COVID-19: losing your sense of smell

Professor Carl Philpott

University of East Anglia

Lecture content

- How common is smell loss in Covid-19?
- Does it get better?
- How does it position relative to other symptoms of the pandemic?
- How is it different to typical smell loss seen with other viruses?
- What about taste?
- Why bother with smell loss?

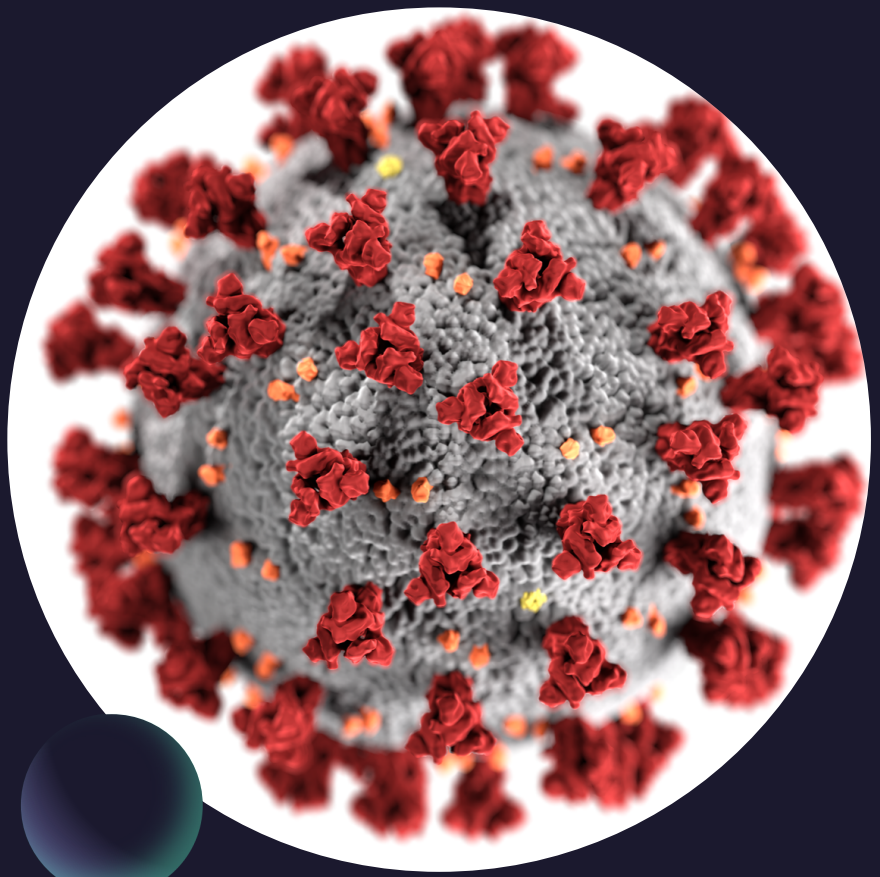
The story of Covid-19 smell and taste loss…

The Covid-19 story of anosmia so far…

- Over 50 million cases to date
- Over 1,000,000 deaths

Chinese reports…

- Initially no mention of smell/taste loss
- Then in a report of 214 hospitalized patients…hypogeusia in 12 (5.6%) and hyposmia in 11 (5.1%)
- Mao et al (https://doi.org/10.1101/2020.02.22.20026500)



Next stop Iran…

- 48.23% of 10069 participants had anosmia/hyposmia of which onset was sudden in 75%
- Bagheri et al https://doi.org/10.1101/2020.03.23.20041889

…and then Italy…

- Of 88 hospitalized patients, 59 were able to be interviewed
- 33.9% reported at least one taste or olfactory disorder and 11 (18.6%) both.
- 20.3% had symptoms before the hospital admission, 13.5% during hospital stay. Taste alterations were more frequently (91%) before hospitalization, whereas after hospitalization taste and olfactory alteration appeared with equal frequency

…and to the rest of Europe…

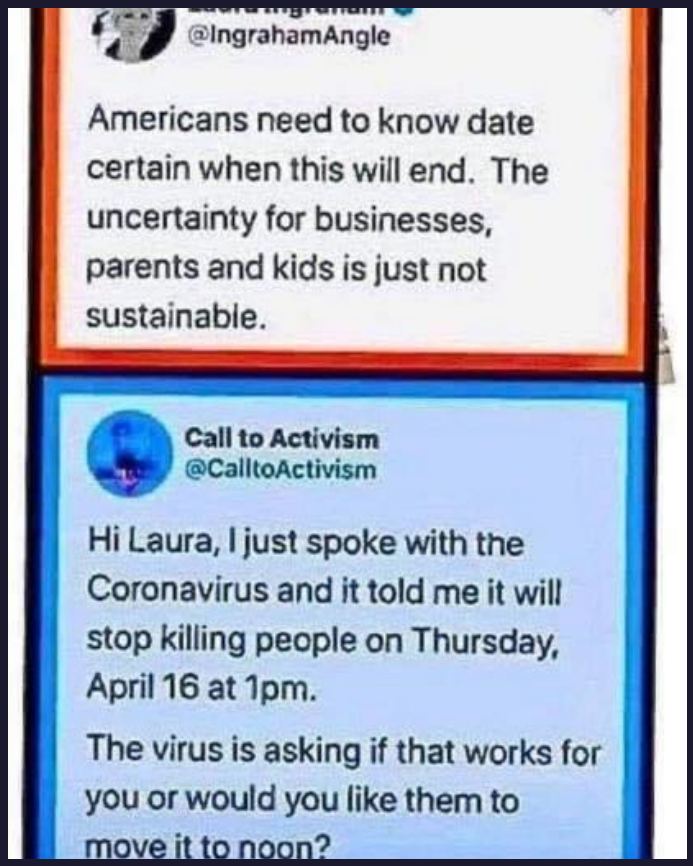
- 417 mild-to-moderate COVID-19 patients
- 85.6% and 88.0% of patients reported olfactory and gustatory dysfunctions
- 12% was the first symptom
- Lechien et al, doi: 10.1007/s00405-020-05965-1.

Corona has landed in Blighty

- 2,618,862 participants
- 18,401 had a SARS-CoV-2 test
- 65.03% reported smell loss in +ve test patients
- 21.71% reported smell loss in –ve test patients
- odds ratio = 6.74; 95% confidence interval = 6.31-7.21)

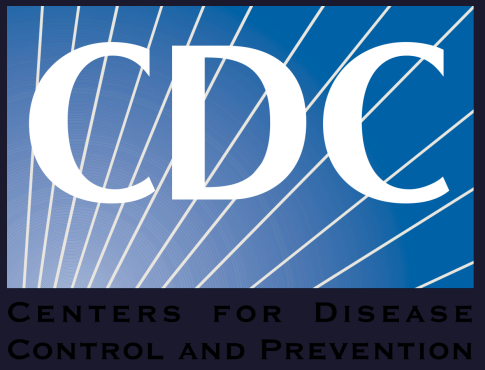
Menni C, Valdes AM, Freidin MB, Sudre CH, Nguyen LH, Drew DA, Ganesh S, Varsavsky T, Cardoso MJ, El-Sayed Moustafa JS, Visconti A, Hysi P, Bowyer RCE, Mangino M, Falchi M, Wolf J, Ourselin S, Chan AT, Steves CJ, Spector TD.
Nat Med. 2020 Jul;26(7):1037-1040. doi: 10.1038/s41591-020-0916-2. Epub 2020 May 11.

The Americans have it too…



Officially a symptom

- CDC – 30th March 2020
- WHO – 17th April 2020
- PHE – 18th May 2020



THE CONVERSATION

Academic rigour, journalistic flair

Many UK healthcare workers may have had coronavirus without knowing it – new survey of

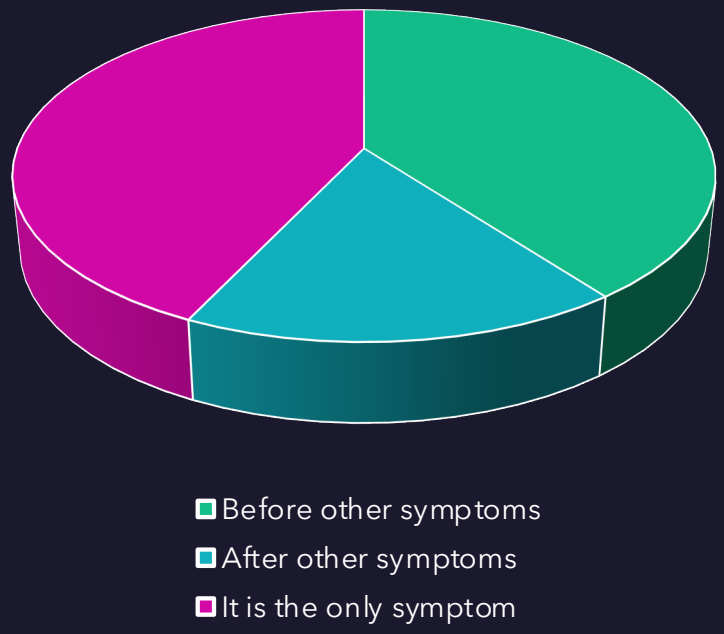
Anosmia and hyposmia in health-care workers with undiagnosed SARS-CoV-2 infection

- Questionnaires were distributed at six NHS trusts; 1041 individuals completed the questionnaires between 27th March and 9th June 2020.
- Nearly two-thirds of participants reported recent sudden loss of sense of smell and/or taste.
- Loss of sense of smell and/or taste was significantly associated with a positive Covid-19 test.

