Seroprevalence of SARS-CoV-2 antibodies in people with an acute loss in their sense of smell and/or taste in a community-based population in London, UK: An observational cohort study

Janine Makaronidis1,2,3, Jessica Mok1,2,3, Nyaladzi Balogun1,2,3, Cormac G. Magee1,2,3, Rumana Z. Omar4, Alisia Carnemolla1,3, Rachel L. Batterham1,2,3*

1 UCL Centre for Obesity Research, Division of Medicine, University College London, London, United Kingdom, 2 Bariatric Centre for Weight Management and Metabolic Surgery, University College London Hospital, London, United Kingdom, 3 National Institute of Health Research, UCLH Biomedical Research Centre, London, United Kingdom, 4 Department of Statistical Science, University College London, London, United Kingdom

* r.batterham@ucl.ac.uk

Abstract

Background

Loss of smell and taste are commonly reported symptoms associated with coronavirus disease 2019 (COVID-19); however, the seroprevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies in people with acute loss of smell and/or taste is unknown. The study aimed to determine the seroprevalence of SARS-CoV-2 antibodies in a community-based population with acute loss of smell and/or taste and to compare the frequency of COVID-19 associated symptoms in participants with and without SARS-CoV-2 antibodies. It also evaluated whether smell or taste loss are indicative of COVID-19 infection.

Methods and findings

Text messages, sent via primary care centers in London, United Kingdom, invited people with loss of smell and/or taste in the preceding month, to participate. Recruitment took place between 23 April 2020 and 14 May 2020. A total of 590 participants enrolled via a web-based platform and responded to questions about loss of smell and taste and other COVID-19–related symptoms. Mean age was 39.4 years (SD ± 12.0) and 69.1% (n = 392) of participants were female. A total of 567 (96.1%) had a telemedicine consultation during which their COVID-19–related symptoms were verified and a lateral flow immunoassay test that detected SARS-CoV-2 immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies was undertaken under medical supervision. A total of 77.6% of 567 participants with acute smell and/or taste loss had SARS-CoV-2 antibodies; of these, 39.8% (n = 175) had neither cough nor fever. New loss of smell was more prevalent in participants with SARS-CoV-2
antibodies, compared with those without antibodies (93.4% versus 78.7%, \( p < 0.001 \)), whereas taste loss was equally prevalent (90.2% versus 89.0%, \( p = 0.738 \)). Seropositivity for SARS-CoV-2 was 3 times more likely in participants with smell loss (OR 2.86; 95% CI 1.27–6.36; \( p < 0.001 \)) compared with those with taste loss. The limitations of this study are the lack of a general population control group, the self-reported nature of the smell and taste changes, and the fact our methodology does not take into account the possibility that a population subset may not seroconvert to develop SARS-CoV-2 antibodies post-COVID-19.

### Conclusions

Our findings suggest that recent loss of smell is a highly specific COVID-19 symptom and should be considered more generally in guiding case isolation, testing, and treatment of COVID-19.

### Trials registration

ClinicalTrials.gov NCT04377815

---

**Author summary**

**Why was this study done?**

- Coronavirus disease 2019 (COVID-19), an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, was declared a pandemic in March 2020.

- COVID-19 can cause loss or reduced ability to smell (anosmia) or taste, without cough or fever, but few countries recommend self-isolation and testing on the basis of smell or taste changes alone.

- This study aimed to find out the proportion of people who have developed SARS-CoV-2 antibodies in a community-based population with a newly developed loss in their sense of smell and/or taste in London, UK.

**What did the researchers do and find?**

- Text messages were sent out to people registered with a number of primary care centers in London inviting people with a new loss in their sense of smell and/or taste to participate.

- Recruited participants completed online questionnaires regarding demographics, their loss of smell and/or taste, and other COVID-19 symptoms, before they had a telemedicine consultation with a healthcare professional who confirmed the history of their symptoms and supervised a test to find out if they had SARS-CoV-2 antibodies.

- A total of 78% of 567 people with smell and/or taste loss had SARS-CoV-2 antibodies; of these, 40% had neither cough nor fever, and participants with loss of smell were 3 times more to have SARS-CoV-2 antibodies, compared with those with loss of taste.
What do these findings mean?

- Loss of smell is a highly specific symptom of COVID-19.
- COVID-19 can present with loss of smell and/or taste without cough or fever.
- Loss of smell should be taken into consideration in case isolation, testing, and treatment strategies for COVID-19.

Introduction

Coronavirus disease 2019 (COVID-19) is an acute infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has spread exponentially, with 27,417,497 cases and 894,241 deaths reported from 216 countries by 9 September 2020 [1]. In the absence of a vaccine and disease-specific treatments, strategies to contain the pandemic are focused on rapid case isolation and testing. Although originally described as a primarily respiratory disease, reports of COVID-19 presenting with other multisystem symptoms, including loss of smell and taste, emerged rapidly. Understanding the symptomatology of COVID-19 and the predictive value of symptoms is crucial for containment strategies. As lockdown policies ease globally, early recognition of COVID-19 symptoms by the public together with rapid self-isolation and testing will be of vital importance to limit disease spread.

