CORRESPONDENCE



Correspondence to "Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold: An ARIA-EAACI-GA2LEN consensus"

Dear Editor,

This is in reference to the EAACI position paper titled Correspondence to "Differentiation of COVID-19 signs and symptoms from allergic rhinitis and common cold: An ARIA-EAACI-GA2LEN consensus" pages 2354–2366 of Volume 76, Issue 8 published in August 2021.¹

Revised: 1 March 2022

The top five most severe symptoms of COVID-19, as agreed upon by consensus (89 doctors from 37 countries) are:

- 1. Taste dysfunction,
- 2. Sneezing (not in bursts),
- 3. Ocular itch,
- 4. Cough,
- 5. Nasal pruritus.

An alternative way to interpret the data to help practitioner rapid triage patients is that the survey respondents felt that only two COVID-19 symptoms might *differentiate* it from the common cold and allergic rhinitis:

- 1. Taste dysfunction,
- 2. Smell dysfunction.

The consensus questionnaire did not ascertain the vaccination status of the patients attended to by the ARIA (Allergic Rhinitis and its Impact on Asthma) practitioner respondents. At the time of the first publication of the consensus results (17 March 2021), there had been 5.13 vaccine doses per 100 people in the world according to the research and statistics organisation Our World in Data ². Since then, and as of 20 September 2021, there have been 75.9 vaccine doses per 100 people in the world, with 31.8% of the total population being double-vaccinated.²

The ZOE COVID Symptom Study is the world's largest ongoing study into the COVID-19 virus. The app is a not-for-profit initiative to collect data (mostly) from the UK population. It was launched at the end of March 2020 by health science company ZOE with scientific analysis provided by King's College London. Since its launch, the pattern of symptoms logged by over 4.6 million users of the app has changed as the virus has evolved, and there appear to be differences in COVID-19 symptoms depending on the vaccination status.³

Interestingly, the ARIA respondents generally agreed that runny nose was "very rare and if present, mild (VAS<5/10)" in COVID-19, compared with the common cold "always," and allergic rhinitis "often." Where conversely, "runny nose" was a top 5 symptom of COVID-19 captured by ZOE, regardless of the vaccination status.

Considering that the original symptoms to watch for, as published on the CDC website on 14 March 2021,⁴ were fever, cough and shortness of breath, it is clear that there is an evolution of clinical presentations. Clinicians need to be made aware that not only symptoms are changing over time but also vaccination status may affect these too.

The evolution of symptoms may result from different virus strains, changed host immune responses due to vaccination doses and organic COVID-19 infections, and environmental factors (e.g. pollution index⁵). There are highly variable presentations in different populations.

At the very minimum, latest data show that symptomatology is affected by vaccination status,⁶ which the ARIA-EAACI-GA2LEN consensus did not capture, thus limiting its utility in clinical practice. The paper is presented published and presented as a "consensus," but on closer scrutiny, it is a survey that has been devised and sent out to ARIA members that neither collected enough data from which conclusions could be drawn nor.

The recent REACT-1 study published on 28 September 2021 of over 1 million UK participants tried to ascertain symptoms of COVID-19.⁷ They found that the top 5 symptoms of COVID-19, which were jointly predictive of PCR positivity and appeared to vary only marginally across age groups, were:

- 1. Loss or change of sense of smell,
- 2. Loss or change of sense of taste,
- 3. Fever,
- 4. New persistent cough,
- 5. Chills.

As of 21 September 2021, these are the top five COVID-19 symptoms in various populations per ZOE and the REACT-1 study compared with the EAACI consensus (Table 1):

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EAACI consensus	ZOE nonvaccinated	ZOE one-dose vax	ZOE 2 vaccinations	REACT-1
Taste dysfunction	Headache	Headache	Runny nose	Smell dysfunction
Sneezing	Runny nose	Runny nose	Headache	Taste dysfunction
Ocular itch	Sore throat	Sore throat	Sneezing	Fever
Cough	Fever	Sneezing	Sore throat	Persistent cough
Nasal pruritus	Persistent cough	Persistent cough	Loss of smell	Chills

TABLE 1 The top five COVID-19 symptoms in various populations per ZOE and the REACT1 study compared to the EAACI consensus

Colours are used to easily view the change of symptoms with vaccination status, different analyses and those proposed with the EAACI consensus.

There has been an evolution of ZOE symptoms in dual vaccinated individuals with loss of smell being the 5th most common symptom in September 2021, and on a final recheck before replying to editorial comments, this has been replaced with "persistent cough" and in the nonvaccinated group, sore throat and runny nose change positions. With new variants, it is possible that clinical phenotypes will change.

The ARIA-EAACI-GA2LEN is divergent with patient-reported symptoms as captured by ZOE and with the REACT-1 study. The rapid evolution of symptoms with both different strains of the virus and postvaccination reduces the utility of the consensus position in clinical practice.

CONFLICT OF INTEREST

OL declare has no conflicts of interests in relation to this work. PS has no conflicts of interest related to this letter. He has current researcher-initiated funding in mucosal and skin immunology supported by GSK and Sanofi respectively. DBP has advisory board membership with AstraZeneca. Boehringer Ingelheim. Chiesi. Mylan, Novartis, Regeneron Pharmaceuticals, Sanofi Genzyme, Thermofisher; has consultancy agreements with Airway Vista Secretariat, AstraZeneca, Boehringer Ingelheim, Chiesi, EPG Communication Holdings Ltd, FIECON Ltd, Fieldwork International, GlaxoSmithKline, Mylan, Mundipharma, Novartis, OM Pharma SA, PeerVoice, Phadia AB, Spirosure Inc, Strategic North Limited, Synapse Research Management Partners S.L., Talos Health Solutions, Theravance and WebMD Global LLC; has grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Boehringer Ingelheim, Chiesi, Mylan, Novartis, Regeneron Pharmaceuticals, Respiratory Effectiveness Group, Sanofi Genzyme, Theravance and UK National Health Service; has payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Mylan, Mundipharma, Novartis, Regeneron Pharmaceuticals and Sanofi Genzyme; has payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim, Mundipharma, Mylan, Novartis, Thermofisher; has stock/stock options from AKL Research and Development Ltd, which produces phytopharmaceuticals, owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 92.61% of Observational and Pragmatic

Research Institute Pte Ltd (Singapore); and has 5% shareholding in Timestamp, which develops adherence monitoring technology, is peer reviewer for grant committees of the UK Efficacy and Mechanism Evaluation programme, and Health Technology Assessment, and was an expert witness for GlaxoSmithKline.

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SUPPORTING INFORMATION

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