

Assessing Attitudes and Perceptions of Dental Professionals Toward
an Oral-Systemic Connection

by

Adam Wiley Brock, DMD

Thesis submitted to the Faculty of the
US Army Advanced Education Program in Periodontics
Uniformed Services University of the Health Sciences
In partial fulfillment of the requirements for the degree of
Master of Science 2017

ACKNOWLEDGMENTS

Much appreciation to MAJ Brandon Coleman for his vision, hustle, and guidance throughout the duration of this project. This project starts and stops with MAJ Coleman. Thank you for the opportunity to participate.

Much gratitude to Dr. Richard Topolski for his expertise with Qualtrics and with the statistical analysis. His contributions were invaluable.

A special thanks to Dr. Douglas Dickinson for his help with the survey design and editing of the manuscript.

And, of course, thank you to all those who gave of their time to participate with the survey—from those who helped with the design and provided feedback in the pilot stages to those who took the survey and circulated it among their friends and colleagues. Your contributions made this project possible.

The author hereby certifies that the use of any copyrighted material in the thesis manuscript entitled:

“Assessing Attitudes and Perceptions of Dental Professionals Toward an Oral-Systemic Connection”

Is appropriately acknowledged and, beyond brief excerpts, is with the permission of the copyright owner.

Adam W. Brock, DMD
US Army Advanced Education Program in Periodontics
Uniformed Services University
05/22/2017

Uniformed Services University of the Health Sciences Manuscript/Presentation Approval or Clearance

Initiator						
1. USU Principal Author (Last, First, Middle Initial)						
2. Academic Title						
3. School/Department/Center						
4. Phone			5. Email			
6. Clearance		Paper	Article	Book	Presentation	Other
7. Title						
8. Intended Publication/Meeting						
9. Required by			10. Date of Submission			
<p>**Note: It is DoD policy that clearance of information or material shall be granted if classified areas are not jeopardized, and the author accurately portrays official policy, even if the author takes issue with that policy. Material officially representing the view or position of the University, DoD, or the Government is subject to editing or modification by the appropriate approving authority.</p> <p>Neither I nor any member of my family have a financial arrangement or affiliation with any corporate organization offering financial support or grant monies for this research, nor do I have a financial interest in any commercial product(s) or service(s) I will discuss in the presentation or publication.</p> <p>The following statement is included in the presentation or publication: The opinions or assertions contained herein are the private ones of the author(s) and are not to be construed as official or reflecting the view of the DoD or the USUHS.</p> <p>The following items have been included in the presentation and/or publication: Student and/or faculty USU affiliation. Examples: 1) LCDR Jane Doe, DMD, Resident, Naval Postgraduate Dental School and Uniformed Services University of the Health Sciences Postgraduate Dental College. 2) COL John Doe, DDS, Endodontics Program Director, Fort Bragg, NC and Associate Professor of Endodontics, Uniformed Services University of the Health Sciences Postgraduate Dental College. 3) USUHS logo included on title slide and/or poster</p>						
Chair/Department Head Approval**						
Name (Last, First, Middle Initial)						
Signature						
Commander Approval** (if applicable)						
Name (Last, First, Middle Initial)						
School						
Higher approval clearance required (for University- DoD, or US Gov't-level policy, communications systems or weapons review)						
Signature						

**Uniformed Services University of the Health Sciences
Manuscript/Presentation Approval or Clearance**

Service Dean Approval**	
Name (Last, First, Middle Initial)	
School	
Higher approval clearance required (for University-, DoD, or US Gov't-level policy, communications systems or weapons review)	
Signature	
Executive Dean Approval**	
Name (Last, First, Middle Initial)	
Higher approval clearance required (for University-, DoD, or US Gov't-level policy, communications systems or weapons review)	
Signature	
Vice President for External Affairs Action	
Name (Last, First, Middle Initial)	
USU Approved	DoD Approval Clearance Required
Submitted to DoD (Health Affairs) on	
Submitted to DoD (Public Affairs) on	
DoD Approved/Cleared (as written)	DoD Approved/Cleared (with changes)
DoD Clearance Date	DoD Disapproval Date
Signature	

Distribution Statement

Distribution A: Public Release.

The views presented here are those of the author and are not to be construed as official or reflecting the views of the Uniformed Services University of the Health Sciences, the Department of Defense or the U.S. Government.

ABSTRACT

Assessing Attitudes and Perceptions of Dental Professionals Toward an Oral-Systemic Connection:

Adam Wiley Brock, Master of Science, 2017

Thesis directed by: MAJ Brandon Coleman, Assistant Director, US Army Advanced Education Program in Periodontics

Background: A basic understanding of statistical concepts is essential to understand research and provide optimal patient care. The relationship between periodontitis and systemic health and how clinicians perceive this literature—along with how they perceive and understand statistics—are of interest in dentistry. To date, little has been reported on how oral-systemic health literature translates to clinical practice and patient care. This project investigates how the dental profession—particularly periodontists and general dentists—perceives statistics and oral-systemic health literature by conducting a survey to inquire about these two subjects.

Methods: This project was influenced by a collection of surveys in the medical literature since the mid-2000s on physicians' attitudes and understanding of statistics (5,7,8,74,82,95,107). One such survey done with medical residents (107) served as a model. After developmental and pilot testing phases, the survey was made available to

dental professionals and organized into four sections: demographics, attitudes toward oral-systemic health, self-reported familiarity with statistics, and knowledge of statistics. The survey was maintained via the web-based survey platform Qualtrics. The project hypothesized that there would be a difference between dental professionals' self-perceived understanding of statistics and their actual knowledge of statistics. The aim was to collect basic information on dental professionals' perceptions and knowledge of statistics and their attitudes toward oral-systemic health.

Results: The numbers of initiated and completed surveys were 324 and 212, respectively. The numbers of periodontists and general dentists that participated were 63 and 84, respectively. The remaining 65 participants were of various dental specialties, such as but not limited to hygienists, prosthodontists, and orthodontists. The focus of this report was on responses from periodontists and general dentists. The mean years of practice were 20.48 for periodontists and 8.86 for general dentists. When considering systemic health conditions in the aggregate—diabetes, cardiovascular disease, and adverse pregnancy outcomes—periodontists were statistically significantly more likely to respond that there is a correlation with periodontitis ($p=0.01$). There was a significant difference between periodontists and general dentists in both self-reported confidence in statistics and performance on the knowledge test ($p=.008$ and $p=.005$, respectively). For those who reported substantial statistical training, they were statistically significantly more likely to discuss an oral-systemic connection with their patients than all other groups ($p=0.01$), except for those who reported a significant

amount of statistical training.

Conclusions: Periodontists and general dentists were relatively self-aware about their statistical knowledge deficiencies when comparing their self-reported attitudes to their performance on the knowledge test. Periodontists were generally consistent with their responses regarding attitudes toward oral-systemic health, familiarity with statistics, and knowledge of statistics. However, results were less consistent for general dentists. This project appears to be the first of its kind among dental professionals at large, particularly among general dentists and periodontists.

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION	10
Statement of the problem	10
CHAPTER 2: REVIEW OF THE LITERATURE	12
Biostatistics and the medical profession	12
Periodontitis and a systemic connection	18
Overview	18
Periodontitis and diabetes	20
Periodontitis and cardiovascular disease	28
Periodontitis and pre-term low birth weight (PTLBW) pregnancy outcomes	32
Biostatistical concepts and their application in the periodontics literature.....	35
Odds and risk ratios	35
The definition of periodontitis, odds ratios, and PTLBW	38
Periodontitis and other systemic conditions	40
How does periodontitis and systemic health literature affect one’s daily practice?..	42
CHAPTER 3: PURPOSE.....	44
CHAPTER 4: HYPOTHESIS.....	46
Hypothesis #1.....	46
Hypothesis #2.....	46
Other research question:	46
CHAPTER 5: SPECIFIC AIMS	47
Aim #1	47
Aim #2	47
Aim #3	47
CHAPTER 6: MATERIALS AND METHODS	48
Overview.....	48
Preparatory work.....	48
Instrument development.....	48
Instrument distribution.....	50
Data analysis	52
CHAPTER 7: RESULTS	53
Overview.....	53
Survey Development.....	54
Table 1: Demographic information (mean responses, except where indicated).....	57
Table 2: Attitudes, perceptions, and behaviors toward a “perio-systemic link” (mean responses).....	57
Table 3: Attitudes toward basic statistical knowledge (mean responses).....	58

Table 4: Assessment of basic statistical knowledge (mean responses)	59
Statistical analysis	60
CHAPTER 8: DISCUSSION.....	62
Overview.....	62
Survey Organization	63
Survey platform and social media publicity	64
Survey development and design	66
Limitations	70
Findings of interest	72
CHAPTER 9: CONCLUSIONS	78
REFERENCES	79

LIST OF TABLES

Table 1: Demographic information (mean responses, except where indicated)	58
Table 2: Attitudes, perceptions, and behaviors toward a “perio-systemic link” (mean responses).....	58
Table 3: Attitudes toward basic statistical knowledge (mean responses).....	59
Table 4: Assessment of basic statistical knowledge (mean responses).....	60

LIST OF FIGURES

Figure 1: Survey website with web link to Qualtrics web site, the administrator of the survey.....	52
Figure 2: The web-platform Qualtrics was used to administrate the survey. This image is from the mobile-device platform, noting the sliding bar feature to respond to survey questions.....	56
Figure 3: The Twitter page for the survey.....	65
Figure 4: The Facebook page for the survey.....	66

CHAPTER 1: INTRODUCTION

STATEMENT OF THE PROBLEM

The medical profession—including dentistry—interacts constantly with statistics. Evidence-based medicine and dentistry requires professionals to properly interpret any number of statistical concepts and subsequently apply such concepts to patient care. Clinical trials, retrospective studies, positive versus negative predictive values, odds ratios, and sensitivity *versus* specificity are just a few statistical concepts medical professionals need to understand in order to translate research into clinical care.

Competency with statistics and its interpretation has been an ongoing discussion in the medical literature. Proper understanding can start anywhere along the spectrum of research—from those engaged in conducting research with the objective of producing findings that can be published to those on the receiving end of such research who read and analyze the findings. It has been argued that medical research has a history of being inadequate due to flaws in design, sampling, analysis, and interpretation—leading to articles being published with poorly conducted research and professionals being unable to recognize flaws in research design (2,3).

Patients—those who are the consumers of medicine—generally can only trust that their health care providers adequately understand statistical concepts, ranging from basic to complex. When a health professional recommends a course of treatment, how can the patient be sure that the provider thoroughly understands research published on a particular drug or material? A breakdown in understanding can occur anywhere along the spectrum, from study design to interpretation of the results, and sometimes both.

In periodontics, clinicians must assess a broad literature base in order to develop a truly evidence-based practice. Beyond clinical practice, the periodontics community has shown great interest in the ongoing research concerning a connection between oral and systemic health. Many of the research publications exploring such a broad topic require clinicians to effectively analyze complex statistical relationships in order to accurately convey the state of an “oral-systemic link” or “perio-systemic link” to patients. Again, patients expect periodontists (and all dentists) to be the vanguard of their oral health, advising and treatment planning appropriately. To date, little has been done to assess how periodontal research translates into clinical practice. More studies are needed to assess the attitudes and perceptions of the dental community toward a potential connection between oral and systemic health, and how biostatistical knowledge may affect clinician perceptions or behavior.

CHAPTER 2: REVIEW OF THE LITERATURE

BIostatISTICS AND THE MEDICAL PROFESSION

For a profession so reliant on clinical trials dealing with pharmacological agents, biocompatible materials, and risk factors, medical professionals receive little graduate training in biostatistics, with exposure often limited to one course during their first or second year (96). With such limited training, one can see how medical journals can routinely publish articles with statistical flaws. One psychiatry journal found statistical errors in 40% of 164 articles (2,66). At the other end of the spectrum, newer research may be more intricately designed with increased sophistication in its methods; as such, a reader's knowledge of basic statistical concepts may not be adequate to sufficiently interpret and analyze newer innovations and approaches to medical research (74).

A relatively large, thoroughly designed and validated survey on medicine residents' understanding of biostatistics found that 75% of residents admitted to low confidence in understanding statistics in the medical literature; accordingly, this population, on average, answered less than 50% of statistics questions correctly (107). The authors found that knowledge scores declined with progression through training. Interestingly, 58% interpreted the meaning of a p-value correctly. However, an article published a year after the survey addressing misconceptions of p-value found that the original survey's question on p-value was actually phrased incorrectly, with none of the answer choices being correct (41), further illustrating the complexity and controversy of applied biostatistics. The survey also found that 87% of respondents identified the purpose of double blind studies correctly and 81% interpreted relative risk correctly—indicating a level of familiarity with certain basic statistical concepts.

Where understanding of statistical concepts starts to wane, for example, is often with the heavily relied upon p-value. Interestingly, the p-value is simultaneously one of the most commonly cited statistical terms and yet one of the most misunderstood (4,32,41). The purpose of the p-value—as introduced by RA Fisher—was to determine whether or not an experiment should be repeated if the calculated p-value falls below the arbitrarily threshold of 0.05. If repeated tests resulted in additional p-values below 0.05—“significant” values, in current parlance—one may conclude that the results are not the result of chance alone. However, the concept of the p-value became much more complex with the advent of hypothesis testing to include issues like acceptance, rejection, type I and II errors, and power (41).

Another statistical concept that is often misunderstood was highlighted during a continuing education seminar for gynecologists on risk communication. One hundred sixty gynecologists were asked to answer a question regarding positive predicative value (PPV) (37). The question was:

Assume you conduct breast cancer screening using mammography in a certain region. You know the follow information about the women in this region: the probability that a woman has breast cancer is 1% (prevalence); if a woman has breast cancer, the probability that she tests positive is 90% (sensitivity); and if a woman doesn't have breast cancer, the probability that she nevertheless tests positive is 9% (false-positive rate). A woman tests positive. She wants to know from you whether that means that she has breast cancer for sure, or what the chances are. What is the best answer?

- A. The probability that she has breast cancer is about 81%
- B. Out of 10 women with a positive mammogram, about 9 have breast cancer
- C. Out of 10 women with a positive mammogram, about 1 has breast cancer (correct answer)
- D. The probability that she has breast cancer is about 1%

Only 21% of respondents answered the question correctly (answer C). The majority overestimated the probability of cancer—47% selected A, 13% selected B—with an additional 19% underestimating its probability (D). The result of this test on PPV was included in a report from 2007 examining doctors and patients understanding of statistics (36). The authors argue that physicians do actually understand statistics, but statistics are often presented in a way that obfuscates their meaning. At the previously mentioned conference, the question on PPV was translated into “natural frequencies”—more intuitive vernacular, essentially—instead of presenting them as “conditional probabilities”—statistically technical jargon. The same 160 participants were presented the same scenario with the following information: “Ten out of every 1000 women have breast cancer; of these 10 women with breast cancer, 9 test positive; and of the 990 women without cancer, about 89 nevertheless test positive.” After translating the scenario into “natural frequencies,” 87% understood that 1 in 10 is the correct answer. Part of the problem with statistics is that its presentation can be complex to understand, not intuitive, and often misleading.

Concepts like absolute risk and relative risk can be confusing. The authors of the same article (36) cite a UK warning from 1995 on oral contraceptive pills in which it was reported that the risk of life-threatening blood clots increased by 100%. Technically, the report was correct—the relative increase was 100%; however, the absolute risk increase from second generation to third generation oral contraceptive pills went from 1 out of 7000 to 2 out of 7000. Yes, the third generation pill had a 100% relative increase in blood clots but an absolute risk increase of just one. Increases in absolute risk tend to be lower quantities while changes in relative risk are much larger (36). This nuanced distinction was not picked up by the UK Committee on Safety of Medicines or the British media, both of

whom made emergency announcements on the perceived “danger” of the third generation medication.

