The burden of olfactory dysfunction during the COVID-19 pandemic in the United Kingdom*

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Dear Editor:

At the onset of the COVID-19 pandemic, the loss of sense of smell (i.e. anosmia) emerged as a cardinal symptom of infection ⁽¹⁻⁴⁾. Recent meta-analyses have demonstrated a prevalence of 43.0% - 52.7% ⁽⁵⁻⁷⁾. In their assessment of olfactory dysfunction in 2,581 mild and moderate-to-critical COVID-19 cases, Lechien et al. observed a prevalence of 85.9% and 4.5-6.9%, respectively ⁽⁸⁾. We utilized a set of questions on olfactory dysfunction (Supplemental Information and Table 1), which had been piloted in a separate trial ⁽⁹⁾, to ascertain patterns of olfactory dysfunction in the general public. The survey was conducted anonymously on 1,160 adults across the UK (Supplemental Table 2) in November 2021. 14.3% (166/1160) of responders reported having experienced a loss of sense of smell since January 2020. Roughly

half recovered their smell within one month (45.0%, 72/160). Smell loss persisted for 1-3 and 3-6 months in 19.9% (33/160) and 15.7% (26/160), respectively. For 10.2% (17/160) and 7.2% (12/160), smell loss persisted beyond 6 and 12 months, respectively.

Parosmia ('my smell is distorted, meaning things smell differently than they used to') and phantosmia ('phantom smell(s), meaning I smell items that are not present in the vicinity') were reported in 23.5% (39/166) and 28.3% (47/166) of those with smell loss, respectively. For the participants who reported parosmia, 15.4% (6/39) had fully recovered by the time of the survey with improvements in 53.8% (21/39). Parosmia remained unchanged or worsened in 15.4% (6/39) and 12.8% (5/39), respectively. For those who reported phantosmia, 34.0% (16/47)

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Table 1. Smell Dysfunction in the UK sample for those who responded "Yes" to having lost their sense of smell or taste in the last 20 months.

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of burning, cooling or tingling in		Not applicable	26	17.5
		Yes	87	54.4
		No	73	45.6

If yes, how often have you experi- enced this? (n=159)Just once3421A few times4125Every day1710	%
A few times 41 25.	1.4
Every day 17 10	5.8
	0.7
Multiple times per day 8 5.	.0
Never experienced 59 37.	7.1
If you have experienced a loss of When the relation of the second	1.2
smell, has this adversely affected your quality of life? (n=160) 78 48	3.8
Has your weight changed sinceI have gained weight4729	9.4
your sense of smell changed? I have lost weight 43 26.	5.9
No change 70 43.	3.8

had fully recovered, whilst 51.1% (24/47) had seen improvements. Phantosmia remained unchanged or worsened in 6.4% (3/47) and 8.5% (4/47), respectively. 54.4% (87/160) reported having experienced sensations of burning, cooling or tingling in their nose or mouth. Of those who reported a loss of sense of smell, 51.2% (82/160) indicated that this had adversely impacted their quality of life.

We next sought to determine the burden of olfactory dysfunction across UK adults by extrapolating prevalence estimates to the entire UK adult population. With the observed 14.3% (95% CI: 12.4% - 16.4%) prevalence of smell loss and taking the current UK population as 67.2 million (World Bank, 2020), this is equivalent to 9.6 million (95% CI: 8.3 million to 11.1 million) people having experienced a loss of smell since the start of the COVID-19 pandemic, across the UK. Crucially, 1.0% (95% CI: 0.6% - 1.2%) of participants reported smell loss beyond 12 months, which extrapolates to 695,331 people in the UK (95% CI: 398,416 - 1.2 million). Lastly, regarding the prevalence of parosmia, 3.4% (95% Cl: 2.5% - 4.6%) of the cohort reported having experienced some degree of parosmia, which extrapolates to 2.3 million people in the UK (95% CI: 1.7 million to 3.1 million). 11 of these participants experienced persistent parosmia, which is equivalent to a prevalence of 0.9% (95% CI: 0.5% - 1.7%) and extrapolates to 637,386 people in the UK (95% Cl: 356,454 – 1,1 million). We have discussed limitations inherent to this type of study in the Supplemental Methods.

