (41.7)
Europe	25 (59.5)	21 (51.2)	22 (75.9)/22 (75.9)[c]	27 (81.8)[d]	13 (31.7)
North America	6 (100)	6 (100)	2 (100)/2 (100)[c]	1 (100)[d]	7 (100)
Inpatient	2 (4.2)	3 (6.4)	1 (3.2)/ 1 (3.2)[c]	1 (2.9)[d]	12 (25.0)
Europe	2 (4.8)	3 (7.3)	1 (3.5)/1 (3.5)[c]	1 (3.0)[d]	10 (24.4)
North America	0	0	0	0	2 (28.6)
Day ward	16 (33.3)	19 (40.4)	7 (22.6)/ 8 (25.8) [c]	1 (2.9) [d]	23 (47.9)
Europe	16 (38.1)	19 (46.3)	7 (24.1)/ 8 (27.6) [c]	1 (3.0) [d]	23 (56.1)
North America	0	0	0	0	0
Laboratory	0	0	1 (3.2)/1 (3.2)[c]	8 (23.5)[d]	0
Europe	0	0	1 (3.5)/ 1 (3.5)[c]	8 (24.2)[d]	0
North America	0	0	0	0	0
Number of patients assessed in the same room—median (IQR)	3 (4)	3 (4)	1 (2)/ 1 (2)[c]	-	3 (3)
Europe	4 (3)	3 (3)	2 (2)/ 1 (2)[c]	-	3 (4)
North America	1 (0.5)	1 (0.5)	1 (0)/ 1 (0)[c]	-	2 (2)
Number of healthcare professionals required to perform each test/procedure—median (IQR)	2 (1)	2 (1)	2 (1)/ 2 (1)[c]	2 (1)/ 2 (1)[e]	3 (1)
Europe	2 (1)	2 (1)	2 (1)/ 2 (1)[c]	2 (1)/ 2 (0)[e]	3 (2)
North America	2 (2)	2 (2)	3 (1)/ 2 (1)[c]	1/ 1[ae]	2 (1)

Abbreviations: IQR, interquartile range; max, maximum; min, minimum.

[a]No IQR and range are presented, as there is only one sIgE estimate from North America.

[b]These values correspond to the average number of testing doses given in a drug provocation test in the context of penicillin allergy (the median percentages for the frequency of patients requiring one, two or more than two drug provocation tests are, respectively, of 70% [IQR: 60%], 18% [IQR: 22%], and 10% [IQR: 19%]).

[c]Values for patch test preparation and application/Values for patch test results' reading.

[d]Values regarding the setting where blood sampling is performed.

[e]Values for blood sampling/Values for specific IgE quantification.