*Lancet Microbe. August 2020. Matt Lechner, Nicholas Counsell, Jacklyn Liu, Nicholas Eynon-Lewis, Santdeep Paun, Valerie J Lund, Sam Jayaraj, *Carl Philpott. DOI:https://doi.org/10.1016/S2666-5247(20)30096-3.*

Timing of symptoms from healthcare workers

When did you notice the loss of smell/taste?	Number (%)
Before other symptoms	98 (40)
After other symptoms	43 (17)
It is the only symptom	106 (43)



Tong et al Systematic Review and Meta-Analysis

10 studies were analysed for olfactory dysfunction (n = 1,627)

53% (95% CI: 29.64-75.23%) prevalence in Covid-19+ve cases

gustatory dysfunction 44% prevalence

validated instruments assessment of OD = 86.60% prevalence

In those testing positive for Covid, how common is smell loss (OD)?

TABLE 2 Meta-analysis of patients with COVID-19-positive PCR result and prevalence of olfactory dysfunction

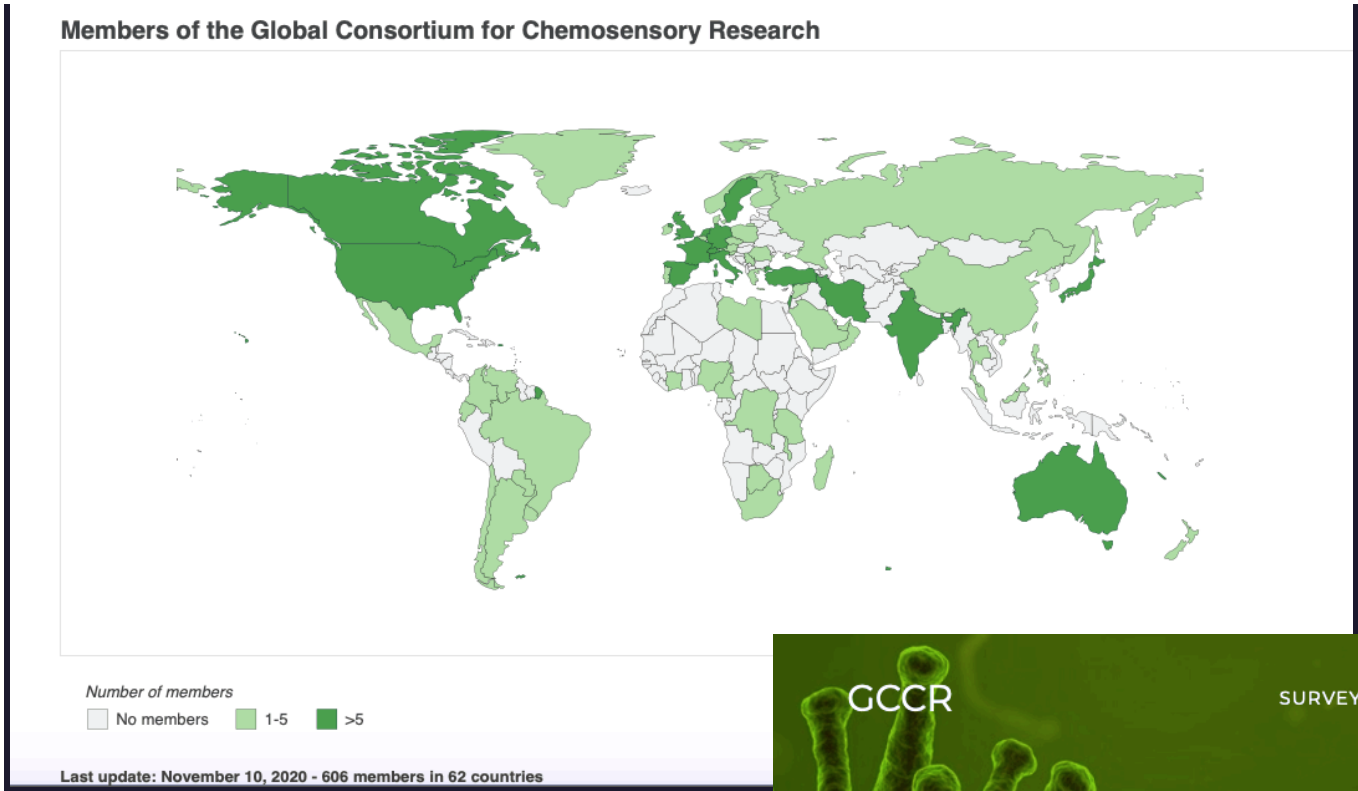
Lead Author	n COVID-19 positive	N with OD	Percentage with OD	Average age with OD	Proportion Female	Setting	Location
C Menni	579	344	59%	41	69%	Outpatient based	UK based
J Lechian	417	357	86%	No data	No data	Inpatient and Outpatient	Belgium, Spain, France, Italy
C Yan	59	40	68%	No data	No data	Outpatient based	USA
ST Moein	60	58	97%	47	33%	Inpatient	Iran
L Mao	214	11	5%	No data	No data	Inpatient	China
Totals	1329	819	62% prevalence of OD in COVID + ve population				

Is loss of sense of smell a diagnostic marker in COVID-19: A systematic review and meta-analysis.
Rocke J, Hopkins C, Philpott C, Kumar N.
Clin Otolaryngol. 2020 Aug 1:10.1111/coa.13620. doi: 10.1111/coa.13620

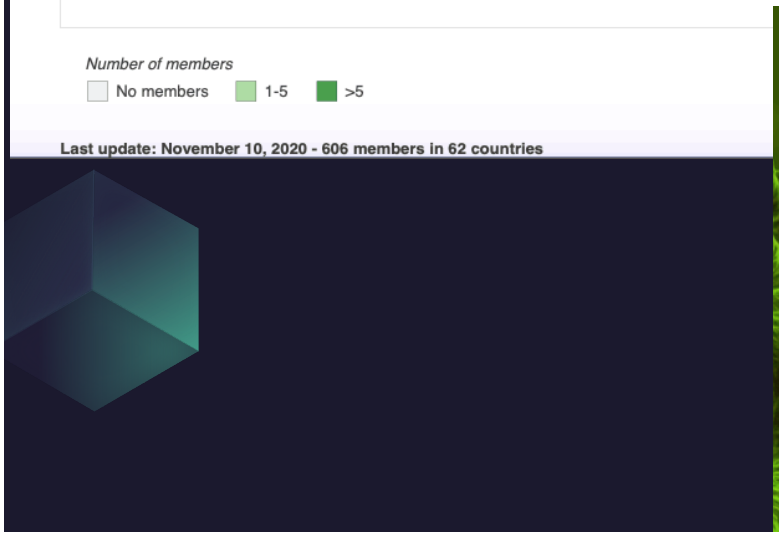
If smell loss is present, how likely is it that they have Covid-19?

TABLE 3 Meta-analysis of patients with new onset olfactory dysfunction and prevalence of COVID-19 positivity

Lead Author	N with OD	N COVID + ve test	Percentage COVID + ve	Average Age	Female	Setting	Location
S Bagheri	10 069	No data	No data	32.5	71%	Outpatient based	Iran
S Gane	11	No data	No data	37.6	27%	Outpatient	UK
C Hopkins	2428	No data	No data	30-39	73%	Outpatient based	UK
I Gengler[a]	55	52	94%	No data	No data	No data	France
C Yan	73	40	55%	No data	No data	Outpatient based	USA
C Menni	557	345	62%	No data	No data	Outpatient based	UK
Bold values where patients with olfactory dysfunction were PCR tested for COVID-19 and included in meta-analysis below (Yan et al, Menni et al):							
Total	630	385	61% PPV for COVID + ve test in OD				


Members of the Global Consortium for Chemosensory Research
Number of members
No members
1-5
>5
Last update: November 10, 2020 - 606 members in 62 countries


GCCR




GCCR
SURVEYS
FOR PATIENTS
COVID-19 PROJECTS
LINKS
MEMBERS
GLOBAL CONSORTIUM
FOR CHEMOSENSORY RESEARCH

GCCR SURVEY

- 4039 participants (2913 women, 1118 men); ages 19-79
- COVID-19 diagnosis either via laboratory tests or clinical assessment
- Self-rating of smell and taste :
  - smell worst affected
  - taste not far behind
  - chemesthesis – tingling and burning in nose and mouth experienced by some
- Smell distortions were relatively rare

