

Seong Buk Gu, Seoul, South Korea.

Email: moole@korea.ac.kr

Minji Kim and Gwanghui Ryu contributed equally to this work.

ORCID

Sang Min Lee  <https://orcid.org/0000-0002-9568-2096>

Hyeon-Jong Yang  <https://orcid.org/0000-0002-7287-4300>

Soo Whan Kim  <https://orcid.org/0000-0002-6917-5998>

REFERENCES

1. Bousquet J, Schunemann 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 e73.
2. Debbaneh PM, Bareiss AK, Wise SK, McCoul ED. Intranasal azelastine and fluticasone as combination therapy for allergic rhinitis: systematic review and meta-analysis. *Otolaryngol Head Neck Surg*. 2019;161(3):412-418.

3. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4(1):1.
4. Gross GN, Berman G, Amar NJ, Caracta CF, Tantry SK. Efficacy and safety of olopatadine-mometasone combination nasal spray for the treatment of seasonal allergic rhinitis. *Annals Allergy Asthma Immunol*. 2019;122(6):630-638 e633.
5. Meltzer EO, Wallace D, Dykewicz M, Shneyer L. Minimal clinically important difference (MCID) in allergic rhinitis: agency for health-care research and quality or anchor-based thresholds? *J Allergy Clin Immunol Pract*. 2016;4(4):682-688. e686.
6. Juniper EF, Guyatt GH, Griffith LE, Ferrie PJ. Interpretation of rhinoconjunctivitis quality of life questionnaire data. *J Allergy Clin Immunol*. 1996;98(4):843-845.

SUPPORTING INFORMATION

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

DOI: 10.1111/all.15416

Presentation of airway and general symptoms in COVID-19 caused by dominant SARS-CoV-2 variants: A follow-up on ARIA consensus

To the Editor,

Several SARS-CoV-2 variants have occurred since the beginning of the COVID-19 pandemic. Mutated *variants of concerns* (VOC; World Health Organization nomenclature) have a variable contamination rate and virulence. COVID-19 symptoms are polymorphic and vary according to VOC.¹ A consensus effort from the ARIA group (*Allergic Rhinitis and its Impact on Asthma*) has been shown that symptoms from common cold, allergic rhinitis, and COVID-19 are likely to be differentiated in a panel of 15 items.²

Although papers have described major clinical manifestations in these new variants,^{3,4} there is no consensus on important symptom changes caused by VOC Delta and Omicron. Following the methods

of the first EAACI-ARIA-GA¹LEN paper,² we assessed globally how physicians seeing COVID-19 patients are rating various symptoms induced by different VOC.

2 | METHODS

A bibliographic survey identified common symptoms induced by VOC Delta and Omicron. Then, a Delphi questionnaire regarding key symptoms associated with SARS-CoV-2 infection was developed based on the items from ARIA-EAACI-GA²LEN consensus² and from literature. Symptoms included common cold (upper airway),

TABLE 1 Tasks of the questionnaire

Symptom	Occurrence	Expected VAS
Runny nose, sneezing, stuffy nose, nasal pruritus, facial/nasal pain, ocular itch, ocular pain, Ocular redness, >3 nasal symptoms, smell dysfunction, taste dysfunction, dyspnea, cough, wheezing, sore throat, headache, fatigue, fever, duration of illness >1 week, undulating symptoms, gastrointestinal symptoms, skin symptoms, body/muscle ache, arthralgia, altered consciousness	Choice between: (none, very rare, possible, common, always) or (yes, no)	(grade from 0–10)

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

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

FIGURE 1 Expected symptom intensity on analogue scale (0: no symptom and 10: strongest symptoms) for wild-type and virus variants of SARS-CoV-2, rated by ARIA specialists. Asterisk indicates significant difference ($p < .01$) for Delta (blue) and Omicron (red), compared to wild type. Symptom groups A/B/C/D are explained in the main text and referred to Figure 2