Additionally, the authors concede that patients often have difficulty understanding statistical concepts, but those same patients likely assume that physicians have the necessary understanding to provide appropriate guidance as subject matter experts. However, it has been shown that the ability to understand statistical concepts does not respect professions—physicians have just as much difficulty. Wegwarth argues that it falls upon physicians to understand potential harm and benefits that an intervention can cause and that “statistically illiterate physicians” often fall back on local treatment customs, poor conclusions, and sales pitches from pharmaceutical companies (105).

Another survey of 4713 obstetrics-gynecology residents highlighted statistical illiteracy among medical professionals (5). The survey consisted of a total of four questions—two questions inquiring about training in statistics, one question assessing knowledge of PPV modeled after the previously discussed question given to gynecologists (36), and one question assessing knowledge of the definition of p-value (“True or false: The p-value is the probability that the null hypothesis is correct”—the correct answer is false). Only 26% answered the question on PPV correctly, while 42% answered the p-value question correctly. Only 12% answered both questions correctly. Interestingly, those who answered the PPV question correctly tended to identify their training as much more inadequate than those who answered the question incorrectly.

In a nuanced report in the psychology literature that analyzed self-perception (56), the authors conducted a series of studies after which they asked the participants to self-assess their ability and test performance. The results showed that unskilled participants not

only performed poorly, but they failed to realize it—those in the bottom quartile of performance not only overestimated their abilities but thought they were above average. Interestingly, the report found that participants recognized their relative incompetence once they received training for their deficiencies and became competent. The authors found this paradoxical—after recognizing one’s own incompetence, they were no longer incompetent. On the other end of the spectrum, extremely competent individuals—those in the top quartile—tended to underestimate their ability and test performance relative to their peers. This underestimation was attributed to a failure to recognize that their proficiency is not shared by their peers—only after learning how poorly their peers performed did top-quartile performers raise their self-assessment to more accurate levels (56).

The findings from this psychology report, sometimes referred to as the Dunning-Kruger Effect (25), are of interest in light of the responses to a number of surveys conducted on medical professionals’ understanding of biostatistics. For example, the obstetrics-gynecology residents that answered the question on PPV correctly viewed their training as insufficient compared to those that answered the question incorrectly. Meanwhile, overconfidence with biostatistics was found with a survey assessing oral and maxillofacial surgery (OMS) residents (7).

The survey for OMS residents was modeled after the previously published survey (107) assessing medicine residents’ knowledge of biostatistics. Ninety-eight percent of OMS residents felt it is important to know something about statistics in order to read the literature intelligently, with 40% claiming to understand almost all statistical concepts they encounter. The mean OMS resident score on the six statistical methods questions was 38% compared to 51% for medicine residents, with 46% correctly identifying a p-value. The

authors found that higher levels of confidence were correlated with poorer levels of knowledge of biostatistics, exemplifying a component of the Dunning-Kruger Effect. Only 49% of OMS residents had taken a course in biostatistics, whereas more than 68% of medicine residents had some training in biostatistics; however, only 69% of medicine residents reported reading journals regularly versus 86% for OMS residents—perhaps indicating that while OMS residents reportedly read journals regularly, they may not understand fully what they read.

The findings from the OMS residents' survey were similar to those of the medicine residents' survey in that authors of both surveys found that residents lack sufficient knowledge of biostatistics to interpret the results of clinical research in the literature. Wegwarth commented that “statistically illiterate physicians are doomed to rely on their statistically illiterate conclusions, on local customs, and on the (mostly) inaccurate promises of pharmaceutical sales representatives and their leaflets. The price for this innumeracy is paid by patients who undergo medical procedures without being correctly informed of what to expect” (105). As an example of the problematic nature of complex statistical concepts, clinicians reading medical literature often skip more complicated sections of an article—such as materials and methods or results—and gravitate toward the abstract (96). Sections like the abstract, however, often don't have complete information, thus readers may be placing limitations on their own understanding (96).

In addition to the previously mentioned surveys, other specialties within medicine and dentistry have conducted surveys to analyze the extent of understanding of concepts of biostatistics within their respective fields (8,74,82,95). The general conclusion among these surveys is that while clinicians within a specialty often place high value or importance on

statistical knowledge, actual understanding of such concepts is lacking (95). As such, there is often a call to educators within the medical profession to better prepare students and young clinicians to understand statistical methodology beyond elementary statistical coursework, which is often limited to one or two classes (96). While demanding change often meets little resistance, actual implementation or functional suggestions seem to be lacking.

PERIODONTITIS AND A SYSTEMIC CONNECTION

Overview

Recent studies have reported the prevalence of periodontitis in the United States to be 45.9% for those aged 30 and older (27). Due to this high prevalence of periodontitis, the dental field has spent considerable time and energy studying potential risk factors to identify susceptible patients. For example, periodontitis has shown a predilection for males, advanced age, Hispanics, non-Hispanic blacks, and those in lower socio-economic status (27). Many of these groups are also at risk for systemic disease, and in which some of the first literature to publish on a potential link between periodontitis and cardiovascular disease emerged in the late 1980s. Authors from Finland published a report finding that patients with acute myocardial infarction had worse dental health than controls matched for age and sex, also highlighting that those with dental disease and ischemic heart disease often share characteristics of low-socioeconomic status, smoking, diabetes, and insulin resistance (65). Articles such as this from the late 1980s inspired a flurry of literature from that time up to the present day investigating the association between oral health and systemic health.

Major areas of research have focused on periodontitis and its relation to a number of diseases, with the common ones often being diabetes mellitus, cardiovascular disease, and pre-term low birth weight pregnancy outcomes. The issue with studying—and more specifically trying to establish a connection between—oral and systemic health, coupled with trying to link treatment of periodontal disease with improved systemic health, is the difficulty in conducting prospective (also termed cohort or longitudinal) studies in which the results of treatment or some other intervention are not known until sometime after the intervention. Also, prospective studies can be used to follow what occurs to a patient after receiving a particular treatment or after exposure to a risk factor (104). Examples of prospective studies in the periodontics literature include the Nebraska and Washington studies—which followed patients longitudinally for several years after receiving periodontal treatment—and found osseous surgery produced the greatest probing depth reduction for deeper pockets (49,77). Some recent studies have attempted to demonstrate prospectively that nonsurgical periodontal treatment affects hemoglobin A1C levels (HbA1C) in diabetics (17,29,30,81).

Although powerful, the general difficulty with prospective studies is ethical in nature—one cannot induce chronic kidney disease or diabetes in a person with periodontitis to assess how these systemic diseases affect their periodontal status, nor can one induce periodontitis in a pregnant woman in an effort to assess the influence of periodontitis on pre-term low birth weight. Additionally, if one develops a disease, it must be treated immediately. Furthermore, such studies can often require many years to complete and are typically very expensive.

While many research groups are trying to study potential links or commonalities

between oral and systemic disease—some authors have even referenced ancient Greece and Hippocrates, who in 400 BC allegedly relieved joint pain after extracting teeth (28)—the problems of conducting prospective studies has forced researchers down the avenues of retrospective (case control) and cross-sectional (prevalence) studies. An example of a cross-sectional study is a relatively recent publication investigating an association between erectile dysfunction and periodontitis (90), in which the authors appeared to be drawn to several shared risk factors between the diseases, such as smoking, diabetes, and cardiovascular disease. The authors found the prevalence of chronic periodontitis was highest among those with severe erectile dysfunction; they also found a positive correlation between the two diseases but with no statistical significance. Studies like these seemingly add little to the oral-systemic link conversation as the authors concede the pathways of vasculogenic erectile dysfunction and chronic periodontitis are complex but necessitate further investigation and longitudinal follow up. Articles such as this one highlight shared characteristics, but the analysis essentially stops there without additional follow up or meaning beyond simple observed commonalities.

Periodontitis and diabetes

Diabetes has long been studied by dental researchers for associations with periodontal health and disease. The interest in a link between the two stems from inflammatory pathways central to the pathophysiology of both diseases. Inflammation precedes the onset of diabetes, leading to pancreatic beta-cell dysfunction, apoptosis, insulin resistance, and diabetes. Periodontal disease, in comparison, is a chronic inflammatory condition in which immune and inflammatory processes are regulated poorly,

leading to host tissue destruction and tooth loss (80). In general, the diabetes and periodontitis literature has made broad assertions that systemic inflammation is at least in part due to oral microbial agents and their virulence factors entering the circulation, with elevated serum C-reactive protein and biomarkers of oxidative stress being evidence of this oral-systemic relationship (19). As such, this has led to conclusions that it is “therefore biologically plausible” that chronic inflammation due to periodontitis increases the risk of developing diabetes and that periodontal inflammatory pathways can affect diabetes control (HbA1C levels), beta-cell function, insulin resistance, and type-2 diabetes (19).

However, the majority of reports regarding periodontitis and diabetes are cross-sectional, analyzing the proportions of individuals with periodontal disease between those with and without diabetes. The bulk of the studies reporting on the prevalence of periodontal disease conclude that the prevalence is greater in who those who have diabetes, and that those with diabetes are more likely to have deeper periodontal pockets and greater attachment loss than those without diabetes (33). For example, the Pima Indian community in Arizona has a strikingly high prevalence of non-insulin dependent diabetes mellitus (NIDDM)—approximately 50% above age 35 are affected (54). Interestingly, a cross-sectional study of this Indian population found that Pima Indians with diabetes had a higher prevalence of periodontitis than those without diabetes across all age groups (91), while a separate longitudinal study found that periodontitis incidence was 2.6 times greater in Pima Indians with diabetes than those without diabetes (71).

A population like the Pima Indians highlights the dilemma of the oral health and systemic health literature. Is the relationship between diabetes and periodontitis nothing more than a simple association with some shared pathologic characteristics? Or is the

relationship between the two causal? Is there an underlying socioeconomic factor, such as poor diet, that predisposes to both diseases, coupled with genetic influences? If the periodontitis is treated, will that affect the diabetic status? These questions may be interrelated, but they may be mutually exclusive; and the distinctions may be subtle and nuanced. As such, there have been reports in the periodontitis literature of attempting to show that treatment of periodontal disease will lead to a decrease in HbA1C levels. (This assumes that periodontal disease affects diabetes and poses the question of directionality, even with a causal relationship—it could also be that diabetes may increase the susceptibility of developing periodontal disease.)

In 1997, a group published a report titled “Treatment of periodontal disease in diabetes reduces glycated hemoglobin” in which the authors assessed HbA1C levels among Pima Indians after nonsurgical periodontal therapy combined with concomitant antimicrobial therapy consisting of water-doxycycline, chlorhexidine-doxycycline, iodine-doxycycline, chlorhexidine-placebo, or water-placebo (control) (43). With diabetes and periodontitis showing a historical link among Pima Indians, the authors of this randomized controlled trial found that nonsurgical periodontal treatment with accompanying antimicrobial therapy reduced HbA1C levels by 0.94% in the water/doxycycline group and by 0.51% in both the chlorhexidine/doxycycline and iodine/doxycycline groups at 3 months. These reductions were reported as significant. The chlorhexidine/placebo and the water-placebo group showed no significant changes. A nuanced look at the data shows, however, that at baseline all four tests groups had HbA1C levels in excess of 10%. At three months there was a reduction to levels below 10% in three of the four test groups, but at six months in these same three groups HbA1C levels returned to baseline levels. The only group to

show a continued reduction in HbA1C at three and six months was the chlorhexidine-placebo group, but even then it was still above 10%.

Interpretation of these findings is difficult. Perhaps the authors hoped to find periodontal treatment would definitively affect diabetic control in a substantial way, but it is difficult to extrapolate clinical significance with reduction of HbA1C levels above 10% to levels above 9%. Additionally, the average HbA1C reduction across the three doxycycline groups was 0.65%, making it unclear if this reduction was due to the antibiotic or the nonsurgical therapy. The more logical conclusions may be that the subjects' lifestyle predisposes to both diabetes and periodontitis without a causal relationship, or that the diabetic dysregulation increases a predisposition to periodontal disease with nonsurgical periodontal therapy necessary to maintain periodontal health. Regardless of their conclusions, the results seemed to have a level of promise for the authors at three months, but any gain was subsequently lost at six months. The greatest affect the treatment provided seemed to be on the subjects' periodontal disease, rather than their diabetic control. The percent of patients positive for *Porphyromonas gingivalis*—an organism strongly associated with periodontal disease and considered a potential periodontal pathogen—before treatment ranged from 43% to 71%. At three months, *P. gingivalis* was below detectable levels in all patients in the water/doxycycline and chlorhexidine/doxycycline groups, while *P. gingivalis* in the iodine/doxycycline, chlorhexidine/placebo, and water/placebo groups was at 16%, 17%, and 22%, respectively.

A 2013 systematic review analyzed evidence for the effects of periodontal disease on diabetes control, complications, and incidence (9). The authors found that current evidence for any effects of periodontal disease on glycemic control is limited, but when

compared to those with periodontal health, those with poor periodontal status and type-2 diabetes or no diabetes have greater risk for developing poorer glycemic control. Also, those with poor periodontal health and type-1 or type-2 diabetes have a greater risk for diabetes-related complications. In a repeated theme throughout periodontitis-diabetes literature, the authors implore that large-scale, long-term studies across multiple populations are necessary to establish definitive evidence that periodontal disease has an adverse effect on glycemic control (9).

This systematic review acknowledges a relationship between poor periodontal health and diabetes but does not establish a definitive causality. The review was utilized by the European Federation of Periodontology (EFP) and the American Academy of Periodontology (AAP) consensus report on periodontitis and systemic diseases as “evidence for directional associations between periodontal diseases and diabetes” (19). However, the significance or meaning of “directional association” is unclear. This same consensus report also cites a different 2013 review that found beneficial effects of nonsurgical periodontal treatment on diabetes outcomes but fails to acknowledge the results of the follow-up randomized clinical trial to this particular review (29,30) Proof-of-principle or biologic plausibility is not the same as clinically relevant. A frank discussion of effect size is warranted, with the burden of proof on those implying causality.

In 2013, Engebretson’s group conducted a systemic review and meta-analysis on the effect of periodontal treatment on diabetes outcomes (30). The authors looked at previous reports that conducted nonsurgical periodontal treatment with or without adjunctive topical or systemic antibiotics and/or topical antiseptics; one study included surgical therapy. They found a statistically significant weighted mean difference of 0.36%

HbA1C reduction in the treatment group. This value of -0.36% HbA1C was comparable, per the authors, to two systematic reviews from 2010 that found mean values of -0.40% (98) and -0.40% (93). Again, the authors were unable to make clinical recommendations, citing a lack of large prospective clinical trials.

Also in 2013, Engebretson conducted a randomized clinical trial to determine if nonsurgical periodontal treatment reduces levels of HbA1C in persons with type-2 diabetes and moderate to advanced chronic periodontitis (29). This trial—termed the Diabetes and Periodontal Therapy Trial (DPTT)—was a single-masked, multicenter, randomized clinical trial that enrolled patients from outpatient medical and dental clinics and communities of five academic medical centers in the United States. A total of 514 patients participated—half in the test group, half in the control group—with HbA1C values between 7% and 9% and moderate to advanced chronic periodontitis. The test group received scaling and root planing at baseline and at three and six months with oral hygiene instructions, while the control group received only oral hygiene instructions at the same time frames. After six months, the control group was offered scaling and root planing. The target six-month reduction of HbA1C was 0.6% or greater. At the time of the study, the DPTT was the largest multicenter randomized clinical trial to investigate the effect of periodontal therapy on glycemic control, per the authors' knowledge.

The study was stopped because at six months, mean HbA1C levels in the test group had increased 0.17%, compared with 0.11% in the control group. At six months, periodontal measures had improved in the treatment group compared with the control group. The authors concluded that nonsurgical periodontal therapy did not improve HbA1C in patients with type-2 diabetes and moderate to advanced chronic periodontitis.

