Keywords
Complete edentulism; comorbid disease; malnutrition; obesity; rheumatoid arthritis; cardiovascular disease; pneumonia; COPD; cancer; dementia; mortality.

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Abstract
The relationship between complete edentulism, which is the terminal outcome of a multifactorial oral disease process and other comorbid diseases, was first reported in 2009. Although the relationship between edentulism and a multitude of systemic diseases was reported, none of the publications studied could determine causality of tooth loss on the incidence of any comorbid disease. Since that publication, there has been a renewed interest in this relationship, and a plethora of new articles have been published. This article will provide an update on articles published since 2008 on the relationship between edentulism and comorbid diseases, and will include the relationship between complete edentulism and such comorbid conditions as malnutrition, obesity, cardiovascular disease, rheumatoid arthritis, pulmonary diseases (including chronic obstructive pulmonary disease), cancer, and even mortality.

As prosthodontists and dentists, we have been treating the clinical condition of complete edentulism for over a millennium. Unfortunately, treatment of the edentulous patient may have in many academic institutions focused on the technical aspects of removable prostheses rather than the clinical rationale for treatment and long-term outcomes. According to World Health Organization (WHO) criteria, the completely edentulous patient meets WHO criteria for being: (1) physically impaired, (2) disabled, and (3) handicapped.1,3

Consider the patient shown in Figure 1, a 23-year-old male with a history of chronic soft drink consumption, who presented in pain for dental treatment. Rather than attempting to salvage some remaining mandibular anterior teeth to retain a removable partial dental prosthesis, the patient was edentulated and allowed to heal. He underwent two additional surgeries before denture fabrication; the first surgery was required due to the failure to recognize and remove lateral bony exostoses that impeded successful prosthesis insertion, and a second surgery was required to remove 5 to 7 mm of alveolar bone due to a lack of adequate interarch space. Finally, complete denture prostheses were inserted on healed alveolar ridges. Given that the average life expectancy in the United States is 78.8 years, what does this 23-year-old edentulous patient have to look forward to over the next 55 years, and how might edentulation at this early age impact his overall systemic health?

Incidence of complete edentulism in the United States and globally

Over a decade ago, Douglas et al4 suggested that complete edentulism in the United States was not declining, and may, in fact, be on the rise. The authors suggested that the apparent decline in edentulism of approximately 10% per decade will be more than offset by the increase in the population growth of adults over the age of 55. They suggested that the completely edentulous population in the United States would increase from 33.6 to 37.9 million by 2020, due to population growth and increased life expectancies for the elderly.

Slade et al5 evaluated edentulism trends in the United States. They investigated population trends in U.S. adults >15 years of age using five national cross-sectional health surveys (1957 to 1958, 1971 to 1975, 1988 to 1998, 1999 to 2002, and 2009 to 2012). These surveys included 155,524 individuals. The authors found that the prevalence of edentulism declined from 18.9% at the 1957 to 1958 cohort to 4.9% in the most recent age cohort. They reported the rate of edentulism in the United

Comorbidity and Edentulism Update

Figure 1 (A) Maximal intercuspation position at initial presentation of 23-year-old male patient exhibiting significant loss of tooth structure and dental caries. (B) Occlusal view of maxillary arch at initial presentation. (C) Occlusal view of mandibular dental arch at initial presentation. (D) Initial panoramic film denoting multiple carious lesions, periapical abscesses, and significant vertical bone height. (E) Panoramic film following tooth extraction, but before alveolar surgery to provide adequate interarch space for removable complete denture prostheses. (F) Definitive prostheses inserted at established occlusal vertical dimension. Note significant amount of tooth display.

States in 2010 at 12.2 million. As might be expected, edentulism was a rare condition in high-income households, and states with higher levels of poverty experienced higher levels of edentulism. Slade et al projected that the rate of decline would slow to 2.6% by 2050; however, they also concluded that rate of decline in edentulism may be offset by population growth and aging. Wu et al reported similar findings. They evaluated social stratification and tooth retention in 11,812 adults 50+ years of age between 1988 and 2004, using NHANES surveys. During this time, the rate of edentulism declined from 24.6% to 17.4%. In addition, the mean number of missing teeth declined from 8.19 to 6.5. Wu et al concluded that tooth loss and edentulism were directly related to race, lower income, and lower education levels. Given these data, it appears that the need for complete denture education must be continued for the next four or five decades in the United States.

Globally, complete edentulism also appears to be on the decline. Kassebaum et al studied the effects of 291 diseases and their 1160 sequelae occurring between 1990 and 2010 globally. A total of 68 studies were selected and included 285,746 people in 26 countries ages 12 and older. A meta-analysis was conducted of the data. The results indicated that the global incidence of complete edentulism decreased from 4.4% to 4.1% between 1990 and 2010. Clearly, dentistry and prosthodontics have made an impact on tooth loss and complete edentulism; however, although a decline has been observed, we have not
eliminated complete edentulism or the need for complete denture education, at least in the United States.

