

PREVALENCE OF OTITIS MEDIA AND DENTAL CARIES IN
PALAUAN CHILDREN: EXPLORING THE ASSOCIATION
BETWEEN TWO COMMON CHILDHOOD DISORDERS

By

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CERTIFICATE OF APPROVAL

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List of Abbreviations

AIC	Akaike Information Criteria
AOM	Acute otitis media
BIC	Bayesian Information Criteria
CSOM	Chronic superlative otitis media
dft	Decayed-filled teeth index (primary dentition)
DMFT	Decayed-Missing-Filled teeth index (permanent dentition)
EH	Enamel hypoplasia
NB	Negative binomial
OM	Otitis media
OME	Otitis media with effusion
RSV	Respiratory syncytial virus
sd	Standard deviation
URI	Upper respiratory infections
ZINB	Zero-inflated negative binomial
ZIP	Zero-inflated Poisson

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*“Teach your child
something new everyday”*



*“Learning is the foundation
of life”*

Abstract

Background

Both otitis media (OM) and dental caries are of special concern as they relate to a child's quality of life and ability to grow and thrive. The etiologies for both tooth decay and OM are complex and multi-factorial with evidence that genetic, lifestyle, and environmental factors all play a role. Furthermore, the relationship between OM and dental caries remains unclear with mixed results from previous studies. Historically, both of these diseases have been highly prevalent in Palau, however, the current state of these conditions is largely unknown. This project aims to describe the current prevalence of each disease within the population, test the hypothesis that the two diseases are associated, and identify significant predictors for both primary and permanent dental caries.

Methods

The Ministry of Health's School Health Program Physical Examination Screenings began in the 2006-07 school year as a tool to identify health concerns and refer students for treatment to address these specific areas. Each year students in odd-numbered grades undergo this comprehensive health survey that includes measurements on ear health (tympanometry), oral health (count of decayed teeth), as well as several other physical, behavioral, and mental health assessment. In the 2011-2012 school year data were collected from 1232 students representing 35% of the total school enrollment. Using these data, we describe the prevalence of otitis media and dental caries, test if these two conditions are associated in primary and permanent dentition, and identify risk factors associated with dental caries.

Results

A total of 1053 students were included in this analysis. The average age of the students was 9.9 years and was evenly distributed between the sexes. Approximately three-quarters of students attend public schools. Over one-quarter of students (28%) had 'abnormal' (Type B or Type C) tympanometry results with 16.4% indicating active infections (Type B). Also, 85% of students experienced tooth decay. The distribution of decayed and filled teeth in the sample was substantial; while a significant proportion of the students remained caries-free, the total number of decayed teeth reached up to 20 in one student. Also, the burden of disease for both of these disorders was higher in public schools. Analysis revealed *age, school type, ethnicity, BMI, and nicotine use* were associated with caries experience in primary dentition while *age, school type, ethnicity, BMI, nicotine and alcohol use, and state of residence* were associated with permanent dentition. Tympanometry findings were not identified as significant predictors in either model.

Discussion

Both otitis media and dental caries are highly prevalent in this population. In fact, Palau ranks among the populations with highest prevalence of otitis media in the world. Although these School Health surveys function as an excellent surveillance tool for child health in Palau, several limitations to the design limit the strength of evidence with which to test the hypothesized association between OM and dental caries. Even so, we found that the burden of both diseases were disproportionately high in public compared with private schools. A school-based intervention designed to improve general hygiene may be an effective intervention for targeting both conditions.

Background

Introduction

The term “childhood diseases” may first bring to mind pneumonia, malaria, and diarrhea—some of the leading causes of death to children under five worldwide. More recently, “lifestyle” diseases—including chronic disease such as obesity—have started to take center stage. While middle ear infections (otitis media, OM) and dental caries are not leading causes of mortality in children, both diseases are highly prevalent around the globe. Preventable for the most part, both OM and dental caries have a significant impact in terms of human and economic costs (Cripps et al, 2005) which are often exacerbated by social conditions.

Although relatively rare, mortality caused by OM or dental caries is not unheard of. Severe and untreated infections in the ears and mouth may create abscesses which spread bacteria to the brain (Kagihara et al, 2009; Monasta et al, 2012). More often, the substantial burden associated with these diseases is cited as having significant impacts on quality of life. For example, the World Health Organization (WHO) estimates that of the 65-330 million individuals that suffer from chronic OM worldwide, 50% will also suffer hearing impairment—a substantial component to quality of life (Acuin, 2004; Monasta, 2012).

Pain and discomfort is associated with both acute otitis media and active caries. Effusions associated with middle ear infections impair hearing and affects communication and language development, psychological and cognitive development, as well as educational progress and achievement (Monasta et al, 2012; Acuin, 2004). Pain associated with dental caries, problems with eating, chewing, and smiling significantly impact a child’s social, mental, and physical development (Schroth et al, 2009). Thus, both diseases restrict activities at school

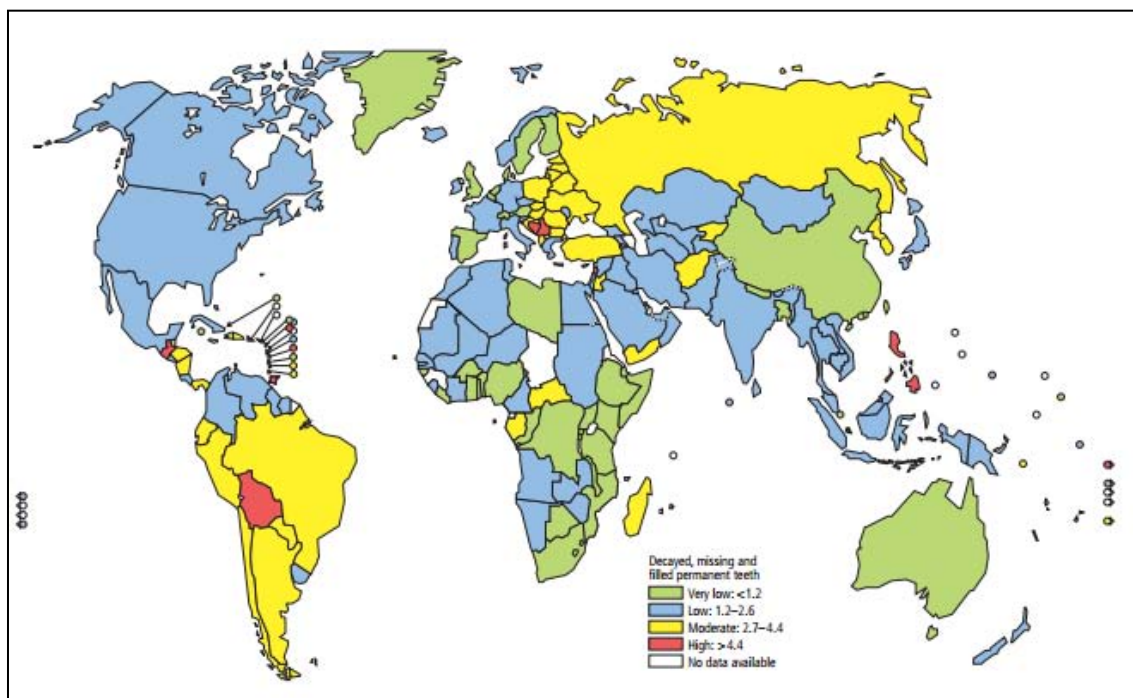
causing millions of school-hours to be lost each year throughout the world (Petersen et al, 2005). Moreover, these developmental disruptions in childhood may last into adulthood, leading to disability affecting educational and career achievement, and social interaction. In the paper 'Otitis media and its consequences: beyond the earache' an international panel of experts on middle ear and pediatric infections discuss the impacts of OM on the population level (Vergison et al, 2010). OM is the leading cause of antibiotic prescriptions in developed countries (Vergison et al, 2010; Gould & Matz, 2010). As such, this disease is directly impacting the global rise of antibiotic-resistant bacteria (Uhari et al, 1998; Vergison et al, 2010; Monasta et al, 2012). It's been estimated in the United States that infants and toddlers spend an average of 42 days on antibiotics in their first year of life, and 49 days in the second year (Paradise et al, 1997; Vergison et al, 2010). Clearly, OM is more than "just an earache" and at the same time oral health is more than "just having good teeth".

Dental caries

Dental caries (also called "cavities" or dental decay) is the most common preventable childhood disease worldwide (Selwitz et al, 2007) and is considered the fourth most expensive disease to treat among industrialized nations (Petersen et al, 2005). Prevalence estimates vary widely between and even within countries. Despite great improvements in oral health in several countries over the past decades (e.g., Scandinavia), the burden of oral disease is particularly high for disadvantaged and poor population groups in both developing and developed countries alike (Petersen et al, 2005). For this reason, prevalence estimates for dental caries in school-aged children range from 60% to 90% in industrialized nations (Petersen et al, 2005). In 1979, the WHO took a large step in combating oral disease by setting a global goal of less than 3

decayed, missing and filled teeth (DMFT) among 12-year-olds by the year 2000 (Petersen, 2003) and establishing the Oral Health Data Bank to monitor the progress of individual nations in realizing this goal. Figure 1 presents the status of oral health, as represented by categories of the DMFT index among 12 year olds, in countries around the world in 2004. Although the WHO goal has been met at the global level—in 2011, the global DMFT was estimated at 1.67 (Malmo University, 2013)—oral health disparities clearly exist around the globe.

Figure 1. Global estimates of oral disease as measured by average decayed-missing-filled teeth (DMFT) index in 12-year-olds (Petersen et al, 2005).



Global estimates range from *Very low* (<1.2 DMFT, nations in green), *Low* (1.2-2.6 DMFT, nations in blue), *Moderate* (2.7-4.4 DMFT, nations in yellow), and *High* (>4.4 DMFT, nations in red). Nations for which no data was available are indicated by white.

Historically, the prevalence of caries was low in most developing countries but has increased in recent years (Petersen et al, 2005). This is generally attributed to increased

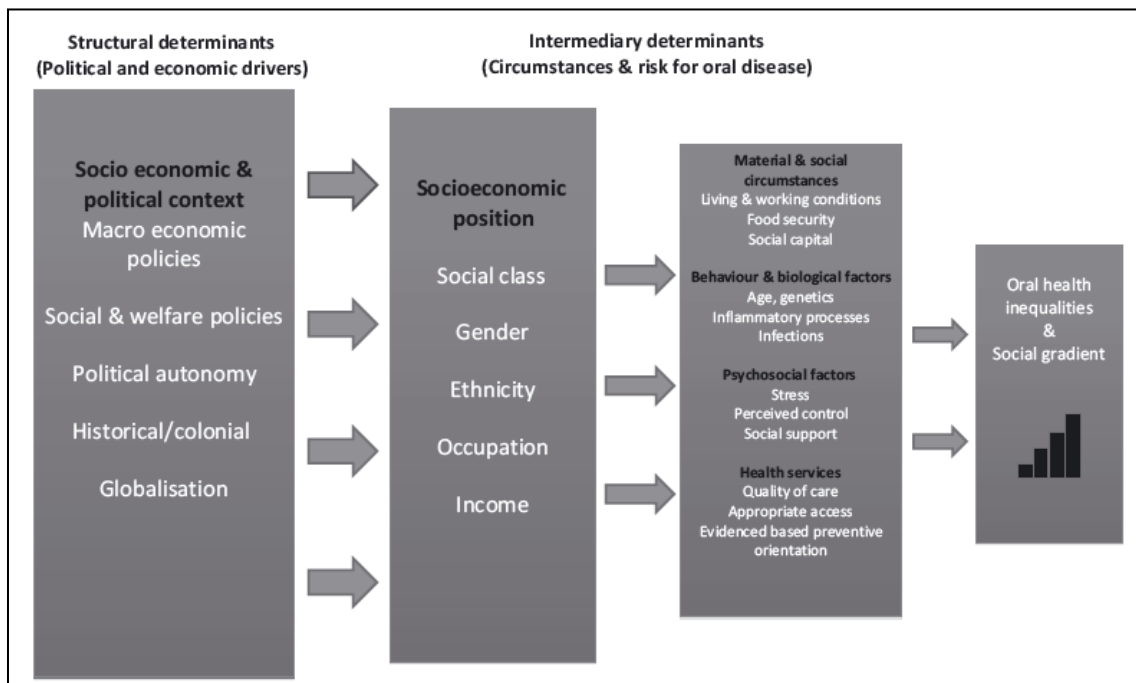
availability and consumption of sugars on a global scale. The process of caries formation—the demineralization of hard dental tissues—is counter-balanced by re-mineralization activity, typically achieved with adequate exposure to fluoride. Higher income countries tend to have high access to both sugar and fluoride (and other preventive services). Low income countries have access to neither (Figure 1 displays low caries burden in many of the African and Asian nations). However, it is in middle income countries where these processes—cariogenic behaviors and preventive services—are thrown out of balance and high caries rates are observed (Kagihara et al, 2009).

Dental cavities are formed by demineralization of hard dental tissues (in both the crown and root) caused by acid produced by bacterial fermentation (Selwitz et al, 2007). This process begins within the bacterial biofilm (dental plaque) which covers a tooth surface and is fueled by dietary carbohydrates. The most common bacteria responsible for this process are *Streptococcus mutans*, *Streptococcus sobrinus*, and *Lactobacillus* spp (Selwitz et al, 2007). Cariogenesis—the process of cavity formation—is further modified by salivary flow and composition, consumption of dietary sugars, hygiene practices, and exposure to fluoride. Considering these factors, cavity formation progresses relatively slowly in most people and then experience further decline with age (Selwitz et al, 2007).

The persistence of this condition, however, can be attributed to biological, environmental, and lifestyle-related factors. Since many of these factors may change over time, a person’s risk of developing carious teeth can also vary. Early childhood caries is often attributed to inappropriate methods of feeding infants (e.g., prolonged use of bottle or training cups with sugar-containing drinks); poor oral hygiene; poor nutrition; insufficient exposure to fluoride; and poverty (Selwitz et al, 2007; Irvine et al, 2011). Biological and genetic factors

which also play a role in cariogenesis include salivary flow; oral bacterial levels; and individual immunological response (Selwitz et al, 2007). Dental decay in the primary teeth is a significant predictor of future decay in permanent teeth in later childhood and adolescence (O’Sullivan & Tinanoff, 1996; Kagihara et al, 2009). Likewise, alcohol, tobacco use (smoking and chewing), and stress are also more likely to contribute to cariogenesis in permanent teeth. A more complete list of risk factors for dental caries is summarized in Figure 2 (below) and Table 1.

Figure 2. Conceptual model of social determinants leading to oral health inequalities.



Conceptual model for understanding social determinants of oral health inequalities developed by Watt & Sheiham (2012).

Table 1. Comparison of common risk factors for dental caries and otitis media

Risk factors for dental caries		Risk factors for otitis media
Low socioeconomic status; No dental insurance coverage; household crowding and/or large family size; Active caries present in mother.	Social	Low socioeconomic status; Day-care attendance; Lack of medical care access.
Poor general hygiene; Poor dietary habits; Certain infant feeding practices; Smoking status.	Behavioral	Certain infant feeding practices (e.g., bottle propping or breast feeding for less than 3 months); Pacifier use.
Inadequate salivary flow (and composition); High levels of cariogenic bacteria; Gingival recession; Immunological components; Need for special health care; Family history; Visible plaque; Enamel hypoplasia.	Biological	Age; Sex; Race and ethnicity; Host response; Atopy; Chronic sinusitis; ciliary dysfunction; Cleft palate and/or craniofacial abnormalities; Down syndrome; Immunocompromising conditions; Family history; Asthma.
Insufficient fluoride exposure.	Environmental	Season; Tobacco smoke and other air pollution.