Additionally, they do not support nonsurgical periodontal treatment in patients with diabetes for the purpose of lowering levels of HbA1C. The strength of the study stems from adequate statistical power from the sample size (n=514) and that the study population was geographically and ethnically diverse. A previous trial with a large sample size (n=157) found a statistically significant reduction in HbA1C at 0.36% at three months compared to controls (94). However, another trial also with a large sample size (n=165) failed to show a positive effect on glycemic control (48), mirroring the 2013 findings. Limitations of the study may be that the HbA1C range was limited to 7% to 9%, giving rise to the thought that patients outside this range may experience changes in HbA1C; additionally, systemic antibiotics were not employed.

As research regarding periodontitis and systemic health—diabetes, in particular—is largely confined to observational studies such as cohort (prospective or longitudinal), case-control (retrospective), or cross-sectional (prevalence) studies, it is rare when a randomized clinical trial with adequate power is completed. Interestingly, the results of this study sparked controversy among the research community. For example, a guest editorial was published in JADA in 2014 (81) to counter some of the dissenting opinions regarding Engebretson’s clinical trial, likely due to the unexpected negative findings. One such dissenting opinion was published as a letter to the editor of JAMA and was written by Chappelle, Borgnakke, and Genco (18)—Chappelle and Genco wrote the consensus report of the EFP/AAP on diabetes and periodontal disease (19)—while Borgnakke was the primary author on the 2013 systematic review regarding diabetes and periodontitis (9). They argued that Engebretson should have included patients with HbA1C levels beyond 9% (mean HbA1C was 7.8%) since a range of 7-9% is close to therapeutic levels; as such, it would be

unlikely that patients in this range would experience much change. They also argued, irrespective of the patients' diabetic conditions, that the trial failed to show adequate periodontal improvement (18).

The guest editorial by Philstrom (81) argued that patients with type-2 diabetes with HbA1C levels higher than 9% and a BMI of less than 30 are rare and states that Engebretson's results should be viewed as generalizable because the "participant sample was typical of patients with diabetes both in terms of HbA1C and obesity." Other concerns beyond pre-treatment HbA1C levels included inadequate periodontal therapy, obesity masking a decrease in inflammatory response, and lack of antimicrobials. These concerns were addressed by Engebretson, however, in the study itself and in subsequent replies to letters to the editor in JAMA. Engebretson counters that periodontal improvements were similar to improvements reported in other multicenter trials involving similar treatments (16,106) and that systemic antibiotics were not indicated because patients were not immunocompromised nor at a greater risk for infections following periodontal treatment.

The pushback toward this randomized clinical trial can be interpreted as somewhat puzzling when viewed in the light of several reports arguing for studies that are larger, more diverse, and longer in duration to adequately assess the effects of periodontal treatment on HbA1C in diabetic patients (9,19,48). While it seems clear that periodontal treatment will affect the periodontal status of diabetics positively, the urge to conclude that nonsurgical periodontal therapy will consistently or reliably affect HbA1C seems somewhat forward, considering studies reporting a benefit are looking at improvement in the range of -0.4. One might argue, however, that a hypothetical improvement from 6.8 to 6.4 or from 6.0 to 5.6 may be clinically meaningful. In some cases, a reduction of 0.4 has

been found to be statistically significant, but the clinical value may be seen as questionable—such as, how reliant should one be on periodontal treatment for a reduction in HbA1C. Philstrom makes the point that *“to urge censorship of the results of a well-designed and executed clinical trial is contrary to the values of academic research and its foundation of ethical open inquiry, transparency, publication, and dissemination of knowledge that must be considered by those who make health care decisions”* (81). It does not seem inappropriate to consider motivations—perhaps reputations, publications, and/or money in marketing periodontal treatment—to minimize the finding of a trial such as this one. Philstrom concludes his editorial by making the point that nonsurgical periodontal treatment should be delivered for the purpose of treatment periodontal disease and not for improving glycemic control in type-2 diabetic patients (81).

In light of this clinical trial and the subsequent opinions it fostered, it becomes clear that motives are complex. Clinicians should take care to avoid accepting any one study as absolute fact and must be able to carefully discern the meaning of a study’s data. It seems less than prudent to take an author’s conclusions at face value; rather, a clinician must possess a somewhat sophisticated appreciation of the publication process and the statistical analysis underlying complex data.

Periodontitis and cardiovascular disease

As with diabetes, much of the literature with periodontitis and atherosclerotic vascular disease (ASVD)—also termed atherosclerotic cardiovascular disease (ACVD)—emphasizes the role of periodontitis as a chronic inflammatory disease, leading to the entry of bacteria into the bloodstream and having effects on distant organs. For example, the

EFP/AAP consensus report lists periodontitis having a “possible impact on general health” (99) and rests its laurels on the “most biologically plausible” explanation for the relationship between periodontitis and ACVD by referencing review articles that offer the explanation of bacteria and/or their products from periodontitis entering the bloodstream and activating inflammatory pathways favoring atheroma formation, maturation, and exacerbation (84,88). Biologic plausibility is only a starting point and may not mimic reality in a complex system such as the human body. In addition, the question of effect size still remains.

The EFP/AAP consensus reports also hinges on what the authors deem “epidemiological evidence” of a relationship between periodontitis and ACVD, which was reported in a systematic review that found “positive associations” between the two diseases (23) by analyzing cohort and case-control studies for associations of clinical or radiographically diagnosed periodontitis and ACVD . The review looked at reports of incident ACVD, including coronary heart disease (CHD), cerebrovascular disease, and peripheral arterial disease. This review is of interest for the amount of detail the authors go into toward reviewing the literature, observation study design, and variation among categorizing periodontal disease.

The review concluded that there is an increased risk of ACVD in patients with periodontitis compared to patients without periodontitis but not necessarily for all groups of the population (23). Importantly, the authors stress that over the past decade the debate has been whether or not the relationship between ACVD and periodontitis is causal; more specifically, if treatment of periodontitis will reduce the risk of cardiovascular events. The authors acknowledge causality can only be determined via randomized controlled clinical

trials and recognize that the low incidence of ACVD in the general population implies that any trial would be among a population with an existing high absolute risk (23).

The allure of a link between periodontitis and a systemic disease, such as ACVD, is the shared inflammatory pathways, with the thought being that inflammatory processes of two separate diseases must share something in common, hence the desire to determine if the relationship is in any way causal. One of the commonly measured and analyzed biomarkers with ACVD and periodontitis is C-reactive protein (CRP), a biomarker of systemic inflammation. Prospective epidemiological studies of individuals without prior history of ACVD have shown that a single non-fasting measure of CRP is a predictor of future vascular events, like stroke, myocardial infarction, and sudden cardiac death (50). Periodontitis is also associated with elevated systemic inflammatory biomarkers, such as CRP, tumor necrosis factor-alpha, IL-6, and IL-8 (61). There has been thought that CRP is a byproduct of the periodontitis lesion, but what has not been determined is if these local levels have a systemic effect (63).

A report was put out by the American Heart Association (AHA) in 2012 to address the association between periodontitis and ACVD. The AHA report also discussed several common risk factors between periodontitis and ACVD, such as smoking, age, and diabetes; furthermore, the report highlights the role of provider expectations and patient education in the relationship (59). This effect can be seen with a simple Google search for periodontitis in Philadelphia, which brought up a web site advertising that “studies have shown a strong link between periodontal disease—even in its early stages—and serious systemic diseases such as heart disease, stroke, diabetes, pre-term low birth weight, cancer, brain abscesses and pneumonia” (58). Another Philadelphia periodontist listed the following on its website:

“Gum disease, or periodontitis, is an epidemic in America that not only affects the health of the teeth and jaw, but is linked to heart disease, diabetes, strokes, and many other systemic health problems” (13). While this latter quote is technically correct, one may argue that it implies causality with words like “epidemic” and “linked” and that periodontal therapy will have a positive effect on systemic conditions.

The AHA’s exhaustive report examined associations between the diseases. It acknowledges a high prevalence of the diseases, but cautions that even with an association between the two, that such information is predominantly derived from observational studies. As such, the association does not demonstrate that periodontitis causes ACVD, nor does it indicate that periodontal therapy prevents heart disease or modify the clinical course of ACVD (59). The AHA report asserts that “statements that imply a causative association between periodontal disease (PD) and specific ASVD events or claim that therapeutic interventions may be useful on the basis of that assumption are unwarranted” (59).

As such, the oral and systemic health literature eventually circles back to its fundamental problem: research is constrained by observational studies that allow for associations to be determined but not so much for causality. Interestingly, the EFP/AAP consensus report concluded, nevertheless, that “there is consistent and strong epidemiologic evidence that periodontitis imparts increased risk for ACVD” (99), while an extensive review of the literature in 2010 reported the continued need for clinical trials to determine if periodontal therapy has a role in preventing cardiovascular events (52).

The arguable crown jewel of the periodontitis and ACVD literature is a pilot study titled “Periodontitis and Vascular Events” (PAVE). In this pilot study, periodontal therapy was executed and then followed by an evaluation of subsequent periodontal status and

systemic levels of CRP as a means to observe prevention of cardiovascular events (6,22,75). The hypothesis was that the intensive treatment group (scaling and root planing with oral hygiene instructions) would have reduced periodontal parameters while simultaneously lowering CRP and GCF IL-1 beta levels compared to the community care group (oral hygiene instructions and a letter of referral to seek periodontal treatment). After six months, there was a significant reduction in mean probing depths; additionally, using intent-to-treat analyses, there was no significant effect on serum CRP at six months. While the authors found that any consideration of treatment versus no treatment showed a significant reduction in the percentage of people with elevated CRP at six months, this reduction was nullified in obese patients (75). What the study clearly showed, however, was that there were significant improvements in periodontal health at six months for those who received periodontal treatment compared to community care.

One may assume that the interest for nonsurgical periodontal therapy to extend its reach beyond simply improving one's periodontal condition to having an influence on systemic pathways is well intentioned. The connections are, indeed, interesting and warrant future investigation. As is the case with the randomized trial with diabetes, the randomized trial with ACVD does not provide any clear systemic benefit to nonsurgical periodontal therapy. The AHA report refutes the idea that periodontitis causes heart disease or that treatment of periodontal disease prevents heart disease (59).

Periodontitis and pre-term low birth weight (PTLBW) pregnancy outcomes

As with periodontitis and cardiovascular disease, the association between periodontitis and PTLBW is muddled, with professionals further clouding the meaning of the association. For example, a Philadelphia periodontist promotes that treatment of

periodontitis can reduce periodontitis-related pregnancy complications, which are listed as “preeclampsia, or low weight of the baby, as well as premature birth... by up to 50%” and that bacteria from periodontitis can enter the bloodstream and cause the liver to produce extra CRP with studies having “overwhelmingly proven that an extremely high rates (sic) of CRP in early pregnancy definitely increases the risk [of preeclampsia]” (92). These anecdotal quotes from websites should highlight the importance of periodontists’ professional message to their patients. Distinguishing between facts and fear-based advertising can be difficult and controversial.

Part of the difficulty with the literature regarding periodontitis and PTLBW is that its significance or meaning is buried in difficult to interpret statistical measures. Risk factors for PTLBW include but are not limited to smoking, alcohol, black race, low socioeconomic status, high maternal body mass index, stress, and previous pre-term birth (24,38); several of these are also risk factors for periodontitis (27,64). The hypothetical mechanism of action for a link between periodontitis and PTLBW argues that infections are an important cause of pre-term birth with 50% of spontaneous pre-term births associated with ascending genital tract infections (60). Bacteria within the uterus may lead to a pro-inflammatory response causing production of substances such as cytokines and prostaglandins, leading to smooth muscle contraction. The idea of infection and its role in pre-term pregnancies (39) may have been the impetus for literature that emerged in the mid- to late-1990s regarding a potential association between periodontitis and pre-term birth (76), but the preciseness of the relationship is murky. Some theories (34) behind the purported relationship include the idea that women with periodontitis may experience more frequent and severe bacteremias than periodontally health women, increasing the chance of

uterine exposure to oral bacteria and their by-products; once bacteria reach the uterus, an inflammatory cascade is initiated. Additionally, cytokines produced in the periodontium may enter the systemic circulation and promote systemic inflammation, leading to pre-term birth.

This potential association was first reported in 1996 in a case-control (retrospective) study looking at periodontal status and PTLBW (76). The number of women in the study was 124 with 90% of them having their periodontal status assessed within three days of birth. Pregnancy status was categorized into cases and controls for two groups of mothers—all mothers and primiparous mothers. The 93 PTLBW cases for all mothers had a mean clinical attachment level (CAL) of 3.10 mm/site, while the 31 normal birth weight (NBW) (control) cases for all mothers had a mean CAL of 2.80 mm/sites. The mean CAL for primiparous-PTLBW cases was 2.98 mm/site, while the mean CAL for primiparous-NBW control cases was 2.56 mm/site. The authors defined periodontal disease as at least a CAL of 3 mm at a minimum of 60% of sites.

A lack of consensus within the periodontics community on a precise definition of periodontal disease creates an additional barrier to interpretable research. Michalowicz, in his 2013 review of periodontitis and PTLBW, concluded that “it is not possible to identify from the existing literature a disease definition that is consistently and strongly associated with preterm birth risk that could be used to define eligibility in future RCTs” (66). Offenbacher and his group concede that they were using CAL as a means to describe prior “evidence of disease” but CAL’s utility comes from measurements taken at different points in time to monitor disease progression or loss of attachment. A simple measure of CAL at a

single point in time only demonstrates the current level of attachment for that particular moment and does not indicate current disease activity.

Offenbacher and his group claim that “periodontal disease is a statistically significant risk factor for PTLBW with adjusted odds ratios of 7.9 and 7.5 for all PTLBW cases and PTLBW, respectively.” Further conclusions are drawn by utilizing an odds ratio of 7.5 against an incidence of 10% for all cases of pre-term low birth weight, setting a risk difference of 18.2% (risk of PTLBW attributable to periodontal disease). Further extrapolation leads to a conclusion that of 250,000 cases of PTLBW annually, approximately 45,000 of those are attributable to periodontitis, presumably if periodontitis is defined as a CAL of 3 mm on at least 60% of sites. The statistical analysis by Offenbacher becomes quite detailed—referencing complex statistical equations to correlate odds ratios with relative risk to establish attributable risk (54) that are beyond the scope of this thesis. This leads to a discussion of odds ratios and their meaning, especially as they correlate with periodontitis and PTLBW.

BIostatistical Concepts and Their Application in the Periodontics Literature

Odds and risk ratios

Odds ratios are difficult to interpret and have been acknowledged as such in the medical literature (1,42,44). Clinicians often think in terms of probability, which is the proportion—or percentage—of times an event would happen if an observation were repeated many times, and thus values range from 0 (never) to 1.0 (always). Or, in a medical context, the number of times a disease occurs divided by the number of times it could potentially occur. This can also be thought of as risk. The next level of analysis after

probability is the relative risk—expressed as a ratio of probabilities from zero to infinity and utilized in longitudinal studies. Relative risk is calculated by taking the probability of outcome in those exposed divided by the probability of the outcome in those not exposed (42). Relative risk expresses how much risk has increased or decreased from an initial level (1) and is thought of as relatively straight forward to understand (51).

An interesting misinterpretation, however, of risk statement is highlighted by Gigerenzer (35) in which he reported a psychiatrist was advising patients that 30-50% of the time sexual problems occur when taking fluoxetine. Patients were interpreting this to mean that when on the drug, 30-50% of their sexual encounters would result in dysfunction, whereas the clinician meant that out of every ten patients taking this drug, 3-5 of them would experience problems. While this example shows how easily statistics can be misinterpreted; once clarified, risk is a relatively straightforward concept.

