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Prevalence and Risk Factors of Taste and Smell Impairment in a Nation-wide Representative Sample of the U.S. Population

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Objectives: To estimate the prevalence of, and explore potential risk factors for, taste and smell dysfunction in the general population of the United States.

Design: A cross-sectional study.

Setting: Data from the National Health and Nutrition Examination Survey (NHANES 2013-2014) conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention.

Participants: A total of 3519 men and women aged 40 years and older who participated in NHANES 2013-2014.

Main Outcome Measures: Bilateral odor identification test scores for the 8 odorants of the two versions of the NHANES Pocket Smell Test™. Scores from whole-mouth and regional taste identification and intensity rating tests employing quinine and sodium chloride.

Results: The estimated prevalence was 13.5% for smell impairment, 17.3% for taste impairment, and 2.2% for both taste and smell impairment. For smell, but not taste, prevalence estimates increased with age and were higher in men and ethnic minorities. Lower educational attainment, lower family income, and a history of asthma or cancer were independently associated with a higher prevalence of smell impairment, whereas light-to-moderate alcohol consumption (1-3 drinks/day) was associated with a lower prevalence of such impairment. After multivariate adjustment, being non-Hispanic Black Americans, consuming ≥4 drinks of alcohol per day, and having a history of cardiovascular disease (CVD) were independently associated with a higher prevalence of taste impairment.

Conclusion: Based upon a nationally representative, complex, and multistage probability survey, an estimated 28.6% of the U.S. population ≥40 years old, i.e., over 43 million people,

suffer from some degree of smell or taste dysfunction. A large number of demographic and lifestyle risk factors were found to be related to smell dysfunction, whereas only ethnicity, heavy alcohol consumption, and CVD history were found to be associated with higher prevalence of taste dysfunction.

Strengths and limitations of this study

- The present study provides a nation-representative estimates of the prevalence of taste and smell impairment among men and women aged 40 years and above in the United States population.
- This study demonstrates associations of a multitude of demographic factors and medical history with chemosensory disorders on a nation-wide scale.
- This is a cross-sectional study, which limits its ability to infer causal relationships between risk factors and taste and smell impairments.

INTRODUCTION

Smell and taste disorders pose a major threat to public health, significantly compromising quality of life, food preferences, nutritional status, and safety from airborne toxins, fire, smoke, spoiled food, and leaking natural gas.[1-4] It is now well established that a disproportionate number of the elderly experience smell dysfunction that has direct consequences for health and safety.[3,5] For example, in one longitudinal study of 1,162 non-demented older persons, the mortality rate over a 4-year period was 45% for those with lowest baseline olfactory test scores, as compared to a rate of 18% in those with the highest test scores, even after controlling for age and other confounders.[6]

Although a large literature suggests that chemosensory disorders are relatively common,[2,7-12] there remains a lack of consensus as to the actual prevalence of such disorders in the general population.[2,7,13,14] Previous studies attempting to address this issue have provided prevalence estimates ranging from 2.7% to 24.5% for smell dysfunction,[7-10,12,13,15,16] and 0.6% to 20% for taste dysfunction.[9,13,16,17] Such variation likely reflects differences in test procedures, criteria for defining dysfunction, and both sample sizes and sampling procedures, as well as variations in sex, age, health, and ethnic composition of the sampled populations.

The relatively recent addition of olfactory and gustatory testing to the National Health and Nutrition Examination Survey (NHANES), a survey that focuses on representative samples of non-institutionalized persons from 15 randomly selected counties or other geographic jurisdictions within the United States, provides a unique opportunity to obtain sound nation-wide estimates of prevalence of chemosensory dysfunction. An evaluation of

the olfactory data collected during the first year of this survey (2012) was suggestive of a 12.4% prevalence for smell dysfunction in the sampled population, although estimates of taste dysfunction were not presented.[18] The present study, based on a much larger sample size from the 2013-2014 NHANES survey, provides estimates of the prevalence of both olfactory and taste dysfunction within the U.S. population. Importantly, it identifies new and critical risk factors for olfactory and taste loss within the population at large.

METHODS

Study Participants

A total of 3708 men and women aged 40 years and older were considered for the taste and smell examination contained in NHANES 2013-2014. A short screening questionnaire and a test of perceived taste intensity were used to assess eligibility for the study.[19] Participants were excluded from smell and taste examinations if they were: 1) pregnant or lactating; 2) allergic to quinine (pertinent to the quinine taste test only); or 3) unable to correctly rate the brightness of a standard series of three lights in an LED luminescence panel (pertinent to understanding the procedures of the taste test only). These exclusions left 3114 participants who completed the quinine and sodium chloride (NaCl) taste tests and 3519 participants who completed the 8-item smell test. The mean (SEM) age of NHANES participants (n=3114) included in the taste test was 57.5 (0.3) years; 48.6% were men. Regarding ethnic distribution, 72.8% were non-Hispanic Whites, 10.1% non-Hispanic Blacks, and 6.6% Mexican Americans. For the smell test, the mean (SE) age of NHANES participants (n=3519) was 57.8 (0.3) years; 47.7% were men. Of these participants, 71.2% were non-Hispanic Whites,

10.6% non-Hispanic Blacks, 6.9% Mexican Americans, and 11.3% other races/ethnicities (including other Hispanic and multi-racial individuals).

The NHANES protocol was approved by the National Center for Health Statistics (NCHS) institutional review board, and written informed consent was obtained from all participants. For additional details of the initial introduction of chemosensory testing to this survey, see Hoffman et al.[18]

Smell and Taste Tests

For smell testing, the two 4-item versions (A & B) of the NHANES Pocket Smell Test™ (Sensonics International, Haddon Heights, NJ), developed in conjunction with NIH, were sequentially administered, resulting in an 8-item "scratch and sniff" test.[19] The eight odorants (chocolate, strawberry, smoke, leather, soap, grape, onion, and natural gas), components of the 40-item University of Pennsylvania Smell Identification Test (UPSIT),[20] were presented in a fixed order. A subject was required, in a forced-choice situation, to identify each odorant from four alternative names. Smell impairment was defined as not being able to correctly identify 6 or more of the 8 odors, each from a list of four possible responses.[7] Of note, our definition of smell impairment approximately corresponds to the definition of being unable to correctly identify 29 or more of the 40 odors using the UPSIT test from which the present items were largely derived, and primarily includes persons who, on the original UPSIT scale, would be classified as having either anosmia, severe microsmia, or moderate microsmia (**Supplementary Table 1**).[12]

The taste tests employed in this NHANES surgery included a tongue tip taste test and a whole mouth taste test. In the tongue tip test, the taste stimuli [0.32 mg/mL quinine (bitter) and 58.5 mg/mL NaCl (salty) in 10 ml solution] were presented on a cotton swab that was gently moved across the tip of the tongue in a standardized manner.[19] Participants were asked to identify the taste (salty, bitter, sour, something else, no taste) and rate the perceived intensity on the Generalized Labeled Magnitude Scale (gLMS).[21] A 30-second interval was interspersed between stimulus presentations, during which time participants rinsed their mouths with water. In the whole mouth taste test, participants swished 10 mL of each tastant solution (19.5 mg/mL NaCl, 58.5 mg/mL NaCl, or 0.32 mg/mL quinine) for 3 seconds, expectorated, and rinsed their mouths with water. The participants then were asked to identify the taste quality and rate the solution's intensity on a standardized scale. In addition, a replication of the whole mouth test was conducted with a salt solution.

A recent test-retest reliability and validity examination of NHANES taste test protocol demonstrated a reasonable correlation between quinine whole mouth measurement (0.32 mg/mL) and other taste measurements, including tongue tip tests of NaCl ($r = 0.53$) and quinine ($r = 0.44$), and whole mouth tests of NaCl ($r = 0.60$ for 19.5 mg/mL NaCl and 0.77 for 58.5 mg/mL NaCl), sucrose, citric acid, and propylthiouracil, suggesting that the whole mouth quinine assessment was a reasonable assessment for overall taste functioning.[19] Thus, in our study, failing to correctly identify quinine in the whole mouth test defined taste dysfunction. In sensitivity analyses, we defined taste impairment as failing to correctly identify quinine (both tongue tip and whole mouth test) or NaCl (both tongue tip and whole mouth test).

Demographics and related information

The NHANES survey employed a computer-assisted personal interview system. The in-home questionnaire obtained information on age, sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, and other), educational attainment (high school or below, some college, college, graduate school or above), ratio of family income to poverty (PIR; categorized as low [PIR<1.3], middle [1.3≤PIR≤3.5], and high [PIR>3.5]),[22] smoking status (never smoker, past smoker, current smoker: <10, 10-20, >20 cigarettes/day), alcohol consumption (nondrinker, 1-3 drinks/day, or ≥4 drinks/day), self-reported chronic diseases (diabetes, cardiovascular disease [CVD], asthma, and cancer), pesticide use in home (yes, no), self-reported taste and smell problems (defined as reporting problems within the past year), and conditions that might influence taste and smell ability (frequent nasal congestion, head injury, tonsillectomy, broken nose/serious injury to face or skull, and sinus infection). Symptoms of depression were assessed using the 9-item Patient Health Questionnaire scale (PHQ-9, possible range 0–27). A cut-off point ≥10 was used to identify participants with moderate to severe depression.[23] To estimate physical activity, metabolic equivalent values (MET-min/week) were calculated by using the sum of the MET score multiplied by the average time per week of specific physical activity and subsequently categorizing the scores into tertile levels of physical activity.[24] Blood pressure (BP) and anthropometric measurements were performed by trained health technicians in the mobile examination centers. Blood pressure was measured three times, and the mean values of the last two measurements were used in the analysis. Hypertension was defined as systolic BP ≥140 or diastolic BP ≥90 mmHg, or positive answers to the questions, "Now taking prescribed

medicine for high BP" or "Told had high BP 2+ times." Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Obesity was defined as BMI ≥30 kg/m^2.

Statistical analysis

Due to the complex NHANES sampling design, weights were incorporated into the analysis whenever possible using SAS version 9.4 (SAS Institute, Cary, NC). We used the number 15 (the number of primary sampling units minus the number of sampling strata) for the degrees of freedom. PROC SURVEYFREQ was used to estimate the prevalence of taste and smell disorders in the total population as well as within subgroups of the population. The comparison between participants with and without taste or smell disorder was tested by using the Wald F-test in the PROC SURVEYREG for continuous variables or the Rao-Scott Chi-Square test in the PROC SURVEYFREQ for categorical variables. Applied with PROC SURVEYLOGISTIC, logistic regression was used to estimate the age- and sex-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of taste and smell disorders for common socioeconomic, demographic, and lifestyle characteristics that may serve as risk factors of the disorders, including BMI, race/ethnicity, educational attainment, family income, smoking status, alcohol use, physical activity, depression, hypertension, obesity, diabetes, CVD, asthma, cancer, pesticide use, frequent nasal congestion, head injury, tonsillectomy, broken nose or serious injury to face or skull, and sinus infection. We used a SAS macro (%StepSvylog) to perform backward model selection for complex survey data. Potential risk factors with P<0.25 were entered together into a multivariable logistic model and then successively removed until all retained variables had a P<0.05.[25] Finally, to assess the

capacity of selected risk factors in predicting smell and taste disorder, we plotted a receiver operating characteristic (ROC) curve and calculated a sample-weighted area under the ROC curve (AUC) that incorporated the NHANES sampling design, using STATA, version 12.0 (Stata Corporation, College Station, Texas). Two-sided $P<0.05$ was considered statistically significant.

RESULTS

The overall estimated prevalence of smell impairment was 13.5%, whereas that for taste impairment was 17.3%. The estimated prevalence of having both a taste and smell disorder was 2.2%. Thus, about 28.6% of the U.S. population appears to have either a smell or taste problem or both.

Figure 1 shows the prevalence estimates of smell and taste disorders according to age, sex, and ethnicity. For smell dysfunction, the estimates significantly increased with age in both men and women. In addition, compared with women, men had a higher prevalence in each age group, especially in the group of 70 years and older (men: 37.2%; women: 25.2%). Regarding race/ethnic distribution, compared with non-Hispanic White Americans, ethnic minorities, namely non-Hispanic Black Americans, Mexican Americans, and other race/ethnicity, had a higher estimated prevalence of smell impairment. In contrast, no such patterns of relationship were found between these demographic variables and the prevalence of taste dysfunction. Paradoxically, the estimated prevalence of taste dysfunction decreased with age in women, but not in men. In the 40-69 year-old age cohort, non-Hispanic Black Americans had a higher prevalence of taste impairment than that in other ethnic groups,

although in the oldest group (comprised of 97 non-Hispanic Black Americans, 41 Mexican Americans, and 82 participants of other races/ethnicities), non-Hispanic Black Americans had the lowest prevalence. Regarding individual smell test items of all the participants, 4.3% incorrectly identified the odor of onion, 6.7% of soap, 9.5% of smoke, 12.3% of natural gas, 16.1% of chocolate, 18.7% of strawberry, 20.6% of leather, and 30.4% of grape. In the age group of 70 years and older, the corresponding proportions reached 21.2% for smoke and 26.3% for natural gas (**Supplementary Figure 2**).

