Liou et al. Alteration of taste and smell in COVID-19 –A systematic review and meta-analysis

This supplement contains the following items:

Liou J-M, *et al*. *Gut* 2021; 70:806–807. doi: 10.1136/gutjnl-2020-322125

Methods

Studies that reported the frequency of alteration in taste (dysgeusia, hypogeusia, ageusia) or smell (dysosmia, hyposmia, anosmia) in patients with laboratory confirmed COVID-19 cases and/or uninfected controls were eligible. Case reports and studies which only included patients with taste or smell alteration were excluded. Review articles or comments on other original studies were also excluded. The references of these articles were also searched for eligibility. The proportion of these symptoms in cases and/or controls and their 95% confidence interval (95% CI) and odds ratio (OR) were analyzed by random effect model using the Comprehensive Meta-analysis software.

Supplementary Table 1. Additional characteristics of eligible studies

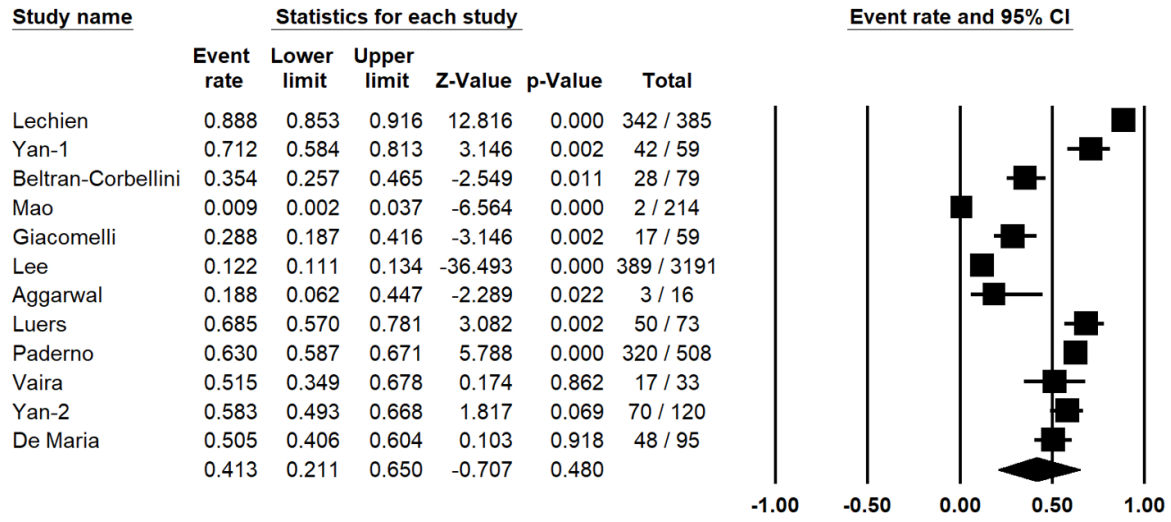
Ref.	Author	Assessment of taste or smell alteration	Diagnosis of COVID-19
1	Lechien[1]	National Health and Nutrition Examination Survey, and the short version of the Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS).	RT-PCR
2	Roland	UCSF COVID-19 Symptom Survey	Self-reported positive test
3	Yan-1	27-question survey	RT-PCR
4	Beltran-Corbellini	self-reported symptoms	RT-PCR
5	Mao	self-reported symptoms	RT-PCR
6	Giacomelli	self-reported symptoms	RT-PCR
7	Lee	telephone interview	RT-PCR
8	Aggarwal	interview	RT-PCR
9	Moein	University of Pennsylvania Smell Identification Test (UPSIT) & symptoms	RT-PCR
10	Luers	Total Nasal Symptom Score (TNSS)	RT-PCR
11	Paderno	questionnaire	RT-PCR
12	Vaira	chemosensitive test	RT-PCR
13	Yan-2	self-reported symptoms	RT-PCR
14	De Maria	self-reported symptoms	RT-PCR
15	Merza	self-reported symptoms	RT-PCR
16	Spinato	telephone interview	RT-PCR
17	Clemency	interview	RT-PCR
18	Menni	app-based symptom tracker	RT-PCR

Ref: reference; COVID-19: coronavirus infectious disease 2019; RT-PCR: reverse transcriptase polymerase chain reaction.