Risk differs from odds, which are less intuitive and more readily used in gambling. Odds are expressed as a proportion, ranging from zero to infinity, and are expressed as the probability of an event happening divided by the probability of the event not happening (42). In medicine, odds are the number of people experiencing an event divided by those that do not—meaning that the numerator is the same as in probability (risk) but the denominator differs in that it is the number of cases without the outcome and not the total cases (1,44). For example, if attempting to roll a three on a single dice roll, the odds are 1/5—one roll of a three for every five other rolls. Where the confusion with odds stems from is with the use of the odds ratio, which is the odds of the exposed group divided by the odds in the unexposed group. Odds ratios are thought of as less intuitive without a simple interpretation, except when its value is similar to that of relative risk (44).

When conditions are rare, risk and odds ratios are about equal. When the proportion starts to rise, however, the values diverge and the meaning or value of odds ratios can become muddled. In a study that compared the knowledge of members of the National Psoriasis Foundation versus non-members regarding the drug calcipotriene, an odds ratio of 24 was reported, implying that members were more than 20-times more likely to know of the drug; meanwhile, the risk ratio was much more modest at 3.5 (1,72). Odds ratios are useful because they can be used in case-control or retrospective studies, such as with periodontitis and systemic health literature. The coefficients of logistical regression models—statistical concepts that are common for case-control data—can be converted into odds ratios; there may be situations when an odds ratio make more sense than relative risk, such as when both values are close to one—but more often than not people think in terms of risk ratios (44). (Zhang and Yu proposed a formula for approximating relative risk from an odds ratio [109].)

Case-control or retrospective studies, for example, have a numerator (cases) but no denominator as with longitudinal studies. As such, retrospective studies cannot determine rates and relative risks. Instead, reports compare the frequency of exposure among cases with the frequency of exposure among controls, such as with the study by Offenbacher in which he compared cases of pre-term low birth for mothers with his definition of periodontitis versus cases of normal birth for mothers without his definition of periodontitis. The odds ratio thus serves as a substitute for relative risk ratios. Odds ratios are also common in meta-analysis, which aggregates research studies to increase power to discover differences (42). Odds ratios serve a means to an end, but their value can be misleading as reports have found differences between odds and risk ratios greater than

20%, magnifying the effects of odds ratios compared to risk ratios (44). Up to 26% of articles interpreted odds ratios as if they were risk ratios (44).

Returning to Offenbacher's article, what does an odds ratio of 7.5 mean? While clearly demonstrating an association, the data utilized stems from retrospective studies. Extrapolating that treatment of periodontal disease could have an effect on 45,000 cases of pre-term birth is an interesting figure. Offenbacher's article is just one analysis on the potential detrimental effect of periodontitis on pregnancy and has been analyzed at length to highlight the inherent difficulty in understanding the specific literature relating to this topic.

The definition of periodontitis, odds ratios, and PTLBW

With this backdrop of odds ratios, it is apropos to revisit the definition of periodontitis as it relates to PTLBW. Manau analyzed the definition of periodontitis at length (64), finding that varying definitions of periodontitis influenced the statistical findings. The review utilized 14 definitions of periodontitis and at least 50 continuous clinical measurements of periodontitis. The detailed analysis looked at 1296 women and found that six of the 14 definitions had statistically significant adjusted odds ratios for some pregnancy outcomes, such as pre-term birth, low birth weight, and PTLBW. No significance was found with the other eight definitions. Out of more than 50 continuous measurements, only 17 showed statistically significant odds ratios with CAL being the measurement that often showed statistical significance (10,34,62,108). Manau concluded that the association between periodontitis and adverse pregnancy outcomes may be influenced by periodontal disease definitions or measurements used. Manau also found

periodontitis associated with adverse pregnancy was not limited to “pre-term low birth weight” but to various adverse pregnancy outcomes (64).

A systematic review by Ide and Papapanou (46) also analyzed how the definition of periodontitis influenced statistical conclusions with pregnancy outcomes. They found periodontitis is “modestly but significantly associated” with low birth weight and preterm birth; however, findings are impacted by periodontitis case definitions and that composite outcome “pre-term low birth weight” should be discontinued. Michalowicz (67) also recommends unified disease definitions for periodontitis and looked at the influence of periodontal treatment on adverse pregnancy outcomes. While Michalowicz acknowledges that associations have been found (46), mechanisms remain largely unclear and the literature contains a host of problematic elements including but not limited to: 1) undefined periodontal disease extent or severity influence on adverse pregnancy outcomes; 2) evidence outlining evidence-based definitive clinical endpoints of periodontal treatment that result in little or no increased risk for adverse outcomes; and 3) lack of randomized trials providing periodontal treatment to women planning on becoming pregnant. Additionally, Michalowicz makes the point that existing randomized controlled trials indicate that periodontal therapy early in pregnancy does not alter rates of preterm birth or low birthweight and that meta-analyses restricted to high-quality or low-bias randomized controlled trials have shown odds ratios of 1.05 and 1.15 favoring no treatment (17,83,102).

One of the studies analyzed by Michalowicz analyzed 11 trials with over 6500 women, looking at pregnant women with periodontitis that were randomized to either treatment with scaling and root planing or no treatment (80). Five of the trials were

considered high quality (low risk of bias), while the rest were considered low quality (high risk of bias). The high quality studies showed treatment had no significant effect on overall rate of preterm birth (odds ratio 1.15) and did not reduce the rate of low birthweight infants (OR 1.07), spontaneous abortions/stillbirths (0.79), or overall adverse pregnancy outcomes (1.09). This review concluded that while periodontal treatment is necessary to maintain periodontal status, women should be told that periodontal treatment during pregnancy is unlikely to reduce risk of pre-term birth or low-birth weight infants (80).

Periodontitis and other systemic conditions

The issues with diabetes, cardiovascular disease, and adverse pregnancy outcomes in relation to periodontitis are just three examples of the dental literature attempting to establish associations between periodontitis and systemic disease. Numerous other diseases have been examined. A case-control report on periodontitis and asthma claimed that “periodontitis influenced severe asthma” due to an adjusted odds ratio of 4.82 (40). The authors also softened their claim by stating their findings “suggest an influence of periodontitis on partially controlled severe asthma” and ultimately call on prospective studies and randomized controlled trials to “better test” and “clarify the biological mechanism” between periodontitis and asthma. While this report is of interest for the potential association between periodontitis and asthma, it is one that relies on a retrospective analysis utilizing odds ratios that seem to imply relative risk. In addition, periodontitis has not only been associated with asthma, but additional reports have been done analyzing dementia, hepatitis, obstructive sleep apnea, rheumatoid arthritis, chronic kidney disease, and even pancreatic cancer (47,68,70,73,78,79,103).

With a vast amount of literature on various systemic conditions and their

relationship to periodontitis, it leaves the clinician to make difficult decisions on behalf of the patients, such as how to inform them of potential oral and systemic health connections. A simple Google search of regional periodontists brought up a web site making the following claim: “Recent research highly suggests the correlation between the bacteria of periodontal disease and systemic risks such as cardiovascular disease, diabetes, stroke, pre-term deliveries for expecting mothers, Alzheimer’s disease, and most recently pancreatic cancer. With this research in mind, periodontal surgery can also dramatically improve and support your overall health!” (26). Framing periodontal surgery as beneficial for prevention of diseases such as Alzheimer’s seems somewhat exaggerated.

As for pancreatic cancer, an association with periodontitis has been explored to a limited extent in the literature (45,68,69). The caché of associating pancreatic cancer with periodontitis has its allure as less than half survive after six months from initial diagnosis with 40,000 deaths annually (97). Colgate promotes the association with a summary of a 2013 article (68) analyzing the purported association on its company website (20). The 2013 report by Michaud and his group utilized a large European database of collected blood samples from over 380,000 participants whose cancer status was tracked over several years. The group identified 578 incident cases of pancreatic cancer with 468 of these cases having a blood specimen. After analyzing for sufficient volume and assay success, 405 cases of pancreatic cancer were analyzed against 416 controls. Antibodies to *Aggregatibacter actinomycetemcomitans*, *P. gingivalis*, and *Tannerella forsythia* were then analyzed with a strain of *P. gingivalis* (ATTC 53978) having the highest concentration. The authors found an odds ratio of 2.14 for this strain and reported a “two fold increase risk of pancreatic cancer.” They additionally found that those with high levels of antibodies to

common oral bacteria had a 45% lower risk of pancreatic cancer compared to those with lower antibody levels. These conclusions seem to contradict each other, leaving one to speculate on the importance of these findings. Certainly promoting a “two fold increase” may catch the attention of patients, but it causes one to ask what it means practically for both patients and clinicians. For example, does periodontitis cause pancreatic cancer? Would scaling and root planing on a person with CALs of 4 mm reduce the chance of being diagnosed with pancreatic cancer? What about the asthma report that had an odds ratio of 4.82, or Offenbacher’s report on PTLBW that had an odds ratio of 7.5? In case-control studies, the percentage of cases does not reflect the risk (baseline prevalence) of the population but the design chosen by the investigators (1).

How does periodontitis and systemic health literature affect one’s daily practice?

The overall complexity of this body of literature makes its interpretation suited for biostatisticians of the highest caliber. The average periodontist could be forgiven for finding the contradictory and nuanced literature confusing. And yet, the clinician is responsible for processing the literature and providing evidence-based recommendations to the patients who rely on their professional expertise. The flurry of periodontitis and systemic health literature, coupled with statements by professionals on their practice websites about the risk of untreated periodontitis on systemic disease, spurred interest to investigate on a broad scale how dental professionals incorporate such information into their daily practices. In particular, how do clinicians promote the association to their patients? At the first sign of periodontitis, do they refer their patients to physicians? How

often, if ever, do clinicians inform their patients that treating periodontal disease will have an effect on HbA1C for type-2 diabetic patients?

Apart from daily practice behavior, it was also thought of interest to investigate the role of dental and medical literature on a clinical practice. Do clinicians read journals? Do they actively seek literature on the association between periodontitis and systemic health? Does the association between periodontitis and systemic health influence how one treatment plans? And lastly, what do clinicians know about statistics? A review of the literature showed few prior studies documenting the actual behaviors and attitudes of practicing clinicians regarding these subjects.

CHAPTER 3: PURPOSE

Medical and dental decision-making is a critical component of the military healthcare system. Clinicians are expected to utilize the best evidence to render optimal care to patients in order to maximize outcomes while minimizing costs or other burdens. However, some medical literature has shown that providers' decision-making processes may be complicated by a variety of factors, particularly systematic failures to properly understand and apply statistical concepts in evaluating the research literature. Little is known about dental specialties and their knowledge of biostatistics and how they practice evidence-based dentistry. The literature in the field of periodontics has concentrated on the association between oral and systemic health, but there have been few reports on how providers view and incorporate knowledge of this association as part of their clinical practice.

The purpose of this study was to evaluate dental professionals' attitudes and perceptions toward the oral-systemic interactions in health and disease. These findings were examined in the context of the subjects' self-reported knowledge of basic biostatistics and research methods (i.e. to what extent do clinicians assess their own knowledge of statistics, and how might that influence their views toward a complex statistical relationship in practice). In addition, the survey included items to allow us to assess differences between subjects' self-reported knowledge of basic biostatistics and research methods and their actual knowledge.

Additionally, the military possibly contains the world's largest group dental practice. In the Army, for example, dental readiness and wellness are the primary target metrics. A truly evidence-based approach to military dentistry could eventually standardize

procedures and best practices. Clinicians may perceive evidence-based dentistry potentially in one of two ways: as a means to improve dental readiness and wellness or as a threat to provider autonomy. True evidence-based dentistry would optimize both costs and wellness/readiness, but only if individual clinicians perceive its value and elect to implement best practices. This study aimed to collect initial data which may eventually contribute to identifying future obstacles faced by military dentistry in implementing best practices. Furthermore, some of the recent goals of the Army Medical Department senior leadership include increased emphasis on inter-professional development. Currently, few, if any studies have looked at how the practice of dentistry may drive long-term medical healthcare through clinician referrals and/or medical surveillance.

CHAPTER 4: HYPOTHESIS

HYPOTHESIS #1

There is a statistically significant difference between dentists' self-perceived understanding of biostatistics and actual knowledge of biostatistics.

HYPOTHESIS #2

Dental professionals with more statistical knowledge will express less confidence in the current state of the art regarding oral-systemic connections.

OTHER RESEARCH QUESTION:

A descriptive survey to assess practice behaviors of multiple groups of clinicians.

CHAPTER 5: SPECIFIC AIMS

AIM #1

This survey study will provide basic information on dentists'—particularly periodontists'—perception and actual knowledge of biostatistics, opinion of evidence-based dentistry, and attitudes toward the association between oral and systemic health.

AIM #2

This pilot study aims to collect a broad range of preliminary data in order to determine whether a more robust, hypothesis generating study is feasible.

AIM #3

This study aims to collect initial data which may eventually contribute to identifying future obstacles faced by military dentistry in implementing best practices.

CHAPTER 6: MATERIALS AND METHODS

OVERVIEW

This protocol divided into four different stages: (1) preparatory work, (2) instrument development, (3) instrument distribution, and (4) data analysis.

PREPARATORY WORK

A research team was assembled containing expertise beyond periodontics. A psychology researcher with experience in survey design and application as well as a statistician were included as part of the project team in order to maximize the utility of the study. The researching resident conducted a manual (PubMed) search prior to initiating the study with two goals: (1) rule out the presence of a similar study in the periodontics or dental literature and (2) collect relevant prior studies in the medical literature in order to use as a potential basis for instrument development. As with other social science or survey-based studies, instrument validity is critically important. No validated instrument was found specific to the periodontal literature.

INSTRUMENT DEVELOPMENT

A single, pilot survey instrument was developed with a target study population of the professional dental community, to include periodontists, general dentists, hygienists, and all other specialties. The survey contained four separate components in order to address the specific aims: (1) demographic information; (2) attitudes, perceptions, and behaviors toward a “perio-systemic link”; (3) attitudes toward basic statistical knowledge; and (4) assessment of basic statistical knowledge.

As no validated instrument could be found for component 2 listed above, the questions were developed by consensus. Components 3 and 4 utilized a fully validated and rigorously developed survey study from the medical literature for its basic structure (107). Several other surveys assessing clinicians' knowledge of biostatistics have been conducted in the past, many of which also used the aforementioned article as a basis for instrument development (5,7,8,36,74,82,95,105,107).

The research team, led by the staff principal investigator and researching resident, compiled an initial draft of a survey instrument, conserving as many validated elements as possible from prior bodies of work. The instrument then underwent multiple rounds of review by the (diversified) research team until a general consensus was reached. Survey instrument design must take into account several factors (e.g. length of time required, clarity of questions, legitimacy of questions, and accuracy of questions to assess what the team wants to assess). In many situations, trade-offs must be made in the design, and such issues were resolved by discussion where possible.

The literature concerning social science / survey research raises several interest concepts and issues to consider. As an example, it has been shown that when respondents encounter a survey question, they typically build "pragmatic meaning" that is a composite of their interpretation of the intent of the question, the question's purpose, and what is an appropriate answer (87). If subjects are asked initially about their confidence in understanding statistical concepts, their answers may bias the answers they give to subsequent questions concerning the oral-systemic link. Part of survey design involves managing the expectations of the participants.

Once a working draft of the survey instrument was developed, it was given out among both faculty and residents of the periodontics program as a “field test.” Again, this step aimed to ensure all questions were clear and error-free. By assessing the objective knowledge of faculty, an informal validation could be confirmed for component 4 prior to conducting the study.

The final survey instrument was converted into a structured web-based questionnaire platform and hosted on the Qualtrics web service. Qualtrics is HIPAA-compliant, anonymous (IP addresses are not stored) and accessible across multiple platforms (to include mobile). While this method does invite questions or concerns of authenticity among subjects, a web-based approach was thought to be the only feasible method of maximizing participation in order to achieve an acceptable n value.