The characteristics of the study population by smell and taste disorder status are shown in **Table 1**. In addition to the demographic characteristics, participants with smell impairment tended to have lower levels of educational attainment, physical activity, family income, and alcohol consumption than other participants. Moreover, they had a higher prevalence of hypertension, diabetes, CVD, cancer, and self-reported taste and smell problems (P<0.05). Other factors, including BMI, smoking, obesity, depression, the history of asthma, pesticide use, nasal congestion, tonsillectomy, and head injury, were not associated with smell dysfunction. Age and ethnicity were associated with the prevalence of taste impairment.

After adjusting for age, gender, and ethnicity, the prevalence of smell and taste disorders was differentially associated with other socioeconomic, lifestyle, and medical history variables (**Table 2**). Educational attainment, family income, physical activity, alcohol consumption, and a history of hypertension, CVD, or cancer were significantly associated with the prevalence of olfactory dysfunction. Educational attainment and a history of asthma were significantly associated with the prevalence of taste dysfunction.

In backward stepwise selection, older age, male gender, ethnic minorities (including

non-Hispanic Black and Mexican American), lower family income, lower educational attainment, and a history of asthma or cancer remained in the model and were independently associated with an increased prevalence of smell impairment (ORs ranging from 1.33-1.91, all $P<0.05$), whereas light-to-moderate alcohol consumption (1-3 drinks/day) was significantly associated with a decreased prevalence of smell impairment (OR and 95% CI, 0.72 [0.58, 0.91], $P<0.01$) (**Table 3**). For taste dysfunction, non-Hispanic Black (OR and 95% CI, 1.46 [1.07, 1.99], $P=0.02$), high alcohol consumption (≥4 drinks/days) (OR and 95% CI, 1.42, [1.04, 1.94], $P=0.03$), and a history of CVD (OR and 95% CI, 1.30, [1.02, 1.67], $P=0.04$) were significantly associated with a higher prevalence of impairment, whereas age was inversely associated with such prevalence (each 5-year increment; OR and 95% CI, 0.93 [0.89, 0.97], $P=0.01$) (**Table 3**).

Age (each 5-year increment; OR and 95% CI, 1.22 [1.08, 1.38], $P<0.01$), physical inactivity (OR and 95% CI, 2.38 [1.21, 4.70], $P<0.05$), and head injury (OR and 95% CI, 2.15 [1.10, 4.18], $P<0.05$) were significantly associated with a higher prevalence of having both taste and smell dysfunction.

Figure 2 shows that age, sex, and ethnicity render an AUC of 0.72 for smell dysfunction. Further inclusion of socioeconomic, lifestyle, and medical risk factors only marginally increased the AUC to 0.74. For taste impairment, an AUC of 0.57 was estimated for a model that included age, ethnicity, heavy alcohol consumption, and a history of CVD.

In the sensitivity analyses, when we defined taste disorder as being unable to correctly identify either quinine or NaCl, we estimated a prevalence of 14.0%. In addition, with this alternate definition, the associations of Black ethnicity, heavy alcohol consumption, and a

CVD history with the prevalence of taste disorder were attenuated to non-significance (OR and 95% CI: 1.25 [0.98, 1.59] for Black ethnicity; 1.20 [0.86, 1.67] for heavy alcohol consumption, and 1.15 [0.85, 1.55] for CVD).

DISCUSSION

In this most current nation-wide representative sample of U.S. men and women aged 40 years and older, the overall estimated prevalence of smell and taste impairment was 13.5% and 17.3%, respectively. Significant differences were observed in the estimated prevalence of smell impairment among subgroups defined by age, gender, and ethnicity. Such differences were not evident for the estimated prevalence of taste dysfunction. In our multivariate analysis, a multitude of potential risk factors, including age, sex, race/ethnicity, family income, educational attainment, alcohol consumption, and a history of asthma or cancer, were independently associated with the prevalence of smell impairment. Non-Hispanic Black ethnicity, high alcohol consumption, and a history of CVD were significantly associated with a higher prevalence of taste impairment after adjustment for confounders.

Our nationally representative estimate of the overall prevalence of smell dysfunction (13.5%) was quite similar to the estimate based on a single-year NHANES survey (12.4%).[18] These estimates were somewhat lower than that reported in other populations whose prevalence ranged from 18.0 to 24.5%,[7,8,10,13] and somewhat higher than that reported by some other studies (2.7%-3.8%).[9,15] Differences between the test procedures (e.g., odorants, psychophysical paradigms) and the study populations (e.g., age, sex, and health status) are presumably involved (**Supplementary Table 2**). Using the 40-item UPSIT, Doty et al. found

little age-related decline in smell function until the 6th decade of life, at which time a precipitous age-related decline occurred, illustrating how age would be expected to markedly influence prevalence.[12] Of particular importance in establishing prevalence are the criteria used to define dysfunction, which vary considerably among studies. In two studies, being unable to identify 75% of either 4 or 12 odorants was defined as dysfunction.[8,12] Other studies have set this criterion at 62.5% for either 8 or 16 odorants,[6,9,14,18] and 40% for 5 odorants.[8] Such variations in criteria significantly influence the estimated prevalence and likely explain much of the variation seen among prevalence studies. Our study, like most others, has the limitation of employing a relatively few number of odorants. Despite this limitation, however, our criterion for defining smell impairment (i.e., <75% or 6/8 items) corresponds to dysfunction defined by the 40-item UPSIT. Correctly identifying 6 out of 8 items corresponds to an UPSIT score of 30, which is the cut point between mild and moderate microsmia. Thus, regardless of the limitations of the number of test items, the NHANES prevalence estimates appear to have strong face validity as compared to a number of previous prevalence estimates.

Only a limited number of epidemiological studies have estimated the prevalence of taste dysfunction.[9,13,16,17] In the 1994 Disability Supplement to the National Health Interview Survey (NHIS-D), based on information from a self-reported taste impairment questionnaire, Hoffman et al. found that only 0.6% of U.S. adults (>18 years) reported having a gustatory problem.[17] In the current study, using standardized taste testing, the prevalence of taste impairment was 17.3%, whereas the prevalence of self-reported taste impairment (defined as reporting taste problems within the past year) was only 5.3%, suggesting that self-reported

estimates significantly underestimated the true prevalence.[7,8,26] Nevertheless, the prevalence of taste impairment in our study was comparable to two other large taste testing studies that reported prevalence of 14.8% and 20.0%.[9,13]

Epidemiological studies that have examined potential risk factors for smell and taste disorders are limited. Several have consistently found the prevalence of smell impairment to increase with age and to be higher in men than in women.[7,10,13,18] In addition, the current analysis demonstrated that certain ethnic groups, such as non-Hispanic Blacks and Mexican Americans, had a higher prevalence of smell impairment than that observed for White Americans. In the National Social Life, Health, and Aging Project study, Pinto et al. also demonstrated that older African Americans and Hispanics had worse olfactory function.[27] While a subtle difference was noted by Doty et al. between White and Black Americans in a large, albeit convenience, sample,[20] other studies observed equivalent UPSIT scores in White and Black American populations and relatively higher scores in Korean American populations,[28] suggesting factors in addition to race/ethnicity, per se, likely account for such differences. In the current study, other potential risk factors for smell impairment were also identified, including lower educational attainment and less family income. Our findings of the influences of such socioeconomic factors were consistent with previous studies.[4,15,16,18,29] Existing evidence has suggested that access to health care, occupation, and overall quality of life potentially explain the link between low socioeconomic status and a higher prevalence of smell disorder.[30] Regarding olfactory function, besides the above findings which were mostly consistent with the data from 2012 NHANES survey,[18] our results additionally demonstrated a link between a history of asthma and cancer and a slightly higher prevalence of smell

dysfunction. For medical history, Alobid et al. reported that a history of persistent asthma had a significant impact on smell loss in patients with nasal polyposis.[31] Moreover, asthma was a predictor of poor olfactory function in patients with chronic rhinosinusitis.[32] Some clinical studies also demonstrated that smell function significantly decreased in patients receiving cancer chemotherapy,[33,34] and the prevalence of self-reported taste and smell alterations could reach as high as 86%.[35] Of note, smoking was not associated with the prevalence of smell impairment in our cross-sectional analysis. Accumulating evidence has suggested that smoking may exert an adverse effect on smell function,[7,13,36] although some studies have not observed significant associations.[10,16,37] These mixed findings may reflect the cross-sectional nature of these studies, as well as the lack of detailed assessments of smoking dose and duration, which are often more informative than dichotomous smoking status. More prospective studies are warranted to elucidate the potential adverse effect of smoking on olfactory function.

In comparison to the data for smell impairment, fewer associations between taste impairment and demographic/health measures were observed. We did find that race/ethnicity, heavy alcohol use, and a history of CVD were associated with a higher prevalence of taste impairment. Compared with non-Hispanic White, non-Hispanic Black had a higher prevalence of both taste and smell disorders. The underlying reason for this observation was unknown, although other socioeconomic factors and genetic susceptibility might partially account for this link. Interestingly, we also found heavy drinking to be associated with an increased prevalence of taste dysfunction, whereas light-to-moderate drinking was associated with a decreased prevalence of smell dysfunction, suggesting that the amount of alcohol

intake may exert distinct effects on chemosensory perception.[18,38,39] In addition, we found a positive association between CVD and the prevalence of altered taste. Evidence has suggested that variations in oral sensation, influenced by both genetic and environmental factors, might increase the risk of CVD by impacting dietary behaviors such as higher intake of high-fat and sweet foods.[40,41] However, in this cross-sectional study, we could not exclude the possibility that the taste function might be influenced by the medications taken by people with CVD. Unexpectedly, an inverse association between age and the prevalence of taste dysfunction was observed in our study, which is in contrast to frequent reports of age-dependent reductions of taste ability.[42,43] Aging may primarily influence the taste sensitivity to low levels of stimuli,[42] but less so for suprathreshold deficits in taste. In most epidemiological studies, relatively high concentrations of tastants (24 mg/ml quinine hydrochloride; 75-100 mg/mL NaCl; 100-200 mg/mL sucrose; 50-165 mg/mL citric acid) have been employed,[9,13] which may not be sensitive enough to detect age-related taste dysfunction.[44] Of note, threshold concentrations are typically set at much lower concentrations (e.g., 3×10^{-4} mg/mL for quinine, 0.585 mg/mL for NaCl, 6.84 mg/mL for sucrose, and 3.84 mg/mL for citric acid).[44] In the NHANES, the tastant concentrations (0.32 mg/mL for quinine, 19.5 mg/mL and 58.5 mg/mL for NaCl) were much higher than the threshold concentrations, albeit comparable to those used in some previous epidemiological studies.[9,13] This may explain the similarity between our NHANES findings and those reported in a German population with taste test at suprathreshold concentrations, in which a decline trend of the prevalence of taste dysfunction was observed in women aged 45-74 years.[13]

The present study provides a nation-representative estimates of the prevalence of taste

and smell impairment among men and women aged 40 years and above in the United States population. Moreover, it has demonstrated that chemosensory disturbances are influenced by a range of demographic and health factors. Importantly, our analysis strongly suggests that a considerable number of Americans suffer from chemosensory disturbances. That being said, this research has its limitations. First, it is a cross-sectional study, which limits its ability to infer causal relationships between risk factors and taste and smell impairments. Second, we utilized only bitter and salt tasting stimuli, excluding sweet and sour tasting ones. Furthermore, the unexpected inverse association of taste dysfunction with age suggests that the test used by NHANES is not sensitive enough to capture age-related declines in taste function. Nonetheless, there is evidence that the whole-mouth quinine test used in our study may be a good proxy for overall taste function, even though there are presently no universally accepted standards to best define taste impairment.[19] Third, we measured taste and smell function on only a single occasion, which may not be representative of longer-term function. Nevertheless, the taste and smell measurements employed in this study have been found to be largely reproducible over a 6-month period.[19] Fourth, the NHANES survey only sampled non-institutionalized and relatively healthy individuals. The prevalence of taste and smell impairment may be significantly higher in persons whose health is otherwise compromised, such as those with neurodegenerative disorders.[45] Finally, since only a limited number of potential risk factors were evaluated, other risk factors may exist that have yet to be identified.