**Tooth loss and comorbid disease**

The relationship between tooth loss and other systemic comorbid conditions is, at best, multifactorial (Fig 2). What, then, is a comorbid condition? Comorbidity is one or more diseases (or disorders) that exist in addition to the primary disorder or disease for a given patient (in this case, complete edentulism). The combined relationship between the primary condition and the comorbidity can have profound impacts on the individual’s overall health. In medicine, the Charlson Comorbidity Index is the most widely used validated method for quantifying the effects of multiple diseases on a patient. It predicts the 1-year mortality rates for individuals with multiple systemic diseases. Of 22 possible conditions the Index uses, oral health is not one of the possible disease entities.
In an evaluation of the relationship between complete edentulism and other systemic comorbid conditions, Felton reported on a multitude of studies indicating that completely edentulous patients had a greater risk of developing coronary artery plaque formation, and for having certain cancers. In addition, edentulous patients had a greater incidence of asthma (OR = 10.52) and diabetes. In addition, one study found a direct relationship between the number of remaining teeth and the incidence of dementia. Unfortunately, none of the studies reviewed could confirm whether the relationship between complete edentulism and these comorbid conditions was causal (i.e., a direct cause and effect relationship) or casual.

The purpose of this report, then, is to provide an updated review of the current literature on the relationship between tooth loss, complete edentulism, and comorbid disease conditions.

**Methods**

To further investigate this relationship, the National Library of Medicine’s PubMed web site was used to search the literature using the following parameters:

1. Articles published since 2008
2. Patient cohorts studied had to have a minimum of 50 patients, and a control group for comparison.
3. MESH terms included complete edentulism, dentures, and tooth loss in combination with the following comorbidities: nutrition, cancer, cardiovascular disease, cognition or dementia, diabetes, mortality, respiratory or chronic obstructive pulmonary disease (COPD), and rheumatoid arthritis (RA).
4. Some portion of the investigated patient cohort had to be completely edentulous
5. Abstracts were reviewed, and articles printed and reviewed to determine if they met the inclusion criteria by a single author.

**Results**

A total of 225 abstracts of potential articles published since the 2009 report were reviewed, resulting in 95 full-text articles for review. Of these, 48 were found to meet the inclusion criteria. These were subdivided into categories evaluating edentulism and its relationship to the following comorbid conditions:

1. Impact on nutrition and obesity
2. Cardiovascular diseases
3. Diabetes
4. RA
5. Respiratory diseases, including COPD
6. Cancer
7. Cognitive disorders
8. Mortality

Tables 1–10 present some of the pertinent data from the 2009 paper highlighted at the start of the table in bold/italic type, and the more recent data in standard type. In addition, some discussion is required to distinguish between the use of “Odds ratio” and “Hazard ratio,” which are reported from many of the manuscripts. As used here, “Odds ratio” is obtained from the use of logistic regression analysis, and relates to the ratio of proportions. In other words, an odds ratio of 2.3 implies that one patient cohort is at a 2.3-time greater risk for developing a systemic comorbidity than a different patient cohort (i.e., edentulous vs. dentate). “Hazard ratio” is obtained from a Cox regression (i.e., survival analysis) statistical evaluation (i.e., the number of new cases of a “disease” occurring per population cohort, per unit time). The hazard ratio is the relative risk of the disease comorbidity occurring based on a comparison of event rates during a given time period.

**Discussion**

**Complete edentulism, nutrition, malnutrition, and obesity**

Malnutrition and obesity are the two general aspects of nutrition that have been studied related to tooth loss and denture wear.

**Nutrition and malnutrition (Table 1)**

In our previous report, Nowjack-Ramer and Sheiham reported that tooth loss negatively influenced nutritional intake, and that edentulous patients were at greater risk for malnutrition than the dentate or partially dentate cohort. In a systematic review, Lancker et al. found a direct correlation between poor oral health and malnutrition. Ioannidou et al. found that tooth loss was related to a decreased intake of vital nutrients, and that the risk was 1.42 times greater for each five teeth lost. De Marchi et al. reported that the edentulous patient cohort did not consume the recommended amount of fruits and vegetables. Han and Kim reported that in the denture-wearing cohort, 12.8% were malnourished while using dentures, whereas 20% experienced malnutrition if dentures were not used. De Marchi et al. found that the edentulous patient was 3.26 times more likely to suffer from malnutrition (OR = 3.26 with one denture) then the partially dentate cohort. In a systematic review, Saarela et al. reported that the denture-wearing patient cohort was better equipped to have an adequate diet, and that complete edentulism without dentures resulted in malnutrition.

**Obesity (Table 2)**

Obesity has emerged as one of the fastest growing medical conditions in the United States. It affects more than a third of the adult U.S. population. Obesity can lead to a multitude of comorbid conditions, including cardiovascular disease, type 2 diabetes, certain types of cancer, and premature death. The estimated annual cost associated with obesity is a significant part of the expenditures for health care in the United States. The incidence of diabetes appears to be age- and ethnicity-related. The U.S. Centers for Disease Control (CDC) estimates of obesity are shown in Figure 3 for 2011; note how that increased by 2013 (Fig 4). Sadly, it is even worse for non-Hispanic blacks. Also note that in NO state is the incidence of obesity less than 20% (U.S. CDC).