INSTRUMENT DISTRIBUTION

This study sought to maximize participation across the dental community and was open to general dentists, all specialties, and hygienists. As this study was exploratory in nature, no power analysis could be conducted. A target n value of 300-500 subjects was considered desirable. The research team expected an attrition rate of up to 30% due in part to the projected length of the survey and in part based on prior, similar literature. Upon IRB review and approval from both Fort Gordon and Augusta University, open enrollment commenced for a period of 3 months. Anonymity was maintained without personally identifiable information being asked or tracked, and all participation was voluntary. No financial gain was offered to participants and the survey team did not receive financial compensation of any kind.

The researching resident attempted to recruit participants such that the sample or study population was as representative as possible; a difficult undertaking. The resident pursued two different strategies: (1) maximize exposure to pre-existing networks of practitioners within the department and school and (2) leverage social media in order to increase exposure to clinicians with a variety of different backgrounds and training experiences. The downside to such an approach was that it might bias the results toward more tech-savvy or social-media friendly subjects. However, the potential downside was thought to be outweighed by the increased subject participation. Social media publicity included Facebook, Twitter, the AAP Forum, websites, and various other dental groups. Participation was voluntary, anonymous, and without any compensation. The survey was made available on the internet at <http://oralhealthstudy.com> and at http://augustastate.co1.qualtrics.com/SE/?SID=SV_bQx3aVKHuTqsVaR.

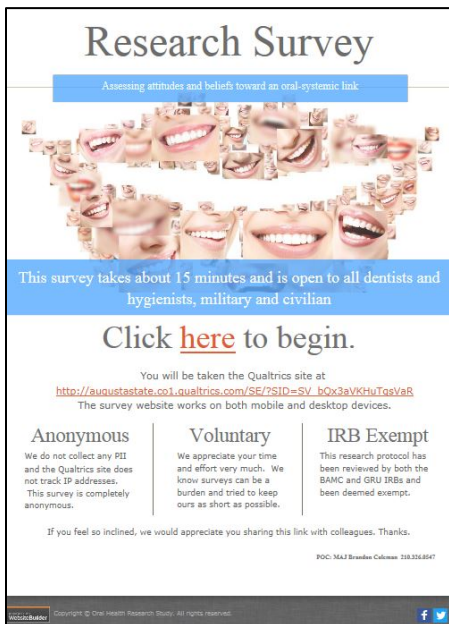


Figure 1: Survey website with web link to Qualtrics web site, the administrator of the survey

DATA ANALYSIS

A strategic plan for data management and statistical analysis was developed and approved by the psychology and statistician consultants in advance. Independent variables included demographic information, with the primary independent variable being whether the clinician was a periodontist, general dentist, or other. The intent of the current study was to compare periodontists and general dentists, but information from other groups may give a basis for future research. For most questions, answers were recorded on a continuous sliding scale in order to improve the applicability of statistical techniques. Basic statistical knowledge, component 4, was analyzed according to the total number correct. The statistician was blinded to identity of the groups when comparing responses.

A regression analysis was considered if participation was high enough; however, the pilot nature of the project and limited participation did not warrant a complex analysis. Data were compared descriptively, and in some questions such as those assessing behavior, a more complex analysis was not pertinent. Further analysis utilized t-tests for comparison between periodontists and general practitioners. An appropriate correction, such as a Bonferroni correction or similar method, was applied to account for the volume of questions asked. Significance was set at $p < 0.05$.

CHAPTER 7: RESULTS

OVERVIEW

The following tables consolidate the survey's findings for periodontists and general dentists. The survey was circulated among a variety of dental professionals, to include dental hygienists, general dentists, and dental specialists. The number of surveys initiated was 324, and the total number of completed surveys was 212. The breakdown of completed surveys by specialty was as follows: periodontists 63, general dentists 84, hygienists 23, endodontists 3, orthodontists 6, pediatric dentists 5, prosthodontists 22, oral surgeons 4, dental public health 1, and unknown 1.

For the purposes of this report, the decision was made to focus on general dentists and periodontists, with the decision partially stemming from simply lower volumes of hygienists and other dental specialists participating in the survey—the lower responses for these groups did not lend themselves to analysis. Future studies and reports may further analyze the results from hygienists and other specialty fields beyond periodontics and general dentistry.

Table 1 comprises the demographic information of the survey's participants, consisting of two questions: years since dental school and exposure to statistics/evidence-based dentistry.

Table 2 comprises the second portion of the survey and consists of eighteen questions. This section is the longest section of the survey and inquires about self-reported information regarding attitudes and perceptions toward the “perio-systemic link” or “oral-systemic link” (OSL). Topics in this section involve questions dealing with periodontitis and its relation to diabetes, cardiovascular disease, and adverse pregnancy outcomes. Other

questions entail inquiring about clinical behavior in managing patients with moderate-to-severe periodontitis.

The third portion of the survey is found in Table 3, which list the questions regarding self-reported attitudes toward basic statistical concepts and confidence in reading and interpreting information found in the dental literature.

SURVEY DEVELOPMENT

The survey went through a rigorous developmental phase, going through multiple drafts and versions. An initial pilot draft was developed and analyzed for fluidity, content, and organization among the principle investigators at Fort Gordon with additional input sought from and given by the periodontics faculty of The Dental College of Georgia at Augusta University. Several versions of the survey went through this initial phase—drafts, reviews, revisions, and new drafts. A much more developed version was then presented to the periodontics residents at Fort Gordon, seeking input on organization, clarity, and ease-of-use.

In addition to collaboration with the Periodontics Department of The Dental College of Georgia, further input and expertise was sought with the Psychology Department of Augusta University. The psychology department was consulted on survey design and creating a user-friendly, web-based format accessible on desktop computers, tablets, and smartphones. The periodontics department was consulted for experience with survey publications in the dental literature and to gain a dental perspective outside of the Army sphere of practice.

The psychology department converted the final draft of the survey into a user-friendly format for multiple platforms via the web-based survey program Qualtrics. Many

of the questions required responses based on a range from “strongly disagree to strongly agree” or “none to complete confidence” with corresponding numerical values of -5 (strongly disagree/none) to 5 (strongly agree/complete confidence). For example, a question such as “I actively pursue reading articles that examine ‘oral-systemic link’ ” had a response ranging from strongly disagree to strongly agree. The Qualtrics design allowed for a sliding-bar scale for certain questions that allowed participants to place their response anywhere along the bar. This allowed for participants to characterize their response within a spectrum or range without having to assign themselves a strict numerical value, such as a two or three out of ten.

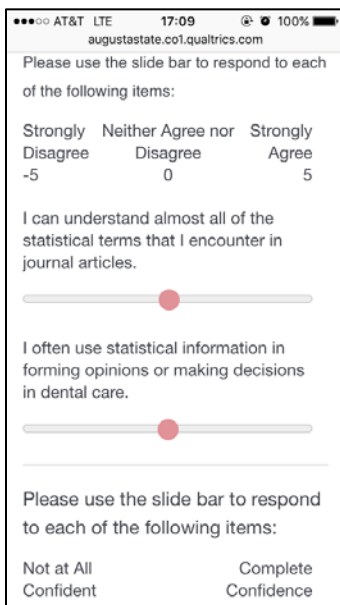


Figure 2: The web-platform Qualtrics was used to administrate the survey. This image is from the mobile-device platform, noting the sliding bar feature to respond to survey questions.

The Qualtrics design allowed the survey to be targeted to two separate groups. The first group was clinicians—hygienists, general dentists, and dental specialists—employed by the Army, either active duty or civilian. The other group was the same professional demographic but non-Army providers. This allowed us to pool responses based on the two

groups, which was of interest to see how Army providers interpret oral health and systemic health literature versus non-Army providers. The split design of the survey allowed for analysis on trends, similarities, and differences among both groups. The design also allowed for participants to identify themselves based on their specialty within dentistry, allowing us to analyze the responses of specific groups, such as periodontitis and general dentists.

The final version of the survey was organized into four sections, listed here chronologically: 1) demographic information; 2) assessing oral and systemic health literature; 3) attitudes and confidence with statistics; and 4) assessing statistical knowledge. Preliminary versions of the survey had sections two and three reversed, but the decision was made later to ask about oral and systemic health before statistics.

TABLE 1: DEMOGRAPHIC INFORMATION (MEAN RESPONSES, EXCEPT WHERE INDICATED)

	Periodontists	General Dentists	Method of assessment
Number of survey completed	63 (total)	84 (total)	Self-identification
Years since dental school	20.48	8.86	Years
Exposure to statistics or EBD	3.94	3.07	1-none; 2-minimal; lectures/seminars 3-some; semester courses 4-significant (residency/course); 5-substantial (residency/courses); 6-advanced degree

TABLE 2: ATTITUDES, PERCEPTIONS, AND BEHAVIORS TOWARD A “PERIO-SYSTEMIC LINK” (MEAN RESPONSES)

	Periodontists	General Dentists	Method of assessment
Actively pursue articles examining “oral-systemic” link (OSL)	2.07	0.28	Slide bar: Strongly agree (5) Strongly disagree (-5)
OSL literature influences my decision making	2.44	1.31	Slide bar: Strongly agree (5) Strongly disagree (-5)
Routinely discuss OSL with my patients	2.04	1.14	Slide bar: Strongly agree (5) Strongly disagree (-5)
Medical community perceives OSL strength?	-2.20	-2.14	Slide bar: Strongly agree (5) Strongly disagree (-5)
Diabetes is associated or correlated with periodontitis	4.11	3.05	Slide bar: Strongly agree (5) Strongly disagree (-5)
CVD is associated or correlated with periodontitis	2.66	2.49	Slide bar: Strongly agree (5) Strongly disagree (-5)
Adverse pregnancy outcomes are associated or correlated with periodontitis	1.95	2.24	Slide bar: Strongly agree (5) Strongly disagree (-5)
Diabetes directly made worse by periodontitis	3.30	2.07	Slide bar: Strongly agree (5) Strongly disagree (-5)
CVD directly made worse by periodontitis	2.16	1.84	Slide bar: Strongly agree (5) Strongly disagree (-5)
Adverse pregnancy outcomes directly made worse by periodontitis	1.51	1.57	Slide bar: Strongly agree (5) Strongly disagree (-5)

TABLE 2: ATTITUDES, PERCEPTIONS, AND BEHAVIORS TOWARD A “PERIO-SYSTEMIC LINK” (CONTINUED) (MEAN RESPONSES)

Impact of untreated periodontal disease on life expectancy	0.03	-1.03	Slide bar: Gain 10 years Lose 10 years
Patient with moderate-to-severe chronic periodontitis— informed patient periodontitis could affect overall health	59.98%	39.00%	Slide bar: 0-100%
Patient with moderate-to-severe chronic periodontitis— prescribed antibiotics as sole therapy	4.43%	4.75%	Slide bar: 0-100%
Patient with moderate-to-severe chronic periodontitis— prescribed antibiotics in conjunction with non-surgical therapy	20.31%	18.67%	Slide bar: 0-100%
Patient with moderate-to-severe chronic periodontitis— referred patient to periodontist	N/A	40.36%	Slide bar: 0-100%
Patient with moderate-to-severe chronic periodontitis— referred to another dental specialist	18.54%	11.56%	Slide bar: 0-100%
Patient with moderate-to-severe chronic periodontitis— referred to a medical provider for medical care	14.37%	9.53%	Slide bar: 0-100%
Future studies in the next 5-10 years will _____ the OSL	2.38	2.91	Slide bar: Strengthen (5) Weaken (-5)

TABLE 3: ATTITUDES TOWARD BASIC STATISTICAL KNOWLEDGE (MEAN RESPONSES)

	Periodontists	General Dentists	Method of assessment
I can understand almost all of the statistical terms I encounter in journal articles	0.78	0.43	Slide bar: Strongly agree (5) Strongly disagree (-5)
I often use statistical information in forming opinions or making decisions in dental care	1.23	1.44	Slide bar: Strongly agree (5) Strongly disagree (-5)
I am confident in interpreting the results of a journal article	2.67	1.55	Slide bar: Complete confidence (5) Not at all (-5)
I am confident in interpreting the P value for a given result	2.33	-0.21	Slide bar: Complete confidence (5) Not at all (-5)
I am confident in assessing whether the correct statistical procedure was used to answer a research question	0.13	-1.34	Slide bar: Complete confidence (5) Not at all (-5)
I am confident in recognizing an error in a study’s statistical analysis	-0.35	-1.49	Slide bar: Complete confidence (5) Not at all (-5)

TABLE 4: ASSESSMENT OF BASIC STATISTICAL KNOWLEDGE (MEAN RESPONSES)

	Periodontists	General Dentists	Correct answer
The purpose of a double-blind or double masked study is to:	43/63 (68.3%)—correct 0/63 (0%)—I don't know	64/84 (76.2%)—correct 3/84 (3.6%)—I don't know	Avoid observer and subject bias
Any systematic error in the design, conduct, or analysis of a study that results in a mistaken estimate of an exposure's effect on the risk of disease is called:	32/63 (50.8%)—correct 18/63 (28.6%)—I don't know	33/84 (39.3%)—correct 35/84 (41.7%)—I don't know	Bias
In a study of a disease, a researcher found an effect for a potential risk factor had a p-value = 0.07. A confidence interval of 95% (95% CI) for relative risk (RR) associated with this risk factor could be:	7/63 (11.1%)—correct 43/63 (68.3%)—I don't know	6/84 (7.1%)—correct 70/84 (83.3%)—I don't know	0.9-1.3
Treatment A was found to have a significant effect with p-value = 0.05 and the treatment B effect was found significant with p value = 0.002. We may conclude that:	19/63 (30.2%)—correct 11/63 (17.5%)—I don't know	21/84 (25.0%)—correct 34/84 (40.5%)—I don't know	It is impossible to compare the size of the effects
Which test should be used for comparison of blood pressure values between subjects belonging to three levels of smoking?	20/63 (31.7%)—correct 24/63 (38.1%)—I don't know	7/84 (8.3%)—correct 58/84 (69.0%)—I don't know	ANOVA
In a placebo-controlled trial of the use of a peri-operative antibiotic to improve implant outcomes, an author states that the results had $P > 0.05$. This means:	27/63 (42.9%)—correct 15/63 (23.8%)—I don't know	27/84 (32.1%)—correct 41/84 (48.8%)—I don't know	The probability is greater than 1 in 20 that a difference this large or larger could occur by chance alone
To determine if delivery of a pre-term, low-birth weight baby is associated with periodontitis, data from 40 women who had a pre-term, low-birth weight baby were collected. These patients were matched with women of the same age/race who had full-term, normal-birth weight babies. The hospital/dental charts of the women who gave birth to pre-term, low-birth weight babies were reviewed to determine if they had periodontitis prior to delivery. This type of study is known as:	5/63 (7.9%)—cross-sectional study 44/63 (69.8%)—retrospective cohort study 10/63 (15.9%)—I don't know	39/84 (46.4%)—retrospective cohort study 9/84 (10.7%)—retrospective cohort study 27/84 (32.1%)—I don't know	A. Cross-sectional study B. Retrospective cohort study (Both responses were considered correct)

A study wishes to assess the characteristics of a bone grafting material. Please indicate the correct choice if the researcher measured the volume of bone graft material:			Continuous
A study wishes to assess the characteristics of a bone grafting material. Please indicate the correct choice if the researcher measured bone graft particle size:**			Ordinal
A study wishes to assess the characteristics of a bone grafting material. Please indicate the correct choice if the researcher measured type of bone graft classified as autogenous, allograft, or xenograft:			Nominal

**This question was eliminated and not included in the analysis of the results. Feedback from survey participants highlighted a lack of clarity with the question.