CONCLUSION

This study, based upon a representative sample of the United States population, strongly suggests that a significant number of American citizens suffer from smell or taste problems. Thus, 13.5% of the study population exhibited smell dysfunction, 17.3% taste dysfunction, and 2.2% both taste and smell dysfunction. Since the 2016 US Census Bureau estimates the U.S. population ≥40 years old to be ~152 million,[46] this translates to over 43 million Americans having some degree of chemosensory dysfunction. The adverse consequences of these disorders are particularly critical to older populations because approximately a fifth of those sampled could not identify the test odors of smoke and natural gas, in accord with other studies on this topic.[47] As shown in the NHANES study, a multitude of demographic, lifestyle, and health factors are potential risk factors for smell dysfunction. Risk factors for taste dysfunction were more limited, being confined only to ethnicity, heavy alcohol consumption, and a history of CVD. Future prospective investigations are needed to establish more clearly the link between these and other risk factors and the development of chemosensory disturbances.

Contributors: Q. Sun was responsible for the study concept. G. Liu, Z. Zong, and Q. Sun were responsible for analysis and interpretation of data. G. Liu wrote the first draft of the manuscript. All authors made great improvement in the content and writing and approved the finally version of the manuscript.

Competing interests: Richard L. Doty is President and major shareholder of Sensonics International, the manufacturer of the NHANES Pocket Smell Test™.

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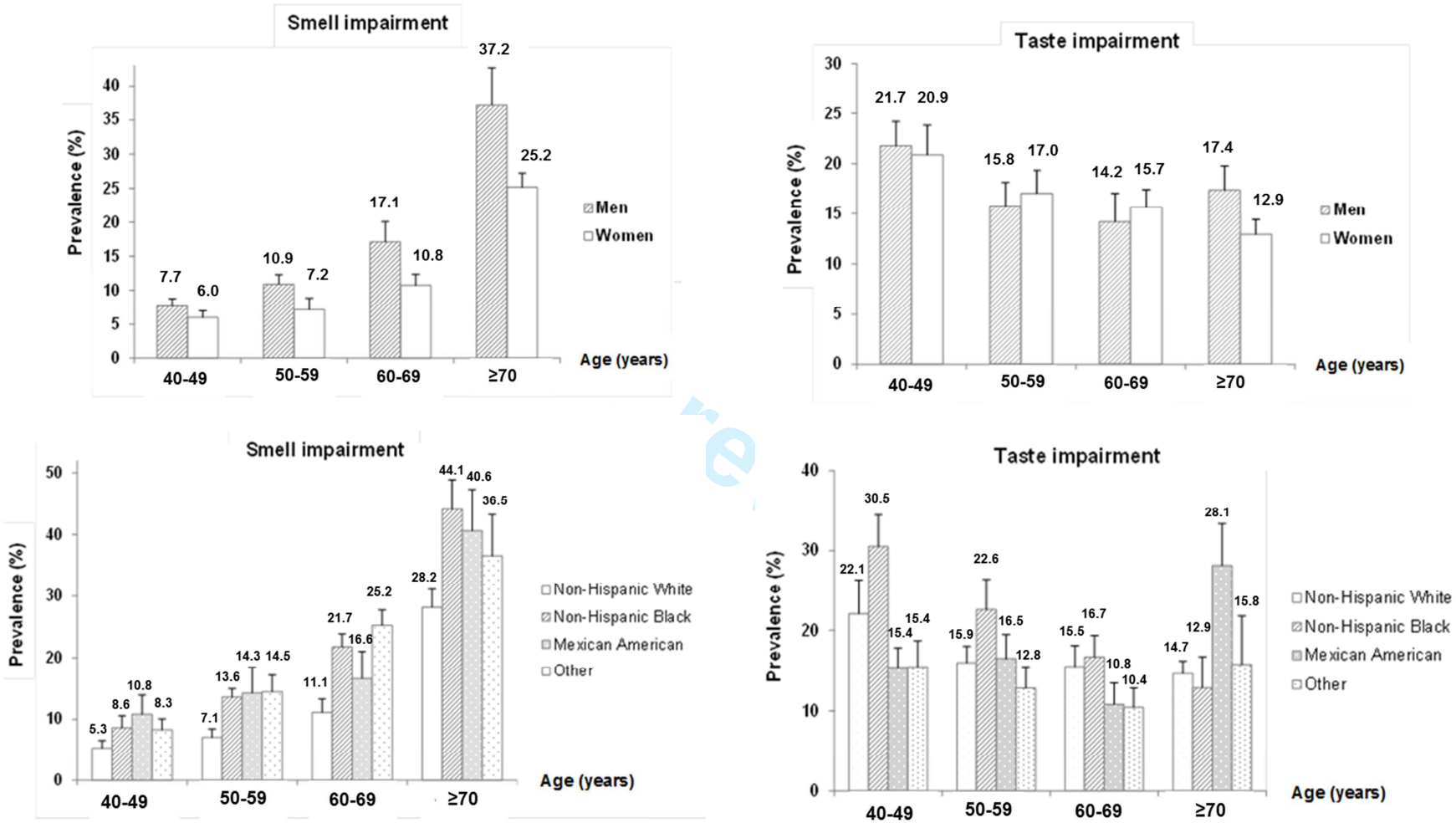


Figure 1. Prevalence of Smell and Taste Impairment According to Age, Sex, and Race/Ethnicity

Table 1. Characteristics of Study Participants According to Smell and Taste Impairment Status*

Characteristic	Smell impairment			Taste impairment		
	Yes (n=630)	No (n=2889)	*P*	Yes (n= 540)	No (n=2574)	*P*
Age, years	65.0±0.6	56.7±0.2	<0.001	55.9±0.6	57.8±0.3	0.01
BMI, kg/m^2	29.5±0.4	29.5±0.2	0.91	29.6±0.5	29.6±0.2	0.99
Men,%	56.2 (3.1)	46.4 (1.0)	0.005	49.2 (1.6)	48.5 (1.0)	0.72
Race/ethnicity, %			0.005			0.04
Non-Hispanic White	64.3 (3.6)	72.3 (3.2)		72.1 (3.9)	72.9 (3.1)	
Non-Hispanic Black	14.1 (2.1)	10.0 (1.4)		13.5 (2.1)	9.5 (1.4)	
Mexican American	7.7 (2.4)	6.8 (1.6)		5.9 (2.0)	6.7 (1.5)	
Other	13.9 (1.2)	10.9 (1.1)		8.5 (1.4)	10.9 (1.2)	
Educational attainment			<0.001			0.29
< High school	49.5 (2.7)	35.4 (2.4)		38.8 (3.0)	35.1 (2.9)	
Some college	25.7 (2.3)	31.3 (1.4)		31.7 (2.2)	31.0 (1.9)	
College graduate or above	24.8 (2.3)	33.3 (2.3)		29.5 (3.6)	33.9 (2.3)	
Physical activity, METs/week			<0.001			0.33
Tertile 1	40.9 (2.0)	29.5 (1.4)		29.7 (1.9)	29.2 (1.3)	
Tertile 2	32.1 (2.4)	32.0 (1.0)		36.7 (4.1)	31.7 (1.1)	
Tertile 3	27.0 (2.2)	38.5 (1.5)		33.6 (3.9)	39.1 (1.9)	
Ratio of family income to poverty, %			<0.001			0.20
<1.3	25.2 (2.4)	19.1 (2.7)		20.1 (2.7)	18.0 (2.8)	
1.3-3.5	43.8 (1.8)	32.8 (1.2)		37.8 (2.5)	33.7 (1.2)	
>3.5	31.0 (3.0)	48.0 (3.0)		42.1 (3.0)	48.2 (3.4)	
Smoking status, %			0.25			0.28
Never	51.8 (2.8)	53.7 (2.0)		50.1 (3.4)	53.6 (2.0)	
Past	33.8 (2.9)	28.2 (1.3)		28.6 (3.4)	29.4 (1.3)	
Current <10 cigarettes/day	8.1 (1.0)	9.7 (0.6)		10.3 (1.6)	9.1 (0.6)	
Current 10-20 cigarettes/day	2.0 (0.9)	2.0 (0.2)		3.0 (1.1)	1.9 (0.3)	
Current >20 cigarettes/day	4.3 (1.6)	6.4 (1.0)		8.0 (1.5)	6.0 (1.1)	
Alcohol consumption (drinks/day)			<0.001			0.07
Nondrinkers	49.4 (2.6)	31.4 (2.1)		31.2 (3.5)	32.2 (2.2)	
1-3 drinks/day	44.1 (2.3)	59.1 (2.3)		55.9 (3.5)	58.9 (2.4)	
≥4 drinks/day	6.5 (1.7)	9.5 (0.8)		12.9 (1.5)	8.9 (0.8)	
Depression symptom, yes, %	10.0 (2.0)	9.1 (0.9)	0.59	7.7 (1.0)	9.0 (1.0)	0.31
Hypertension, yes, %	63.9 (2.4)	46.4 (1.1)	<0.001	49.6 (2.3)	47.5 (1.5)	0.51
Obesity, yes, %	37.9 (2.2)	40.3 (1.5)	0.36	42.7 (2.9)	39.7 (1.6)	0.31
Diabetes, yes, %	21.2 (1.5)	14.8 (1.0)	<0.001	15.7 (2.3)	15.0 (1.0)	0.75
CVD, yes, %	24.4 (2.0)	11.2 (0.7)	<0.001	12.7 (1.6)	12.3 (0.8)	0.79
Asthma, yes, %	16.5 (2.0)	13.9 (0.8)	0.20	16.0 (2.1)	13.8 (0.7)	0.26
Cancer, yes, %	23.9 (2.1)	14.8 (0.6)	<0.001	12.7 (1.9)	16.6 (1.0)	0.16
Pesticide use, yes, %	18.1 (1.6)	18.4 (1.0)	0.90	16.3 (1.9)	18.6 (0.9)	0.26

Self-report taste problem, yes, %	10.7 (1.6)	4.1 (0.4)	<0.001	3.8 (1.1)	4.7 (0.6)	0.55
Self-report smell problem, yes, %	19.5 (2.2)	6.1 (0.9)	<0.001	8.9 (1.3)	7.8 (0.9)	0.36
Frequent nasal congestion, yes, %	28.3 (2.0)	31.4 (0.9)	0.21	29.8 (2.8)	31.2 (1.0)	0.67
Head injury, yes, %	15.0 (1.5)	16.7 (1.0)	0.25	17.4 (2.1)	16.9 (1.2)	0.84
Tonsillectomy, %	34.9 (3.2)	32.3 (1.3)	0.41	32.0 (2.8)	32.7 (1.3)	0.80
Broken nose or serious injury to face/skull, yes, %	18.1 (1.6)	17.5 (1.4)	0.78	18.9 (2.4)	17.7 (1.4)	0.51

* Data are means (SE), or % (SE). 28 participants with missing values for BMI; 112-279 participants with missing values for hypertension, family income, pesticide use, and depression symptom; 2-7 participants with missing values for self-reported taste problem, self-reported smell problem, frequent nasal congestion, head injury, and broken nose or serious injury to face/skull.

Table 2. Demographic-adjusted Odds Ratios of Smell and Taste Impairment by Socioeconomic Characteristics, Lifestyle Factors, and Medical History*

	Smell impairment		Taste impairment	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*
Education level				
Low vs high	1.69 (1.30, 2.20)	<0.001	1.29 (1.00, 1.67)	0.05
Ratio of family income to poverty				
<1.3 vs >3.5	1.80 (1.35, 2.40)	<0.001	1.28 (0.84, 1.94)	0.25
Smoking status				
Past vs never	0.99 (0.78, 1.27)	0.96	1.11 (0.80, 1.56)	0.53
<10 cigarettes/day vs never	1.06 (0.75, 1.50)	0.76	1.12 (0.77, 1.65)	0.55
10-20 cigarettes/day vs never	1.36 (0.50, 3.68)	0.55	1.66 (0.70, 3.93)	0.25
>20 cigarettes/day vs never	1.00 (0.44, 2.28)	0.99	1.39 (0.99, 1.95)	0.06
Alcohol use				
1-3 drinks/day vs nondrinkers	0.58 (0.47, 0.71)	<0.001	0.83 (0.63, 1.10)	0.20
≥4 drinks/day vs nondrinkers	0.66 (0.33, 1.30)	0.23	1.22 (0.90, 1.65)	0.21
Physical activity				
Tertile 1 vs tertile 3	1.61 (1.27, 2.05)	<0.001	1.28 (0.90, 1.83)	0.17
Depression	1.17 (0.77, 1.79)	0.46	0.85 (0.62, 1.18)	0.34
Hypertension	1.31 (1.03, 1.67)	0.03	1.23 (0.95, 1.59)	0.13
Obesity	1.02 (0.80, 1.30)	0.87	1.10 (0.84, 1.44)	0.48
Diabetes	1.15 (0.91, 1.44)	0.24	1.15 (0.81, 1.62)	0.44
CVD	1.53 (1.16, 2.02)	0.003	1.19 (0.93, 1.52)	0.15
Asthma	1.36 (0.96, 1.91)	0.08	1.45 (1.05, 2.00)	0.03
Cancer	1.35 (1.02, 1.80)	0.04	0.80 (0.47, 1.37)	0.43
Pesticide use	0.87 (0.64, 1.17)	0.34	0.86 (0.65, 1.14)	0.30
Frequent nasal congestion	0.90 (0.71, 1.15)	0.40	0.95 (0.70, 1.27)	0.70
Head injury	0.99 (0.75, 1.31)	0.93	1.03 (0.72, 1.46)	0.88
Tonsillectomy	0.93 (0.66, 1.32)	0.69	1.05 (0.78, 1.43)	0.74
Broken nose or serious injury to face/skull	1.19 (0.89, 1.59)	0.25	1.08 (0.84, 1.39)	0.56

* Adjusted for age, sex, and race/ethnicity.

