

# Associations between oral health and general health: a survey-wide association study of the NHANES

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**Objective:** This proof of concept study uses data from the National Health and Nutrition Examination Survey (NHANES) to explore potential associations between oral and systemic health in a survey-wide association study (SWAS). **Basic research design:** Data from n=9,971 records in the 2015-2016 NHANES survey were used to evaluate associations between self-rated oral health and the various systemic health conditions that are included in the survey. Associations were estimated using survey-weighted linear regression models adjusted for age, sex, race, and smoking status. **Results:** Substantial associations with self-rated oral health were evident after correction for multiple comparisons. The study revealed associations in categories of mental health, cardiovascular disease, and diabetes adding to the body of evidence. The study also suggested associations with physical functioning, vision, hearing, genitourinary symptoms, and the prevalence of hepatitis. **Conclusions:** The SWAS method demonstrated the ability to identify associations between oral health and systemic health. Suggested associations should be investigated further investigated with emphasis on both biologic and societal mechanisms. The noteworthy associations with mental health, physical activity, and cardiovascular disease in this study inform clinicians from each of these disciplines that they may benefit from collaborations with oral health care providers to promote whole-person health.

**Keywords:** NHANES; SWAS; oral health; general health; mental health

## Introduction

The well-established connections between oral health and general health are constantly growing in number and becoming more well-established (Dorfer *et al.*, 2017; Kane, 2017). Unfortunately, the divide between medicine and dentistry often presents a roadblock toward the identification of associations between oral and non-oral conditions through segregation of health care data. For example, as electronic medical record (EMR) studies become more frequent in the medical literature, similar dental studies of good quality lag behind because much documentation of dental history lies outside the hospital EMR. This segregation of data can lead to problems with data being missing not at random due to the fundamental differences between those who utilize hospitals and emergency departments as their main source of oral care (Sun *et al.*, 2015). This limitation in some EMR based studies can threaten the generalizability of findings beyond the hospital system they were conducted in.

Despite these logistic difficulties, studies have managed to demonstrate associations between oral health and cardiovascular disease (Beck *et al.*, 1996; DeStefano *et al.*, 1993), diabetes mellitus (Loe, 1993), mental health (O'Neil *et al.*, 2014; Park *et al.*, 2014) and other conditions outside the oral cavity. Though these started as mere associations, further studies have elucidated potential mechanistic connections which have been cited as evidence for the importance of oral care. For example, multiple investigators have reported that patients with periodontal disease have increased endothelial dysfunction and systemic inflammation providing a potential mechanistic

connection between oral health and cardiovascular disease (Amar *et al.*, 2003; Higashi *et al.*, 2008). Identifying these connections allows the field of dentistry to suggest new ways in which oral health might impact on patients' overall health and advocate for its importance.

To overcome the challenges of obtaining integrated data on oral and general health where both were collected systematically, it is vital that we use what data we do have in creative ways. This manuscript borrows methodology from the field of genetic epidemiology, and in particular from phenome-wide association studies (PheWAS) (Denny *et al.*, 2016). In a PheWAS study, the exposure of interest is a single nucleotide polymorphism (SNP), and the goal is large-scale evaluation of the EMR to identify associated disease phenotypes. This is accomplished by categorizing International Classification of Disease codes, Current Procedural Terminology codes, and other information in the EMR into validated clinical phenotypes. The investigator can then look for potential associations of the SNP with a wide range of conditions that may not have obvious mechanistic connections (Denny *et al.*, 2010).

This study uses data from the National Health and Nutrition Examination Survey (NHANES) and applies a PheWAS-type method. The exposure of interest in this case is self-reported oral health status as recorded on the NHANES oral health questionnaire, and the goal is to evaluate associations with various medical conditions recorded on the various other questionnaires. Similar to the PheWAS, this survey-wide association study will allow us to assess associations between self-reported oral health and a wide array of general health conditions.

## Methods

The NHANES is a cross-sectional study conducted every two years (Center for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS), 2018). Care is taken to ensure that the sample obtained for the study is representative of the national population with underrepresented classes being oversampled. Survey weights are then applied to the data to reach estimates representative of the population. The data was obtained from the NHANES website and includes data from the 2015-2016 questionnaires.

Conducting this type of study on survey data requires special attention toward the coding of survey results. For example, many of the items on the NHANES' questionnaires are coded in opposite directions with worse disease outcomes being given high values on some items and low values on others. For this study, all outcomes were recoded so that their direction was consistent such that positive associations are always represented by positive regression coefficients.