STATISTICAL ANALYSIS

The responses to the cluster of questions listed in table 2 concerning systemic conditions and their association with periodontitis—diabetes/CVD/adverse pregnancy outcomes are associated or correlated with periodontitis—had a statistically significant difference when taken in aggregate when comparing responses from periodontists and general dentists. With this particular cluster of questions, which were grouped together on the survey, periodontists were more willing to support an association among these systemic conditions ($p=0.01$). Respondents were given a range to assess the association from strongly agree (5) to strongly disagree (-5). The individual responses from periodontists and general dentists, respectively, were as follows: diabetes, 4.11 vs. 3.05; CVD, 2.66 vs. 2.49; and adverse pregnancy outcomes, 1.95 vs. 2.24. Interestingly, periodontists gave more credence to diabetes being associated with periodontitis with cardiovascular disease to a lesser extent; however, general dentists felt that adverse pregnancy outcomes were associated with periodontitis more than periodontists. Even with those individual differences, when looking at the three questions together, periodontists were statistically significantly more likely to respond there is an association.

Another finding of interest stems from the first section of the survey in which participants asked about their exposure to statistics or evidence-based dentistry. Respondents could choose from six options: 1) none; 2) minimal, limited to lectures or seminars; 3) some, to include a semester course or two; 4) significant, such as residency and a few semester courses; 5) substantial, meaning residency and multiple courses; and 6) an advanced degree, such as an MPH or PhD. The mean for periodontists was 3.94, while for general dentists the mean was 3.07. For those who reported substantial training, they were statistically more likely to discuss an oral-systemic connection with their patients than all other groups ($p=0.01$) except for those who report a significant amount of statistical training..

There was also a significant difference between general dentists and periodontitis in both their self-reported confidence in statistics and research methods and their actual performance on the statistics test, with periodontists performing higher in both instances ($p=.008$ and $p=.005$, respectively). While there is a statistically significant difference, it should be noted that the performance is low for both groups with the mean percentage for test performance at 28.44% for general dentists and 38.98% for periodontists.

CHAPTER 8: DISCUSSION

OVERVIEW

Surveys in the medical literature assessing clinicians' knowledge of biostatistics have been completed in the past (5,7,8,36,74,82,95,105,107). The long-term objective of the present study of the dental field was to gather preliminary information, identify trends, and determine what areas merit further investigation. To address the collective issues in one format, a survey of dental professionals was designed to assess the following: 1) demographics to include specialty, years of practice, and exposure to statistics; 2) attitudes toward the periodontitis-systemic health literature and how periodontitis may or may not affect systemic health; 3) self-reported familiarity with statistical concepts; and 4) actual knowledge of basic statistics. The present survey was modeled primarily after one previously published survey conducted with medicine residents (107) due to its rigorous design and validation, giving the present survey at a minimum a framework to investigate dental professionals' experience with biostatistics.

In addition to this study with medicine residents, several other previously published surveys (7,8,74) were influential in constructing the present survey for dental professionals. We are not aware of any other survey targeted either to the dental profession at large or toward periodontists regarding self-assessment and actual knowledge of biostatistics. In addition, this survey targeted not just residents but practicing clinicians as well.

SURVEY ORGANIZATION

As previously discussed, the final version of the survey was organized into four sections, listed here chronologically: 1) demographic information; 2) assessing oral and systemic health literature; 3) attitudes and confidence with statistics; and 4) assessing statistical knowledge. Early versions of the survey had sections two and three reversed, but the decision was made later to ask about oral and systemic health before statistics.

The decision to swap sections two and three was a subtle but an interesting one. When respondents encounter a survey question, they typically build “pragmatic meaning” that is a composite of their interpretation of the intent of the question, the question’s purpose, and what is an appropriate answer (87). With this in mind, the thought was that if they were asked about their attitudes and confidence with statistics first, they may be less honest about how they perceive periodontitis and systemic health literature, possibly under reporting the value they place in it, after considering questions such as “I can understand almost all of the statistical terms that I encounter in journal articles.” The section on periodontitis and oral health literature was thus placed before the section on statistics so that participants would, ideally, be as honest as possible about how much they value it.

Another reason for the switch was to build sequentially, in a relatively ordered manner, an inquiry about periodontitis and systemic health literature, a self-report regarding familiarity with statistics, and an assessment of statistical knowledge. Respondents have a tendency to expand or restrict the meaning of concepts in a question (87). As an example, contributions to a progressing conversation typically express new information; if respondents are first asked about their marriage followed by their lives as a whole, they may interpret the second question as being about their lives without

considering their marriage (87,89,100). With this in mind, the survey was organized to build upon new information and an ordered sequence of questioning.

SURVEY PLATFORM AND SOCIAL MEDIA PUBLICITY

Publicity for the survey was a grassroots effort. The research team utilized personal contacts to attract initial responses and then asking them to funnel the survey to their contacts or co-workers. Several colleagues willingly posted the survey link on their Facebook, Twitter, or Instagram pages. Within the Army, the research team contacted clinicians at various installations, asking them to forward the survey to the dental professionals of their respective clinics and/or installations. Some contacts were willing to do so, others were not—this may suggest bias for those who did forward the survey but is also indicative of limitations with survey research in that the results are dependent upon voluntary participation. As previously discussed, the research team created Facebook and Twitter pages to promote the survey. Some moderate success was achieved on these social media platforms as several organizations and individuals followed our social media sites.



Figure 3: The Twitter page for the survey



Figure 4: The Facebook page for the survey

As this was the first survey to be done within the Fort Gordon periodontics department, several ideas were discussed in order to promote the survey. The decision to pursue a social media platform was based on the idea that it could potentially be an efficient way to increase awareness. For example, with the Facebook page, the thought was that friends and colleagues of the project could simply “like” the survey page, which would then appear on their individual Facebook feeds and presumably be seen by their friends and colleagues, creating a cascade effect.

The approach with Twitter was a bit different in that once the account was created we sought to follow a number of different dental-based accounts, such as dental schools, alumni networks, clinics, non-profit organizations, companies, and individual and group practices. The hope was that the followers of such accounts would then make their way to the survey page. Some success was achieved as the Twitter account gained over one hundred followers with several accounts re-tweeting our tweets. Overall, it is unclear how effective the Facebook and Twitter platforms were, but by utilizing them the department gained experience navigating social should it engage in future survey projects.

Additionally, the periodontics department of Fort Gordon contacted the American Academy of Periodontology’s open forum—the AAP Connect—and requested permission

to post the URL to the survey on the forum's message board where it was eventually posted and given broad exposure among the periodontics community. It was also timed in conjunction with the AAP's annual meeting in November 2015. The research team also contacted several hygienist groups, but these groups declined to publicize the survey to their members.

The survey link was live for four weeks, from mid-November through mid-December 2015. It became apparent that the amount of participants would be contingent on word-of-mouth and publicity. Simply emailing one or two colleagues realistically leads to maybe one or two responses. As such, we began to ask colleagues to forward the survey to as many of *their* colleagues as possible. Also, as previously mentioned, we attempted to increase our presence on our social media platforms by liking and following multiple dental professionals and organizations with the hope of gaining traffic to our social media pages. This approach may have had an influence on survey participants and favored clinicians who may be more technologically inclined than those without a presence on dental-sponsored social media groups.

SURVEY DEVELOPMENT AND DESIGN

The survey went through several iterations. Early drafts were ambitious in nature with close to forty questions. This was thought by the periodontics department of Augusta University to be problematic, fearing that a lengthy survey would lead to an increased incompleteness rate. Unfortunately, this advice was not fully appreciated as the final survey had over thirty questions—down from forty—but the advice turned out to be prophetic as the dropout rate was over 30%. Other suggestions from Augusta University's periodontics

department consisted of the following: 1) the inclusion of a question regarding properly defining meta-analysis; 2) the inclusion of a question regarding the value of randomized clinical trials; and 3) the elimination of a knowledge question—which was adapted from the medicine residents’ survey (107)—pertaining to odds ratios that was too lengthy. The odds ratio questions was eventually eliminated, which is somewhat regrettable that a version of it was not included in the final survey since the review of the literature consisted of a lengthy discussion of the value of understanding odds ratios. In retrospect, questions regarding meta-analysis and randomized controlled clinical trials may have been of interest in lieu of multiple questions regarding p-values and ANOVA, for example.

A preliminary draft of the survey was eventually presented to the residents of the US Army’s Advanced Education Program in Periodontics in May of 2015 to assess clarity, organization, and flow. For example, early drafts of the statistical knowledge portion of the survey included questions and multiple choice answers; however, there was not an option of “I don’t know” to the questions, which the residents felt would be an important addition so that participants weren’t simply guessing the right answer and giving a potentially skewed version of actual knowledge. This suggestion was heeded as an option of “I don’t know” was included in all of the knowledge questions and provided information of interest to know how many respondents opted for this answer choice on certain questions.

Other concerns included cumbersome phrasing, such as terms like “active, untreated, moderate-to-severe chronic periodontitis” and altering them to simpler phrases such as “active, untreated periodontal disease.” Ultimately, this suggestion was discarded as the phrase “active, untreated, moderate-to-severe chronic periodontitis” remained in the survey, though in hindsight while this phrasing may be adequate for periodontists, its

nuance probably not appreciated by general dentists and other dental specialists. As such, the residents felt periodontics-specific terminology may seem clumsy to non-periodontists. To this point, pre-term low birth weight was initially referred to in the survey as “PTLBW,” which may be an abbreviation familiar to medical physicians or periodontists but not necessarily to other dental professionals at large.

The psychology department also recommended a key suggestion to survey organization. Initially, the survey was organized as follows: section 1—demographic information; section 2—attitudes and confidence with statistics; section 3—assessing oral and systemic health literature; and section 4—assessing statistical knowledge. The psychology department felt it prudent to switch sections 2 and 3 in order to ask about oral and systemic literature first before asking about attitudes and confidence with statistics. The thought behind the switch was that if participants were asking about their perception of statistics first, they would be less honest—more conservative, probably—in their responses about oral and systemic health literature.

A potential pitfall of surveys in general is that cognitive psychologists believe that memories and autobiographical reports of events are as much constructed as retrieved (87). For example, if a respondent can quickly recall a particular event in the past, they may misinterpret that one event as being frequent—a phenomenon known as the availability heuristic (101). Also, if the memory is strong, a respondent may feel that the event happened more recently than it actually did (12,14). Also, respondents who believed they have changed—or even remained the same—may be influenced by such beliefs when recalling past event (85).

As far as responses to the survey go, it is difficult to speculate on the different

experiences respondents may have had with the oral-systemic health literature. It could be limited, or it could be extensive. They may overvalue their knowledge of statistics, relying on the memory of doing well in a prior course of statistics, even if it was years ago. In addition, sections 1-3 were predominantly agree/disagree questions and straightforward. The tenor of the survey was altered once reaching the knowledge section, and perhaps respondents felt frustrated at the change of tone. Anecdotally, some verbal feedback from respondents acquainted with the research team commented that the survey was of interest through section three, but then felt startled by the abrupt change once reaching the knowledge section. Paradoxically, the research team felt that the knowledge section was best kept at the end of the survey so as to not frustrate respondents early and cause potential drop outs; however, due to the length of the survey, it is possible respondents dropped out before even reaching the knowledge section.

A pitfall with the survey design may be the reliance upon the agree/disagree format for responses. Some respondents are inclined to agree with any assertion (86), perhaps the result of a disposition to please and avoid conflict (21,37). Another reason may be the agree/disagree format unintentionally suggests to respondents that those conducting the survey believe the statements themselves, and if respondents believe themselves to be of lower status than those conducting the survey, they may defer to what they think the researcher's opinion may be (15,57). Lastly, the "theory of survey satisficing"—a trend discussed by Krosnick (55)—argues that survey respondents tend toward confirmation than disconfirmation by shortcutting responses in order to simply agree with an assertion.

When considering these three points, it is interesting to reflect on design of the survey from this point of view. Is the simple structure of the survey being predominantly

agree/disagree jading responses toward agreeing, even if one does not agree? Do respondents feel inclined to agree simply to please, because they shy away from disagreement as a personality trait? It is interesting to consider the phenomenon of “expertise” as the survey was created by dental professionals for dental professionals, so in theory, respondents should not feel inclined to agree with the researchers, since it was disclosed up front that the survey was part of a periodontics residency research project. Given this disclosure, respondents may have been unintentionally jaded into feeling as though they should respond in way they perceive the resident would want them to respond. For those that have been through a dental residency, is there an inclination toward sympathy or empathy, wanting to help in any way possible? Additionally, for the dental hygienists, was there an inclination to agree with most of the questions due to a feeling of deferring what they think the researchers’ opinions would be? It is of interest to analyze these issues, as the research team contacted several hygienists groups seeking participation, but all groups were reluctant to endorse the survey, perhaps for fear of exposure for lack of statistical knowledge, or for being compared to dentists and specialists. This is only speculation, but it may have been a factor. (The survey did, however, have some participation from hygienists, just no endorsement from the hygienist professional organizations to push the survey out to their members.)

LIMITATIONS

Hindsight offers clarity. The aim of the project in assessing dental professionals’ views toward oral-systemic literature, attitudes toward statistics, and actual statistical knowledge had a fair amount of success—total respondents were over two hundred and

word-of-mouth among the research team's colleagues was mostly positive. A project such as this had not been attempted among general dentists and other dental specialists beyond oral and maxillofacial surgery and orthodontics. The data demonstrate not only a lack of statistical knowledge but a level of self-awareness among respondents regarding their lack of experience and confidence in understanding statistical concepts. The research team readily acknowledges its own deficiencies regarding statistics and its application in the literature—this project simply reinforces the needs for widespread improvement in a broad sense.

As previously discussed, a clear limitation in retrospect was the length of the survey. Other surveys analyzing medical professionals' knowledge of statistics utilized a limited approach, such as limiting assessments to as little as two questions (12,36). The medicine residents' survey was comparable in length to ours. The medicine residents' survey had a series of demographical questions, followed by nine questions assessing attitudes/confidence regarding statistics, and then sixteen knowledge questions (105). Their knowledge test was based from statistical methods most frequently represented in research studies published in journals such as the *BMJ*, *JAMA*, and *New England Journal of Medicine*, as well as from a previously published Danish survey on physicians' statistical knowledge, along with materials from a statistics course at Johns Hopkins Bloomberg School of Public Health. Their instrument was validated, and as such, we thought it prudent to base our instrument off of theirs, following suit with subsequent surveys that too were modeled from the medicine residents' survey. We recognize, however, that even with following a validated instrument, our instrument is not inherently validated—it was an approximation we attempted to make.

Even with an instrument similar in length, we felt ours may have been too broad in scope, attempting to investigate not only attitudes and actual knowledge of statistics but to also investigate attitudes toward oral-systemic health literature. A portion of the oral-systemic health questions were in some ways redundant, inquiring about associations and then causality, though the purpose behind such questions was to investigate how providers perceive how periodontitis interacts with other systemic conditions. It may have been prudent to have split the instrument into two separate projects—one on oral-systemic health and a second on attitudes/knowledge of statistics. After-the-fact discussions have speculated that the second section of the survey—the oral-health systemic health section—may have been too cumbersome with eighteen questions alone.

The survey was made available on both desktop and mobile platforms. The length and wording of the survey may have been too cumbersome on the mobile devices with respondents possible being impatient with the formatting.

FINDINGS OF INTEREST

There was a disparity in years since dental school when comparing periodontists and general dentists, perhaps accounting for the increased performance on the knowledge portion of the survey, albeit 38.98% vs. 28.44% may not be considered much of a difference (it was not found to be significantly different). The average years of practice for periodontists were 20.48, while it was 8.86 for general dentists. Additionally, when it comes to the following three categories—1) actively pursue articles examining oral-systemic link literature; 2) oral-systemic literature influences my decision making; and 3) routinely discuss oral-systemic literature with my patients—general dentists all reported

less activity than periodontists with averages of 0.28, 1.31, and 1.14 vs. 2.07, 2.44, and 2.04, respectively, on a scale of strongly agree (5) to strongly disagree (-5), though these differences were not found to be significant.

