

# Smell and taste dysfunction testing

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Policy contains: Chemosensory impairment; electrogustometry; smell disorder; smell testing; taste disorders; taste testing.

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## Coverage policy

Smell and taste dysfunction testing is clinically proven, and therefore may be medically necessary for various populations, including members with neurological disorders, COVID-19 infection, and olfactory and gustatory dysfunction, for which results will change care management and when the following testing and medical necessity criteria are met (Doty, 2019; Oppo, 2020; Whitcroft, 2020):

Any of the following odor identification and smell tests:

- Odor identification testing.
- 40-odorant University of Pennsylvania Smell Identification Test (UPSIT).
- 12-odor Brief-Smell Identification Test (B-SIT).
- 3-odor Pocket Smell Test (PST) (Sensonics, Inc., Haddon Heights, NJ).
- Smell threshold (detection) testing.
- Smell suprathreshold testing.
- Smell unilateral testing.

Any of the following taste tests:

- Whole-mouth taste suprathreshold testing.
- Taste quadrant (regional) testing.

Any of the following indications (Malaty, 2013; Doty, 2019):

- Diagnose unexplained symptoms of an olfactory or gustatory disorder.
- Determine the nature and degree of chemosensory dysfunction.
- Detect malingering (full test versions only, e.g., University of Pennsylvania Smell Identification Test or Sniffin' Sticks tests).
- Monitor functional changes over time.
- Assess treatment efficacy.

### Limitations

The following indications of psychophysical smell and taste identification tests are experimental/investigational and not clinically proven:

- Identifying asymptomatic members at risk for neurodegenerative diseases (e.g., Alzheimer's dementia or Parkinson's disease) (Jung, 2019; Kotecha, 2018; Silva, 2018).
- Screening asymptomatic members for cognitive impairment (Patnode, 2019; U.S. Preventive Services Task Force, 2020).
- Routine testing in the absence of a complaint of or suspicion for smell or taste dysfunction (Malaty, 2013).
- Detection of malingering using shorter-version validated smell tests (e.g., Quick Smell Identification Test or Q-sticks) (Malaty, 2013; Morley, 2018).

Electrophysiological chemosensory tests for unexplained smell and taste dysfunction (e.g., electrogustometry or evoked potential testing) may be considered on a case-by-case basis for the differential diagnosis as part of a specialty examination (Doty, 2008, 2015; Gamper, 2012).

### Alternative covered services

- Allergy testing.
- Biopsy of the olfactory mucosa.
- Drug assays and chemical analyses for suspected medication or nutritional etiologies.
- Electroencephalography for members with a history of seizures.
- Hematological tests (e.g., hematocrit count, hemoglobin level, white blood cell count, urea nitrogen level, creatinine level, glucose level, erythrocyte sedimentation rate, eosinophil count, and immunoglobulin E level).
- Nasal endoscopy.
- Neuroimaging (e.g., computed tomography or magnetic resonance imaging) to rule out intracranial or peripheral nerve abnormalities.
- Nerve blocks.
- Neurological, otolaryngological, or psychiatric consultation.
- Medical evaluation (complete medical history and physical examination).
- Thyroid function studies.

## Background

Up to 5% of the general population suffers from gustatory dysfunction, whereas up to 20% of people have olfactory impairment (Landis, 2004; Welge-Lüssen, 2011). These chemosensory disorders frequently lower quality of life, resulting in a variety of problems with daily living such as increased or decreased eating, difficulties with cooking, and ingestion of damaged food (Mainland, 2020; Niklassen, 2022). Smell disorders especially expose patients to serious injury as they can prevent them from detecting such things as fire, poisonous fumes, and leaking gas (Mainland, 2020; Niklassen, 2022).

