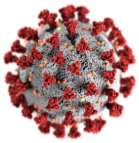
ACCESS
vACCine covid-19  monitoring readinESS

EVENT DEFINITION FORM

Event: Anosmia and ageusia
Outcome/covariate: outcome
Version: **1**
Status: final

Contributing authors

authors	Role	Date
Tuur Egbers	Medical /draft	July 2020
Miriam Sturkenbom	Codemapper	August 13, 2020
Leila Belbachir	Medical review	August 22, 2020
Caitlin Dodd	Algorithm proposal	03-09-2020
Carlos Durán	Rev. narrow/possible assignment	29-03-2021
Miriam Sturkenboom	Inclusion of codes used in final ACCESS report	23-08-2021

1. Event definition

Anosmia[1], [2]

Anosmia: Absent smell function

Two causes for anosmia:

1) conductive and/or traumatic
2) sensorineural

1) Obstructive nasal diseases, such as chronic rhinosinusitis (CRS), nasal polyposis, allergic rhinitis, and nasal masses, can obstruct nasal airflow to the olfactory cleft.
(excluding) Chronic rhinosinusitis as a cause of diminished smell

There must be a time limit, non-necessarily

Chronic rhinosinusitis after immunisation is possible

Approximately 20-30% of patients who experience head trauma develop some degree of olfactory dysfunction, whereas up to 5% experience anosmia.

Exclusion of recent trauma

2) A recent history of URI is reported by 20-30% of patients with acquired olfactory dysfunction.
Excluding congenital anosmia? Yes
Kallmann syndrome (congenital), which can be distinguished by the presence of hypogonadotropic hypogonadism, must be ruled out in similar cases because the presentation can be similar. Damage to the olfactory bulb can also be seen with many neurodegenerative diseases, such as Alzheimer disease and Parkinson disease.

Exclusion of anosmia as a part of another disease.

Numerous commonly prescribed medications, such as antihypertensive and antihyperlipidemic drugs, are associated with smell disturbance.

Exclusion of anosmia caused by the use of specific medication.

Angiotensin-converting-enzyme inhibitors, diuretics, calcium channel blockers, and statins

Ageusia

Ageusia: Absent taste function

[1] Boesveldt S, Postma EM, Boak D, Welge-Luessen A, Schöpf V, Mainland JD, Martens J, Ngai J, Duffy VB. Anosmia-A Clinical Review. Chem Senses. 2017 Sep 1;42(7):513-523. doi: 10.1093/chemse/bjx025. Erratum in: Chem Senses. 2017 Sep 1;42(7):607. PMID: 28531300; PMCID: PMC5863566.

[2] Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and Ageusia: Common Findings in COVID-19 Patients. Laryngoscope. 2020 Jul;130(7):1787. doi: 10.1002/lary.28692. Epub 2020 Apr 15. PMID: 32237238; PMCID: PMC7228304.

Staging system to assess whether the patient has ageusia or dysgeusia. A scale that ranges from 0, which refers to no taste, to 4, which refers to total taste loss, may be useful in evaluation[3] [4].

Ageusia is the loss of taste functions of the tongue
Anosmia the loss of the ability to detect one or more smells

2. Synonyms / lay terms for the event

Anosmia:

- Olfaction (is a chemoreception that, through the sensory olfactory system, forms the perception of smell)
- Anosphresia
- anosmic

ageusia

- Loss of the sense of taste
- Hypogeusia
- Gustation (taste perception)
- Taste perception
- Ageusic

3. Laboratory tests that are specific for event

Ageusia and anosmia

A complete blood count, sedimentation rate, plasma creatinine, liver function tests, antinuclear antibodies, and a thyroid profile are an essential part of the initial evaluation. Detection of antibodies to Ro/SSA and LA/SSB may be valuable in identifying patients with Sjögren's syndrome, while measurement of lead, arsenic, and other heavy metal concentrations may be warranted in selected patients with dysgeusia.