Liou J-M, *et al*. *Gut* 2021; 70:806–807. doi: 10.1136/gutjnl-2020-322125

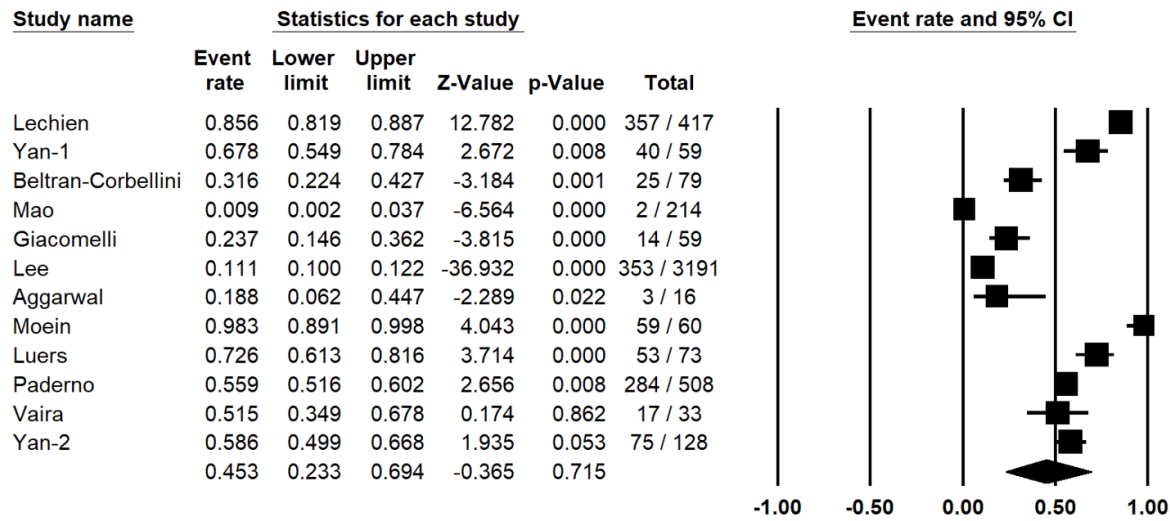
Supplementary Figures

Figure S1. Forrest plots of the proportion of taste alteration in COVID-19 patients



Heterogeneity: Q=1160, I^2=99.1%, p<0.001

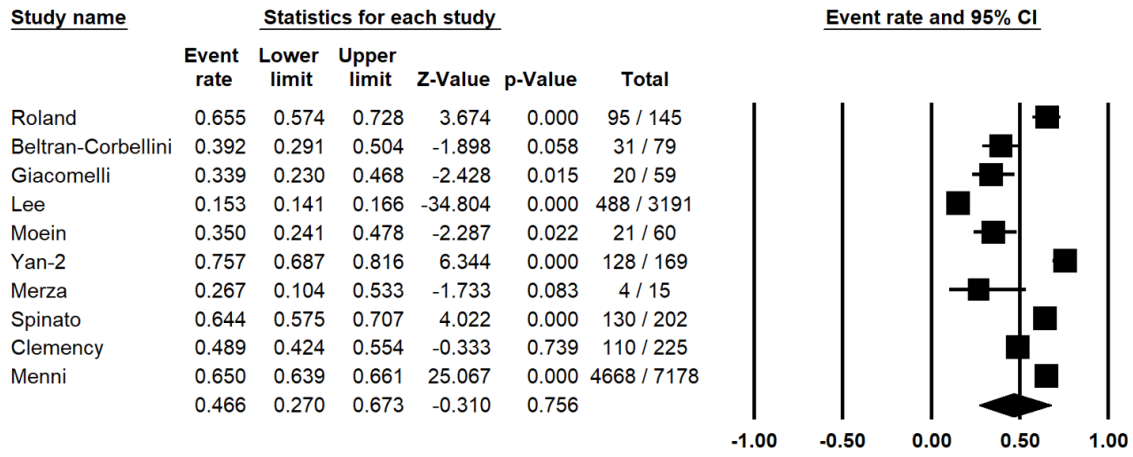
Figure S2. Forrest plots of the proportion of smell alteration in COVID-19 patients