Chemosensory dysfunction gained greater awareness during the COVID-19 pandemic as disorders related to these senses were a common indicator of SARS-CoV-2 infection (Tong, 2020). Prevalence of gustatory and olfactory disorders is expected to increase due to lasting post-COVID effects and an increasingly aging U.S. population (Claus, 2022). The prevalence of smell and taste dysfunctions increases with age (Hoffman, 2016; Rawal, 2016). Smell dysfunction is more common in men, ethnic minorities (i.e., non-Hispanic Blacks and Mexican Americans), and in those with lower educational attainment or family income (Hoffman, 2016). Studies of the prevalence of chemosensory disorders in pediatric populations are rare, and their detection presents several challenges, particularly among children ages 3 to 5 years (Dalton, 2009). A meta-analysis of 10 studies (n = 21,601) revealed olfactory impairment is significantly associated (hazard ratio = 1.52) with all-cause mortality (Pang, 2022).

Initial evaluation of altered taste and smell dysfunction relies heavily on patient history and physical examination to identify the most common causes. Some altered sensation may appear without any apparent stimulus (Doty, 2008). Taste dysfunction may have primary causes but is often a result of retronasal olfactory dysfunction. Retronasal olfaction is the perception of odors emanating from the oral cavity during eating and drinking, rather than sniffing (orthonasal olfaction) (Landis, 2005). The distinction between true gustatory loss and olfactory loss lies in the inability to detect bitter, sweet, salty, sour, or umami (gustatory dysfunction) from the inability to perceive complex food flavors (olfactory dysfunction).

Olfactory testing comprises electrophysiological tests and psychophysical testing to determine the nature and severity of impairment (Doty, 2015). Electrophysiological testing measures cortical neural responses to an odor stimulus (odor event-related potentials) and olfaction detection thresholds (the electro-olfactogram). Psychophysical smell testing uses a patient's response to unilateral or bilateral olfactory stimuli via orthonasal and retronasal routes to quantify odor detection, identification, discrimination, memory, and suprathreshold intensity perception. Structural and functional imaging may be used to clarify the etiology of functional loss.

Taste testing is more challenging to perform and interpret than smell testing, as multiple nerves are involved, taste receptors are variably distributed over the tongue and oral cavity, and taste thresholds are sensitive to a number of factors (Doty, 2008). Taste threshold testing comprises electrogustometry of tongue regions (passing anodal current to the tongue to generate a taste perception) and direct application of liquid stimuli or taste strips to the tongue using the whole mouth taste threshold, taste suprathreshold, and taste-quadrant tests. Gustatory evoked potentials may also be used.

## Findings

### Guidelines

The American Academy of Family Physicians guideline (Malaty, 2013) addresses assessment of smell and taste dysfunction in a primary care setting. The differential diagnosis encompasses a range of subjective and objective tools that can be performed relatively expeditiously in primary care to identify the most common and treatable etiologies. These include validated office-based tests for smell and taste disorders. Referral to a specialty smell and taste center or a specialist (e.g., otolaryngologist or neurologist) is indicated if the patient's quality of life is significantly impaired by a persistent smell or taste disorder that has no easily treatable cause.

Standardized questionnaires can aid in identifying self-reported sensory loss or distortion (Malaty, 2013). Physical examination entails direct visualization; anterior rhinoscopy; and neurologic (e.g., cranial nerve I for olfactory loss and cranial nerves VII, IV, and X for gustatory loss), cognitive, and motor assessment to identify common neurodegenerative etiologies. Anterior rhinoscopy can identify significant rhinitis, nasal polyps, or findings indicative of inflammation or infection pathologies that correlate with sinonasal pathology affecting smell. When anterior rhinoscopy is inconclusive and sinonasal pathology is suspected, nasal endoscopy and computed

tomography of the nasosinuses may be indicated. Magnetic resonance imaging of the brain is indicated when intracranial lesions are a concern.

### Evidence review

Validated smell and taste dysfunction tests (i.e., psychophysical and electrophysiological tests) are well-established clinical tools for assessing chemosensory identification and threshold impairment following the completion of a standard history and physical examination. They can determine the nature and degree of chemosensory dysfunction, detect malingering, monitor functional changes over time, and assess treatment efficacy.

The scientific evidence supporting the reliability and validity of smell testing is more robust than that of taste testing. The main limitations of the overall literature are the absence of normative data by age and gender and standardized testing methods. Reliability assessment is not always possible, although the individual may serve as their own control.

