World Workshop on Oral Medicine VI: Controversies regarding dental management of medically complex patients: assessment of current recommendations

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Objectives. Current recommendations for safe and effective dental management are less than optimal for some medical conditions because of limited evidence, conflicting conclusions, or both. This review (1) compiled and evaluated dental management recommendations for select medical conditions; (2) summarized recommendations and their assigned levels of evidence; (3) identified areas of conflict, ambiguity, or both; and (4) identified issues that warrant future research, enhanced consensus statements, or both.

Study Design. Systematic literature searches were performed for guideline publications, systematic and narrative reviews, and opinion documents containing recommendations for (1) medication-related osteonecrosis of the jaw (MRONJ); (2) cardiovascular diseases (CVDs); (3) prosthetic joints (PJs); and (4) systemic steroid therapy (SST).

Results. The search yielded the following numbers of publications that met the inclusion criteria: MRONJ − 116; CVDs − 54; prosthetic joints − 39; and systemic steroids − 12.

Conclusions. Very few of the compiled recommendations were assigned or linked to levels of evidence by their authors. Key conclusions include the following: MRONJ—expert recommendations trend toward proceeding with dental treatment with little to no modification in osteoporotic patients on bisphosphonates; CVDs—current recommendations are primarily directed to general surgery and applied to dentistry; PJs—routine antibiotic prophylaxis is not indicated for dental treatment; and SST—steroid supplementation is not indicated for most patients undergoing dental procedures under local anesthesia. (Oral Surg Oral Med Oral Pathol Oral Radiol 2015;120:207-226)

Medically complex patients are frequently encountered in dental practice, with their medical conditions, the consequences of systemic disease management, or a combination of both directly impacting dental care. Of concern is the risk of adverse systemic complications resulting from dental treatment, as well as the impact of the medical conditions on dental outcomes. Utilization of high-quality, contemporary, evidence-based guidelines can translate into safe and effective clinical results. For many medical conditions encountered in dental practice, international evidence-based protocols would be the best reference for guiding dentists in standards of care. However, current clinical practice may be based on multiple sources, including publications and textbooks, pre- and postgraduate dental curriculum, and continuing education courses, all of which may provide recommendations of varying quality, levels of evidence, or obsolescence (Figure 1).

Current standards of practice for selected medical conditions are limited by several factors: (1) Recommendations are not evidence based or linked to levels of

Statement of Clinical Relevance

Knowledge of clinical management recommendations and the extent to which they are evidence based are important to treat patients safely and effectively. This review outlines key recommendations for four medical conditions commonly encountered in dental practice, and highlights unresolved issues for future research and enhanced guidelines.

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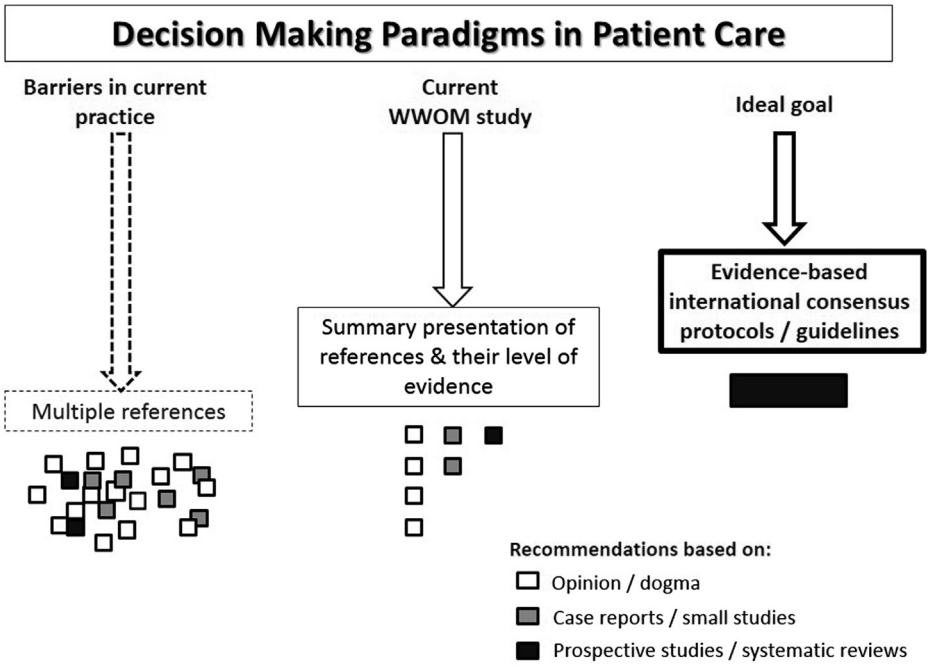

Fig. 1. Decision making paradigms for clinicians based on available reference sources. (1) Barriers in current clinical dental practice are due to varying recommendations (*left panel*). (2) The current WWOM study was designed to assess and present the current status and state-of-the-science of the guideline literature and; identify areas of controversy and opportunities for research (*middle panel*). (3) This leads to the ideal goal of achieving high-quality, evidence-based, internationally applicable consensus treatment protocols and guidelines (*right panel*).

evidence; (2) recommendations are conflicting or contradictory; (3) recommendations are often vague, not practical, or applicable to community-based clinical practice; and (4) published data and conclusions from scientific studies are interpreted differently. These limitations restrict the opportunity for dentists to provide safe and effective treatment, and consequently, confusion and outdated or potentially ineffective or unnecessary practices may persist.

A review group of oral medicine experts convened by the World Workshop on Oral Medicine VI (WWOM-VI) was tasked with reviewing several specific and prevalent medical conditions that are controversial in terms of accepted standards for dental care. The group's objective was to assess the current status of published recommendations from the literature on each issue (see Figure 1). The specific aims were (1) to identify, compile, and evaluate published guidelines and recommendations; (2) summarize recommendations and conclusions and report their level of evidence as provided by the publications' authors; (3) identify areas of conflict, controversy, or ambiguity; and (4) determine current concerns and unresolved issues that would benefit from further research and enhanced consensus group statements.

Feedback from a cohort of practicing American dentists provided initial focus to the selection of potential review topics. A survey was distributed to members of the American Dental Association (ADA), requesting their input regarding the most prevalent and controversial issues encountered in their practice relative to dental management of patients with various medical conditions. Detailed description of the survey will be reported in a subsequent publication.

Based on survey results, as well as subsequent discussions among group members, the WWOM-VI review group came to a consensus on the following topics for review:

1. Medication-related osteonecrosis of the jaw (MRONJ)
2. Cardiovascular diseases (CVDs)
3. Prosthetic joints
4. Systemic steroid therapy.

METHODS

Literature review

The review group devised lists of keywords comprising clinical keywords relevant to each topic (see respective sections); keywords pertaining to dentistry (i.e., dentistry, dental treatment, dental surgery, dental extraction, dental scaling, dentoalveolar procedure); and keywords for desired publication types (i.e., guideline, practice guideline, recommendation, standard of care, practice standard, professional standard, algorithm, clinical algorithm, practice algorithm, clinical guideline, expert consensus). Literature searches were performed by the research

Table I. List of guideline websites for which literature search was performed

Professional organization	*Website address*
National Guideline Clearinghouse	www.guidelines.gov
Scottish Intercollegiate Guidelines Network	www.sign.ac.uk
Canadian Medical Association Infobase for Clinical Practice Guidelines	www.cma.ca/index.php/ci_id/54316/la_id/1.htm
Guidelines International Network	www.g-i-n.net
Evidence-Based Medicine Guidelines	www.ebm-guidelines.com
National Institute for Clinical Excellence	www.nice.org.uk
Clinical Practice Guidelines published in CMAJ	www.cmaj.ca/site/misc/service/guidelines.xhtml
Clinical Practice Guidelines Archive	www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/archive.html
Australia's Clinical Practice Guidelines Portal	www.clinicalguidelines.gov.au/
ACP Guidelines Page	www.acponline.org/clinical_information/guidelines/guidelines/

CMAJ, Canadian Medical Association Journal; *ACP,* American College of Physicians.

librarian (JC) between late July and early August 2013, in English language journals and electronic publications for guidelines and recommendations related to these topics. Searches were performed in Medline (OVID; [publications from 1946 to 2013]), Embase (OVID; [publications from 1947 to 2013]), the Cochrane Library (Wiley), CINAHL (Cumulative Index to Nursing and Allied Health Literature *via* EBSCO [Elton B. Stevens Co. database; publications from 1981 to 2013]) and the Web of Science (Thomson Reuters; [publications from 1900 to 2013]). In addition, (1) guideline websites were identified and searched for relevant publications (Table I); (2) the review group members compiled a list of relevant professional organizations (Table II) and performed searches within those websites for publications containing relevant guidelines and recommendations; and (3) searches were conducted in point-of-care medical references UpToDate (www.uptodate.com) and Dynamed (dynamed.ebscohost.com).

Inclusion and exclusion criteria

Publications were included if they presented information specifically for, or potentially relevant to, dental management of the specified patient cohort. Publication types included consensus and guideline statements, systematic reviews (including meta-analyses), narrative reviews, and opinion documents (which included editorials). An initial review of the articles' titles and abstracts was then performed; those deemed potentially relevant were subject to full review. In addition, the articles were also evaluated for potential additional citations in their bibliographies. After full review, publications were excluded if it there were no recommendations or conclusions relevant to the specific respective subject matter.

Guideline or recommendation review

Management recommendations were extracted and analyzed and conclusions recorded. Levels of evidence and classes of recommendation, if presented by the authors of those publications, were included. Definitions of the respective classification systems used by publication authors were documented.

This report highlights key recommendations for select issues within the subject matter, with publication references included in respective summary tables for each topic. However, due to page limitations, this report does not encompass all recommendations and issues from all publications that met inclusion criteria, as these will be presented in subsequent publications.

DENTAL MANAGEMENT OF PATIENTS WITH MRONJ

Methods

Inclusion and exclusion criteria. Subject-specific search terms included, but were not limited to, the following: osteonecrosis; avascular necrosis; phosphorous necrosis; osteopathology; jaw; jaws; drug-induced; bisphosphonate; oral; IV; diphosphonates; RANKL inhibitors; denosumab; VEGF inhibitors; antiangiogenesis; bevacizumab; sunitinib; antirheumatic drugs; methotrexate; BRONJ; BIONJ; ONJ; BION; BON; local risk factors; systemic risk factors; susceptibility; etiology; diagnosis; prevention; treatment; and management.

Publications were included if they contained recommendations developed for the management of patients exposed to drugs associated with MRONJ. This included bisphosphonates (BPs), receptor activator of nuclear factor κ-B ligand (RANKL) inhibitors, vascular endothelial growth factor (VEGF) inhibitors or antiangiogenesis drugs, and antirheumatic drugs for treatment of osteoporosis or for cancer therapy.

Results

The search identified 134 citations from an initial screening of titles and abstracts. Seventeen additional citations were identified from other sources, yielding a total of 151 citations available for full review. One

Table II. List of professional organization websites searched for literature review

Professional organization	*Website address*
Physicians/Surgeons	
American Heart association	www.heart.org/HEARTORG/
British Heart Association	www.bhf.org.uk/#&panel1-5
The Association of Bone and Joints Surgeons	www.abjs.org/
American Association of Colleges of Osteopathic Medicine	www.aacom.org/Pages/default.aspx
NHLBI − Health Information for Professionals	www.nhlbi.nih.gov/health/indexpro.htm
American Association/Academy of Orthopaedic Surgeons	www.aaos.org
National Institute for Health and Care Excellence	www.nice.org.uk
New South Wales Government	www.health.nsw.gov.au/policies/pages/default.aspx
Scottish Dental Clinical Effectiveness Programme	www.sdcep.org.uk/index.aspx?o=2270
American Society of Clinical Oncology	www.cancer.net/publications-and-resources/what-know-ascos-guidelines
Scottish Intercollegiate Guidelines Network	www.sign.ac.uk/guidelines/index.html
British Orthopaedic Association	www.boa.ac.uk/Pages/Welcome.aspx
American Association of Clinical Endocrinologists	www.aace.com/publications/guidelines
Endocrine Society	www.endocrine.org/
Dental (General)	
American Dental Association	www.ada.org
International Association for Dental Research	www.iadr.com/i4a/pages/index.cfm?pageid=1
FDI World Dental Federation	www.fdiworldental.org/home.aspx
British Dental Association	www.bda.org
Oral Medicine/Oral Pathology	
The American Academy of Oral Medicine	www.aaom.com/
British Society of Oral Medicine	www.bsom.org.uk/index.html
European Association of Oral Medicine	www.eaom.eu/
The Academy of Oral and Maxillofacial Pathology	www.aaomp.org/
International Association of Oral Pathologists	www.iaop.com/
British Society of Oral and Maxillofacial Pathology	www.bsomp.co.uk/
Oral and Maxillofacial Surgery	
American Association on Oral and Maxillofacial Surgery	www.aaoms.org/members/resources/aaoms-advocacy-and-position-statements
British Association of Oral and Maxillofacial Surgeons	www.baoms.org.uk/
European Association for Craniomaxillofacial Surgery	www.eurofaces.com
International Association of Oral and Maxillofacial Surgeons	www.iaoms.org
European Board of Oromaxillofacial Surgery	www.ebomfs.net/eng_index.php
Other Dental Specialties	
The American Academy of Pediatric Dentistry	www.aapd.org
American Academy of Periodontology	www.perio.org
British Society of Periodontology	www.bsperio.org.uk
European Federation of Periodontology	www.efp.org/news.php
International Team for Implantology	www.iti.org

NHLBI, National Heart, Lung and Blood Institute; *FDI*, Fédération dentaire internationale.

citation was identified from bibliographies, and 36 articles were excluded after full review, yielding a final total of 116 articles that met inclusion criteria, and these included 19 consensus and guideline statements, 10 systematic reviews, 69 narrative reviews, and 18 opinion documents. Among these articles, 4 contained recommendations pertaining to non-BPs implicated in osteonecrosis of the jaw (i.e., denosumab, bevacizumab, sunitinib).

Clinical practice recommendations from consensus guidelines and systematic reviews. The following analysis is directed to dental management of patients receiving oral or intravenous (IV) BPs for osteoporosis, since this subject area was specifically identified in the ADA-based survey that was initially conducted. Key recommendations from the consensus guidelines as well as systematic reviews are presented in Table III.

Individual recommendations and subsequent discussion regarding oncology patients receiving IV BPs, non-BP drugs implicated in MRONJ, and treatment of established MRONJ will be addressed in subsequent publications.

Level of evidence for recommendations. None of the recommendations concerning the dental management of patients receiving oral or IV-BPs for osteoporosis were assigned or linked to levels of evidence by their authors.

Discussion

Levels of evidence were not assigned to the recommendations from consensus statements and systematic reviews concerning dental management of patients on oral or IV-BPs for osteoporosis. Of note, such recommendations from one early classic systematic review

explicitly stated they were based on "published literature," and "personal experience," since recommendations were not directly based on the review's data.[1]

Among publications, potential risk factors for the development of MRONJ were reported in relation to local risk factors (i.e., oral disease, invasive dental procedures) and systemic factors. One meta-analysis of 3 controlled trials of cancer patients found that the association with systemic risk factors was not as pronounced as that of local oral risk factors for MRONJ.[2] However, whether this also applies to the case of patients with osteoporosis remains to be established.

The recommendations for the dental management of this patient cohort collectively emphasized the following key issues: (1) attaining optimal dental health before the initiation of BPs, although not as stringent a requirement as in the case of initiation of IV-BPs for oncology patients; (2) the importance of maintaining optimal dental health for decreasing the risk, albeit very small, of developing MRONJ; and (3) proceeding with all dental care with little to no modifications in the setting of complete and well-documented informed consent. In this context, the series of publications from the ADA Council of Scientific Affairs (2006 guidelines, with updates in 2008 and 2011) are the most comprehensive publications for this patient population.[3-5]

Areas of controversy among recommendations from all eligible publications. C-TELOPEPTIDE TEST. The role of testing the serum bone turnover marker C-telopeptide (CTX) level as an indicator of risk for MRONJ in this patient population remains controversial. Some publications recommend serum CTX levels before invasive dental procedures to predict an individual's risk of developing MRONJ, with dental treatment modifications based on those results.[4,6-11] However, other publications, including the latest ADA guideline, have indicated that serum CTX levels display neither reliability nor accuracy in predicting the risk for MRONJ and do not recommend routine testing.[5,12,13]

DRUG HOLIDAYS. Considerable disparity exists among recommendations regarding deferral of initiation of drug therapy, or interruption of drug therapy for purposes of invasive dental procedures. Although some suggest that there are no contraindications or requirements to modify routine dental care as a result of oral BP use,[4,14,15] some narrative reviews and opinion documents advocate drug holidays before invasive procedures based on length of oral BP use (e.g., 3 year benchmark) with or without medical, clinical, or radiographic risk factors.[8,11,16-22] Other publications recommend withholding the drug until complete healing has occurred (i.e., site epithelialization, osseous healing) with waiting periods ranging from 14 days to 3 months, or 1 to 6 months before and after dental treatment.[14,20] However, statements from the ADA and the American Academy of Oral and Maxillofacial Surgeons (AAOMS) suggest that there is insufficient evidence to recommend drug holidays or waiting periods before initiation of BP therapy.[5,9,23-29] One publication acknowledges that lack of support for drug holidays is in line with the physiology behind bone remodeling and the pharmacokinetics of BPs. However, they still advocate some degree of coordination between prescribing physicians and treating dentists for BP dose adjustment and timing of treatment to potentially reduce the risk of MRONJ.[30]

PROPHYLACTIC ANTIBIOTIC THERAPY. There are conflicting and varying recommendations regarding prophylactic antibiotic therapy before and after dental treatment for prevention of MRONJ. One recommendation cites that antibiotics are not indicated for "routine dentistry," (term not defined), whereas others recommend varying regimens of systemic antibiotics before and/or after invasive therapy.[6,7,12,31-35]

Unresolved issues for future research and consensus statements. The precise pathophysiology of BP associated MRONJ as it relates to individual patient risk remains undefined. This is of particular relevance for identifying a priori the small proportion of at-risk patients who develop clinical MRONJ, as well as effective measures to prevent MRONJ (i.e., dental treatment planning, antibiotic therapy, drug holidays, CTX testing). The role, if any, of oral commensal bacteria in this infectious process remains unclear and thus contributes to the unclear value of prophylactic antibiotic therapy. Further investigation into mechanisms underlying MRONJ would strategically enhance development of evidence-based guidelines.

Of further note are suggestions to avoid use of vasoconstrictor in local anesthetics; however, it is not known if this decreases risk of development of MRONJ.[31,34,36] In addition, questions remain regarding degrees of invasiveness of dental procedures as they relate to risk of development of MRONJ.

Conclusions

Questions concerning dental treatment of patients on IV or oral BPs for osteoporosis are summarized in Table IV. The portfolio of recommendations suggests proceeding with dental care with no modifications, given the low risk of MRONJ development, and provision for adequate informed consent; however, no recommendation is assigned a level of evidence. It is anticipated that ongoing basic science and clinical studies will provide the basis for future production by consensus groups of guidelines with a more robust evidence base. Given the dynamic evolution of the science of this relatively recent pathobiologic paradigm, clinicians should continually seek and follow updated guidelines as they emerge over time.

Table III. Key recommendations from guideline statements and systematic reviews: dental management of patients receiving bisphosphonates for osteoporosis (none of the publications assigned levels of evidence for any of the recommendations)

	Level of evidence[*] *Class of recommendation*[†]
In all patients, clinicians should discuss:	
• Importance of maintaining good oral hygiene[19]	NA
• Lifestyle changes, such as smoking cessation for those at high risk for MRONJ[19]	NA
• Very rare occurrence of MRONJ[19]	NA
Risk assessment and treatment planning - Potential risk factors for MRONJ:	
Oral risk factors:	
• Recent dentoalveolar trauma[91-93]	NA
• Dental extraction[90,91]	NA
• Dentoalveolar surgery[91]	NA
• Poor oral hygiene[91]	NA
• Oral infections[91]	NA
• Periodontal disease[91]	NA
Systemic risk factors:	
• Greater frequency of administration[91]	NA
• Larger BP dose[91]	NA
• Longer treatment regimens[91]	NA
• Radiation therapy[91]	NA
• Infectious disease[91]	NA
• Concomitant therapy with corticosteroids[90,92]	NA
• Compromised immune status or immunodeficiency[92]	NA
• Advanced age[92]	NA
• Chronic diseases[92]	NA
Asymptomatic patients receiving BP therapy	
• Before initiation of BP therapy — optimal period to address medically necessary dental care. (i.e., removal of teeth with long-term poor prognosis and/or presenting high risk for infection over time [e.g.: Partially impacted, nonrestorable, or advanced bone loss])[2,5,19,94]	NA
○ *Note:* This pre-BP dental management is a less stringent requirement than with patients using these drugs as part of cancer therapy)[2,5,19,93]	
• Routine dental care — effective oral hygiene practices and regular (i.e., semiannual) examinations and cleaning are especially important in these patients.[4,5,19,92,95]	NA
• Urgent or emergent invasive dental procedures — take precedence over the concern for MRONJ (regardless of the magnitude of the surgery).[5,19]	NA
• Treat immediately periapical pathoses, sinus tracts, purulent periodontal pockets, severe periodontitis, and active abscesses that involve the medullary bone.[4]	NA
• Elective dentoalveolar surgery is not contraindicated.[24,93]	NA
• Surgical procedures — trial segmental or sextant approach may help limit risk of MRONJ (although there are no prospective studies).[5]	NA
• Chlorhexidine rinses — advised before and after any surgical procedures involving bone (i.e., periosteal or medullary bone exposure).[4,5]	NA
• BP therapy greater than 2 years — proceed with routine dental care (to include invasive procedures); however, do inform the patient that risk for MRONJ continues to increase with extended drug use.[5]	NA
Deferred interventions	
• Alteration of BP use — patients need to first consult their treating physician. This should be a medical decision based primarily upon risk for skeletally related events (e.g., fractures) secondary to low bone density, not due to the potential risk of MRONJ.[4,5]	NA
• Drug holidays — there is insufficient evidence to recommend a "drug holiday" or waiting period for invasive dental procedures.[5]	NA
• Routine dental treatment — generally should not be modified solely because of the patient's use of BPs. They do not require any special precautions.[4,93]	NA
Restorative dentistry and prosthodontics	NA
• Malocclusion or masticatory forces — there is no evidence that these increase risk for MRONJ.[3-5]	NA
• Routine restorative care of carious teeth — perform with the goal of minimizing the risk of bone infection.[2-5]	NA
• Prosthodontic appliances — should be carefully adjusted for fit to minimize the chance for ulceration and possible bone exposure.[4,5]	NA
Oral and maxillofacial surgery	
• There are no strict contraindications to oral and maxillofacial surgical procedures, although treatment plans that minimize periosteal and/or intrabony exposure or disruption are preferred.[5]	NA
• Informed consent — patients undergoing invasive procedures should be informed of the risk, albeit small, of developing MRONJ.[3-5]	NA
• Dental extractions — alternative treatment plans should be discussed with the patient, which include endodontics (including treatment followed by removal of clinical crown); allowing roots to exfoliate (instead of extraction); and fixed and removable partial dentures (instead of implants).[3-5]	NA

(*continued on next page*)

Table III. Continued

	Level of evidence[*] *Class of recommendation*[†]
• Conservative surgical technique − primary tissue closure is advised, with placement of semipermeable membranes over extraction sites if primary closure is not possible.[3-5]	NA
Management of periodontal diseases	
• Nonsurgical therapy − appropriate forms advised, with monitoring on a regular basis (e.g., every 4−6 weeks).[3-5]	NA
• Periodontal surgery − can be employed if there is no response to nonsurgical therapy, using modest bone-recontouring techniques and primary soft tissue closure.[3,4]	NA
Implant placement and maintenance	
• Extensive implant placement, guided bone regeneration, bone replacement grafts:	
• No evidence exists regarding risk of MRONJ or the success of implant treatment following such procedures.[3-5]	NA
• There may be at increased risk of developing MRONJ, therefore use of such techniques should be judiciously considered based on risks and patient needs.[3-5]	NA
• There is no rationale for antibiotic prophylaxis for implant surgery.[96]	NA
• Peri-implantitis:	
• Appropriate forms of nonsurgical therapy combined with a prolonged phase of initial therapy should be considered for patients with peri-implantitis.[3,4]	NA
• If peri-implantitis does not resolve, surgical revision of soft tissues around the implant(s) may be appropriate and, when necessary, modest bone recontouring.[3,4]	NA
Endodontics	
• Endodontic treatment − is preferable to surgical manipulation if a tooth is salvageable.[3-5]	NA
• Technique − routine endodontic technique should be used, with care not to perforate the apex.[3-5]	NA
• Periapical healing − there is limited evidence to suggest that healing after endodontic therapy is similar to patients without a history of BP use.[5]	NA
• Endodontic surgical procedures − should be guided by the same precautions used for oral and maxillofacial surgical procedures.[4,5]	NA
Orthodontics	
• There is no evidence concerning the effect of BPs on orthodontic treatment, although case reports suggest that orthodontic movement may be compromised.[4,5]	NA
• It is possible that orthodontic treatment duration will be longer for BP users.[4,5]	NA

NA, not assigned a level of evidence; *BP*, bisphosphonate; *MRONJ*, medication-related osteonecrosis of the jaw.

*Level of evidence:[44]

A−based on multiple randomized controlled trials (RCT).

B−based on data from a single RCT or nonrandomized studies.

C−expert opinion.

†Class of recommendation:[44]

I benefit of patients clearly outweighs any risks, procedure should be performed.

II conflicting evidence and/or a divergence of opinion about the usefulness of a procedure or treatment.

IIa benefit seems to outweigh the risk, weight of evidence in favor of usefulness, it is reasonable to perform the procedure.

IIb benefit seems to outweigh the risk, usefulness is less well established, it is not unreasonable to perform the procedure.

III evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful−risk outweighs the benefit; if it may be harmful and unhelpful, procedure should not be performed.

Table IV. Key questions for research and/or expert consensus: dental management of patients receiving bisphosphonates for osteoporosis

To what extent does tissue-based genetic governance of risk contribute to clinical development of the lesion in the small subset of patients who develop clinical medication-related osteonecrosis of the jaw (MRONJ)?
What is the mechanistic role of oral commensal bacteria in the etiopathogenesis of MRONJ?
To what extent does testing of serum bone turnover marker C-telopeptide (CTX) levels identify risk of MRONJ?
To what extent (if any) do the following dental management factors affect treatment outcomes or risk of development of MRONJ:
• Delaying initiation or interruption of BP therapy for invasive dental procedures?
• Degree of invasiveness of dental procedure?
• Antibiotic prophylaxis (topical and systemic)?
• Vasoconstrictors in local anaesthetic solutions?

DENTAL MANAGEMENT OF PATIENTS WITH CARDIOVASCULAR DISEASE

Methods

Inclusion and exclusion criteria. Subject-specific search terms included the following: cardiopathy; cardiomyopathy; coronary artery disease; ischemic heart disease; hypertension; cardiac arrhythmias; angina pectoris; myocardial infarction (MI); pacemaker; implanted defibrillator; heart failure; and stroke.

Publications were included if they contained recommendations concerning dental care for patients with CVDs as it pertains specifically to provision of care

without adverse events and dental considerations as a result of these medical conditions. Due to previous extensive reviews on these subject matters, the review group did not include recommendations pertaining to antibiotic prophylaxis (AP) for prevention of infective endocarditis, the link between CVD and periodontal disease; management of cardiac emergencies in the dental office; and the management of patients on antithrombotic therapy.[37,38]

Results

Our search identified an initial list of 81 citations from an initial screening of titles and abstracts. An additional 19 citations were identified from other sources, yielding a total of 100 citations that were subjected to full review. Eleven additional citations were identified through the analysis of bibliographies, and 57 articles were excluded after full review, yielding a total of 54 articles that met inclusion criteria. Of the eligible articles, there were 7 consensus and guideline statements, 1 systematic review, 38 narrative reviews, 7 opinion documents, and 1 brief posting on the ADA website.

Clinical practice recommendations from consensus guidelines and systematic reviews. Key recommendations concerning the prevention of adverse events or complications during, or as a direct result of dental care, from the consensus and guideline statement publications and systematic review, are presented in Table V. Recommendations that refer generally to "noncardiac surgery" and can be applicable to dental treatment were also included.

Level of evidence for recommendations. Recommendations in the literature concerning the prevention of adverse events on CVD patients were primarily directed to general surgery. Select recommendations were derived from single randomized controlled trials (Class B), and most recommendations were derived from expert opinion or not linked to levels of evidence.

Discussion

Given the substantial number of narrative reviews regarding dental management of the cardiac patient, the paucity of formal guideline publications is surprising. Among the consensus and guideline statements, only 3 were developed specifically in context of the dental management of patients with CVD: 1 of these statements was a consensus statement from a Canadian dental hygiene association regarding angina pectoris,[39] and the other 2 addressed dental care of stroke patients as reported by British and Canadian groups.[40,41] Of the remaining guideline publications, 2 represented the 2009 European Society of Cardiology (ESC) guidelines for non-cardiac surgery,[42,43] 1 represented the 2007 American College of Cardiology and American Heart Association (ACC/AHA) guidelines for noncardiac surgery,[44] and 1 represented the 2010 AHA guideline for cardiovascular implantable electronic devices.[45]

Based on the publications' classification system, recommendations that were assigned a level of evidence of B or higher (i.e., based on single randomized controlled trials or nonrandomized studies) were concerned with functional capacity as a risk assessment predictor; active cardiac conditions for which treatment be deferred and the condition treated (which include recent MI, unstable angina, significant arrhythmias, and severe valvular disease) and recommended waiting periods before treatment for patients who had undergone revascularization procedures (i.e., bare metal stent implementation, drug-eluting stent implementation, and balloon angioplasty).[44] Levels of evidence of C (i.e., based on consensus or expert opinion) were assigned to recommendations concerning proceeding with emergent noncardiac surgery despite cardiac status[44] and not recommending antibiotic prophylaxis for patients with cardiac implantable electronic devices.[45]

Regarding AHA risk stratification of 30-day cardiac event rates based on type of surgery,[44] there was one suggestion that routine dental procedures be placed under the "low risk" category (<1%) and more complex oral and maxillofacial surgery procedures be placed under the "intermediate risk" category (1%–5%); however, levels of evidence were not provided.[42,43]

Among the collective recommendations, absolute contraindications to proceeding with noncardiac surgery were limited to those patients already experiencing a cardiac event, such as unstable angina and acute coronary syndrome.[44] With respect to the patient with hypertension, one recommendation cited limited evidence from a randomized controlled trial that there was no benefit to deferring long-term treatment of patients with hypertension with diastolic blood pressures between 110 and 130 mm Hg and no previous cardiac conditions.[44] This strategy could be logically interpreted as being safe to proceed with dental treatment for these patients.

Areas of controversy among recommendations from all eligible publications. HYPERTENSION. There was minor disagreement regarding recommended frequency of blood pressure monitoring in patients with hypertension or other risk factors. Some authors advocated monitoring at every dental appointment,[46-52] and others recommended monitoring only during appointments when "significant dental procedures" are being undertaken.[53,54]

Although most publications concurred that patients with normal blood pressure (≤120/80 mm Hg), prehypertension (120–139/80–89 mm Hg) and well-controlled hypertension or stage I hypertension (140–159/90–99 mm Hg) could receive routine dental care,[46,48,49,54,55] there was disparity in recommendations concerning patients with stage II hypertension (160–179/

Table V. Key recommendations and levels of evidence (if assigned), from guideline statements and systematic reviews: management of patients with cardiovascular disease, as it pertains to the prevention of adverse events during provision of care

	*Level of evidence** / *Class of recommendation*[†]
Surgical interventions can be divided into cardiac risk groups with estimated 30-day cardiac event rates (i.e., cardiac death and MI):[43,44]	NA
• Low risk (<1%)	
○ Represent the lowest risk and are rarely associated with excess morbidity and mortality.[44]	
○ Routine dental procedures are considered low risk.[43]	
• Intermediate risk (1%−5%)	
○ Morbidity and mortality vary depending on the surgical location and extent of the procedure. (i.e., short with minimal fluid shifts vs. prolonged with large fluid shifts, greater potential for postoperative myocardial ischemia and respiratory depression). Therefore, must exercise judgment to correctly assess perioperative surgical risks and the need for further evaluation.[44]	
○ Major oral and maxillofacial surgery (head and neck) is classified as intermediate risk.[43]	
• High risk (>5%)	
Risk assessment based on functional capacity:	
• Functional capacity ≥4 METs without symptoms − proceed with planned treatment.[44]	**B, IIa**
• Functional capacity poor (i.e., <4 METs) or unknown, and no clinical risk factors[‡] − proceed with planned treatment.[44]	**B, I**
• Functional capacity poor (i.e., ≤4 METs) or unknown functional capacity, and 1−3 clinical risk factors,[‡] scheduled for intermediate risk surgery − proceed with planned surgery with heart rate control.[44]	**B, IIa**
Emergency noncardiac surgery − should be treated in the operating room and continue perioperative surveillance and postoperative risk stratification and risk factor management.[44]	**C, I**
Active cardiac conditions for which patients should undergo evaluation and treatment before noncardiac surgery:[44]	**B, I**
• Unstable coronary syndromes: unstable or severe angina (CCS class III or IV); recent MI (i.e., <30 days)	
• Decompensated heart failure (NYHA classification III, IV)	
• Significant arrhythmias (e.g., high-grade AV block, Mobitz II AV block, third-degree AV block, symptomatic ventricular arrhythmias, supraventricular arrhythmias [including AF) with HR greater than 100 beats/min at rest, symptomatic bradycardia, newly recognized ventricular tachycardia)	
• Severe valvular disease (severe aortic stenosis, symptomatic mitral stenosis)	
Specific conditions	
• Hypertension − stage 3 (>180/110 mm Hg) − the potential benefits should be weighed against the risk of delaying the procedure. One randomized trial was unable to demonstrate a benefit from delaying surgery in patients with hypertension on long-term treatment, who presented for noncardiac surgery with diastolic blood pressure between 110 and 130 mm Hg and who had no previous cardiac conditions.[44]	NA
• Unstable angina − if noncardiac surgery can be postponed safely, it is recommended that patients be diagnosed and treated before noncardiac surgery.[43]	NA
• Acute coronary syndrome (ACS) − in the unlikely combination of a life-threatening clinical condition requiring urgent noncardiac surgery and ACS, it is recommended that surgery be given priority with aggressive medical treatment and myocardial revascularization on immediate follow-up.[43]	NA
• Coronary artery disease − Although the overwhelming risk factor for perioperative morbidity, procedures with different levels of stress are associated with different levels of morbidity and mortality.[44]	NA
• Bare metal stent implantation − elective noncardiac surgery is not recommend within 4−6 weeks (optimally 3 months) following the intervention.[43,44]	**B, III**
• Recent balloon angioplasty − elective noncardiac surgery is not recommend within 2−4 weeks following the intervention.[43,44]	**B, III**
• Cardiovascular implantable electronic devices (CIED) − antimicrobial prophylaxis is not recommended for dental procedures to prevent CIED infection.[45]	**C, III**

NA, not assigned a level of evidence; *MI*, myocardial infarction; *MET*, metabolic equivalent; *CCS*, Canadian Cardiovascular Society; *NYHA*, New York Heart Association; *AV*, atrioventricular; *AF*, atrial fibrillation; *HR*, heart rate; *beats/min*, beats per minute.

*Level of evidence:[44]

A−based on multiple randomized controlled trials (RCT).

B−based on data from a single RCT or nonrandomized studies.

C−expert opinion.

[†]Class of recommendation:[44]

I benefit of patients clearly outweighs any risks, procedure should be performed.

II conflicting evidence and/or a divergence of opinion about the usefulness of a procedure or treatment.

IIa benefit seems to outweigh the risk, weight of evidence in favor of usefulness, it is reasonable to perform the procedure.

IIb benefit seems to outweigh the risk, usefulness is less well established, it is not unreasonable to perform the procedure.

III evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful−risk outweighs the benefit; if it may be harmful and unhelpful, procedure should not be performed.

[‡]Clinical risk factors include[44] ischemic heart disease, compensated or prior heart failure (HF), diabetes mellitus, renal insufficiency, and cerebrovascular disease.

100−109 mm Hg). In this latter case, selected publications advocated providing only emergency care, especially if there are medical risk factors,[47,53] whereas others advocated selective "noninvasive" dental care in addition to emergency care.[46,48,49,54,56] However, some (including the ACC/AHA guideline) advised that treatment was safe if there are no medical risk factors, if the metabolic equivalent (MET) was >4, and/or if the patient was chronically treated with medications, as previously suggested for patients with diastolic pressures up to 130 mmHg.[44,47,53]

Discrepancies also existed regarding treatment of patients at higher blood pressure readings (e.g., ≥180/≥110−119 mm Hg), with some advising that all dental treatment was contraindicated[51-54,57] and others advocating emergency treatment only using local anesthetic (LA) without vasoconstrictor, if benefit of treatment outweighed the risk.[46,49,58]

Dental treatment after MI. Several publications in dental hygiene journals by the same author interpreted the AHA/ACC recommendation of deferring noncardiac surgery for patients with recent MI, to imply that one may proceed with dental treatment after a waiting period of at least 30 days.[51,52] However, other authors recommended that only emergency care be performed after this period, without stating suitable waiting periods for regular care.[53,55,57,59] The longstanding recommendation advising a waiting period of 6 months before emergency dental care in a hospital setting was based on older reports that cited risk of cardiac events for general surgical procedures under general anesthesia.[60]

Local anesthetic with vasoconstrictor. There was disparity among recommendations regarding use of LA with vasoconstrictor in patients with CVD. There were several medical conditions (e.g., unstable angina, MI within past 6 months, recent coronary artery bypass surgery [CABG]), for which absolute contraindication, strict avoidance, and caution with the use of LA with vasoconstrictor were advised, but there was lack of consistency among publications.[39,48,49,58,61,62] There was also variation regarding recommended safe amount of epinephrine for these patients, with some advocating a maximum dose of 0.04 mg of epinephrine (two anesthetic carpules with vasoconstrictor at 1:100,000 concentration)[48,51,52,54-57,60,63,64] and others suggesting 0.054 mg (three anesthetic carpules).[47,58,62]

Balloon angioplasty. There was minor disparity regarding waiting periods following balloon angioplasty, as the ESC guidelines recommended a waiting period of 2 weeks,[42] and the ACC/AHA guidelines recommended a waiting period of 4 weeks,[44] with the latter being linked to a Class B level of evidence.

Unresolved issues for future research and consensus statements. Although selected recommendations advocated comprehensive dental evaluation and removal of all sources of active dental disease before CABG, it remains unknown whether dental disease or the presence of oral infection has any impact on post-CABG outcomes.[53] What is also unclear is the length of time that dental treatment be deferred after surgery. For example, there is one recommendation from the ESC guidelines that patients who had undergone "…previous CABG in the last 5 years can be sent for noncardiac surgery without further delay"; however, this statement is ambiguous, as it does not distinguish between a waiting time of 5 years and administration of treatment within the past 5 years, and whether that includes the period immediately after CABG.[42]

The ESC and AHA/ACC guidelines recommend a 12-month waiting period following drug-eluting stent implementation before noncardiac surgery, and the AHA/ACC guideline has the added qualifier that it relates to surgeries in which antiplatelet therapy is discontinued preoperatively (Level of evidence B).[42,44] However, this does not specifically address procedures performed on patients whose antiplatelet therapy had not been discontinued. Thus, there are no recommendations applying to noninvasive dental procedures of varying stress levels, and the AHA recommended practice of performing invasive dental or oral surgical procedures without discontinuing antiplatelet therapy.[65]

Conclusions and future directions

Questions concerning dental treatment of CVD patients are summarized in Table VI. While dental treatment falls within the lowest risk category for adverse cardiac events, potential patient morbidity for such events creates concern among dentists. With lack of consensus statements, guidelines, or systematic reviews focused on these specific issues related to dental treatment for patients with CVD, the vast majority of current recommendations are not linked to levels of evidence and are presumably derived from expert opinion. Additionally, the infrequent occurrence of adverse cardiac events in the dental setting makes the design of adequately powered clinical studies challenging. There is, thus, significant need for formal consensus statements specific to dentistry for each of these cardiac scenarios, even if extrapolated from nondental surgical data.

DENTAL MANAGEMENT OF PATIENTS WITH PROSTHETIC JOINTS

Methods

Inclusion and exclusion criteria. Initial subject specific search terms included the following: prosthetic joint replacements; prosthetic joint infections; antibiotic prophylaxis; oral source bacteremia; immunocompromising factors; topical antimicrobials; systemic antimicrobials;

Table VI. Key questions for research and/or expert consensus: dental management of patients with cardiovascular diseases, as it pertains to the prevention of adverse events during the provision of care

For each cardiac condition, what is the accurate risk stratification for specific dental procedures with varying levels of stress and invasiveness?
What are appropriate recommended modifications for dental procedures for patients with stage II hypertension (both treated and not actively treated) and previous cardiac disease?
What, if any, are the potential risks from catecholamine-containing local anesthetics in patients with various cardiac conditions? Optimal evidence-based protocols for their usage during dental treatment are needed.
What parameters determine the safest time to deliver dental treatment: • After myocardial infarction (treated and not actively treated)? • After balloon angioplasty? • After drug-eluting stents, in which antiplatelet therapy is not discontinued? • After coronary artery bypass grafting?

hip surgery; hip replacement; joint surgery; joint replacement; knee surgery; knee replacement; shoulder surgery; and shoulder replacement.

Publications were included if they contained recommendations concerning the prevention of prosthetic joint infections (PJI) as it relates to invasive dental treatment.

Results

We identified 47 citations for full text review through initial screening of titles and abstracts. No additional citations were identified from other sources, and 13 additional citations were identified through the analysis of bibliographies. We excluded 21 articles after full review, yielding a total of 39 articles that met inclusion criteria. Of these articles, there were 8 consensus and guideline statements, 13 narrative reviews, and 18 opinion documents. Of note, 2 of the eligible guideline publications referred to the same 2012 joint guideline by the American Dental Association (ADA) and American Association of Orthopedic Surgeons (AAOS).

Clinical practice recommendations from consensus guidelines and systematic reviews. The ADA and AAOS published joint guidelines in 1997,[66] 2003,[67] and 2012,[68] and the New Zealand Dental Association has a "code of practice" published in 2003.[69] The AAOS published a unilateral guideline in 2009, which superseded the joint ADA/AAOS 2003 guidelines.[70] The American Association of Pediatric Dentists (AAPD) published a 2012 guideline for pediatric patients at risk of infection (to include those with prosthetic joints),[71] and the Canadian Dental Association (CDA) published a guideline in 2013, making reference to the ADA/AAOS 2012 guideline.[72] Table VII compares recommendations derived from published guidelines from 1997 to 2012, and Table VIII compares the recommendations from the 2012 ADA/AAOS and 2013 CDA guidelines.

Level of evidence for recommendations. Recommendations before 2012 concerning prevention of PJI as it relates to invasive dental treatment were not assigned or linked to levels of evidence. The primary ADA/AAOS 2012 recommendation of discontinuing the routine practice of antibiotic prophylaxis for patients with prosthetic joints was assigned as a "limited recommendation," which is cited as being derived from limited, nondefinitive data.

Discussion

There was minimal variation between the 1997 and 2003 ADA/AAOS guidelines, with their recommendations of antibiotic prophylaxis not being indicated for most patients with prosthetic joints when undergoing invasive dental procedures, and limited indications for antibiotic prophylaxis for 2 years after placement and for those with selected medical risk factors. None of these recommendations was assigned a level of evidence by the authors. In their "code of practice," the New Zealand Dental Association essentially adopted the 2003 ADA/AAOS guideline statement, with the added recommendation of attainment of optimal oral health before and after prosthetic joint replacement.[69] The same can be said for the AAPD; however, these authors also referred to the 2007 AHA guidelines for infective endocarditis to delineate specific dental procedures for which AP is indicated.[73] Of the reviewed articles, the 2012 ADA/AAOS guideline was the only one that assigned levels of evidence. Its main recommendation, although based on "limited" evidence, was "considering" discontinuing the routine use of antibiotic prophylaxis, while giving other recommendations that were assigned levels of "expert" opinion or "inconclusive" evidence.[68] By comparison, the CDA's guideline the following year adopted a stronger stance by stating that "routine antibiotic prophylaxis is not indicated," although not incorporating level of evidence to the recommendation.[72]

Areas of controversy among recommendations from all eligible publications. AAOS 2009 INFORMATION STATEMENT. The AAOS 2009 information statement was controversial, as it reversed and, thus, contradicted previous guidelines, suggesting that all patients with prosthetic joints have antibiotic prophylaxis for all potentially bacteremia-causing procedures and for the patients' lifetime.[70] In response, several opinion documents

Table VII. Comparison of recommendations: dental management of patients with prosthetic joints (1997 to 2012)

ADA/AAOS 1997,[66] ADA/AAOS 2003,[67] NZDA 2003,[69] AAPD 2012[71]	*Class of recommendation*	*AAOS 2009[70]*	*Class of recommendation*
Patients scheduled for or with pre-existing prosthetic joint replacement (NZDA 2003) − all should have a dental examination and treatment, as required, to reduce and remove sources of oral bacteremia.[69]	NA		
AP is not indicated for dental patients with pins, plates and screws.[66,67,69,71]	NA		
Routine AP for all PJ patients is not justified, as premedication is **not indicated for most dental patients with prosthetic joints.**[66,67,69,71]	NA	"…**consider antibiotic prophylaxis for all total joint replacement patients before any invasive procedure that may cause bacteremia**."	NA
AP could be considered for dental procedures producing significant bacteremia in a **small number of patients with prosthetic joints at increased risk:**[66,67,69] • **Two years following joint replacement**[66,67,69] • Previous prosthetic joint infection[66,67,69] • Immunocompromised/immunosuppressed patients[66,67,69] • Inflammatory arthropathies (i.e., RA, SLE)[67,69] • Drug- or radiation-induced immunosuppression[67] • Insulin dependent diabetes[66,67,69] • Malnourishment[66,67,69] • Hemophilia[66,67,69] • Malignancy[67]	NA	"This is **particularly important for those patients with one or more of the following risk factors:**" • All patients with prosthetic joint replacement. • Previous prosthetic joint infection • Immunocompromised/immunosuppressed patients • Inflammatory arthropathies (i.e., RA, SLE) • Drug- or radiation-induced immunosuppression • Insulin-dependent (type 1) diabetes • Malnourishment • Hemophilia • Malignancy • **Obesity** • **Smoking** • **Megaprostheses**	NA
Specific indications based on dental procedure (AAPD 2012):[71] • Antibiotics may be considered when high-risk dental procedures (i.e., all dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa)[73] • The following procedures and events do not need prophylaxis:[73] • Routine anesthetic injections through noninfected tissue • Taking dental radiographs • Placement of removable prosthodontic or orthodontic appliances • Adjustment of orthodontic appliances • Placement of orthodontic brackets • Shedding of deciduous teeth • Bleeding from trauma to the lips or oral mucosa	NA		

Significant differences are highlighted in bold (none of the publications assigned levels of evidence for any of the recommendations).
ADA, American Dental Association; *AAOS*, American Academy of Orthopedic Surgeons; *NZDA*, New Zealand Dental Association; *AAPD*, American Academy of Pediatric Dentists; *NA*, not assigned a class of recommendation; *AP*, antibiotic prophylaxis; *PJ*, prosthetic joint(s).

recommended that the dentist contact the patient's orthopedic surgeon and follow the 2003 guidelines until a new joint consensus statement was approved.[74,75] Although several recommendations stated that the patients' clinician was ultimately responsible for making treatment recommendations (including antibiotic prophylaxis), based on their professional judgment, some suggested that orthopedic surgeons, not dentists, should write the prescription if they recommend antibiotic prophylaxis for patients otherwise not recommended for prophylaxis by previous joint ADA/AAOS guidelines.[74,76,77]

Unresolved issues for future research and consensus statements. The joint 2012 guideline from the ADA and AAOS effectively reversed the AAOS 2009 "information statement," basing their recommendations on systematic reviews and linking them to levels of evidence. However, the guideline remains unclear as to whether "discontinuing the practice of routinely prescribing prophylactic antibiotics" for these patients translates to discontinuing the practice altogether, or whether clinicians should consider prescribing in a limited number of cases, as indicated in previous guidelines. This led to a state of confusion, which was expressed by many respondents to our ADA survey of practicing dentists.

Several questions must be answered in order to develop clear and evidence based recommendations, for example, the likelihood that bacteremia from an oral source can cause or are associated with PJI; whether

Table VIII. Comparison of recommendations: dental management of patients with prosthetic joints (2012−2013)

*ADA/AAOS, 2012**	*Class of recommendation*[70]	*#CDA, 2013†*	*Class of recommendation*[70]
In the absence of reliable evidence linking poor oral health to prosthetic joint infection, it is the opinion…that patients with prosthetic joint implants or other orthopedic implants ***maintain appropriate oral hygiene***.	**Consensus**	Patients should ***be in optimal oral health*** before having total joint replacement and should ***maintain good oral hygiene and oral health*** following surgery. Orofacial infections in all patients, including those with total joint prostheses, should be treated to eliminate the source of infection and prevent its spread.	NA
The practitioner might ***consider discontinuing the practice of routinely prescribing prophylactic antibiotics*** for patients with hip and knee prosthetic joint implants undergoing dental procedures.	**Limited**	Patients should not be exposed to the adverse effects of antibiotics when there is no evidence that such prophylaxis is of any benefit. ***Routine antibiotic prophylaxis is not indicated*** for dental patients with total joint replacements or for patients with orthopedic pins, plates, and screws.	NA
We are ***unable to recommend for or against the use of topical oral antimicrobials*** in patients with prosthetic joint implants or other orthopaedic implants undergoing dental procedures.	**Inconclusive**		

Limited recommendation:[70]
Quality of the supporting evidence that exists is unconvincing, or well-conducted studies show little clear advantage to one approach versus another. Practitioners should be cautious in deciding whether to follow recommendation and should exercise judgment and be alert to emerging publications that report evidence. Patient preference should have a substantial influencing role.
Inconclusive recommendation:[70]
There is lack of compelling evidence, resulting in an unclear balance between benefits and potential harm. Practitioners should feel little constraint in deciding whether to follow recommendation and should exercise judgment and be alert to future publications that clarify existing evidence for determining balance of benefits versus potential harm. Patient preference should have a substantial influencing role.
Consensus recommendation:[70]
Expert opinion supports the guideline recommendation, even though there is no available empirical evidence that meets the inclusion criteria. Practitioners should be flexible in deciding whether to follow recommendation, although they may set boundaries on alternatives. Patient preference should have a substantial influencing role.

Levels of evidence were assigned as indicated for the American Dental Association/American Association of Orthopedic Surgeons' 2012 guideline statement.
NA, not assigned class of recommendation.
*American Dental Association (ADA) and American Academy of Orthopedic Surgeons (AAOS) 2012 guideline statement.[70]
†Canadian Dental Association (CDA) 2013 guideline statement.[72]

Table IX. Key research questions: dental management of patients with prosthetic joints

Are selected invasive dental procedures are associated with prosthetic joint infections (PJI), and if so, what is the strength of this association?
If this association exists, does prophylaxis, either via systemic antibiotic administration or topical antimicrobial oral rinses reduce the risk of PJI?
What is the incidence, nature, and magnitude of oral bacteremia from daily activities (e.g., oral hygiene, eating), in relation to the risk for development of PJI?
To what extent, if any, does pre-existing oral disease increase the risk of development of PJI?

poor oral hygiene or bacteremia from daily oral hygiene practices are associated with or cause PJI; and whether antibiotic prophylaxis is effective in preventing such infections. One retrospective matched case-control study did not identify any association between dental procedures and increased risk of PJI; however, the authors acknowledged the low power of their study.[78]

In response to the confusion and ambiguity of the 2012 ADA/AAOS guidelines, the ADA published an updated guideline statement in 2015, after the WWOM review group literature search had been completed. This recently published updated ADA guideline statement does not recommend antibiotic prophylaxis for dental procedures for patients with prosthetic joints, citing lack of evidence from their systematic review, which found no association between dental procedures and PJI.[79]

Conclusions and future directions

Although published guidelines since 1997 have trended toward ceasing the practice of providing antibiotic prophylaxis for this patient cohort, additional studies, as summarized in Table IX, are needed to provide recommendations that are based on higher levels of evidence.

DENTAL MANAGEMENT OF PATIENTS ON SYSTEMIC STEROID THERAPY

Methods

Inclusion and exclusion criteria. Initial search terms included the following: adrenal crisis; adrenal suppression; adrenal insufficiency (AI); steroid supplementation; systemic steroids; steroid cover; steroid prophylaxis; and preoperative steroids.

Publications were included if they contained guidelines or recommendations developed for the prevention of adverse events (i.e., Adrenal crisis) during the dental care of patients exposed to systemic steroid therapy. Additional publications were also included pertaining to general surgery procedures, if deemed applicable to dental treatment.

Results

Our initial search revealed 11 citations which were pulled for full text review. One additional citation was identified from other sources, and 7 additional citations were identified through the analysis of bibliographies. Seven articles were excluded after full article review, yielding a total of 12 articles that met inclusion criteria.

Of the eligible publications, 2 were deemed as formal guideline publications (1 of which specifically pertained to dental treatment), 1 was a systematic review, 8 were narrative reviews, and 1 was an opinion document.

Clinical practice recommendations from consensus guidelines and systematic reviews. Key recommendations from the consensus guideline publications[80,81] and systematic review[82] relating to patients specifically at risk of adrenal suppression due to systemic steroid therapy are presented in Table X.

Level of evidence for recommendations. Only one of the recommendations concerning the prevention of adverse events during the dental care of patients exposed to systemic steroid therapy was assigned or linked to levels of evidence.

Discussion

The systematic review was a Cochrane review pertaining to general surgery for patients with AI, based on two randomized controlled trials.[82] The authors of these trials concluded that they were unable to support or refute the use of supplemental steroids during surgery and that patients' daily maintenance dosages of steroids may be sufficient in the majority of patients with adrenal suppression. The one dental-specific guideline article created a risk stratification based on invasiveness of dental procedures, suggesting that most routine dental procedures, as well as minor surgical procedures under LA, do not require supplemental steroid dosing beyond the daily maintenance dose. Steroid supplementation was only considered for patients who are undergoing procedures under general anesthesia; however, the authors noted a lack of evidence to demonstrate any benefit. These recommendations were not linked to levels of evidence by their authors.[80]

Areas of controversy among recommendations from all eligible publications. Degree of hypoadrenalism or risk of AI for individuals on chronic systemic steroid use. It has been suggested that patients receiving less than 10 mg prednisolone per day (or equivalent) have normal hypothalamic–pituitary–adrenal (HPA) axes and therefore do not require further HPA axis testing or additional steroid

supplementation.[83,84] However, there were contradictory suggestions that those patient receiving more than 7.5 mg prednisolone per day or equivalent for more than 30 days, or more than 20 mg prednisolone per day for more than 2 weeks, are at risk for AI.[81]