Reports linking loss of the sense of smell and/or taste to COVID-19 emerged in March 2020 [2–4]. SARS-CoV-2 enters the human body via the angiotensin-converting enzyme-2 (ACE-2) receptor, highly expressed in the nasal epithelium [5]. Consequent inflammatory changes in the olfactory neuroepithelium could disrupt olfactory neuron function, leading to smell loss [6,7]. Thus, from a pathophysiological perspective, it is logical for COVID-19 to impact smell [5,6]. Smell and taste are highly interlinked, with an element of taste (flavor) perception mediated through retronasal olfaction; hence, loss of smell results in taste changes [6]. However, within the oral cavity, ACE-2 is highly expressed on tongue epithelial mucosal cells [5], raising the possibility that taste loss results from a direct effect of SARS-CoV-2 on the tongue and that taste loss alone could occur in the absence of smell loss.

Available data suggest a prevalence of smell and/or taste loss in the range of 31%–85% in COVID-19 patients [8–10]. In a prospective epidemiological study, 85.6% and 88.0% of patients with a polymerase chain reaction (PCR)-confirmed COVID-19 diagnosis reported a loss of their sense of smell and taste, respectively [9].

The largest data set of potential COVID-19 related symptoms stems from a web-based app that collected self-reported symptoms from 2,618,862 users in the United Kingdom (UK) and the United States (US). This included the question “Do you have a loss of smell/taste?”. The authors reported a strong association between loss of smell/taste and a diagnosis of COVID-19, and as a consequence, loss of smell/taste are now recognized presentations of COVID-19 in the UK [11,12]. Their methodology did not, however, enable them to differentiate between smell and taste loss [12,13].

The importance of acute loss of smell or taste, in isolation or combination, as a predictor of COVID-19 in a population presenting with chemosensory symptoms is unknown. Currently, recommendations for self-isolation and testing based upon acute loss of smell/taste have only been adopted by a limited number of countries; the majority are focused on fever and respiratory symptoms (Table 1). We therefore set out to quantify the seroprevalence of SARS-CoV-2...
specific antibodies in a community-based cohort with a new loss of their sense of smell and/or taste during the COVID-19 outbreak in London, UK. Additionally, we compared the effect of isolated loss of smell and isolated loss of taste separately and then in combination and investigated whether new smell and/or taste loss are indicative of COVID-19 in our study population.

### Table 1. Recognition of smell and/or taste loss as symptoms of COVID-19 in the 30 countries with the highest number of reported cases globally.