Heterogeneity: Q=1168, I^2=99%, p<0.001

Liou J-M, *et al. Gut* 2021; 70:806–807. doi: 10.1136/gutjnl-2020-322125

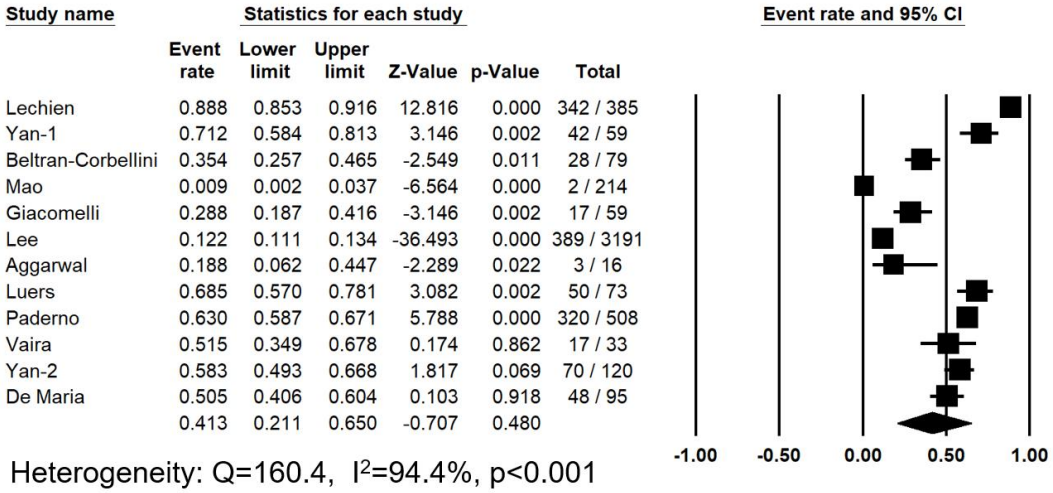
Figure S3. Forrest plots of the proportion of taste or smell alteration in COVID-19 patients



Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total
Roland	0.655	0.574	0.728	3.674	0.000	95 / 145
Beltran-Corbellini	0.392	0.291	0.504	-1.898	0.058	31 / 79
Giacomelli	0.339	0.230	0.468	-2.428	0.015	20 / 59
Lee	0.153	0.141	0.166	-34.804	0.000	488 / 3191
Moein	0.350	0.241	0.478	-2.287	0.022	21 / 60
Yan-2	0.757	0.687	0.816	6.344	0.000	128 / 169
Merza	0.267	0.104	0.533	-1.733	0.083	4 / 15
Spinato	0.644	0.575	0.707	4.022	0.000	130 / 202
Clemency	0.489	0.424	0.554	-0.333	0.739	110 / 225
Menni	0.650	0.639	0.661	25.067	0.000	4668 / 7178
	0.466	0.270	0.673	-0.310	0.756	