Table 3. Backward Stepwise Logistic Regression Model for Smell and Taste Disorders

Variable	Smell impairment		Taste impairment	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (per 5-year increment)	1.37 (1.30, 1.45)	<0.001	0.93 (0.89, 0.97)	0.01
Sex		<0.001		
Women	1 (Reference)			
Men	1.68 (1.27, 2.22)		--	
Race/ethnicity		<0.001		
Non-Hispanic White	1 (Reference)		1 (Reference)	
Mexican American	1.68 (1.02, 2.76)		--	
Non-Hispanic Black	1.91 (1.36, 2.67)		1.46 (1.07, 1.99)	0.02
Ratio of family income to poverty		0.03		
<1.3vs >3.5	1.45 (1.04, 2.01)		--	
Education level		<0.001		
Low vs high	1.33 (1.17, 1.51)		--	
Alcohol use		<0.01		
1-3 drinks/day vs nondrinker	0.72 (0.58, 0.91)		--	
≥4 drinks/day vs nondrinker	--		1.42 (1.05, 1.93)	0.03
CVD	--		1.30 (1.02, 1.67)	0.04
Cancer	1.38 (1.05, 1.83)	0.02	--	
Asthma	1.39 (1.02, 1.89)	0.03	--	

-- Not included in the final model.

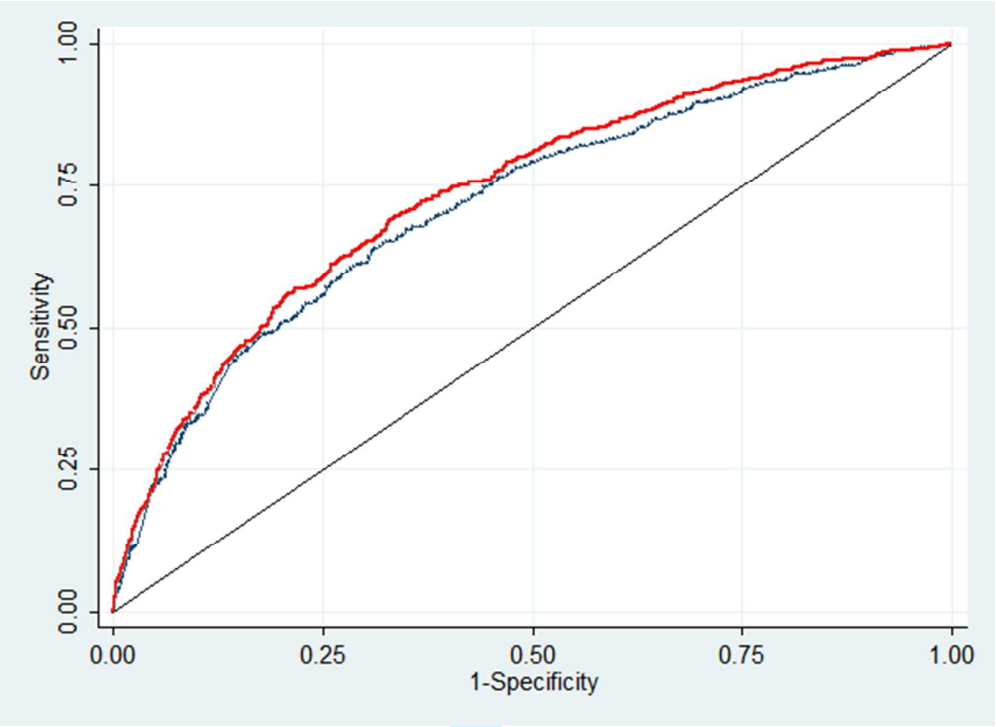
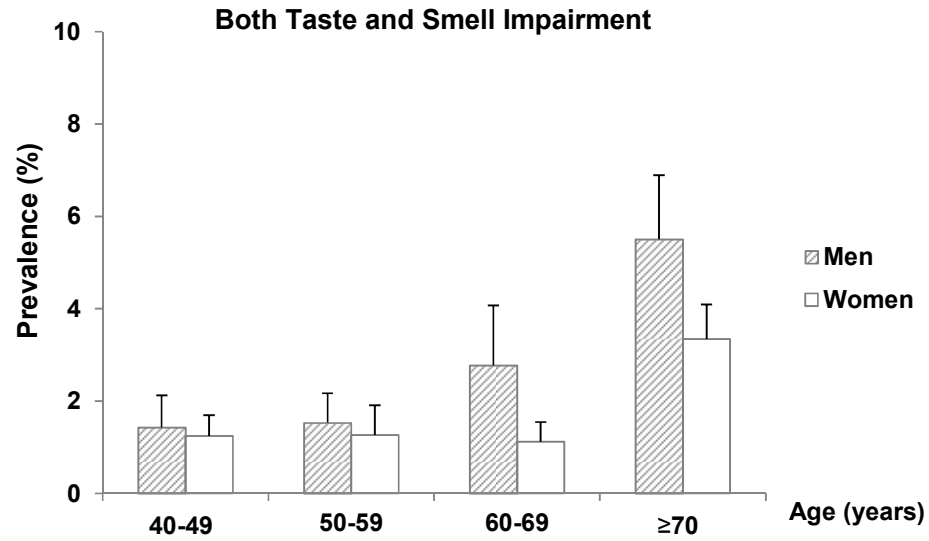
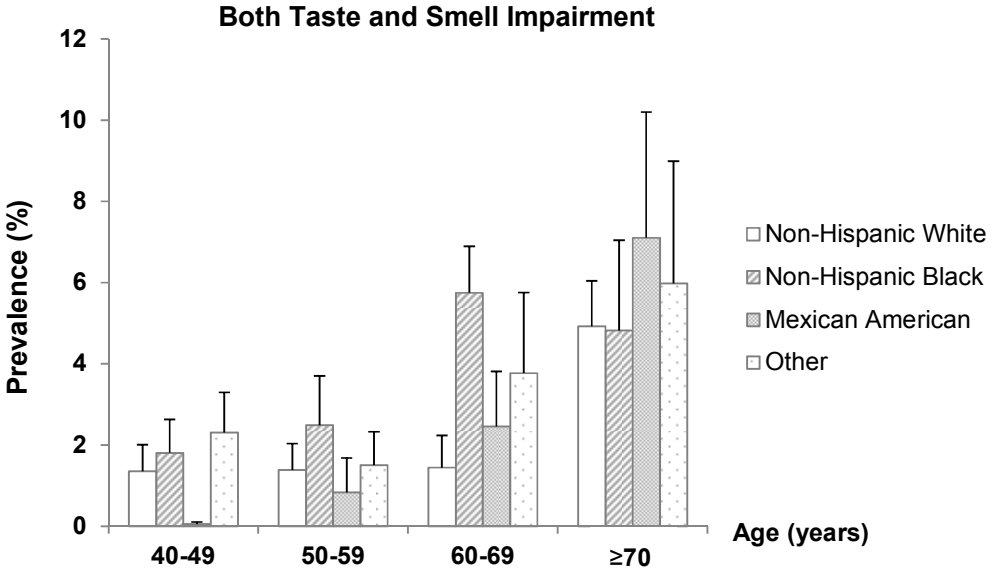


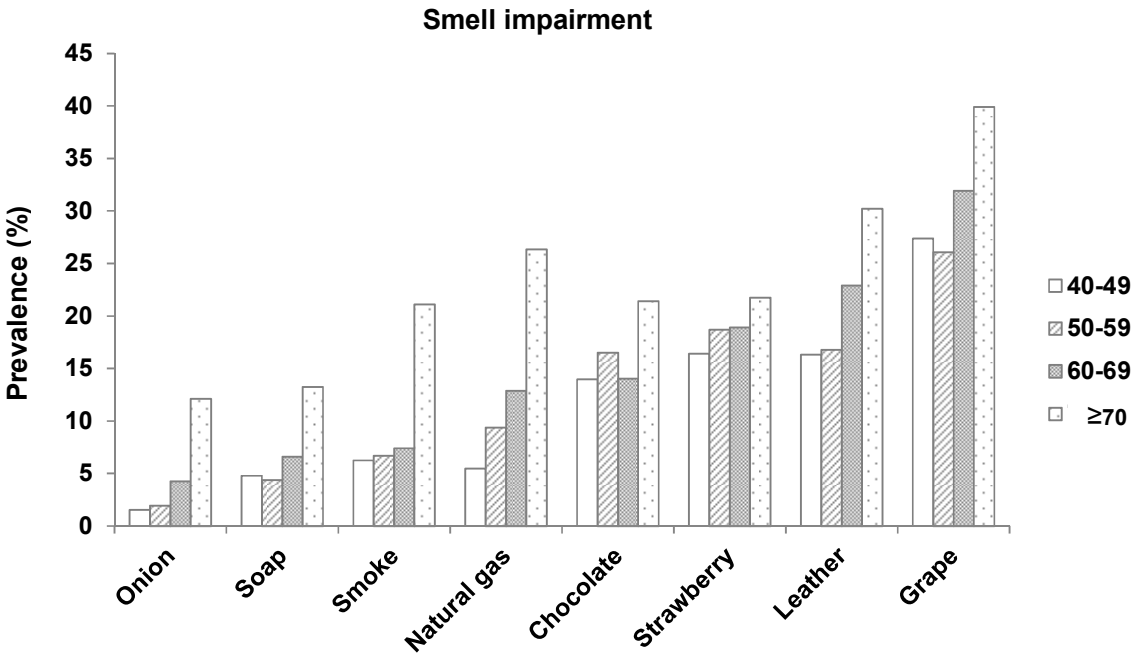
Figure 2. Receiver operating characteristic (ROC) curves showing the capacity of selected risk factors in predicting smell impairment in US men and women, National Health and Nutrition Examination Survey, 2013–2014. Blue curve is for the model adjusted for age, gender, and ethnicity. Red curve is for the model further adjusted for family income, educational attainment, alcohol consumption, and a history of asthma or cancer. The area under the ROC was 0.72 for blue curve and 0.74 for red curve.

Supplementary Figure 1. Prevalence of Both Taste and Smell Impairment by Age, Sex, and Ethnicity





Supplementary Figure 2. Prevalence of Smell Impairment for Specific Odor



Supplementary Table 1. Comparison of the Prevalence of Smell Impairment between UPSIT Study and Current Study

	Prevalence of Smell Impairment		
Age(years)	Total	Men	Women
Current Study (defined as <6 out of 8 odors)			
40-49	6.9%	7.7%	6.0%
50-59	9.0%	10.9%	7.2%
60-69	13.8%	17.1%	10.8%
70+	30.4%	37.2%	25.2%
UPSIT Study (defined as <29 out of 40 odors)			
40-49	3.0%	6.0%	0%
50-59	10.3%	15.9%	4.9%
60-69	17.1%	22.4%	13.1%
70+	33.5%	37.5%	30.1%

Supplementary Table 2. Comparisons of the prevalence of smell impairment and participants' characteristics across studies

Studies	Sample size	Prevalence (%)	Definition	Age (years)*	Men (%)
Murphy C et al. (2002)[6]	2491	24.5%	<6 (8 odors)	68.7 (53-97)	42%
Mullol J et al. (2012)[7]	9348	19.4%	<4 (4 odors)	43.4 (5-91)	34.3%
Boesveldt S et al. (2011)[8]	2778	2.7%	<2 (5 odors)	69.3 (57-85)	48.4%
Bramerson A et al. (2004)[9]	1387	19.1%	<13 (16 odors)	20-80+	48.4%
Vennemann M et al. (2008)[12]	1312	18%	<10 (12 odors)	52.1 (25-75)	47.1%
Schubert CR et al. (2012)[14]	2838	3.8%	<6 (8 odors)	49 (21-84)	45.6%
Current study	3519	13.5%	<6 (8 odors)	57.8 (40+)	47.7%

* Mean (range)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Page 5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	Page 7
Study size	10	Explain how the study size was arrived at	Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 9
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 10-12
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 12-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 19
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 20

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Prevalence and Risk Factors of Taste and Smell Impairment in a Nation-wide Representative Sample of the U.S. Population: a Cross-sectional Study

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Secondary Subject Heading:	Ear, nose and throat/otolaryngology
Keywords:	Taste Impairment, Smell Impairment, Prevalence, Risk factors

Prevalence and Risk Factors of Taste and Smell Impairment in a Nation-wide Representative Sample of the U.S. Population: a Cross-sectional Study

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Objectives: To estimate the prevalence of, and explore potential risk factors for, taste and smell dysfunction in the general population of the United States.