In our previous report, only Sheiham et al. reported that the edentulous population was at an increased risk for obesity. De Marchi et al. found that a 3.28-time higher risk of obesity...
### Table 1: Edentulism, nutrition, and malnutrition

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Study type</th>
<th>Age (years)</th>
<th>Measured</th>
<th>Outcome</th>
<th>Risk, if reported, as OR/HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nowjack-Ramer and Sheiham 2007(^{11})</td>
<td>6985</td>
<td>Cross-sectional</td>
<td>60</td>
<td>Tooth loss, dietary intake</td>
<td>Reduced dentition had reduced intake of fruits and vegetables</td>
<td></td>
</tr>
<tr>
<td>Sahyoun et al 2003(^{12})</td>
<td>5958</td>
<td>Cross-sectional</td>
<td>50-</td>
<td>Healthy eating index (HEI) and tooth loss</td>
<td>&lt;4 pairs of posterior teeth resulted = malnutrition. Edentulous = malnutrition</td>
<td></td>
</tr>
<tr>
<td>Slade 1996(^{13})</td>
<td>1160</td>
<td>Cross-sectional</td>
<td>60</td>
<td>Chewing ability, #remaining teeth</td>
<td>58% of denture wearers reported difficulty chewing</td>
<td></td>
</tr>
<tr>
<td>Saarela et al 2014(^{19})</td>
<td>1475</td>
<td>Cross-sectional</td>
<td>60</td>
<td>Nutritional status</td>
<td>Edentulism without a prosthesis = malnutrition</td>
<td></td>
</tr>
<tr>
<td>De Marchi et al 2008(^{16})</td>
<td>471</td>
<td>Cross-sectional</td>
<td>60 to 92</td>
<td>Malnutrition</td>
<td>26% at risk for malnutrition; one to eight teeth protective against malnutrition</td>
<td>OR = 3.26 with 1 denture</td>
</tr>
<tr>
<td>Lancker et al 2012(^{14})</td>
<td>10,916</td>
<td>Systematic review</td>
<td>60 to 89.6</td>
<td>Malnutrition</td>
<td>Association exists between oral health and malnutrition</td>
<td></td>
</tr>
<tr>
<td>Ioannidou et al 2014(^{15})</td>
<td>2749</td>
<td>Cross-sectional NHANES III</td>
<td>≥60</td>
<td>Protein and caloric intake</td>
<td>Tooth loss = decreased intake of vital nutrients</td>
<td>OR = 1.42 for each 5 teeth lost</td>
</tr>
<tr>
<td>De Marchi et al 2011(^{16})</td>
<td>471</td>
<td>Cross-sectional</td>
<td>60 to 89</td>
<td>Fruit, vegetable intake</td>
<td>44% were edentulous 49% did not consume recommended F-V</td>
<td></td>
</tr>
<tr>
<td>Han &amp; Kim 2014(^{17})</td>
<td>1168</td>
<td>Cross-sectional KNHANES</td>
<td>75.1 (mean)</td>
<td>Nutritional intake</td>
<td>With dentures: 12.8% malnourished; without dentures: 20%</td>
<td>OR = 1.89</td>
</tr>
</tbody>
</table>
Table 2  Edentulism and obesity

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Study type</th>
<th>Age (years)</th>
<th>Measured</th>
<th>Outcome</th>
<th>Risk, if reported, as OR/HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheiham et al 2002&lt;sup&gt;20&lt;/sup&gt;</td>
<td>629</td>
<td>Cross-sectional</td>
<td>65+</td>
<td>&lt;21 teeth, or edentulous</td>
<td># remaining teeth, body mass index (BMI)</td>
<td>OR = 3.0</td>
</tr>
<tr>
<td>De Marchi et al 2012&lt;sup&gt;21&lt;/sup&gt;</td>
<td>471</td>
<td>Cross-sectional</td>
<td>60 to 92</td>
<td>Obesity</td>
<td>Central obesity</td>
<td>OR = 3.28</td>
</tr>
<tr>
<td>Do Nascimento et al 2013&lt;sup&gt;22&lt;/sup&gt;</td>
<td>900</td>
<td>Cross-sectional</td>
<td>72.7 (mean)</td>
<td>Obesity</td>
<td>Not wearing dentures</td>
<td>OR = 2.88</td>
</tr>
</tbody>
</table>

Table 3  Edentulism and cardiovascular disease

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Study type</th>
<th>Age (years)</th>
<th>Measured</th>
<th>Outcome</th>
<th>Risk, if reported, as OR/HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taguchi et al 2004&lt;sup&gt;24&lt;/sup&gt;</td>
<td>67</td>
<td>Cross-sectional</td>
<td>44 to 68</td>
<td>Tooth loss, hypertension</td>
<td>Tooth loss = increased risk of hypertension</td>
<td>OR = 3.59</td>
</tr>
<tr>
<td>Desvarieux et al 2003&lt;sup&gt;25&lt;/sup&gt;</td>
<td>711</td>
<td>Cross-sectional</td>
<td>57 to 75</td>
<td>Tooth loss, periodontal health</td>
<td>Tooth loss = increased incidence of carotid artery plaques</td>
<td>OR = 1.88</td>
</tr>
<tr>
<td>Schwahn et al 2004&lt;sup&gt;26&lt;/sup&gt;</td>
<td>2738</td>
<td>Cross-sectional</td>
<td>20 to 59</td>
<td>Tooth loss, plasma fibrinogen</td>
<td>Periodontal, tooth loss with inflammation</td>
<td>OR = 1.88</td>
</tr>
<tr>
<td>Medina-Solis et al 2014&lt;sup&gt;27&lt;/sup&gt;</td>
<td>13,966</td>
<td>Cross-sectional</td>
<td>50.9</td>
<td>Tooth loss, angina pectoris</td>
<td>10.2% were edentulous</td>
<td>OR = 12.93</td>
</tr>
<tr>
<td>Polzer et al 2012&lt;sup&gt;28&lt;/sup&gt;</td>
<td>108 to 41,407</td>
<td>Systematic review-meta analysis</td>
<td>18 to 85</td>
<td>Tooth loss, circulatory mortality</td>
<td>Circulatory mortality linked to tooth loss. All-cause mortality linked</td>
<td>OR = 12.93</td>
</tr>
</tbody>
</table>