4. Diagnostic tests that are specific for event

From Uptodate

Anosmia

[3] Maes A, Huygh I, Weltens C, Vandevelde G, Delaere P, Evers G, Van den Bogaert W. De Gustibus: time scale of loss and recovery of tastes caused by radiotherapy. Radiother Oncol. 2002 May;63(2):195-201. doi: 10.1016/s0167-8140(02)00025-7. PMID: 12063009.

[4] Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and Ageusia: Common Findings in COVID-19 Patients. Laryngoscope. 2020 Jul;130(7):1787. doi: 10.1002/lary.28692. Epub 2020 Apr 15. PMID: 32237238; PMCID: PMC7228304.

Although not always indicated, imaging can often provide valuable information regarding the etiology of olfactory dysfunction. **Computed tomography (CT)** can help assess the degree of opacification of olfactory clefts in patients with chronic rhinosinusitis (CRS).

An unremarkable history and physical examination, in combination with persistence of olfactory dysfunction, warrant further workup with imaging because the cost-effectiveness of **magnetic resonance imaging** in idiopathic olfactory loss has already been established. Magnetic resonance imaging remains the imaging study of choice in patients with suspicion of tumor or to verify the absence of olfactory bulbs in Kallmann syndrome.

"Sniffin' Sticks" test, a test of nasal chemosensory performance developed in 1996 and that consists of tests for odor threshold, discrimination, and identification, has gained popularity due to its test-retest reliability and validity.

Perhaps the most widely used and published screening test remains the University of **Pennsylvania Smell Identification Test**, which is a forced-choice, 40-question test that has been given to >500,000 patients. With the ability to detect malingering and with a test-retest reliability of 0.94, the University of Pennsylvania Smell Identification Test remains a powerful tool in detecting and monitoring olfactory dysfunction.

Butanol threshold test

The patient is presented with bottles containing either water or odorant

Ageusia

Electro-gustometry and chemo-gustometry

Electrogustometry has its basis the principle of applying weak electrical currents to the different taste buds in the oral cavity, whereas the chemogustometry uses specific taste solutions to examine the taste sensitivity.

Spatial analysis

In this test, a cotton swab is dipped in a particular taste solution. The patient is then asked to assess the quality and intensity of the taste.

Psychophysical evaluation: This is essential to identify the patient's complaints and in measuring the degree of permanent taste loss. The clinician must also be sensitive to the psychological state of the patient. Depression can result from a taste problem or contribute to a taste complaint.

Medical Imaging: Imaging techniques (CT and MRI) help in ruling out or confirm the presence of any damage to the structures of the central nervous system, particularly to the brain stem, thalamus, or pons.

Whole-mouth taste test

Whole-mouth taste testing assesses the patient's ability to detect, identify, and rate the intensity of various concentrations of sweet, sour, salty, and bitter taste solutions

Flavour discrimination test

The flavor discrimination test is used to evaluate the combination of both taste and smell sensation. Four different stimulant solutions are made available which differ in the amount of sweetener present.

5. Drugs that are used to treat event

Anosmia

Corticosteroids

Overall, further studies are needed before a formal recommendation of either topical or systemic corticosteroid treatment can be made.

- fluticasone nasal spray in chronic rhinosinusitis (CRS)
- In URI (upper respiratory infection), CRS, and idiopathic-associated olfactory dysfunction concluded that systemic steroids (oral prednisolone) improved smell across all measures, whereas local steroids (mometasone nasal spray) showed no significant improvement in olfaction.

Theophylline (phosphodiesterase inhibitor)

Overall, the moderate response rate, in addition to the substantial adverse effects profile, has limited the use of theophylline in clinical practice.

Alpha-Lipoic Acid

Alpha-lipoic acid and its active metabolite dihydrolipoic acid are well known to stimulate the expression of nerve growth factor, enhance conduction velocity of motor nerves, and possess antioxidative effects.

Results that indicated that 61% of the patients had moderate-to-significant improvement led to the recommendation of its use for treatment in postviral cases. Overall, the use alpha-lipoic acid in the clinical setting remains limited given the lack of definitive data.