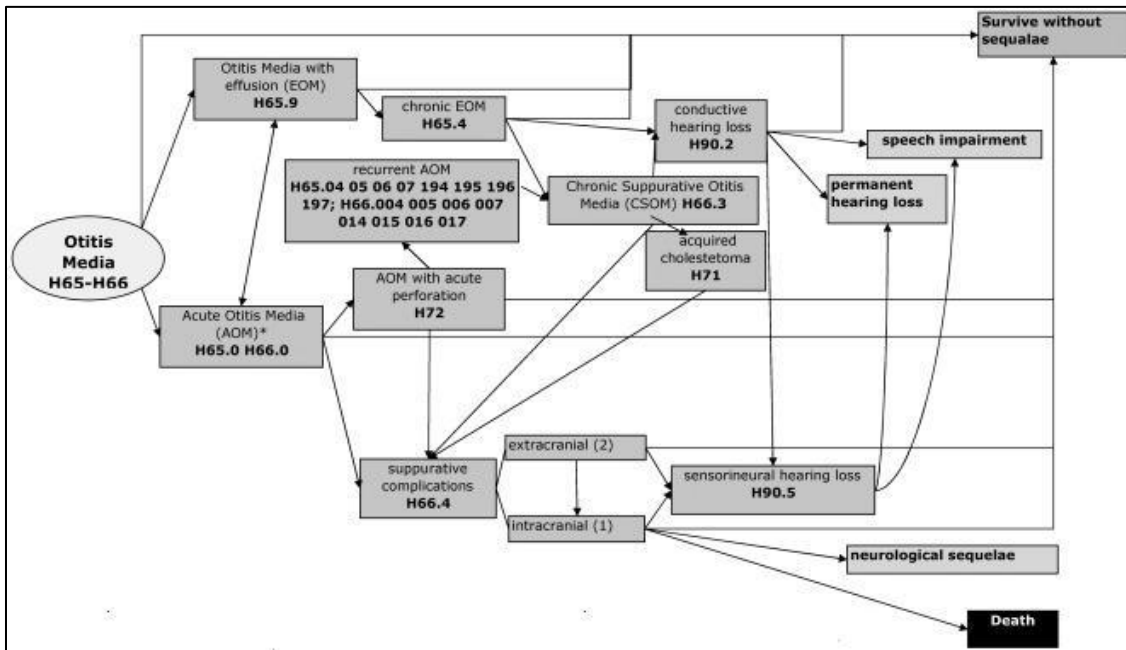
Sources: Selwitz et al, 2007; Irvine et al, 2011; Kagihara et al, 2009; Chan et al, 1993; Gould & Matz, 2010; Cunningham et al, 2012).

Otitis media

Otitis media is an umbrella term which covers all inflammations of the middle ear. OM can be broadly dichotomized into otitis media with effusion and acute otitis media (AOM). As illustrated in Figure 3, one challenge in reporting precise prevalence estimates of OM lays in the frequent overlap of conditions and subsequent difficulties in accurate diagnosis. In the United States, it is estimated that by a child’s third birthday 80% will have experienced at least one episode of AOM (Teele et al, 1989; Vergison et al, 2010; Monasta et al, 2012). Another report from the WHO states that over 90% of the burden of OM (specifically chronic suppurative otitis media) is found in countries in Southeast Asia and Western Pacific, Africa, and other ethnic groups of the Pacific Rim (Acuin, 2004). For instance, a 2012 systematic review found AOM

incidence rates for children under 5 to be highest in sub-Saharan Africa and Oceania with children in these areas having an average of more than one episode of AOM in a given one year period (Monasta et al, 2012). Despite the variation in estimates and definitions, middle ear infections remain common in many parts of the world with the highest burden falling on social and economically disadvantaged groups.

Figure 3. Sequelae of otitis media with ICD-1—CM diagnosis codes (Monasta et al, 2012).



Normally, the middle ear space maintains a slightly negative air pressure relative to the outside environment which is periodically relieved by opening the Eustachian tube during yawning and chewing (Gould & Matz, 2010; Cunningham et al, 2012). Therefore, this negative pressure is directly dependent on the functioning of the Eustachian tube and if the tube is impaired, excessive negative pressure may build. A higher relative negative pressure increases the likelihood that nasopharyngeal contents will reflux into the middle ear space during

transient openings of the Eustachian tube. Additionally, increased negative pressure in the middle ear can cause increased vascular permeability and can lead to development of effusion (Gould & Matz, 2010).

Eustachian tube dysfunction occurs in 75% of children who have viral upper respiratory infections (URIs; Gould & Matz, 2010), leading to impaired drainage of the middle ear and promoting the growth of bacterial and viruses which are causes of otitis media. The bacterial pathogens most commonly identified include: *Streptococcus pneumoniae*, non-typeable *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pyogenes*, and—less commonly—*Staphylococcus aureus* (Gould & Matz, 2010). Additionally, viruses such as influenza (A and B) and parainfluenza (types 1, 2, 3), and respiratory syncytial virus (RSV) may affect host immune response and facilitate bacterial colonization in the middle ear (Gould & Matz, 2010). Recurrent acute otitis media is estimated to occur up to 20% of children who develop AOM before age 3. It is not unusual for otitis media with effusion to persist beyond 3 months. Chronic OM, specifically chronic suppurative otitis media, is estimated to cause significant hearing loss in 60% of cases (Gould & Matz, 2010). Risk factors for OM include: child's age, family history, race, genetic factors, exposure to tobacco smoke and other air pollutants, allergies, breastfeeding history, and child care attendance (see Table 1, Page 6).

Hypothesized association

The etiologies for both tooth decay and OM are complex and multi-factorial with evidence that genetic, lifestyle, and environmental factors all play a role. In the mid-1990s, several studies in Finland proposed a connection between the two childhood diseases (Uhari et al, 1996; Uhari et al, 1998; Nelson et al 2005). This hypothesis was suggested by findings that xylitol chewing

gum—which has historically been used for the prevention of dental caries (Muehleemann et al, 1970; Makinen et al, 1995; Uhari et al, 1998)—reduced the incidence of AOM in pre-school age children (Uhari et al, 1996). Xylitol, a common sugar substitute, prevents dental caries by inhibiting the growth of *S mutans*. In these Finnish studies, researchers found that xylitol could also inhibit the growth of *S pneumonia* (Knuuttila & Makinen, 1975; Vadeboncoeur et al, 1983; Kantiokari et al, 1995).

Since then, two additional studies attempted to establish an association between OM and dental caries but have produced mixed results. The first was a case-control study which found no difference in ear infection history (past year and lifetime history) between 71 children experiencing dental caries (defined as $dmft \geq 1$) and 55 that were caries-free ($dmft=0$; Nelson et al, 2005). However, they did find a trend toward significance ($p=0.07$) for the mean number of ear infections to be higher in the dental caries versus caries-free groups.

The second study—a retrospective cohort study using a database of Medicaid records—demonstrated an association between OM and dental caries (Alaki et al, 2008). With over 30,000 records, clinical visits (claims) were made within the first year of life by 49% and 69% of children for AOM and respiratory infection, respectively. These children were at a 29% higher risk (hazard ratio=1.29, $p<0.001$) for developing caries after the first year of life compared to those with no claims. However, when evaluated individually, children with OM-claims were only at 11% higher risk (HR=1.11, $p=0.05$) while children with claims for respiratory tract infections were 34% higher risk (HR=1.34, $p<0.001$) for developing caries after that first year of life.

Evidently, the association between these two childhood disorders remains unclear. Fueling this uncertainty is the small body of evidence investigating the connection as well as the

uncertainty behind the mechanisms possibly connecting the two diseases. However, at least two biological hypotheses have been proposed to explain this relationship:

Biological hypothesis 1: *Otitis media causes the development of dental caries.*

Many childhood medical problems, including infections such as OM, have been linked to a condition known as enamel hypoplasia (EH; Pascoe & Seow, 1994) which results from a disruption in enamel formation (Alaki et al, 2008). Dental enamel is the hardest substance in the body however the specialized cells that form enamel—ameloblasts—are very sensitive to insults. Since dental caries are lesions in the enamel, any disruption in ameloblast activity leaves a child more susceptible to enamel erosion.

This phenomenon has been observed at the population level, especially among indigenous groups. For example, the prevalence of EH among indigenous children in Guatemala is approximately 73%. These children also experience nearly twice the prevalence of infectious diseases in early life than those without a history of EH (Infante & Gillespie, 1974; Alaki et al, 2008). Another study with Australian Aboriginal children found 99% of the population (ages 4 to 6) to suffer from EH (Pascoe & Seow, 1994). EH was also identified as a significant risk factor for dental caries ($\chi^2=92.1$, $p<0.01$).

Biological hypothesis 2: *Both otitis media and dental caries are caused by common risk factors and commonly co-morbid conditions.*

This hypothesis postulates that the two conditions are un-related biologically; however, both conditions are occurring co-morbidly due to common risk factors. For example, in young children, bottle use increases the colonization of *S mutans* and *S pneumonia*—the infectious agents responsible for OM and dental caries, respectively (Knuuttila & Makinen,

1975; Vadebonocoeur et al, 1983; Kontiokari et al, 1995). Common risk factors may also include personal hygiene and other factors related to general living conditions, among others (Table 1).

Republic of Palau—Context and rationale

The island nation of Palau serves as an interesting study setting as it sits at several “crossroads” defined by geography, culture, and economic development. Located in the Western Pacific, the nation gained independence in 1994 when it entered into a Compact of Free Association with the United States. The country spans several hundred islands, with only eight being permanently inhabited. The present population of Palau is approximately 21,000 and is primarily composed of ethnic Palauans and Filipino immigrants (The World Factbook, 2009). Before World War II, Palau was also colonized by Spain, Germany, and most significantly, Japan. Therefore, Palau experiences a unique mixture and influence of Eastern and Western cultures balanced with their own traditional native culture.

The Japanese occupation of Palau in the earlier part of the 19th century saw great economic development in Palau. This development has continued to increase during Palau’s association with the US. Today, the World Bank classifies Palau as being an “upper middle income” country with an estimated GDP of approximately \$165.5 million (World Bank). As a relatively young nation, Palau continues to “develop” in key areas of healthcare such as simple healthcare delivery (complicated by the geography of the nation) and health information systems (possibly due to a shortage in human resources; Cuboni et al, 2010; Dueler & Maskarinec, 2007).

Both OM and dental caries have previously been identified as being highly prevalent in Palau, however, these epidemiologic studies are few and far between. In 1985 as part of the 'Micronesia Otitis Media Training Project,' 16% of Head Start children and 10% of elementary school children were determined to have "active disease" (class 4-6 on the OM disease severity scale; Dever et al, 1990; Appendix, Table A1). There is one other report on ear health specific to Palau from 1993, but as a case-series study, was inadequately designed to make general conclusions about the state of ear health in the population (Chan et al, 1993). Although the specific burden of OM is not clearly established, anecdotally, the disease is regarded as one of the most common handicapping conditions among Palau's children (Dever et al, 1990).

Slightly better documented is the "silent epidemic" of dental caries—a term coined by former US Surgeon General Dr. David Satcher (Greer et al, 2003). In 2003, a comparative analysis of oral health in Palau, Hawai'i and Guam concluded dental caries were "excessively high" in the region (Greer et al, 2003). They also reported the age-weighted mean for decayed and filled primary teeth (dft) of children ages 5 to 9 to be 3.0 times the US national mean (Palau mean dft=5.56 vs US mean dft 1.88). Whether this "excess" is due to genetic or socioeconomic factors is unclear, however these factors appear to have an active role in both diseases.

This thesis research is not able to evaluate the causal mechanisms underlying these two diseases. However, data from the high quality survey of oral health and AOM status in a large sample of Palauan school children allows the characterization of prevalence and a cross-sectional evaluation of the co-occurrence of these conditions.

Specific Aims

1. Describe the current state of ear and oral health among children in Palau:
 - a. Determine the overall frequency of tympanometry results and stratified by predictors;
 - b. Determine the overall mean number of decayed teeth in primary and permanent dentition and stratified by predictors.
2. Test the association between dental caries in primary dentition and tympanometry results:
 - a. Select an appropriate generalized linear model based on the primary predictors;
 - b. Continue building a full model with predictors and potential confounders;
 - c. Perform analysis of deviance to determine if tympanometry results significantly improve final model;
 - d. Conclude whether or not dental caries in primary dentition and tympanometry results are significantly associated.
3. Test the association between dental caries in permanent dentition and tympanometry results:
 - a. Select an appropriate generalized linear model based on the primary predictors;
 - b. Continue building a full model with predictors and potential confounders;
 - c. Perform analysis of deviance to determine if tympanometry results significantly improve final model;
 - d. Conclude whether or not dental caries in permanent dentition and tympanometry results are significantly associated.

Methods

Data source

The Ministry of Health's School Health Program Physical Examination Screenings began in the 2006-07 school year as a tool to identify health concerns and refer students for treatment to address these specific areas. Our data sample is based on the 2nd edition of this screening tool (revised August 2010). Both physical and mental health is examined and data is collected on demographics, medical and family history, vital signs, body mass, vision, dental, hearing, substance use, and depression, among others. Each year, the screenings are conducted on the odd-numbered grades so that, in theory, the same students are captured every other year. This data is collected by a team of medical professionals from the Ministry of Health.

Study subjects

Screenings were conducted only on those students who returned a signed consent form. During the 2011-2012 screenings, no information was collected on students residing in Sonsorol or Hatohebei states, however the larger states and population centers in Palau were included. From an original sample of 1232 students from both elementary and high schools, we restricted our analysis to students between the ages of 5 and 15 years. Although this reduced the sample to 1094 students, this number is equivalent to 31% of the total school enrollment for that year, and arguably representative of the total population of youth, ages 5-15 years in the country of Palau.

Measurement and data collection

The following data were collected between August 16, 2011 and November 18, 2011.

Table 2. Biologic and analytic outcome variables of interest.

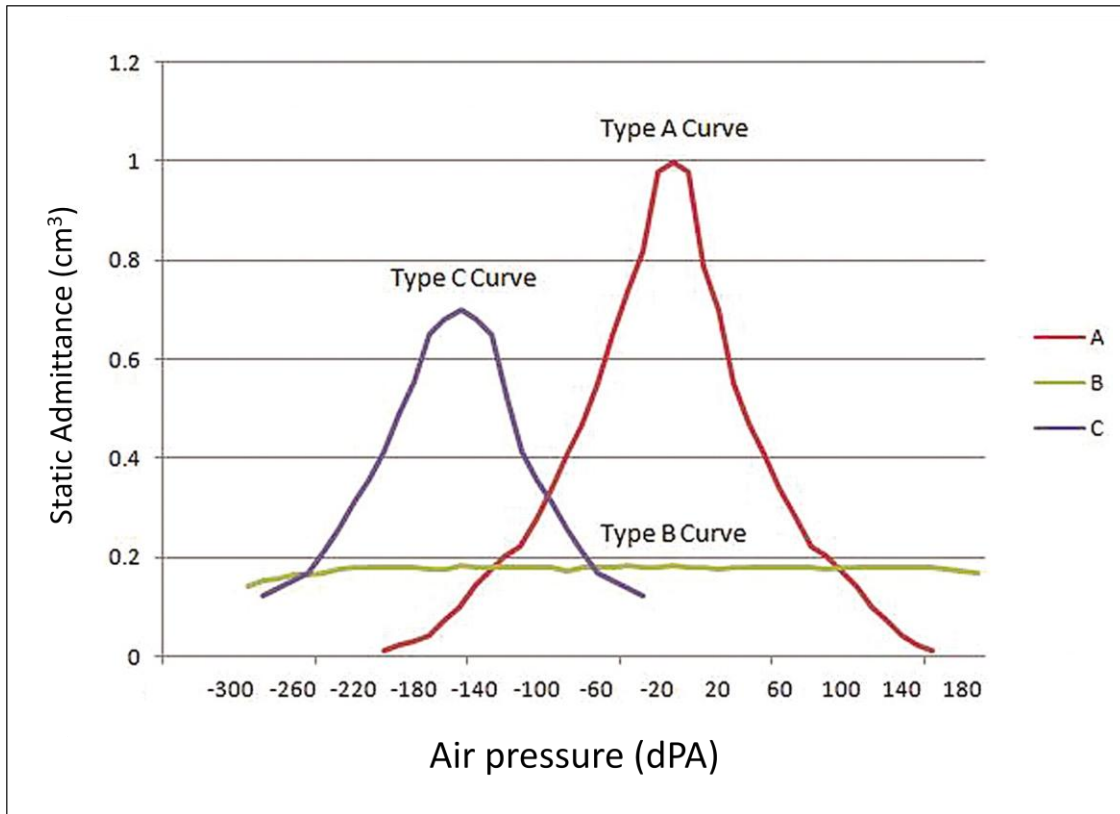
Measure	Type of variable	Possible response
Total caries	Discrete	0 to 32 ^a
Primary caries	Discrete	0 to 20
Permanent caries	Discrete	0 to 32
Tympanometry	Categorical	Type A; Type B; Type C
Tympanometry	Binary	Normal; Abnormal

Note: (a) These are theoretical upper limits. A full set of primary and permanent dentition include 20 and 32 teeth, respectively (Malmo University, 2013).

Dental nurses counted the number of decayed (treated and untreated) teeth in the mouth of each child and identified if the decay was in the primary or permanent dentition. Each tooth was exclusively healthy, decayed (“cariou”) or previously treated decay (“filled”) and recorded as a dichotomous healthy or decayed. From this, we created a *Total caries* variable which is simply the summation of all decayed teeth in each child. We also created two more variables which represent the total number of decayed primary teeth (*Primary caries*) and decayed permanent teeth (*Permanent caries*).