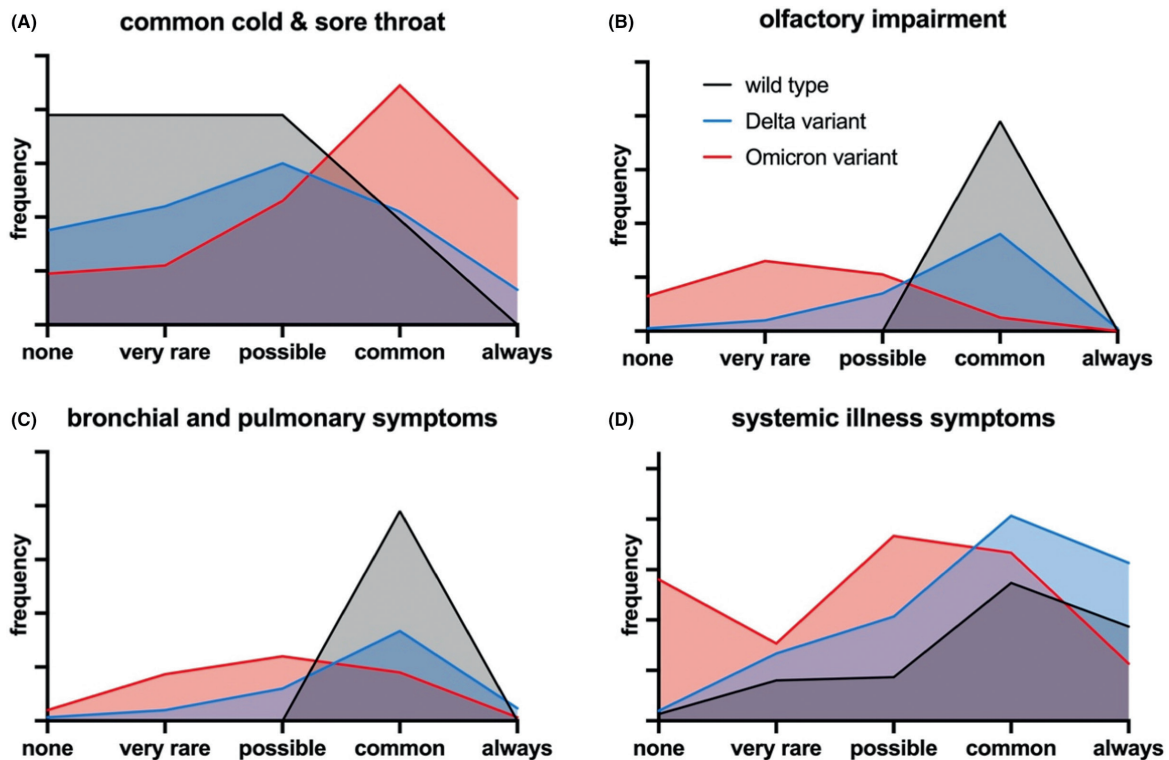
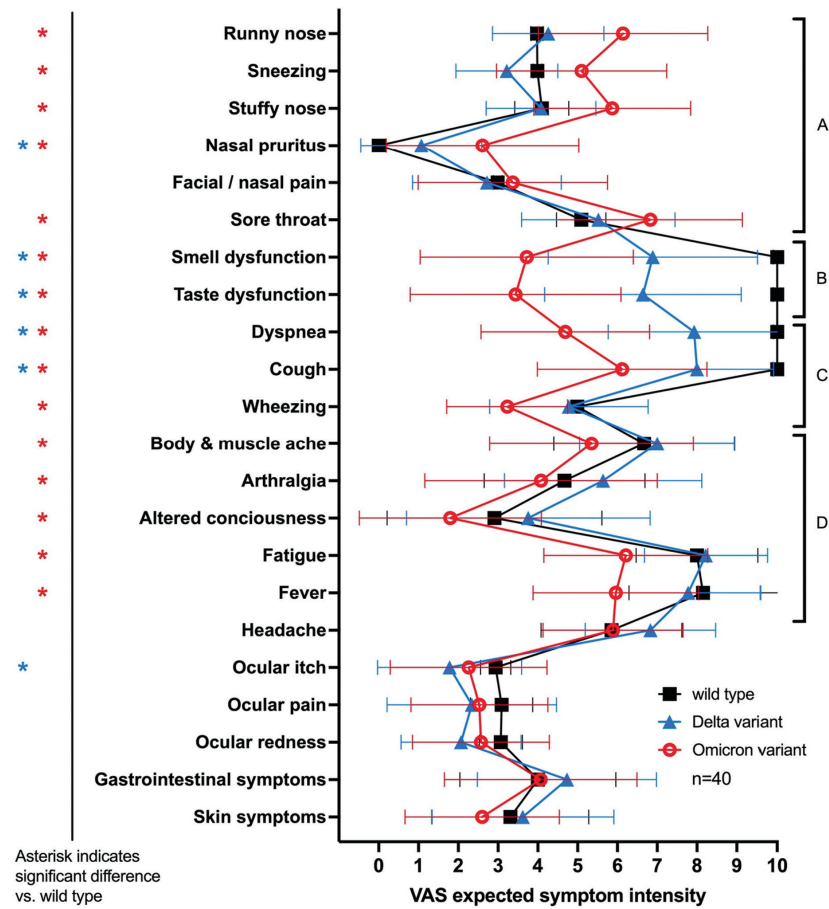