Electrophysiological testing of smell and taste was introduced as early as the 1950s. In the history of smell testing, there is longer clinical experience with electrophysiological testing, but more definitive research supporting psychophysical testing. Electrophysiological smell testing is less practical than psychophysical testing for routine clinical use because of patient intolerance of the electrodes, technical issues that lower test sensitivity and reliability, and the high costs and length of testing (Doty, 2015). Results of early studies of electrogustometry suggested a role in increasing the understanding of the mechanisms of taste transduction, but its value relative to aqueous methods for taste threshold assessment is less clear, and professional consensus regarding the routine use of electrogustometry is lacking.

The optimal psychophysical tests are highly sensitive, reliable, relatively inexpensive, and practical for routine use. Several tests meet these requirements and are commercially available for screening gross dysfunction or more detailed examination.

### Smell testing

The strongest evidence supports orthonasal olfaction tests with psychometric properties of high sensitivity, test-retest reliability, and validity in adult populations. Examples of the most widely examined psychophysical smell tests are the 40-item University of Pennsylvania Smell Identification Test (Whitcroft, 2019) for odor identification; the Sniffin' Sticks tests (Gellrich, 2017; Schriever, 2014) for odor threshold, discrimination, and identification; and the University of Connecticut Test Battery (Whitcroft, 2019) for odor threshold and odor identification. They have sex- and age-related normative data that enable determination of a patient's percentile rank relative to peers.

Several shorter iterations of these tests have been validated for screening gross olfaction loss in adult and pediatric populations. Screening tests are quick, relatively inexpensive, and easy to administer across a variety of settings. They typically include three- and four-odor versions that can be self-administered using "scratch and sniff" technology, e.g., the Quick Smell Identification Test (Hummel, 2010) and the three-item quick sticks (Q-sticks) (Malaty, 2013). Screening tests are highly sensitive for detecting anosmia; however, they are less sensitive than the longer versions for detecting hyposmia and cannot be relied upon to detect malingering (Doty, 2008; Malaty, 2013). Comprehensive testing with the longer-item tests is generally reserved for use by specialized smell and taste centers or specialists when a patient's quality of life is significantly impaired by a persistent chemosensory disorder that has no easily treatable cause (Malaty, 2013).

A systematic review of 30 studies (Ozay, 2019) identified the retronasal smell test, the candy smell test, and odorant presentation containers as the three most widely used and accepted retronasal olfaction test methods. Significant shortcomings in the literature limit the routine use of these tests in clinical practice. These limitations are a lack of established optimal concentrations and test agents and the absence of a procedure to detect threshold sensation tests, because retronasal testing had been conducted within the suprathreshold zone.

## Neurocognitive screening and assessment

While evidence suggests an association between hyposmia and Alzheimer's disease, the clinical utility of smell identification testing for early detection or prediction of Alzheimer's remains unclear. Several meta-analyses found smell testing identified changes associated with mild cognitive impairment and Alzheimer's (Jung, 2019; Kotecha, 2018; Silva, 2018), but longitudinal studies are still needed to determine if smell tests can reliably predict disease onset. The evidence also has limitations around test specificity and identifying influencing factors (Jung, 2019; Kotecha, 2018; Silva, 2018). The U.S. Preventive Services Task Force (2019) concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening for cognitive impairment in older adults. The systematic review (Patnode, 2019) upon which their decision was based included randomized controlled trials for numerous screening tools, but none for olfaction met criteria for inclusion.

In contrast, olfactory dysfunction is highly prevalent and persistent in Parkinson's disease. The European Federation of Neurological Societies recommends olfactory testing to differentiate Parkinson's disease from other parkinsonian disorders including recessive forms of Parkinson's disease (Berardelli, 2013). Smell identification tests show potential as an early biomarker for Parkinson's diagnosis, differential diagnosis from other conditions, and prediction of clinical outcomes (Morley, 2018; Oppo, 2020). Tests like the University of Pennsylvania Smell Identification Test and Sniffin' Sticks have demonstrated ability to detect anosmia or hyposmia common in Parkinson's patients (Morley, 2018). Shorter versions of these tests also retain much of their accuracy for this population (Morley, 2018), but as yet no uniform set of odorants or normative data specific to Parkinson's disease has been identified.