Specialists from the Ear, Nose, and Throat Clinic conducted tympanometry tests in each ear. Tympanometry is a non-invasive measurement of the condition of the middle ear—or specifically the mobility of the eardrum and conduction bones—using electroacoustics (Lous et al, 2012). The findings of this test are classified according to three types of curves, as presented in Figure 4.

Figure 4. Examples of common tympanometry curves (Gould et al, 2010).



This figure diagrams the three most common tympanometry curves. Type A curve indicates normal tympanic membrane compliance. Type B reflects low static admittance or poor compliance. Type C curves are shifted left on the graph indicating slightly higher negative pressure in the idle ear space (Gould & Matz, 2010).

Tympanometry has a high sensitivity and specificity in diagnosing middle ear effusions in children with a positive predictive value of 0.93 for effusion in the middle ear of a flat tympanogram (Type B) and a negative predictive value of 0.94 for a normal tympanogram (Type A; Palmu et al, 1999; Lous et al, 2012). Both Type B and Type C are considered “abnormal” results. We created an overall result (*Tympanometry*) based on the worse compliance in the two ears with Type A representing the best compliance, Type C representing moderate compliance, and Type B representing poor compliance. A second tympanometry (binary) variable differentiates between ‘normal’ and ‘abnormal’ results.

Table 3. Main predictor variables for analysis of otitis media and dental caries.

Measure	Type of variable	Possible response
Age (years)	Discrete	5 to 15
Sex	Binary	Male; Female
School type	Binary	Public; Private

We used age, sex, and school type as primary predictors for both OM and dental caries under the assumption that these three variables would explain the majority of disease. Previous studies in Palau found total caries burden (non-differentiated by primary and permanent dentition) to be significantly higher in younger age (Appanaitis et al, 2013). Furthermore, OM incidence is highest in early childhood (generally between 6 months and 2 years; Gould & Matz, 2010). Gender differences in tooth eruption and exfoliation rates may account for differences in caries prevalence (between primary and permanent dentition; Greer et al, 2003). School type was used as an indicator for socioeconomic status (Piovesan et al, 2011).

Table 4. Potential confounders considered in analysis.

Measure	Type of variable	Possible response
Ethnicity	Binary	Palauan; Other
BMI	Continuous	
Weight category	Ordinal	Underweight; Healthy weight; Overweight; Obese
Physical activity level	Ordinal	Light; Moderate; Vigorous
School location	Binary	Urban; Rural
State of residence	Nominal	1-14
Nicotine	Binary	Yes; No
Alcohol	Binary	Yes; No

Table 1 (*Background*) highlights the role of genetics in the etiologies of both OM and dental caries. Globally, OM is higher in certain populations. Previous epidemiologic studies have found the prevalence of chronic OM to be highest among Inuits (12-46%), Australian Aboriginals (12-25%), and Native Americans (4-8%) and South Pacific Islanders (4-6%; WHO, 1996). From these data, we believe that Palauans may share a similarly elevated prevalence of OM to their Pacific-rim neighbors. Due to the homogeneity of the population, though, ethnicity was dichotomized into Palauan versus “other” ethnicity. “Other” ethnicities may include Filipino and other Asians, other Micronesians, or other Pacific Islanders.

BMI was calculated based on weight and height measurements, and recorded as both a continuous and categorical variable based on the CDC’s categorization for children and teens. In the present analysis, BMI was used an indicator for other lifestyle factors such as diet and exercise. Categorical BMI was not used in regression analysis due to the nature in which it is

calculated and categorized, and subsequent difficulty with interpretations. Physical activity levels were self-reported by students as light, moderate, or vigorous. Substance use (i.e., nicotine or alcohol use) could be potential confounders for the older children.

Statistical analysis

Regression analysis for Specific Aim 2 and 3 began by selecting an appropriate generalized linear model. Since caries are discrete counts, we examined regression models in the Poisson family: Poisson (corrected for over-dispersion and zero-inflated) and negative binomial (also zero-inflated). For simplicity, these models were compared based on the three primary predictors. Following model selection, we used univariate analysis of independent variables to identify significant predictors ($p < 0.2$) for the “full candidate model”. Based on this “full candidate,” we removed variables with the highest significance levels, one at a time, until all variables within the full model achieved significance at the $p < 0.1$ level. Here we then added tympanometry into the model to test if this variable significantly improved the final model, specifically considering this set of related hypothesis:

H0: Tympanometry results do not significantly predict the mean number of dental caries.

H1: Tympanometry results significantly predict the mean number of dental caries in primary teeth.

H1: Tympanometry results significantly predict the mean number of dental caries in permanent teeth.

Significant predictors are based on Wald χ^2 statistics at the $p < 0.01$ level. Candidate models were compared using Nagelkerke (adjusted) R^2 statistics, Akaike Information Criteria (AIC), and Bayesian Information Criteria (BIC).

Human Subjects Protection

The project dataset was de-identified prior to data analysis. Permission to use these data was granted by Palau's Ministry of Health and with approval from Palau's Institutional Review Board (IRB). The statistical analysis protocol was also reviewed by the IRB of Oregon Health & Science University (IRB00009196).

Results

From the 1094 students age 5-15 years, 41 had missing data points. These students were removed from further analysis leaving our final sample at 1053 students. The mean age of students was 9.85 years and the sample was evenly distributed between male (50.7%) and female (49.3%) students. Nearly 60% of the students came from urban schools; this approximately equal to the number of students who reside in Koror (61.3%), the largest state in Palau. Three-quarters of students attended public schools. Both nicotine and alcohol use were significantly ($p < 0.001$) associated with age (OR=2.21 and OR=1.90, respectively) and each other (OR=90.05, $p < 0.001$).

Table 5. Population characteristics of children survey in 2011-2012 Physical Examination Screening (n=1053).

		Primary dentition			Permanent dentition			
		Mean decay, all students	Percentage of students decay-free	Mean decay, students with decay	Mean decay, all students	Percentage of students decay-free	Mean decay, students with decay	
Sex	Male	50.7%	2.40 (3.41)	49.6	4.76 (3.45)	2.45 (2.90)	33.2	3.66 (2.85)
	Females	49.3%	2.19 (3.21)	54.7	4.84 (3.14)	2.57 (2.89)	29.9	3.66 (2.81)
School type	Private	25.3%	1.39 (2.43)	63.5	3.82 (2.64)	1.94 (2.34)	40.2	3.25 (2.21)
	Public	74.7%	2.60 (3.51)	48.3	5.03 (3.41)	2.70 (3.04)	28.6	3.78 (2.97)
Ethnicity	Palauan	91.2%	2.34 (3.34)	51.8	4.86 (3.29)	2.58 (2.92)	29.9	3.68 (2.85)
	Other	8.8%	1.81 (3.05)	55.9	4.10 (3.43)	1.75 (2.44)	48.4	3.40 (2.44)
BMI (kg/m²)		19.57						

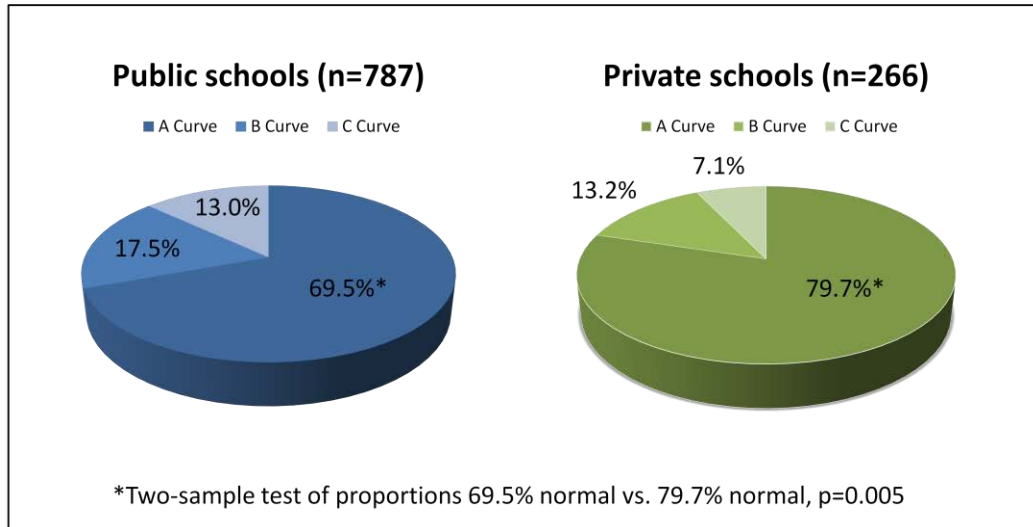
	(5.36)						
BMI (cat)							
Underweight	4.9%	3.23 (3.72)	40.4	5.42 (3.35)	2.77 (2.58)	25.0	3.69 (2.33)
Healthy weight	64.5%	2.53 (3.48)	48.9	4.96 (3.42)	2.57 (2.99)	31.4	3.75 (2.93)
Overweight	12.4%	1.80 (3.02)	59.2	4.42 (3.30)	2.11 (2.63)	36.9	3.34 (2.62)
Obese	18.2%	1.54 (2.53)	62.0	4.04 (2.60)	2.48 (2.80)	30.2	3.55 (2.72)
Physical Activity							
Light PA	13.0%	2.01 (3.07)	56.9	4.68 (3.06)	2.35 (2.72)	33.6	3.54 (2.63)
Moderate PA	73.3%	2.24 (3.27)	52.7	4.75 (3.28)	2.52 (2.92)	31.0	3.66 (2.87)
Vigorous PA	13.7%	2.84 (3.70)	44.4	5.11 (3.60)	2.56 (2.90)	32.6	3.80 (2.78)
School location							
Urban	59.5%	2.12 (3.08)	54.2	4.61 (3.03)	2.62 (2.93)	31.3	3.81 (2.83)
Rural	40.5%	2.56 (3.62)	49.2	5.04 (3.64)	2.34 (2.83)	31.9	3.44 (2.82)
Nicotine							
No	90.0%	2.49 (3.36)	48.0	4.80 (3.27)	2.39 (2.81)	33.1	3.58 (2.76)
Yes	10.0%	0.50 (2.11)	89.5	4.73 (4.92)	3.55 (3.37)	17.14	4.29 (3.25)
Alcohol							
No	96.9%	2.35 (3.34)	51.2	4.81 (3.31)	2.45 (2.83)	32.3	3.61 (2.76)
Yes	3.1%	0.67 (1.87)	81.8	3.67 (3.01)	4.39 (4.06)	9.1	4.83 (4.00)
Tympanometry							
Type A	72.1%	2.17 (3.22)	54.0	4.71 (3.24)	2.48 (2.93)	31.9	3.64 (2.89)
Type B	16.4%	2.77 (3.57)	45.1	5.05 (3.41)	2.42 (2.54)	31.8	3.54 (2.33)
Type C	11.5%	2.41 (3.49)	50.4	4.87 (3.56)	2.79 (3.14)	28.9	3.93 (3.06)

Note: Columns 3, 5, 6, and 8 present mean decay (standard deviation in parenthesis).

Description of tympanometry results

Approximately 72.0% of the students had a normal tympanometry finding (A Curve) while 28.0% had abnormal results (16.4% B Curve and 11.5% C Curve). Abnormal results ranged from 16% in the 15 year olds to 37% in the 7 year olds, with a significant (inverse) association between age and proportion of abnormal tympanometry results (OR=0.94, $p<0.01$). There were no significant differences in tympanometry results between the sexes (two-sample test of proportions: $z=0.00$, $p=1.0$), but differences were observed between school types. Among children who attend public schools, only 69.5% had normal tympanometry results while 79.7% of children attending private schools had normal results (two-sample test of proportions: $z=-2.82$ $p=0.005$; Figure 5 and Appendix for corresponding tables).

Figure 5. Tympanometry results of Palauan children by school type.



Description of dental caries

Caries experience—both treated and untreated decay—was identified in 84.7% of all students.

The mean number of primary and permanent teeth with caries experience is summarized in

Figure 6. A significant negative correlation was observed between total number of teeth with caries and student age ($\rho=-0.25$, $p<0.001$). There was no significant difference in total number of teeth with caries between male and female students in public school (5.47 vs 4.13; rank-sum test, $p=0.28$) nor in private school (3.06 vs 3.63; rank-sum test, $p=0.08$) settings. However, there was a significant difference between the same sexes in different school types; students in public schools had 1.5 times the mean number of teeth with caries than children in private schools. For example, the mean number of total teeth with caries for males in public schools was 5.47 (sd 4.13) but only 3.06 (sd 3.15) in private schools (rank-sum test, $p<0.001$). Also, the mean number of total teeth with caries for females in public schools was 5.13 (sd 3.98) compared to 3.63 (sd 3.07) in private schools (rank-sum test, $p<0.001$; Figure 7 and Appendix for corresponding tables).

Figure 6. Mean number of primary and permanent teeth with caries.

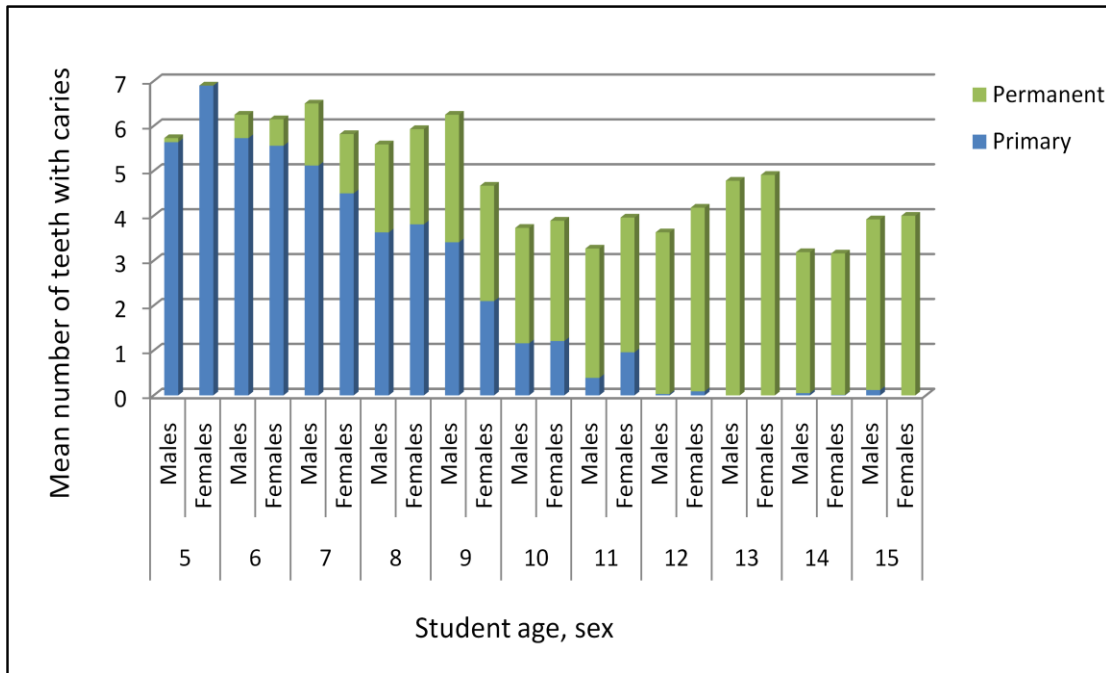
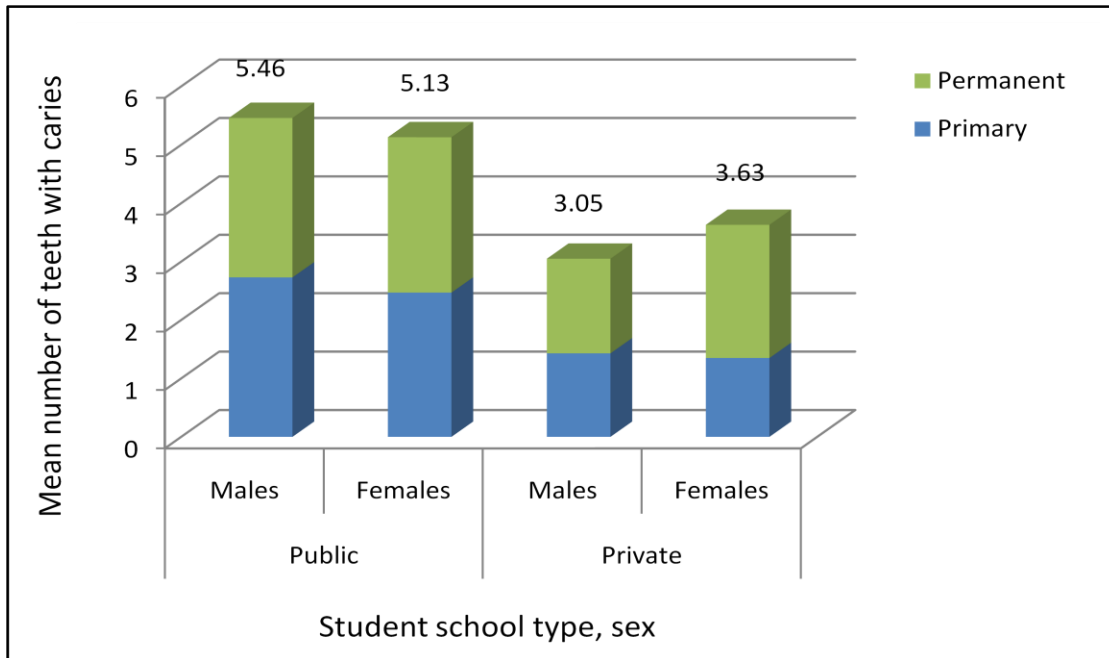


Figure 7. Distribution of caries burden in primary and permanent teeth by school type.