occurred if fewer than eight natural teeth remained (OR = 3.28). For edentulous patients, Do Nascimento et al<sup>22</sup> reported that the edentulous patient cohort that did not wear dentures were at an increased risk of being obese (OR = 2.88). Finally, Hamdan et al<sup>23</sup> in a randomized control trial, compared the nutritional intake of patients with well-fitting complete dentures, and those with implant-retained mandibular overdentures, but found no difference between the cohorts.

Clearly, the evidence appears to support the premise that the edentulous patient appears at risk for poor nutritional intake, malnutrition, and obesity. Our abilities to provide exceptional complete denture prostheses are essential to correct this situation.

Complete edentulism and cardiovascular diseases (Table 3)

Cardiovascular disease is the leading cause of death in the United States, killing more than 370,000 adults annually. The primary risk factors for cardiovascular disease are high blood pressure, high LDL cholesterol levels, and smoking, although other risk factors also play a role in the disease progression (U.S. CDC).

Our previous investigation pointed to the relationship between tooth loss and atherosclerotic plaque formation. Taguchi et al<sup>24</sup> reported that tooth loss increased the risk of hypertension. Desvarieux et al<sup>25</sup> demonstrated that tooth loss was associated with an increase in the formation of carotid artery plaques, and Schwahn et al<sup>26</sup> showed that tooth loss and periodontal disease were associated with increased levels of inflammatory markers in the bloodstream. Since that report, two additional studies merit consideration.

Medina-Solis et al<sup>27</sup> in a cross-sectional survey of 13,966 participants with a mean age of nearly 51 years, found a rate of complete edentulism of 10.2%. They found that the effect of edentulism on angina pectoris was correlated with age, being more prevalent in the younger age group (OR = 12.93). Polzer et al<sup>28</sup> conducted a systematic review and meta-analysis to determine whether the number of remaining teeth...
Table 4  Edentulism and diabetes

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Study type</th>
<th>Age (years)</th>
<th>Measured</th>
<th>Outcome</th>
<th>Risk, if reported, as OR/HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cleary and Hutton 1995²⁹</td>
<td>370</td>
<td>Cross-sectional</td>
<td>50 to 95</td>
<td>Health, #teeth, non-insulin diabetes</td>
<td>Edentulous = higher risk of developing non-insulin dependent diabetes mellitus</td>
<td>OR = 4.06</td>
</tr>
<tr>
<td>Medina-Solis et al 2006³⁰</td>
<td>14,000</td>
<td>Cross-sectional</td>
<td>18 to 90</td>
<td>#teeth, health status</td>
<td>30.6% edentulous above 65 years. Edentulism increased risk of diabetes</td>
<td>OR = 1.82</td>
</tr>
<tr>
<td>Azogui-Levi and Dray-Spira 2012³¹</td>
<td>19,231</td>
<td>Cross-sectional</td>
<td>35+</td>
<td>± diabetes and dental problems</td>
<td>Diabetes = dental problems. Diabetes = removable prostheses</td>
<td>OR = 1.47, OR = 2.17</td>
</tr>
<tr>
<td>Patel et al 2013³²</td>
<td>2508</td>
<td>Cross-sectional</td>
<td>50+</td>
<td>#teeth and diabetes</td>
<td>Edentulism = 28% diabetic v 14% (nondiabetic)</td>
<td>OR = 2.25</td>
</tr>
</tbody>
</table>

Table 5  Edentulism and rheumatoid arthritis

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Study type</th>
<th>Age (years)</th>
<th>Measured</th>
<th>Outcome</th>
<th>Risk, if reported, as OR/HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Pablo et al 2008³⁴</td>
<td>4461</td>
<td>Cross-sectional</td>
<td>60+</td>
<td>#remaining teeth, perio disease, edentulism</td>
<td>RA patients = higher incidence of perio, more missing teeth, greater risk of edentulism</td>
<td>OR = 1.82 for perio disease, OR = 2.27 if edentulous, OR = 1.92 if edentulous</td>
</tr>
<tr>
<td>Demmer et al 2011³⁵</td>
<td>9702</td>
<td>Cross-sectional</td>
<td>25 to 74</td>
<td>#remaining teeth, perio disease, edentulism</td>
<td>Perio disease and &gt;5 missing teeth = higher incidence of RA (but not statistically significant). Edentulism = greater risk of RA</td>
<td>OR = 1.82 for perio disease, OR = 2.27 if edentulous, OR = 1.92 if edentulous</td>
</tr>
</tbody>
</table>

is associated with circulatory mortality or all-cause mortality, and to determine whether the replacement of missing teeth would provide protection for the patient from mortality. They identified 23 studies that met their inclusion criteria, including five that met moderate to high levels of quality. Their assessment found a relationship between circulatory mortality and the number of remaining teeth, as well as a relationship between all-cause mortality and the number of remaining teeth. Unfortunately, no studies determined whether the replacement of missing teeth protected the patient against mortality. Polzer et al indicated that the effects of denture use on circulatory mortality needed to be studied.