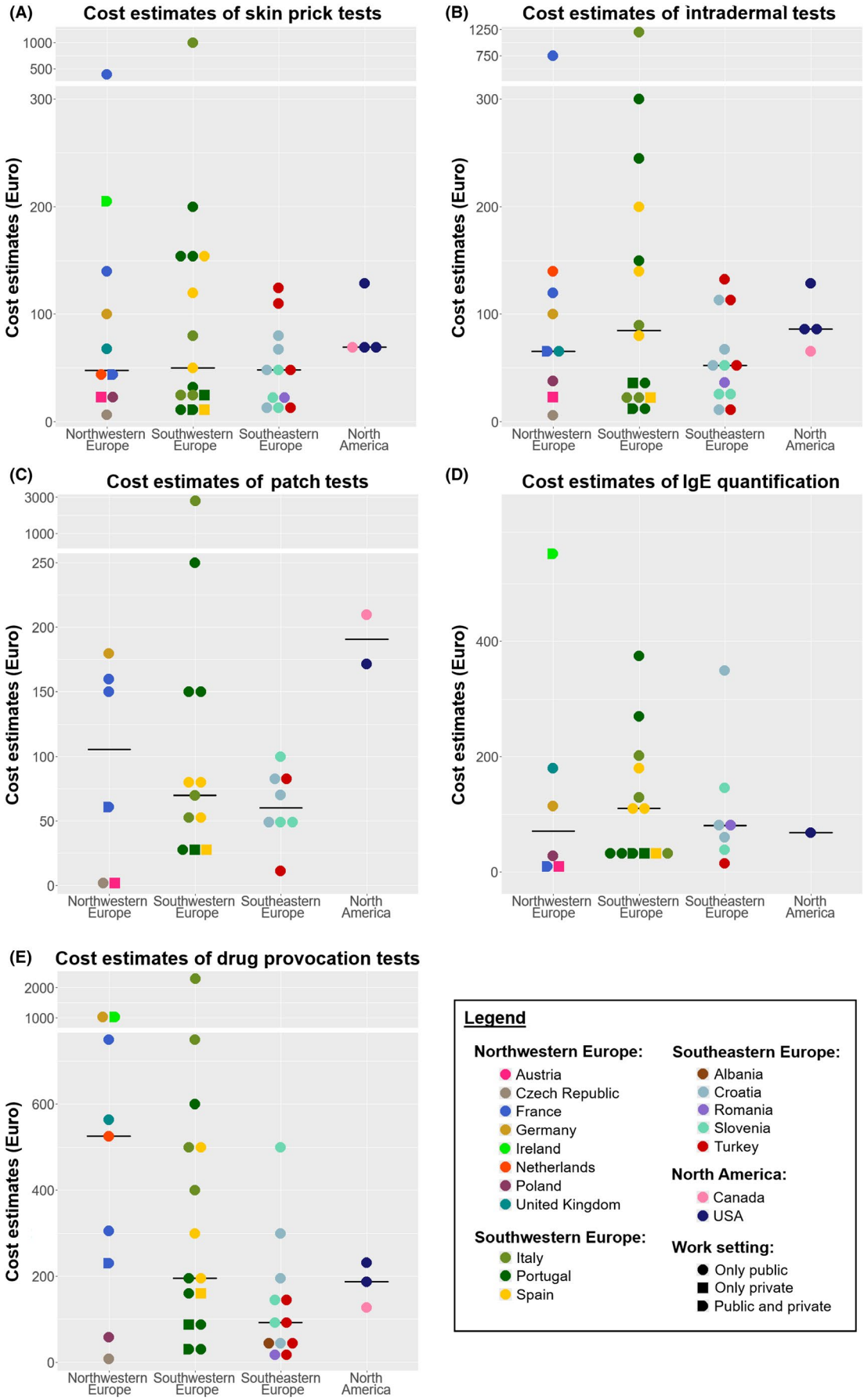

FIGURE 1 Respondent-reported cost estimates (in 2018 Euro) of skin prick tests (A), intradermal tests (B), patch tests (C), IgE quantification (D), and drug provocation tests (E) in patients with suspected penicillin allergy, by respondents' region, country, and work setting

We obtained 51 responses to our questionnaire from 19 countries (out of 389 individuals from 34 countries to whom the questionnaire was directly sent, corresponding to a response rate of 13.1%). Respondents were predominantly female (n = 33) and had a mean age of 46.4 years (Table S1). Most respondents were practicing allergists (n = 44) and worked in the public sector (n = 45). Forty-four responses were from Europe, and 7 were from North America. In all, 38 emails were sent to confirm outlier values, with 27 (71%) responses received.

More than 90% of respondents had experience in performing skin prick tests (SPT), DPT, and intradermal tests for penicillin allergy evaluations (Table 1). In patients with suspected penicillin allergy, intradermal tests and DPT were the most frequently performed tests (median frequency = 80%), followed by SPT (75%), specific IgE (sIgE) (30%), patch tests (15%), and basophil activation test (BAT) and lymphocyte transformation test (LTT) (10%) (Appendix S1). The median required time was of 45 minutes to perform SPT and intradermal tests; for DPT, the median time was 5 hours. More than half respondents reported performing SPT (65%), intradermal tests (57%), and patch tests (77%) in the outpatient setting; DPT were most commonly reported to be performed in the day ward (48%) (Appendix S1). A median of 2 healthcare professionals was necessary to perform all tests except DPT (with a median of 3 professionals).

Regarding cost estimates, the highest median costs for assessing a patient were reported for DPT (€190.0), followed by BAT/LTT (€90.0 for both), specific IgE quantification (€81.0), patch tests (€75.1), intradermal tests (€66.6), and SPT (€50.0) (Figure 1; Table S2; Appendix S1). Most reported cost estimates were either of medium or of low confidence (Table S2). Using multiple linear regression models, we observed that higher cost estimates were most frequently associated with the number of involved healthcare professionals (particularly for SPT and intradermal tests) and working in Northwestern Europe (for intradermal tests and DPT) (Appendix S1).

