



Clinical practice guidelines for dental management prior to radiation for head and neck cancer

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ABSTRACT

Purpose: Limited evidence exists linking the specific preventative dental care provided prior to radiation therapy (RT) for head and neck cancer to outcomes like osteoradionecrosis (ORN). This study utilized expert consensus to develop tooth-specific dental treatment pathways for head and neck cancer patients prior to radiation.

Materials and Methods: Dental oncologists from across a single nation were engaged in a Modified Delphi process. Three rounds of questionnaires were performed followed by an in-person meeting. Domains included radiation dose, timing of dental treatment, and treatment of dental caries, periodontal disease and third molars.

Results: The response rate from the 32 participants between rounds was > 70%. Consensus was reached for all but 4 questions. The radiation dose at which participants would prophylactically remove teeth to prevent ORN was established as 70 Gy in the maxilla and 60 Gy in the mandible. Treatment pathways were developed for maxillary and mandibular anterior/premolar and molar teeth receiving a dose at or above this threshold. Risk factors were established for carious, periodontally involved and third molar teeth. In general, periodontally involved teeth and mandibular molars were most frequently recommended for extraction. Only symptomatic third molars were recommended for extraction when adequate healing time was available prior to commencement of RT.

Conclusion: Tooth-level clinical practice guidelines were developed using expert consensus via the modified Delphi process. The treatment pathways developed in this study will be prospectively tested to evaluate the outcomes associated with tooth-specific dental treatments.

Introduction

Head and neck cancer (HNC) made up approximately 2.6% of all new North American cancer cases in 2020 [1,2]. Fortunately, HNC has a relatively high cure rate, with an estimated 5-year survival rate of 66.2% from 2010 to 2016 [1], in part due to a demographic shift towards Human Papillomavirus-related HNC which carries a relatively better prognosis [3,4,5]. A large portion of HNC is treated with radiation therapy (RT) either primarily or in conjunction with surgery [1,6,7,8,9]. Unfortunately, dental complications are often experienced by patients who are exposed to therapeutic radiation. Damage to the major salivary

glands that fall within the high-dose RT volume can lead to profound xerostomia and post-radiation caries [10]. Damage to bone can take years to manifest in the form of osteoradionecrosis (ORN) and is often precipitated by dental extractions [8,11]. The demographic shift toward HPV-related HNC has presented a significant challenge for dental oncologists faced with balancing maintaining a functional dentition for patients while attempting to minimize prolonged risk of ORN [12].

Increasingly, focus is being placed on the value of appropriate pre-RT dental care in minimizing or preventing the significant long-term sequelae following RT for HNC [13,14,15]. Comprehensive systematic reviews of pre-RT dental considerations are able to provide evidence for

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risk factors for ORN but fall short of specific tooth-level treatment recommendations tailored to HNC patients [16,17]. These reviews have not been able to provide concise answers as to the best preventative treatment measures to reduce the long-term oral side effects of RT [17,18,19,20]. Rather, it has been suggested that prospective studies be conducted with well-defined criteria for oral foci of infection, a description of the foci that were eliminated and how, and systematic recording of oral problems that occur post-RT [17]. It is generally accepted that in the absence of high-level evidence, expert consensus may be used to develop clinical practice guidelines [21]. We thus set out to develop consensus-based guidelines for the prophylactic dental care delivered prior to RT for HNC with the eventual intent of prospectively testing the guidelines through a national multi-center study. For the remainder of this manuscript, the guidelines will be referred to as the Canadian Dental Oncology Network (CDON) Head and Neck Guidelines.

Methods

The CDON Head and Neck Guidelines were developed using a modified Delphi approach. The modified Delphi process utilizes rounds of questionnaires followed by an in-person meeting as a means of developing consensus guidelines based on expert opinion [22,23]. A detailed description of the modified Delphi process used, and strategies employed has been previously reported [24]. The three rounds of questionnaires and questions from the final in-person meeting can be found in the supplemental figures.

Panel Development: Invitation letters were sent via email to dental oncologists across Canada. For the purposes of this study, a dental oncologist was defined as a hospital-based dentist treating primarily cancer patients. Contact details were obtained by reviewing websites of known institutions offering dental oncology services and via snowballing sampling technique [25]. Inclusion criteria for panelist selection included: 1) Experience at a Canadian hospital-based dental clinic treating cancer patients for at least two years or completion of a fellowship in Dental Oncology; and 2) Willingness to consent to participate in the study. Written consent was obtained from participants through response via email.

Question generation: A literature review was performed to generate questions for round 1 of the Delphi process. During this round, both closed-ended and open-ended questions were used to allow participants to guide questions for future rounds. In round 2, close-ended questions were developed based on the responses from round 1 and the literature review performed.

The literature review focused on the tooth- and patient-level criteria that lead to a decision to extract or maintain a tooth prior to RT. The questions for round 1 were generated by two dental oncologist and radiation oncologist at the host site and validated by two experienced dental oncologists from two other Canadian sites.