Analyses of the association between oral and general health items were conducted sequentially via a survey-weighted linear regression model adjusted for age, race, and smoking status utilizing the weights provided in the NHANES data set. Variables related to income and education were specifically omitted because oral health has been linked to problems at work, lower education and income meaning there could be partially causal pathways between oral health and the outcome that are mediated by income. Additional analyses were conducted which did adjust for socioeconomic variables. Education level is a categorical response from 1-5 representing: less than 9<sup>th</sup> grade, 9-12<sup>th</sup> grade with no diploma, high school graduate/GED, some college or AA degree, and college graduate or above respectively. Income was similarly categorical and was recoded to be a categorical variable ranging from 1-12 with the lowest group representing \$0-\$4,999/yr and the highest group represents >\$100,000/yr. These analyses must be interpreted with caution as they are almost certainly biased toward the null since these factors likely mediate the association of interest. For the sake of presentation, continuous outcomes with a high degree of variability like low-density lipoprotein (LDL) cholesterol, A1C level, and weight in pounds were standardized prior to analysis. In these analyses, the regression coefficients for binary items represent risk differences and for ordinal/continuous outcomes they represent the average change in the outcome per change in the exposure. At the completion of the analysis a Bonferroni correction was applied to account for multiple comparisons (Dunn, 1961). Although it is a very aggressive correction, it is presented here for consistency with the PheWAS literature where it is often employed. All analyses were conducted using R statistical software.

For the purposes of this study, the term self-rated oral health was used to represent NHANES question OHQ845: Rate the health of your teeth and gums, which is evaluated from Excellent to poor on the traditional 5 point Likert scale. Items were added for specific types of cancer grouped by thyroid, skin, sarcoma, lung, head and neck, hematologic, gynecologic, genitourinary, gastrointestinal, or breast.

## Results

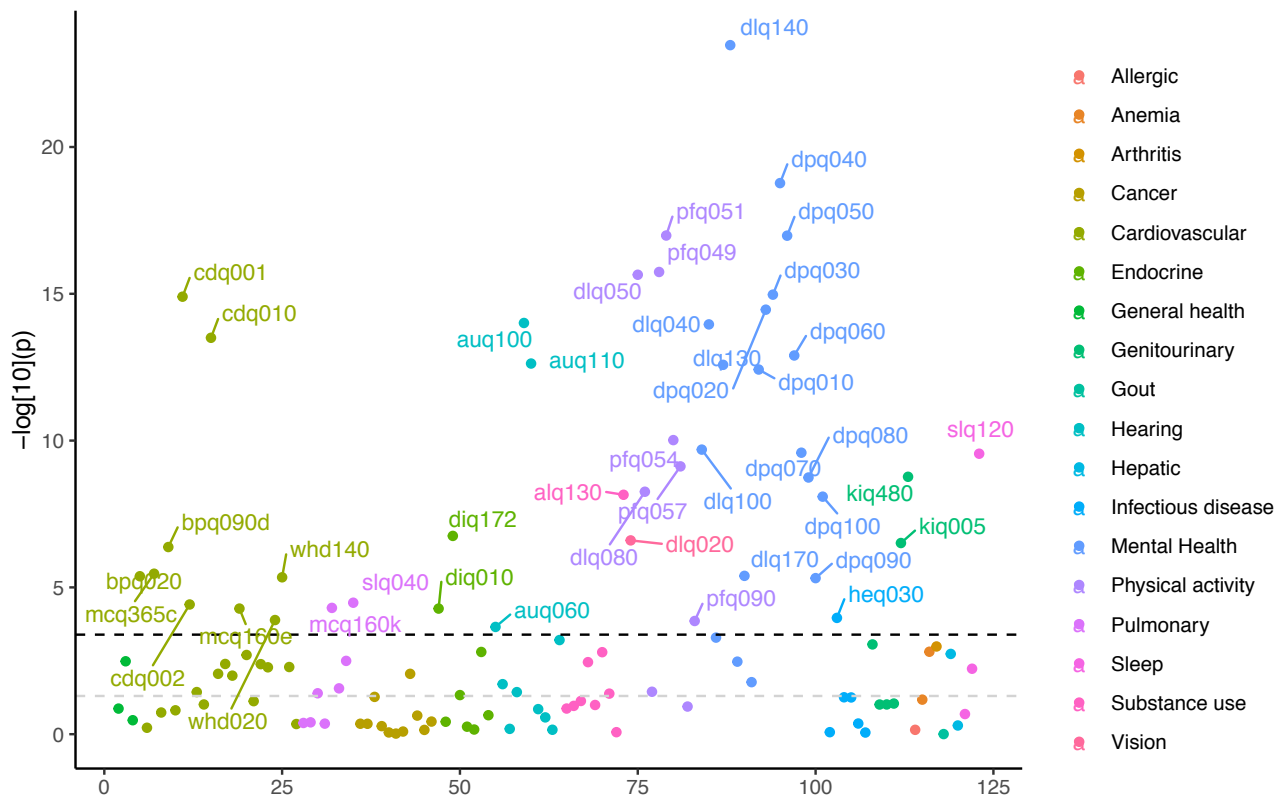
A total of 9,971 records were included in the 2015-2016 NHANES. Each analysis consists of the number of pairwise complete observations available for self-rated oral health and the given general health question. Sample sizes for individual comparisons ranged from 43 to 5976 with a median of 5690 (Interquartile Range (IQR): 3656, 5967). Demographics for the participants are summarized in Table 1 and are consistent with a nationally representative sampling. Most participants considered their oral health to be 'good' (31.30%, 95%CI: 29.95, 32.62). With only 23.42% (95% CI: 22.26, 24.58) describing their oral health as either 'fair' or 'poor.'

