

Pre-Registration of Questions for ‘The effect of income and education on the estimation of olfactory ability’

BACKGROUND

Socio-economic status is a key driver of COVID-19 health outcomes [1]. A US-based report examined the proportionally high rate of deaths relative to national wealth by examining SES status and race data (not reported in clinical settings) for fine-grained regions. The community-level consequences of poverty, economic insecurity, and systemic racism have created higher COVID-19 mortality in areas with predominantly low income households and/or minority race households. Olfactory function evaluated by lab test is a key predictor of COVID-19 [2,3], as is self-reported olfactory function [4,5], however, there are indications the diagnostic value of this symptom may not be sufficient [6], certainly not for all variants. Pre-pandemic studies showed with validated tests that factors such as race, age and lower cognitive function are associated with (un)awareness of olfactory dysfunction[7]. A recent study suggests that this is particularly true when considering race and SES in the United States [8]. A discrepancy between olfactory function and awareness of olfactory function in minoritized populations may be problematic when self-reported olfactory function is used to predict COVID-19. However, it is also possible that olfactory function and awareness of olfactory function may be more consistent when there are “sudden” changes in taste-smell ability, such as experienced with COVID-19 [9], which was not specifically considered in previous studies of awareness of olfactory function.

Low income and minority populations have been found to have greater risk for olfactory dysfunction due to the effects of environmental racism [10-12]. Our GCCR_NDS004 study was aimed at testing whether taste and smell were important factors in COVID-19 infection in low income and minoritized groups. Phase 1 survey data (“NDS004 dataset US”) for 520 low-income participants (<\$41,000 USA) in the United States included an equal sample of low income black, white, and hispanic individuals (via self-identified race categories). We found that white low income most consistently reported worse olfactory ability than black and hispanics and none reported low olfactory ability. We also found that each group reported differing degrees of olfactory ability changes due to COVID-19 infection. A contradictory finding was that the lowest income groups do not seek a diagnosis of COVID-19 due to smell and taste loss, indicating that consideration of SES is a significant factor when assessing the predictive power

of smell and taste loss for identifying COVID-19 infection. These groups may not have the ability to take time off for a doctor's visit, or may feel that a non-life-threatening symptom is worth taking time off. Alternatively, not seeking a diagnosis due to taste/smell loss in these groups may also be explained by the aforementioned dissociation between self-reported olfactory ability and odor awareness [7-8]. The EDS data will shed light on this discrepancy by allowing us to test the difference between self-reported ability (awareness) and ratings of household items (olfactory function) relative to educational status and income.

DATA COLLECTION METHODS

The only method used for data collection is a survey. The data has already been collected at the time of this preregistration. The data are available via the GCCR004 project (aka "home test"/"Smell & Taste Self Check") assessed the relationship between self-reported chemosensory abilities and experienced chemosensory intensities of common household items in participants with or without lab-test confirmed COVID-19. Variables and measurements include demographics (age, gender, region, country, education, SES, smoking, pregnant), self-reported ratings for abilities to smell, and experienced intensities of home/food items, including four smell items [(1) scented cosmetics or detergents, (2) spices, herbs, or food ingredients, (3) fruit, fruit juice, or vegetables, and (4) other items], and two taste-with-odour items [(1) vinegar or lemon/lime juice, and (2) coffee or black/green tea leaves].

PARTICIPANT CHARACTERISTICS

Data were collected using a crowd-sourced, multilingual, online study with a global reach: the GCCR Smell-&-Taste-Check in 12 languages (English, German, French, Italian, Dutch, Russian, Japanese, Portuguese, Spanish, Czech, Turkish, Farsi). The data tranche from 26 June 2020 to 23 March 2021 included 10,918 eligible respondents, as described in "GCCR004" paper (in preparation, pre-registration: <https://osf.io/6bfua>). The demographics of this earlier tranche are described below. Note that data collection has continued since 23 March 2021. We will start analysis with the data tranche up to 15 August 2023, with a sample size of 17,314+ participants **before eligibility screening**. The final sample size will be **smaller** after cleaning and removing duplicates. We expect the distribution across the relevant demographic data to have remained similar. Notably, the sample sizes in the categories of the variables education and SES are symmetric and reasonably balanced.

