

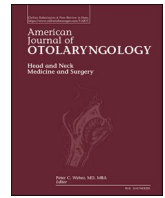


Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

American Journal of Otolaryngology–Head and Neck Medicine and Surgery

journal homepage: www.elsevier.com/locate/amjoto

COVID-19 related persistent olfactory disorders represent an unprecedented challenge

ARTICLE INFO

Keywords

Anosmia
Ageusia
COVID-19
Olfactory function
Olfactory dysfunction
SARS-CoV-2
Coronavirus
Smell
Taste
Taste dysfunction
Maxillo-facial surgery

Dear Editor,

We have read with interest the recent article by McWilliams et al. [1] which reported data on the recovery of olfactory function 2 years after severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Prior to this, only one other study was published with such long follow-up detecting a 2-year prevalence of OD at 11.7 % but in a population that did not include only patients who had OD during infection [2]. Such a long follow-up is essential to obtain reliable results, as the recovery of post-viral olfactory dysfunctions (OD) can occur spontaneously even more than a year after infection [3,4]. The results collected by McWilliams et al. are emblematic of the seriousness of the problem we are facing: more than 60 % of patients who had an OD during the infection do not fully recover their sense of smell at two years. The authors used a methodology based on patient interview. These types of studies allow for a large amount of data to be collected quickly, at low cost, and individuals can act as self-control by comparing their current olfactory function to that before infection. However, compared to psychophysical studies, they significantly underestimate the prevalence of residual OD as patients often confuse significant recovery with complete recovery. It is therefore likely that the prevalence of persistent OD is even higher [5,6]. Such a high prevalence means that in the next few years we will have a very high number of requests for assistance for this disabling morbidity [7]. The sense of smell is a fundamental determinant of the quality of life and its reduction can expose individuals to a large number of environmental risks that we normally identify with the sense of smell [8,9]. OD has often been overlooked in the past, there are no shared therapeutic guidelines and health systems are therefore not ready to face this challenge. Studies such as that of McWilliams et al. may provide us with a solid epidemiological basis from which to draw clinical and therapeutic indications.

About this, analyzing the results reported in the study, it is interesting to note that the percentage of individuals who self-reported a

complete recovery did not change significantly over time (38.7 % at 3 months, 38.9 % at one year, 38.2 % at two years). This means that although there is room for improvement, after 3 months, the risk of having long-term OD is very high. Patients should therefore be initiated to specific therapies early and, after 3 months [10–12], experimental therapies may be considered, such as the injection of platelet-rich plasma into the olfactory cleft [13].

Another important finding is that recovery, at least partial, can occur spontaneously even at a great distance from the OD onset. This must push us to reassure patients and, in any case, start specific therapies whatever the time of observation. In particular, olfactory training has proved to be an effective and side-effect-free instrument for improving olfactory scores even in individuals with long-lasting OD [14,15].

Finally, the study by McWilliams et al. provides an indication that older individuals are at greater risk of incurring persistent OD. This is probably linked to a lower ability, in these subjects, to respond to damage to the olfactory epithelium [16]. The identification of risk factors for the development of persistent OD, which has so far yielded poor results [17–19], is essential for identifying populations of patients at risk, to be subjected to early treatment protocols.

CRedit authorship contribution statement

LAV: literature research, first draft, final approval. GDR, GS, FM PBR, JRL: literature research, critical revision of the manuscript, final approval.

Founding sources

None declared.

<https://doi.org/10.1016/j.amjoto.2022.103667>

Received 16 August 2022

Available online 17 October 2022

0196-0709/© 2022 Published by Elsevier Inc.

Declaration of competing interest

The authors declare that they have no conflict of interests.

Acknowledgements

None declared.