Analysis of caries in primary dentition

Generalized linear models (GLM) were explored to fit the data with primary caries as our outcome of interest (Table 6). GLM are appropriate for variables that stray from the normal distribution pattern. We expected the count of dental caries to follow a Poisson-like distribution. With the mean number of primary caries (in all students) to be 2.30 and a variance of 10.98, we saw evidence that the data was likely over-dispersed. A Poisson regression assumes that the conditional variance is equal to the conditional mean (Simonoff, 2003) so that the ratio of the variance to the mean is 1.

In order to select an appropriate model and continue with the analysis we tested several models in the Poisson family against our predictors *age*, *sex*, and *school type*. With the Poisson

model, the Pearson chi-square statistic (2194) exceeded the model degrees of freedom (df=1049), providing evidence of over-dispersion. Additionally, the Akaike Information Criterion (AIC) was 3880.07 for the Poisson model and can be used to assess adequacy of this model relative to other later choices. Computation of the AIC is such that lower numbers indicate a better model and is defined as:

$$AIC = -2\text{LogL} + 2v$$

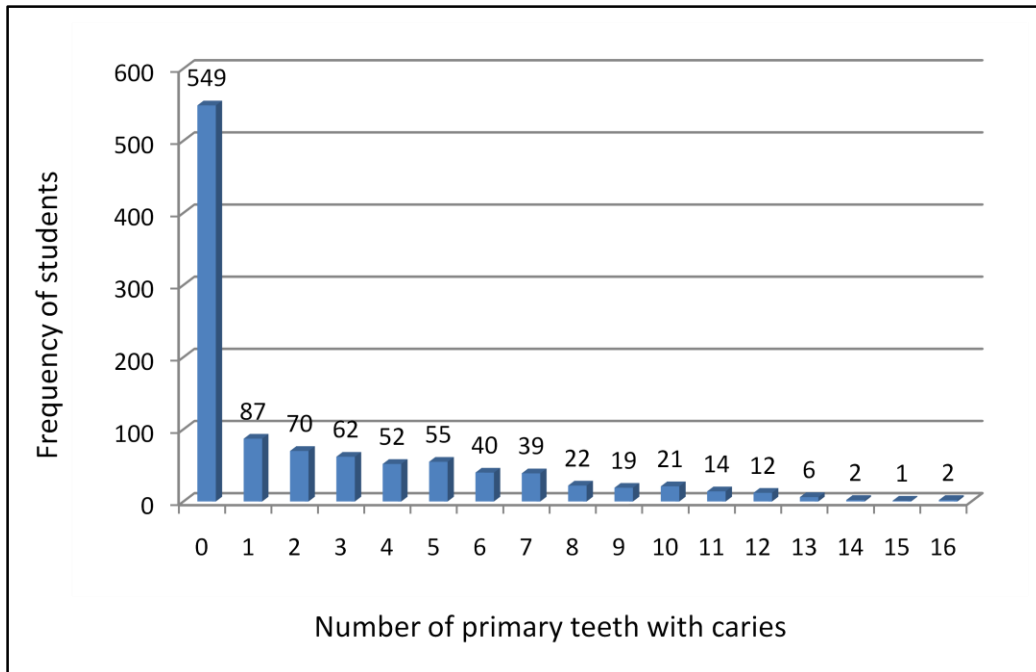
where 'LogL' is the log-likelihood function and 'v' is the number of estimated parameters in the model (Simonoff, 2003). AIC not only "rewards" goodness-of-fit for a given model but also considers (and "penalizes" for) the number of estimated parameters.

To correct for over-dispersion, residual variance was estimated by the Pearson chi-square statistic divided by residual degrees of freedom (~2.09) and standard errors for parameter estimates multiplied by the square root of this quantity (~1.44; McCullagh & Nelder, 1989). The negative binomial (NB) distribution is an alternative to the Poisson in that it directly allows for and incorporates the extra Poisson variation through an additional parameter (alpha) that must be estimated from the data. The AIC for the NB model was 3315.07, suggesting a better fit than the Poisson.

Also important to consider is the large proportion of the sample that were caries-free (primary caries=0 in 52.1% of the sample; Figure 8). This is explained by the large age range of the sample and the smaller window of age in which children have primary teeth. The Poisson model predicts that only 34.8% of the students would be caries-free in primary dentition, and the NB model does slightly better predicting 47.3% to be caries-free. To address the observed proportion of caries-free students being above either Poisson or NB model predictions, a zero-inflated Poisson model (ZIP) and zero-inflated negative binomial (ZINB) were also considered.

ZIP assumes that the data comes from a mixture of two populations; one where the count is always zero, and another where the count has a Poisson distribution with mean that changes as a function of the explanatory variables of interest. In this model, zero counts come from either population, while positive counts come only from the second one. The probability of a zero count originating from the first (static) population can also be modeled as depending on explanatory variables of interest. Therefore, the ZIP model yields two sets of estimates (Table 6). Similarly, the ZINB model has a conditional mean of the target identical to ZIP but uses a different function for the conditional variance (Simonoff, 2003).

Figure 8. Distribution of caries in primary teeth of Palauan school children (n=1053).



As a function of age, both ZIP and ZINB models accurately predict the proportion of students with no primary caries (52.2% and 52.1%, respectively) with similar odds of belonging to the caries-free group for each additional 1 year increase in age (OR=1.93 and OR=1.99,

respectively). ZINB, however, had a lower AIC and was selected as the best option to model our data. Additionally, a likelihood ratio test concerning the dispersion parameter found significant (LR $\chi^2_{df=1} = 87.04$, $p < 0.001$) evidence of over-dispersion, thereby giving further evidence in favor of the ZINB relative to the ZIP model. Taken together, we completed regression analysis for caries in primary teeth following the ZINB model.

Table 6. Comparison of generalized linear models relating caries in primary dentition with predictor variables.

β (se)	Poisson	Negative Binomial	Zero-inflated Poisson	Zero- inflated Neg Bin
age	-0.423 (0.01)	-0.53 (0.02)	-0.25 (0.01)	-0.27 (0.02)
sex	-0.07 (0.04)	-0.07 (0.08)	-0.01 (0.04)	-0.02 (0.06)
school type	0.45 (0.06)	0.45 (0.10)	0.33 (0.06)	0.37 (0.08)
constant	3.68 (0.15)	4.49 (0.27)	2.86 (0.16)	2.92 (0.23)
age^a			0.66 (0.04)	0.69 (0.06)
constant			-6.48 (0.43)	-6.91 (0.57)
Alpha (dispersion parameter)^b		0.78 (0.07)		0.19 (0.04)
Pr (0 caries age)	34.8%	47.3%	52.2%	52.1%
Log likelihood	-1936.04	-1652.54	-1612.04	-1568.52
Akaike Information Criterion (AIC)	3880.07	3315.07	3236.08	3151.03
Bayesian Information Criterion (BIC)	3899.91	3339.87	3265.83	3185.75

Notes: (a) Estimates of Pr(caries=0) as a function of age.

(b) Estimated variance = mean (1+alpha*mean).

ZINB models were inflated by age with the assumption that age explains the excess of zero counts. Univariate analysis was conducted to assess the individual influence of each predictor on primary caries (Appendix, Table A7). To minimize any type II error, significant predictors were identified at $\alpha < 0.2$ level. Following this criteria, age ($p < 0.001$), school type

($p < 0.001$), ethnicity ($p = 0.082$), BMI ($p < 0.001$), and school location ($p = 0.056$) were identified as significant predictors of primary caries in univariate analyses.

We began the process of building the final model by regressing caries in primary teeth on age, school type, ethnicity, BMI, and school location. From this model, containing all predictors that achieved $p < 0.20$ significance in univariate analysis, we eliminated variables that did not achieve a stricter $p < 0.10$ significance and tested the improvement based on a Wald test statistic. After eliminating school location based on this method, we tested several other variables in various models (Appendix, Table A12). Here, we found that nicotine significantly improved the final model (based on AIC and Naglekerke R-squared). With a final model including age, school type, ethnicity, BMI and nicotine use, we tested the hypothesis that tympanometry was a significant predictor of caries in primary teeth. Neither Type B nor Type C tympanometry findings were significant at the $p < 0.1$ level ($p = 0.865$ and $p = 0.934$, respectively). Based on these results the final prediction model for primary caries in Palauan children included the variables age, school type, ethnicity, BMI, and nicotine use (Table 7).

Table 7. Final zero-inflated negative binomial (ZINB)^a multivariate model^b relating mean number of caries in primary dentition in Palauan children.

Variable	β	95%CI	Multiplicative effect ^c	95% CI	p-value
Constant ^d	1.73	1.60, 1.90			
Age	-0.27	-0.31, -0.23	0.76	0.73, 0.79	<0.001
School type					0.001
Private	referent		1		
Public	0.28	0.12, 0.45	1.33	1.13, 1.56	
Ethnicity					0.028
Palauan	referent		1		
Other	-0.26	-0.48, -0.03	0.77	0.62, 0.97	
BMI (1 kg/m ²)	-0.03	-0.05, -0.02	0.97	0.95, 0.98	<0.001
Nicotine					0.023
No	referent		1		
Yes	0.47	0.07, 0.88	1.61	1.07, 2.41	

Notes: (a) Estimates of Pr(caries=0) inflated by age; estimated dispersion parameter =0.17 (95%CI:0.12, 0.25).

(b) AIC= 3129; BIC=3174; Nagelkerke (adjusted) R-square= 0.16.

(c) Multiplicative effect for a Poisson-like regression is the ratio of two means.

(d) Centered for a 6-year-old student with a BMI of 16 kg/ m².

Analysis of caries in permanent dentition

Here again we began with the model selection process for caries in permanent teeth with the primary predictors age, sex, and school type. The mean number of caries in permanent teeth in all 1053 students was found to be 2.51 with a variance of 8.39; again indicating over-dispersion. We compared the results from four generalized linear models in Table 8. Nearly one-third of our sample experienced no caries in permanent dentition (Figure 9) and both ZIP and ZINB had significant ($p < 0.0001$) Vuong tests compared to the Poisson and NB models, respectively, confirming excess proportions of 0 counts in the data (permanent dentition). Both ZIP and ZINB

models estimated similar proportions of students to be caries-free in permanent dentition (ZIP 31.4%, ZINB 29.8%) but differed substantially how this group was influenced by age. For instance, in the ZIP model the estimated odds of being caries-free decreased by just over 20% with each additional 1 year of age (OR=0.78) while the ZINB model estimated this effect to be closer to 90% (OR=0.11). Based on these results, ZINB was selected as the most appropriate model to continue with regression analysis.

Figure 9. Distribution of caries in permanent teeth of Palauan school children (n=1053).

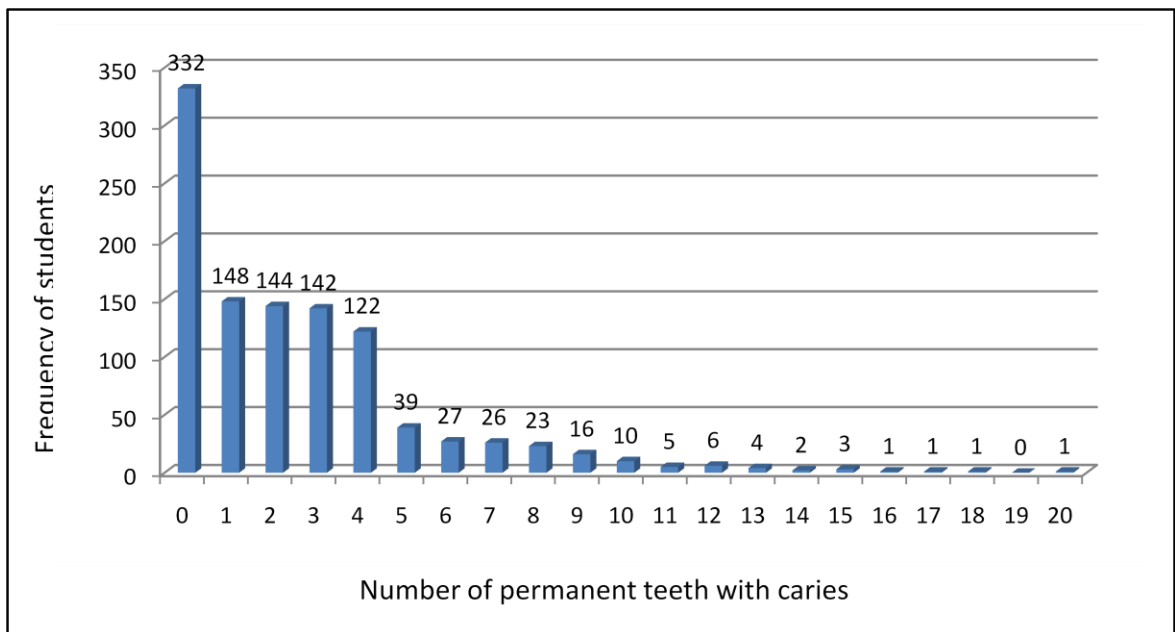


Table 8. Comparison of generalized linear models relating caries in permanent dentition with predictor variables.

β (se)	Poisson	Negative Binomial	Zero-inflated Poisson	Zero-inflated Neg Bin
age	0.17 (0.01)	0.19 (0.01)	0.12 (0.01)	0.13 (0.01)
sex	-0.002 (0.038)	0.02 (0.07)	-0.01 (0.04)	0.03 (0.06)
school type	0.48 (0.05)	0.48 (0.08)	0.33 (0.05)	0.46 (0.08)
constant	-1.70 (0.14)	-1.98 (0.23)	-0.27 (0.12)	-0.69 (0.18)
age^a			-0.25 (0.03)	-2.19 (0.54)
constant			1.41 (0.31)	13.40 (3.24)
Alpha (dispersion parameter)^b		0.68 (0.06)		0.54 (0.05)
Pr (0 caries age)	14.1%	27.90%	31.4%	29.8%
Log likelihood	-2400.28	-2092.43	-2182.17	-2044.90
Akaike Information Criterion (AIC)	4808.56	4194.87	4376.35	4103.80
Bayesian Information Criterion (BIC)	4828.39	4219.66	4406.10	4138.51

Notes: (a) Estimates of Pr(caries=0) as a function of age.

(b) Estimated variance = mean (1+alpha*mean).

Univariate analysis of each independent variable found age ($p < 0.001$), school type ($p < 0.001$), ethnicity ($p = 0.007$), school location ($p = 0.038$), state ($p < 0.001$) as well as both nicotine ($p = 0.030$) and alcohol use ($p = 0.0087$) to be significant predictors of permanent caries at the $\alpha < 0.2$ level (Appendix, Table A11). We began to build a final model by regressing caries in permanent teeth on these variables. After eliminating school location at the $p < 0.10$ level, we explored the addition of other variables of interest (Appendix, Table A12). Several of these models had relatively similar goodness-of-fit measures. A final model was selected based on goodness-of-fit as well as concordance with the model for caries in primary teeth and other known risk factors. This final model included age, school type, ethnicity, BMI, nicotine and alcohol use as well as state of residence. From this model we tested the significance of tympanometry in predicting permanent caries; neither of the tympanometry variables met the

$p < 0.1$ level of significance (Type A vs. Type B vs. Type C), $p = 0.381$; Normal vs. Abnormal, $p = 0.166$). The final model relating the mean number of caries in permanent teeth is summarized in Table 9.

Table 9. Final zero-inflated negative binomial (ZINB)^a multivariate model^b relating mean number of caries in permanent dentition of Palauan children.