FIGURE 2 Expected frequency of symptoms with regard to wild-type and virus variants. The sum of mentions in the questionnaire responses are plotted. (A) common cold/sore throat (rhinorrhea, nasal obstruction, sneezing, facial pain, sore throat, multiple nasal symptoms); (B) chemosensory symptoms (smell and taste dysfunction); (C) bronchial and pulmonary symptoms (wheezing, cough, dyspnea); (D) signs of systemic illness (body ache, arthralgia, fever, fatigue, illness duration, vigilance)

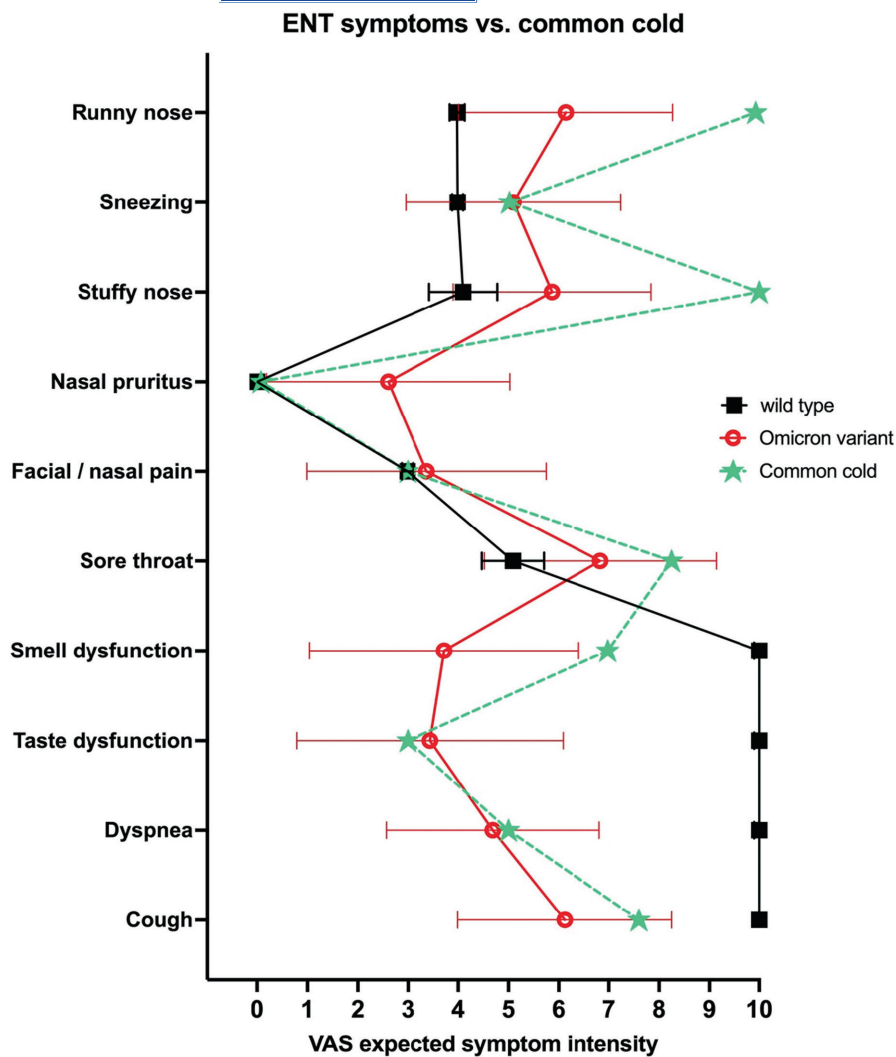


FIGURE 3 Expected symptom intensity on analogue scale (0: no symptom and 10: strongest symptoms) for wild-type and Omicron virus variant of SARS-CoV-2, rated by ARIA specialists

chemosensory, bronchial, and pulmonary as well as systemic illness symptoms (Table 1).