| Country                  | Cases¹ | Deaths¹ | Recognition of smell/taste loss as COVID-19 symptoms | Reference² |
|--------------------------|--------|---------|------------------------------------------------------|------------|
| United States of America | 6,328,099 | 186,699 | Yes | [https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html](https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html) |
| India                    | 4,370,128 | 73,890 | No | [https://www.mygov.in/covid-19](https://www.mygov.in/covid-19) |
| Brazil                   | 4,162,073 | 127,464 | Yes | [https://coronavirus.saude.gov.br/](https://coronavirus.saude.gov.br/) |
| Russia                   | 1,037,526 | 18,080 | No | [https://covid19.rosminzdrav.ru/](https://covid19.rosminzdrav.ru/) |
| Peru                     | 691,575 | 29,976 | No | [https://www.gob.pe/8665-sintomas-del-coronavirus-conocer-si-puedo-haber-contraido-el-covid-19](https://www.gob.pe/8665-sintomas-del-coronavirus-conocer-si-puedo-haber-contraido-el-covid-19) |
| Colombia                 | 679,181 | 21,813 | No | [https://d2jsqrio60m94k.cloudfront.net/](https://d2jsqrio60m94k.cloudfront.net/) |
| Mexico                   | 642,860 | 64,484 | No | [https://coronavirus.gob.mx/](https://coronavirus.gob.mx/) |
| South Africa             | 640,441 | 15,086 | No | [https://sacoronavirus.co.za/](https://sacoronavirus.co.za/) |
| Spain                    | 534,513 | 29,594 | Yes | [https://www.mscbs.gob.es/profesionales/saludPublica/ccayalertas/Actual/nCov-China/img/COVID19_sintomas.jpg](https://www.mscbs.gob.es/profesionales/saludPublica/ccayalertas/Actual/nCov-China/img/COVID19_sintomas.jpg) |
| Argentina                | 500,034 | 10,405 | Yes | [https://www.argentina.gob.ar/coronavirus/glosario/caso-sospechoso](https://www.argentina.gob.ar/coronavirus/glosario/caso-sospechoso) |
| Chile                    | 425,034 | 11,682 | No | [https://www.minsal.cl/nuevo-coronavirus-2019-ncov/](https://www.minsal.cl/nuevo-coronavirus-2019-ncov/) |
| Iran                     | 393,425 | 22,669 | No | [https://test.corona.ir/coronaTest](https://test.corona.ir/coronaTest) |
| France                   | 373,718 | 30,770 | Yes | [https://www.gouvernement.fr/info-coronavirus/comprendre-la-covid-19](https://www.gouvernement.fr/info-coronavirus/comprendre-la-covid-19) |
| United Kingdom           | 354,934 | 41,675 | Yes | [https://www.nhs.uk/conditions/coronavirus-covid-19/check-if-you-have-coronavirus-symptoms/](https://www.nhs.uk/conditions/coronavirus-covid-19/check-if-you-have-coronavirus-symptoms/) |
| Bangladesh               | 331,078 | 4,593 | No | [https://corona.gov.bd/faq](https://corona.gov.bd/faq) |
| Saudi Arabia             | 322,237 | 4,137 | No | [https://www.moh.gov.pk/en/HealthAwareness/EducationalContent/PublicHealth/Pages/corona.aspx](https://www.moh.gov.pk/en/HealthAwareness/EducationalContent/PublicHealth/Pages/corona.aspx) |
| Pakistan                 | 299,659 | 6,359 | Yes | [http://covid.gov.pk/](http://covid.gov.pk/) |
| Turkey                   | 283,270 | 6,782 | No | [https://covid19.saglik.gov.tr/TR-66300/covid-19-nedir-.html](https://covid19.saglik.gov.tr/TR-66300/covid-19-nedir-.html) |
| Italy                    | 280,153 | 35,563 | Yes | [http://www.salute.gov.it/portale/nuovocoronavirus/dettaglioFaqNuovoCoronavirus.jsp?lingua=english&id=230#i](http://www.salute.gov.it/portale/nuovocoronavirus/dettaglioFaqNuovoCoronavirus.jsp?lingua=english&id=230#i) |
| Iraq                     | 269,578 | 7,657 | No | [https://moh.gov.iq/](https://moh.gov.iq/) |
| Germany                  | 255,626 | 9,342 | Yes | [https://www.zusammengegencorona.de/en/inform/recognize-symptoms/#faqitem=5750383b-e61b-5792-afa6-f36cf48b2a7f](https://www.zusammengegencorona.de/en/inform/recognize-symptoms/#faqitem=5750383b-e61b-5792-afa6-f36cf48b2a7f) |
| Philippines              | 245,143 | 3,986 | Yes | [https://www.covid19.gov.ph/](https://www.covid19.gov.ph/) |
| Indonesia                | 203,342 | 8,336 | No | [https://www.kemkes.go.id/index.php?lg=LN02](https://www.kemkes.go.id/index.php?lg=LN02) |
| Ukraine                  | 146,511 | 3,034 | No | [https://covid19.gov.ua/en](https://covid19.gov.ua/en) |
| Israel                   | 138,719 | 1,040 | Yes | [https://govextra.gov.il/ministry-of-health/corona/corona-virus-en/corona-symptoms-en/](https://govextra.gov.il/ministry-of-health/corona/corona-virus-en/corona-symptoms-en/) |
| Canada                   | 135,757 | 9,203 | Yes | [https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/symptoms.html](https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/symptoms.html) |
| Bolivia                  | 122,308 | 7,097 | No | [https://www.boliviasegura.gob.bo/covid-19.php](https://www.boliviasegura.gob.bo/covid-19.php) |
| Qatar                    | 120,579 | 205 | No | [https://www.moph.gov.qa/english/Pages/Coronavirus2019FAQs.aspx](https://www.moph.gov.qa/english/Pages/Coronavirus2019FAQs.aspx) |
| Ecuador                  | 110,757 | 10,627 | No | [https://www.salud.gob.ec/coronavirus-covid-19/](https://www.salud.gob.ec/coronavirus-covid-19/) |
| Kazakhstan               | 106,498 | 1,634 | No | [https://www.gov.kz/memleket/entities/dsm/activities/6626?lang=en&parentId=6625](https://www.gov.kz/memleket/entities/dsm/activities/6626?lang=en&parentId=6625) |

¹ Reported cases as per John Hopkins University of Medicine Coronavirus Resource Centre [14], accessed 9 September 2020.

² Accessed 9 September 2020.

COVID-19, coronavirus disease 2019.

[https://doi.org/10.1371/journal.pmed.1003358.t001](https://doi.org/10.1371/journal.pmed.1003358.t001)
Methods

Study design

The study was conducted in London, UK, and recruited between 23 April 2020 and 14 May 2020 at a time when loss of smell and/or taste were not recognized as COVID-19 symptoms. Recruitment was timed to capture people who experienced symptoms during the peak of the COVID-19 outbreak in London. Antibody testing was delivered using a telemedicine consultation. This approach was chosen to capture positive cases without the limitations of the time window restrictions of PCR and to enable testing and participation without face-to-face contact, reducing the infection risk to both participants and researchers.

Adults registered with 4 participating primary care centers in London were sent text messages to their mobile telephones inviting those who experienced a new loss of their sense of smell and/or taste in the preceding month to participate. The text message read: "Has your sense of smell or taste reduced in the last month? If yes and you’d like to be part of a COVID-19 research study go to [link]". Participants were then directed to an online platform (hosted by Dendrite Clinical Systems) with the study information and an eligibility check. Inclusion criteria were age ≥18 years, proficiency in written and spoken English, and access to video-calling. Exclusion criteria were any preexisting loss of the sense of smell or taste of longer than a month’s duration. Participation was voluntary, and written informed consent was obtained electronically. Enrolled participants completed an online questionnaire (see S1 Text), capturing their sex, age, ethnicity, smoking status, previous COVID-19 testing, questions about their smell and taste symptoms, as well as other symptoms of COVID-19.