Oral zinc

Other **Antihistamines** may be indicated in cases of allergic rhinitis. Attention should also be given to factors in the home (eg, molds, pets) that might add to allergic problems. Desensitization is necessary in some cases. **Leukotriene inhibitors** can reduce the size of nasal polyps and improve smell in some patients with polyps and anosmia/hyposmia. Treatment of chronic sinusitis and nasal polyposis, however, has variable effectiveness for improving anosmia.

Ageusia

Supplements are an option, such as: **zinc gluconate**, particularly in patients undergoing radiotherapy/chemotherapy in the dosage of 140mg/day or **alpha-lipoic acid** in the dosage of 600 mg/day for few months may restore taste.

In cases of dysgeusia and burning mouth disorder, tricyclic antidepressants and clonazepam are a possibility. With severe dysgeusia, topical anesthetics such as lidocaine gel may help.

6. Procedures used specific for event treatment

Anosmia

Olfactory training

Exposure to certain odors may modulate the regenerative capacity of olfactory receptor neurons. Olfactory training was most helpful in postinfection anosmia

Endoscopic sinus surgery (ESS)

Improvement of CRS-related olfactory dysfunction remains difficult to predict, and further studies are needed before the role of ESS for CRS-related olfactory dysfunction can be further defined.

ESS is also used in the treatment of nasal polyposis

Ageusia

Sometimes, a cure is often challenging to obtain. In such cases, the most crucial aspect of treatment is educating the patient on how to cope with the disorder.

7. Setting (outpatient specialist, in-hospital, GP, emergency room) where condition will be most frequently /reliably diagnosed

Primary care

8. Diagnosis codes or algorithms used in different papers to extract the events in Europe/USA: seek literature for papers that have studied this event, and see how they extracted/measured the event.

ICD-10 Version:2019

Anosmia R43.0

Parageusia (including ageusia) R43.2

ICD-9-CM version: 2015

Disturbances of sensation of smell and taste (781.1)

Anosmia 781.1

- psychogenic 306.7
- traumatic 951.8

Ageusia 781.1

9. Codes used in ACCESS

Coding system	Code	Code name	Concept	Concept name	Algorithm
ICD10/CM	G52.0	Disorders of olfactory nerve	C0751937	Olfactory Nerve Diseases	Possible
ICD10/CM	R43.0	Anosmia	C0003126	Anosmia	Narrow

ICD10/CM	R43.1	Parosmia	C1510410	Sense of smell altered	Narrow
ICD10/CM	R43.2	Parageusia	C0013378	Dysgeusia	Narrow
ICD9CM	781.1	Disturbances of sensation of smell and taste			narrow
ICD9CM	352.0	Disorders of olfactory (1st) nerve	C0751937	Olfactory Nerve Diseases	Possible
ICPC	N16	Disturbances of sensation of smell and taste			narrow
RCD2	1924.	Loss of taste	C2364111	Actual Inability To Taste	Narrow
RCD2	1B45.	Anosmia - loss of smell sense	C0003126	Anosmia	Narrow
RCD2	F320.	Olfactory nerve disorders	C0751937	Olfactory Nerve Diseases	Possible
RCD2	R0110	[D]Anosmia	C0003126	Anosmia	Narrow
RCD2	R0111	[D]Parosmia	C1510410	Sense of smell altered	Narrow
RCD2	R0112	[D]Parageusia	C0013378	Dysgeusia	Narrow
RCD2	ZV415	[V]Problems with smell/taste	C0013378	Dysgeusia	Narrow
SCTSPA	1932001	disgeusia	C0013378	Dysgeusia	Narrow
SCTSPA	36955009	ageusia	C2364111	Actual Inability To Taste	Narrow
SCTSPA	44525005	percepción anormal y desagradable de un aroma fuerte	C0234266	Abnormal unpleasant perception of strong scent	Narrow
SCTSPA	68982002	trastorno del nervio olfatorio	C0751937	Olfactory Nerve Diseases	Possible
SCTSPA	112105008	parosmia	C1510410	Sense of smell altered	Narrow
SCTSPA	129820002	alteración olfativa	C1510410	Sense of smell altered	Narrow
SCTSPA	206813000	[D]anosmia	C0003126	Anosmia	Narrow
SCTSPA	206814006	[D]parosmia	C1510410	Sense of smell altered	Narrow
SCTSPA	206815007	[D]parageusia	C0013378	Dysgeusia	Narrow
SCTSPA	247318005	gusto anormal en la boca	C0423564	Abnormal taste in mouth	Narrow
SCTSPA	247320008	las cosas huelen diferente	C0423569	Things smell different	Narrow
SCTSPA	271801002	alteración del sentido del gusto	C0013378	Dysgeusia	Narrow
SCTSPA	697990000	hipogeusia	C0151934	Hypogeusia	Narrow
SCTSPA	708673009	parosmia	C1510410	Sense of smell altered	Narrow
SNOMEDCT_US	1932001	Adverse taste perception	C0013378	Dysgeusia	Narrow
SNOMEDCT_US	44525005	Abnormal unpleasant perception of strong scent	C0234266	Abnormal unpleasant perception of strong scent	Narrow
SNOMEDCT_US	68982002	Disorder of olfactory nerve	C0751937	Olfactory Nerve Diseases	Possible
SNOMEDCT_US	112105008	Sense of smell altered	C1510410	Sense of smell altered	Narrow