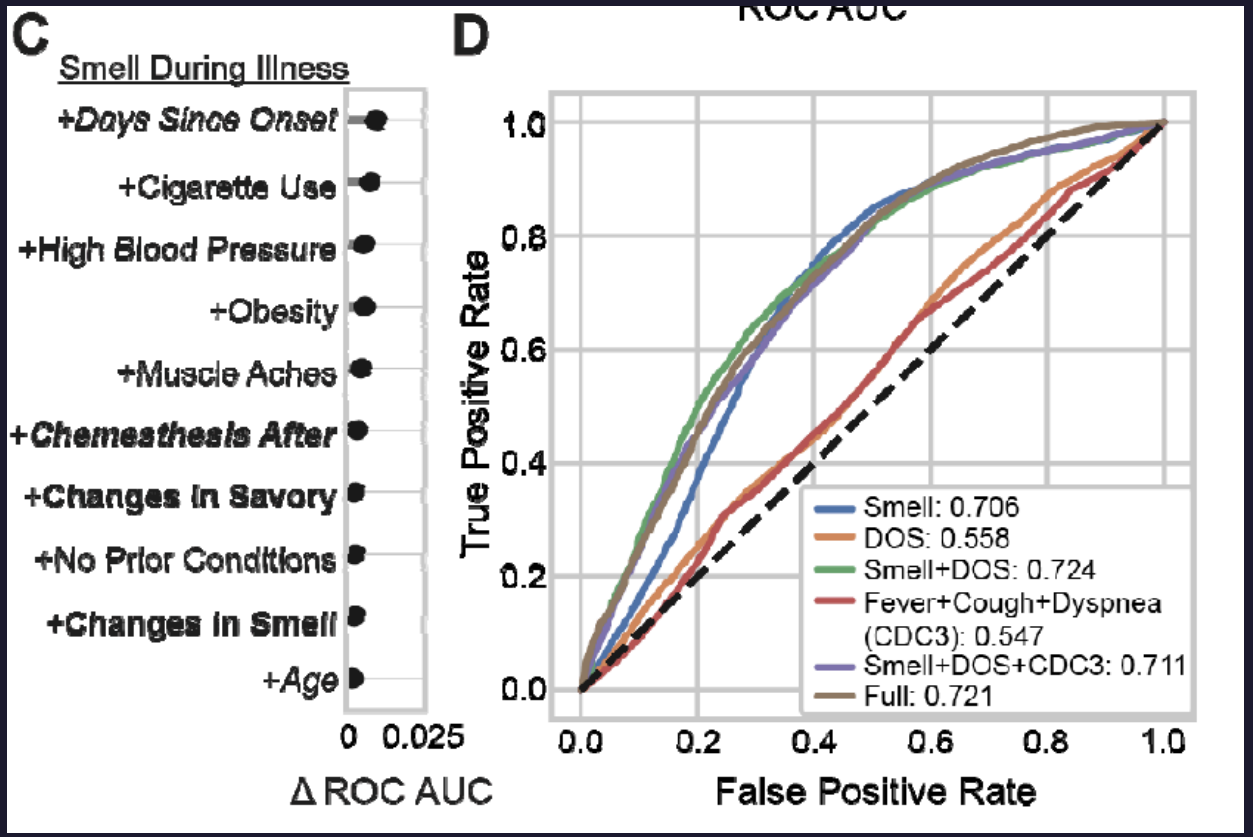
GCCR #2: 4694 subjects

- Both C19+ and C19- groups exhibited smell loss, but it was significantly worse in C19+ participants (mean of 83/100 compared to 60/100)
- Smell loss during illness was the best predictor of COVID-19
- VAS ratings of smell loss were more predictive than binary chemosensory yes/no-questions or other cardinal symptoms, such as fever or cough.

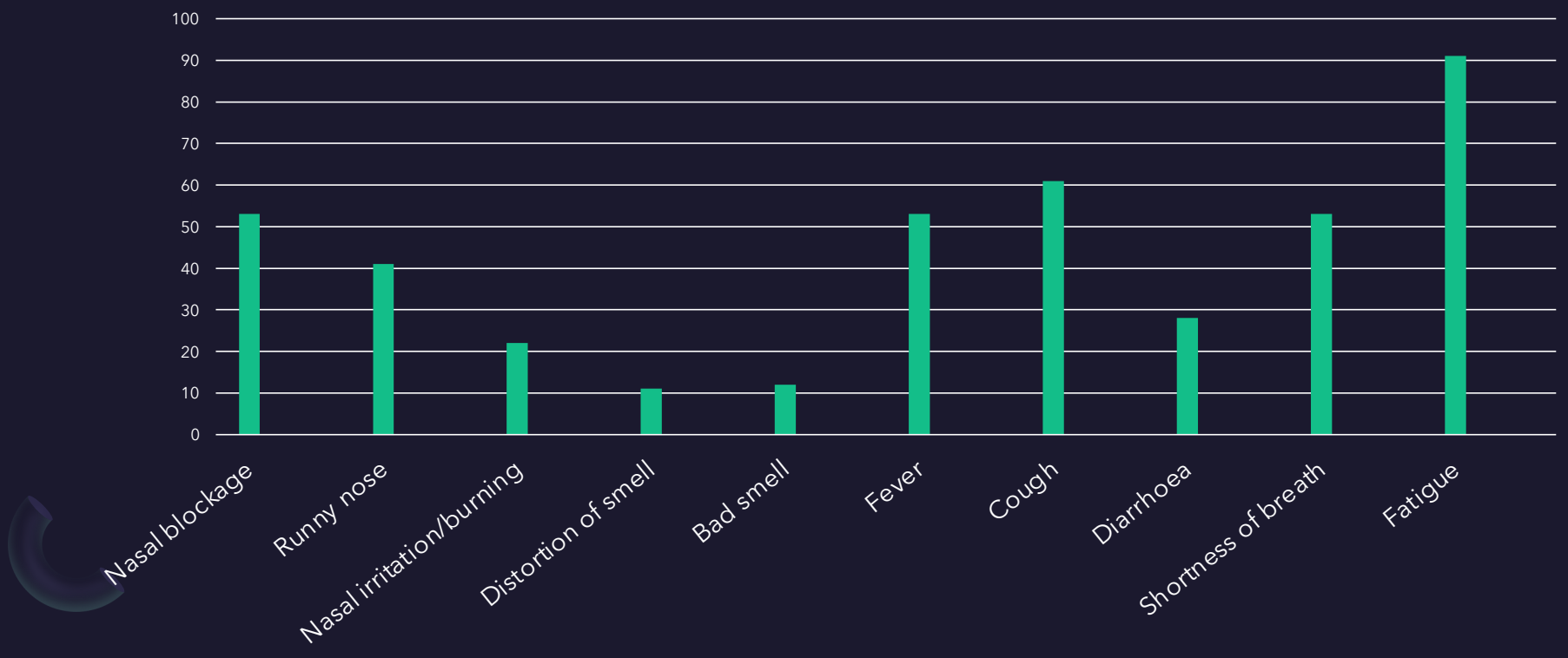
Smell loss scale

- As smell loss is the best predictor of COVID-19, we developed the ODoR-19 tool, a 0-10 scale to screen for recent olfactory loss.
- Numeric ratings ≤2 indicate high odds of symptomatic COVID-19 (4<Odds Ratio <10), which can be deployed when viral lab tests are impractical or unavailable

Is smell loss better than other symptoms in predicting Covid-19?



Other symptoms? (n=142)