Participants were subsequently sent a point-of-care testing kit detecting the presence of immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies to SARS-CoV-2. A healthcare professional arranged a telemedicine video consultation with each participant. At the beginning of the consultation, they asked the participant to describe the changes that they had experienced in their sense of smell and/or taste. Participants were then supervised in performing the antibody test using a finger-prick sample of whole blood, and their results were discussed with them. Photographs of the test cassette were obtained and reviewed independently by a second healthcare professional to confirm the result. Participants with a prior COVID-19 PCR test result were offered antibody testing irrespective of their result. Testing was carried out between 24 April 2020 and 22 May 2020.

The antibody test used detects the presence of IgM and IgG antibodies to SARS-CoV-2 via lateral flow immunoassay (Wuhan UNscience Biotechnology Co., Ltd. COVID-19 Antibody IgM/IgG) [15]. As part of the test’s validation, 1,585 cases were tested: 421 (positive) clinically confirmed (including PCR) COVID-19 patients and 1,164 controls. These showed that the product has a relative sensitivity of 98.8% (95% CI 97.3%–99.6%) and a relative specificity of 98.0% (95% CI 97.15%–98.7%) [15].

The study received ethical approval from the National Health Service Queen’s Square Research Ethics Committee (IRAS Project ID 282668, ClinicalTrials.gov: NCT04377815) and was conducted in line with the declaration of Helsinki and Good Clinical Practice.

Statistical analysis

A sample size calculation was undertaken in order to determine the study’s recruitment target, using the information on reported symptoms from the web-based COVID symptom study app developed by King’s College London and symptom reporting between the 24–29 March 2020 [16]. To calculate an estimate of 50% (95% CI 45%–55%) as the proportion who would test positive amongst those who reported a change in smell or taste, we needed 385 participants in the study [17]. Assuming a 15% attrition, we needed 453 participants in the study. The
recruitment target was set to 500 participants to allow for larger attrition and increase accuracy. This was exceeded to improve the accuracy of the data and enable additional analyses to further describe the pattern of loss of smell and/or taste in the study populations with and without SARS-CoV-2 antibodies. Data were analyzed using GraphPad Prism version 8 (https://www.graphpad.com/scientific-software/prism/) and STATA version 15 (https://www.stata-uk.com/). Data analysis was planned on completion of SARS-CoV-2 antibody testing. There was no prospective study protocol or analysis plan, and no data-driven changes to analyses took place. Descriptive analyses included the calculation of means (plus standard deviation [SD]) for continuous variables and numbers (n, with percentages) for categorical variables. Chi-squared tests were performed on categorical data as part of the secondary analysis. The significance level was adjusted for multiple comparisons by applying a Bonferroni correction when comparing symptoms other than loss of smell or taste. Logistic regression analysis was performed to estimate the association between loss of smell and/or taste and the presence of SARS-CoV-2 antibodies.

Results

Study population

A total of 33,650 text messages were sent out to people registered with 4 participating primary care centers. A total of 650 participants completed the registration process; 60 participants were ineligible and excluded. The participant flowchart [18] is illustrated in Fig 1. Out of 590 eligible participants, 567 (96.1%) had a SARS-CoV-2 antibody test. The mean participant age was 39.4 years (±12.0); 69.1% (n = 392) were female, 30.5% (n = 173) male, and 0.4% (n = 2) of other sex. A total of (n = 311) 79.3% of female participants had a positive test result, compared with 73.4% (n = 127) of male participants (p = 0.120).

Frequency of loss of sense of smell and taste in the study population

Among the 590 participants who completed questionnaires, 90.0% (n = 531) reported loss of their sense of smell. This was described as complete smell loss by 69.9% (n = 371) and as partial smell loss by 30.1% (n = 160). No smell loss was reported in 10.0% (n = 59). A total of 89.8% (n = 530) of participants reported loss of their sense of taste. This was described as complete by 47.4% (n = 251) and as partial by 52.6% (n = 279). No taste loss was reported in 10.1% (n = 60) of participants. Combined loss of smell and taste was reported by 80.0% (n = 472).

Seroprevalence of SARS-CoV-2 antibodies in people with acute loss of their sense of smell and/or taste

Of 590 eligible participants, 567 participants (96.1%) underwent SARS-CoV-2 testing. A total of 77.4% (n = 439) had a positive SARS-CoV-2 result (IgG [n = 303], IgG and IgM [n = 122], and IgM [n = 14]). One further participant was included with a positive PCR result (77.6% [n = 440] positive). Participants with and without SARS-CoV-2 antibodies were comparable in terms of age, sex, ethnicity, smoking status, and frequency of other reported symptoms (Table 2). Importantly, 52.1% (n = 229) of the participants with SARS-CoV-2 antibodies had no history of cough, and 39.8% (n = 175) had neither a fever nor a cough.