Variable	β	95%CI	Multiplicative effect ^c	95% CI	p-value
Constant^d	0.08	-0.38, 0.54			
Age	0.14	0.11, 0.17	1.15	1.11, 1.18	<0.001
School type					<0.001
Private	referent		1		
Public	0.51	0.36, 0.66	1.66	1.43, 1.93	
Ethnicity					0.003
Palauan	referent		1		
Other	-0.35		0.70	0.56, 0.89	
BMI (1 kg/m²)	-0.01	-0.03, -0.003	0.99	0.97, 1.00	0.015
Nicotine					0.076
No	referent		1		
Yes	-0.19	-0.41, 0.02	0.82	0.66, 1.02	
Alcohol					0.041
No	referent		1		
Yes	0.34	0.01, 0.66	1.40	1.01, 1.94	
State					<0.001
1	referent		1		
2	0.49	0.02, 0.96	1.63	1.02, 2.60	
3	-1.86	-3.38, -0.34	0.16	0.03, 0.71	
4	-0.49	-1.70, 0.73	0.61	0.18, 2.07	
5	0.93	0.49, 1.37	2.54	1.63, 3.95	
6	0.04	-0.64, 0.71	1.04	0.53, 2.03	
7	0.65	0.10, 1.19	1.91	1.11, 3.29	
8	0.67	0.12, 1.22	1.95	1.13, 3.38	
9	0.80	0.15, 1.46	2.24	1.16, 4.29	
10	0.47	-0.08, 1.03	1.61	0.92, 2.81	
11	0.66	0.11, 1.22	1.94	1.12, 3.38	
12	-0.37	-1.01, 0.26	0.69	0.36, 1.29	
13	0.08	-0.59, 0.75	1.08	0.55, 2.12	
14	0.61	0.06, 1.15	1.83	1.06, 3.17	

Notes: (a) Estimates of Pr(caries=0) inflated by age; Estimated dispersion parameter =0.40 (95%CI:0.33, 0.50).

(b) AIC= 4019; BIC=4133; Nagelkerke (adjusted) R-square= 0.19.

(c) Multiplicative effect for a Poisson-like regression is the ratio of two means.

(d) Centered for a 12-year-old student with a BMI of 22 kg/ m².

Discussion

Findings from the 2011-2012 student health surveys indicate that dental caries and otitis media remain prevalent conditions in the population with nearly 85% of students surveyed had at least one tooth with signs of decay and over one-quarter of children with abnormal (Type B and Type C) tympanograms. Moreover, 16.4% of Palauan students had a Type B tympanogram, a sign of poor or no mobility in the tympanic membrane, and indicative of an active middle ear infection (Gould & Matz, 2010).

The prevalence of OM in this population is higher than that previously reported by Dever et al (1990) whose focus was restricted to a younger population (i.e., Headstart students). Type B tympanograms were even more prevalent among students ages 5 and 6 (19.1% and 22.1%, respectively), however, not significantly higher (with a two-sample test of proportions) than the overall prevalence most likely due to the small number of students at these ages (Age 5, Type B: n=4; Age 6, Type B: n=38).

The World Health Organization has identified several Pacific Rim populations as having the highest prevalence of (chronic) OM: Inuits, 12-46% and Australian Aboriginals, 12-25% (WHO, 1996). The current prevalence of active OM within Palau's student population appears to be among the highest in the world. Including the students with Type C tympanograms—“near-normal” compliance and a precursor for effusion¹—the prevalence of abnormal tympanograms grows to 28.0%. Additionally, we found that there exist disparities regarding ear health among private and public schools. Students attending public schools had a higher proportion of abnormal tympanometry results. An estimated 17.5% of students in public

¹ Type C curves are shifted to the left, or negative, side of the graph indicating progressive negative pressure in the middle ear space. See Figure 4.

schools show signs of active middle ear infections. A second WHO report indicated that populations with greater than 4% prevalence of OM (specifically CSOM) had a “massive public health problem” that required urgent attention (Acuin, 2004).

The burden of oral disease also appears to be significant public health concern in Palauan children. The overall prevalence of dental caries is relatively high at 85% but falls within the range of prevalence estimates reported by Petersen et al (2005) for industrialized countries (i.e., 60-90%). Previously, Greer et al (2003) reported 87.7% of 6-year-olds in Palau to have decay in primary teeth; in our sample, that prevalence was slightly lower at 84.5% (n=168). Of great concern, however, is the severity and distribution of the oral disease within the population.

The number of teeth with caries ranged from 0 to 16 in primary dentition, and 0 to 20 in permanent dentition. In the students with at least one cavity in a primary tooth, the mean number of cavities was 4.80 (n=504, sd 3.31). Likewise, in students with at least one cavity in permanent teeth, the mean number of cavities was 3.66 (n=721, sd 2.83). As with otitis media, the type of school a child attends is a significant predictor of dental caries with children in public schools having a greater burden of disease. We also found total caries burden to be higher among younger children (age-total caries, $r=-0.25$, $p<0.001$).

Although the severity of disease appears to have declined slightly over the past decade, the current level of disease is much higher than the global goal established by the WHO. For instance, Greer et al (2003) reported the mean number of decayed and filled primary teeth (dft) for 6 year-olds to be 6.90 (sd 4.53). We estimate this number to be 20% lower at a mean of 5.64 (sd 4.14). Our prevalence estimates are somewhat limited since our survey only recorded decayed and filled teeth. A more robust indicator would also include missing teeth, such as the

global decayed, missing, filled teeth index (DMFT) for permanent dentition. The mean DMFT for 12-year-olds is generally used as an indicator of oral health status within a given population. The mean number of decayed and filled permanent teeth for 12-year-old Palauans from the school health survey is 3.88 (n=138, sd 3.79). Even though an underestimation, this prevalence remains above the WHO's goal of 3.0 DMFT.

Through Specific Aims 2 and 3, we identified significant predictors for dental caries (treated and untreated decay) in the population. For caries in primary teeth, these included: age; the type of school a child attended; ethnicity; BMI; and nicotine use. Particular groups at risk of for having a higher mean number of dental caries were children that attended public schools, self-identified Palauan, and nicotine users. Additionally, both age and BMI were inversely related with mean number of caries in primary teeth. Of these predictors, nicotine use had the largest multiplicative effect in multivariate analysis (1.61, 95%CI:1.07,2.41).

Several significant predictors for decay in primary dentition were also significant predictors in permanent dentition. These factors included: age; school type; ethnicity; BMI; and nicotine use. Additional predictors for caries in permanent teeth included alcohol use and state of residence. Several alternative models were considered that showed reasonably good fit for the data. The selection for our final model relating permanent caries was based on known risk factors, concordance with the primary caries model, and overall goodness-of-fit. This strategy was adopted to make it easier for public health officials to focus resources when addressing the issue of childhood caries in Palau.

The strongest predictor of caries in permanent dentition was the type of school a child attended. This variable, as well as the variable of age, was found to be highly significant across several models. In fact, Nagelkerke's adjusted R-squared for just age and sex predicting mean

primary caries is 0.140 compared to 0.162 for the final model. This comparison isn't as strong in permanent dentition where age and school type only produce an adjusted R-squared of 0.097, compared to the final R-squared of 0.194.

Another phenomenon to note in the model for caries in permanent dentition is the association with nicotine use. In univariate analysis, nicotine use was found to have a (significant) positive multiplicative effect (1.24, 95%CI: 1.02, 1.50). However, in the final model this effect is reversed so that nicotine users are predicted to have a lower mean number of caries (multiplicative effect 0.82, 95%CI: 0.66, 1.02). When age was removed from the final model with nicotine use (Appendix, Table A12, Model #4), nicotine again predicted a higher mean number of caries in permanent teeth, however the association became non-significant. There was no significant interaction found between age and nicotine use during the model building process, however, age is a qualitative confounder of nicotine use when predicting the mean number of caries in permanent dentition. Comparing substance use among age groups revealed that the prevalence of exclusive alcohol use was quite low across all ages, however, in the oldest age group (13 to 15 years) the mean number of decayed teeth in permanent dentition was highest among this cohort of four students (i.e., exclusive alcohol use) while at the same time mean decay decreased among exclusive nicotine users and users of both substances (Table A14).

Although both conditions (dental caries and otitis media) are highly prevalent in school children in Palau, this study failed to establish an association between the two. Neither major tympanometry results (Normal vs abnormal) nor individual type of tympanograms (Type A vs Type B vs Type C) were significant in the models for caries in primary and permanent teeth.

Several strengths and limitations should be considered in the context of these findings. First, the sample population was large and representative and provides good prevalence estimates for the general population of Palauan children (Specific Aims 1). We believe the potential for selection bias to be very low because this was a systematic survey which aimed to capture every student in odd-numbered grades. With this methodology, we would anticipate 50% of the total student population to be represented in the sample, however, approximately 33% was included in the survey. Part of this loss is due to students being absent from school and/or otherwise not presenting signed consent forms. If a school absence was explained by an illness then it is possible that our sample represents a slightly healthier sub-set of the population. However, because an unknown proportion of students were present but did not have a signed consent form, it is impossible to determine how this “missing” group skews the data—most likely it is a non-differential bias. Also, for our analysis we excluded students older than 15 years of age, reducing the generalizability of our findings to adolescents and young adults.

We must also consider the accuracy of our measurements. Although these surveys were not designed to precisely measure oral or ear health, the measurements used were both non-invasive and clinically valid. As previously mentioned, the “gold standard” for oral health status is the dft and DMFT indices. The mean number of decayed and filled teeth (i.e., untreated and treated caries) that we reported serve as an underestimation of these measures since we did not record the number of missing permanent teeth; however, this difference should be considered small. Following the 2011-2012 survey year, the Ministry of Health revised the screening forms to assess missing teeth and now include dft/DMFT measurements.

Tympanometry is generally recommended as a supplementary diagnostic tool when otoscopy² is unavailable. Nonetheless, tympanometry remains a useful tool with a high positive predictive value and negative predictive value³. Due to the high prevalence of disease, however, previously reported diagnostic characteristics (i.e., specificity and negative predictive values) may be overestimated in this particular population. Even so, the use of otoscopy may be less desirable in this population due to the pain and/or discomfort associated with this procedure.

The WHO reported a “shortage of accurate, standardized data with which to compare the size of the problem between different parts of the world.” (WHO, 1996). This quote was made in the context of OM, however, we found the same difficulties in this study concerning OM and dental caries alike. As we noted previously, both disorders are categorized and reported under a variety of qualifiers. With the large sample size and reliable measurements, this study provides strong baseline data for Palau (i.e., ear health) and updates other out-dated estimates (i.e., oral health). We acknowledge several limitations to the current study inherent in the design of the school health surveys. Specifically, we believe a stronger design would focus on a younger age group (since OM incidence is highest in early childhood) and follow the cohort over time (to establish or infer causality). Additional research studies are needed to build a body of evidence in order to definitively conclude if an association exists between otitis media and dental caries.

² The United States Clinical Practice Guideline recommends pneumatic otoscopy as the primary diagnostic method for OME and gives tympanometry as an optional tool to confirm diagnosis and document effusion duration (Lous et al, 2012).

³ Based on the Finnish Otitis Media Vaccine Trial with 58 infants (2-11 months of age; Palmu et al, 1999).

Conclusions

The school health surveys serve as an important tool for monitoring the health of Palauan children. Since these surveys were introduced in 2006, they have served as means for identifying individual health concerns and referring students for treatment. To date, however, the surveys have not reached full potential for identifying health concerns within the population. Over the years these surveys have generated large amounts of comprehensive health data. As was evident in the background literature search, the data have not been used to support translational research. Palau's oral healthcare model continues to rely on activities that dental practitioners can deliver to patients rather than preventive strategies that can target the population at large.

Through this study we identified both otitis media and dental caries as being highly prevalent in the school-aged population of Palau. Although we failed to demonstrate a significant association between the two diseases, we did identify school type as a significant predictor of caries in both primary and permanent teeth, as well as a predictor of otitis media. While we do not have sufficient information to conclude that these disparities are related to socioeconomics, we can confidently say that children that attend public schools share a higher burden of these diseases in Palau. We do not know if the determinants of health are related to the families of the students attending the school types (e.g., education, income), or a feature of the school types (e.g., better school environment or health education).

While the burden of dental caries and OM is elevated in both school types, interventions should emphasize the apparent higher need in public schools. School-based interventions may be an effective strategy for addressing these conditions. Schools are not merely education facilities for children but also serve as centers of community life and may play a large role in

modifying environmental exposures (Benzian et al, 2012). The 'Fit for School' program in the Philippines, is a large-scale, evidence based model which incorporates teacher-supervised daily hand washing with soap and tooth brushing with fluoride toothpaste as well as biannual de-worming (Benzian et al, 2012). This program has reportedly reduced the prevalence of high intensity worm infections by 50%, prevented 40% of oral infections, lowered school absenteeism by 30% and boasts 20% fewer malnourished children after only one year of implementation (Fit for School Inc., 2011). The program is supported by the Department of Education and local community members (including local toothpaste manufacturer) and costs around 0.50 USD per child per year to maintain (Monse et al, 2010).

The *Fit for School* intervention follows the "3S" framework: it's *Simple* (evidence-based and cost-effective, easy to implement), *Scalable* (using existing structures and resources) and, most importantly, *Sustainable* (donor-independent and requires community involvement; Benzian et al, 2012). A cost-effective and sustainable intervention that specifically promotes general hygiene may be effective in reducing both OM and dental caries in Palau. The concept of "community-ownership" in terms of healthcare and services is a specific strength of Palauan culture (Duerler & Maskarinec, 2007). Recruiting community participation in a school-based intervention will ensure the sustainability of such a project and increase community awareness of these issues. Despite potential genetic and individual factors related to risk of OM and dental caries, improving hygiene standards and community knowledge of preventive strategies may effectively reduce the burden of these two common childhood disorders in Palau.

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Appendix

Table A1. Revised otitis media disease severity scale used in the 'Micronesia Otitis Media Training Project' (Dever et al, 1990).

Class	Severity Scale
0	Inability to visualize (i.e., obstructing cerumen, atresia)
1	Neutral, white, mobility normal, translucent
2	Neutral or slight retraction; white or pink; mobile or slight decrease; slight tympanosclerosis; slight opacity
3	Retracted, healed perforation; extensive tympanosclerosis; decreased mobility
4	Bulging pink, grey, amber, red; decreased mobility
5	Severe retraction; markedly decreased mobility
6	Perforation
FB	Foreign body

Note: Class 1—normal tympanic membrane; Classes 2 and 3—past mild disease; Classes 4 to 6—active disease requiring therapy.

Table A2. Tympanometry results of Palauan children stratified by age.

	A Curve n (%)	B Curve n (%)	C Curve n (%)	“Abnormal” B + C curve
Age 5 (n=21)	15 (71.4%)	4 (19.1%)	2 (9.5%)	6 (28.6%)
Age 6 (n=168)	113 (67.3%)	37 (22.0%)	18 (10.7%)	55 (32.7%)
Age 7 (n=62)	29 (62.9%)	12 (19.4%)	11 (17.7%)	23 (37.1%)
Age 8 (n=167)	123 (73.7%)	23 (13.8%)	21 (12.6%)	44 (26.4%)
Age 9 (n=67)	44 (65.7%)	16 (23.9%)	7 (10.5%)	23 (34.3%)
Age 10 (n=151)	104 (68.9%)	27 (17.9%)	20 (13.3%)	47 (31.1%)
Age 11 (n=57)	41 (71.9%)	10 (17.5%)	6 (10.5%)	16 (27.1%)
Age 12 (n=138)	112 (81.2%)	12 (8.7%)	14 (10.1%)	26 (18.8%)
Age 13 (n=64)	47 (74.6%)	9 (14.3%)	7 (11.1%)	16 (25.4%)
Age 14 (n=110)	80 (72.7%)	17 (15.5%)	13 (11.8%)	30 (27.3%)
Age 15 (n=49)	41 (83.7%)	6 (12.2%)	2 (4.1%)	8 (16.3%)

Table A3. Tympanometry results of Palauan children stratified by sex

	A Curve n (%)	B Curve n (%)	C Curve n (%)	“Abnormal” B + C curve
Male (n=534)	285 (72.1%)	81 (15.2%)	68 (12.7%)	149 (27.9%)
Female (n=519)	374 (72.1%)	92 (17.7%)	53 (10.2%)	145 (27.9%)

Table A4. Tympanometry results of Palauan children stratified by school type.