Participants (not involved in the study design process) were asked to estimate frequency (none, very rare, possible, common, always) and expected symptom intensity (visual analogue scale/VAS, 0 to 10) according to their experience as of March 2022 when seeing VOC Delta and Omicron COVID-19 patients. Wild-type symptom rating was performed in 2020 during the first waves of the pandemic by the same participants. Participants are ARIA airway specialists working in hospitals (in- and outpatient, ICU, and specialty clinic) and/or smaller offices.

Statistical analysis (ANOVA/*t*-test for multiple/two groups) and data analysis were performed through GraphPad Prism (USA).

3 | RESULTS

Among 47 questionnaires sent out, 40 were received within 7-day notice. Physicians saw an average of 43.5 COVID-19 patients per month. Responses originated in 26 countries.

Symptom intensity differed significantly between wild type and VOC (Figure 1). ANOVA test analyses revealed several significant

differences of the symptom intensity between the three variants (Figure 1, left). Nasal symptoms (anterior rhinorrhea, nasal congestion, and pruritus) ($p < .001$) and sore throat ($p < .001$) were more pronounced in VOC Omicron, compared to wild type. Olfactory function loss was significantly less marked in VOC Delta and Omicron ($p < .001$). The same patterns occurred for pulmonary symptoms and signs of severe disease (Figure 1). Symptom intensity also differed significantly between VOC Delta and Omicron for all symptoms mentioned above ($p < .01$).

Significantly differing symptoms were grouped concerning common cold and sore throat, chemosensory, bronchial and pulmonary, as well as systemic (Figure 2). VOC Omicron induce “common cold symptoms” and sore throat more often than wild-type and VOC Delta infections (Figures 2 and 3).

4 | DISCUSSION

Our data from ARIA airway specialists across the globe indicate that VOC Delta and Omicron cause various airway symptoms that significantly differ in terms of intensity and composition to those of

wild-type SARS-CoV-2. A recent human challenge study to wild-type virus confirmed none to mild rhinitis symptoms with high proportion of olfactory loss.⁵ Few studies mostly carried out in the UK showed that sore throat is common with VOC Omicron, whereas chemosensory symptoms were less common.⁶ A UK-based COVID symptom tracker app "Zoe's Covid Symptom Study" collected millions of symptom samples and showed sore throat, runny nose, sneezing, headache, fever, and persistent cough were the most symptoms in symptoms in VOC Delta.⁷ The role of vaccination on upper airway symptoms is unclear. Smith et al. found only one symptom alteration over the course of two doses of vaccine, possibly also influenced by alteration of virus strain.⁸ Initial reports on mRNA vaccines entirely preventing infections are challenged by recent observations by Yochay et al. of high-viral load infections with VOC Omicron, despite multiple previous vaccinations. There are several limitations for our study. Our study is a consensus based on expert opinions. Recall bias due to long intervals between presentations and our study is possible, although small variation in answers supports reliability. These results, for the first time, provide a more global view of the problem. Ultimately, we cannot differentiate here what triggers the effects we have described (vaccination, infections previously experienced by part of the population, other virus properties, etc.), but we do want to provide physicians with a decision-making aid for the current situation.

Patients are likely to present variable airway and other symptoms in future that can be misinterpreted as common cold. Thus, the prevention of severe outcomes remains the main goal of current vaccination efforts.

ACKNOWLEDGEMENT

Open Access funding enabled and organized by Projekt DEAL.