**Complete edentulism and diabetes (Table 4)**

Diabetes is the seventh leading cause of mortality in the United States. In 2012, over 29 million adults were diagnosed with the disease, and it is estimated that one in four people do not know they have the disease. In addition, 86 million are considered prediabetic, and without diet and exercise, up to 30% of these individuals will become type 2 diabetics within 5 years (U.S. CDC). According to the WHO, diabetes is projected to be one of the world’s main killers and disable within the next 25 years. Nearly 171 million globally are estimated to be affected by diabetes. Our previous report suggested that edentulous patients had a higher risk of developing noninsulin dependent diabetes (Cleary and Hutton,²⁹ and Medina-Solis et al³⁰).

More recently, Azogui-Levi and Dray-Spira³¹ evaluated this relationship in a French population of 19,231 participants aged 35 and older. They collected data from their patient cohort over three visits in a 2-year period and found that diabetics were older (mean age of 66 years vs. 52 years for nondiabetics), more likely to be obese (35% vs. 12%), and had a higher prevalence of oral health problems (16.4%) than nondiabetics (13.4%). They also determined that diabetics were more likely to experience dental problems (OR = 1.47), and were more than twice as likely to wear removable prostheses (62%) than nondiabetics were (33%; OR = 2.17).

Patel et al³² analyzed NHANES 2003 to 2004 data of 2508 participants 50 years of age and older. They found
the prevalence of edentulism was 28% for the diabetic population, but only 14% for the nondiabetic cohort. Multiple regression analysis indicated that patients with diabetes were more likely to be edentulous than those without diabetes (OR = 2.25).

Complete edentulism and RA (Table 5)

RA is a systemic inflammatory disease that can manifest itself in numerous joints in the body. The inflammation primarily affects the synovial membrane, leading to cartilage and bone erosions and occasionally, to joint deformity. Common joint manifestations include pain, swelling, and redness. It is believed to be the result of a faulty immune response. RA affects nearly 1.3 million in the United States, with women being affected 2.5 times as frequently as men (U.S. CDC). For a good review of the etiology and pathogenesis of RA, see Culshaw et al. In our previous study, we reported that de Pablo et al found that patients with RA were at a 2.27-time greater risk for being edentulous than those with remaining teeth. This risk was 3.34 times greater when the patient cohorts were adjusted for confounders (sex, age, smoking, and race-ethnicity). In a study of 9702 women using NHANES I data in a cross-sectional analysis, Demmer et al found that completely edentulous patients experienced a statistically significant increase in the risk of incident RA (OR = 1.92) compared to those patients who had lost fewer than five teeth; however, the causality of RA as it relates to complete edentulism has not been demonstrated to date.

Complete edentulism, respiratory diseases, and COPD (Tables 6 and 7)

Chronic obstructive pulmonary disease (COPD) is characterized clinically by the inability to inspire and expire; it is generally associated with inflammation of the lung tissues. The major risk factor is smoking, but poor air quality may be implicated as well. COPD is the third leading cause of death in the United States, and fifth leading cause globally. It is expected to become the fourth leading cause of death globally by 2030. In the United States, COPD affects an estimated 24 million adults, and results in 700,000 hospital admissions and 124,000 deaths annually (U.S. CDC). Individuals with this disease are classified using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification system; stages I to IV are identified, based on spirometry assessments.
In our last report, which focused on asthma, we noted that Xie et al. had reported that asthma was more likely to occur in the edentulous adult, and that the use of inhaled corticosteroids could lead to increased alveolar ridge resorption in the maxillary arch. Six studies were identified that reported on the association between tooth loss and respiratory diseases, including COPD and pneumonia.

**Respiratory infections (Table 6)**

Several studies have investigated tooth loss and denture use as it relates to the development of upper respiratory tract infections and dysphagia. A plausible mechanism of pneumonia could be associated with aspiration of oral pathogens from the mouth or associated prosthetic appliances.

Sjogren et al. conducted a systematic review of the effects of good oral hygiene on respiratory tract infection and pneumonia in hospitals and nursing homes. They estimated that a reduction of 10% of the cases of death from pneumonia in nursing home residents could be associated with improving oral hygiene of the patients.

Inuma et al. investigated a population of community-dwelling elders in Japan. A total of 524 patients age 85+ years were assessed over 36 months. The investigators found that nocturnal denture wear was significantly associated with a higher risk (OR = 2.3) of pneumonia.

Przybylowska et al. evaluated the composition of denture plaque biofilm on the oral mucosa in 51 patients, 37 diagnosed with COPD. Of these patients, 62% had complete dentures, 24% had transitional RDPs, and 13.5% had metal-based RDPs. All control group patients had complete dentures. Bacterial sampling was conducted on all patients. The investigators found pathogenic bacteria in 92% of the COPD patients. In addition, 70.3% of the hospitalized patients had denture stomatitis with C. albicans infection. Abundant biofilm was detected in 27% of the COPD patients, but only in 7% of the control group. The investigators concluded that poor oral hygiene in the denture-wearing COPD patient can lead to COPD-related events.

Finally, Ortega et al. evaluated the oral health status of elderly patients with oropharyngeal dysphagia compared to a control group without swallowing difficulties. The investigators found that 40% of the dysphagia patients were edentulous, 16% of the patients had confirmation of aspiration into the lung tissues, 80% had signs of biofilm penetration into the larynx, and 32% had oropharyngeal residue of the denture biofilm. Ortega et al concluded that elderly patients with oropharyngeal dysphagia had a high risk of developing aspiration pneumonia.