Importantly, in addition to the health and safety consequences of olfactory dysfunction, a large proportion of individuals reported a negative impact on quality of life, emphasizing its emotional and psychological toll. Few treatment approaches have been validated and are in routine-use for the management of olfactory dysfunction. These are often restricted to specialist centres. Charitable organizations, such as Fifth Sense, have emerged as important points-of-contact for patients during the pandemic, serving as a useful resource for those affected. Altogether, these results demonstrate the multifactorial burden of persistent olfactory dysfunction and hold important implications for healthcare planning in the years to come.

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Authorship contribution

Acquisition, analysis, or interpretation of data: ML, JL, NC, DG, DC, NHT, KJ, RG, JR, CW, AT, RA, SK, RLB, CHY, TAT, JCM, JW, RB, JB, MH, MA, FCH, RC, JVN, PHH, ZMP, SP, NE, BNK, SJ, CH, CP, VJL

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Conflict of interest

The authors declare no relevant COIs.

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SUPPLEMENTARY MATERIAL

Supplementary methods

Further background

At the beginning of the COVID-19 pandemic, our group was one of the first to report Covid-19-associated smell loss in health care workers ⁽⁴⁾ and we started to plan the COVANOS UK trial ⁽⁹⁾. For this purpose, and in view of the fact that many currently used questionnaires were not applicable to the lockdown situation during the pandemic setting (e.g. asking questions whether individuals were still enjoying going out to restaurants, etc.), we reviewed questionnaires and selected a set of questions on olfactory dysfunction, which we called 'Smell-Qx'. We piloted these in the COVANOS UK trial ⁽⁹⁾ and in the presented UK-wide study. The Smell-Qx questionnaire is currently undergoing further validation. Smell-Qx items used for the COVANOS UK trial, and the presented UK wide study are presented in Supplemental Table 1.

Survey method

The Smell-Qx assessment tool was used to obtain fully anonymised data on a gender and age-matched sample of adults in the United Kingdom between 10th November and 15th November 2021. This was accomplished in a step-wise approach where the survey was distributed in stages, where, at the end of each, age and gender rates were assessed to ensure a final cohort, which was well balanced (Supplemental Table 2). In addition to this, the survey was distributed to responders in England, Scotland, Wales and Northern Ireland to ensure wide geographical distribution of survey responses. The survey was completely anonymous and delivered electronically to participants in a pre-registered database via an open call (information provided and title of the survey, 'UK Awareness and Public Health Survey', did not include any information on smell loss or Covid-19 to avoid any response bias). The study was exempt from IRB on the basis that data collection was fully anonymised and no vulnerable participants were involved (a confirmation number was provided by Stanford University; reference IRB no. vb 59838) and according to previous advice from Harrow NHS REC and UCL REC.

Statistical analysis

Participant demographics and history are reported as descriptive statistics, with frequencies, means and standard deviations presented. Further extrapolations to the UK population were done using the proportional test with R version 3.6.2, with proportions and 95% confidence intervals presented.

Limitations

Although aiming to minimise any biases, the potential for recall bias is inherent to the type of this study, as it relies on self-reported outcomes, with a long duration between the experienced smell dysfunction and reporting in some cases. Furthermore, it was not feasible for participants to also undertake psychophysical testing due to the large number of participants (n > 1000) and the design of the study. Moreover, there is a possibility that a small proportion of participants lost their sense of smell due to other causes, as confirmation of COVID-19 status at the time of smell loss was beyond the scope of the present study. Nevertheless, we believe that this proportion is very low in comparison to smell dysfunction due to COVID-19 amidst this global pandemic, and likely not to have had a significant impact on the findings, given the other recent prevalence estimates published, the large sample size and substantial prevalence estimates observed. Regarding age and gender, we ensured a balanced distribution across all age groups and across gender to obtain a highly representative sample of the UK population (The Sex Ratio in the UK in 2021 was 97.75 males per 100 females) and we have also worked hard on including participants from all UK countries and ethnicities to obtain a sample as representative of the UK population as possible. In conclusion, despite some limitations, our results underscore the significant burden of olfactory dysfunction during the COVID-19 pandemic and highlight the long-term challenges and the need for urgent clinical trials to address this unmet clinical need.