	A Curve n (%)	B Curve n (%)	C Curve n (%)	“Abnormal” B + C curve
Public (n=787)	547 (69.5%)	138 (17.5%)	102 (13.0%)	240 (30.5%)
Private (n=266)	212 (79.7%)	35 (13.2%)	19 (7.1%)	51 (20.3%)

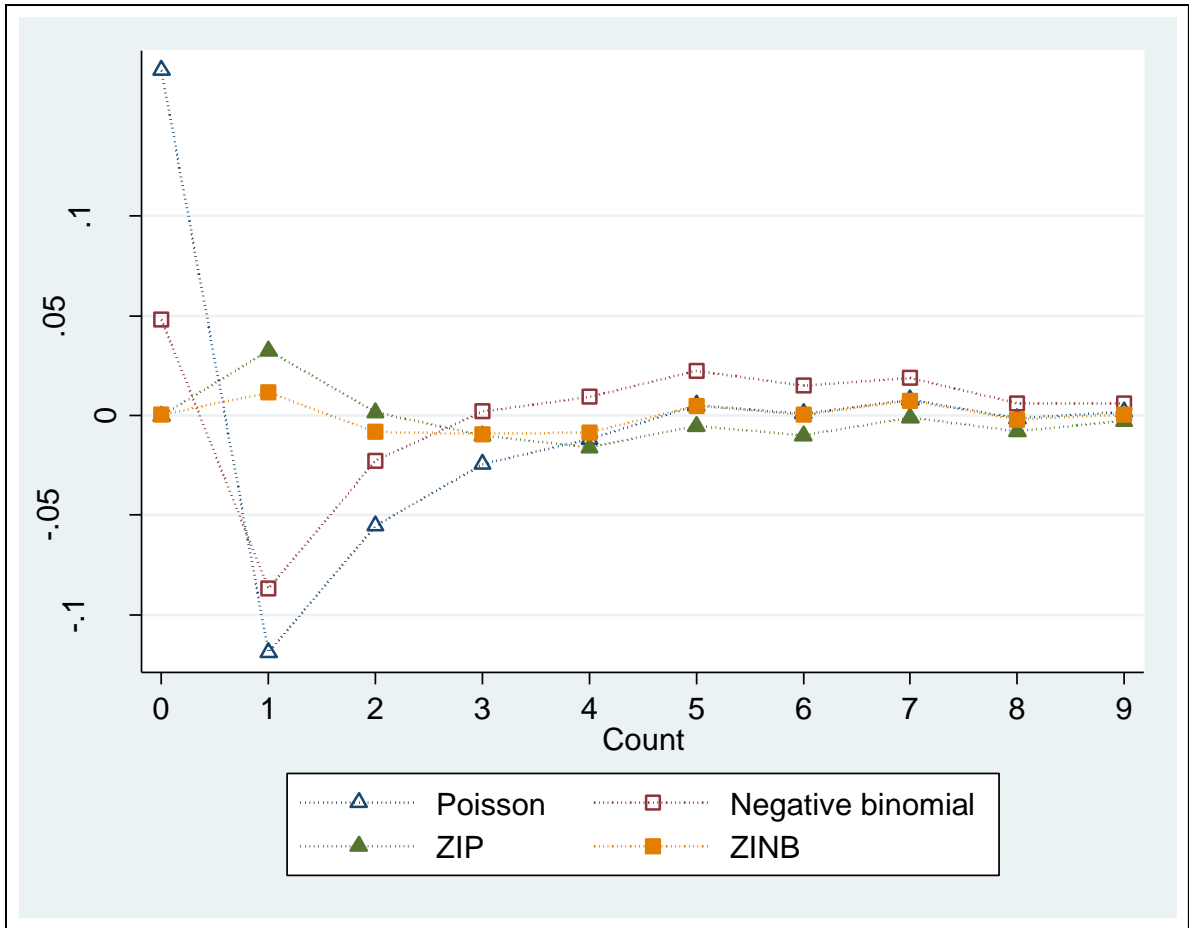
Table A5. Burden of dental caries in Palauan children stratified by age and sex.

	Total caries		Mean (sd)	
	Caries Free	Range	Primary	Permanent
Age 5 (n=21)	4 (19.1%)	0-15	6.24 (4.78)	0.05 (0.22)
Male			5.64 (5.03)	0.09 (0.30)
Female			6.9 (4.68)	0.00 (0.00)
Age 6 (n=168)	25 (14.9%)	0-17	5.64 (4.14)	0.56 (1.02)
Male			5.73 (4.23)	0.52 (1.02)
Female			5.56 (4.07)	0.59 (1.02)
Age 7 (n=62)	10 (16.1%)	0-17	4.84 (3.50)	1.35 (1.43)
Male			5.12 (3.75)	1.38 (1.48)
Female			4.50 (3.21)	1.32 (1.39)
Age 8 (n=167)	18 (10.8%)	0-15	3.71 (2.93)	2.03 (1.67)
Male			3.63 (3.07)	1.96 (1.69)
Female			3.81 (2.74)	2.12 (1.64)
Age 9 (n=67)	3 (4.5%)	0-14	2.82 (2.50)	2.72 (1.70)
Male			3.41 (2.81)	2.84 (1.82)
Female			2.1 (1.86)	2.57 (1.57)
Age 10 (n=151)	18 (11.9%)	0-14	1.19 (1.59)	2.63 (2.49)
Male			1.16 (1.67)	2.57 (2.54)
Female			1.21 (1.52)	2.68 (2.45)
Age 11 (n=57)	13 (22.8%)	0-14	0.63 (1.41)	2.93 (2.84)
Male			0.39 (0.97)	2.88 (3.12)
Female			0.96 (1.83)	3.00 (2.47)
Age 12 (n=138)	31 (22.5%)	0-15	0.07 (0.30)	3.88 (3.79)
Male			0.03 (0.18)	3.60 (4.00)
Female			0.09 (0.37)	4.09 (3.64)
Age 13 (n=63)	9 (14.3%)	0-20	0.00 (0.00)	4.83 (4.49)
Male			0.00 (0.00)	4.78 (4.46)
Female			0.00 (0.00)	4.91 (4.66)
Age 14 (n=110)	23 (20.9%)	0-16	0.03 (0.21)	3.15 (3.10)
Male			0.05 (0.31)	3.14 (2.96)
Female			0.01 (0.12)	3.15 (3.21)
Age 15 (n=49)	7 (14.3%)	0-15	0.06 (0.32)	3.90 (3.44)
Male			0.12 (0.44)	3.80 (3.14)
Female			0.00 (0.00)	4.00 (3.79)

Table A6. Burden of dental caries in Palauan children stratified by school type.

	Total caries		Primary	Permanent
	Caries Free	Range	mean (sd)	mean (sd)
Public (n=787)	96 (12.2%)	0-20	2.60 (3.51)	2.70 (3.04)
Male (n=396)	47 (11.9%)	0-18	2.73 (3.64)	2.73 (3.02)
Female (n=391)	49 (12.5%)	0-20	2.47 (3.38)	2.66 (3.05)
Private (n=266)	65 (24.4%)	0-13	1.39 (2.43)	1.94 (2.34)
Male (n=138)	36 (26.1%)	0-13	1.43 (2.45)	1.62 (2.31)
Female (n=128)	29 (22.7%)	0-12	1.35 (2.43)	2.28 (2.32)

Figure A1. Comparison of four generalized linear models in model selection process for predicting caries in primary dentition (range 0-9 teeth with dental caries).



Note: Zero-inflated Poisson (ZIP) and zero-inflated negative binomial (ZINB).

Table A7. Zero-inflated negative binomial (ZINB)^a univariate regression relating mean number of teeth with caries in primary dentition to independent variables.

Variable	β	95% CI	Mult. Effect ^b	95% CI	LR test ^c (df)	p-value	R ² ^d
Constant	1.428				d		
Age	-0.27	-0.32, -2.23	0.76	0.73, 0.79	130.74 (1)	<0.0001	0.122
Sex					0.03 (1)	0.8683	<0.001
Male	referent		1				
Female	-0.01	-0.16, 0.14	0.99	0.85, 1.15			
School type					18.38 (1)	<0.0001	0.018
Private	referent		1				
Public	0.42	0.23, 0.61	1.53	1.26, 1.85			
Ethnicity					2.93 (1)	0.0867	0.003
Palauan	referent		1				
Other	-0.25	-0.53, 0.03	0.78	0.59, 1.03			
BMI (cont.)	-0.06	-0.08, -0.04	0.94	0.92, 0.96	35.16 (1)	<0.0001	0.034
Physical Activity					1.61 (2)	0.4473	0.002
Light PA	referent		1				
Moderate PA	0.05	-0.18, 0.28	1.05	0.83, 1.33			
Vigorous PA	0.17	-0.12, 0.45	1.18	0.89, 1.57			
School location					3.67 (1)	0.0553	0.004
Urban	referent		1				
Rural	0.15	-0.003, 0.30	1.16	1.00, 1.35			
State					15.22 (13)	0.2937	0.015
1	referent		1				
2	0.53	-0.07, 1.13	1.71	0.94, 3.10			
3	-0.05	-1.01, 0.91	0.95	0.37, 2.49			
4	1.07	0.09, 2.05	2.91	1.09, 7.76			
5	0.43	-0.14, 1.00	1.53	0.87, 2.71			
6	0.30	-0.52, 1.12	1.35	0.60,			

				3.07			
7	0.87	0.18, 1.55	2.38	1.20, 4.72			
8	0.56	-0.14, 1.26	1.76	0.87, 3.53			
9	0.30	-0.69, 1.28	1.36	0.51, 3.59			
10	0.73	0.05, 1.41	2.07	1.05, 4.09			
11	0.60	-0.18, 1.38	1.82	0.84, 3.97			
12	0.47	-0.28, 1.21	1.59	0.76, 3.35			
13	0.20	-0.65, 1.05	1.23	0.52, 2.87			
14	0.50	-0.20, 1.20	1.65	0.82, 3.31			
Nicotine					0.08 (1)	0.7708	<0.001
No	referent		1				
Yes	0.08	-0.45, 0.61	1.08	0.64, 1.84			
Alcohol					0.18 (1)	0.6692	<0.001
No	referent		1				
Yes	-0.16	-0.90, 0.58	0.85	0.41, 1.78			
Tymp					1.88 (2)	0.3911	0.002
Type A	referent		1				
Type B	0.13	-0.06, 0.33	1.14	0.94, 1.39			
Type C	0.004	-0.06, 0.33	1.00	0.80, 1.27			
Tymp					1.02 (1)	0.3132	0.001
Normal	referent		1				
Abnormal	0.08	-0.08, 0.25	1.09	0.92, 1.28			

Notes: (a) Estimates of Pr(carries=0) inflated by age.

(b) Multiplicative effect for a Poisson-like regression is the ratio of two means.

(c) Likelihood ratio test for overall significance of variable; variables with multiple levels have p-values based on Wald's test for overall significance of variable.

(d) Nagelkerke (adjusted) R-square values (Nagelkerke, 1991) based on a (null) log likelihood of -164.3.93 with a maximum R-squared value of 0.956.

(e) Log-likelihood for null model is -1643.93 (4df).

Table A8. Candidate models for zero-inflated binomial regression (ZINB)^a of teeth with caries in primary dentition.

Model	Variable	p ^b	Mult. effect ^c	95% CI	R ² ^d	AIC ^e	BIC
1	Age	<0.001	0.77	0.74, 0.80	0.158	3133.04	3177.67
	School type	0.005	1.29	1.08, 1.54			
	Ethnicity	0.031	0.78	0.62, 0.98			
	BMI	<0.001	0.97	0.95, 0.98			
	School location	0.293	0.94	0.94, 1.22			
2	Age	<0.001	0.77	0.74, 0.80	0.157	3132.14	3171.81
	School type	<0.001	1.34	1.14, 1.58			
	Ethnicity	0.027	0.77	0.61, 0.97			
	BMI	<0.001	0.97	0.95, 0.98			
3	Age	<0.001	0.76	0.73, 0.79	0.162	3129.04	3173.67
	School type	0.0007	1.33	1.13, 1.56			
	Ethnicity	0.0283	0.77	0.62, 0.97			
	BMI	0.0001	0.97	0.95, 0.98			
	Nicotine	0.0227	1.61	1.07, 2.41			
4	Age	<0.001	0.76	0.73, 0.79	0.181	3131.63	3240.74
	School type	0.0015	1.30	1.11, 1.54			
	Ethnicity	0.0337	0.79	0.63, 0.98			
	BMI	0.0001	0.97	0.95, 0.98			
	Nicotine	0.0082	1.72	1.15, 2.57			
	State	0.0331					
5	Age	<0.001	0.76	0.73, 0.79	0.163	3129.80	3179.39
	School type	0.0062	1.28	1.07, 1.52			
	Ethnicity	0.0318	0.78	0.62, 0.98			
	BMI	0.0001	0.97	0.95, 0.99			
	Nicotine	0.0208	1.61	1.08, 2.42			
	School location	0.2646	1.07	0.95, 1.22			
6	Age	<0.001	0.76	0.73, 0.80	0.162	3130.90	3180.49
	School type	0.0007	1.33	1.13, 1.56			
	Ethnicity	0.0286	0.78	0.62, 0.97			
	BMI	0.0001	0.97	0.95, 0.98			
	Nicotine	0.0591	1.73	0.98, 3.06			
	Alcohol	0.7091	0.86	0.39, 1.90			
7	Age	<0.001	0.76	0.73, 0.79	0.181	3133.45	3247.52
	School type	0.0014	1.31	1.11, 1.54			
	Ethnicity	0.0339	0.79	0.63, 0.98			
	BMI	0.0001	0.97	0.95, 0.98			
	Nicotine	0.0295	1.87	1.06, 3.30			
	Alcohol	0.6752	0.84	0.38, 1.86			
8	Age	<0.001	0.76	0.73-0.79	0.16	3150.98	3250.16
	School type	0.0006	1.34	1.13, 1.59			
	Ethnicity	0.0296	0.78	0.62, 0.98			
	State	0.0688					

9	Age	<0.001	0.77	0.74, 0.80	0.176	3136.40	3240.55
	School type	0.0009	1.32	1.12, 1.56			
	Ethnicity	0.0309	0.78	0.62, 0.98			
	BMI	0.0001	0.97	0.95, 0.98			
	State	0.0544					

Notes: (a) Estimates of Pr(caries=0) inflated by age.

(b) Significance level for Wald χ^2 test statistic.

(c) Multiplicative effect for a Poisson-like regression is the ratio of two means.

(d) Nagelkerke (adjusted) R-square values (Nagelkerke, 1991) based on a (null) log likelihood of -164.3.93 with a maximum R-squared value of 0.956.

(d) Akaike and Bayesian Information Criterion.

Table A9. Hypothesis testing of final zero-inflated negative binomial (ZINB)^a multivariate regression model relating teeth with caries in primary dentition for association with tympanometry results.

Model	Variable	p ^b	Mult. effect ^c	95% CI	R ² ^d	AIC ^e	BIC
1	Age	<0.001	0.76	0.73, 0.79	0.162	3129.04	3173.67
	School type	0.0007	1.33	1.13, 1.56			
	Ethnicity	0.0283	0.77	0.62, 0.97			
	BMI	0.0001	0.97	0.95, 0.98			
	Nicotine	0.0227	1.61	1.07, 2.41			
2	Age	<0.001	0.76	0.73, 0.79	0.162	3132.75	3187.30
	School type	0.0007	1.33	1.13, 1.56			
	Ethnicity	0.0302	0.78	0.62, 0.98			
	BMI	0.0001	0.97	0.95, 0.98			
	Nicotine	0.0211	1.61	1.07, 2.43			
	Tympanometry	0.8653					
	Type A		1				
Type B		0.97	0.84, 1.13				
Type C		1.03	0.86, 1.24				
3	Age	<0.001	0.76	0.73, 0.79	0.162	3131.03	3180.63
	School type	0.0007	1.33	1.13, 1.56			
	Ethnicity	0.0282	0.77	0.62, 0.97			
	BMI	0.0001	0.97	0.95, 0.98			
	Nicotine	0.0229	1.60	1.07, 2.41			
	Abnormal tymp	0.9337	0.99	0.88, 1.13			

Notes: (a) Estimates of Pr(caries=0) inflated by age.

(b) Significance level for Wald χ^2 test statistic.

(c) Multiplicative effect for a Poisson-like regression is the ratio of two means.

(d) Nagelkerke (adjusted) R-square values (Nagelkerke, 1991) based on a (null) log likelihood of -164.3.93 with a maximum R-squared value of 0.956.

(e) Akaike and Bayesian Information Criterion.

Table A10. Observed frequency of teeth with caries in primary dentition in student population compared to the counts predicted by the final zero-inflated negative binomial (ZINB) model.

No. of untreated and treated decay (primary caries)	Observed frequency of students	Predicted frequency of students	Difference (observed-expected) in frequency
0	549	549	0
1	87	78	9
2	70	79	-9
3	62	72	-10
4	52	60	-8
5	55	49	6
6	40	39	1
7	39	31	8
8	22	24	-2
9	19	19	0
10	21	14	7
11	14	11	3
12	12	8	4
13	6	6	0
14	2	4	-2
15	1	3	-2
16	2	2	0

Note: Predicted probabilities sum to 0.994 and predicted counts sum to 1048. The total difference in observed and expected frequencies is 5.