References

- [1] . McWilliams MP, Coelho DH, Reiter ER, Costanzo RM. Recovery from COVID-19 smell loss: two-years of follow up. *Doi:10.1016/j.amjoto.2022.103607*.
- [2] Boscolo-Rizzo P, Fabbris C, Polesel J, Emanuelli E, Tirelli G, Spinato G, Hopkins C. Two-year prevalence and recovery rate of altered sense of smell or taste in patients with mildly symptomatic COVID-19. *JAMA Otolaryngol. Head Neck Surg.* 2022. <https://doi.org/10.1001/jamaoto.2022.1983>.
- [3] Lee DY, Lee WH, Wee JH, Kim JW. Prognosis of postviral olfactory loss: follow-up study for longer than one year. *Am. J. Rhinol. Allergy.* 2014;28:419–22.
- [4] Vaira LA, De Riu G, Salzano G, Maglitter F, Boscolo-Rizzo P, Lechien JR. The rate of persistent COVID-19 related chemosensory dysfunctions can be established only after one year. *Oral. Dis.* 2022. <https://doi.org/10.1111/odi.14298>.
- [5] Mazzatenta A, Neri G, D'ardes D, De Luca C, Marinari S, Porreca E. Smell and taste in severe CoViD-19: self reported vs. testing. *Front. Med. (Lausanne)* 2020;7:589409.
- [6] Lechien JR, Saussez S, Maniaci A, Vaira LA. The study of recovery rates of COVID-19 olfactory and gustatory dysfunctions requires psychophysical evaluations. *Am. J. Otolaryngol.* 2021;42:103168.
- [7] Boscolo-Rizzo P, Polesel J, Vaira LA. Smell and taste dysfunction after COVID-19. *BMJ* 2022. <https://doi.org/10.1136/bmj.o1635>.
- [8] Boscolo-Rizzo P, Hopkins C, Menini A, Dibattista M, Cancellieri E, Gardenal N, et al. Parosmia assessment with structured questions and its functional impact in patients with long-term COVID-19-related olfactory dysfunction. *Int. Forum Allergy Rhinol.* 2022. <https://doi.org/10.1002/alr.23054>.
- [9] Vaira LA, Gessa C, Deiana G, Salzano G, Maglitter F, Lechien JR, et al. The effects of persistent olfactory and gustatory dysfunctions on quality of life in long-COVID-19 patients. *Life (Basel).* 2022;12:141.
- [10] Abdelalim AA, Mohamady AA, Elsayed RA, Elawady MA, Ghallab AF. Corticosteroid nasal spray for recovery of smell sensation in COVID-19 patients: a randomized controlled trial. *Am. J. Otolaryngol.* 2021;42:102884.
- [11] Di Stadio A, D'Ascanio L, Vaira LA, Cantone E, De Luca P, Cingolani C, et al. Ultramicronized palmitoylethanolamide and luteolin supplement combined with olfactory training to treat post-COVID-19 olfactory impairment: a multi-center double-blinded randomized placebo-controlled clinical trial. *Curr. Neuropharmacol.* 2022. <https://doi.org/10.2174/1570159X20666220420113513>.
- [12] O'Byrne L, Webster KE, MacKeith S, Philpott C, Hopkins C, Burton MJ. Interventions for the treatment of persistent post-COVID-19 olfactory dysfunction. *Cochrane Database Syst. Rev.* 2021;7:CD013876.
- [13] Steffens Y, Le Bon SD, Lechien J, Prunier L, Rodriguez A, Saussez S, et al. Effectiveness and safety of PRP on persistent olfactory dysfunction related to COVID-19. *Eur. Arch. Otorhinolaryngol.* 2022. <https://doi.org/10.1007/s00405-022-07560-y>.
- [14] Altundag A, Yilmaz E, Kesimli MC. Modified olfactory training is an effective treatment method for COVID-19 induced parosmia. *Laryngoscope* 2022;132:1433–8.
- [15] Lechner M, Liu J, Counsell N, Gillespie D, Chandrasekharan D, Ta NH, et al. The COVANOS trial – insight into post-COVID olfactory dysfunction and the role of smell training. *Rhinology* 2022. <https://doi.org/10.4193/Rhin21.470>.
- [16] Kondo K, Kikuta S, Ueha R, Suzukawa K, Yamasoba T. Age-related olfactory dysfunction: epidemiology, pathophysiology, and clinical management. *Front. Aging Neurosci.* 2020;12:208.
- [17] Tan BKJ, Han R, Zhao JJ, Tan NKW, Quah ESH, Tan CJ, et al. Prognosis and persistence of smell and taste dysfunction in patients with covid-19: meta-analysis with parametric cure modelling of recovery curves. *BMJ* 2022. <https://doi.org/10.1136/bmj-2021-069503>.
- [18] Vaira LA, De Vito A, Deiana G, Pes C, Giovanditto F, Fiore V, et al. Systemic inflammatory markers and psychophysical olfactory scores in coronavirus disease 2019 patients: is there any correlation? *J. Laryngol. Otol.* 2021;135:723–8.
- [19] Saussez S, Sharma S, Thiriard A, Ollslagers V, Vu Duc I, Le Bon SD, et al. Predictive factors of smell recovery in a clinical series of 288 coronavirus disease 2019 patients with olfactory dysfunction. *Eur. J. Neurol.* 2021;28:3702–11.

Luigi Angelo Vaira^{a,b,*}, Giacomo De Riu^a, Giovanni Salzano^{c,d},
Fabio Maglitter^d, Paolo Boscolo-Rizzo^e, Jerome R. Lechien^{f,g}

^a Maxillofacial Surgery Operative Unit, Department of Medical, Surgical and Experimental Sciences, University of Sassari, Sassari, Italy

^b Biomedical Science Department, PhD School of Biomedical Science, University of Sassari, Sassari, Italy

^c ENT and Maxillofacial Surgery Unit, Istituto Tumori G. Pascale of Naples, Naples, Italy

^d Maxillofacial Surgery Unit, University Hospital of Naples “Federico II”, Naples, Italy

^e Department of Medical, Surgical and Health Sciences, Section of Otolaryngology, University of Trieste, Trieste, Italy

^f Department of Anatomy and Experimental Oncology, Mons School of Medicine, UMONS Research Institute for Health Sciences and Technology, University of Mons (UMons), Mons, Belgium

^g Department of Otolaryngology-Head Neck Surgery, Elsan Polyclinic of Poitiers, Poitiers, France

* Corresponding author at: Maxillofacial Surgery Unit, University Hospital of Sassari, Viale San Pietro 43/B, Sassari, Italy.
E-mail address: lavaira@uniss.it (L.A. Vaira).