Supplemental Table 1. Smell-Qx items.

Item	Question
Smell Rating	How would you rate your sense of smell today (0 being completely lost/no sense of smell, 10 being a completely normal sense of smell)?
Taste Rating	How would you rate your perception of taste (salt/sweet/sour/bitter/savoury) today (0 being completely lost/no percep- tion of taste, 10 being a completely normal perception of taste)?
Social	Has the loss of smell affected you socially? (i.e. in your work and personal life)
Social Q1	The changes in my sense of smell make me feel isolated.
Social Q2	Because of the changes in my sense of smell, I have problems with taking part in activities of daily life.
Social Q3	The changes in my sense of smell make me feel angry.
Eating	Has the loss of smell affected your eating habits?
Eating Q1	Because of the changes in my sense of smell, I cook less often than I used to (or visit restaurants less often than I used to).
Eating Q2	Because of the changes in my sense of smell, I don't enjoy drinks or food as much as I used to.
Eating Q3	Because of the changes in my sense of smell, I eat less than I used to or more often than I used to.
Anxiety	Has the loss of smell affected your anxiety levels?
Anxiety Q1	Because of the changes in my sense of smell, I feel more anxious than I used to feel.
Anxiety Q2	Because of the changes in my sense of smell, I feel more socially isolated.
Anxiety Q3	Because of the changes in my sense of smell, I have to try harder to relax.
Annoyance	To what degree is the loss of smell annoying to you?
Annoyance Q1	I am worried that I will never get used to the changes in my sense of smell.
Annoyance Q2	The change in my sense of smell annoys me when I am eating.

Supplemental Table 2. Demographics of UK sample, N = 1160.

		N	%
Age	18-24	164	14.1%
	25-34	165	14.2%
	35-44	174	15.0%
	45-54	169	14.6%
	55-64	167	14.4%
	65-74	166	14.3%
	75 or older	155	13.4%
Gender	Female	580	50.0%
	Male	578	49.8%
	Non-binary	2	0.2%
Education	Less than high school	25	2.2%
	Some high school	44	3.8%
	GCSEs or equivalent	275	23.7%
	A-levels or equivalent	223	19.2%
	Higher educational qualification (below degree level)	106	9.1%
	Vocational qualifications (e.g. NVQ)	137	11.8%
	Degree level (e.g BA, BSc)	251	21.6%
	Post-graduate degree	99	8.5%
Ethnicity	Other (please specify):	7	0.6%
	White	1028	88.6%
	Mixed Race	21	1.8%
	Asian or Asian British	51	4.4%
	Black or Black British	38	3.3%
	Chinese or Chinese British	10	0.9%
	Unknown	1	0.1%
	Prefer not to say	4	0.3%
Geography	England	981	84.6%
	Scotland	89	7.7%
	Wales	59	5.1%
	Northern Ireland	30	2.6%
Smoking History	Current smoker or chewing tobacco user (less than or equal to 20 cigarettes/day)	251	21.6%
	Current smoker or chewing tobacco user (21-35 cigarettes/day)	64	5.5%
	Current smoker or chewing tobacco user (More than 35 cigarettes/day)	26	2.2%
	Ex-smoker or previous tobacco chewing	319	27.5%
	Never smoked/chewed tobacco	500	43.1%
Alcohol History	I never drink alcohol	244	21.0%
Aconorristory	1-14	753	64.9%
	15-21	104	9.0%
	Over 21	59	5.1%
	Total	1160	100.0%
Do you have more than 4 drinks (units not		1100	100.0%
Do you have more than 4 drinks/units per day? (1 unit is approximately equal to a 1/2 pint of beer or a small glass of wine).	Yes	262	22.6%
	No	798	68.8%
	Not applicable	100	8.6%