Design: A cross-sectional study.

Setting: A cross-sectional analysis of data collected in the National Health and Nutrition Examination Survey (NHANES 2013-2014).

Participants: A total of 3519 men and women aged 40 years and older who participated in NHANES 2013-2014.

Main Outcome Measures: Using the NHANES Pocket Smell Test™, smell impairment was defined as failing to correctly identify 6 or more of the 8 odors. Taste impairment was defined as failing to correctly identify quinine or sodium chloride.

Results: The estimated prevalence was 13.5% for smell impairment, 17.3% for taste impairment, and 2.2% for both taste and smell impairment. For smell, but not taste, prevalence estimates increased with age and were higher in men and ethnic minorities. In backward stepwise logistic regression, low educational attainment, low family income, and a history of asthma or cancer were independently associated with a higher prevalence of smell impairment, whereas light-to-moderate alcohol consumption (1-3 drinks/day) was associated with a lower prevalence of this condition. After multivariate adjustment, being non-Hispanic Black Americans, consuming ≥4 drinks of alcohol per day, and having a history of cardiovascular disease (CVD) were independently associated with a higher prevalence of taste impairment.

Conclusion: Based upon a nationally representative multistage probability survey among the U.S. population aged 40 years and older, smell and taste dysfunction affected approximately

20.5 million (13.5%) and 26.3 million (17.3%) individuals, respectively. Age, gender, ethnicity, educational attainment, family income, light-to-moderate alcohol consumption, and history of asthma or cancer were significant risk factors for smell dysfunction, whereas only ethnicity, heavy alcohol consumption, and CVD history were associated with a higher prevalence of taste dysfunction.

Strengths and limitations of this study

- The present study provides a nation-representative estimates of the prevalence of taste and smell impairment among men and women aged 40 years and above in the United States population.
- This study demonstrates associations of age, gender, ethnicity, educational attainment, family income, alcohol consumption, and history of asthma, cancer, or CVD with chemosensory disorders on a nation-wide scale.
- This is a cross-sectional study, which limits its ability to infer causal relationships between risk factors and taste and smell impairments.

INTRODUCTION

Smell and taste disorders pose a major threat to public health, significantly compromising quality of life, food preferences, nutritional status, and safety from airborne toxins, fire, smoke, spoiled food, and leaking natural gas.[1-4] It is now well established that a disproportionate number of the elderly experience smell dysfunction that has direct consequences for health and safety.[3,5,6] For example, in one longitudinal study of 1,162 non-demented older persons, the mortality rate over a 4-year period was 45% for those with lowest baseline olfactory test scores, as compared to a rate of 18% in those with the highest test scores, even after controlling for age and other confounders.[7]

Although a large literature suggests that chemosensory disorders are relatively common,[2,8-16] there remains a lack of consensus as to the prevalence of such disorders in population-based epidemiological studies.[8,12,17-22] Previous studies attempting to address this issue have provided prevalence estimates ranging from 2.7% to 24.5% for smell dysfunction,[8-11,13,17,19,20] and 0.6% to 20% for taste dysfunction.[10,17,20,22] Such variation likely reflects differences in test methods, criteria for defining dysfunction, and both sample sizes and sampling procedures, as well as variations in sex, age, health, and ethnic composition of the sampled populations.

The relatively recent addition of olfactory and gustatory testing to the National Health and Nutrition Examination Survey (NHANES), a survey that focuses on representative samples of non-institutionalized persons from 15 counties or other geographic jurisdictions randomly selected within the United States each year, provides a unique opportunity to obtain sound nation-wide estimates of prevalence of chemosensory dysfunction. An evaluation of

the olfactory data collected during a single year survey (2012) reported a 12.4% prevalence for smell dysfunction in the sampled population, although estimates of taste dysfunction were not presented.[21] In the present study, based on a larger sample size from the NHANES 2013-2014 survey among U.S. population aged 40 years and older, we aimed to estimate the prevalence of both olfactory and taste dysfunction in the U.S. population, and explore potential risk factors for these conditions.

METHODS

Study Participants

NHANES is a cross-sectional survey designed to assess the health and nutritional status of adults and children in the United States. Each year, the survey examines a nationally representative sample of about 5,000 people who are located in 15 counties randomly selected across the country. The taste and smell examination was a new health examination component which was performed among participants aged 40 years and older.[18] A total of 3708 men and women were enrolled in the taste and smell examination. A short screening questionnaire and a test of perceived taste intensity were then used to assess eligibility for the study.[23] Participants were excluded from smell and taste examinations if they were: 1) pregnant or lactating; 2) allergic to quinine (pertinent to the quinine taste test only); or 3) unable to correctly rate the brightness of a standard series of three lights in an LED luminescence panel (pertinent to understanding the procedures of the taste test only). These exclusions left 3114 participants who completed the quinine and sodium chloride (NaCl) taste tests and 3519 participants who completed the 8-item smell test. The mean (SEM) age of

NHANES participants (n=3114) included in the taste test was 57.5 (0.3) years; 48.6% were men. Regarding ethnic distribution, 72.8% were non-Hispanic Whites, 10.1% non-Hispanic Blacks, and 6.6% Mexican Americans. For the smell test, the mean (SE) age of NHANES participants (n=3519) was 57.8 (0.3) years; 47.7% were men. Of these participants, 71.2% were non-Hispanic Whites, 10.6% non-Hispanic Blacks, 6.9% Mexican Americans, and 11.3% other races/ethnicities (including other Hispanic and multi-racial individuals).

The NHANES protocol was approved by the National Center for Health Statistics (NCHS) institutional review board, and written informed consent was obtained from all participants.

Smell and Taste Tests

For smell testing, the two 4-item versions (A & B) of the NHANES Pocket Smell Test™ (Sensonics International, Haddon Heights, NJ), developed in conjunction with the NIH, were sequentially administered, resulting an 8-item "scratch and sniff" test.[23] The eight odorants (chocolate, strawberry, smoke, leather, soap, grape, onion, and natural gas) were presented in a fixed order. A subject was required, in a forced-choice situation, to identify each odorant from four alternative names. Smell impairment was defined as not being able to correctly identify 6 or more of the 8 odors, each from a list of four possible responses.[8] A recent validation study demonstrated moderate-to-good test–retest reliability of the NHANES smell protocol (intraclass correlations were 0.82 and 0.69 for 2-week and 6-month intervals, respectively).[23] Of note, the eight odorants used in NHANES test are components of the 40-item University of Pennsylvania Smell Identification Test (UPSIT).[24] Our definition of

smell impairment approximately corresponds to the definition of being unable to correctly identify 29 or more of the 40 odors using the UPSIT test (**Supplementary Table 1**).

The taste tests employed in this NHANES survey included a tongue tip taste test and a whole mouth taste test. In the tongue tip test, the taste stimuli [0.32 mg/mL quinine (bitter) and 58.5 mg/mL NaCl (salty) in 10 ml solution] were presented on a cotton swab that was gently moved across the tip of the tongue in a standardized manner.[23] Participants were asked to identify the taste (salty, bitter, sour, something else, no taste) and rate the perceived intensity on the Generalized Labeled Magnitude Scale (gLMS).[25] A 30-second interval was interspersed between stimulus presentations, during which time participants rinsed their mouths with water. In the whole mouth taste test, participants swished 10 mL of each tastant solution (19.5 mg/mL NaCl, 58.5 mg/mL NaCl, or 0.32 mg/mL quinine) for 3 seconds, expectorated, and rinsed their mouths with water. The participants then were asked to identify the taste quality and rate the solution's intensity on a standardized scale. As a replication test, another whole month taste test for salt was performed at the end of the chemosensory test. The participants were randomized to receive either a 0.32 M NaCl or a 1 M NaCl salt solution.

A recent test-retest reliability and validity examination of NHANES taste test protocol demonstrated a reasonable correlation between quinine whole mouth measurement (0.32 mg/mL) and other taste measurements, including tongue tip tests of NaCl ($r = 0.53$) and quinine ($r = 0.44$), and whole mouth tests of NaCl ($r = 0.60$ for 19.5 mg/mL NaCl and 0.77 for 58.5 mg/mL NaCl), sucrose, citric acid, and propylthiouracil, suggesting that the whole mouth quinine assessment was a reasonable assessment for overall taste functioning.[23] Thus,

in our study, instead of intensity ratings, failing to correctly identify quinine in the whole mouth test was used to define taste dysfunction. In sensitivity analyses, we defined taste impairment as failing to correctly identify quinine (both tongue tip and whole mouth test) or NaCl (both tongue tip and whole mouth test).

Demographics and related information

The NHANES survey employed a computer-assisted personal interview system. The in-home questionnaire obtained information on age, sex, race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, and other race),[26] educational attainment (high school or below, some college, college, graduate school or above), ratio of family income to poverty (PIR; categorized as low [PIR<1.3], middle [1.3≤PIR≤3.5], and high [PIR>3.5]),[26] smoking status (never smoker, past smoker, current smoker: <10, 10-20, >20 cigarettes/day), alcohol consumption (nondrinker, 1-3 drinks/day, or ≥4 drinks/day), self-reported chronic diseases (diabetes, cardiovascular disease [CVD], asthma, and cancer), pesticide use in home (yes, no), self-reported taste and smell problems (defined as reporting problems within the past year), and conditions that might influence taste and smell ability (frequent nasal congestion, head injury, tonsillectomy, broken nose/serious injury to face or skull, and sinus infection). Symptoms of depression were assessed using the 9-item Patient Health Questionnaire scale (PHQ-9, possible range 0–27). A cut-off point ≥10 was used to identify participants with moderate to severe depression.[27] To estimate physical activity, metabolic equivalent values (MET-min/week) were calculated by using the sum of the MET score multiplied by the average time per week of specific physical activity and subsequently categorizing the scores into tertile levels of physical activity.[28] Blood pressure (BP) and

anthropometric measurements were performed by trained health technicians in the mobile examination centers. Blood pressure was measured three times, and the mean values of the last two measurements were used in the analysis. Hypertension was defined as systolic BP ≥140 or diastolic BP ≥90 mmHg, or positive answers to the questions, "Now taking prescribed medicine for high BP" or "Told had high BP 2+ times." Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Obesity was defined as BMI ≥30 kg/m^2.

Statistical analysis

Due to the NHANES sampling design, the sample weights were incorporated into the analysis whenever possible. We used the number 15 (the number of primary sampling units minus the number of sampling strata) for the degrees of freedom. A SAS procedure—PROC SURVEYFREQ—was used to estimate the weighted prevalence of taste and smell disorders in the total population as well as within subgroups of the population. The comparison between participants with and without taste or smell disorder was tested using the Wald F-test in the PROC SURVEYREG for continuous variables or the Rao-Scott Chi-Square test in the PROC SURVEYFREQ for categorical variables. Logistic regression (PROC SURVEYLOGISTIC) was used to estimate the age- and sex-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of taste and smell disorders for common socioeconomic, demographic, and lifestyle characteristics that may serve as risk factors of the disorders, including BMI, race/ethnicity, educational attainment, family income, smoking status, alcohol use, physical activity, depression, hypertension, obesity, diabetes, CVD, asthma, cancer, pesticide use, frequent nasal congestion, head injury, tonsillectomy, broken nose or serious

injury to face or skull, and sinus infection. To minimize sample reduction due to missing covariates, indicator variables were used for missing categorical variables. We used a SAS macro (%StepSvylog) to perform backward model selection for the survey data. Potential risk factors with $P<0.25$ were entered together into a multivariable logistic model and then successively removed until all retained variables had a $P<0.05$.[29] Finally, to assess the capacity of selected risk factors in predicting smell and taste disorder, we plotted a receiver operating characteristic (ROC) curve and calculated a sample-weighted area under the ROC curve (AUC) that incorporated the NHANES sampling design.

Data were analyzed with the SAS software package, version 9.4 (SAS Institute, Inc., Cary, North Carolina), and STATA, version 12.0 (Stata Corporation, College Station, Texas). Two-sided $P<0.05$ was considered statistically significant.