The outcome variables were grouped into disease categories by two independent reviewers with disputes resolved by consensus. The categories used were: general health (4 items), cardiovascular (23 items), pulmonary (8 items), cancer (11 items), endocrine (8 items), hearing (10 items), substance abuse (9 items), vision (1 item), physical activity (9 items), mental health (18 items), infectious disease (6 items), genitourinary (6 items), allergic (1 item), anemia (2 items), arthritis (1 item), gout (1 item), hepatic (2 items), and sleep disorder (3 items).

The analysis for associations with self-rated oral health resulted in 75 significant associations among the 123 items. After the Bonferroni correction, 45 of these comparisons retained statistical significance (Figure 1). Categories with significant associations included: cardiovascular disease (9 items: current weight, greatest weight, told by physician to reduce salt, ever told you had heart attack, shortness of breath on stairs, pain in chest, pain in chest while walking, ever told high blood pressure, take medication for high cholesterol), diabetes (2 items: told by MD you have diabetes, feel you may be at risk for diabetes), pulmonary (2 items: chronic bronchitis, snort/snore while sleeping), hearing (3 items: difficulty following conversation in noise, frustration hearing while talking, hear a whisper from across a quiet

**Table 1.** Characteristics of participants of the 2015-16 NHANES weighted to represent the national population

	%
Sex	
Male	48.84
Female	51.16
Race	
Mexican American	10.52
Other Hispanic	7.10
Non-Hispanic White	60.62
Non-Hispanic Black	11.94
Non-Hispanic Asian	5.59
Other Race	4.23
Self-Reported Oral Health	
Excellent	18.26
Very Good	26.73
Good	31.30
Fair	16.46
Poor	7.26



**Figure 1.** Manhattan plot showing associations between self-rated oral health and other systemic conditions. The black dashed line is the Bonferroni corrected significance bound whereas the light grey dashed line is the nominal significance bound.