CONFLICT OF INTEREST

There are no conflicts of interest to declare with regard to this project.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Jan Hagemann¹ 
 Gabrielle Onorato²
 Christopher Seifen¹
 Sven Becker³
 Tilman Huppertz¹
 Heidi Olze⁴
 Piotr Kuna⁵
 Joaquim Mullol⁶
 Sanna Toppila Salmi⁷ 
 Joao Fonseca^{8,9,10,11}

Philip Rouadi^{1,2} 
 Torsten Zuberbier^{4,13} 
 Jean Bousquet^{2,13,14} 
 Ludger Klimek^{1,15} 
 the ARIA group

¹Department of Otolaryngology, Head and Neck Surgery, Universitätsmedizin Mainz, Mainz, Germany

²University Hospital Montpellier, Montpellier, France

³Department of Otolaryngology, Head and Neck Surgery, Universitätsmedizin Tübingen, Tübingen, Germany

⁴Department of Otolaryngology, Charité Universitätsmedizin Berlin, Humboldt-Universität zu Berlin, Berlin, Germany

⁵Division of Internal Medicine, Asthma and Allergy, Barlicki University Hospital, Medical University of Lodz, Lodz, Poland

⁶Department of Otolaryngology, University Hospital Barcelona, Barcelona, Spain

⁷Skin and Allergy Hospital, Helsinki University Hospital, Helsinki, Finland

⁸Faculdade de Medicina da Universidade do Porto, Porto, Portugal

⁹Center for Research in Health Technologies and Information Systems, CINTESIS, Universidade do Porto, Porto, Portugal

¹⁰Allergy Unit, Instituto CUF Porto e Hospital CUF Porto, Porto, Portugal

¹¹Health Information and Decision Sciences Department - CIDES, Faculdade de Medicina, Universidade do Porto, Porto, Portugal

¹²Department of Otolaryngology-Head and Neck Surgery, Eye and Ear University Hospital, Beirut, Lebanon

¹³Comprehensive Allergy Center, Department of Dermatology and Allergy, Berlin, Germany

¹⁴MACVIA-France, Montpellier, France

¹⁵Center for Rhinology and Allergology, Wiesbaden, Germany

Correspondence

Jan Hagemann, Department of Otolaryngology, Head and Neck Surgery, Universitätsmedizin Mainz, Langenbeckstr. 1, 55131 Mainz, Germany.

Email: jan.hagemann@unimedizin-mainz.de

The ARIA group members are listed in Appendix A.

ORCID

Jan Hagemann  <https://orcid.org/0000-0002-9846-7850>
 Sanna Toppila Salmi  <https://orcid.org/0000-0003-0890-6686>
 Philip Rouadi  <https://orcid.org/0000-0002-5365-9568>
 Torsten Zuberbier  <https://orcid.org/0000-0002-1466-8875>
 Jean Bousquet  <https://orcid.org/0000-0002-4061-4766>
 Ludger Klimek  <https://orcid.org/0000-0002-2455-0192>

REFERENCES

1. He J, Guo Y, Mao R, Zhang J. Proportion of asymptomatic coronavirus disease 2019: a systematic review and meta-analysis. *J Med Virol.* 2021;93(2):820-830.
2. Hagemann J, Onorato GL, Jutel M, et al. Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold: an ARIA-EAACI-GA(2) LEN consensus. *Allergy.* 2021;76(8):2354-2366.
3. Meo SA, Meo AS, Al-Jassir FF, Klonoff DC. Omicron SARS-CoV-2 new variant: global prevalence and biological and clinical characteristics. *Eur Rev Med Pharmacol Sci.* 2021;25(24):8012-8018.
4. Iacobucci G. Covid-19: runny nose, headache, and fatigue are commonest symptoms of omicron, early data show. *BMJ.* 2021;375:n3103.
5. Killingley B, Mann AJ, Kalinova M, et al. Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge in young adults. *Nat Med.* 2022;28:1031-1041.
6. United Kingdom Government. Technical briefing. 34-14. 2022. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050236/technical-briefing-34-14-january-2022.pdf
7. ZOE Symptom Study. <https://www.ej-med.org/index.php/ejmed/article/view/1120>. 2022.
8. Smith P. Correspondence to "Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold: An ARIA-EAACI-GA2LEN consensus". *Allergy.* 2022;77:2571-2573.

APPENDIX A

ARIA GROUP

Alan Kaplan, International Primary Care Respiratory Group (ICPRG).