**COPD (Table 7)**

In a prospective 5-year cohort study of 11,387 patients ages 45 to 64, Barros et al. studied the inflammatory biomarkers and COPD. They found an increase of IL-6 in the COPD patient cohort, and a significant pathogenic biofilm on dentures; these patients were found to be at higher risk for COPD-related events. Barros et al found that the completely edentulous patient cohort had a 2.37 times higher risk for COPD hospitalization and COPD-related death than the dentate or partially dentate cohorts (OR = 2.37 for GOLD stage 1 and 2).

Offenbacher et al. in a cross-sectional study of 13,465 patients age 45 to 64 (of whom 2084 were completely edentulous) found that 28.3% of the edentulous patient cohort had COPD vs. 19.6% of the dentate patients. The risk (OR) of development of COPD in denture wearers was 1.3 times higher for GOLD stage 2 and 2.5 times higher for GOLD stage 3 COPD.

**Complete edentulism and cancer (Table 8)**

Cancer is the second-leading cause of mortality annually in the United States, resulting in nearly 585,000 deaths in 2011. Currently, the U.S. CDC reports that two of every three individuals diagnosed with cancer live at least 5 years after their diagnosis. Of great interest to prosthodontists, cancer of the head...
Table 9 Edentulism and cognitive impairment

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>Study type</th>
<th>Age (years)</th>
<th>Measured</th>
<th>Outcome</th>
<th>Risk, if reported, as OR/HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stein et al 2007^10</td>
<td>144</td>
<td>Prospect for 40 years</td>
<td></td>
<td>Memory impairment</td>
<td>tooth loss, brain histology</td>
<td>22% had one or more copies of Alzheimer's gene. # missing teeth = incr dementia incidence</td>
</tr>
<tr>
<td>Okamoto et al 2014^50</td>
<td>2335</td>
<td>Prospect for 5 years</td>
<td></td>
<td>Memory impairment and tooth loss</td>
<td>Fewer teeth + decreased cognition 10.3% declined edent was worse</td>
<td>OR = 1.02 in dentate 2.39 in edent</td>
</tr>
<tr>
<td>Eshkoor et al 2014^51</td>
<td>1210 with dementia</td>
<td>National cross-sectional</td>
<td></td>
<td>Oral health, physical and cognitive impairment</td>
<td>Falls incr 17%</td>
<td>OR = 1.58 (funtal decline) OR = 0.66</td>
</tr>
<tr>
<td>Kisely et al 2011^52</td>
<td>27,843 cont.</td>
<td>Meta-analysis</td>
<td></td>
<td>Oral health, dementia</td>
<td>Edentulism increased risk of dementia</td>
<td>OR = 3.4</td>
</tr>
<tr>
<td>Naorungroj et al 2014^53</td>
<td>5878</td>
<td>Cross-sectional over 6 years</td>
<td>45 to 64</td>
<td>Cognitive function, oral health</td>
<td>18.2%. Cognitive change in 6 years greater in edent</td>
<td></td>
</tr>
<tr>
<td>Naorungroj et al 2014^53</td>
<td>558</td>
<td>Cross-sectional over 8 years</td>
<td>52 to 75</td>
<td>Oral health, cognitive function</td>
<td>13.8% edentulous. Greater cognitive decline in edent (NS)</td>
<td></td>
</tr>
<tr>
<td>Paganini-Hill et al 2012^54</td>
<td>5468</td>
<td>52 to 105</td>
<td></td>
<td>Cognitive function, oral health</td>
<td>Greater risk for dementia if NOT wearing dentures</td>
<td>HR = 1.91</td>
</tr>
<tr>
<td>Tsakos et al 2015^55</td>
<td>3166</td>
<td>Longitudinal</td>
<td>60+</td>
<td>Cognitive function, oral health</td>
<td>Edent recalled 0.88 fewer words, at slower rate; edent = cognitive decline</td>
<td></td>
</tr>
<tr>
<td>Zenthofer et al 2014^56</td>
<td>94</td>
<td>Cross-sectional</td>
<td>Mean 82.9</td>
<td>OHRQoL index, oral health</td>
<td>No teeth = lower OHRQoL scores 39.4% edent</td>
<td></td>
</tr>
</tbody>
</table>

and neck region (larynx, pharynx, and oral cavity) accounts for 12% of malignancies globally. An estimated 300,000 mortalities are annually associated with head and neck cancer. The leading types of cancer, according to the U.S. CDC, are shown in Figure 5.

Our previous report suggested that complete edentulism was related to various types of cancers, including lung, esophageal, and bladder cancer.\(^9,46\) Three additional studies have been found since our last publication. In the first, by Ansai et al,\(^47\) 656 Japanese community-dwelling participants were studied over 12 years, to determine if tooth loss was associated with oro-digestive cancer mortality. A significant association was found between tooth loss and cancer death; however, this became insignificant when adjusted for confounders. Survival rates were lowest in the completely edentulous cohort, especially for female denture wearers, when compared to the dentate cohort having 20 or more remaining teeth (\(p = 0.047\)).