INFORMED CONSENT & ETHICS

All volunteers provided consent and confirmed that they were 18 years old or older. The Institutional Review Board of the Faculty of Psychology & Sports Science at the Westfälische Wilhelms-Universität Münster approved the study (no. 2020-27-NB). Additional approval was obtained for the Russian test version by the Bioethics Committee at the A.N. Severtsov Institute of Ecology & Evolution RAS (no. 2020-41-NC). The data are anonymized, there is no token or any link that can be used to identify the participants in this study.

ESTIMATE OF REQUIRED SAMPLE SIZE

We have 2 sources for an estimate of the effect size for demographic variables associated with SES and race:

- 1) From Adams et al.2022 paper: Over-reporting of ability in a representative group of elderly US respondents, self-reported ability was compared with an objective odor identification test. In black respondents (relative to white respondents) the odds-ratio of incorrectly self-reporting normosmia was 3.03 (95% CI: 1.80-5.10, $p < .001$) compared to correctly self-reporting normosmia ($n=1156$). For respondents with some college or higher vs no college or lower education the odds-ratio was 1.07 (95% CI: 0.73-1.58, $p = .721$). There was no demographic variable that directly addressed SES.
<https://doi.org/10.1093/chemse/bjw108>

- 2) NDS004 Data: Olfactory Change effect size by SES: In a subset sample of 158 individuals who experienced taste and smell loss due to respiratory illness (including COVID and others) from a sample of 496 individuals, we estimate a negligible effect of 0.07 from SES for change in self-reported olfactory ability, with lower incomes reporting greater change. We estimate a smaller effect size of 0.04 for SES and self-reported olfactory ability, with lower income groups noting a higher ability.

HYPOTHESES AND DATA ANALYSIS PLAN

Overview. The key dependent variable in this study is the discrepancy between olfactory function and awareness of olfactory function, which we operationalized as the difference between “at home odor intensity test” and “self-reported ability”. At home odor intensity ratings will be subtracted from self-reported ability, so that positive values indicate an overestimated ability and negative values indicate an underestimated ability.

Hypothesis. We hypothesize that a discrepancy between self-reported ability and at-home odor intensity test will be greater in lower income and marginalized groups. The hypothesis will be tested via multivariate regression using demographic categories as independent variables and discrepancy between self-reported ability and at-home odor intensity test as the dependent variable. As “self-reported ability today” may be dependent on “COVID-group”, covid group as categorized in the GCCR004 paper (6 groups: COVID+, COVID?, COVID-, smell/taste changes, other symptoms and no symptoms) will be included as a covariate. If significant in the model, other demographic variables such as age and gender will also be included as covariates.

Context variables for regression influencing . Demographic categories used as independent variables are income (4 categories and “missing”), education (4 categories), region (5 continents), and country (136 countries, including 46 countries with at least 10 participants). The dependent variable “olfactory ability discrepancy index” is calculated as “self-reported ability today” MINUS at-home odor intensity test. To determine the “at-home odor intensity test” we will first attempt to determine if and how the various rated items can be reduced into a single item or fewer than 6 items with a principal components analysis(PCA). We will conduct a collinearity test prior to downstream analysis—in this case, country and region may be correlated and income and education may also be correlated. In the case of collinearity, we will use income and country.

Data Reduction. To determine whether the “at-home odor intensity test” measure can be captured by a single item, we will perform an exploratory analysis with a PCA that includes the intensity ratings of at most four odor items (from the categories cosmetics, spices, fruits and other) and the intensity ratings of at most two food items that were orally sampled (flavored stimuli from the categories sour and bitter). If we meet our calculated sample size threshold (see above), we will determine if missing data are randomly distributed and, if so, then use k nearest neighbor method to impute missing values for PCA. If multiple factors are identified, we will conclude that our “at-home odor intensity test” measure cannot be reduced to a single item and additional outcome variables will be created accordingly.

Analysis. After data are reduced, we will test what social demographic factors influence discrepancy between self-rating (of olfactory ability) and self-testing (at-home odor intensity test) via regression analysis. We will use data from a parallel set of data (in the EDS dataset) for taste to determine if discrepancy between self-rating and self-testing is specific to olfaction or

extends to the gustatory modality (self-reported taste ability and pure sweet and salt ratings). In addition, we will attempt to replicate results from our prior studies in this dataset, e.g. the association between income and reported olfactory ability.