The reason these figures are of interest is when taking into considerations how each group reported their attitudes and behaviors regarding the oral-systemic connection. With the question “periodontitis associated or correlated with adverse pregnancy outcomes,” general dentists had an average score of 2.24 while periodontists were at 1.95. This seems a bit puzzling considering general dentists reported a mean score of 1.31, while periodontists reported a mean score of 2.44 for “OSL literature influences my decision making.” Perhaps general dentists associated periodontitis with adverse pregnancy outcomes more than periodontists because they assumed that was the answer the survey was seeking (15,57). While these findings were not statistically significant, they do highlight interesting trends.

Interestingly, periodontists reported that diabetes, CVD, and adverse pregnancy outcomes are associated with periodontitis with values mean values of 4.11, 2.66, and 1.95 on a scale of strong agree (5) vs. strongly disagree (-5). Periodontists were less convinced that diabetes, CVD, or adverse pregnancy outcomes are made worse by periodontitis with mean values of 3.30, 2.16, and 1.51, respectively. These findings perhaps highlight sentiments for emphasizing the oral-systemic health connection within the periodontics community, even as recent reports have stressed that the purpose of periodontal treatment is to maintain or improve one’s periodontal condition—not as a means to prevent or improve one’s status with diabetes, CVD, or adverse pregnancy outcomes (59,80,81).

Within the limits of the survey’s finding and as a reflection of the population that participated with the survey, it seems periodontists trended toward interpreting an oral-

systemic health connection as casual, not simply an association. The attraction of promoting periodontal treatment as an elixir for systemic conditions is a powerful one with potential for financial gain. An anecdotal illustration of this can be seen via a Google search of periodontists in the Atlantic City region of New Jersey where an office from that region states on its practice website: “Periodontal disease, if left untreated, can contribute to other health problems including heart disease and diabetes. If you’re pregnant, having periodontal disease is also linked to premature birth or low birth weight. Your smile’s health affects the overall health of your body” (31).

Periodontists reported a mean score of 3.94 for exposure to statistics—a score of 4 represents a “significant” amount of exposure to include residency and a course in statistics, yet they reported a mean score of 0.78 for being able to “understand almost all of the statistical terms I encounter in journal articles.” Even with exposure to statistics from a residency, periodontists still reported a low value for statistical understanding and scored about 38% on the knowledge test—yet, periodontists trended toward responding that periodontitis can make diabetes, CVD, and pregnancy outcomes worse.

A thought to consider when looking at the survey’s findings is the idea of “geography is destiny,” in which a medical (or dental) practice is based less or superficially on scientific evidence but rather on local habits (36). Some have argued that collective statistical illiteracy may be due to regional customs that outweigh evidence. As such, if one’s dental world is framed around the idea that periodontitis and diabetes or adverse pregnancy outcomes are related, then perhaps that explains some of the trends found in the survey. The mean years of practice reported for periodontists was just over twenty years—

interestingly, Offenbacher's article on periodontitis and pre-term low birth weight was published twenty years ago in 1996.

Part of what makes the findings intriguing regarding statistics, attitudes about statistics, and actual knowledge of statistics is the trends that come to the forefront. It is impossible to know what the motivations were for how periodontists and general dentists responded to questions in the survey. It may be that for certain aspects of the survey, the general dentists felt pressure to respond in a manner reflecting how they perceived the survey team would want them to respond. Another factor to consider may be an idea termed the "illusion of certainty." This concept refers to an emotional need for certainty where none exists (36). As such, perhaps both periodontists and even the general dentists felt compelled to respond to questions with a sense of certainty, even if they were actually uncertain about the questions being asked, or even if they disagreed. General dentists reported a mean value of 1.14 for "routinely discussing oral-systemic literature with my patients" but responded with mean averages higher than 1.14 for the questions inquiring about periodontitis being correlated with directly affecting diabetes, CVD, or pregnancy outcomes.

The illusion of certainty also may have manifested itself in section 3—attitudes toward basic statistical knowledge. For example, periodontists and general dentists responded with mean values of 2.67 and 1.55, respectively, for the question "I am confident in interpreting the results of a journal article," while also responding with mean values of 0.13 and -1.34 for the question "I am confident in assessing whether the correct statistical procedure was used to answer a research question." The responses for both groups for these two questions seem to be conflicting, but the results from the survey are

not necessarily clearly defined. In some ways, the periodontists' mean of 2.67 for confidence in interpreting results in an article represents a Dunning-Kruger-like effect—those who know the least are unable to recognize their lack of knowledge, which is evidenced by the periodontists' score of 38% on the knowledge test. However, periodontists also seemingly admit that they are not confident in understanding if the correct statistical procedure was utilized, showing a level of self-awareness.

The scope of this project was initially intended to be small in nature, but it afforded exploration along multiple avenues of literature and disciplines—dentistry, periodontics, systemic health, medicine, statistics, survey design, and psychology. The background investigation into these subjects was extraordinarily captivating, riveting, and highly enjoyable. All these avenues culminated in two hypotheses: 1) there would be a statistically significant difference between dentists' self-perceived understanding of biostatistics and actual knowledge of statistics; and 2) dental professionals with more statistical knowledge will express less confidence in the current state of the art regarding oral-systemic connections. Essentially, the opposite was found: periodontists and general dentists, while scoring low on the knowledge test, were relatively self-aware about their knowledge deficiencies with statistics. In addition, for those who reported “substantial” statistical training, they were statistically significantly more likely to discuss oral-systemic connection with their patients than all other groups, except for those who reported a significant amount of training. In other words, those with more training in statistics were more likely to discuss oral-systemic connections. These are interesting findings and perhaps illustrate that a concept such as the “Dunning-Kruger effect,” while an interesting report in the psychology literature, is not a definitive phenomenon. With survey projects,

the results are a reflection of the participants. While our analysis may attempt to explain and contextualize the results, we ultimately can only fall back on the face value of the results.

The projects' aims were indeed met—basic information was obtained on providers' perception and knowledge of statistics and oral-systemic health. What would be of interest, perhaps, is to follow up with a shorter survey with a handful of focused questions on statistics in a few years, mirroring some of the more recent surveys in the medical literature on clinicians' knowledge of statistics. Additionally, the findings also lend to curiosity about how other disciplines within dentistry perceive and interact with statistics. Another potential survey might be one explicitly focused on assessing how providers interpret systematic reviews, meta-analyses, and case reports. Ultimately, this project sparked curiosity about a number of potential information-gathering surveys to assess how dental professionals interact with treatment philosophies, literature, and statistics.

CHAPTER 9: CONCLUSIONS

The results of the project highlight interesting trends regarding knowledge and perceptions of statistics and oral-systemic health for periodontists and general dentists. Oral-systemic health literature centers on retrospective studies, odds ratios, and an inability to reach a consensus on the definition of periodontitis. As such, those that are left in the dark are patients, who must rely on their dental providers to adequately understand and explain how periodontitis and systemic health may or may not be related. There seems to be a proclivity for promoting the notion that periodontal treatment will have a positive effect on preventing systemic conditions such as adverse pregnancy outcomes, controlling diabetes, and preventing cardiovascular disease; the reality is, however, that the literature has shown associations, and an association does not mean causality. Groups like the American Heart Association have stated that periodontal treatment should not be promoted as a means to either prevent or treat cardiovascular disease, but that has not stopped providers from promoting it as such. As was demonstrated with the knowledge test, periodontists and general dentists have room for improvement with understanding statistical concepts. Dental training—whether in dental school and/or residency—should make greater strides to equip their students and residents with the necessary skills to adequately understand statistical concepts.

REFERENCES

1. A'Court, C., Stevens, R., & Heneghan, C. (2012). Against all odds? improving the understanding of risk reporting. *British Journal of General Practice*, 62(596), 160.
2. Altman, D. G. (2002). Poor-quality medical research: What can journals do? *Jama*, 287(21), 2765-2767.
3. Altman, D. G. (1994). The scandal of poor medical research. *BMJ (Clinical Research Ed.)*, 308(6924), 283-284.
4. Andersen, B. (1990). *Methodological errors in medical research: An incomplete catalogue* Blackwell Scientific.
5. Anderson, B. L., Williams, S., & Schulkin, J. (2013). Statistical literacy of obstetrics-gynecology residents. *Journal of Graduate Medical Education*, 5(2), 272-275.
6. Beck, J. D., Couper, D. J., Falkner, K. L., Graham, S. P., Grossi, S. G., Gunsolley, J. C., . . . Stewart, D. D. (2008). The periodontitis and vascular events (PAVE) pilot study: Adverse events. *Journal of Periodontology*, 79(1), 90-96.
7. Best, A. M., & Laskin, D. M. (2013). Oral and maxillofacial surgery residents have poor understanding of biostatistics. *Journal of Oral and Maxillofacial Surgery*, 71(1), 227-234.
8. Bookstaver, P. B., Miller, A. D., Felder, T. M., Tice, D. L., Norris, L. B., & Sutton, S. S. (2012). Assessing pharmacy residents' knowledge of biostatistics and research study design. *The Annals of Pharmacotherapy*, 46(7-8), 991-999.
9. Borgnakke, W. S., Ylöstalo, P. V., Taylor, G. W., & Genco, R. J. (2013). Effect of periodontal disease on diabetes: Systematic review of epidemiologic observational evidence. *Journal of Periodontology*, 84(4-s), S135-S152.
10. Bošnjak, A., Relja, T., Vučićević-Boras, V., Plasaj, H., & Plančak, D. (2006). Pre-term delivery and periodontal disease: A case-control study from Croatia. *Journal of Clinical Periodontology*, 33(10), 710-716.
11. Bradburn, N. M., Rips, L. J., & Shevell, S. K. (1987). Answering autobiographical questions: The impact of memory and inference on surveys. *Science (New York, N.Y.)*, 236(4798), 157-161.
12. Bramwell, R., West, H., & Salmon, P. (2006). Health professionals' and service users' interpretation of screening test results: Experimental study. *BMJ (Clinical Research Ed.)*, 333(7562), 284.
13. Brown, I. S. The perio group. Retrieved from http://www.theperigroup.com/periodontics_philadelphia/what_is_perio.html

14. Brown, N. R., Rips, L. J., & Shevell, S. K. (1985). The subjective dates of natural events in very-long-term memory. *Cognitive Psychology*, *17*(2), 139-177.
15. Carr, L. G. (1971). The role items and acquiescence. *American Sociological Review*, *36*, 287-293.
16. Caton, J. G., Ciancio, S. G., Blieden, T. M., Bradshaw, M., Crout, R. J., Hefti, A. F., . . . Walker, C. (2000). Treatment with subantimicrobial dose doxycycline improves the efficacy of scaling and root planing in patients with adult periodontitis. *Journal of Periodontology*, *71*(4), 521-532.
17. Chambrone, L., Pannuti, C. M., Guglielmetti, M. R., & Chambrone, L. A. (2011). Evidence grade associating periodontitis with preterm birth and/or low birth weight: II. A systematic review of randomized trials evaluating the effects of periodontal treatment. *Journal of Clinical Periodontology*, *38*(10), 902-914.
18. Chapple, I. L., Borgnakke, W. S., & Genco, R. J. (2014). Hemoglobin A1c levels among patients with diabetes receiving nonsurgical periodontal treatment. *Jama*, *311*(18), 1919-1920.
19. Chapple, I. L., & Genco, R. (2013). Diabetes and periodontal diseases: Consensus report of the joint EFP/AAP workshop on periodontitis and systemic diseases. *Journal of Clinical Periodontology*, *40*(s14)
20. Colgate. (2016). Oral bacteria may signal risk for pancreatic cancer. Retrieved from <http://www.colgate.com/en/us/oc/oral-health/conditions/cancer/article/ada-10-oral-bacteria-may-signal-risk-for-pancreatic-cancer>
21. Costa Jr, P. T., & McCrae, R. R. (1988). From catalog to classification: Murray's needs and the five-factor model. *Journal of Personality and Social Psychology*, *55*(2), 258.
22. Couper, D. J., Beck, J. D., Falkner, K. L., Graham, S. P., Grossi, S. G., Gunsolley, J. C., . . . Stewart, D. D. (2008). The periodontitis and vascular events (PAVE) pilot study: Recruitment, retention, and community care controls. *Journal of Periodontology*, *79*(1), 80-89.
23. Dietrich, T., Sharma, P., Walter, C., Weston, P., & Beck, J. (2013). The epidemiological evidence behind the association between periodontitis and incident atherosclerotic cardiovascular disease. *Journal of Clinical Periodontology*, *40*(s14)
24. Djelantik, A., Kunst, A., Van Der Wal, M., Smit, H., & Vrijkotte, T. (2012). Contribution of overweight and obesity to the occurrence of adverse pregnancy outcomes in a multi-ethnic cohort: Population attributive fractions for Amsterdam. *BJOG: An International Journal of Obstetrics & Gynaecology*, *119*(3), 283-290.
25. Dunning, D. (2011). Chapter 5, The dunning-kruger effect: On being ignorant of one's own ignorance. *Advances in Experimental Social Psychology*, *44*, 247.

26. Edelstein, B. (2012). Periodontal disease treatment. Retrieved from <http://www.mygumdoc.com/periodontal-disease-treatment/>
27. Eke, P. I., Dye, B. A., Wei, L., Slade, G. D., Thornton-Evans, G. O., Borgnakke, W. S., . . . Genco, R. J. (2015). Update on prevalence of periodontitis in adults in the united states: NHANES 2009 to 2012. *Journal of Periodontology*, 86(5), 611-622.
28. Emerging Risk Factors Collaboration. (2010). C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: An individual participant meta-analysis. *The Lancet*, 375(9709), 132-140.
29. Engebretson, S. P., Hyman, L. G., Michalowicz, B. S., Schoenfeld, E. R., Gelato, M. C., Hou, W., . . . Oates, T. W. (2013). The effect of nonsurgical periodontal therapy on hemoglobin A1c levels in persons with type 2 diabetes and chronic periodontitis: A randomized clinical trial. *Jama*, 310(23), 2523-2532.
30. Engebretson, S., & Kocher, T. (2013). Evidence that periodontal treatment improves diabetes outcomes: A systematic review and meta-analysis. *Journal of Clinical Periodontology*, 40(s14)
31. Frankel, J., & Frankel, A. (2016). Frankel periodontal, restorative, and implant dentistry. Retrieved from <http://www.frankeldental.com/periodontal-faq.php>
32. García-Berthou, E., & Alcaraz, C. (2004). Incongruence between test statistics and P values in medical papers. *BMC Medical Research Methodology*, 4(1), 1.
33. Genco, R. J., & Williams, R. C. (2010). *Periodontal disease and overall health: A clinician's guide* Professional Audience Communications.
34. Gibbs, R. S. (2001). The relationship between infections and adverse pregnancy outcomes: An overview. *Annals of Periodontology*, 6(1), 153-163.
35. Gigerenzer, G. (2003). *Reckoning with risk: Learning to live with uncertainty* Penguin UK.
36. Gigerenzer, G., Gaissmaier, W., Kurz-Milcke, E., Schwartz, L. M., & Woloshin, S. (2007). Helping doctors and patients make sense of health statistics. *Psychological Science in the Public Interest : A Journal of the American Psychological Society*, 8(2), 53-96.
37. Goldberg, L. R. (1990). An alternative" description of personality": The big-five factor structure. *Journal of Personality and Social Psychology*, 59(6), 1216.
38. Goldenberg, R. L., Culhane, J. F., Iams, J. D., & Romero, R. (2008). Epidemiology and causes of preterm birth. *The Lancet*, 371(9606), 75-84.
39. Goldenberg, R. L., Andrews, W. W., & Hauth, J. C. (2002). Choriodecidual infection and preterm birth. *Nutrition Reviews*, 60(5 Pt 2), S19-25.