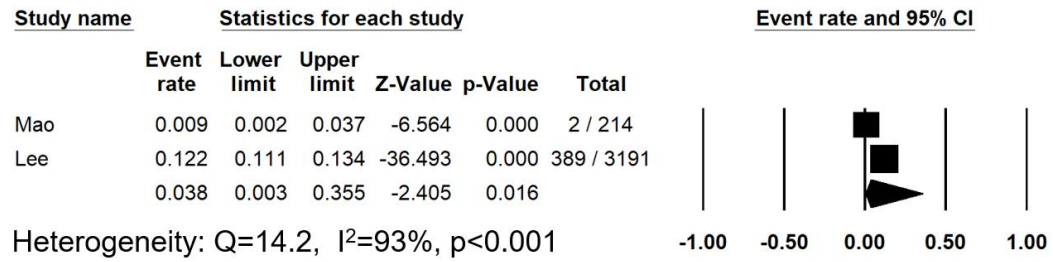
Heterogeneity: Q=1870, I^2=99.5%, p<0.001

Figure S4. Forrest plots of the proportion of taste alteration in COVID-19 patients in East Asia versus non-East Asia



Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total
Lechien	0.888	0.853	0.916	12.816	0.000	342 / 385
Yan-1	0.712	0.584	0.813	3.146	0.002	42 / 59
Beltran-Corbellini	0.354	0.257	0.465	-2.549	0.011	28 / 79
Mao	0.009	0.002	0.037	-6.564	0.000	2 / 214
Giacomelli	0.288	0.187	0.416	-3.146	0.002	17 / 59
Lee	0.122	0.111	0.134	-36.493	0.000	389 / 3191
Aggarwal	0.188	0.062	0.447	-2.289	0.022	3 / 16
Luers	0.685	0.570	0.781	3.082	0.002	50 / 73
Paderno	0.630	0.587	0.671	5.788	0.000	320 / 508
Vaira	0.515	0.349	0.678	0.174	0.862	17 / 33
Yan-2	0.583	0.493	0.668	1.817	0.069	70 / 120
De Maria	0.505	0.406	0.604	0.103	0.918	48 / 95
	0.413	0.211	0.650	-0.707	0.480	

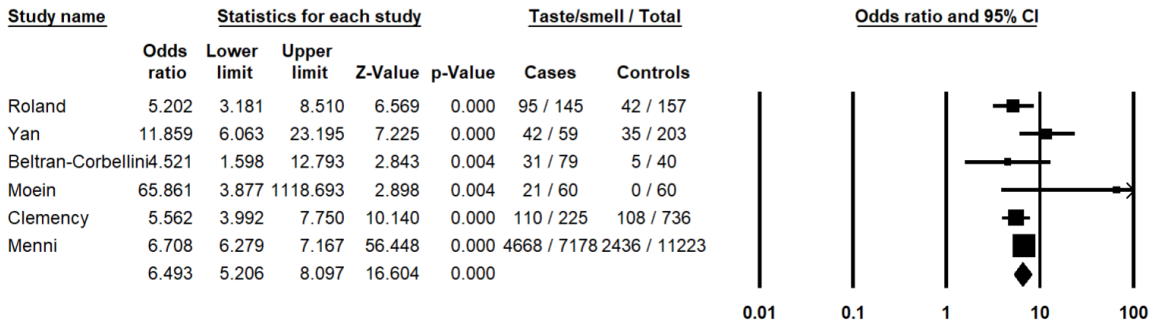
Heterogeneity: Q=160.4, I^2=94.4%, p<0.001



Study name	Event rate	Lower limit	Upper limit	Z-Value	p-Value	Total
Mao	0.009	0.002	0.037	-6.564	0.000	2 / 214
Lee	0.122	0.111	0.134	-36.493	0.000	389 / 3191
	0.038	0.003	0.355	-2.405	0.016	