SNOMEDCT_US	129820002	Olfactory alteration	C1510410	Sense of smell altered	Narrow
SNOMEDCT_US	139277004	Loss of taste (& symptom)	C2364111	Actual Inability To Taste	Narrow
SNOMEDCT_US	139523002	Loss of sense of smell	C0003126	Anosmia	Narrow
SNOMEDCT_US	158191003	[D]Anosmia	C0003126	Anosmia	Narrow
SNOMEDCT_US	158192005	[D]Parosmia	C1510410	Sense of smell altered	Narrow
SNOMEDCT_US	158193000	[D]Parageusia	C0013378	Dysgeusia	Narrow
SNOMEDCT_US	162012003	Loss of taste	C2364111	Actual Inability To Taste	Narrow
SNOMEDCT_US	162254006	Anosmia - loss of smell sense	C0003126	Anosmia	Narrow
SNOMEDCT_US	206813000	[D]Anosmia	C0003126	Anosmia	Narrow
SNOMEDCT_US	206814006	[D]Parosmia	C1510410	Sense of smell altered	Narrow
SNOMEDCT_US	206815007	[D]Parageusia	C0013378	Dysgeusia	Narrow
SNOMEDCT_US	230501005	Loss of sense of smell	C0003126	Anosmia	Narrow
SNOMEDCT_US	247318005	Abnormal taste in mouth	C0423564	Abnormal taste in mouth	Narrow
SNOMEDCT_US	247320008	Things smell different	C0423569	Things smell different	Narrow
SNOMEDCT_US	267164004	Loss of taste	C2364111	Actual Inability To Taste	Narrow
SNOMEDCT_US	271800001	Sense of smell altered	C1510410	Sense of smell altered	Narrow
SNOMEDCT_US	271801002	Taste sense altered	C0013378	Dysgeusia	Narrow
SNOMEDCT_US	272028008	C/O - anosmia			narrow
SNOMEDCT_US	272041007	C/O - loss of taste sense			narrow
SNOMEDCT_US	275462005	[V]Problems with smell			narrow
SNOMEDCT_US	697990000	Hypogeusia	C0151934	Hypogeusia	Narrow
SNOMEDCT_US	708673009	Parosmia	C1510410	Sense of smell altered	Narrow
SNOMEDCT_US	2611000119103	[D]Smell and taste disorder			

11. Algorithm proposal

Broad Algorithm:

- Concept sets (Anosmia, Dysgeusia, Possible_anosmia).
- Index date = first occurrence of a code from the concept sets (Anosmia, Dysgeusia, Possible_anosmia)

Narrow Algorithm:

- Concept sets (Anosmia, Dysgeusia).

- Index date = first occurrence of a code from the concept sets (Anosmia, Dysgeusia)

12. Background rates

No incidence reference was found only prevalence