The questions fell under six domains: 1) The radiation dose above which a clinician begins making decisions to prophylactically remove teeth prior to RT, herein referred to as the "Critical Radiation Threshold", or CRT; 2) The ideal timing of pre-RT dental care; 3) The treatment of teeth with various forms of dental caries and/or periapical lesions; 4) The treatment of third molars; 5) The treatment of teeth with periodontal disease; and 6) General questions.

Once the CRT was established, participants were asked to consider the teeth being described in the questions as falling at or above their CRT. Where relevant, questions were stratified based on tooth location (Maxilla or mandible), position (anterior/premolar, first/second molar or third molar) and radiation dose (low risk - below the CRT, or high risk - at or above the CRT).

Questions related to treatment decisions that did not reach consensus after round 1 were stratified based on patient risk of complications post-RT. To define patient risk, participants were asked open-ended questions in round 1 about the risk factors that impact their decision making when deciding to extract or maintain teeth at future risk of ORN. A Likert scale

was used to determine which risk factors reached consensus amongst the expert panel [26]. These risk factors were applied to various treatment planning scenarios and used to define three risk levels: Mild (Patients at low risk of complications post-RT), Moderate (Patients at moderate risk of complications post-RT) and High (Patients at high risk of complications post-RT). Descriptions of periodontal disease severity (Grades I, II, III and IV) were based on the classification system developed at the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions [27,28].

A goal was set for at least a 70% response rate for each round with a 75% threshold for consensus. A 9-point Likert Scale was used to determine the level of agreement for certain questions and participant confidence in the guideline development process [22,29]. Questions that did not reach consensus during a round were moved to the next round, or the in-person meeting if it became evident after 2 rounds that consensus could not be reached without discussion.

Ethics approval was obtained from the University Health Network Research Ethics Board to conduct the study.

Results

Three rounds of questionnaires were sent to participants from March 2020 to October 2020, followed by a virtual meeting in December of 2020. In total, 44 invitations were sent out with 32 participants consenting to take part in the study (72.7%). There was participant representation from eight of the ten Canadian provinces. The mean years of clinical practice of the 32 participants was 17.2. The response rate for Round 2 was 25/32 (78.2%) and 23/25 (92.0%) for Round 3. Eighteen (78.3%) participants took part in the in-person meeting. In the first round, 51 questions were asked with consensus reached for 14. In round 2, 101 questions were posed with consensus reached on 61. The remaining 50 questions were split between Round 3 and the in-person meeting. Only 4 questions did not reach consensus after the in-person meeting (Figure 1).

The CDON Head and Neck Guidelines that were generated using the modified Delphi process consist of general recommendations and treatment pathways. The general recommendations for referrals, radiation dose, timing of dental treatment prior to RT, risk factors to be considered in decision making, and preventative strategies are as follows.

General Recommendations:

Referrals:

- (1) All patients, both dentate and edentulous, will benefit from a referral to a dental oncology clinic.

Radiation dose and timing:

Anticipated radiation dose (CRT) should be considered when choosing whether or not to extract a tooth prior to radiation.

- (2) Ideally, the CRT should be consistent within an institution. Establishment of a CRT should involve both dental oncologists, radiation oncologists, and other team members involved in treatment of ORN such as oral and maxillofacial surgeons or radiation oncologists specialized in late effects of radiation.

Ideally at least 7–14 days of healing should be allowed between extraction or other surgical procedures before the commencement of RT.

If an extraction or surgical procedure is required and there are less than 7 days available prior to the RT start date, a clinician would need to use their judgement as to whether or not a tooth presents a significant enough risk of future ORN (for example, a tooth with severe bone loss and mobility) to warrant extraction prior to RT. This decision should be