Heterogeneity: Q=14.2, I^2=93%, p<0.001

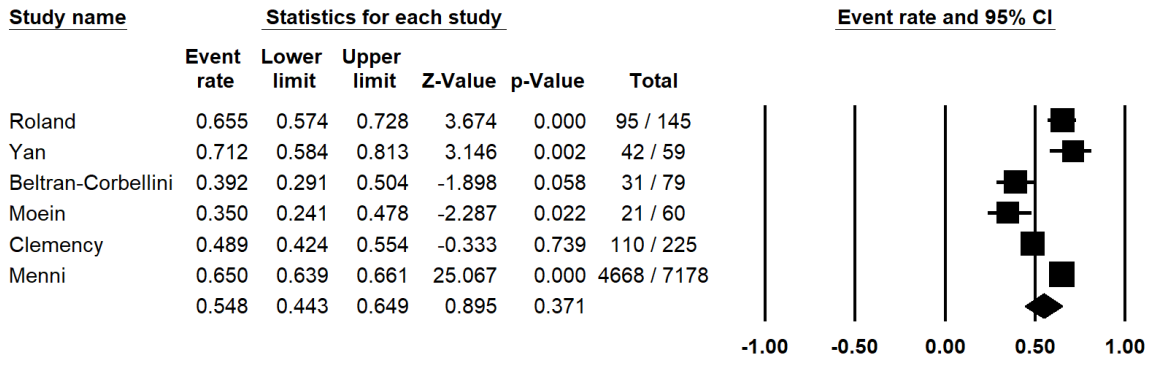
Figure S5. Forrest plot of the association of taste or smell alteration and COVID-19



Heterogeneity: Q=1160, I^2=99.1%, p<0.001

Figure S6. Forrest plot of (A) sensitivity, (B) specificity, (C) Positive prediction value, (D) Negative prediction value, and (E) Accuracy of taste or smell alteration in the prediction of COVID-19

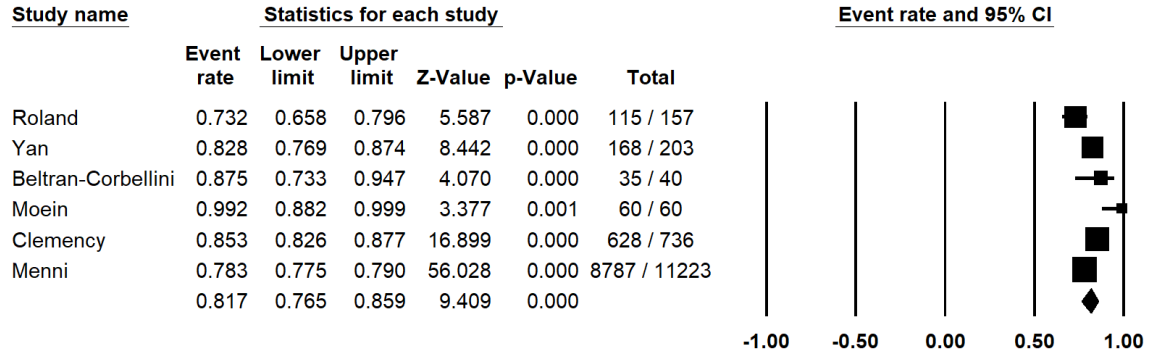
(A)Sensitivity



Heterogeneity: Q=65.1, I^2=92.3%, p<0.001

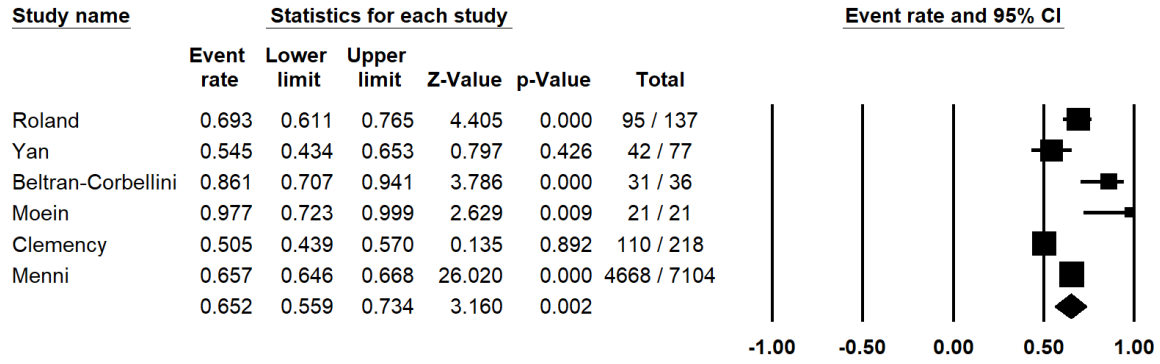
Liou J-M, *et al. Gut* 2021; 70:806–807. doi: 10.1136/gutjnl-2020-322125