RESULTS

The overall estimated prevalence of smell impairment was 13.5%, whereas it was 17.3% for taste impairment. The estimated prevalence of having both a taste and smell disorder was 2.2%. Thus, about 28.6% of the U.S. adult population aged 40 years and older appears to have either a smell or taste problem or both.

Figure 1 shows the prevalence estimates of smell and taste disorders according to age, sex, and ethnicity. For smell dysfunction, the estimates significantly increased with age in both men and women. In addition, compared with women, men had a higher prevalence in each age group, especially in the group of 70 years and older (men: 37.2%; women: 25.2%). Regarding race/ethnic distribution, compared with non-Hispanic White Americans, ethnic

minorities, namely non-Hispanic Black Americans, Mexican Americans, and other races/ethnicities, had a higher estimated prevalence of smell impairment. In contrast, no such patterns of relationship were found between these demographic variables and the prevalence of taste dysfunction. Paradoxically, the estimated prevalence of taste dysfunction decreased with age in women, but not in men. **Supplementary Figure 1** shows mean (SE) NHANES Pocket Smell Test™ scores according to age and gender. Regarding taste impairment, non-Hispanic Black Americans had a higher prevalence of than that in other ethnic groups (22.9% for non-Hispanic Black, 17.1% for non-Hispanic White, 15.6% for Mexican American, and 13.9% for other race). **Supplementary Figure 2** demonstrates the prevalence of both taste and smell impairment by age, sex, and ethnicity. Regarding individual smell test items of all the participants, 4.3% incorrectly identified the odor of onion, 6.7% of soap, 9.5% of smoke, 12.3% of natural gas, 16.1% of chocolate, 18.7% of strawberry, 20.6% of leather, and 30.4% of grape. In the age group of 70 years and older, the corresponding proportions reached 21.2% for smoke and 26.3% for natural gas (**Supplementary Figure 3**).

The characteristics of the study population by smell and taste disorder status are shown in **Table 1**. In univariate comparisons, in addition to the demographic characteristics, participants with smell impairment tended to have lower levels of educational attainment, physical activity, family income, and alcohol consumption than other participants. Moreover, they had a higher prevalence of hypertension, diabetes, CVD, cancer, and self-reported taste and smell problems ($P<0.05$). Other factors, including BMI, smoking, obesity, depression, the history of asthma, pesticide use, nasal congestion, tonsillectomy, and head injury, were not associated with smell dysfunction. Age and ethnicity were associated with the prevalence of

taste impairment.

After adjusting for age, gender, and ethnicity, the prevalence of smell and taste disorders was differentially associated with other socioeconomic, lifestyle, and medical history variables (**Table 2**). Educational attainment, family income, physical activity, alcohol consumption, and a history of hypertension, CVD, or cancer were significantly associated with the prevalence of olfactory dysfunction. Educational attainment and a history of asthma were significantly associated with the prevalence of taste dysfunction.

In backward stepwise selection, older age, male gender, ethnic minorities (including non-Hispanic Black and Mexican American), low family income, low educational attainment, and a history of asthma or cancer remained in the model and were independently associated with an increased prevalence of smell impairment (OR and 95% CI was 1.37 [1.30, 1.45] for age, 1.68 [1.27, 2.22] for men, 1.91 [1.36, 2.67] for non-Hispanic Black, 1.45 [1.04, 2.01] for low family income, 1.33 [1.17, 1.52] for low education attainment, 1.38 [1.05, 1.83] for cancer, and 1.39 [1.02, 1.89] for asthma; all $P<0.05$). In contrast, light-to-moderate alcohol consumption (1-3 drinks/day) was significantly associated with a decreased prevalence of smell impairment (OR and 95% CI, 0.72 [0.58, 0.91], $P<0.01$) (**Table 3**). For taste dysfunction, non-Hispanic Black (OR and 95% CI, 1.46 [1.07, 1.99], $P=0.02$), high alcohol consumption (≥4 drinks/days) (OR and 95% CI, 1.42, [1.04, 1.94], $P=0.03$), and a history of CVD (OR and 95% CI, 1.30, [1.02, 1.67], $P=0.04$) were significantly associated with a higher prevalence of impairment, whereas age was inversely associated with the prevalence of this condition (each 5-year increment; OR and 95% CI, 0.93 [0.89, 0.97], $P=0.01$) (**Table 3**).

Age (each 5-year increment; OR and 95% CI, 1.22 [1.08, 1.38], $P<0.01$), physical inactivity (OR and 95% CI, 2.38 [1.21, 4.70], $P<0.05$), and head injury (OR and 95% CI, 2.15 [1.10, 4.18], $P<0.05$) were significantly associated with a higher prevalence of having both taste and smell dysfunction.

Figure 2 shows that age, sex, and ethnicity render an AUC of 0.72 for smell dysfunction. Further inclusion of socioeconomic, lifestyle, and medical risk factors only marginally increased the AUC to 0.74. For taste impairment, an AUC of 0.57 was estimated for a model that included age, ethnicity, heavy alcohol consumption, and a history of CVD.

In a secondary analysis, similar results regarding the risk factors for taste and smell impairment were observed when analyses were restricted to the participants aged 40-60 years, although some of the associations did not reach statistical significance probably due to reduced power (data not shown). In the sensitivity analyses, when we defined taste disorder as being unable to correctly identify either quinine or NaCl, we estimated a prevalence of 14.0%. In addition, with this alternate definition, the associations of Black ethnicity, heavy alcohol consumption, and a CVD history with the prevalence of taste disorder were attenuated to non-significance (OR and 95% CI: 1.25 [0.98, 1.59] for Black ethnicity; 1.20 [0.86, 1.67] for heavy alcohol consumption, and 1.15 [0.85, 1.55] for CVD).

DISCUSSION

In this most current nation-wide representative sample of U.S. men and women aged 40 years and older, a significant number of U.S. adults were found to experience smell or taste problems. The overall estimated prevalence of smell and taste impairment was 13.5% and

17.3%, respectively. Significant differences were observed in the estimated prevalence of smell impairment among subgroups defined by age, gender, and ethnicity. Such differences were not evident for the estimated prevalence of taste dysfunction. In our multivariate analysis, a multitude of potential risk factors, including age, sex, race/ethnicity, family income, educational attainment, alcohol consumption, and a history of asthma or cancer, were independently associated with the prevalence of smell impairment. Non-Hispanic Black ethnicity, high alcohol consumption, and a history of CVD were significantly associated with a higher prevalence of taste impairment after adjustment for confounders.

Our nationally representative estimate of the overall prevalence of smell dysfunction (13.5%) was quite similar to the estimate based on a single-year NHANES survey (12.4%).[21] These estimates were somewhat lower than that reported in other populations whose prevalence ranged from 18.0 to 24.5%,[8,9,11,17] and somewhat higher than that reported by some other studies (2.7%-3.8%).[10,19] Differences between the test procedures (e.g., odorants, psychophysical paradigms) and the study populations (e.g., age, sex, and health status) are presumably involved (**Supplementary Table 2**). Using the 40-item UPSIT, Doty et al. found little age-related decline in smell function until the 6th decade of life, at which time a precipitous age-related decline occurred, illustrating how age would be expected to markedly influence prevalence.[13] Of particular importance in establishing prevalence are the criteria used to define dysfunction, which vary considerably among studies. In two studies, being unable to identify 75% of either 4 or 12 odorants was defined as dysfunction.[9,12] Other studies have set this criterion at 62.5% for either 8 or 16 odorants,[6, 14,21] and 40% for 5 odorants.[9] Such variations in criteria significantly influence the estimated prevalence and likely explain

much of the variation seen among prevalence studies. Our study, like most others, has the limitation of employing a relatively few number of odorants. Despite this limitation, however, our criterion for defining smell impairment (i.e., <75% or 6/8 items) corresponds to dysfunction defined by the 40-item UPSIT. Correctly identifying 6 out of 8 items corresponds to an UPSIT score of 30, which is the cut point between mild and moderate microsmia.[24]

Only a limited number of epidemiological studies have estimated the prevalence of taste dysfunction.[10,17,20,22] In the 1994 Disability Supplement to the National Health Interview Survey (NHIS-D), based on information from a self-reported taste impairment questionnaire, Hoffman et al. found that only 0.6% of U.S. adults (>18 years) reported having a gustatory problem.[22] In the current study, using standardized taste testing, the prevalence of taste impairment was 17.3%, whereas the prevalence of self-reported taste impairment (defined as reporting taste problems within the past year) was only 5.3%, suggesting that self-reported estimates significantly underestimated the true prevalence.[8,9,30] Nevertheless, the prevalence of taste impairment in our study was comparable to two other large taste testing studies that reported prevalences of 14.8% and 20.0%.[10,17]

Epidemiological studies that have examined potential risk factors for smell and taste disorders are limited. Several have consistently found the prevalence of smell impairment to increase with age and to be higher in men than in women.[8,11,17,21] In addition, the current analysis demonstrated that certain ethnic groups, such as non-Hispanic Blacks and Mexican Americans, had a higher prevalence of smell impairment than that observed for White Americans. In the National Social Life, Health, and Aging Project study, Pinto et al. also demonstrated that older African Americans and Hispanics had worse olfactory function.[31]

Williams et al. observed significant differences between Hispanics, African Americans, and non-Hispanic Whites in taste perception.[32] While a subtle difference was noted by Doty et al. between White and Black Americans in a large, albeit convenience, sample,[24] another study observed equivalent UPSIT scores in White and Black American populations and relatively higher scores in Korean American populations.[33] The discrepant results may reflect differences in population characteristics, testing methods, and definitions for smell impairment.

In the current study, other socioeconomic risk factors for smell impairment that are independent of ethnicities were also identified, including low educational attainment and low family income. Our findings of the influences of these socioeconomic factors were consistent with previous studies.[4,19-21,34] Existing evidence has suggested that access to health care, occupation, and overall quality of life potentially explain the link between low socioeconomic status and a higher prevalence of smell disorder.[35] Regarding olfactory function, besides the above findings which were mostly consistent with the data from 2012 NHANES survey,[21] our results additionally demonstrated a link between a history of asthma and cancer and a slightly higher prevalence of smell dysfunction. For medical history, Alobid et al. reported that a history of persistent asthma had a significant impact on smell loss in patients with nasal polyposis.[36] Moreover, asthma was a predictor of poor olfactory function in patients with chronic rhinosinusitis.[37] Some clinical studies have also demonstrated that smell function is significantly decreased in patients receiving cancer chemotherapy,[38,39] and at least one study suggest that the prevalence of self-reported taste and smell alterations could reach as high as 86%.[40] Of note, smoking was not associated with the prevalence of smell

impairment in our cross-sectional analysis. Accumulating evidence has suggested that smoking may exert an adverse effect on smell function,[8,17,41] although some studies did not observe such a link.[11,20,42] In another cross-sectional population-based study, Mullol et al. reported that smoking and exposure to noxious substances were even mild protective factors for smell recognition.[9] These mixed findings may reflect the cross-sectional nature of these studies, as well as the lack of detailed assessments of smoking dose and duration, which are often more informative than dichotomous smoking status. More prospective studies are warranted to elucidate the potential adverse effect of smoking on olfactory function.