Estimates of the median paid amount for each test were highest for DPT (€112.7) and lowest for intradermal tests (€30.0), SPT (€28.8), and sIgE (€27.0) (Table S2; Appendix S1). For all assessed tests/procedures, the reimbursement to cost ratio (perceived amount paid dividing by the overall reported cost estimates) was lower than 100%, ranging from 44.4% for patch tests to 73.8% for DPT; these percentages were higher in Europe than in North America for SPT, intradermal tests, and DPT.

In our comprehensive literature review, we identified six publications assessing the costs of penicillin allergy diagnostic tests (namely skin tests and DPT),[3,5-9] five of which performed in North America[3,5-8] and one in Europe[9] (Table S3)—our median reported material and personnel cost estimates were generally consistent with the values presented in those studies, while reported facilities costs may have been overestimated when compared to the value obtained in the only publication formally calculating space costs (€3).[8] Our cost assessment in a Portuguese private Allergy Unit identified a total cost per patient for skin tests of €41.7 (€14.3 for material costs + €27.4 for personnel costs) and for DPT of €78.6 (€10.1 for material costs + €68.5 for personnel costs) (Table S4). In the public sector, our cost assessment identified skin tests costs per patient of €95.0 (€73.5 for material costs + €21.5 for personnel costs) and DPT costs of €77.0 (€11.0 for material costs + €66.0 for personnel costs).

The estimates reported in this study provide unique contextual information on the need for context-based cost assessments and on when penicillin allergy testing might be cost-saving. This is particularly relevant as previous studies have shown that patients with a penicillin allergy label may have higher treatment costs due to the use of more expensive antibiotics and increased risk of hospital-acquired infections (resulting in longer hospital stays), readmissions, and more ambulatory visits[1-3]—therefore, by prompting an allergy delabeling in most patients, generalized testing could possibly be cost-saving.

This study has some important limitations regarding its sample size and low response rate. While the questionnaire length might have dissuaded some experts, we tried to minimize response fatigue by allowing skip patterns. Another potential limitation concerns the possibility of literacy-related sample biases, although we re-contacted respondents to clarify outliers/potential mistakes. Potential strengths include results novelty, the combined use of different methodologies, and the possibility of results exploration using an interactive app.

In conclusion, this study suggests that there is wide diversity in penicillin allergy testing practice and reported cost estimates, with median values ranging from €50.0 for SPT to €190.0 for DPT. Of note, respondents had not provided actual costs, but rather estimates based on their perceptions, and largely with low-medium confidence. The fact that cost estimates were largely higher than reported paid amounts merits further attention, as it might negatively influence penicillin allergy diagnostic practice, which may result in worse clinical outcomes and in an increased healthcare burden.

ACKNOWLEDGMENTS

This work was supported by the Portuguese Ministry for Science, Technology, and Higher Education (Ministério da Ciência, Tecnologia e Ensino Superior), through the Portuguese Foundation for Science and Technology (Fundação para a Ciência e Tecnologia) [grant number PD/BD/129836/2017]. The funding source had no involvement in study design, data collection, analysis and interpretation, report writing, or in the decision to submit the article for publication.

CONFLICTS OF INTEREST

Eric Macy has received research grants from ALK (the sellers of Pre-Pen in the United States) and consulted for and is serving on a data and safety monitoring board for Audentes. No other author has conflicts of interest to declare within the scope of this study.

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REFERENCES

1. Su T, Broekhuizen B, Verheij T, Rockmann H. The impact of penicillin allergy labels on antibiotic and health care use in primary care: a retrospective cohort study. *Clin Transl Allergy*. 2017;7(1):7-18.
2. Sousa-Pinto B, Cardoso-Fernandes A, Araújo L, Fonseca JA, Freitas A, Delgado L. Clinical and economic burden of hospitalizations with registration of penicillin allergy. *Ann Allergy Asthma Immunol*. 2018;120(2):190-194.
3. Macy E, Contreras R. Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: a cohort study. *J Allergy Clin Immunol*. 2014;133(3):790-796.

