



# Smell and taste dysfunction after covid-19

## Health systems are unprepared for the scale of the challenge

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Cite this as: *BMJ* 2022;378:o1653

<http://dx.doi.org/10.1136/bmj.o1653>

Published: 27 July 2022

The sense of smell is an ancient and vital perception in mammals, with the olfactory receptor gene family making up 1% of the mammalian genome, and the human olfactory system being able to discriminate among thousands of airborne chemicals at concentrations below the detection limits of the most complex analytical systems.<sup>1</sup> However, people only realise the importance of smell when it is lost. The covid-19 pandemic has put both smell and taste disturbances in the spotlight because of the functional impact and severe distress caused by the loss of these senses, their fundamental diagnostic value,<sup>2</sup> and, more recently, the high rate of long term dysfunction.<sup>3</sup>

The linked meta-analysis by Tan and colleagues (doi:10.1136/bmj-2021-069503) gives a clear picture of the challenge humans face.<sup>4</sup> About 5% of people who report initial changes to their sense of smell or taste after covid-19 still report smell and taste dysfunction six months later and, given that an estimated 550 million cases of covid-19 have been reported worldwide as of July 2022, large numbers of patients will be seeking care for these disabling morbidities. Health systems should therefore be ready to provide support to these patients who often report feeling isolated when their symptoms are overlooked by clinicians.<sup>5</sup>

More than other senses, smell and taste include emotional and affective elements of experience. These senses cannot be communicated through social networks—as with ideas, imaging, and music, sharing them requires coexistence. Loss of smell and taste adversely affects quality of life by depriving those affected of several everyday pleasures and social bonds.<sup>6</sup> People can also experience anorexia, food aversions, malnutrition, anxiety, and depression.<sup>7</sup> All these disturbances can be greatly amplified by the onset of qualitative alterations, in particular by parosmia. Parosmia, a fluctuant distorted smell perception, is a common sequela of the olfactory dysfunction associated with covid-19, arising on average three months after SARS-CoV-2 infection.<sup>8</sup> For the overwhelming majority, parosmia transforms a pleasant odour into an unpleasant one, and daily activities such as smelling coffee and sensing the flavour of food can become disgusting and emotionally distressing.

Studies in the meta-analysis by Tan and colleagues were conducted by interviewing patients.<sup>4</sup> Such studies are cheap, quick, and, most importantly, self-controlled, because each patient's subjective perception of smell is compared before and after the onset of covid-19. But, as with sight and hearing, sense of smell and taste are measurable mainly through psychophysical tests, and this more objective

evaluation can provide more accurate and valuable information. Numerous studies have consistently observed that subjective evaluation tends to underestimate the real prevalence of olfactory dysfunctions compared with psychophysical tests.<sup>9,10</sup>

Using pen-like odour dispensing devices, these psychophysical tests can measure odour thresholds as well as olfactory discriminative and identification abilities.<sup>11</sup> In a recent case-control study of patients one year after covid-19, we observed that participants who self-reported complete resolution of their loss of smell had statistically significant lower psychophysical olfactory scores than people with no history of covid-19 matched on sex and age.<sup>3</sup> Although an unconscious alteration of sense of smell may not impact quality of life, it exposes people to possible risks. In addition to eating behaviour, nutrition, and social communication, both smell and taste are crucial for vital functions such as warning against environmental hazards, including fires, poisonous fumes, leaking gas, and spoiled food.<sup>12</sup>

The treatment of chemosensory disorders is still frustrating, as few evidence based options are available. Knowing the pathogenetic mechanisms of SARS-CoV-2 induced olfactory loss can provide a more solid basis for the development of new treatment strategies. Although the involvement of olfactory bulb and central olfactory pathways cannot be excluded, most evidence points to the virus targeting supporting cells of the olfactory neuroepithelium. These cells—not olfactory neurons—express the molecular make-up necessary for entry of the virus.

One recent high quality study suggests that viral or cellular components released from infected supporting cells cause widespread downregulation of olfactory receptors and of their signalling components in olfactory sensory cells.<sup>13</sup> Thus, the primary target of the treatment for post-covid-19 anosmia should be the olfactory neuroepithelium.

Olfactory training, started as soon as possible after the onset of symptoms, is the only disease specific intervention with evidence of efficacy for the treatment of post-infectious olfactory dysfunction. First proposed by Thomas Hummel in 2009, olfactory training exploits the unique regenerative capabilities of the olfactory neuroepithelium.<sup>14</sup> Patients are advised to sniff and try to identify a sequence of four strong smelling scents—usually rose, eucalyptus, lemon, and clove—for 15 seconds twice a day over the course of several months.

In addition to the use of nasal steroids, which aim to resolve SARS-CoV-2 induced inflammation, other treatments that have shown some, albeit marginal, benefit in small clinical trials include intranasal

vitamin A and supplements of alpha lipoic acid and omega 3 fatty acids.<sup>15</sup> As olfactory neuroepithelium is located in the hidden posterior roof of the nasal cavity, specific delivery systems able to distribute drugs to the olfactory region could improve the efficacy of intranasal treatment options.

The large number of people with long lasting chemosensory dysfunction after covid-19 offers a unique opportunity to test new treatments in large multicentre trials. Health leaders, policy makers, and research funders should realise the extraordinary importance of good chemosensory function for the wellbeing of humans, allocate adequate resources to support chemosensory research, and sustain medical specialists faced with an exceptional number of patients with smell and taste dysfunction.

The BMJ has judged that there are no disqualifying financial ties to commercial companies.

The authors declare the following other interests: None.

Further details of The BMJ policy on financial interests here: <https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-coi-form.pdf>."

Provenance and peer review: Commissioned; not externally peer reviewed.

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