In comparison to the data for smell impairment, fewer associations between taste impairment and demographic/health measures were observed. We did find that race/ethnicity, heavy alcohol use, and a history of CVD were associated with a higher prevalence of taste impairment. Compared with non-Hispanic White subjects, non-Hispanic Black subjects had a higher prevalence of both taste and smell disorders. The underlying reason for this observation was unknown, although other socioeconomic factors and genetic susceptibility might partially account for this link. Interestingly, we also found heavy drinking to be associated with an increased prevalence of taste dysfunction, whereas light-to-moderate drinking was associated with a decreased prevalence of smell dysfunction, suggesting that the amount of alcohol intake may exert distinct effects on chemosensory perception.[21,43,44] In addition, we found a positive association between CVD and the prevalence of altered taste. Evidence has suggested that variations in oral sensation, influenced by both genetic and environmental factors, might increase the risk of CVD by impacting dietary behaviors such as higher intake of high-fat and sweet foods.[45,46] However, in this cross-sectional study, we

could not exclude the possibility that the taste function might be influenced by the medications taken by people with CVD. Unexpectedly, an inverse association between age and the prevalence of taste dysfunction was observed in our study, which is in contrast to frequent reports of age-dependent reductions of taste ability.[47,48] Aging may primarily influence the taste sensitivity to low levels of stimuli,[47] but less so for suprathreshold deficits in taste. In most epidemiological studies, relatively high concentrations of tastants (24 mg/ml quinine hydrochloride; 75-100 mg/mL NaCl; 100-200 mg/mL sucrose; 50-165 mg/mL citric acid) have been employed,[10,17] which may not be sensitive enough to detect age-related taste dysfunction.[49] Of note, threshold concentrations are typically set at much lower concentrations (e.g., 3×10^{-4} mg/mL for quinine, 0.585 mg/mL for NaCl, 6.84 mg/mL for sucrose, and 3.84 mg/mL for citric acid).[49] In the NHANES, the tastant concentrations (0.32 mg/mL for quinine, 19.5 mg/mL and 58.5 mg/mL for NaCl) were much higher than the threshold concentrations, albeit comparable to those used in some previous epidemiological studies.[10,17] This may explain the similarity between our NHANES findings and those reported in a German population with taste test at suprathreshold concentrations, in which a decline trend of the prevalence of taste dysfunction was observed in women aged 45-74 years.[17]

The present study provides a nation-representative estimate of the prevalence of taste and smell impairment among men and women aged 40 years and older in the United States population. Most previous studies were only conducted among older adults.[8,10,12,14,15] Moreover, it has demonstrated that chemosensory disturbances are influenced by a range of demographic and health factors. Importantly, our analysis strongly suggests that a

considerable number of Americans suffer from chemosensory disturbances. That being said, this research has its limitations. First, it is a cross-sectional study, which limits its ability to infer causal relationships between risk factors and taste and smell impairments. Second, we utilized only bitter and salt tasting stimuli, excluding sweet and sour tasting ones. Furthermore, the unexpected inverse association of taste dysfunction with age suggests that the test used by NHANES is not sensitive enough to capture age-related declines in taste function. Nonetheless, there is evidence that the whole-mouth quinine test used in our study may be a good proxy for overall taste function, even though there are presently no universally accepted standards to best define taste impairment.[23] Third, we measured taste and smell function on only a single occasion, which may not be representative of longer-term function. Nevertheless, the taste and smell measurements employed in this study have been found to be largely reproducible over a 6-month period.[23] In addition, although a recent study demonstrated that the NHANES taste and smell protocol has moderate-to-good test–retest reliability,[23] the face validity of the protocol was not proven. Furthermore, the impact of cognitive function on the validity of assessments of smell and taste functions cannot be evaluated in this investigation. Fourth, the NHANES survey only sampled non-institutionalized and relatively healthy individuals. The prevalence of taste and smell impairment may be significantly higher in persons whose health is otherwise compromised, such as those with neurodegenerative disorders.[50] Finally, since only a limited number of potential risk factors were evaluated, other risk factors may exist that have yet to be identified.

CONCLUSION

This study, based upon a representative sample of the United States population, strongly suggests that a significant number of American citizens suffer from smell or taste problems. Thus, 13.5% of the study population exhibited smell dysfunction, 17.3% taste dysfunction, and 2.2% both taste and smell dysfunction. Since the 2016 US Census Bureau estimates the U.S. population ≥40 years old to be ~152 million,[51] this translates to over 43 million Americans having some degree of chemosensory dysfunction. The adverse consequences of these disorders are particularly critical to older populations because approximately a fifth of those sampled could not identify the test odors of smoke and natural gas, in accord with other studies on this topic.[52] As shown in the NHANES study, age, gender, ethnicity, educational attainment, family income, light-to-moderate alcohol consumption, and history of asthma or cancer were potential risk factors for smell dysfunction. Risk factors for taste dysfunction were more limited, being confined only to ethnicity, heavy alcohol consumption, and a history of CVD. Future prospective investigations are needed to establish more clearly the link between these and other risk factors and the development of chemosensory disturbances.

Contributors: Q. Sun was responsible for the study concept. G. Liu, Z. Zong, and Q. Sun were responsible for analysis and interpretation of data. G. Liu wrote the first draft of the manuscript. R. L. Doty contributed to results interpretation, statistical analysis, and critical revision of the manuscript. All authors approved the finally version of the manuscript.

Competing interests: Richard L. Doty is President and major shareholder of Sensonics International, the manufacturer of the NHANES Pocket Smell Test™.

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Figure 1. Prevalence of Smell and Taste Impairment According to Age, Sex, and Race/Ethnicity. A and B are the prevalence of smell and taste impairment in men and women according to each age group. C and D are the prevalence of smell and taste impairment in different ethnicities according to each age group.

Figure 2. Receiver operating characteristic (ROC) curves showing the capacity of selected risk factors in predicting smell impairment in US men and women, National Health and Nutrition Examination Survey, 2013–2014. Blue curve is for the model adjusted for age, gender, and ethnicity. Red curve is for the model further adjusted for family income, educational attainment, alcohol consumption, and a history of asthma or cancer. The area under the ROC was 0.72 for blue curve and 0.74 for red curve.

Table 1. Characteristics of Study Participants According to Smell and Taste Impairment Status*

Characteristic	Smell impairment			Taste impairment		
	Yes (n=630)	No (n=2889)	*P*	Yes (n= 540)	No (n=2574)	*P*
Age, years (mean±SE)	65.0±0.6	56.7±0.2	<0.001	55.9±0.6	57.8±0.3	0.01
BMI, kg/m^2 (mean±SE)	29.5±0.4	29.5±0.2	0.91	29.6±0.5	29.6±0.2	0.99
Men,%	56.2 (3.1)	46.4 (1.0)	0.005	49.2 (1.6)	48.5 (1.0)	0.72
Race/ethnicity, %			0.005			0.04
Non-Hispanic White	64.3 (3.6)	72.3 (3.2)		72.1 (3.9)	72.9 (3.1)	
Non-Hispanic Black	14.1 (2.1)	10.0 (1.4)		13.5 (2.1)	9.5 (1.4)	
Mexican American	7.7 (2.4)	6.8 (1.6)		5.9 (2.0)	6.7 (1.5)	
Other	13.9 (1.2)	10.9 (1.1)		8.5 (1.4)	10.9 (1.2)	
Educational attainment			<0.001			0.29
< High school	49.5 (2.7)	35.4 (2.4)		38.8 (3.0)	35.1 (2.9)	
Some college	25.7 (2.3)	31.3 (1.4)		31.7 (2.2)	31.0 (1.9)	
College graduate or above	24.8 (2.3)	33.3 (2.3)		29.5 (3.6)	33.9 (2.3)	
Physical activity, METs/week			<0.001			0.33
Tertile 1	40.9 (2.0)	29.5 (1.4)		29.7 (1.9)	29.2 (1.3)	
Tertile 2	32.1 (2.4)	32.0 (1.0)		36.7 (4.1)	31.7 (1.1)	
Tertile 3	27.0 (2.2)	38.5 (1.5)		33.6 (3.9)	39.1 (1.9)	
Ratio of family income to poverty, %			<0.001			0.20
<1.3	25.2 (2.4)	19.1 (2.7)		20.1 (2.7)	18.0 (2.8)	
1.3-3.5	43.8 (1.8)	32.8 (1.2)		37.8 (2.5)	33.7 (1.2)	
>3.5	31.0 (3.0)	48.0 (3.0)		42.1 (3.0)	48.2 (3.4)	
Smoking status, %			0.25			0.28
Never	51.8 (2.8)	53.7 (2.0)		50.1 (3.4)	53.6 (2.0)	
Past	33.8 (2.9)	28.2 (1.3)		28.6 (3.4)	29.4 (1.3)	
Current <10 cigarettes/day	8.1 (1.0)	9.7 (0.6)		10.3 (1.6)	9.1 (0.6)	
Current 10-20 cigarettes/day	2.0 (0.9)	2.0 (0.2)		3.0 (1.1)	1.9 (0.3)	
Current >20 cigarettes/day	4.3 (1.6)	6.4 (1.0)		8.0 (1.5)	6.0 (1.1)	
Alcohol consumption (drinks/day)			<0.001			0.07
Nondrinkers	49.4 (2.6)	31.4 (2.1)		31.2 (3.5)	32.2 (2.2)	
1-3 drinks/day	44.1 (2.3)	59.1 (2.3)		55.9 (3.5)	58.9 (2.4)	
≥4 drinks/day	6.5 (1.7)	9.5 (0.8)		12.9 (1.5)	8.9 (0.8)	
Depression symptom, %	10.0 (2.0)	9.1 (0.9)	0.59	7.7 (1.0)	9.0 (1.0)	0.31
Hypertension, %	63.9 (2.4)	46.4 (1.1)	<0.001	49.6 (2.3)	47.5 (1.5)	0.51
Obesity, %	37.9 (2.2)	40.3 (1.5)	0.36	42.7 (2.9)	39.7 (1.6)	0.31
Diabetes, %	21.2 (1.5)	14.8 (1.0)	<0.001	15.7 (2.3)	15.0 (1.0)	0.75
CVD, %	24.4 (2.0)	11.2 (0.7)	<0.001	12.7 (1.6)	12.3 (0.8)	0.79
Asthma, %	16.5 (2.0)	13.9 (0.8)	0.20	16.0 (2.1)	13.8 (0.7)	0.26
Cancer, %	23.9 (2.1)	14.8 (0.6)	<0.001	12.7 (1.9)	16.6 (1.0)	0.16
Pesticide use, %	18.1 (1.6)	18.4 (1.0)	0.90	16.3 (1.9)	18.6 (0.9)	0.26

Self-report taste problem, %	10.7 (1.6)	4.1 (0.4)	<0.001	3.8 (1.1)	4.7 (0.6)	0.55
Self-report smell problem, %	19.5 (2.2)	6.1 (0.9)	<0.001	8.9 (1.3)	7.8 (0.9)	0.36
Frequent nasal congestion, %	28.3 (2.0)	31.4 (0.9)	0.21	29.8 (2.8)	31.2 (1.0)	0.67
Head injury, %	15.0 (1.5)	16.7 (1.0)	0.25	17.4 (2.1)	16.9 (1.2)	0.84
Tonsillectomy, %	34.9 (3.2)	32.3 (1.3)	0.41	32.0 (2.8)	32.7 (1.3)	0.80
Broken nose or serious injury to face/skull, %	18.1 (1.6)	17.5 (1.4)	0.78	18.9 (2.4)	17.7 (1.4)	0.51

* Data are mean ± SE, or % (SE). BMI: body mass index; CVD: cardiovascular disease. There were 28 participants with missing values for BMI; 112-279 participants with missing values for hypertension, family income, pesticide use, and depression symptom; 2-7 participants with missing values for self-reported taste problem, self-reported smell problem, frequent nasal congestion, head injury, and broken nose or serious injury to face/skull.

Table 2. Demographic-adjusted Odds Ratios (OR) of Smell and Taste Impairment by Socioeconomic Characteristics, Lifestyle Factors, and Medical History*

	Smell impairment		Taste impairment	
Variable	OR (95% CI)	*P*	OR (95% CI)	*P*
Education level				
Low vs high	1.69 (1.30, 2.20)	<0.001	1.29 (1.00, 1.67)	0.05
Ratio of family income to poverty				
<1.3 vs >3.5	1.80 (1.35, 2.40)	<0.001	1.28 (0.84, 1.94)	0.25
Smoking status				
Past vs never	0.99 (0.78, 1.27)	0.96	1.11 (0.80, 1.56)	0.53
<10 cigarettes/day vs never	1.06 (0.75, 1.50)	0.76	1.12 (0.77, 1.65)	0.55
10-20 cigarettes/day vs never	1.36 (0.50, 3.68)	0.55	1.66 (0.70, 3.93)	0.25
>20 cigarettes/day vs never	1.00 (0.44, 2.28)	0.99	1.39 (0.99, 1.95)	0.06
Alcohol use				
1-3 drinks/day vs nondrinkers	0.58 (0.47, 0.71)	<0.001	0.83 (0.63, 1.10)	0.20
≥4 drinks/day vs nondrinkers	0.66 (0.33, 1.30)	0.23	1.22 (0.90, 1.65)	0.21
Physical activity				
Tertile 1 vs tertile 3	1.61 (1.27, 2.05)	<0.001	1.28 (0.90, 1.83)	0.17
Depression	1.17 (0.77, 1.79)	0.46	0.85 (0.62, 1.18)	0.34
Hypertension	1.31 (1.03, 1.67)	0.03	1.23 (0.95, 1.59)	0.13
Obesity	1.02 (0.80, 1.30)	0.87	1.10 (0.84, 1.44)	0.48
Diabetes	1.15 (0.91, 1.44)	0.24	1.15 (0.81, 1.62)	0.44
CVD	1.53 (1.16, 2.02)	0.003	1.19 (0.93, 1.52)	0.15
Asthma	1.36 (0.96, 1.91)	0.08	1.45 (1.05, 2.00)	0.03
Cancer	1.35 (1.02, 1.80)	0.04	0.80 (0.47, 1.37)	0.43
Pesticide use	0.87 (0.64, 1.17)	0.34	0.86 (0.65, 1.14)	0.30
Frequent nasal congestion	0.90 (0.71, 1.15)	0.40	0.95 (0.70, 1.27)	0.70
Head injury	0.99 (0.75, 1.31)	0.93	1.03 (0.72, 1.46)	0.88
Tonsillectomy	0.93 (0.66, 1.32)	0.69	1.05 (0.78, 1.43)	0.74
Broken nose or serious injury to face/skull	1.19 (0.89, 1.59)	0.25	1.08 (0.84, 1.39)	0.56

* Adjusted for age, sex, and race/ethnicity. CVD: cardiovascular disease.