(B) Specificity



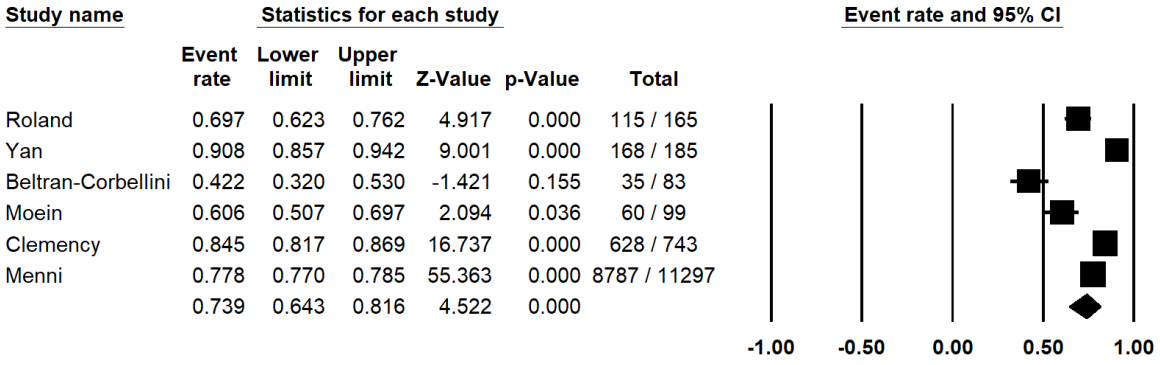
Heterogeneity: Q=32.6, I^2=84.7%, p<0.001

(C) Positive prediction value



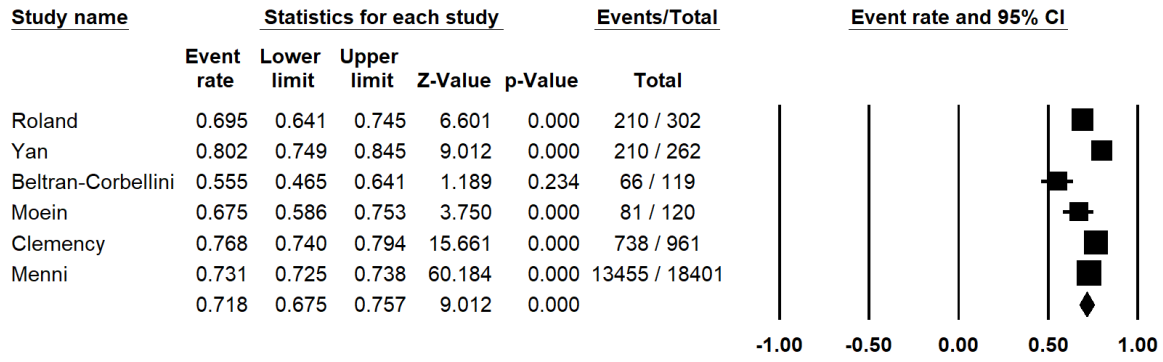
Heterogeneity: Q=36.8, I^2=86.4%, p<0.001