REFERENCES

1. A Poor People's Pandemic Report [Internet]. Poor People's Campaign. [cited 2023 Oct 13]. Available from: <https://www.poorpeoplescampaign.org/pandemic-report/>
2. Hannum ME, Ramirez VA, Lipson SJ, Herriman RD, Toskala AK, Lin C, et al. Objective Sensory Testing Methods Reveal a Higher Prevalence of Olfactory Loss in COVID-19–Positive Patients Compared to Subjective Methods: A Systematic Review and Meta-Analysis. *Chemical Senses*;45(9):865–74. Available from: <https://doi.org/10.1093/chemse/bjaa064>
3. Rocke J, Hopkins C, Philpott C, Kumar N. Is loss of sense of smell a diagnostic marker in COVID-19: A systematic review and meta-analysis. *Clinical Otolaryngology* 45(6):914–22. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1111/coa.13620>
4. Menni C, Valdes AM, Freidin MB, Sudre CH, Nguyen LH, Drew DA, et al. Real-time tracking of self-reported symptoms to predict potential COVID-19. *Nature Medicine*. 2020;26:1037–40.
5. Gerkin RC, Ohla K, Veldhuizen MG, Joseph PV, Kelly CE, Bakke AJ, et al. Recent smell loss is the best predictor of COVID-19 among individuals with recent respiratory symptoms. *Chemical Senses* [Internet]. 2020 Dec 25 [cited 2021 Jan 13];(bjaa081). Available from: <https://doi.org/10.1093/chemse/bjaa081>
6. Hoang MP, Staibano P, McHugh T, Sommer DD, Snidvongs K. Self-reported olfactory and gustatory dysfunction and psychophysical testing in screening for COVID-19: A systematic review and meta-analysis. *International Forum of Allergy & Rhinology* 12(5):744–56. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1002/alr.22923>
7. Adams DR, Wroblewski KE, Kern DW, Kozloski MJ, Dale W, McClintock MK, et al. Factors Associated with Inaccurate Self-Reporting of Olfactory Dysfunction in Older US Adults. *Chem Senses* [Internet]. 2017 Mar 1 [cited 2022 Jan 17];42(3):223–31. Available from: <https://doi.org/10.1093/chemse/bjw108>
8. Cao Z, Yang A, D'Aloisio AA, Suarez L, Deming-Halverson S, Li C, et al. Assessment of Self-reported Sense of Smell, Objective Testing, and Associated Factors in Middle-aged and Older Women. *JAMA Otolaryngol Neck Surg* [Internet]. 2022 Mar 10 [cited 2022 Mar 15]; Available from: <https://doi.org/10.1001/jamaoto.2022.0069>
9. Lötsch J, Hummel T. Clinical Usefulness of Self-Rated Olfactory Performance—A Data Science-Based Assessment of 6000 Patients. *Chem Senses* [Internet]. 2019 Jul 17 [cited 2020

May 20];44(6):357–64. Available from:

<https://academic.oup.com/chemse/article/44/6/357/5488092>

10. Samoli E, Stergiopoulou A, Santana P, Rodopoulou S, Mitsakou C, Dimitroulopoulou C, et al. Spatial variability in air pollution exposure in relation to socioeconomic indicators in nine European metropolitan areas: A study on environmental inequality. *Environ Pollut* [Internet]. 2019 Jun 1;249:345–53. Available from:

<http://www.sciencedirect.com/science/article/pii/S026974911834908X>

11. Rivas I, Kumar P, Hagen-Zanker A. Exposure to air pollutants during commuting in London: are there inequalities among different socio-economic groups? *Environ Int* [Internet]. 2017 Apr 1;101:143–57. Available from:

<http://www.sciencedirect.com/science/article/pii/S0160412016305803>

12. Hoover KC. Sensory Disruption in Modern Living and the Emergence of Sensory Inequities. *Yale J Biol Med* [Internet]. 3;91(1):53–62. Available from:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5872642/>