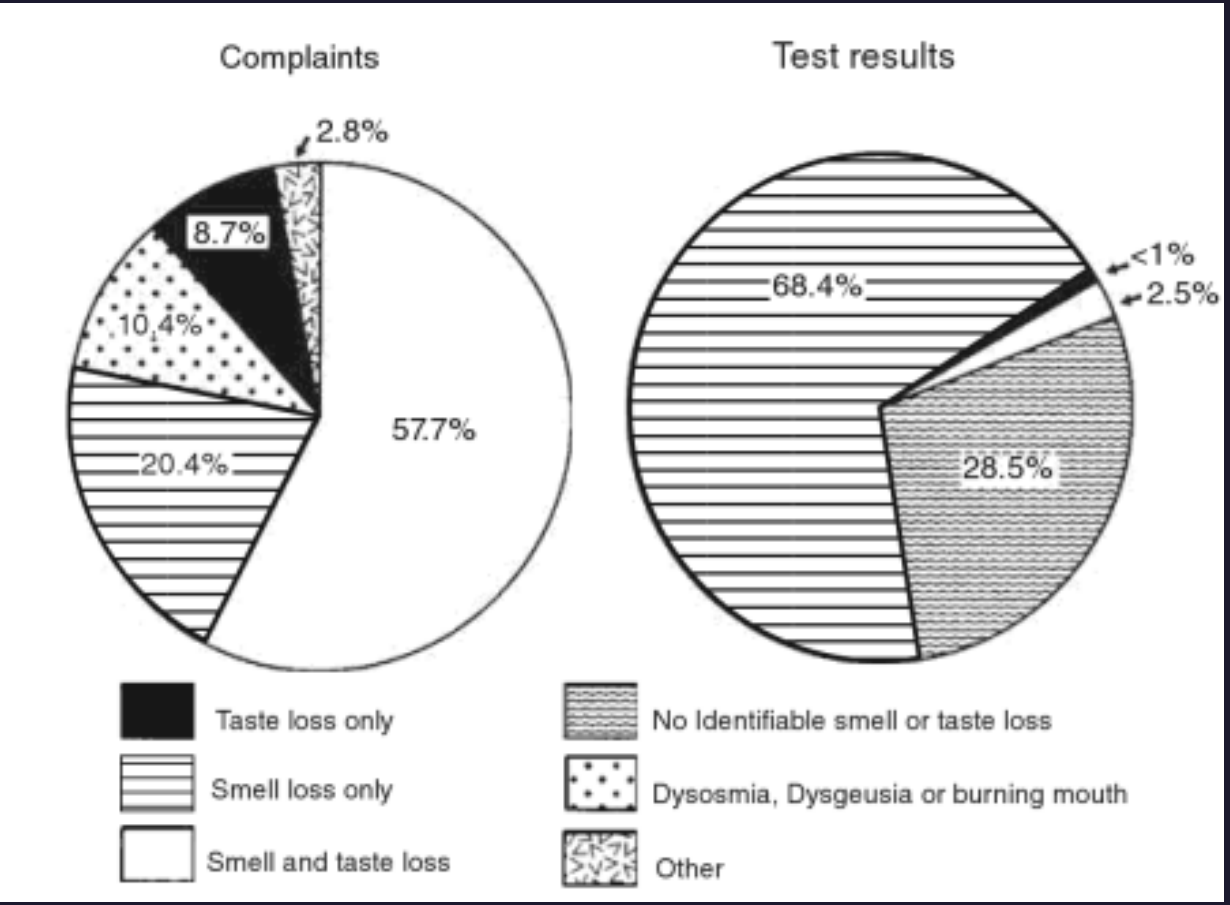
Taste disturbances in the GCCR survey

Table 3. Frequency of responses, by group, for changes of specific taste qualities during COVID-19

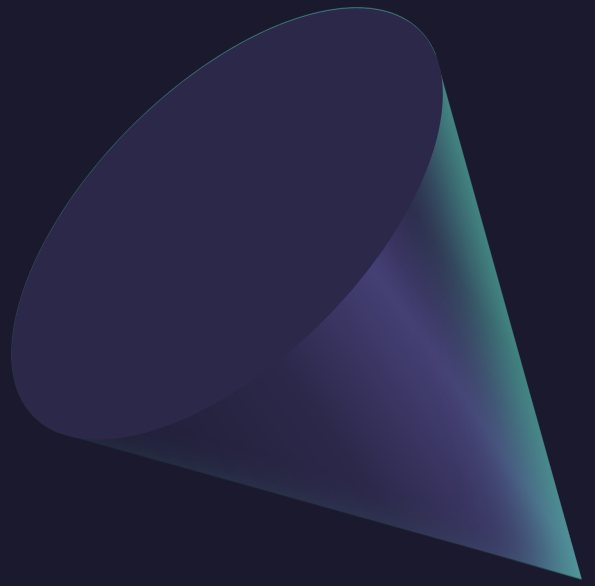
Taste change	Clinical Assessment (N = 2637)	Lab Test (N = 1402)
Sweet	1160	628
Salt	1211	629
Bitter	1036	550
Sour	980	531
Umami	668	411

Contrast between patient symptoms and test results

Is it just smell or is taste involved too?



Post-viral (infectious) olfactory loss (dysfunction)



Epidemiology

Probably represents about 11% of all olfactory loss but 20-25% in smell & taste clinics

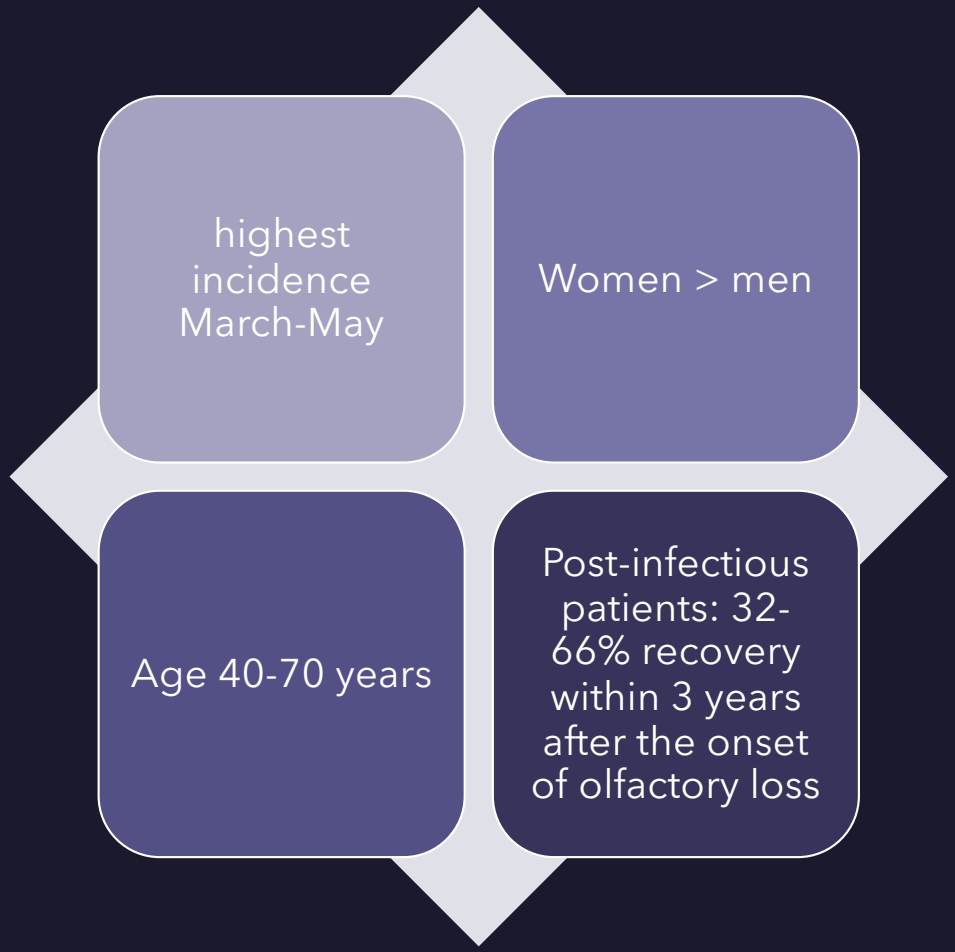
Viral respiratory illness is associated with loss of smell that does not return when other symptoms abate

Infection is recalled as “more severe”

Patients often describe preceding URTIs causing temporary smell loss

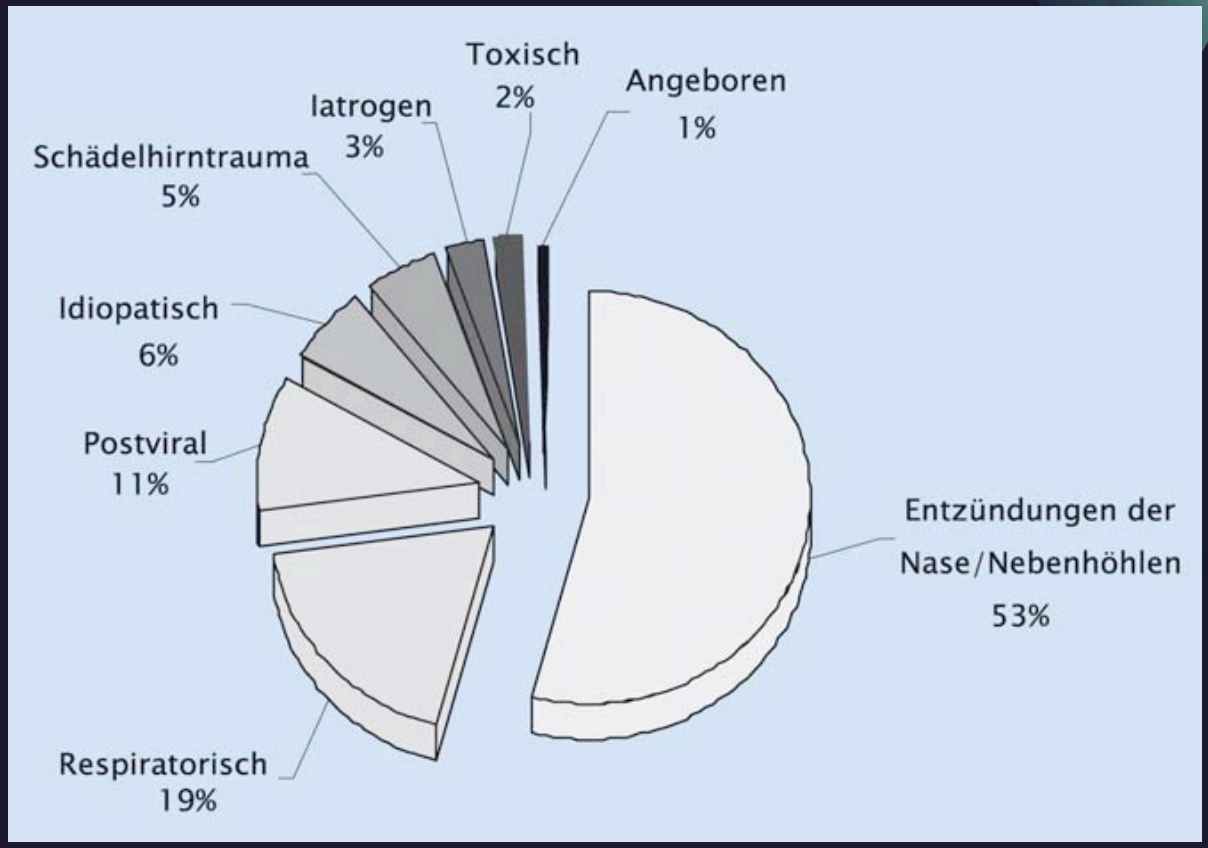
Sometimes there is crossover with CRS/cleft disease

