Supplementary Material

Smell and Taste Dysfunction in Patients With COVID-19:

A Systematic Review and Meta-analysis

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| Section/topic          | # | Checklist item                                                                 | Reported on page # |
|-----------------------|---|---------------------------------------------------------------------------------|--------------------|
| **TITLE**             |   |                                                                                 |                    |
| Title                 | 1 | Identify the report as a systematic review, meta-analysis, or both.             | 1                  |
| **ABSTRACT**          |   |                                                                                 |                    |
| Structured summary    | 2 | Provide a structured summary including, as applicable: background; objectives;  | 3-4                |
|                       |   | data sources; study eligibility criteria, participants, and interventions;      |                    |
|                       |   | study appraisal and synthesis methods; results; limitations; conclusions and    |                    |
|                       |   | implications of key findings; systematic review registration number.            |                    |
| **INTRODUCTION**      |   |                                                                                 |                    |
| Rationale             | 3 | Describe the rationale for the review in the context of what is already known.  | 6                  |
| Objectives            | 4 | Provide an explicit statement of questions being addressed with reference to   | 6                  |
|                       |   | participants, interventions, comparisons, outcomes, and study design (PICOS).    |                    |
| **METHODS**           |   |                                                                                 |                    |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g.,   | 7-8                |
|                       |   | Web address), and, if available, provide registration information including     |                    |
|                       |   | registration number.                                                           |                    |
| Eligibility criteria  | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report    | 7-8                |
|                       |   | characteristics (e.g., years considered, language, publication status) used     |                    |
|                       |   | as criteria for eligibility, giving rationale.                                  |                    |
| Information sources   | 7 | Describe all information sources (e.g., databases with dates of coverage,      | 7-8                |
|                       |   | contact with study authors to identify additional studies) in the search and    |                    |
|                       |   | date last searched.                                                            |                    |
| Search                | 8 | Present full electronic search strategy for at least one database, including    | Table S2           |
|                       |   | any limits used, such that it could be repeated.                               |                    |
| Study selection       | 9 | State the process for selecting studies (i.e., screening, eligibility, included | 7-8                |
|                       |   | in systematic review, and, if applicable, included in the meta-analysis).       |                    |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms,         | 7-8                |
|                       |   | independently, in duplicate) and any processes for obtaining and confirming    |                    |
|                       |   | data from investigators.                                                       |                    |
| Data items            | 11 | List and define all variables for which data were sought (e.g., PICOS, funding | 7-8                |
|                       |   | sources) and any assumptions and simplifications made.                         |                    |
| Risk of bias in       | 12| Describe methods used for assessing risk of bias of individual studies          | 7-8                |
| individual studies    |   | (including specification of whether this was done at the study or outcome      |                    |
|                       |   | level), and how this information is to be used in any data synthesis.          |                    |
| Summary measures      | 13| State the principal summary measures (e.g., risk ratio, difference in means).  | 7-8                |
| Synthesis of results  | 14| Describe the methods of handling data and combining results of studies, if     | 7-8                |
|                       |   | done, including measures of consistency (e.g., $I^2$) for each meta-analysis.  |                    |
| Section/topic                  | #  | Checklist item                                                                 | Reported on page # |
|-------------------------------|----|-------------------------------------------------------------------------------|--------------------|
| Risk of bias across studies   | 15 | Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies). | Table S3           |
| Additional analyses           | 16 | Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. | 7-8                |
| RESULTS                      |    |                                                                                |                    |
| Study selection               | 17 | Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. | 9                  |
| Study characteristics         | 18 | For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. | 9                  |
| Risk of bias within studies   | 19 | Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). | Table S4           |
| Results of individual studies | 20 | For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. | 10-11              |
| Synthesis of results          | 21 | Present results of each meta-analysis done, including confidence intervals and measures of consistency. | 10-11              |
| Risk of bias across studies   | 22 | Present results of any assessment of risk of bias across studies (see Item 15). | 10-11              |
| Additional analysis           | 23 | Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). | 10-11              |
| DISCUSSION                   |    |                                                                                |                    |
| Summary of evidence           | 24 | Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). | 11-12              |
| Limitations                   | 25 | Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). | 11-12              |
| Conclusions                   | 26 | Provide a general interpretation of the results in the context of other evidence, and implications for future research. | 11-12              |
| FUNDING                      |    |                                                                                |                    |
| Funding                       | 27 | Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. | Title page         |
|   | Search strategy                                      |
|---|-----------------------------------------------------|
| 1 | anosmia.mp.                                         |
| 2 | anosmia.m_titl.                                     |
| 3 | hyposmia.mp.                                        |
| 4 | hyposmia.m_titl.                                    |
| 5 | dysosmia.mp.                                        |
| 6 | dysosmia.m_titl.                                    |
| 7 | olfaction disorder.mp. or exp Olfaction Disorders/  |
| 8 | olfactory dysfunction.mp.                           |
| 9 | olfactory dysfunction.m_titl.                       |
| 10| smell dysfunction.mp.                               |
| 11| smell dysfunction.m_titl.                           |
| 12| aguesia.mp.                                         |
| 13| hypogeusia.mp.                                      |
| 14| dysgeusia.mp.                                       |
| 15| aguesia.m_titl.                                     |
| 16| hypogeusia.m_titl.                                 |
| 17| dysgeusia.m_titl.                                  |
| 18| taste dysfunction.mp.                              |
| 19| taste dysfunction.m_titl.                           |
| 20| gustatory dysfunction.mp.                           |
| 21| neurological.mp.                                    |
| 22| neurological.m_titl.                               |
| 23| 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 |
| 24| COVID-19.mp.                                        |
| 25| Coronavirus Infections/                             |
| 26| 2019 novel coronavirus.mp.                          |
| 27| COVID-19.m_titl.                                    |
| 28| Coronavirus Infection.m_titl.                       |
| 29| 2019 novel coronavirus.m_titl.                      |
| 30| 2019-nCoV.mp.                                       |
| 31| 2019-nCoV.m_titl.                                   |
| 32| SARS-CoV-2.m_titl.                                  |
| 33| SARS-CoV-2.mp.                                      |
| 34| 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 |
| 33| 23 and 34                                           |
| Domains      | Leading explanatory questions                                                                 |
|--------------|-----------------------------------------------------------------------------------------------|
| Selection    | 1) Does the patient(s) represent(s) the whole experience of the investigator (centre) or is the selection method unclear to the extent that other patients with similar presentation may not have been reported? |
| Ascertainment| 2) Was the exposure adequately ascertained?                                                   |
|              | 3) Was the outcome adequately ascertained?                                                    |
| Causality    | 4) Were other alternative causes that may explain the observation ruled out?                  |
|              | 5) Was there a challenge/rechallenge phenomenon?                                               |
|              | 6) Was there a dose–response effect?                                                          |
|              | 7) Was follow-up long enough for outcomes to occur?                                            |
| Reporting    | 8) Is the case(s) described with sufficient details to allow other investigators to replicate the research or to allow practitioners make inferences related to their own practice? |
Table S4: Methodological assessment of studies’ quality based on the criteria by Murad et al (Table S3)