Frequency of loss of smell and taste in participants with and without SARS-CoV-2 antibodies

Among the participants who underwent SARS-CoV-2 antibody testing (n = 567), 89.9% (n = 510) reported loss of their sense of smell and 89.7% (n = 509) taste loss. The frequency of reported loss of smell and taste in participants with and without SARS-CoV-2 antibodies are
Fig 1. Participant flowchart illustrating participant flow through the recruitment process. Participant flowchart illustrating the participant flow through the recruitment process, from text invitations, through eligibility screening, questionnaire completion and testing [18]. Figures presented as % with total number (n). Age presented as mean age in years with standard deviation.

https://doi.org/10.1371/journal.pmed.1003358.g001
presented in Fig 2 and Table 3. A total of 80.4% of participants with smell loss and 86.0% (n = 307) of those with complete smell loss had a positive test result. A total of 77.8% of participants with taste loss and 86.0% of those with complete taste loss (n = 209) had a positive test result. Extracts from questionnaire responses from participants with positive SARS-CoV-2 antibodies describing their loss of smell and taste can be seen in Table 4.

Loss of smell predicts positive SARS-CoV-2 antibody status in a community-based population with an acute loss of their sense of smell and/or taste

Logistic regression was used to explore the relative importance of loss of smell and loss of taste, alone and in combination, as symptoms of COVID-19 infection, assessed by the presence of
SARS-CoV-2 antibodies in our study population with acute loss of smell and taste. Isolated loss of smell and combined loss in the sense of smell and taste were compared with an isolated loss of taste (Table 5).

Participants with loss of smell alone were nearly 3 times more likely than participants with isolated taste loss to have SARS-CoV-2 antibodies (OR 2.86, 95% CI 1.37–6.36; \( p < 0.001 \)), and participants with combined loss of smell and taste were 4 times more likely to have SARS-CoV-2 antibodies (OR 3.98, 95% CI 2.24–7.08; \( p < 0.001 \)). These findings remained unchanged after adjusting for sex, age, ethnicity, and smoking status.

Discussion

In this community-based cohort study, undertaken during the peak of the COVID-19 outbreak in London, the seroprevalence of SARS-CoV-2 antibodies in participants with new onset loss of sense of smell and/or taste, was 77.6%. A total of 39.8% (n = 175) of the study population with acute loss of smell and taste. Isolated loss of smell and combined loss in the sense of smell and taste were compared with an isolated loss of taste (Table 5).

Participants with loss of smell alone were nearly 3 times more likely than participants with isolated taste loss to have SARS-CoV-2 antibodies (OR 2.86, 95% CI 1.37–6.36; \( p < 0.001 \)), and participants with combined loss of smell and taste were 4 times more likely to have SARS-CoV-2 antibodies (OR 3.98, 95% CI 2.24–7.08; \( p < 0.001 \)). These findings remained unchanged after adjusting for sex, age, ethnicity, and smoking status.
participants reported neither cough nor fever. In our study cohort, loss of smell was more prevalent in participants with SARS-CoV-2 antibodies compared with those without antibodies (93.4% versus 78.7%, \( p < 0.001 \)), whereas taste loss was equally prevalent (90.2% versus 89.0%, \( p = 0.738 \)). Furthermore, participants with acute smell loss were 3 times more likely to be seropositive for SARS-CoV-2 (OR 2.86; 95% CI 1.27–6.36; \( p < 0.001 \)) compared with those with taste loss.

Loss of smell and taste were evaluated as separate symptoms, which enabled a direct comparison of their relationship to SARS-CoV-2 antibodies. Among participants, loss of sense of smell and/or taste was more prevalent in those with SARS-CoV-2 antibodies compared with those without antibodies. Table 3 details the reported loss of sense of smell and/or taste in participants with positive and negative SARS-CoV-2 antibodies.

**Table 3. Reported loss of sense of smell and/or taste in participants with positive and negative SARS-CoV-2 antibodies.**

| Sense of smell                        | SARS-CoV-2 antibody positive \( (n = 440) \) | SARS-CoV-2 antibody negative \( (n = 127) \) | \( p \)-value |
|--------------------------------------|---------------------------------------------|---------------------------------------------|-------------|
| Loss of the sense of smell (complete and partial) | 93.4% \( (n = 411) \) | 78.7% \( (n = 100) \) | \( p < 0.001 \) |
| Complete loss of smell               | 69.8% \( (n = 307) \) | 39.4% \( (n = 50) \) | \( p < 0.001 \) |
| Partial loss of smell                | 23.6% \( (n = 104) \) | 39.4% \( (n = 50) \) | \( p < 0.001 \) |

| Sense of taste                        | SARS-CoV-2 antibody positive \( (n = 397) \) | SARS-CoV-2 antibody negative \( (n = 113) \) | \( p \)-value |
|--------------------------------------|---------------------------------------------|---------------------------------------------|-------------|
| Loss of the sense of taste (complete and partial) | 90.2% \( (n = 397) \) | 89.0% \( (n = 113) \) | \( p = 0.738 \) |
| Complete loss of taste               | 47.5% \( (n = 209) \) | 26.8% \( (n = 34) \) | \( p < 0.001 \) |
| Partial loss of taste                | 42.7% \( (n = 188) \) | 62.2% \( (n = 79) \) | \( p < 0.001 \) |

| Combined loss of sense of smell and taste | SARS-CoV-2 antibody positive \( (n = 368) \) | SARS-CoV-2 antibody negative \( (n = 86) \) | \( p \)-value |
|----------------------------------------|---------------------------------------------|---------------------------------------------|-------------|
| Loss of sense of smell and taste (complete and partial) | 83.6% \( (n = 368) \) | 67.7% \( (n = 86) \) | \( p < 0.001 \) |
| Complete loss of both smell and taste | 50.5% \( (n = 186) \) | 20.5% \( (n = 26) \) | \( p < 0.001 \) |
| Complete loss of smell, partial loss of taste | 25.6% \( (n = 94) \) | 15.7% \( (n = 20) \) | \( p = 0.060 \) |
| Partial loss of smell, complete loss of taste | 4.6% \( (n = 17) \) | 3.9% \( (n = 5) \) | \( p = 0.642 \) |
| Partial loss of both smell and taste | 19.3% \( (n = 71) \) | 27.6% \( (n = 35) \) | \( p < 0.001 \) |