Antonino Romano, Department of Laboratories/Unit of Pediatrics and Medical Genetics/Allergology, Associazione OASI Maria SS: Troina, Sicilia, IT.

Bilun Gemicioglu, Department of Pulmonary Diseases, Cerrahpaşa Faculty of Medicine, İstanbul University-Cerrahpaşa, İstanbul, Turkey.

Boleslaw Samoliński, Medical University of Warsaw, Department of the Prevention of Environmental Hazards and Allergology, Warsaw, Poland.

Branislava Milenkovic, Clinic for Pulmonary Disease, University Clinical Center of Serbia, Belgrade, Serbia.

Brian Lipworth, Scottish Centre for Respiratory Research, University of Dundee, Scotland.

Cemal Cingi, Otolaryngology Department, Eskisehir University, Eskisehir, Turkey.

Charlotte Suppli Ulrik, Department of Respiratory Medicine, Copenhagen University Hospital, Denmark.

Christian Bergmann, Allergie-Centrum-Charité, Berlin.

Désirée Larenas-Linnemann, Centro de Excelencia en Asma y Alergia, Hospital Médica Sur, Ciudad de México, Mexico.

Dirceu Solé, Division of Allergy, Clinical Immunology and Rheumatology, Department of Pediatrics, Universidade Federal de Sao Paulo, Brazil.

Ewa Jassem, Department of Pulmonology and Allergology, Medical University of Gdansk, Debinki str 7, 90-211 Gdańsk, Poland.

Florin Mihaltan. National Institute of Pneumology M Nasta, Bucharest, Romania.

Ioanna Tsiligianni, International Primary Care Respiratory Group (ICPRG).

Jaime C. Sousa, International Primary Care Respiratory Group (ICPRG).

Jaron Zuberbier, Charité Virchow-Klinikum, Humboldt-Universität zu Berlin.

Juan Carlos Ivancevich, Department of Allergy and Immunology, Medical Faculty of Universidad del Salvador, Buenos Aires, Argentina.

Kimi Okubo, Department of Otolaryngology, Nippon Medical School, Tokyo, Japan.

Luis R. Caraballo, Institute for Immunological Research, University of Cartagena, Cartagena de Indias, Colombia.

Maia Gotua, Center of Allergy and Immunology, Tbilisi, Georgia.

Mario Zernotti, Department of ENT, Catholic University of Cordoba, Cordoba, Argentina.

Mark Dykewicz, Section of Allergy & Immunology, Division of Infectious Diseases, Department of Internal Medicine, St. Louis, USA.

Maximiliano Gomez, ALLERGY & ASTHMA UNIT HOSPITAL SAN BERNARDO, SALTA - ARGENTINA.

Menachem Rottem, Division of Allergy and Clinical Immunology, Ha'Emek Medical Center, Afula 18,101, Israel.

Michael Makris, Allergy Unit, 2nd Dpt. of Dermatology and Venereology, University Hospital Athens, Greece.

Motohiro Ebisawa, Clinical Research Center for Allergy and Rheumatology, National Hospital Organization Sagami National Hospital, Kanagawa, Japan.

Musa Khaitov, NRC Institute of Immunology FMBA, Moscow, Russia.

Neil Fitch, International Primary Care Respiratory Group (ICPRG).

Nelson Augusto Rosario Filho, Department of Pediatrics, Federal University of Parana, Curitiba, PR, Brazil.

Neven Miculinic, Croatian Pulmonary Society Zagreb Croatia.

Osman Yusef, International Primary Care Respiratory Group (ICPRG).

Tari Haahtela, Skin and Allergy Hospital, Helsinki University Hospital, University of Helsinki, Helsinki, Finland.

Tiago Maricoto not Maricoti, International Primary Care Respiratory Group (ICPRG).

Todor A. Popov, University Hospital Sv. Ivan Rilski, Sofia, Bulgaria.

Tomohisa Iinuma, Department of Otolaryngology, Head and Neck Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan.

Tuula Vasankari, Filhary and University of Turku, Pulmonary diseases and Clinical Allergology, Turku, Finland.

Vincenzo Patella, Division of Internal Medicine and Allergy/Immunology, Faculty of Medicine and Surgery, University of Naples Federico II, Naples, Italy.

Yoshitaka Okamoto, Department of Otolaryngology, Head and Neck Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan.