How concerns for bisphosphonate-induced osteonecrosis of the jaw affect clinical practice among dentists: a study from the South Texas Oral Health Network

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Bisphosphonate-induced osteonecrosis of the jaw (BONJ) represents a growing concern for dentists and patients in that it may alter clinical care. This study assessed the knowledge and perceptions of practicing dentists in relation to the risk of BONJ and how their knowledge and perceptions influence their decisions when developing treatment plans. For this study, a sample of dentists (n = 93) in South Texas completed a 38-item survey about BONJ knowledge and perception and their current clinical practices for patients undergoing bisphosphonate therapy. Knowledge score groupings reflected differences between low knowledge and high knowledge dentists in terms of their behavior concerning medical history, alternative treatments offered, and routine blood testing for patients on bisphosphonate therapy. 

Key words: bisphosphonate osteonecrosis of the jaw, dental care

B isphosphonates are antiresorptive agents that are used commonly for managing diseases that require decreased osteoclast activity, including osteoporosis, multiple myeloma, Paget’s disease, and cancers (such as lung, breast, and prostate) that metastasize to bone.1,3 Currently, there are 7 approved bisphosphonates available commercially in the United States: alendronate, etidronate, ibandronate, pamidronate, risedronate, tiludronate, and zoledronic acid.4 Those approved for treatment related to malignancy are available primarily in intravenous (IV) formulations. Bisphosphonates approved for osteoporosis and Paget’s disease generally are oral formulations; however, some are available for short IV infusion also. Studies have demonstrated the efficacy of bisphosphonates in increasing bone mineral density and decreasing the risk of nontraumatic fractures in patients with osteoporosis.2–4 Administering bisphosphonates to cancer patients at risk for metastases to bone dramatically reduces both tumor invasion of bone and corresponding bone pain and fractures.7–19

Patients on antiresorptive agents may be at risk of developing bisphosphonate-induced osteonecrosis of the jaw (BONJ).4 According to the American Association of Oral and Maxillofacial Surgeons (AAOMS), BONJ occurs when bone in the maxillofacial region is exposed for >8 weeks in a patient who has received a bisphosphonate with no prior history of radiation therapy.26 While BONJ is very rare, it can result in devastating maxillary and/or mandibular bone loss. This bone loss typically follows dental procedures, but may also occur spontaneously.4,14,21

Management of BONJ is primarily supportive, focusing on pain management and prevention or treatment of secondary infections with antibiotics. When BONJ approaches later stages, debridement and other surgical interventions may be warranted.4,20 Hence, BONJ is a major concern among dental practitioners due to the severity of this drug-induced complication and the limited management options currently available.

The exact etiology of BONJ is unknown and no known pathogens are associated with its development. Studies indicate that BONJ occurs more frequently in the mandible than the maxilla and is associated with pre-existing dental disease, tobacco use, diabetes, dentures, and invasive dental procedures that involve dental alveolar bone, such as dental extractions.2,4,16,22–27 While BONJ can occur following the use of any bisphosphonate, studies indicate the risks of developing BONJ are more likely with high potency bisphosphonates (for example, zoledronic acid or pamidronate), IV administration, higher dosage regimens, and longer durations of therapy.1 A previous study by the National Dental Practice-Based Research Network (NDPBRN) collaborative group found the incidence of BONJ to be 0.63:100,000 patient years; 87% of the patients in this cohort were taking oral bisphosphonates.28 Low doses of orally administered bisphosphonates, such as those used to treat osteoporosis, are linked to BONJ following at least 2 years of treatment.7 By contrast, high doses of IV-administered bisphosphonates—which often are administered to cancer patients—over short periods—are more highly linked to the development of BONJ, with a reported risk up to 4.4 times higher than low dose oral administration.1,4,20,29–31 The risk of patients developing BONJ after therapy is discontinued is unknown, since it is not clear how long bisphosphonates remain in alveolar bone.27,32,33 As a result, dentists must be aware if a patient has ever received bisphosphonates as a part of their cancer therapy. Ideally, patients will complete all necessary invasive dental work prior to starting antiresorptive therapy.

While much remains unknown regarding the risks of bisphosphonate use, the concerns are real, and ongoing dental care is necessary for patients taking these medications. Currently, there is little research available as to how a dentist’s concern for patients developing BONJ influences his or her practice patterns. This study sought to assess the knowledge and perceptions of
practicing dentists in relation to BONJ risk and how their knowledge and perceptions influence their decisions when developing treatment plans. The importance of this study is indicated by the results, which show that dentists may over- or undertreat this patient population, depending on their understanding (or lack thereof) and comfort level. The secondary objective of this study was to clarify the risk for BONJ based on the literature and to improve evidence-based decision making for dentists who may not identify or treat BONJ routinely.

**Materials and methods**

This study was conducted as a project for the *South Texas Oral Health Network* (STOHN), which is an NDPBRN. The Institutional Review Board at the University of Texas Health Science Center at San Antonio (UTHSCSA) approved the conduct of this study. A subcommittee consisting of private practitioners from STOHN and the academic faculty from UTHSCSA was formed to develop this project further. The subcommittee consisted of 2 general dentists, 2 oral surgeons, 1 periodontist, 1 pharmacist, and 1 statistician. Based on an extensive literature review, this subcommittee designed a survey to assess the knowledge, perceptions, and practice behavior of dental practitioners in relation to bisphosphonate therapy and oral health.

At present, there is no known literature concerning dentists’ perceptions and subsequent clinical practice related to BONJ; however, a 2010 pilot study assessed BONJ knowledge among dentists and dental students in Murcia, Spain, revealing that 50% of students and 68% of dentists had up-to-date knowledge about BONJ but that only 13% of students and 33% of dentists knew how to treat established BONJ. Some of the knowledge-based questions in the present study were extracted and modified from the 2010 study. The final 38-item survey was prepared in English and made available to dental practitioners through either an online survey (SurveyMonkey) or a paper-based format. STOHN members (n = 60), faculty from the UTHSCSA Dental School (n = 318), members of the San Antonio Dental District Society (n = 700), and the Laredo Dental District Society (n = 30) were invited to complete the survey; of these, 93 dental practitioners (8.4%) volunteered to participate in this study by completing the survey either online (n = 86) or on paper during a STOHN meeting (n = 7).

Background data for each practitioner were collected, including their title/role (that is, dentist, faculty, or resident), dental specialty (general, periodontics, endodontics, pediatric dentistry, orthodontics, oral/maxillofacial surgery, prosthodontics, or other), year in which the highest level of dental training was completed (prior to 1970, 1970-1979, 1980-1989, 1990-1999, and 2000-2010), and STOHN membership (yes or no).

The participants’ knowledge and perception of BONJ were assessed on the basis of their responses to survey questions concerning the risk of developing BONJ, treatment of BONJ, and the practitioner’s current practices. A total of 38 questions (4 demographic-based, 9 knowledge-based, and 25 perception-based) were evaluated. Knowledge and perception questions could be answered with estimated percentages or numbers, with answers of either true/false/don’t know, always/sometimes/rarely/never, or strongly agree/agree/neutral/disagree/strongly disagree. A STOHN-developed knowledge score was calculated based upon correct answers to the 9 knowledge-based questions. Correct answers were those deemed most supported by current literature.

Knowledge questions for which limited or inconclusive information was available were viewed as correctly answered by the
less definitive responses of agree/neutral/disagree. A knowledge score equal to the sum of correct answers was constructed. Participants were classified as having a high knowledge score (7-9 questions answered correctly) or a low knowledge score (0-6 questions answered correctly). Strongly agree, agree, always, and sometimes were interpreted as positive survey responses; strongly disagree, disagree, rarely, and never were viewed as negative responses. Contingency tables of knowledge score category versus each survey item response and reported positive or negative responses (in %) were constructed.

### Statistical analysis

Descriptive statistics were used to summarize each of the survey questions, and knowledge score mean, standard deviation, median, and interquartile range were computed. Specialty categories were collapsed into 3 groups: General Dentistry (general and pediatric), Surgical (endodontics, periodontics, and oral surgeons), and Nonsurgical (orthodontics, prosthodontics, other). Associations between practitioner characteristics and continuous knowledge score were assessed using the Kruskal-Wallis test. Associations between survey response and knowledge score category (that is, high or low) were assessed using Fisher’s exact test. All statistical tests were performed at the 2-sided 0.05 level of statistical significance, and all statistical analyses were conducted using statistical analysis software (SAS Version 9.2, SAS Institute, Inc.).

### Results

From September 2010 through July 2011, 93 dental practitioners took the 38-item survey to assess their knowledge and perception of BONJ incidence, risk factors, the effects of performing dental treatment before and after initiating bisphosphonate therapy, and each respondent’s current practices as they relate to bisphosphonates and the risk for developing BONJ. Practitioner estimates of BONJ in their practices are presented in Charts 1-3. The majority of practitioners surveyed were dentists (83%), while 9% were faculty, 7% were identified as both dentist and faculty, and 1% was in residency. A majority of respondents were classified as general dentists (69%), while 25% were classified as dental surgeons, and 6% worked in a nonsurgical specialty. The median year in which dental training was completed was 1990 [range = 1954-2010]. Among the practitioners, 18% were members of STOHN. The distribution of survey responses observed for the 9 questions included in the knowledge score is presented in Table 1.

Table 1. Key to answers and observed responses to “Knowledge Score” questions.

<table>
<thead>
<tr>
<th>Question</th>
<th>Correct answer</th>
<th>True</th>
<th>False</th>
<th>Don’t know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonate-induced osteonecrosis of the jaw (BONJ) occurs at a higher frequency in the mandible than in the maxilla.</td>
<td>True</td>
<td>68 (76)</td>
<td>1 (1)</td>
<td>21 (23)</td>
</tr>
<tr>
<td>Intravenous use of bisphosphonates is correlated with higher risk of BONJ than oral use.</td>
<td>True</td>
<td>82 (89)</td>
<td>3 (3)</td>
<td>7 (8)</td>
</tr>
<tr>
<td>Sources of infection should be eliminated prior to beginning intravenous bisphosphonate therapy.</td>
<td>True</td>
<td>86 (94)</td>
<td>0 (0)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Elective invasive dental treatment should be avoided during and after intravenous bisphosphonate therapy.</td>
<td>True</td>
<td>72 (79)</td>
<td>11 (12)</td>
<td>8 (9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question</th>
<th>Correct answer</th>
<th>Strongly agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sound oral hygiene practices and regular dental care can reduce the risk of BONJ.</td>
<td>Strongly agree/Agree</td>
<td>41 (45)</td>
<td>38 (41)</td>
<td>7 (8)</td>
<td>6 (6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>There is evidence linking BONJ with alcohol and tobacco use.</td>
<td>Agree/Neutral/Disagree</td>
<td>6 (6)</td>
<td>17 (18)</td>
<td>55 (60)</td>
<td>12 (13)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>There is evidence linking BONJ with pre-existing dental disease.</td>
<td>Strongly agree/Agree</td>
<td>12 (13)</td>
<td>35 (38)</td>
<td>35 (38)</td>
<td>9 (10)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>The risk of BONJ increases with duration/dose of bisphosphonate therapy.</td>
<td>Strongly agree/Agree</td>
<td>46 (50)</td>
<td>37 (40)</td>
<td>6 (6)</td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>The risk of BONJ decreases to normal after discontinuing bisphosphonate therapy.</td>
<td>Agree/Neutral/Disagree</td>
<td>2 (2)</td>
<td>12 (13)</td>
<td>17 (18)</td>
<td>36 (39)</td>
<td>25 (27)</td>
</tr>
</tbody>
</table>
The survey results revealed that 51% of the participants were aware of the link between BONJ and untreated/pre-existing dental disease. When participants were grouped by knowledge level, 78% of the dental practitioners in the high knowledge group reported they were well informed about BONJ compared to 54% in the low knowledge group (P = 0.03).

Both high knowledge and low knowledge participants (86% and 79%, respectively) correctly believed that patients should not undergo elective invasive treatments during IV bisphosphonate use. Regardless of BONJ knowledge score, most participants would avoid elective invasive procedures for patients taking any form of bisphosphonates and will refer patients who require invasive dental treatment and are undergoing bisphosphonate therapy to an appropriate specialist.

Based on the survey results, 94% of high knowledge practitioners will ask their patients if they are taking bisphosphonates, compared to only 71% of low knowledge practitioners (P = 0.01). When practitioners are aware that a patient is receiving oral bisphosphonate therapy, 93% of all participating practitioners (regardless of knowledge score) will discuss the risk of developing BONJ with their patients. In addition, 80% of all participants will modify their treatment recommendation if the patient is taking oral bisphosphonates, while 97% of high knowledge practitioners will modify treatment for patients receiving IV bisphosphonates, compared to 79% of low knowledge practitioners (P = 0.06). While most participants will modify their treatment plans for patients taking bisphosphonates, approximately 63% of all participants reported they did not have informed consent forms that outline the risks that BONJ may result after invasive dental treatment. Practitioners were asked whether they routinely ordered blood work for patients taking bisphosphonates to evaluate circulating levels of C-terminal cross-linking telopeptide (CTX) prior to invasive treatment. Among respondents, 30% of high knowledge participants reported ordering this blood work compared to 9% of low knowledge participants (P = 0.05).

While high knowledge and low knowledge participants (76% and 58%, respectively) claim to be confident they could identify a case of BONJ, neither group would be comfortable managing such a case. Regardless of knowledge level, 65% of practitioners perceive their patients are not well informed about BONJ, while 47% reported their patients are unconcerned about developing BONJ. Approximately 55% of all participants reported that their patients will choose to delay dental care due to pre-existing bisphosphate use. Conversely, 42% of high knowledge practitioners and 21% of low knowledge practitioners reported that their patients will elect to delay the start of bisphosphonate therapy until dental care is completed. It should be noted that 85% of all participants indicated that they were concerned about the possibility of their patients developing BONJ and would like more guidelines regarding BONJ identification, risk, and management.

Discussion
The results of the present study show that practitioner knowledge of BONJ risk influences how those surveyed conduct their practices. Furthermore, the level of knowledge relates directly to the practitioner’s self-perception of understanding; that is, the high knowledge group better recognized their higher level of understanding compared to the low knowledge group. This result is consistent with previous studies, suggesting greater accuracy for self-perception of one’s level of understanding in relation to one’s true knowledge base. The findings from the present study document the direct relationship between the practitioner’s knowledge base and correct practice behaviors for this patient population, reinforcing the value of incorporating research findings into clinical care. In this context, it must also be noted that most dental practitioners (~90%) had an adequate knowledge of BONJ, answering at least 6 of the 9 knowledge questions from the survey correctly.

One known risk factor of BONJ is the use of IV bisphosphonates that are prescribed to patients with hypercalcemia of malignancy or metastases to bone. In keeping with recommendations from the AAOMS, practitioners from both the high and low knowledge groups agreed that elective dental treatment should not be performed during IV bisphosphonate therapy. While no statistical difference was observed between the groups, there was a trend indicating more practitioners in the high knowledge group would modify dental treatment for patients on IV bisphosphonates compared to those in the low knowledge group.

Evidence suggests oral bisphosphonates are associated with a lower risk of inducing BONJ compared to IV bisphosphonates. One key observation in the present study was that 80% of all practitioners surveyed stated they would modify their treatment recommendations for patients taking oral bisphosphonates, regardless of their knowledge score. This finding demonstrates clearly that the respondents are not comfortable with treating low-risk patients on oral bisphosphonates; as a result, these patients may be foregoing dental treatment unnecessarily. Eighty percent of the participants in the low knowledge group report modifying treatment for patients on oral bisphosphonates and IV bisphosphonates equally. This finding suggests a lack of understanding of the different risks for developing BONJ among patients taking oral bisphosphonates and those taking IV bisphosphonates. As a result, patients who have received IV bisphosphonates may be overtreated and patients taking low-dose oral bisphosphonates undertreated.

Another noted difference in practice behavior involved asking patients whether they are currently using (or have ever used) bisphosphonates. The value in obtaining this important medical information is appreciated by more practitioners in the high knowledge group. However, once practitioners become aware of their patient’s history of bisphosphonate use, more than 90% of all practitioners (regardless of knowledge score) will discuss the risk of BONJ with their patients. This behavior is consistent with the treatment recommendations made by the American Dental Association (ADA) Council on Scientific Affairs in 2011. Dental practitioners should routinely discuss the risks and benefits of dental care and the risk of BONJ with patients taking bisphosphonates. Similarly, knowledge base had little influence on practitioner behavior related to providing specific informed consent and referring at-risk patients for invasive dental treatment. Of those surveyed, 63% do not have informed consent forms...
related specifically to the risk of developing BONJ. Regardless of the respondent’s knowledge score, most participants will avoid invasive procedures on patients who are taking any form of bisphosphonate and report referring patients to a specialist for required invasive treatment.

Differences were also noted between groups regarding CTX blood work. While a minority of practitioners overall reported using this marker to guide treatment, the high knowledge group reported using it more often. It has been hypothesized in the literature that CTX in the urine or blood may serve as an indicator of increased risk for BONJ. However, a recent prospective study evaluated CTX levels in patients who were taking bisphosphonates and suggested that CTX is not predictive of the development of BONJ following invasive dental treatment. Bisphosphonates can remain in the bone for up to 10 years; however, it is unclear how this long half-life translates into risk of patients developing BONJ after short- or long-term bisphosphonate use. At present, there is little evidence to delineate when the risk for BONJ decreases after bisphosphonate therapy is discontinued. Available data suggests that discontinuing oral bisphosphonates for 6-12 months may result in spontaneous sequestration or resolution of existing BONJ. Given the low incidence of BONJ and the long half-life of bisphosphonates in the alveolar bone, this important question proves difficult to study. Importantly, patients who need invasive dental treatment due to infection and/or pain should receive treatment regardless of bisphosphonate use. Only elective invasive dental procedures should be avoided to eliminate the risk of developing BONJ. If possible, patients who need IV bisphosphonate therapy should complete all invasive dental care prior to initiating bisphosphonate treatment.

This study also surveyed practitioners’ perceptions of their patients’ concern about and knowledge of BONJ and their resultant treatment decisions. Many practitioners (~65%) believed their patients were not well-informed about BONJ and approximately 50% believed their patients were not concerned about developing BONJ. Interestingly, slightly more than 50% believed their patients would choose to delay dental treatment due to concerns related to previous bisphosphonate use. This survey revealed that 42% of high knowledge practitioners report that their patients will elect to delay bisphosphonate therapy until dental care is completed, compared to 21% of low knowledge practitioners, a finding that relates to the lower percentage of low knowledge practitioners who inquire about bisphosphonate use. Unfortunately, the appropriateness of these practitioners’ decisions, along with their relative risks and benefits, remains unknown.

Lastly, it was determined that 85% of practitioners wanted more information and guidelines for providing dental care to patients taking bisphosphonates. The AAOMS published a position paper on BONJ in 2007 that outlined the staging and treatment of BONJ. This position paper was updated in 2009; at that time, the staging of BONJ was modified to include the Stage 0 category and to define Stage 3 disease more accurately; the updated recommendations are summarized in Table 2.

In consideration of these treatment recommendations, general practitioners should make treatment and referral decisions based on their knowledge and experience in treating patients on bisphosphonates or patients with existing BONJ. According to the AAOMS recommendations, patients with Stage 0 or 1 disease should be monitored every 3 months to determine disease progression and verify healing.

A 2011 article by Hellstein et al summarized the recommendations from the ADA Council on Scientific Affairs regarding the care of patients receiving antiresorptive therapy for preventing and treating osteoporosis. After an extensive review of the current literature, the panel concluded that the risk of BONJ in a patient not afflicted with cancer is low; the highest prevalence estimate was 0.10%. To date, no conclusive studies have assessed BONJ incidence; however, the ADA Council has provided prevention strategies for patients

### Table 2. AAOMS-recommended staging and treatment strategies for BONJ.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>Treatment strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No clinical evidence of necrotic bone but nonspecific clinical findings and symptoms</td>
<td>Systemic management, including use of pain medication and antibiotics</td>
</tr>
<tr>
<td>1</td>
<td>Exposed and necrotic bone in asymptomatic patients without evidence of infection</td>
<td>Antibacterial mouthrinse, clinical follow-up on quarterly basis, patient education and review of indications for continued bisphosphonate therapy</td>
</tr>
<tr>
<td>2</td>
<td>Exposed and necrotic bone associated with infection as evidenced by pain and erythema in region of exposed bone with or without purulent drainage</td>
<td>Symptomatic treatment with oral antibiotics, oral antibacterial mouthrinse, and pain control, and superficial debridement to relieve soft tissue irritation</td>
</tr>
<tr>
<td>3</td>
<td>Exposed and necrotic bone in patients with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone (that is, inferior border and ramus in the mandible; maxillary sinus and zygoma in the maxilla), resulting in pathologic fracture; extraroral fistula, oral antral/oral nasal communication; and osteolysis extending to the inferior border of the mandible or the sinus floor</td>
<td>Antibacterial mouthrinse, antibiotic therapy and pain control, surgical debridement/resection for long-term palliation of infection, and pain progressors</td>
</tr>
</tbody>
</table>

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receiving antiresorptive therapy for osteoporosis and treatment recommendations for specific dental conditions (Table 3). Ideally, patients will complete all necessary dental care prior to starting bisphosphonate treatment, which should be followed by good oral hygiene and routine dental care. However, many patients may have already begun bisphosphonate therapy when they are initially evaluated in the dental clinic; as a result, it is essential to inform patients about the risks of developing BONJ prior to dental care. Council-recommended points of discussion include the following: antiresorptive therapy for low bone mass puts osteoporosis patients at a very low risk (0.10%) of developing BONJ; the low risk can be minimized but not eliminated; and sound oral hygiene and routine dental care may be the best approach for minimizing the risk of BONJ. There are no diagnostic tests that determine which patients are at risk of developing BONJ, and discontinuing bisphosphonate therapy may not eliminate the risk of developing BONJ but may have a negative impact on osteoporosis. There is no data proving that a drug holiday is useful in reducing the risk of BONJ. In addition, discontinuing treatment should be a medical decision based on the risk of skeletal related events (bone fractures) rather than the potential risk of BONJ.

Intended as a pilot project of the STOHN NDPBRN, the population of the present study consisted of a convenience sample of dental practitioners in the areas of San Antonio and South Texas and was limited by the number of surveys completed voluntarily. The findings of this study could be biased, as those who replied to the survey may have been those most aware of BONJ. Conducting a similar survey with a larger sample may yield more generalized results. Future studies should incorporate more specific knowledge questions such as those addressing drug potency and duration of therapy, 2 known predisposing factors for BONJ. Additionally, future studies should evaluate physicians’ knowledge and perceptions related to BONJ to determine if physicians are aware of the risk of patients developing BONJ following bisphosphonate therapy, if they are discussing these risks with their patients, and if they are referring patients to complete dental care prior to starting antiresorption treatment. These findings may improve collaborations between physicians and dental practitioners when managing patients who are undergoing bisphosphonate therapy and require dental care.

Conclusion
The results of this survey demonstrate the importance of a dental practitioner understanding BONJ and communicating risks to patients and how this knowledge affects their treatment recommendations. While much remains unknown regarding the risk of BONJ, position statements and recommendations for managing patients on bisphosphonate therapy are available. This study reinforces the value of disseminating and translating this evidence for dental practitioners.

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Manufacturers

SurveyMonkey, Palo Alto, CA  www.surveymonkey.com

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