40. Gomes-Filho, I. S., Soledade-Marques, K. R., Seixas da Cruz, S., de Santana Passos-Soares, J., Trindade, S. C., Souza-Machado, A., . . . Costa de Santana, T. (2014). Does periodontal infection have an effect on severe asthma in adults? *Journal of Periodontology*, *85*(6), e179-e187.
41. Goodman, S. (2008). A dirty dozen: Twelve p-value misconceptions. *Seminars in Hematology*, *45*(3) 135-140.
42. Grimes, D. A., & Schulz, K. F. (2008). Making sense of odds and odds ratios. *Obstetrics and Gynecology*, *111*(2 Pt 1), 423-426. doi:10.1097/01.AOG.0000297304.32187.5d [doi]
43. Grossi, S. G., Skrepcinski, F. B., DeCaro, T., Robertson, D. C., Ho, A. W., Dunford, R. G., & Genco, R. J. (1997). Treatment of periodontal disease in diabetics reduces glycosylated hemoglobin. *Journal of Periodontology*, *68*(8), 713-719.
44. Holcomb Jr, W. L., Chaiworapongsa, T., Luke, D. A., & Burgdorf, K. D. (2001). An odd measure of risk: Use and misuse of the odds ratio. *Obstetrics & Gynecology*, *98*(4), 685-688.
45. Hujoel, P. P., Drangsholt, M., Spiekerman, C., & Weiss, N. S. (2003). An exploration of the periodontitis–cancer association. *Annals of Epidemiology*, *13*(5), 312-316.
46. Ide, M., & Papapanou, P. N. (2013). Epidemiology of association between maternal periodontal disease and adverse pregnancy outcomes–systematic review. *Journal of Clinical Periodontology*, *40*(s14)
47. Ioannidou, E., Swede, H., Fares, G., & Himmelfarb, J. (2014). Tooth loss strongly associates with malnutrition in chronic kidney disease. *Journal of Periodontology*, *85*(7), 899-907.
48. Jones, J. A., Miller, D. R., Wehler, C. J., Rich, S. E., Krall-Kaye, E. A., McCoy, L. C., . . . Garcia, R. I. (2007). Does periodontal care improve glycemic control? the department of veterans affairs dental diabetes study. *Journal of Clinical Periodontology*, *34*(1), 46-52.
49. Kaldahl, W. B., Kalkwarf, K. L., Patil, K. D., Molvar, M. P., & Dyer, J. K. (1996). Long-term evaluation of periodontal therapy: I. response to 4 therapeutic modalities. *Journal of Periodontology*, *67*(2), 93-102.
50. Kaptoge, S., Di Angelantonio, E., Lowe, G., Pepys, M., Thompson, S., Collins, R., & Danesh, J. (2010). Emerging risk factors collaboration: C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: An individual participant meta-analysis. *Lancet*, *375*(9709), 132-140.
51. Katz, K. A. (2006). The (relative) risks of using odds ratios. *Archives of Dermatology*, *142*(6), 761-764.

52. Kebschull, M., Demmer, R. T., & Papapanou, P. N. (2010). "Gum bug, leave my heart alone!"--epidemiologic and mechanistic evidence linking periodontal infections and atherosclerosis. *Journal of Dental Research*, 89(9), 879-902.
53. Kleinbaum, D. G., Kupper, L. L., & Morgenstern, H. (1982). *Epidemiologic research: Principles and quantitative methods*. (pp. 144-145) John Wiley & Sons.
54. Knowler, W. C., Bennett, P. H., Hamman, R. F., & Miller, M. (1978). Diabetes incidence and prevalence in pima indians: A 19-fold greater incidence than in rochester, minnesota. *American Journal of Epidemiology*, 108(6), 497-505.
55. Krosnick, J. A. (1991). Response strategies for coping with the cognitive demands of attitude measures in surveys. *Applied Cognitive Psychology*, 5(3), 213-236.
56. Kruger, J., & Dunning, D. (1999). Unskilled and unaware of it: How difficulties in recognizing one's own incompetence lead to inflated self-assessments. *Journal of Personality and Social Psychology*, 77(6), 1121.
57. Lenski, G. E., & Leggett, J. C. (1960). Caste, class, and deference in the research interview. *American Journal of Sociology*, , 463-467.
58. Levine, R., & Fava II, P. (2014). Pennsylvania center for dental implants & periodontics. Retrieved from <http://www.padentalimplants.com/periodontal-therapy-procedures/>, accessed 24 Jan 2016
59. Lockhart, P. B., Bolger, A. F., Papapanou, P. N., Osinbowale, O., Trevisan, M., Levison, M. E., . . . American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, Council on Epidemiology and Prevention, Council on Peripheral Vascular Disease, and Council on Clinical Cardiology. (2012). Periodontal disease and atherosclerotic vascular disease: Does the evidence support an independent association?: A scientific statement from the American Heart Association. *Circulation*, 125(20), 2520-2544.
60. Lockwood, C. J. (2002). Predicting premature delivery—no easy task. *New England Journal of Medicine*, 346(4), 282-284.
61. Loos, B. G. (2005). Systemic markers of inflammation in periodontitis. *Journal of Periodontology*, 76(11-s), 2106-2115.
62. Lopez, N. J., Smith, P. C., & Gutierrez, J. (2002). Higher risk of preterm birth and low birth weight in women with periodontal disease. *Journal of Dental Research*, 81(1), 58-63.
63. Lu, Q., & Jin, L. (2010). Human gingiva is another site of C-reactive protein formation. *Journal of Clinical Periodontology*, 37(9), 789-796.

64. Manau, C., Echeverria, A., Agueda, A., Guerrero, A., & Echeverria, J. J. (2008). Periodontal disease definition may determine the association between periodontitis and pregnancy outcomes. *Journal of Clinical Periodontology*, *35*(5), 385-397.
65. Mattila, K. J., Nieminen, M. S., Valtonen, V. V., Rasi, V. P., Kesaniemi, Y. A., Syrjala, S. L., . . . Jokinen, M. J. (1989). Association between dental health and acute myocardial infarction. *BMJ (Clinical Research Ed.)*, *298*(6676), 779-781.
66. McGuigan, S. M. (1995). The use of statistics in the british journal of psychiatry. *The British Journal of Psychiatry : The Journal of Mental Science*, *167*(5), 683-688.
67. Michalowicz, B. S., Gustafsson, A., Thumbigere-Math, V., & Buhlin, K. (2013). The effects of periodontal treatment on pregnancy outcomes. *Journal of Clinical Periodontology*, *40*(s14)
68. Michaud, D. S., Izard, J., Wilhelm-Benartzi, C. S., You, D. H., Grote, V. A., Tjonneland, A., . . . Riboli, E. (2013). Plasma antibodies to oral bacteria and risk of pancreatic cancer in a large european prospective cohort study. *Gut*, *62*(12),
69. Michaud, D. S., Josphipura, K., Giovannucci, E., & Fuchs, C. S. (2007). A prospective study of periodontal disease and pancreatic cancer in US male health professionals. *Journal of the National Cancer Institute*, *99*(2), 171-175.
70. Nagao, Y., Kawahigashi, Y., & Sata, M. (2014). Association of periodontal diseases and liver fibrosis in patients with HCV and/or HBV infection. *Hepatitis Monthly*, *14*(12), e23264. doi:10.5812/hepatmon.23264 [doi]
71. Nelson, R. G., Shlossman, M., Budding, L. M., Pettitt, D. J., Saad, M. F., Genco, R. J., & Knowler, W. C. (1990). Periodontal disease and NIDDM in pima indians. *Diabetes Care*, *13*(8), 836-840.
72. Nijsten, T., Rolstad, T., Feldman, S. R., & Stern, R. S. (2005). Members of the national psoriasis foundation: More extensive disease and better informed about treatment options. *Archives of Dermatology*, *141*(1), 19-26.
73. Nizam, N., Basoglu, O. K., Tasbakan, M. S., Nalbantsoy, A., & Buduneli, N. (2014). Salivary cytokines and the association between obstructive sleep apnea syndrome and periodontal disease. *Journal of Periodontology*, *85*(7), e251-e258.
74. Novack, L., Jotkowitz, A., Knyazer, B., & Novack, V. (2006). Evidence-based medicine: Assessment of knowledge of basic epidemiological and research methods among medical doctors. *Postgraduate Medical Journal*, *82*(974), 817-822. doi:82/974/817 [pii]
75. Offenbacher, S., Beck, J. D., Moss, K., Mendoza, L., Paquette, D. W., Barrow, D. A., . . . Graham, S. P. (2009). Results from the periodontitis and vascular events (PAVE) study: A pilot multicentered, randomized, controlled trial to study effects

- of periodontal therapy in a secondary prevention model of cardiovascular disease. *Journal of Periodontology*, 80(2), 190-201.
76. Offenbacher, S., Katz, V., Fertik, G., Collins, J., Boyd, D., Maynor, G., . . . Beck, J. (1996). Periodontal infection as a possible risk factor for preterm low birth weight. *Journal of Periodontology*, 67(10s), 1103-1113.
 77. Olsen, C. T., Ammons, W. F., & van Belle, G. (1985). A longitudinal study comparing apically repositioned flaps, with and without osseous surgery. *The International Journal of Periodontics & Restorative Dentistry*, 5(4), 10-33.
 78. Ortiz, P., Bissada, N., Palomo, L., Han, Y., Al-Zahrani, M., Panneerselvam, A., & Askari, A. (2009). Periodontal therapy reduces the severity of active rheumatoid arthritis in patients treated with or without tumor necrosis factor inhibitors. *Journal of Periodontology*, 80(4), 535-540.
 79. Payne, J. B., Golub, L. M., Thiele, G. M., & Mikuls, T. R. (2015). The link between periodontitis and rheumatoid arthritis: A Periodontist's perspective. *Current Oral Health Reports*, 2(1), 20-29.
 80. Phipps, K. R., & Stevens, V. J. (1995). Relative contribution of caries and periodontal disease in adult tooth loss for an HMO dental population. *Journal of Public Health Dentistry*, 55(4), 250-252.
 81. Pihlstrom, B. L., & Buse, J. B. (2014). Diabetes and periodontal therapy. *Journal of the American Dental Association (1939)*, 145(12), 1208-1210.
 82. Polychronopoulou, A., Eliades, T., Taoufik, K., Papadopoulos, M. A., & Athanasiou, A. E. (2011). Knowledge of european orthodontic postgraduate students on biostatistics. *European Journal of Orthodontics*, 33(4), 434-440.
 83. Polyzos, N. P., Polyzos, I. P., Zavos, A., Valachis, A., Mauri, D., Papanikolaou, E. G., . . . Messinis, I. E. (2010). Obstetric outcomes after treatment of periodontal disease during pregnancy: Systematic review and meta-analysis. *BMJ (Clinical Research Ed.)*, 341, c7017.
 84. Reyes, L., Herrera, D., Kozarov, E., Roldán, S., & Progulske-Fox, A. (2013). Periodontal bacterial invasion and infection: Contribution to atherosclerotic pathology. *Journal of Clinical Periodontology*, 40(s14)
 85. Ross, M., & Conway, M. (1986). Remembering one's own past. *The Handbook of Motivation and Cognition*, , 122-144.
 86. Saris, W. E., Revilla, M., Krosnick, J. A., & Shaeffer, E. M. (2010). Comparing questions with agree/disagree response options to questions with item-specific response options. *Survey Research Methods*, , 4(1) 61-79.

87. Schaeffer, N. C., & Presser, S. (2003). The science of asking questions. *Annual Review of Sociology*, , 65-88.
88. Schenkein, H. A., & Loos, B. G. (2013). Inflammatory mechanisms linking periodontal diseases to cardiovascular diseases. *Journal of Clinical Periodontology*, 40(s14)
89. Schwarz, N., Knäuper, B., Hippler, H., Noelle-Neumann, E., & Clark, L. (1991). Rating scales numeric values may change the meaning of scale labels. *Public Opinion Quarterly*, 55(4), 570-582.
90. Sharma, A., Pradeep, A., & Raju P, A. (2011). Association between chronic periodontitis and vasculogenic erectile dysfunction. *Journal of Periodontology*, 82(12), 1665-1669.
91. Shlossman, M., Knowler, W. C., Pettitt, D. J., & Genco, R. J. (1990). Type 2 diabetes mellitus and periodontal disease. *The Journal of the American Dental Association*, 121(4), 532-536.
92. Sierakowski, S. R. (2016). Brandywine periodontics, LLC. Retrieved from <http://www.brandywineperio.com/periodontal-disease/the-mouth-body-connection>
93. Simpson, T. C., Needleman, I., Wild, S. H., Moles, D. R., & Mills, E. J. (2010). Treatment of periodontal disease for glycaemic control in people with diabetes. *Australian Dental Journal*, 55(4), 472-474.
94. Sun, W., Chen, L., Zhang, S., Wu, Y., Ren, Y., & Qin, G. (2011). Inflammatory cytokines, adiponectin, insulin resistance and metabolic control after periodontal intervention in patients with type 2 diabetes and chronic periodontitis. *Internal Medicine*, 50(15), 1569-1574.
95. Susarla, S. M., & Redett, R. J. (2014). Plastic surgery residents' attitudes and understanding of biostatistics: A pilot study. *Journal of Surgical Education*, 71(4), 574-579.
96. Switzer, S. S., & Horton, N. J. (2007). What your doctor should know about statistics (but perhaps doesn't...). *Chance*, 20(1), 17-21.
97. Tarver, T. (2012). Cancer facts & figures 2012. american cancer society (ACS) atlanta, GA: American cancer society, 2012. 66 p., pdf. available from. *Journal of Consumer Health on the Internet*, 16(3), 366-367.
98. Teeuw, W. J., Gerdes, V. E., & Loos, B. G. (2010). Effect of periodontal treatment on glycemic control of diabetic patients: A systematic review and meta-analysis. *Diabetes Care*, 33(2), 421-427.

99. Tonetti, M. S., & Dyke, T. E. (2013). Periodontitis and atherosclerotic cardiovascular disease: Consensus report of the joint EFP/AAP workshop on periodontitis and systemic diseases. *Journal of Clinical Periodontology*, 40(s14)
100. Tourangeau, R., Rasinski, K. A., & Bradburn, N. (1991). Measuring happiness in surveys: A test of the subtraction hypothesis. *Public Opinion Quarterly*, 55(2), 255-266.
101. Tversky, A., & Kahneman, D. (1973). Availability: A heuristic for judging frequency and probability. *Cognitive Psychology*, 5(2), 207-232.
102. Uppal, A., Uppal, S., Pinto, A., Dutta, M., Shrivatsa, S., Dandolu, V., & Mupparapu, M. (2010). The effectiveness of periodontal disease treatment during pregnancy in reducing the risk of experiencing preterm birth and low birth weight: A meta-analysis. *The Journal of the American Dental Association*, 141(12), 1423-1434.
103. Watts, A., Crimmins, E. M., & Gatz, M. (2008). Inflammation as a potential mediator for the association between periodontal disease and Alzheimer's disease.
104. Weaver, A., & Goldberg, S. (2011). *Clinical biostatistics and epidemiology* (1st ed.) MedMaster, Inc.
105. Wegwarth, O. (2013). Statistical illiteracy in residents: What they do not learn today will hurt their patients tomorrow. *Journal of Graduate Medical Education*, 5(2), 340-341.
106. Williams, R. C., Paquette, D. W., Offenbacher, S., Adams, D. F., Armitage, G. C., Bray, K., . . . Fiorellini, J. P. (2001). Treatment of periodontitis by local administration of minocycline microspheres: A controlled trial. *Journal of Periodontology*, 72(11), 1535-1544.
107. Windish, D. M., Huot, S. J., & Green, M. L. (2007). Medicine residents' understanding of the biostatistics and results in the medical literature. *Jama*, 298(9), 1010-1022.
108. Wood, S., Frydman, A., Cox, S., Brant, R., Needoba, S., Eley, B., & Sauve, R. (2006). Periodontal disease and spontaneous preterm birth: A case control study. *BMC Pregnancy and Childbirth*, 6(1), 1.
109. Zhang, J., & Kai, F. Y. (1998). What's the relative risk?: A method of correcting the odds ratio in cohort studies of common outcomes. *Jama*, 280(19), 1690-1691.