Shakeri et al,\(^48\) in a case-controlled study in Iran, studied 309 patients with confirmed diagnoses of gastric adenocarcinoma, and 613 age- and sex-matched controls. They found that participants with eight or more remaining teeth were more likely to have gastric cancer than those with fewer than 8 remaining teeth (OR = 1.6), or those who were edentulous (OR = 1.6); however, the authors reported there was insufficient evidence for a clear pattern of association between the risk of gastric adenocarcinoma and oral health.
Finally, in a similar study, Zeng et al. conducted a meta-analysis of 11 articles to determine the association between tooth loss and cancer of the head and neck region. They found a direct association between tooth loss and head and neck cancer. They reported that the loss of 6 to 15 teeth increases the risk (OR = 1.58), the loss of 15 to 19 teeth increases the risk (OR = 1.72), and the completely edentulous condition increases the risk even further (OR = 1.89).

Complete edentulism and cognitive impairment (Table 9)

Cognitive disorders, also known as dementia, are characterized by memory impairment, as well as marked difficulty in speaking, motor activity, object recognition, and disturbance of executive function (ability to plan, organize, and abstract). Alzheimer’s Disease is the most common form of dementia. It is a progressive disease that begins with mild memory loss, and is thought to involve parts of the brain that control thought, memory, and language. The cause remains unclear. In 2013, up to 5 million adults had been diagnosed with Alzheimer’s in the United States. The number of individuals with the disease doubles every 5 years after the age of 65. By 2050, the number of affected individuals is projected to rise to 14 million, nearly a three-fold increase above current levels. The best-known risk factor is age, although genetics may play a role. Alzheimer’s, and other cognitive disorders, are the sixth leading cause of mortality in the United States. Nearly 84,767 deaths were reported to result from Alzheimer’s disease in 2011. In nursing
In our previous work, we reported on the relationship between tooth loss and cognitive disorders that was first reported by Stein et al. In a prospective longitudinal study of 144 Roman Catholic nuns in Milwaukee, WI, detailed dental records were managed by a single dental practitioner over a 40-year period. In addition, cognitive assessments were performed on the patients over a 12-year period. Finally, cranial tissues were obtained post-mortem, and analyzed by a trained neuropathologist blinded to the nuns’ cognitive function scores. The findings were impressive, as 22% of the study participants...
had one or more copies of the gene for Alzheimer’s. In addition, the investigators found a direct correlation between the incidence of dementia and the number of missing teeth. This initial publication has led to additional interest in the relationship between tooth loss and cognitive disorders since 2007.

Okamoto et al. evaluated 2335 community-dwelling patients for memory loss as a function of tooth loss in a prospective 5-year clinical trial. They found that the completely edentulous patient experienced a greater decline in cognitive function when compared to the dentate cohort. The risk of decline in cognitive function was 2.39 times greater (OR = 2.39) in the edentulous population. The risk of patients with 1 to 8 remaining teeth becoming edentulous within 5 years was 4.68 times greater than that of patients with more teeth.

Eshkoor et al. examined 1210 patients with diagnosed dementia in a national cross-sectional study. They evaluated oral health, gait, and physical and cognitive impairment as a function of tooth loss. They reported that the incidence of falls increased 17% in the edentulous population (OR = 1.58), and that the incidence of falls decreased for those edentulous patients who wore their dentures (OR = 0.66) and for partially dentate patients (OR = 0.59).

Kisely et al. conducted a systematic review and meta-analysis of 2784 patients with severe mental illness and a control group of 31,084 patients. Nine studies were selected from 550 citations that met the inclusion criteria. The authors reported that the rate of complete edentulism varied from 3% (India) to 65% (England and Denmark). Patients with severe mental illness had a 3.4-time greater risk of being completely edentulous, and had 6.2 more decayed, missing, and filled surfaces than the control group.

Naorungroj et al. used a subset of the Atherosclerosis Risk in Communities study, a community-based study of vascular disease of 558 adult 52- to 75-year olds studied over 8 years. The authors reported that 13.8% of the cohort was edentulous, and that there was a greater, but not clinically significant, decline in cognitive function in the edentulous cohort over the 8-year evaluation period. No causal effect could be determined.

Paganini-Hill et al. evaluated the oral health and cognitive abilities of 5468 older community-dwelling adults with a mean
age of 81 years over an 18-year period. The authors found that 90% of those patients with inadequate natural masticatory function were edentulous. The edentulous patients who did not wear dentures demonstrated a 91% greater risk for dementia (HR = 1.91) than those who were partially dentate. For the partially dentate cohort, poor oral hygiene resulted in a greater risk for dementia (22% to 65%) than those who performed proper brushing daily. The authors concluded that the wearing of removable prostheses appeared to be beneficial in terms of reducing the risk of dementia.

Tsakos et al55 evaluated cognitive function in 3166 community-dwelling adults 60+ years of age. All assessments were done at baseline and at 5-year intervals (10 years total). Completely edentulous patients were found to recall 0.88 fewer words, and were 0.09 m/sec slower than partially dentate controls. The authors stated that complete edentulism was independently associated with cognitive decline and physical decline in older English adults, and that tooth loss may be a potential early marker of cognitive decline in the elderly.

Zenthofer et al56 in a cross-sectional study, assessed oral health related quality of life (OHRQoL) in institutionalized patients. They found that edentulous patients reported lower QoL scores than those with FDPs and RDPs, but higher than those who were edentulous and had no replacement dentures.