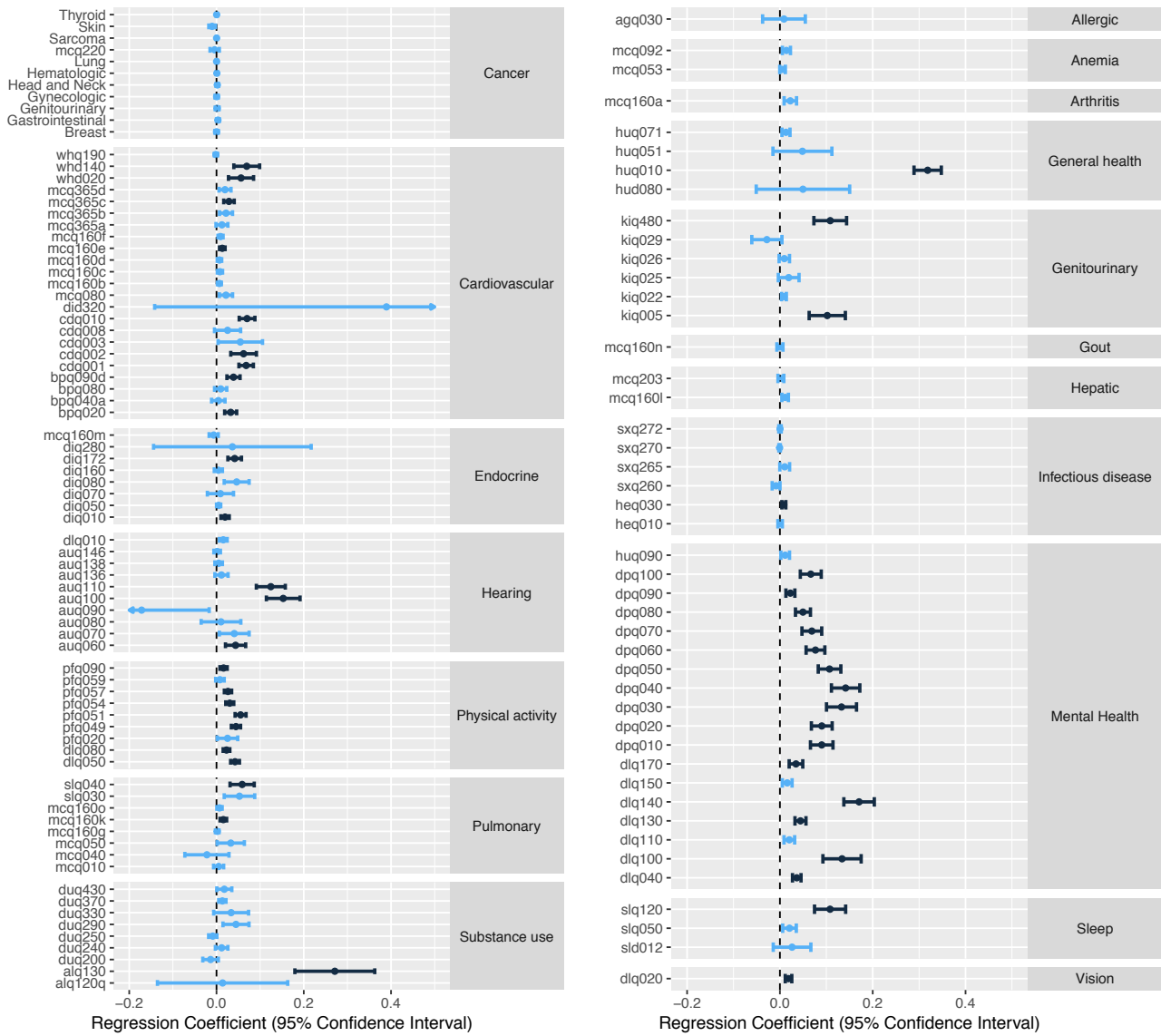
room), infectious disease (1 item: hepatitis C), mental health (15 items: little interest in doing things, feeling down/depressed/hopeless, trouble sleeping or too much sleeping, feeling tired, poor appetite or overeating, feeling bad about yourself, trouble concentrating, moving or speaking slowly or too fast, thought you would be better off dead, difficulty associated with these problems, how depressed you feel, how often you feel depressed, how worried or anxious you are, how often worried or anxious, and serious difficulty concentrating), physical functioning (7 items: require special healthcare equipment, confusion/memory problems, special equipment to walk, limited in amount of work you can do, limitations keep you from working, serious difficulty walking, difficulty doing errands alone), substance abuse (1 item: number of drinks/day in past 12mo), general health (1 item: rate general health condition), genitourinary (2 items: frequency, urinary leakage), sleep disturbances (1 item: how often you feel overly sleepy during the day), vision (1 item: serious difficulty seeing). Figure 2 shows the magnitude and that all the associations were positive.

Following this initial analysis, a secondary analysis was adjusted for household income and educational status. When these additional adjustments were performed 14 items were no longer significant (See supplementary table at [https://biostat.app.vumc.org/wiki/pub/Main/SmithTable2/Table\\_2.pdf](https://biostat.app.vumc.org/wiki/pub/Main/SmithTable2/Table_2.pdf)). Associations that lost significance were some items related to cardiovascular health, diabetes, disabilities, physical functioning, and several other single items. Generally, these were associations that were close to the significance cutoff before adjustment for socioeconomic factors that became marginally significant after their addition.

## Discussion

The NHANES data has shown a number of associations between self-reported oral health and general health conditions known to be impacted by oral health. This result serves as a proof of principle for the use of a survey-wide association study methodology. Using techniques from PheWAS, it was possible to identify associations we know exist, such as those between oral health and cardiovascular disease (Demmer and Desvarieux, 2006; Holmlund *et al.*, 2017; Meurman *et al.*, 2004), mental health (Hassel *et al.*, 2011; Okoro *et al.*, 2012), and diabetes (Lamster *et al.*, 2008). These findings demonstrate convergent validity of the method.