Epidemiology (2)



German – Austrian – Swiss Survey

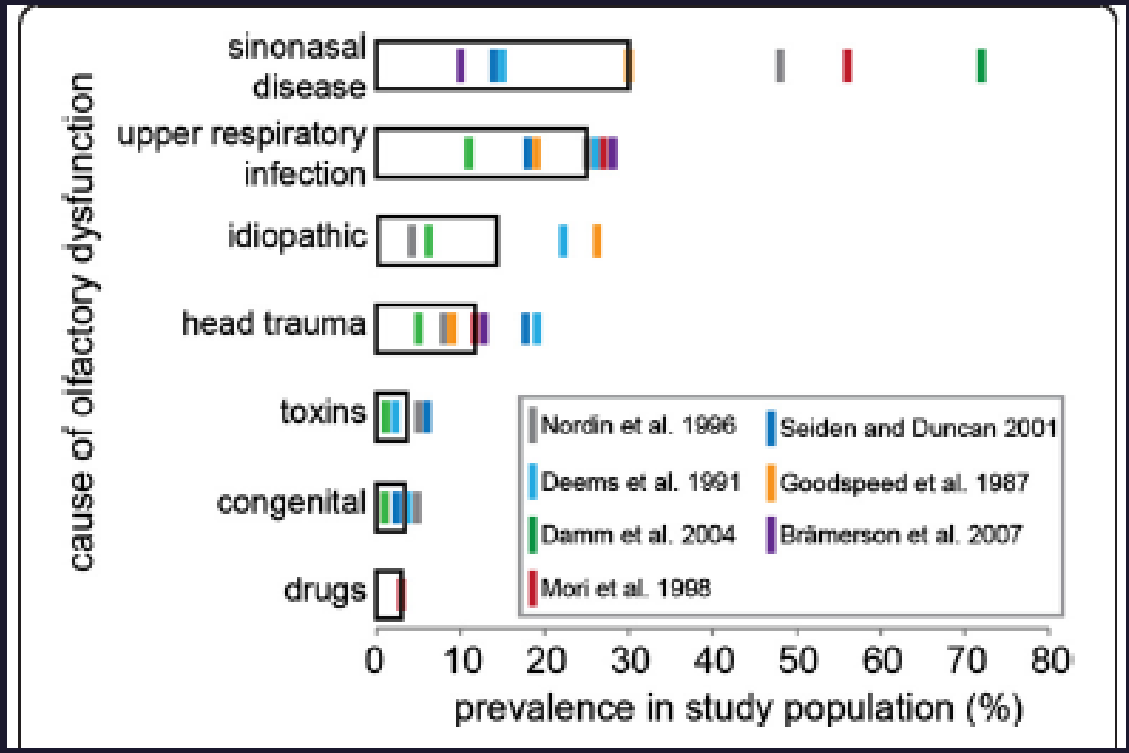
- 72% sinonasal disease
- 11% post-viral olfactory loss



Damm M, Temmel A, Welge-Lussen A, Eckel HE, Kreft MP, Klussmann JP, et al. [Olfactory dysfunctions. Epidemiology and therapy in Germany, Austria and Switzerland]. HNO 2004;52(2):112-20

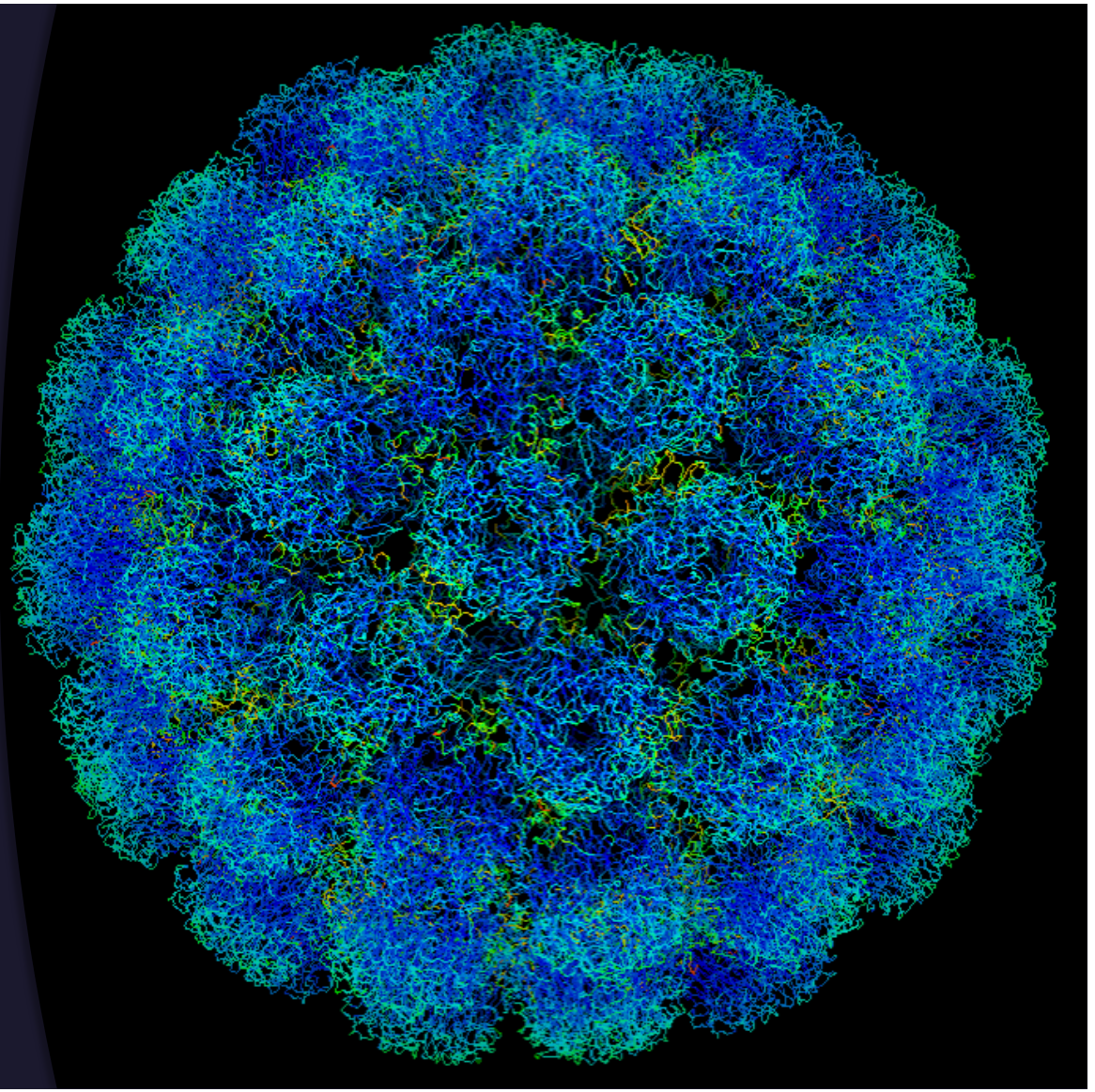
International survey

- Keller and Malaspina BMC Ear, Nose and Throat Disorders 2013, 13:8 http://www.biomedcentral.com/1472-6815/13/8



Aetiology

- Pathological agents include:
  - rhinoviruses (30-50%)
  - parainfluenza (5%)
  - **Coronavirus 10-15%**
  - Influenza (5-15%)
  - Coxsackie (<5%)
  - adenoviruses (<5%)
  - respiratory syncytial viruses (10%)



Pathophysiology

Reduced number of ciliated olfactory receptors means at the epithelial surface there is a lack of dendrites and vesicles

Results in a decrease in the area available for odour molecule detection.

So how is Covid-19 Smell Loss Different to typical PVOL?

CLASSICAL PVOL

- 2:1 female to male
- Age 40-70
- Typically noticed when other symptoms abate

COVID OD

- 70-90% female
- Younger – ave. age 30-40; 50% <40 yrs
- May be only symptom and typically sudden
- Short-lived? in 90%?
- Actual gustatory function?