Consequently, narrative reviews and opinion publications proposed diverse indications for steroid supplementation based on patients' steroid regimen. There was one recommendation that patients who had received glucocorticoid therapy for more than 3 weeks by any route receive steroid supplementation, presumably regardless of dose.[85] There was another recommendation that steroid supplementation is required if the patient's daily dose was less than the recommended surgical dose; however, a recommended target surgical dose was not specified.[86]

One notable narrative review involved a systematic search for case reports in the literature for adrenal crises associated with dental treatment and cited a number of risk factors for adrenal crisis and, thus, indications for steroid supplementation. These risk factors included significant adrenal insufficiency; use of corticosteroids greater than 4 years; poor health status and stability at the time of dental treatment; history of infectious disease; stressful invasive procedures; general anesthesia; and use of drugs that inhibit the synthesis or metabolism of cortisol.[87]

Conversely, suggested thresholds for not requiring supplementation varied from prednisolone 5 mg per day or less,[88] 30 mg hydrocortisone per day or less (7.5 mg prednisolone),[89] more than 30 mg hydrocortisone (7.5 mg prednisolone) per day for less than 30 days, discontinued more than 2 weeks previously,[89] and prednisone 10 mg per day or less.[83,84,86] There were also suggestions that supplementation was not required if steroid treatment had been discontinued for more than three months[83,84,86] or if steroids were being administered on an alternate day basis.[88,89]

Risk stratification based on surgical stress. Several articles provided specific recommendations based on risk stratification of the procedures. (i.e., mild, moderate, and high[81]; minor or major surgery[87]). However, none of the publications specifically defined which procedures fall under a given category. In addition, there was one recommendation that a procedure exceeding 1 hour be performed in a hospital setting with steroid supplementation.[90]

Steroid supplementation regimens. Among the narrative reviews and opinion documents, there were diverse regimens for preoperative steroid supplementation, including the widely propagated practice of doubling the normal dose of steroids on the day of treatment,[89] and target ranges varying from 5 mg prednisone (or equivalent) to 25 mg prednisone on the day of surgery.[83-87,89,90] One publication stratified the supplementation regimen based on surgical stress, with 25 to 75 mg hydrocortisone equivalent on the day of surgery for minor surgery, and 100 to 150 mg hydrocortisone equivalent for the day of major surgery and the following day; however, definitions for major and minor surgery were not provided.[87] The single guideline publication suggested that doubling the daily dose was recommended for those on "high doses of steroids," although a definition was not provided.[80]

Unresolved issues for future research and consensus statements. Although many of the recommendations pertained specifically to patients with iatrogenic adrenal suppression due to exogenous steroid supplementation, there remain questions regarding the management of patients who have other causes of adrenal suppression (e.g., adrenalectomy, radiation to the pituitary, Cushing disease) and who do or do not require supplemental steroid therapy.

Conclusions and future directions

Clinical questions and future opportunities for research are highlighted in Table XI. There is no strong evidence to support or refute the practice of steroid supplementation in general, given the very limited scientific evidence. The general trend from expert opinion and less formal consensus is toward not providing supplementation for most routine dental and minor oral surgical procedures under LA[80,82] and reserving steroid supplementation for more stressful procedures, for those performed with the patient under general anesthesia, when the patient's health is poor, and when drugs that metabolize cortisol or inhibit its synthesis are used. Since the risk of adverse outcomes from short term steroid supplementation is low; this may be a significant factor relative to the continued practice of steroid supplementation.

SUMMARY

This study assessed the degree to which current literature for dental management of selected medical conditions provided high-quality recommendations. Knowledge of these clinical management recommendations, the extent of their basis on science and clinical translation, and how they relate to each other, is important to provide safe and effective care. This report also delineated the current state-of-the-science, key recommendations, as well as controversial and unresolved issues to provide a basis for new research and formulation of high-quality consensus guideline statements.

To maximize clinical relevance regarding areas of current controversy in dental practice, the four topics were selected by group consensus based on a survey of practicing American dentists. Conclusions for each topic are as follows:

Table X. Key recommendations and levels of evidence (if assigned) derived from guideline statements and systematic reviews: dental management of patients on systemic steroid therapy

	*Level of evidence** *Class of recommendation†*
No need for mineralocorticoid supplementation.[81]	**C, I**
Unable to support or refute the use of supplemental perioperative steroids during surgery, as there is currently insufficient evidence to support the use of supplemental perioperative steroids in patients with adrenal insufficiency.[82]	NA
It is likely that administration of the patient's daily maintenance dose of corticosteroid may be sufficient in the majority of adrenally suppressed patients undergoing surgery and that supplemental doses may not be required.[82]	NA
General Dental Procedures	
Does not warrant supplementation with additional glucocorticoids.[80]	NA
Minor surgery under local anesthesia	
Patients are at very low risk, if any, for developing adrenal crisis.[80]	NA
Evidence suggests that supplementation is unnecessary for local anesthetic procedures. These patients should simply maintain their usual dose of glucocorticoids.[80]	NA
Surgery under general anesthesia	
There is no evidence that glucocorticoid supplementation exceeding physiologic levels of cortisol induced by stress is beneficial.[80]	NA
The need for perioperative glucocorticoid supplementation for patients on exogenous steroids should be determined by the severity of the surgery and the pre-existing glucocorticoid dose.[80]	NA

NA, not assigned a level of evidence.
*Level of evidence:[81]
A—based on multiple randomized controlled trials (RCT).
B—based on data from a single RCT or nonrandomized studies.
C—expert opinion.
†Class of recommendation:[81]
I benefit of patients clearly outweighs any risks, procedure should be performed.
II conflicting evidence and/or a divergence of opinion about the usefulness of a procedure or treatment.
IIa benefit seems to outweigh the risk, weight of evidence in favor of usefulness, it is reasonable to perform the procedure.
IIb benefit seems to outweigh the risk, usefulness is less well established, it is not unreasonable to perform the procedure.
III evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful—risk outweighs the benefit; it may be harmful and is unhelpful, procedure should not be performed.

Table XI. Key questions for research and/or expert consensus: dental management of patients on systemic steroid therapy

What is the range of adrenal suppression for the most common regimens of steroid drug doses?
What are (a) the physiologic response levels of cortisol associated with and, thus; (b) appropriate target steroid supplementation dosages for:
• Specific dental and surgical procedures?
• Procedures performed in different settings (i.e.: Local anesthesia vs. sedation vs. general anesthesia)?
• Anxious and/or fearful dental patients?
• Dental patients with systemic causes of adrenal suppression? (e.g., Cushing syndrome, history of adrenalectomy, radiotherapy or previous surgery to the pituitary gland, autoimmune disorders)

- Medication-related osteonecrosis of the jaw:
  - Current non—evidence-based recommendations are trending toward proceeding with dental care, with little or no treatment modifications for patients on IV or oral BPs for osteoporosis.
  - With ongoing research studies and consensus groups, it is anticipated that evidence-based recommendations are forthcoming.
- Cardiovascular disease:
  - There are very few evidence-based recommendations for prevention of adverse events during dental treatment in this patient cohort, all of which are derived from recommendations pertaining to general surgery.
  - Given limitations in producing adequately powered studies, consensus guideline statements specifically pertaining to the dental management of patients with CVD are needed, even if based on the general surgery literature.
- Prosthetic joints:
  - Consensus based on emerging evidence is trending toward not providing AP for dental procedures for this patient cohort.
- Systemic steroid therapy:
  - General expert recommendations trend toward not providing steroid supplementation for most dental procedures under LA, and only doing so for more stressful procedures, for those performed with

patient under general anesthesia, when the patient's health is poor, and when drugs that metabolize cortisol or inhibit its synthesis are used.
- Risks of adrenal crisis, cortisol levels in response to surgical stress, and appropriate supplemental steroid dosages have yet to be determined.

Forthcoming papers by this WWOM-VI review group will include a detailed report on the results of the ADA survey of dental practitioners, which informed the choice of topics covered in this report, and more detailed reports on these four individual patient cohorts. Critical and objective appraisals of the quality of formal organizational consensus and guideline documents will be included by using various tools, such as the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument (http://www.agreetrust.org/) and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.

Future opportunities include surveys of dental practitioners from other countries and regions, and the analysis of the validity and application of specific guidelines in clinical practice.

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