Figure A2. Observed versus predicted frequency of teeth with caries in primary dentition based on final model.

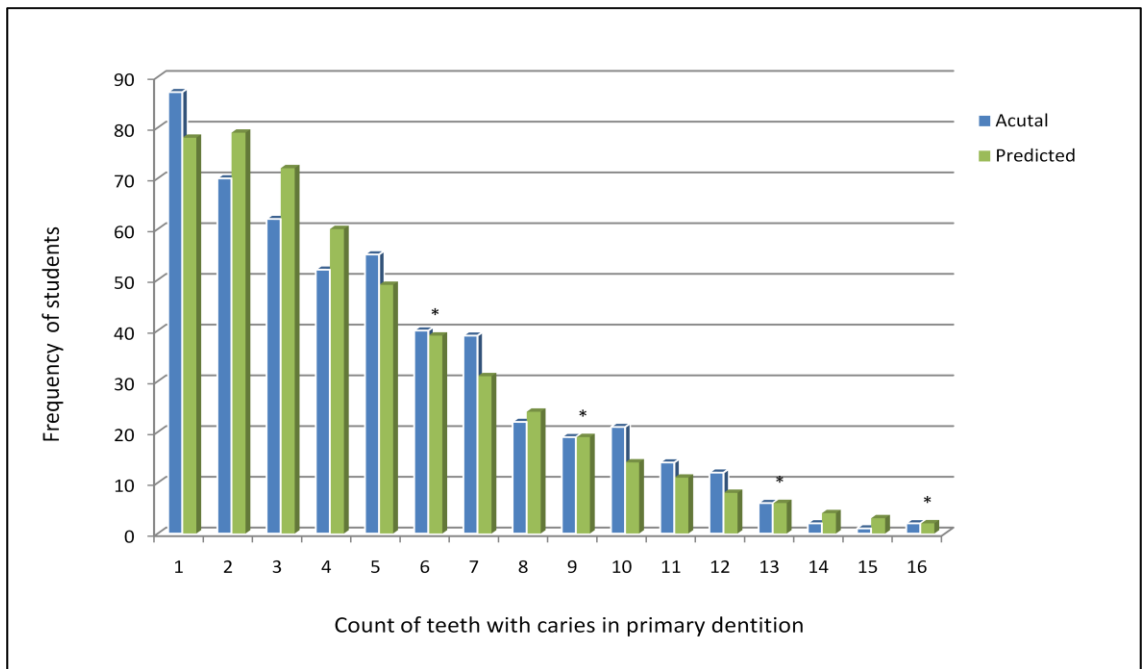
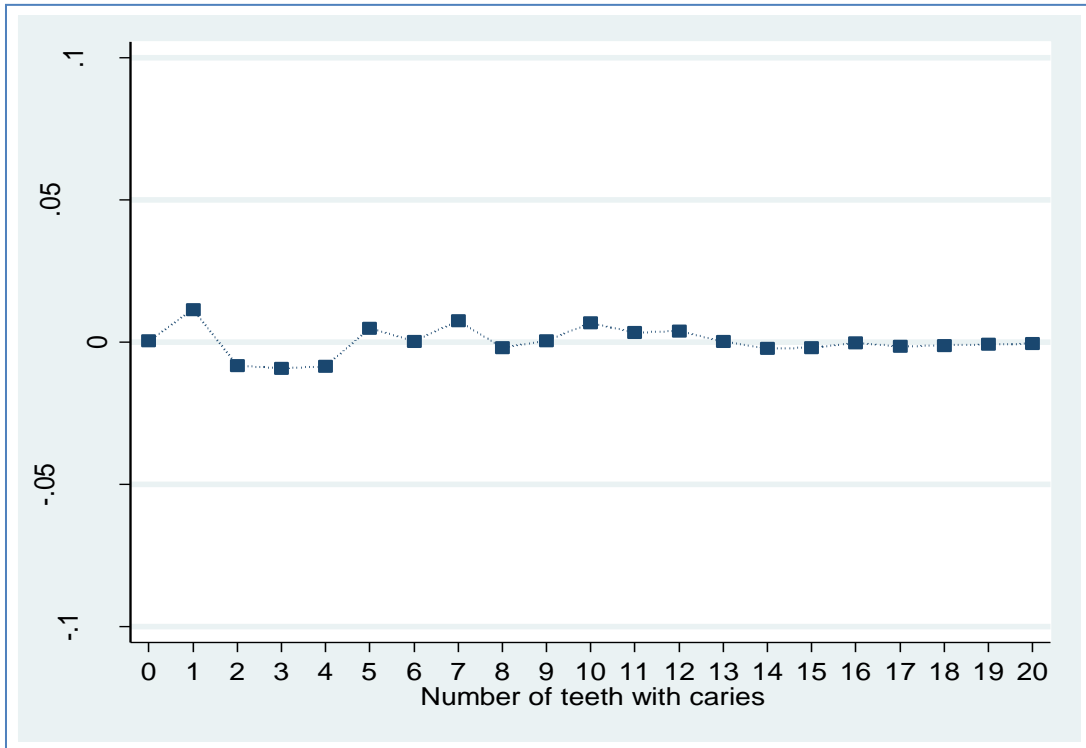
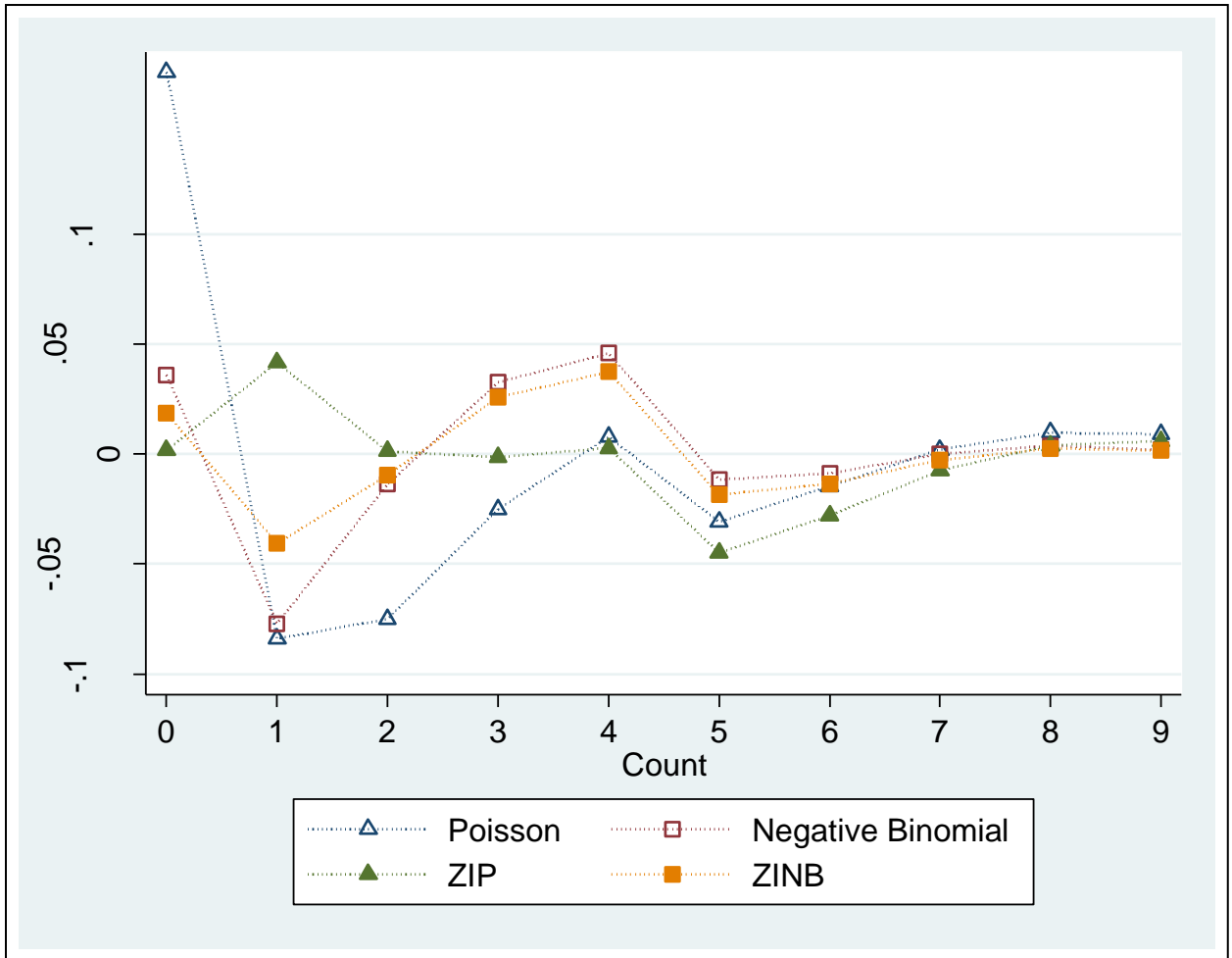


Figure A3. Deviation of predicted probabilities of caries in primary teeth based on final model from observed probabilities.



Note: Positive deviations shows under-predictions.

Figure A4. Comparison of four generalized linear models in model selection process for predicting caries in permanent dentition (range 0-9 teeth with dental caries).



Note: Zero-inflated Poisson (ZIP) and zero-inflated negative binomial (ZINB).

Table A11. Zero-inflated negative binomial (ZINB)^a univariate regression relating mean number of teeth with caries in permanent dentition to independent variables.

Variable	β	95% CI	Mult. Effect ^b	95% CI	LR test ^c (df)	p-value	R ² ^d
Constant	1.09	1.02, 1.15			d		
Age	0.12	0.09, 0.14	1.12	1.09, 1.16	69.64 (1)	<0.0001	0.065
Sex					0.36 (1)	0.5510	<0.001
Male	referent		1				
Female	0.04	-0.09, 0.17	1.04	0.91, 1.18			
School type					20.13 (1)	<0.0001	0.019
Private	referent		1				
Public	0.35	0.20, 0.51	1.43	1.22, 1.66			
Ethnicity					7.06 (1)	0.0079	0.007
Palauan	referent		1				
Other	-0.34	-0.59, -0.09	0.71	0.56, 0.91			
BMI (cont.)	0.003	-0.009, 0.02	1.00	0.99, 1.02	0.28 (1)	0.5980	<0.001
Physical Activity					0.51 (2)	0.7737	<0.001
Light PA	referent		1				
Moderate PA	0.03	-0.17, 0.22	1.03	0.84, 1.25			
Vigorous PA	0.09	-0.17, 0.34	1.09	0.85, 1.41			
School location					4.31 (1)	0.0379	0.004
Urban	referent		1				
Rural	-0.14	-0.27, -0.008	0.87	0.76, 0.99			
State					82.27 (13)	<0.0001	0.077
1	referent		1				
2	0.28	-0.21, 0.76	1.32	0.81, 2.15			
3	-1.94	-3.50, -0.39	0.14	0.03, 0.68			
4	-0.80	-2.05, 0.45	0.45	0.13, 1.57			
5	0.70	0.24, 1.16	2.01	1.27, 3.18			
6	-0.03	-0.73, 0.67	0.97	0.48,			

				1.95			
7	0.66	0.09, 1.24	1.94	1.09, 3.44			
8	0.55	-0.02, 1.13	1.74	0.98, 3.09			
9	0.80	0.12, 1.49	2.23	1.13, 4.42			
10	0.30	-0.28, 0.88	1.35	0.75, 2.41			
11	0.61	0.04, 1.19	1.85	1.04, 3.29			
12	-0.52	-1.17, 0.14	0.60	0.31, 1.15			
13	-0.14	-0.84, 0.56	0.87	0.43, 1.74			
14	0.48	-0.09, 1.06	1.62	0.91, 2.88			
Nicotine					4.69 (1)	0.0304	0.005
No	referent		1				
Yes	0.21	0.02, 0.41	1.24	1.02, 1.50			
Alcohol					6.89 (1)	0.0087	0.007
No	referent		1				
Yes	0.41	0.10, 0.73	1.51	1.10, 2.08			
Tymp					1.57 (2)	0.4568	0.002
Type A	referent		1				
Type B	0.001	-0.18, 0.18	1.00	0.84, 1.20			
Type C	0.13	-0.08, 0.33	1.14	0.93, 1.39			
Tymp					0.57 (1)	0.4501	<0.001
Normal	referent		1				
Abnormal	0.06	-0.09, 0.20	1.06	0.92, 1.22			

Notes: (a) Estimates of Pr(caries=0) inflated by age.

(b) Multiplicative effect for a Poisson-like regression is the ratio of two means.

(c) Likelihood ratio test for overall significance of variable; variables with multiple levels have p-values based on Wald's test for overall significance of variable.

(d) Nagelkerke (adjusted) R-square values (Nagelkerke, 1991).

(d) Log-likelihood for null model is -2097.60 (4df).

Table A12. Candidate models for zero-inflated binomial regression (ZINB)^a of teeth with caries in permanent teeth.

Model	Variable	p ^b	Mult. effect ^c	95% CI	R ² ^d	AIC ^e	BIC
1	Age	<0.0001	1.14	1.10, 1.17	0.190	4024.44	4138.50
	School type	<0.0001	1.69	1.45, 1.97			
	Ethnicity	0.0070	0.72	0.57, 0.92			
	School location	0.7994	1.02	0.87, 1.20			
	State	<0.0001					
	Nicotine	0.0749	0.82	0.66, 1.02			
	Alcohol	0.0446	1.40	1.01, 1.93			
2	Age	<0.0001	1.14	1.10, 1.17	0.190	4022.50	4131.61
	School type	<0.0001	1.70	1.47, 1.97			
	Ethnicity	0.0071	0.73	0.57, 0.92			
	State	<0.0001					
	Nicotine	0.0744	0.82	0.66, 1.02			
	Alcohol	0.0447	1.40	1.01, 1.93			
3	Age	<0.0001	1.15	1.11, 1.18	0.194	4018.65	4132.71
	School type	<0.0001	1.66	1.43, 1.93			
	Ethnicity	0.0032	0.70	0.56, 0.89			
	State	<0.0001					
	Nicotine	0.0764	0.82	0.66, 1.02			
	Alcohol	0.0406	1.40	1.01, 1.94			
	BMI	0.0153	0.99	0.97, 1.00			
4	School type	<0.0001	1.58	1.36, 1.85	0.124	4102.57	4211.67
	Ethnicity	0.0111	0.73	0.57, 0.93			
	State	<0.0001					
	Nicotine	0.1731	1.16	0.94, 1.42			
	Alcohol	0.0456	1.40	1.01, 1.97			
	BMI	0.6046	1.00	0.99, 1.01			
5	Age	<0.0001	1.14	1.11, 1.17	0.190	4019.81	4123.95
	School type	<0.0001	1.66	1.43, 1.93			
	Ethnicity	0.0056	0.72	0.57, 0.91			
	State	<0.0001					
	BMI	0.0162	0.99	0.97, 1.00			
6	Age	<0.0001	1.14	1.12, 1.18	0.191	4020.88	4129.99
	School type	<0.0001	1.66	1.43, 1.92			
	Ethnicity	0.0048	0.71	0.46, 0.90			
	State	<0.0001					
	BMI	0.0168	0.99	0.97, 1.00			
	Nicotine	0.3357	0.91	0.75, 1.10			
7	Age	<0.0001	1.13	1.10, 1.16	0.186	4023.56	4122.75
	School type	<0.0001	1.70	1.47, 1.97			
	Ethnicity	0.0118	0.74	0.59, 0.94			
	State	<0.0001					

Notes: (a) Estimates of Pr(caries=0) inflated by age.

(b) Significance level for Wald χ^2 test statistic.

(c) Multiplicative effect for a Poisson-like regression is the ratio of two means.

(d) Nagelkerke (adjusted) R-square values (Nagelkerke, 1991) based on a (null) log likelihood of -2097.601 with a maximum R-squared value of 0.981.

(e) Akaike and Bayesian Information Criterion.

Table A13. Hypothesis testing of final zero-inflated negative binomial (ZINB)^a multivariate regression model relating teeth with caries in permanent dentition for association with tympanometry results.