Worse smell and taste in Covid -19

- 10 COVID-19 patients (PCR diagnosed, assessed on average 2 weeks after infection)
- 10 common cold patients (assessed before the COVID-19 outbreak)
- 10 healthy controls, matched for age and sex
- Smell and taste tests undertaken

Comparison of COVID-19 and common cold chemosensory dysfunction. Huart C, Philpott C, Konstantinidis I, Altundag A, Whitcroft KL, Trecca EMC, Cassano M, Rombaux P, Hummel T. Rhinology. 2020 Aug 19. doi: 10.4193/Rhin20.251.

Worse smell and taste in Covid-19

- Smell discrimination and identification scores of COVID-19 patients were significantly lower compared to common cold patients (p= 0.015)
- 100% sensitivity and 80% specificity for a cut-off value of 10 out of 16
- We found that olfactory dysfunction had a favourable recovery in both groups, as all patients reported improvement in the weeks following the infectious event.
- Particularly, all COVID-19 patients all reported improvement at a mean follow-up of 18 days (±6 days), although only 30% reported complete recovery.

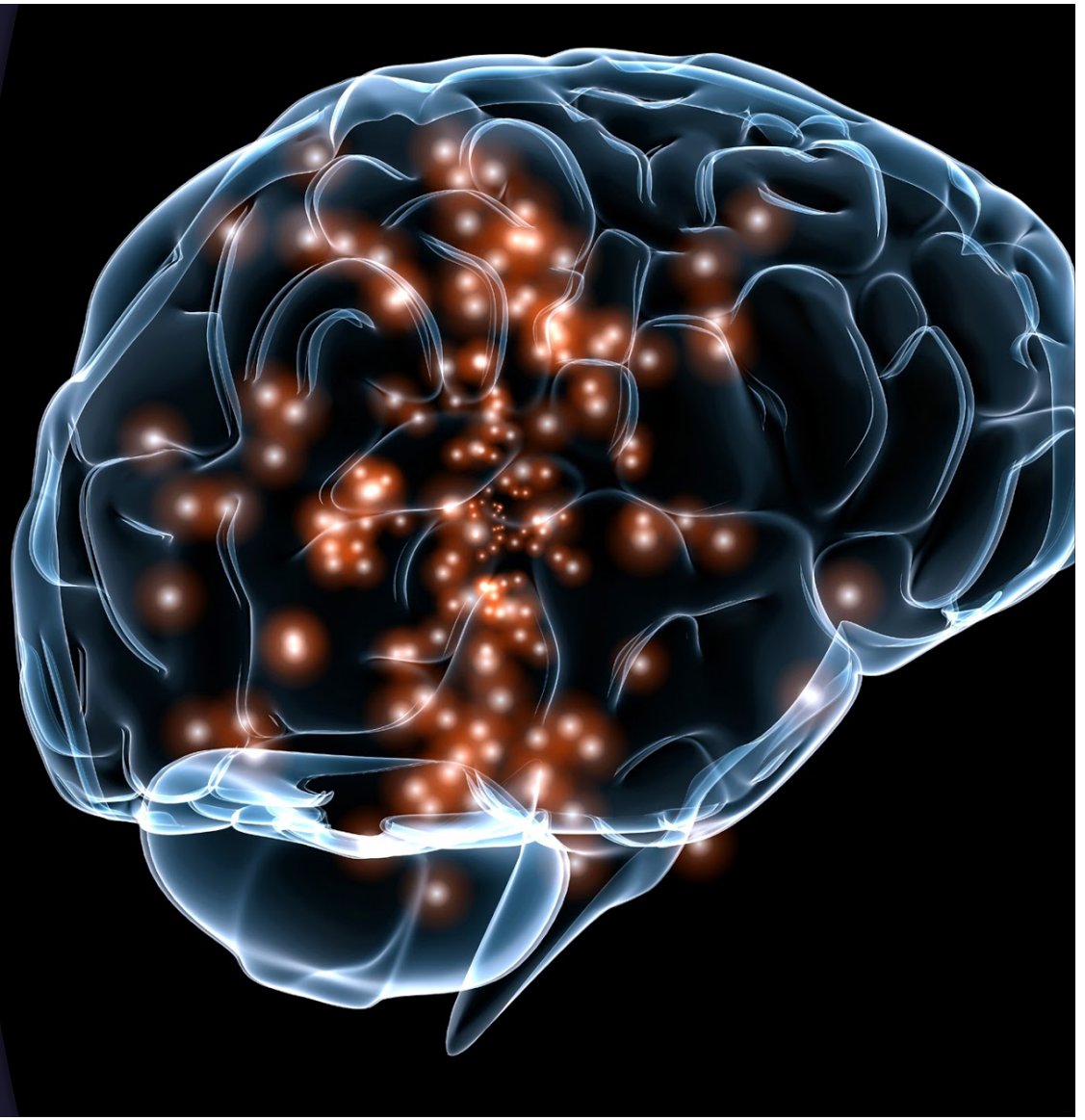
Worse smell and taste in Covid-19

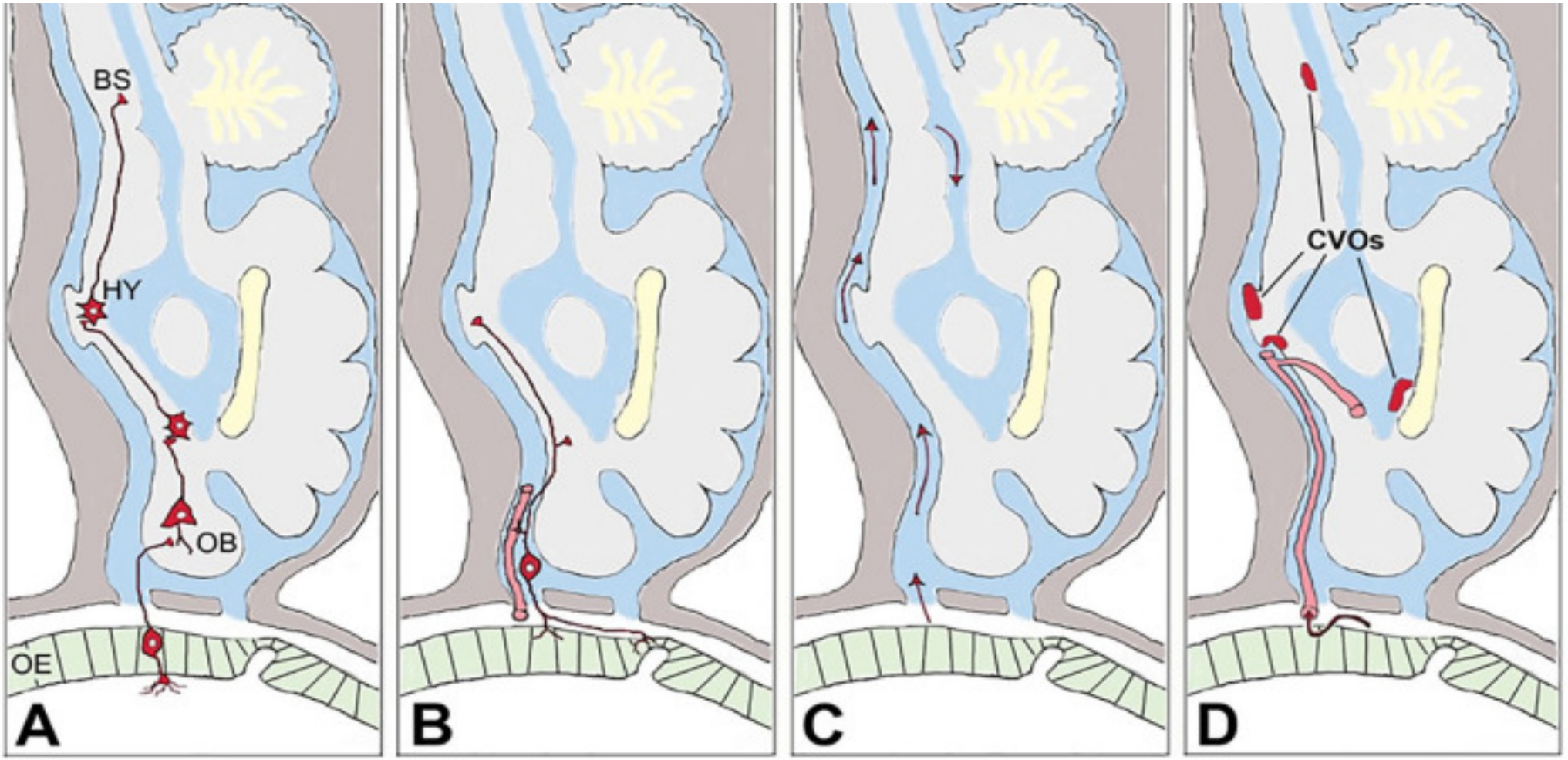
- COVID-19 patients had worse global, sweet and bitter taste scores ($p<0.05$)
- Bitter stimulus showed an excellent discrimination performance with 90% sensitivity and 80% specificity

Covid 19 is a crafty virus…

Neuroinvasive??