The most consistent associations were found between self-reported oral health and mental health, which is consistent with previously published findings (O'Neil *et al.*, 2014; Park *et al.*, 2014). Although this could partially be due to the number of items related to mental health, all 18 items that were categorized to mental health were significant at the  $p < 0.05$  level with 15 items maintaining their statistical significance after Bonferroni correction. Unravelling this association is difficult as it is difficult to tease out whether poor oral health contributes to things that have a negative impact on mental health, like poor body image, social isolation, and embarrassment or whether a person gets depressed and lapses on their self-care regimen resulting in poor oral health or perception thereof. Though more research is needed to substantiate this claim, it is likely that both of these mechanisms are correct which gives oral health care providers the opportunity to play a role in both the prevention and treatment of mental health related like



**Figure 2.** Forrest Plot of associations with self-rated oral health. Confidence intervals are unadjusted. Observations in black were significant after Bonferroni correction.

anxiety and depression. It is also possible that those with depression are also more pessimistic about their health generally, so that their self-perception is naturally lower.

There was also a consistent association between oral health and tiredness or fatigue. In particular, two items from the mental health questionnaire and one item from the sleep questionnaire (dpq030: Trouble sleeping or sleeping too much, dpq040: Feeling tired or having little energy, and slq120: How often do you feel overly sleepy during the day) were all highly significant with large estimated effect sizes. It is possible these are directly related to the potential association between mental health and oral health, but there are also many other reasons this association might exist such as sleep disturbances related to oral pain.

A number of less well-known associations were also identified. Some of these associations have a relatively straightforward explanation, i.e. physical functioning is likely related to obesity and cardiovascular health, which are positively correlated with oral health. In other cases, the reason for the potential association is unclear, including those between oral health and vision, hearing, genitourinary problems, and Hepatitis C. Some of these

relationships may have a biologic mechanism that is yet to be identified. Others likely have their roots in behavioral commonalities, effects of the health system and the social determinants of health. For example, areas where oral health providers are scarce may also be short of providers who might address vision and hearing problems in the community. Perhaps, there is some stigma related to Hepatitis C infection, which has been documented (Northrop, 2017; Temple-Smith *et al.*, 2006), leading people to be less willing to see an oral health provider. Both of these situations would lead to the population level associations identified in this study.

It is well-documented that poor oral health can result both in and from lower education and household income (Farmer *et al.*, 2016; Mejia *et al.*, 2018; Mitby *et al.*, 2003; Parsons *et al.*, 2012; Paulander *et al.*, 2003; Singh *et al.*, 2019; Smith and Murphy, 2019; Vano *et al.*, 2015). Therefore, these aspects of socioeconomic status operate as both a potential confounder of and a potential mediator of the association between oral health and general health conditions. Care must therefore be taken in interpreting the findings that lost significance after adjustment for these factors. It is possible that the initial



associations were spurious, but it is also very probable that they represent legitimate associations for which a portion of the impact of oral health was adjusted away in this analysis as the link between poor oral health and difficulties with employment are well established (Al-Sudani *et al.*, 2016; Hall *et al.*, 2013) and provide a plausible social mechanism for which both education and household income would be potential mediators.

This study lends additional evidence to the association between cardiovascular disease and oral health. Additionally, the items in the cardiovascular category that were significant represent a wide variety of conditions that fall under the cardiovascular umbrella including obesity, high cholesterol, hypertension, and angina. Each of these represents an opportunity to investigate potential reasons for this association. For example, it is possible that the same dietary behaviors that lead to obesity cause poor oral health. If this hypothetical proved true on further study, it would lend greater weight to population and individual level efforts to modify diets.

The strength of this study is the meticulous care taken in the administration of the NHANES study and the breadth of health topics covered. The care taken in sampling means that these results will be more generalizable than those coming from a single center EMR study, which is essentially a convenience sample. This study is limited by the self-report nature of the data. Although the NHANES also contains data from examinations, the number of well-defined disease phenotypes in the questionnaires allowed for a much broader comparison than would be possible using the provider-reported data. The self-report nature of the data may have led to under-reporting and biases especially as it relates to outcomes that may have stigma attached.

## Conclusions

This study demonstrated that a large variety of general health conditions are associated with oral health. Whether these associations represent a mechanistic connection (either via a biological or behavioral/social mechanism) and can therefore be targeted by preventative intervention will require further study. Regardless, these associations help identify comorbid conditions of people with poor self-rated oral health, and thus inform oral health practitioners of potential comorbidities their patients may present with. This information can be used by public health professionals to suggest what sort of medical professionals would be good partners for implementing public health initiatives. In the happiest of circumstances, these medical providers can be recruited to promote oral health within their practice and participate in oral health initiatives.

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