Model	Variables	p ^b	Mult. effect ^c	95% CI	R ² ^d	AIC ^e	BIC
1	Age	<0.0001	1.15	1.11, 1.18	0.194	4018.65	4132.71
	School type	<0.0001	1.66	1.43, 1.93			
	Ethnicity	0.0032	0.70	0.56, 0.89			
	BMI	0.0153	0.99	0.97, 1.00			
	Nicotine	0.0764	0.82	0.66, 1.02			
	Alcohol	0.0406	1.40	1.01, 1.94			
	State	<0.0001					
	1	1					
	2	1.63	1.02, 2.60				
	3	0.16	0.03, 0.71				
	4	0.61	0.18, 2.07				
	5	2.54	1.63, 3.95				
	6	1.04	0.53, 2.03				
	7	1.91	1.11, 3.29				
	8	1.95	1.13, 3.38				
9	2.24	1.16, 4.29					
10	1.61	0.92, 2.81					
11	1.94	1.12, 3.38					
12	0.69	0.36, 1.29					
13	1.08	0.55, 2.12					
14	1.83	1.06, 3.17					
2	Age	<0.0001	1.45	1.12, 1.18	0.196	4020.71	4144.70
	School type	<0.0001	1.65	1.42, 1.92			
	Ethnicity	0.0034	0.71	0.56, 0.89			
	BMI	0.0143	0.99	0.97, 1.00			
	Nicotine	0.0828	0.83	0.67, 1.02			
	Alcohol	0.0432	1.40	1.01, 1.93			
	State	<0.0001					
	1	1					
	2	1.61	1.01, 2.56				
	3	0.15	0.03, 0.71				
	4	0.61	0.18, 2.04				
	5	2.53	1.63, 3.93				
	6	1.04	0.53, 2.04				
	7	1.88	1.09, 3.24				
	8	1.95	1.12, 3.37				
9	2.20	1.15, 4.23					
10	1.59	0.91, 2.77					
11	1.97	1.13, 3.43					
12	0.69	0.37, 1.31					
13	1.07	0.54, 2.08					
14	Tympanometry	1.82	1.05, 3.15				

	Type A	0.3810					
	Type B		1				
	Type C		1.09	0.93, 1.29			
			1.10	0.92, 1.33			
3	Age	<0.0001	1.15	1.12, 1.18	0.196	4018.72	4137.75
	School type	<0.0001	1.65	1.42, 1.92			
	Ethnicity	0.0034	0.71	0.56, 0.89			
	BMI	0.0142	0.99	0.97, 1.00			
	Nicotine	0.0830	0.83	0.67, 1.03			
	Alcohol	0.0434	1.40	1.01, 1.93			
	State	<0.0001					
	1		1				
	2		1.61	1.01, 2.56			
	3		0.15	0.03, 0.71			
	4		0.61	0.18, 2.05			
	5		2.53	1.63, 3.93			
	6		1.04	0.53, 2.04			
	7		1.88	1.09, 3.24			
	8		1.95	1.13, 3.37			
	9		2.20	1.15, 4.23			
	10		1.59	0.91, 2.77			
	11		1.97	1.13, 3.43			
	12		0.69	0.37, 1.31			
	13		1.07	0.55, 2.08			
	14		1.82	1.05, 3.15			
	Abnormal tymp	0.1657	1.10	0.96, 1.25			

Notes: (a) Estimates of Pr(caries=0) inflated by age.

(b) Significance level for Wald χ^2 test statistic.

(c) Multiplicative effect for a Poisson-like regression is the ratio of two means.

(d) Nagelkerke (adjusted) R-square values (Nagelkerke, 1991).

(e) Akaike and Bayesian Information Criterion.

Table 14. Observed frequency of teeth with caries in permanent dentition in student population compared to the counts predicted by the final zero-inflated negative binomial (ZINB) model.

No. of untreated and treated decay (permanent caries)	Observed frequency of students	Predicted frequency of students	Difference (observed-expected) in frequency
0	332	312	20
1	148	192	-44
2	144	155	-11
3	142	115	27
4	122	82	40
5	39	58	-19
6	27	41	-14
7	26	28	-2
8	23	20	3
9	16	14	2
10	10	9	1
11	5	7	-2
12	6	5	1
13	4	3	1
14	2	2	0
15	3	2	1
16	1	1	0
17	1	1	0
18	1	1	0
19	0	1	-1
20	1	0	1

Note: Predicted probabilities sum to 0.999 and predicted counts sum to 1049. The total difference in observed and expected frequencies is 4.

Figure A5. Observed versus predicted frequency of permanent caries based on final model.

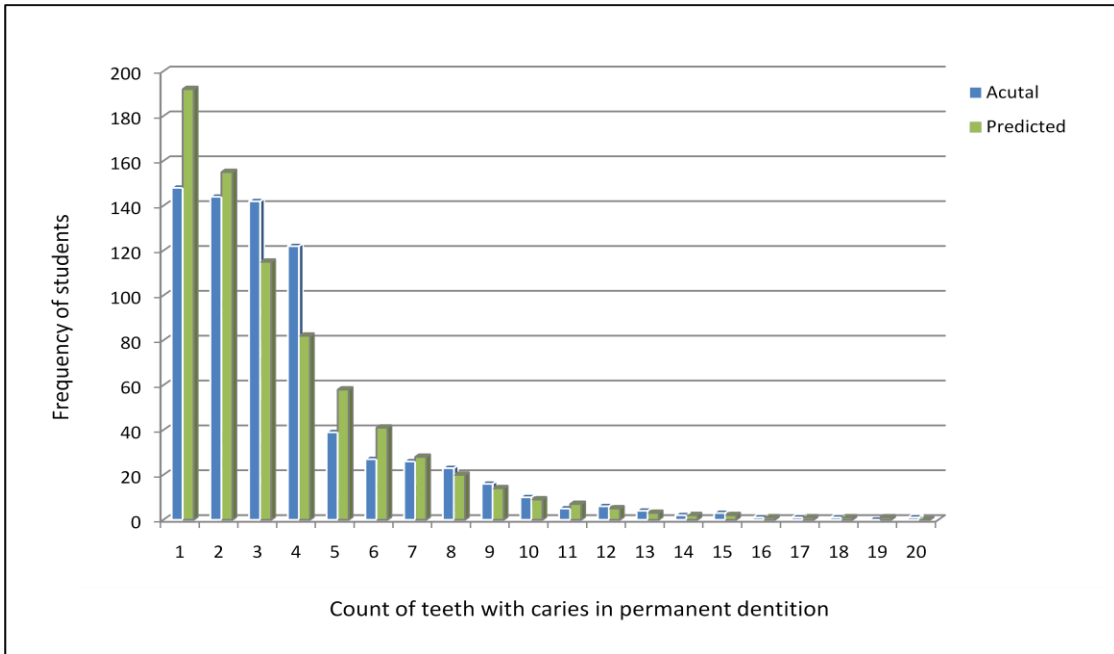
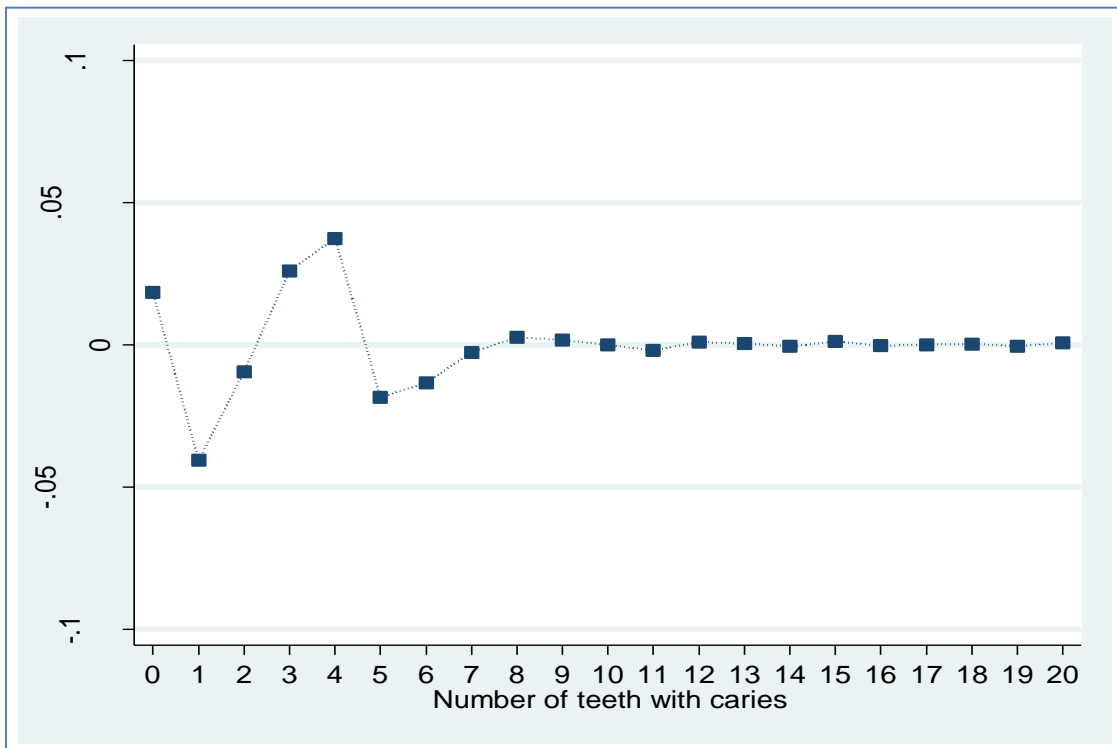


Figure A6. Deviation of predicted probabilities of primary caries based on final model from observed probabilities.



Note: Positive deviations shows under-predictions.

Table A11. Frequency of students reporting substance use by age group.

		Ages 5-8		Ages 9-12		Ages 13-15	
Nicotine Use		No	Yes	No	Yes	No	Yes
Alcohol Use	No	416	1	392	16	136	59
	Yes	0	1	0	5	4	23
		N=418		N=413		N=222	

Table A12. Percentage of students reporting substance use by age group.

		Ages 5-8		Ages 9-12		Ages 13-15	
Nicotine Use		No	Yes	No	Yes	No	Yes
Alcohol Use	No	99.5%	0.02%	94.9%	3.9%	61.3%	26.6%
	Yes	0	0.02%	0	1.2%	1.8%	10.4%
		N=418		N=413		N=222	

Figure A7. Percentage of students reporting substance use by age group.

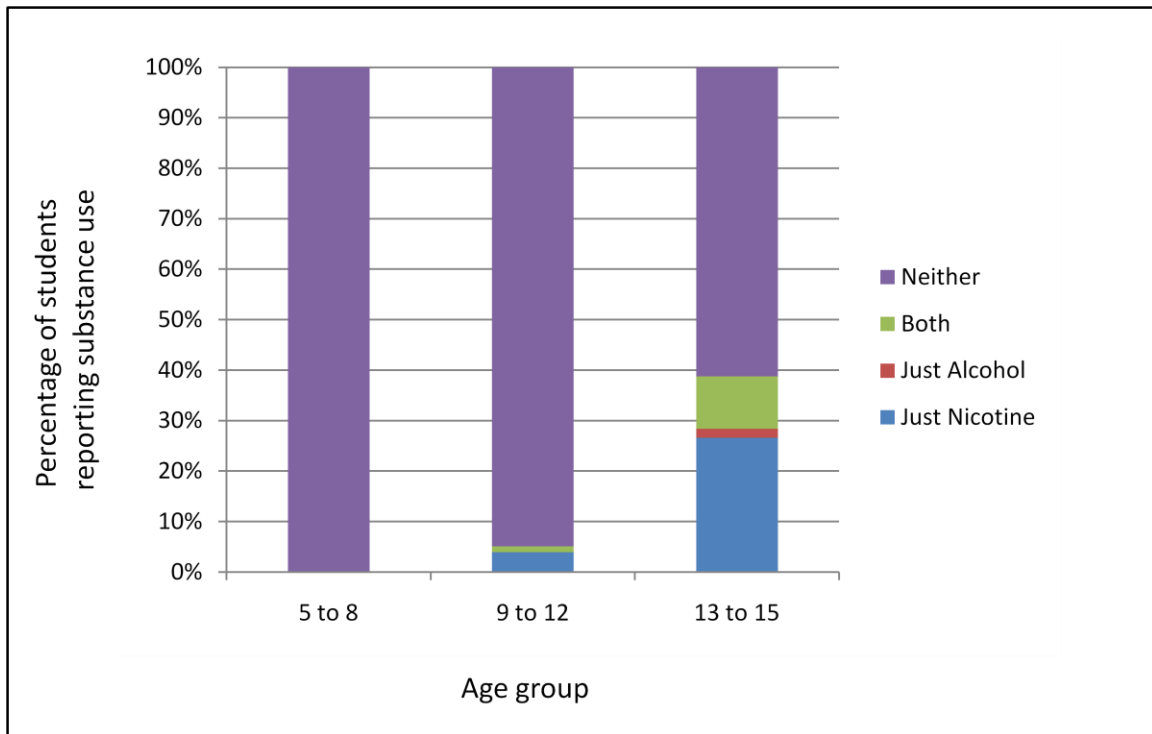


Table A13. Mean number of decayed teeth in primary dentition according to reported substance use and age group.

		Ages 5-8		Ages 9-12		Ages 13-15	
		No	Yes	No	Yes	No	Yes
Alcohol Use	No	4.75 (3.71)	16 (0)	0.99 (1.70)	0.75 (2.49)	0.02 (1.19)	0.03 (0.26)
	Yes	0	7 (0)	0	2.8 (3.03)	0	0.04 (0.21)

Note: Mean decay (standard deviation in parenthesis).

Figure A8. Mean number of teeth with caries in primary dentition according to reported substance use and age group.

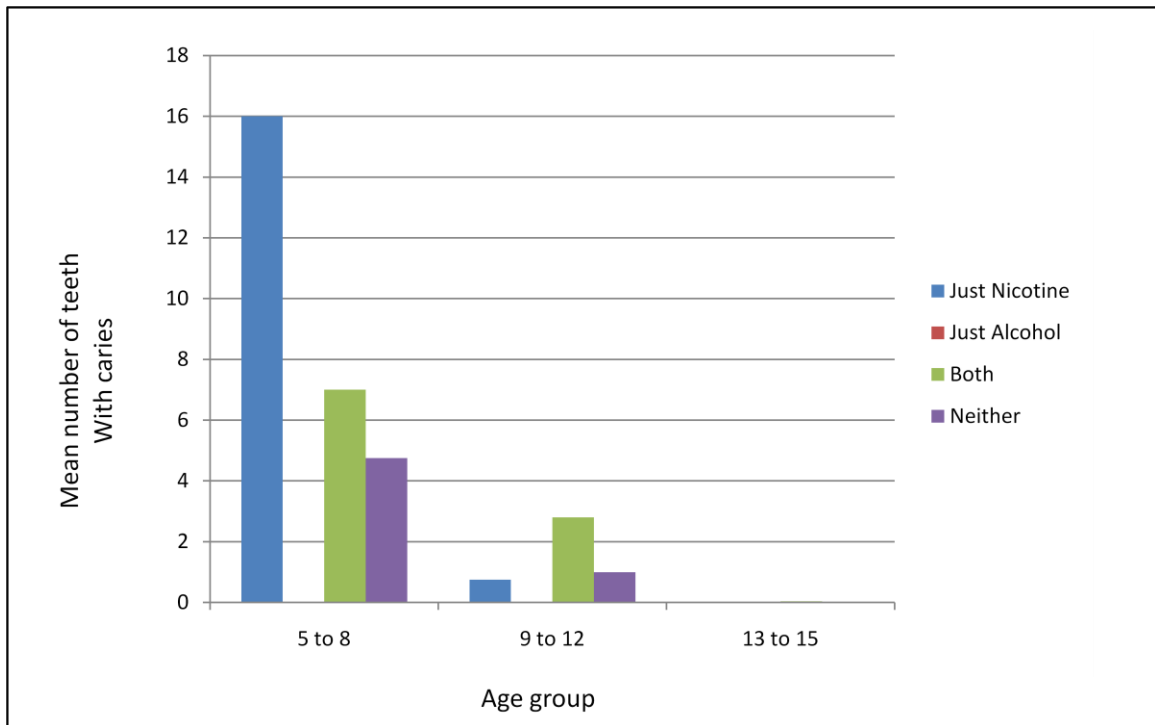


Table A14. Mean number of decayed teeth in permanent dentition according to reported substance use and age group.

		Ages 5-8		Ages 9-12		Ages 13-15	
Nicotine Use		No	Yes	No	Yes	No	Yes
Alcohol Use	No	1.23 (1.52)	1 (0)	3.07 (2.94)	3.38 (4.13)	3.92 (3.72)	3.25 (3.14)
	Yes	0	4 (0)	0	5 (1.58)	4.75 (8.18)	4.22 (3.78)

Note: Mean decay (standard deviation in parenthesis).

Figure A9. Mean number of decayed teeth in permanent dentition according to reported substance use and age group.