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

**Table 4. Extracts from participants’ descriptions of their loss of smell and/or taste taken from questionnaire responses from participants with positive SARS-CoV-2 antibodies.**

| Examples of descriptions of participants’ loss of their sense of smell | Examples of descriptions of participants’ loss of their sense of taste |
|---------------------------------------------------------------------|---------------------------------------------------------------------|
| “Sense of smell vanished, couldn’t smell anything from garlic to bleach to aromatherapy oils.” | “I could not taste even the spiciest of foods or sweetest. I tried different chillies too but nothing had a taste.” |
| “I lost my sense of smell but did not have a blocked nose which was very strange. I have to say I couldn’t smell anything for roughly 14 days.” | “I could not taste anything. Including a large teaspoon of hot sauce.” |
| “I couldn’t smell anything. The neighbours apartment caught on fire one night and if it wasn’t for my flatmate (or the fire brigade later) I wouldn’t have realised.” | “I could taste absolutely nothing. I tested various food and drink but absolutely nothing. I did not have a cold.” |
| “It was as if the nerves had fried. My nose was not blocked, I just suddenly was unable to smell anything.” | “I couldn’t taste chillies or any food. Drinks were just liquid.” |
| “Zero smell... not even strong things like frying garlic and perfumes. It was unlike when I have had similar experiences with colds because my nasal passages were not blocked and I could breathe normally.” | “I could taste absolutely nothing. I tested various food and drink but absolutely nothing.” |

SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
smell, but not taste, was significantly more prevalent in participants with SARS-CoV-2 antibodies, compared with those without. Moreover, within our study cohort with smell and taste loss, participants with loss of smell alone were 3 times more likely than participants with loss of taste alone to have SARS-CoV-2 antibodies. Participants who reported both a loss of smell and taste were 4 times more likely to have SARS-CoV-2 antibodies compared with participants with isolated taste loss. These findings suggest that a loss of smell is a highly specific symptom of COVID-19, in contrast to a loss of taste, despite their comparable frequency. Sense of taste and smell are interlinked, with retronasal olfaction being a major component of taste (flavor); thus, it is plausible that the loss of taste reported by participants who also report loss of smell reflects impaired retronasal olfaction and hence, represents loss of flavor perception, as a consequence of smell loss. Interestingly, 6.6% of participants with SARS-CoV-2 antibodies reported an isolated loss in their sense of taste, in the absence of smell loss, suggesting the presence of a rarer, alternative pathophysiological mechanism targeting gustatory function in isolation. Lingual mucosal epithelium ACE2 could provide a plausible explanation [19].

Globally, as populations are released from lockdown, early identification by the public of COVID-19 symptoms and rapid self-isolation and testing will be of vital importance to limit disease spread. Currently, as highlighted in Table 1, a large number of countries are not advising that loss of smell and/or taste are COVID-19 symptoms. This could have potentially devastating consequences. Importantly, 40% of our seropositive cohort reported neither fever nor cough. Similarly, a recent UK-based survey reported that cough and/or fever were only present in 51% of people with COVID-19 [3]. Counterintuitively, people with minor symptoms, such as isolated smell loss, who remain systemically well pose the highest public health threat.

SARS-CoV-2 specific antibody testing performed via telemedicine consultation enabled us to confirm participants’ reported symptomatology and verify their identity and test results, which adds to the quality of our data. Although viral nucleic acid detection using real-time PCR remains the gold standard for diagnosis, there are several limitations to this method, including a high processing time, labor intensity, and a high false negative rate [20–22]. Furthermore, there is a narrow window to perform testing before the virus becomes undetectable by PCR [23]. In contrast, seroconversion to IgM and IgG antibodies occurs as early as day 4 [24]. The Center for Disease Control and Prevention recommends antibody testing for diagnostic purposes using high specificity kits to minimize false positives [22]. Given the very high prevalence in our study cohort and the specificity of our chosen test, we could expect a high positive predictive value [22]. The sensitivity of our antibody test is 98.8%. These data were generated in people who were PCR positive, suggesting a very high seroconversion rate.