**Complete edentulism and mortality (Table 10)**

Current life expectancy in the United States is 78.8 years, and nearly 2.6 million deaths are reported annually, from a multitude of causes (U.S. CDC). In our 2009 paper, there were no reports of the relationship between complete tooth loss, edentulism, and mortality.9 Although several papers reviewed above8,40,44,47 have discussed the relationship between tooth loss and mortality, several more deserve consideration.

Brown57 provided one of the initial studies of the relationship between edentulism and mortality. In a cross-sectional survey of 41,000 adults 18+ years of age. Mortality information was collected after 15 years. He found that 12.3% of the participants were completely edentulous (46% rate at 75+ age cohort), and that complete edentulism that occurred before age 65 was associated with all-cause mortality. After adjustment for all confounders, the risk of death was 1.5 times greater for the edentulous patient than for the partially and fully dentate patient cohorts. An association between complete edentulism and cardiovascular mortality was also demonstrated.

Holm-Pedersen et al58 evaluated 573 nondisabled community-dwelling individuals at baseline, and at 5-year intervals for 20 years. They found that 40% of the entering participants were edentulous, and by 21 years, 88% had died. Edentulous patients had a statistically higher risk for mortality (HR = 1.26) when compared to partially dentate patients. Holm Pedersen et al suggested that tooth loss was independently associated with mortality and that tooth loss may be an early predictor of accelerated aging.

Osterberg et al59 evaluated whether the number of teeth remaining at age 70 in a Swedish population influenced mortality. In their study of 1803 participants, they found that the 7-year mortality rates were highest in completely edentulous men (42% to 47%). They reported that the number of remaining teeth was an independent, significant 7-year predictor of mortality in both sexes: each remaining tooth reduced 7-year mortality by 4%. The number of remaining teeth was shown to be a significant predictor of mortality in the elderly, regardless of socioeconomic status, health factors, or lifestyle.

Ansari et al60 studied 656 patients over a 12-year period. They found a significant association between cancer death and tooth loss (HR = 1.03). Survival rates for female patients (only) were lowest in the edentulous patient cohort, and were statistically worse than those with 20 or more teeth.

Janket et al61 evaluated the role of removable prostheses on cardiovascular survival in a 15-year cross-sectional study. In 256 participants, they found that partially edentulous patients with an RDP had a lower risk for cardiovascular mortality than those who were fully dentate; however, those with complete dentures, or with a complete denture opposing an RDP had a higher risk of mortality. This study suggested that the periodontal health of the remaining teeth, if present, may influence cardiovascular survival; the authors suggested that reducing inflammation of remaining teeth and replacement of missing teeth appears to impact longevity.

Polzer et al62 conducted a systematic review in which 23 studies were selected. They reported that a relationship existed between the number of remaining teeth and both circulatory and all-cause mortality; however, no study in their investigation demonstrated whether replaced teeth protect the patient against mortality.

In contrast, Schwahn et al63 studied 1803 patients over a 10-year period to determine if missing, but un-replaced teeth had an effect on mortality. In their patient cohort, 188 had un-replaced missing teeth. They found that having nine or more un-replaced teeth was directly related to all-cause mortality (OR = 1.53) in this patient cohort; those patients with nine or more un-replaced teeth had a two-fold increase for cardiovascular mortality. Interestingly, they demonstrated that an induction period of at least 9 years appears to be required for this relationship to develop. When adjusting for confounders, the OR for all-cause mortality was 1.43, and 1.88 for cardiovascular death. A reduced, but nonreplaced dentition appears to be associated with an increased risk for mortality.

Watt et al64 studied 12,831 participants for 8 years. After adjusting for confounders, edentulous participants demonstrated a significantly higher risk for all-cause mortality (HR = 1.3 generally, HR = 1.49 for cardiovascular death mortality) compared to participants with natural teeth. Edentulous patients had a 2.97-time greater risk for mortality related to stroke. The authors concluded that being edentulous was shown to be an independent predictor of cardiovascular disease mortality.

Finally, Liljestrand et al65 in cross-sectional study of 8446 patients in Finland, evaluated the dental status of their patient cohort at baseline and over the next 13 years. National registers were used to obtain information on various comorbidities and mortality. The authors reported that the edentulous patient was at increased risk for development of cardiovascular disease (HR = 1.40), coronary heart disease (HR = 1.5), diabetes mellitus (HR = 1.56), and death (HR = 1.68). In comparison to patient cohorts with remaining teeth, they were at the greatest risk for death.
Conclusions

According to the research found and evaluated in this study, it appears that:

1. Tooth loss, as well as complete edentulism, is associated with a multitude of systemic comorbid conditions.
2. The edentulous patient is at risk for reduced nutritional intake and for obesity.
3. Edentulous patients are at an increased risk of COPD-related events.
4. Poorly maintained removable prostheses may be associated with increases in pneumonia-related hospitalizations.
5. Tooth loss and complete edentulism may be associated with an increased risk of head and neck cancer.
6. The risk of decline in cognitive function appears to be greater in the edentulous population.
7. Edentulism is an independent predictor of cardiovascular disease mortality.
8. A reduced, but nonreplaced dentition is associated with an increased risk for mortality.
9. Wearing of optimal removable prostheses may help protect patients against some types of comorbid disease conditions.
10. We need to educate patients and caregivers as to the potential long-term harmful outcomes of tooth extraction, and of poorly maintained removable prostheses.

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