Alonso and colleagues (2021) conducted a systematic review and meta-analysis focusing on the assessment of olfactory impairment in Parkinson's disease patients and its capacity for differential diagnosis. In their study, they sought to understand the testing methods used to assess olfactory function in Parkinson's disease patients (n = 1,544) and gauge these tests' capacity to differentiate Parkinson's disease from other neurological conditions. Out of 5,304 studies that were reviewed, 35 met their inclusion criteria, revealing six distinctive smell tests. Meta-analyses of data from 1,144 patients showcased poorer olfactory performance in Parkinson's disease patients compared to those with conditions like progressive supranuclear palsy and essential tremor. However, the distinction was less clear when compared to idiopathic rapid eye movement sleep behavior disorder. The University of Pennsylvania Smell Identification Test emerged as the predominant method for evaluating olfactory function in Parkinson's disease.

## Taste testing

The most widely used tests for taste dysfunction are electrogustometry, the whole mouth taste threshold test, the taste suprathreshold test, and the taste quadrant test (van den Brink, 2021). Normative data have been developed for electrogustometry threshold testing in adult populations and more recently in pediatric populations. Normative data exist for some psychophysical threshold tests, but not for the more practical and popular psychophysical suprathreshold tests.

Electrogustometry assesses taste detection thresholds rather than recognition thresholds and is not applicable for measuring basic taste qualities (Gamper, 2012). A systematic review (Moura, 2015) of nine studies found quantitative taste testing in children was feasible as long as the tests were condition- and age-specific. The authors were unable to perform a meta-analysis due to variations in sample size (with a range of 34 to 432 participants), age of the population (ages 0 to 12 years), evaluation methods, and study objectives. All but two of the studies enrolled populations of healthy children. The other two studies enrolled children with specific taste-limiting conditions — chronic otitis media with effusion and invasive developmental disorders. The taste testing methods were psychophysical (six studies), electrogustometry (two studies), and a four-point questionnaire (one study). Despite the limitations in the literature, psychophysical taste testing and electrogustometry are recognized diagnostic tools in pediatric clinical practice and specialized clinics.

In a systematic review of 19 studies, Kwak (2023) examined an association between gustatory function and Parkinson's disease. Studies used various gustatory tests, such as taste strips, questionnaires, taste solutions, propylthiouracil/phenylthiocarbamide perception tests, and electrogustometry. While the overall evidence was limited, contradictory, and lacked normative data, the results suggest patients with Parkinson's disease may experience significantly lower gustatory function than control participants. However, studies with larger populations and normalized gustatory function tests are needed.

In 2020, we updated the references. New literature is emerging on chemosensory loss among patients with SARS-CoV-2 infection. Two systematic reviews and meta-analyses demonstrated that objective methods were more sensitive than subjective methods for identifying smell loss as a result of infection with SARS-CoV-2 (Hannum, 2020; Tong, 2020). These findings warrant no coverage change.

In 2021, we removed several older references and added a systematic review that failed to establish the utility and efficacy of olfactory testing in the management of temporal lobe epilepsy (Hwang, 2020). No policy changes are warranted.

In 2022, we added a systematic review/meta-analysis of 37 studies (n = 8,035 chronic rhinosinusitis patients) that investigated links between computerized tomography scoring systems and measures of olfaction. The study identified a significant link between Lund-Mackay with Smell Identification Test-40 and Sniffin' Sticks; a near-significant link with Brief Smell Identification Test; and no link with Toyota & Takagi olfactometry (Chen, 2023).

In 2024, we updated the references and made no policy changes.

## References

On September 6, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "Olfaction Disorders" (MeSH), "Smell" (MeSH), "Taste Disorders" (MeSH), "olfactory testing," "gustometry," "smell test," "anosmia," "hyposmia," "dysosmia," and "taste test." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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## Policy updates

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