Table 5. Logistic regression exploring the seroprevalence of SARS-CoV-2 antibodies in people with loss in the sense of smell in isolation, loss in the sense of taste in isolation, and a loss both in the sense of smell and taste in combination.

| Condition                             | Odds ratio (95% CI) (unadjusted) | p-value | Odds ratio (95% CI) (adjusted) | p-value |
|---------------------------------------|----------------------------------|---------|--------------------------------|---------|
| Loss in the sense of taste only (baseline) | 1.00                             |         | Loss in the sense of taste only | 2.72 (95% CI 1.21–6.14) | 0.016 |
| Loss in the sense of smell only       | 2.86 (95% CI 1.27–6.36)          | <0.001  | Combined loss in the sense of smell and taste | 4.11 (95% CI 2.29–7.37) | <0.001 |
| Combined loss in the sense of smell and taste | 3.98 (95% CI 2.24–7.08)          | <0.001  | Constant                       | 2.91 (0.75–11.35) | 0.123 |
| Constant                              | 1.07 (95% CI 0.64–1.81)          | 0.789   |                                |         |

1 For sex, age, ethnicity, and smoking status.
CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

https://doi.org/10.1371/journal.pmed.1003358.t005
However, evidence with regard to the rate of patients with confirmed COVID-19, who seroconvert to generate an antibody response remains limited. Current data suggest seroconversion rates of up to 100% in hospital patients, which may be related to disease severity but also time from symptom onset [20,25,26]. Although a recent study demonstrated a 99.4% seroconversion rate in hospital staff following a mild COVID-19 illness, in which 47.5% of the study population reported anosmia [27], no data are available yet reporting the rate of seroconversion in confirmed COVID-19 patients with anosmia.

Limitations
The main limitation of our study is the lack of a general population control group without loss of smell and/or taste. The study only recruited participants who reported acute smell and/or taste loss. Although this enabled us to study this presentation and its relevance to COVID-19, this also presents a degree of selection bias; hence, our findings refer to a population subset with new acute loss of smell and/or taste. In addition, although we used a questionnaire to assess COVID-19 symptoms and subsequently validated participants’ responses during the telemedicine interview, we did not undertake any objective assessments of smell or taste. However, from a COVID-19 disease containment perspective, the general public are unlikely to have rapid access to formal objective smell/taste testing. Moreover, our data show a high seroprevalence of SARS-CoV-2 antibodies in people who recognized a loss of their sense of smell. Furthermore, as our study relied on antibody testing via telemedicine, we were unable to account for COVID-19 patients who may not have seroconverted to develop IgG or IgM antibodies, which may lead to our findings underestimating the prevalence of COVID-19 in this population. However, our findings suggest that a key public health message is that people who notice a loss in their ability to smell everyday house-hold odors such as garlic, onions, coffee, and perfumes should self-isolate and seek PCR testing.

The majority of our participants were female; this finding may reflect previous findings that females have a higher frequency of loss of smell and/or taste with COVID-19 than males [3,9,28]. We found no differences in sex, but this may reflect the lower number of males recruited.

Conclusions
In a community-based population, the vast majority of participants with new onset loss of smell were seropositive for SARS-CoV-2 antibodies. Acute loss of sense of smell needs to be considered globally as a criterion for self-isolation, testing, and contact tracing in order to contain the spread of COVID-19.

Supporting information
S1 STROBE checklist. STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.
(DOCX)

S1 Text. Questionnaires used to capture demographics (part 1) and symptoms in study participants (part 2).
(DOCX)

S1 Data. Study data set.
(XLSX)
Acknowledgments
We thank Jed Wingrove for designing the participant instruction leaflet and Charalampos Markakis for his help in the organisation and running of the study. We also thank the Hampstead Group Practice, The Northern Medical Centre, the James Wigg Practice, and the Queen’s Crescent Practice for their collaboration in sending out the invitation text messages to their registered patients.

Author Contributions
Conceptualization: Janine Makaronidis, Alisia Carnemolla, Rachel L. Batterham.
Data curation: Janine Makaronidis, Jessica Mok, Nyaladzi Balogun, Rachel L. Batterham.
Formal analysis: Janine Makaronidis, Jessica Mok, Rumana Z. Omar, Alisia Carnemolla, Rachel L. Batterham.
Funding acquisition: Rachel L. Batterham.
Investigation: Janine Makaronidis, Jessica Mok, Nyaladzi Balogun, Cormac G. Magee, Alisia Carnemolla, Rachel L. Batterham.
Methodology: Cormac G. Magee, Alisia Carnemolla, Rachel L. Batterham.
Project administration: Alisia Carnemolla.
Resources: Rachel L. Batterham.
Validation: Janine Makaronidis.
Writing – original draft: Janine Makaronidis, Jessica Mok, Nyaladzi Balogun, Cormac G. Magee, Rumana Z. Omar, Alisia Carnemolla, Rachel L. Batterham.
Writing – review & editing: Janine Makaronidis, Jessica Mok, Nyaladzi Balogun, Cormac G. Magee, Rumana Z. Omar, Alisia Carnemolla, Rachel L. Batterham.