- Genetically similar SARS-CoV virus can spread via a synapse-connected route to the medullary cardiorespiratory centre
- Coronaviral RNA has been identified post-mortem concentrated in the brain-stem of human patients during the previous SARS-CoV pandemic
- Mice studies have shown that coronaviruses can invade intracranially
- At a central level, SARS-CoV-2 may involve the nucleus of the solitary tract, which is part of the taste pathways
- Smell, sweet and bitter receptors share some similarities: G-Protein coupled receptors (GPCRs





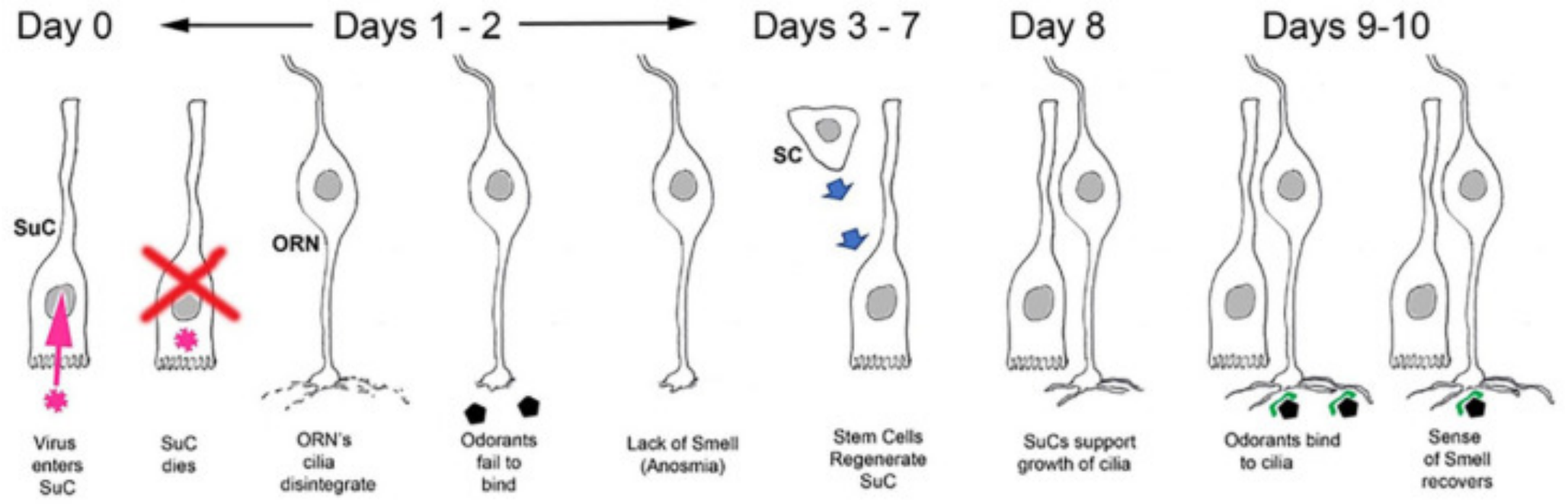
Four potential routes of SARS-CoV-2 virus from the nose to the brain through the cribriform plate. (A) Olfactory circuits. (B) Nervus terminalis. (C) Cerebrospinal fluid. (D) Vasculature. BS, brainstem; CVOs, circumventricular organs; HY, hypothalamus; OB, olfactory bulb; OE, olfactory epithelium.

Architectural disturbance?

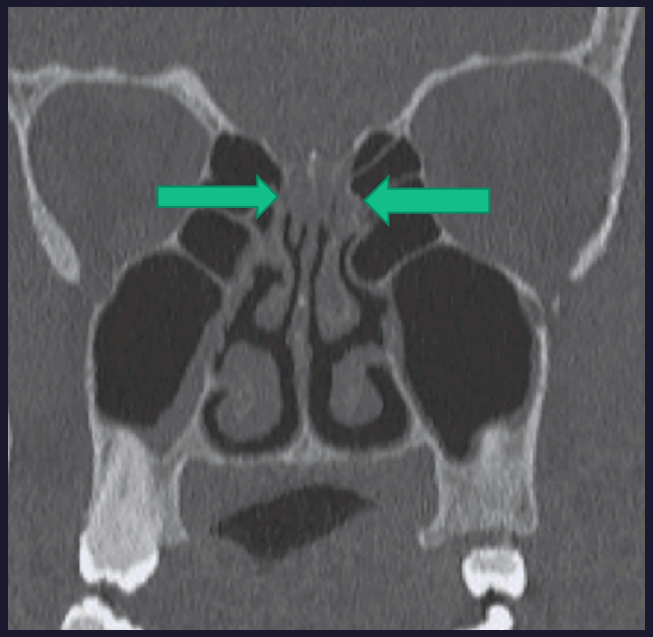
- Virus attacks supporting cells in the olfactory epithelium
- Results in “squeezing” of sensory neurons
- Perhaps explains temporary effect in the majority

Time course of olfactory dysfunction

(DOI: 10.1177/1073858420956905; Butowt and Barthold)



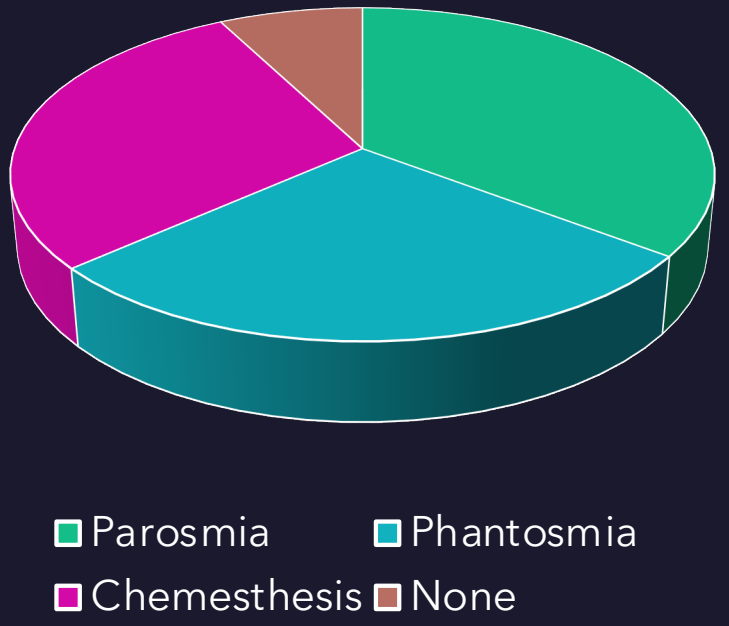
Localised oedema?



- Elizier et al
- doi:10.1001/jamaoto.2020.0832

Qualitative disturbances

Symptom	N (%)
Parosmia	115 (42)
Phantosmia	92 (34)
Chemesthesis	94 (35)



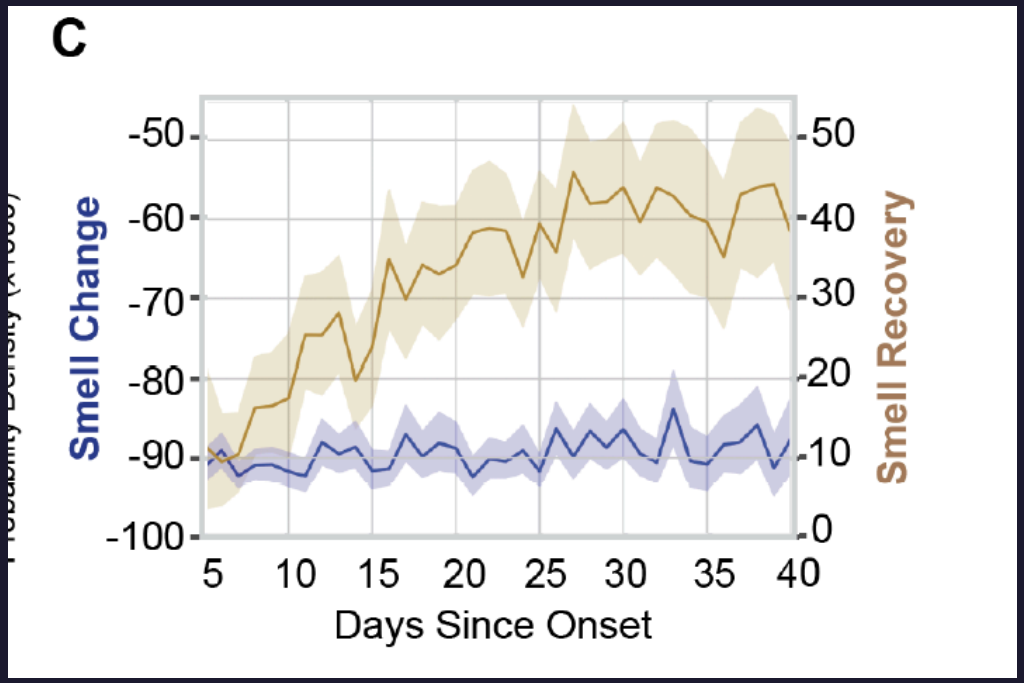
So how many in the UK have smell/taste problems due to covid-19?