(D) Negative prediction value



Heterogeneity: Q=107.8, I^2=95.4%, p<0.001

(E) Accuracy



Heterogeneity: Q=34.9, I^2=85.7%, p<0.0001

References

1. Lechien JR, Chiesa-Estomba CM, De Siati DR, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study [published online ahead of print, 2020 Apr 6]. *Eur Arch Otorhinolaryngol.* 2020;1-11.
2. Roland LT, Gurrola JG 2nd, Loftus PA, Cheung SW, Chang JL. Smell and taste symptom-based predictive model for COVID-19 diagnosis [published online ahead of print, 2020 May 4]. *Int Forum Allergy Rhinol* 2020;10.1002/alr.22602. doi:10.1002/alr.22602
3. Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms [published online ahead of print, 2020 Apr 12]. *Int Forum Allergy Rhinol* 2020;10.1002/alr.22579. doi:10.1002/alr.22579
4. Beltrán-Corbellini Á, Chico-García JL, Martínez-Poles J, et al. Acute-onset smell and taste disorders in the context of Covid-19: a pilot multicenter PCR-based case-control study [published online ahead of print, 2020 Apr 22]. *Eur J Neurol* 2020;10.1111/ene.14273.

doi:10.1111/ene.14273

5. Mao L, Jin H, Wang M, et al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 2020;e201127.
6. Giacomelli A, Pezzati L, Conti F, et al. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. *Clin Infect Dis.* 2020;ciaa330.
7. 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.
8. Aggarwal S, Garcia-Telles N, Aggarwal G, Lavie C, Lippi G, Henry BM. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): Early report from the United States. *Diagnosis* (Berl). 2020;7:91-6.
9. Moein ST, Hashemian SMR, Mansourafshar B, Khorram-Tousi A, Tabarsi P, Doty RL. Smell dysfunction: a biomarker for COVID-19 [published online ahead of print, 2020 Apr 17]. *Int Forum Allergy Rhinol* 2020;10.1002/alr.22587. doi:10.1002/alr.22587
10. Luers JC, Rokohl AC, Loreck N, et al. Olfactory and Gustatory Dysfunction in Coronavirus Disease 19 (COVID-19) [published online ahead of print, 2020 May 1]. *Clin Infect Dis* 2020;ciaa525. doi:10.1093/cid/ciaa525
11. Paderno A, Schreiber A, Grammatica A, et al. Smell and taste alterations in Covid-19: a cross-sectional analysis of different cohorts. *Int Forum Allergy Rhinol* 2020;10.1002/alr.22610.
12. Vaira LA, Salzano G, Petrocelli M, Deiana G, Salzano FA, De Riu G. Validation of a self-administered olfactory and gustatory test for the remotely evaluation of COVID-19 patients in home quarantine [published online ahead of print, 2020 May 1]. *Head Neck* 2020;10.1002/hed.26228. doi:10.1002/hed.26228
13. Yan CH, Faraji F, Prajapati DP, Ostrander BT, DeConde AS. Self-reported olfactory loss associates with outpatient clinical course in Covid-19 [published online ahead of print, 2020 Apr 24]. *Int Forum Allergy Rhinol* 2020;10.1002/alr.22592. doi:10.1002/alr.22592

14. De Maria A, Varese P, Dentone C, Barisione E, Bassetti M. High prevalence of olfactory and taste disorder during SARS-CoV-2 infection in outpatients [published online ahead of print, 2020 May 8]. *J Med Virol* 2020;10.1002/jmv.25995. doi:10.1002/jmv.25995
15. Merza MA, Haleem Al Mezori AA, Mohammed HM, Abdulah DM. COVID-19 outbreak in Iraqi Kurdistan: The first report characterizing epidemiological, clinical, laboratory, and radiological findings of the disease. *Diabetes Metab Syndr* 2020;14(4):547-54.
16. Spinato G, Fabbris C, Polesel J, et al. Alterations in Smell or Taste in Mildly Symptomatic Outpatients With SARS-CoV-2 Infection. *JAMA* 2020;e206771.
17. Clemency BM, Varughese R, Scheafer DK, et al. Symptom Criteria for COVID-19 Testing of Heath Care Workers. *Acad Emerg Med* 2020;10.1111/acem.14009.
18. Menni C, Valdes AM, Freidin MB, et al. Real-time tracking of self-reported symptoms to predict potential COVID-19. *Nat Med* 2020;10.1038/s41591-020-0916-2.