References
1. WHO. Coronavirus disease (COVID-19) pandemic 2020 [Internet]. [cited 2020 9 September]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019
2. Spinato G, Fabbris C, Polesel J, Cazzador D, Borsetto D, Hopkins C, et al. Alterations in Smell or Taste in Mildly Symptomatic Outpatients With SARS-CoV-2 Infection. JAMA. 2020; 323(20):2089–90. https://doi.org/10.1001/jama.2020.6771 PMID: 32320008
3. Hopkins C, Surda P, Kumar N. Presentation of new onset anosmia during the COVID-19 pandemic. Rhinology. 2020; 58(3):295–298. https://doi.org/10.4193/Rhin20.116 PMID: 32777751.
4. Kaye R, Chang CWD, Kazahaya K, Brereton J, Denny JC 3rd. COVID-19 Anosmia Reporting Tool: Initial Findings. Otolaryngol Head Neck Surg. 2020; 163(1):132–134. Epub 2020/04/29. https://doi.org/10.1177/0194599820922992 PMID: 32340555.
5. Hou YJ, Okuda K, Edwards CE, Martinez DR, Asakura T, Dinnon KH, et al. SARS-CoV-2 Reverse Genetics Reveals a Variable Infection Gradient in the Respiratory Tract. Cell. 2020; 18(2):429–446. https://doi.org/10.1016/j.cell.2020.05.042.
6. Whitcroft KL, Hummel T. Olfactory Dysfunction in COVID-19: Diagnosis and Management. JAMA. 2020; 323(24):2512–2514. https://doi.org/10.1001/jama.2020.8391 PMID: 32432682.
7. Hwang CS. Olfactory neuropathy in severe acute respiratory syndrome: report of A case. Acta neurologica Taiwanica. 2006; 15(1):26–8. Epub 2008/04/08. PMID: 16699291.
8. Lee Y, Min P, Lee S, Kim SW. Prevalence and Duration of Acute Loss of Smell or Taste in COVID-19 Patients. J Korean Med Sci. 2020; 35(18):e174. Epub 2020/05/10. https://doi.org/10.3346/jkms.2020.35.e174 PMID: 32393370.
9. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease
10. Klopfenstein T, Kadiane-Oussou NJ, Toko L, Royer PY, Lepiller Q, Gendrin V, et al. Features of anosmia in COVID-19. Med Mal Infect. 2020; 50(5):436–439. https://doi.org/10.1016/j.medmal.2020.04.006 PMID: 32305563; PubMed Central PMCID: PMC7511233.

11. Zayet S, Klopfenstein T, Mercier J, Kadiane-Oussou NJ, Lan Cheong Wah L, Royer PY, et al. Contribution of anosmia and dysgeusia for diagnostic of COVID-19 in outpatients. Infection. 2020;1–5. Epub 2020/05/16. https://doi.org/10.1007/s15010-019-01387-2 PMID: 31919762; PubMed Central PMCID: PMC7221233.

12. Streeck H, Schulte B, Kuemmer B, Richter E, Hoeller T, Fuhrmann C, et al. Infection fatality rate of SARS-CoV-2 infection in a German community with a super-spreading event. medRxiv. 2020:2020.05.04.20090076. https://doi.org/10.1101/2020.05.04.20090076.

13. Menni C, Valdes AM, Freedin MB, Sudre CH, Nguyen LH, Drew DA, et al. Real-time tracking of self-reported symptoms to predict potential COVID-19. Nat Med. 2020; 26:1037–1040. https://doi.org/10.1038/s41591-020-0916-2 PMID: 32393804.

14. JHU. Coronavirus Resource Center: John Hopkins University of Medicine; [cited 2020 9 September]. Available from: https://coronavirus.jhu.edu/map.html.

15. Elabscience. COVID-19 IgG and IgM. [cited 2020 30 May]. Available from: https://www.elabscience.com/p-covid_19_igg_igm_rapid_test-375335.html.

16. ZOE. COVID symptom study [Internet]. [cited 2020 April]. Available from: https://covid.joinzoe.com/data.

17. Machin D, Campbell M, Tan S, Tan S-H. Sample Size Tables for Clinical Studies, Third Edition. United Kingdom: Wiley-Blackwell; 2011. 314 p.

18. Schulz KF, Altman DG, Moher D. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Med. 2010; 8:18. Epub 2010/03/26. https://doi.org/10.1186/1741-7015-8-18 PMID: 20334633; PubMed Central PMCID: PMC2860339.

19. Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci. 2020; 12(1):8. https://doi.org/10.1038/s41368-020-0074-x PMID: 32094336.

20. CDC. Interim Guidelines for COVID-19 Antibody Testing [Internet]. 2020. [cited 2020 May 28]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antibody-tests-guidelines.html.

21. Hou H, Wang T, Zhang B, Luo Y, Mao L, Wang F, et al. Detection of IgM and IgG antibodies in patients with coronavirus disease 2019. Clin Transl Immunol. 2020; 9(5):e01136. Epub 2020/05/10. https://doi.org/10.1002/cti2.1136 PMID: 32382418; PubMed Central PMCID: PMC7202656.

22. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Clinical Infectious Diseases. 2020;ciaa344. https://doi.org/10.1093/cid/ciaa344 PMID: 32221519.

23. Fafi-Kremer S, Bruel T, Madec Y, Grant R, Tondeur L, Grzelak L, et al. Serologic responses to SARS-CoV-2 infection among hospital staff with mild disease in eastern France. medRxiv. 2020:2020.05.19.20101832. https://doi.org/10.1101/2020.05.19.20101832.

24. Giacomelli A, Pezzati L, Conti F, Bernacci M, Siano M, Oreni L, et al. Self-reported Olfactory and Taste Disorders in Patients With Severe Acute Respiratory Coronavirus 2 Infection: A Cross-sectional Study. Clinical Infectious Diseases. 2020; 71(15):889–890. https://doi.org/10.1093/cid/ciaa330 PMID: 32215618.