- 1,192,013 cases to date
- 715,208 estimated to have experienced smell/taste loss

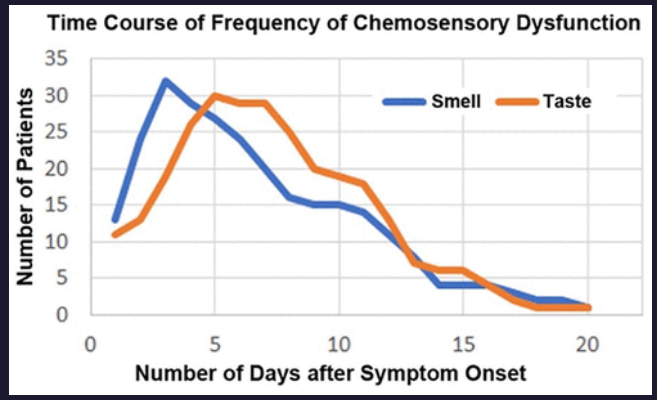
Smell recovery

- NHS staff: For those in who loss of smell and/or taste occurred at least four weeks prior to the survey, only half had fully recovered, indicating the need for further research into the long-term management of the sequelae of Covid-19 infection.
- GCCR survey: Olfactory recovery within 40 days was reported for ~50% of participants and was best predicted by time since illness onset.

Recovery of smell loss

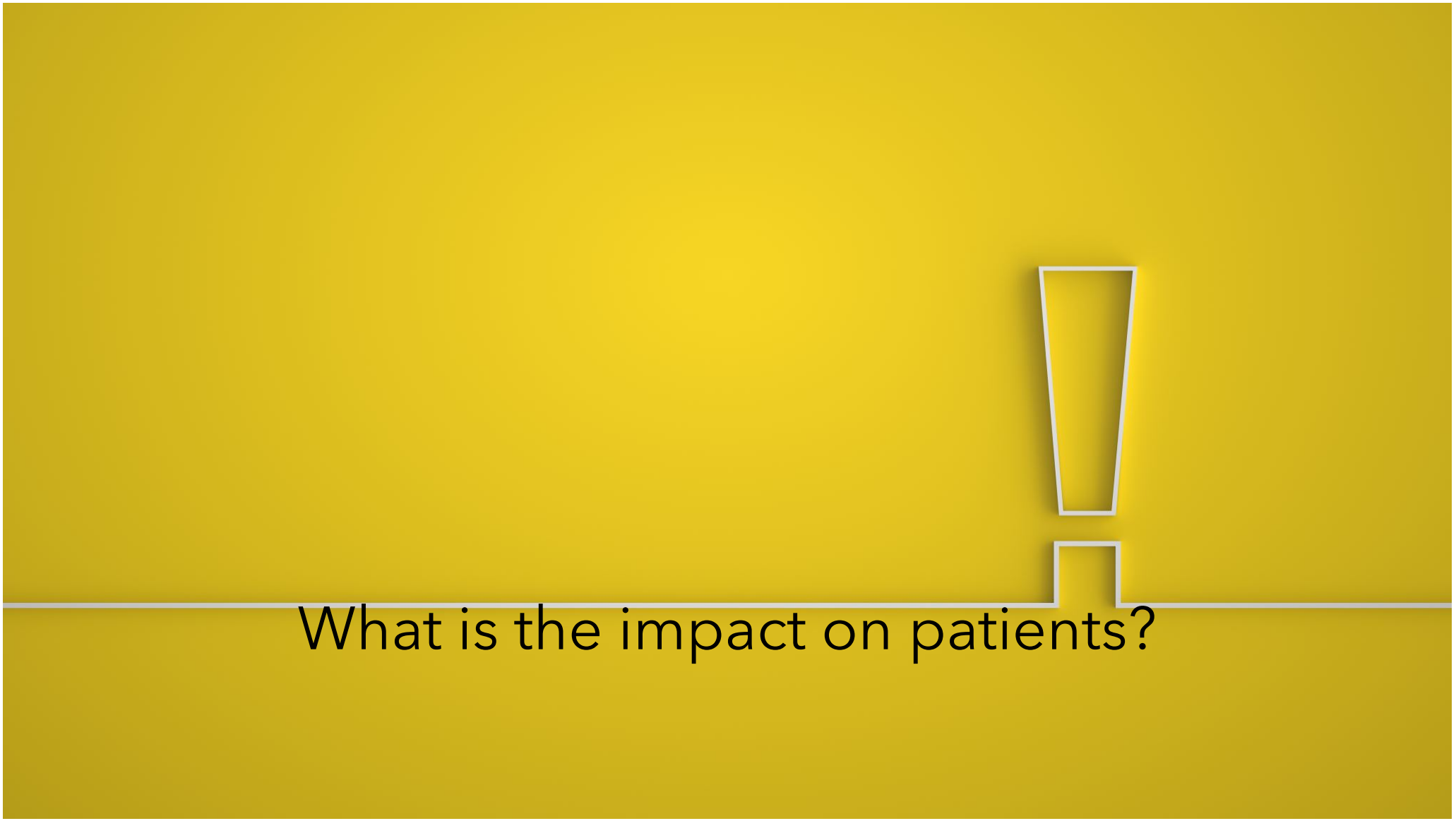


10-17% recover within 3-4 weeks of onset



But if 10% don’t get better…

- 50,266,033 cases globally to date
- 60% with olfactory dysfunction = 30,159,619
- 10% with persistent olfactory dysfunction = over 3 million
- UK = about 71,500 people


What is the impact on patients?


N°5
CHANEL
PARIS
PARFUM

“When I lost my sense of smell it was like being struck blind. Life lost a good deal of its savour...My whole world was radically poorer”

Exert from “The Man Who Mistook His Wife For a Hat” by O. Sacks as featured in “Aroma”

Fifth sense member survey

The Impact of Olfactory Disorders in the United Kingdom
Carl M. Philpott and Duncan Boak
Chem. Senses 39: 711–718, 2014 doi:10.1093/chemse/bju043

- 500 members in the UK polled
- Depression and anxiety = 61% of sufferers
- 28% have received treatment (e.g. antidepressants, counselling)
- Further 25% have taken over the counter remedies or sought alternative medicines/therapies
- 30% have suffered weight loss
- 35% have suffered weight gain

Priority Setting Partnership for Smell & Taste Disorders

James Lind Alliance
Priority Setting Partnerships

Home | About the JLA | The PSPs | Top 10s | JLA Guidebook | News and Publications | Making a differenc

You are in: Home » The PSPs » Smell and Taste Disorders

Smell and Taste Disorders

A man's nose and mouth

The Smell & Taste Disorders Priority Setting Partnership (PSP) has its origins in the beginnings of Fifth Sense, the charity set up to support those with smell and taste disorders. The charity has been planning to do the PSP for a number of years and it formed one part of the development plan that was submitted to the National Lottery Community Fund in 2019. The fund provided the budget to support this project and finally enable it to happen.

A diverse group of stakeholders have come together to form this PSP to find out what matters to patients, carers and clinicians in the field of smell and taste disorders. Professor Carl Philpott, Professor of Rhinology and Olfactology at the University of East Anglia and Director of Research and Medical Affairs at Fifth Sense is the professional lead for the PSP Steering Group and is supported by clinicians across ENT, Neurology, Psychology and Primary Care, and patient and carer representatives from a range of conditions and causes.

Fifth Sense
Smell, Taste, Life.

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/ Uncategorised

Fifth Sense Announce Smell And Taste Disorders James Lind Alliance Pric

Fifth Sense Announce Smell And Taste Disorders James Lind Alliance Priority Setting Partnership

21/09/2020 / Nina Hill /

Working Together to Establish Research Priorities for Smell and Taste Disorders

James Lind Alliance
Priority Setting Partnerships

Fifth Sense is excited to announce the launch of a James Lind Alliance Priority Setting Partnership (PSP) to establish future research priorities of patients, carers and clinicians in the field of smell and taste disorders.

The PSP steering group will lead the development of a survey aimed at all those affected by smell and taste disorders, and includes carers and family, health or social care professionals and representatives of relevant organisations. The survey will cover obvious symptoms, such as a reduction or complete lack of smell or taste, to qualitative symptoms, such as smell distortions or hallucinations. The partnership will result in a vital list of informed priorities which will be a catalyst for future research into conditions that have a serious quality of life impact on so many.

COMMUNITY FUND

Led by Professor Carl Philpott (Director of the UK's first NHS clinic focusing on smell and taste disorders) and supported by funding from the National Lottery Community Fund, the partnership will build on the increased awareness of smell and taste disorders that has resulted from the Covid-19 pandemic and provide a unique opportunity to engage patients and their families and friends, as well as the clinicians who support them.

Prof Philpott said: "This partnership will work hard to reach people with a smell or taste disorder– people whose voices are frequently not heard in research."

Summary

- Undeniable link with olfactory and possible gustatory loss; worse than typical viral infections
- Younger and female – more so than typical PVOL
- Qualitative disturbances also common
- If your colleague can't smell, send them home!
- Local or central effect? – may vary from case to case
- Self-limiting? In the majority, but at least 10% have smell related long-Covid
- What to do? Seek support – Fifth Sense

Any questions?

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