Table 3. Backward Stepwise Logistic Regression Model for Smell and Taste Disorders

Variable	Smell impairment		Taste impairment	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (per 5-year increment)	1.37 (1.30, 1.45)	<0.001	0.93 (0.89, 0.97)	0.01
Sex		<0.001		
Women	1 (Reference)			
Men	1.68 (1.27, 2.22)		--	
Race/ethnicity		<0.001		
Non-Hispanic White	1 (Reference)		1 (Reference)	
Mexican American	1.68 (1.02, 2.76)		--	
Non-Hispanic Black	1.91 (1.36, 2.67)		1.46 (1.07, 1.99)	0.02
Ratio of family income to poverty		0.03		
<1.3vs >3.5	1.45 (1.04, 2.01)		--	
Education level		<0.001		
Low vs high	1.33 (1.17, 1.51)		--	
Alcohol use		<0.01		
1-3 drinks/day vs nondrinker	0.72 (0.58, 0.91)		--	
≥4 drinks/day vs nondrinker	--		1.42 (1.05, 1.93)	0.03
CVD	--		1.30 (1.02, 1.67)	0.04
Cancer	1.38 (1.05, 1.83)	0.02	--	
Asthma	1.39 (1.02, 1.89)	0.03	--	

-- Not included in the final model. OR: odds ratio; CVD: cardiovascular disease.

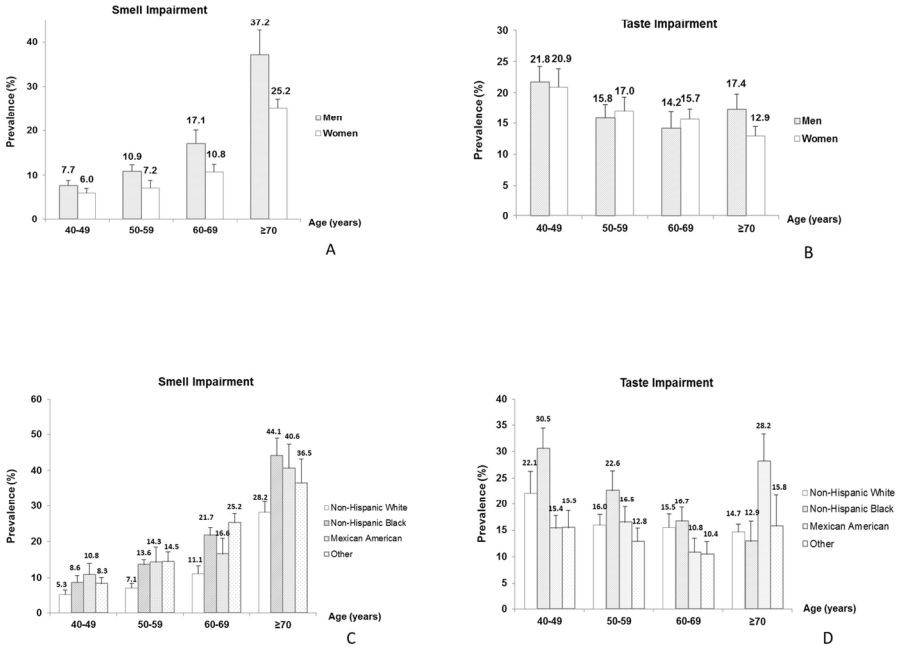

Figure 1. Prevalence of Smell and Taste Impairment According to Age, Sex, and Race/Ethnicity. A and B are the prevalence of smell and taste impairment in men and women according to each age group. C and D are the prevalence of smell and taste impairment in different ethnicities according to each age group.

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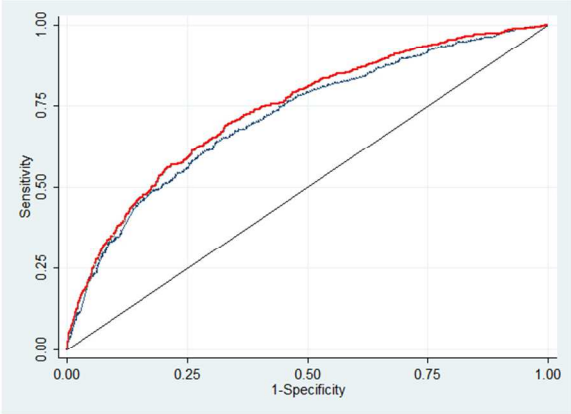


Figure 2. Receiver operating characteristic (ROC) curves showing the capacity of selected risk factors in predicting smell impairment in US men and women, National Health and Nutrition Examination Survey, 2013–2014. Blue curve is for the model adjusted for age, gender, and ethnicity. Red curve is for the model further adjusted for family income, educational attainment, alcohol consumption, and a history of asthma or cancer. The area under the ROC was 0.72 for blue curve and 0.74 for red curve.

90x90mm (300 x 300 DPI)

Supplementary Table 1. Comparison of prevalence of smell impairment between the UPSIT study and the current study in NHANES population

	Prevalence of Smell Impairment		
Age(years)	Total	Men	Women
Current Study (defined as <6 out of 8 odors)			
40-49	6.9%	7.7%	6.0%
50-59	9.0%	10.9%	7.2%
60-69	13.8%	17.1%	10.8%
70+	30.4%	37.2%	25.2%
UPSIT Study (defined as <29 out of 40 odors)			
40-49	3.0%	6.0%	0%
50-59	10.3%	15.9%	4.9%
60-69	17.1%	22.4%	13.1%
70+	33.5%	37.5%	30.1%

Supplementary Table 2. Comparisons of the prevalence of smell impairment and participants' characteristics across studies

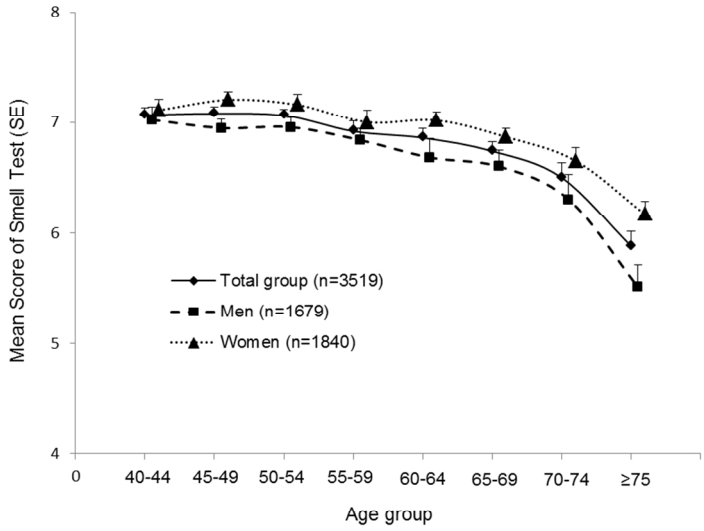
Studies	Sample size	Prevalence (%)	Definition	Age (years)*	Men (%)
Murphy C et al. (2002)[6]	2491	24.5%	<6 (8 odors)	68.7 (53-97)	42%
Mullol J et al. (2012)[7]	9348	19.4%	<4 (4 odors)	43.4 (5-91)	34.3%
Boesveldt S et al. (2011)[8]	2778	2.7%	<2 (5 odors)	69.3 (57-85)	48.4%
Bramerson A et al. (2004)[9]	1387	19.1%	<13 (16 odors)	20-80+	48.4%
Vennemann M et al. (2008)[12]	1312	18%	<10 (12 odors)	52.1 (25-75)	47.1%
Schubert CR et al. (2012)[14]	2838	3.8%	<6 (8 odors)	49 (21-84)	45.6%
Current study	3519	13.5%	<6 (8 odors)	57.8 (40+)	47.7%

* Mean (range)

Supplementary Figure 1. Mean (SE) NHANES Pocket Smell Test™ scores according to age and gender.

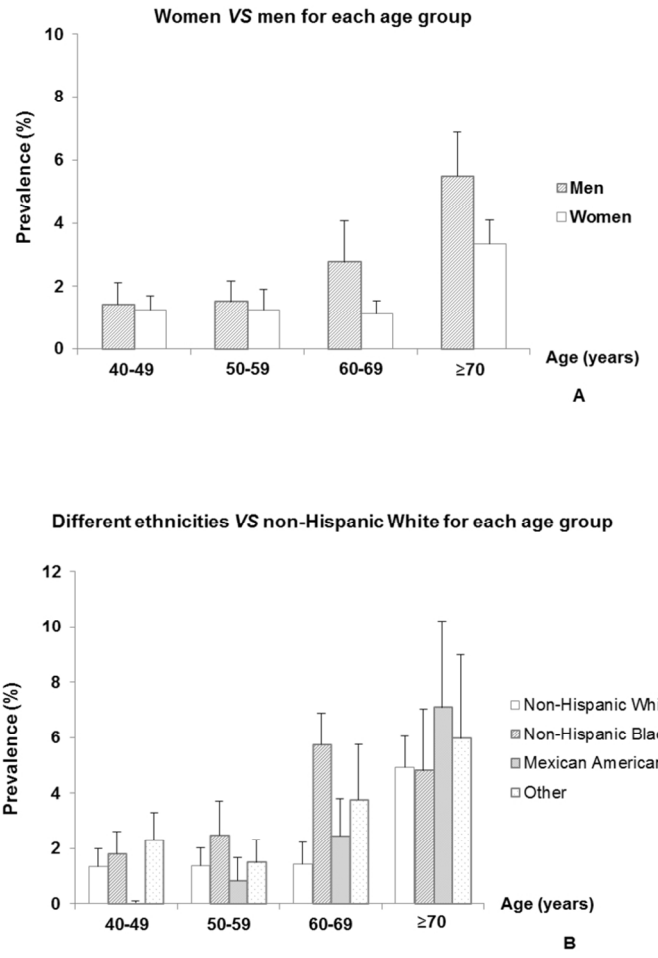
Supplementary Figure 2. Prevalence of Both Taste and Smell Impairment by Age, Sex, and Ethnicity. A is the prevalence of both smell and taste impairment in men and women according to each age group. B is the prevalence of both smell and taste impairment in different ethnicities according to each age group.

Supplementary Figure 3. Prevalence of Smell Impairment for Specific Odor



Supplementary Figure 1. Mean (SE) NHANES Pocket Smell TestTM scores according to age and gender.

101x90mm (300 x 300 DPI)



Supplementary Figure 2. Prevalence of Both Taste and Smell Impairment by Age, Sex, and Ethnicity. A is the prevalence of both smell and taste impairment in men and women according to each age group. B is the prevalence of both smell and taste impairment in different ethnicities according to each age group.

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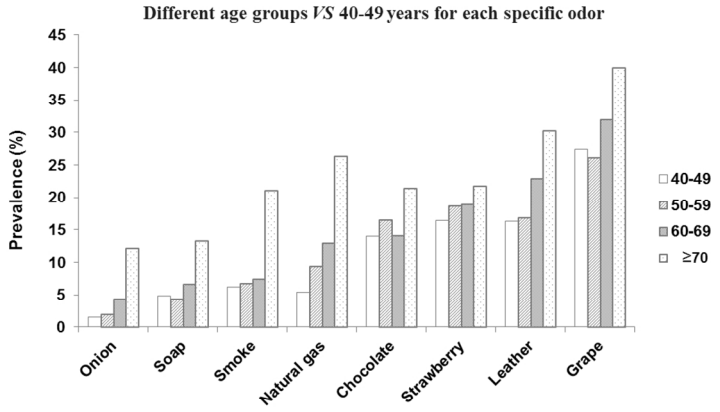

Supplementary Figure 3. Prevalence of Smell Impairment for Specific Odor

113x90mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Page 2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 5
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Page 5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	N/A
Bias	9	Describe any efforts to address potential sources of bias	Page 7
Study size	10	Explain how the study size was arrived at	Page 5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Page 9
		(*b*) Describe any methods used to examine subgroups and interactions	Page 13
		(*c*) Explain how missing data were addressed	Page 10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	Page 9
		(*e*) Describe any sensitivity analyses	

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N/A
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	N/A
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Page 10-12
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Page 12-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 19
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 20

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.