| Study                      | Selection | Ascertainment | Domains | Causality | Reporting |
|----------------------------|-----------|---------------|---------|-----------|-----------|
|                            | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
| Tostmann et al             | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Giacomelli et al           | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Benézit et al              | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Klopfenstein et al         | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Tomlins et al              | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Luers et al                | Y | Y | N  | Y  | n.a | n.a | Y  | Y |
| Vaira et al                | Y | Y | Y  | Y  | n.a | n.a | Y  | Y |
| Yan et al                  | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Beltrán-Corbellini et al   | Y | Y | N  | Y  | n.a | n.a | Y  | Y |
| Moein et al                | Y | Y | Y  | N  | n.a | n.a | Y  | Y |
| Mao et al                  | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Levinson et al             | Y | Y | N  | Y  | n.a | n.a | Y  | Y |
| Fontanet et al             | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Vaira et al                | Y | Y | Y  | Y  | n.a | n.a | Y  | Y |
| Lechien et al              | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Aggarwal et al             | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Lee et al                  | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Hornuss et al              | Y | Y | Y  | Y  | n.a | n.a | Y  | Y |
| Just et al                 | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Lechien et al              | Y | Y | Y/N | Y  | n.a | n.a | Y  | Y |
| Borobia et al              | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Cavagna et al              | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Härter et al               | Y | Y | N  | N  | n.a | n.a | Y  | Y |
| Allenbach et al            | Y | Y | N  | N  | n.a | n.a | Y  | Y |

*aused different approaches for olfactory and gustatory; N= no; Y = yes; n.a = not applicable
Figure S1: Funnel plot for olfactory dysfunction
Figure S2: Funnel plot for gustatory dysfunction
References

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