4. Torres MJ, Celik GE, Whitaker P, et al. A EAACI drug allergy interest group survey on how European allergy specialists deal with β-lactam allergy. *Allergy*. 2019;74(6):1052-1062.
5. Dodek P, Phillips P. Questionable history of immediate-type hypersensitivity to penicillin in Staphylococcal endocarditis: treatment based on skin-test results vers-us empirical alternative treatment–a decision analysis. *Clin Infect Dis*. 1999;29(5):1251-1256.
6. King EA, Challa S, Curtin P, Bielory L. Penicillin skin testing in hospitalized patients with β-lactam allergies: effect on antibiotic selection and cost. *Ann Allergy Asthma Immunol*. 2016;117(1):67-71.
7. Chen JR, Tarver SA, Alvarez KS, Wei W, Khan DA. Improving aztreonam stewardship and cost through a penicillin allergy testing clinical guideline. *Open Forum Infect Dis*. 2018;5(6):ofy106.
8. Blumenthal KG, Li Y, Banerji A, Yun BJ, Long AA, Walensky RP. The cost of penicillin allergy evaluation. *J Allergy Clin Immunol Pract*. 2018;6(3):1019-1027.
9. Ferré-Ybarz L, Salinas Argente R, Gómez Galán C, Duocastella Selvas P, Nevot FS. Analysis of profitability in the diagnosis of allergy to beta-lactam antibiotics. *Allergol Immunopathol*. 2015;43(4):369-375.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

DOI: 10.1111/all.13987

Anisakis is a major cause of anaphylaxis in seaside areas: An epidemiological study in Japan

To the Editor,

Anaphylaxis is a common condition observed in emergency departments and is sometimes associated with a fatal outcome. Following the establishment of standard criteria for anaphylaxis, several epidemiological studies have reported increasing incidence rates ranging from 50 to 112 per 100 000.[1]

We undertook this retrospective case-based study by identifying cases of anaphylaxis among the residents of two cities (Tateyama and Minami-Boso) in the Awa region of the southernmost part of Boso Peninsula, Japan (Figure S1). We identified patients who had been diagnosed with anaphylaxis at two hospitals, namely the Kameda Medical Center (KMC) and Awa Regional Medical Center (ARMEC), between September 2010 and August 2015. Most emergency patients in the Awa region attend these emergency departments as there are few emergency hospitals within this rural area (these two hospitals accepted 78.4% of all emergency patients in the region; in-house data). Episodes of anaphylaxis were identified by searching electronic medical records using diagnostic anaphylaxis-related codes. In all cases, the diagnosis of anaphylaxis was confirmed based on the World Allergy Organization anaphylaxis criteria.[2] In patients with two or more events, each anaphylactic event was counted separately. We excluded all patients with drug hypersensitivity–related anaphylaxis because of incomplete data collection. The inciting factors were determined in each case, based on patient history and examinations mainly involving in vitro-specific immunoglobulin E (IgE) testing. We report the age-adjusted incidence of anaphylaxis and its causes. Incidence rates were calculated according to the number of residents in the two cities. The World Health Organization[3] standard population distribution was used for age adjustment. A Fisher's test of variance was used to compare values between multiple groups. The study was approved by the KMC (approval number: 15-081) and ARMEC (approval number: 14) review boards according to the Ethical Guidelines for Medical and Health Research Involving Human Subjects of the Japanese Ministry of Health, Labor, and Welfare. The requirement to obtain informed consent from each participant was waived by the ethics committee in favor of posting an opt-out document on the hospital website (Method S1).

A total of 232 cases of anaphylaxis were identified in 203 patients. The total age-adjusted incidence rate was calculated as 56.0 cases (95% confidence interval [CI], 45.1-66.9) per 100 000 person-years. Of 203 patients, 67.2% were male. The incidence associated with each culprit is shown in Table 1. The age distribution (Figure 1) exhibits two peaks at 0-4 and 55-69 years of age. Most cases occurring in the sixth and seventh decades were due to ingested fish.

In 93 (45.8%) patients, specific IgE antibodies to putative allergens were investigated. As shown in Table 1 and Figure S2, ingested fish was the most frequent allergen (n = 128, 55.2%). Specific IgE antibodies were tested in 45 of 128 (35.2%) of cases involving ingested fish, and of these, 41 (91%) were positive for *Anisakis*-specific IgE antibodies, while specific IgE antibody tests for fish types (including mackerel, salmon, tuna, moth, and sardine) were negative.

A detailed list of symptoms categorized by presumed cause is provided in the Table S1. Gastrointestinal symptoms were markedly more frequent with ingested fish–related anaphylaxis compared with other food-related anaphylaxis (P = .029). The average time from ingestion to anaphylaxis onset was longer in cases of ingested fish–related anaphylaxis (Table 1). A biphasic reaction was identified in only five patients (2.2%). There were no cases of fatal anaphylaxis.

The estimated incidence rate in our study (56.0 per 100 000 person-years) may have been underestimated because we excluded drug-hypersensitivity cases. The large number of patients with ingested fish–related anaphylaxis was a distinctive feature of this study.