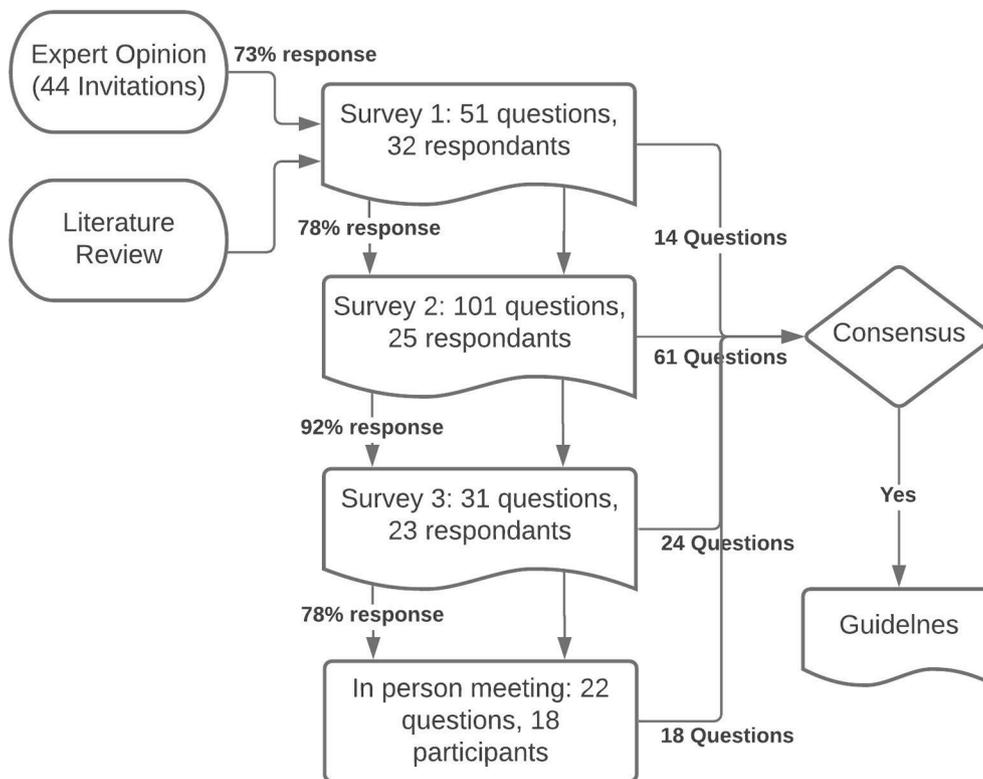


Figure 1. Modified Delphi Rounds and Responses.

made in conjunction with the patient’s radiation oncologist. It is recognized that in practice, there is often less than 7–14 days of healing available between extractions and commencement of RT.

(3) In the maxilla, the established radiation dose whereby clinicians would decide to prophylactically extract a tooth (the CRT) with a dental condition that placed it at future risk of ORN (a “tooth at risk”) was 70 Gy. Consensus was nearly reached at 60 Gy (73.9%) (Figure 2).

In the mandible, the CRT was 60 Gy. Sixty percent of participants would decide to prophylactically extract a tooth at risk receiving 50 Gy (Figure 2).

Patient and Dental Risk Factors:

Dental Caries: The risk factors that should be considered when deciding to extract or restore a tooth with dental caries that will receive a radiation dose at or above the CRT, ranked in order of importance, are:

1. Risk of infection
2. Oral health status
3. Cancer type/prognosis
4. Compliance/motivation

Factors that would indicate a patient or tooth be considered “Low risk” of complications related to dental caries during and post-RT include: A tooth at risk with dental caries where there is low risk of infection during RT; a patient with good oral health status; a patient with a poor long-term prognosis and unlikely to experience late effects; and a good history of compliance with oral care. Factors considered high risk of complications would include: A tooth at risk with dental caries where there is high risk of infection during and post-RT; a patient with poor oral health status, poor previous compliance with oral care, or a patient who will be receiving a dose at the high range of the CORT to structures of concern, or who is expected to have a significant lifespan post-RT.

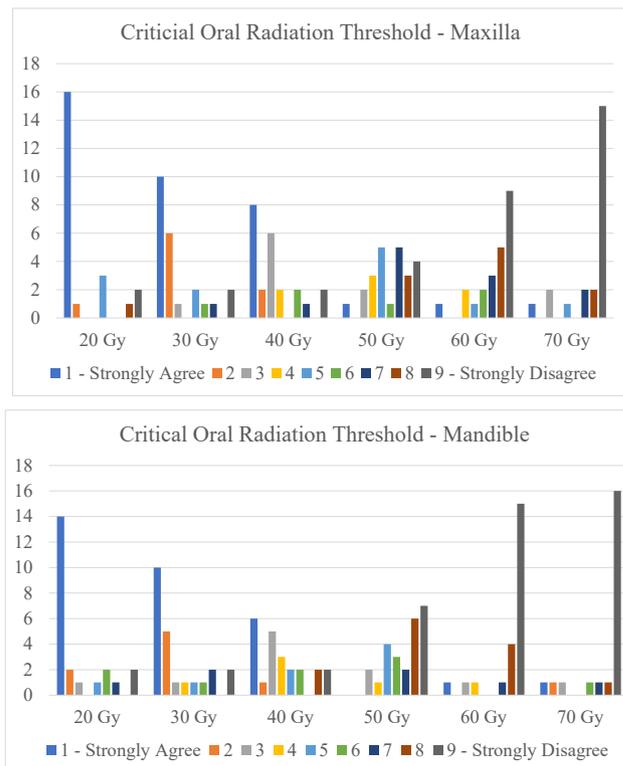


Figure 2. Critical Radiation Threshold (Colour to be Used in Print).

Third Molars: When considering third molar teeth that fall at or above the CRT, the risk factors that should be considered, ranked in order of importance, are the following:

1. Cancer type and prognosis
2. Time available for healing between extraction and commencement of RT.
3. Patient compliance

4. Oral hygiene status

Here, a patient at high risk of complications from third molars post RT would be a patient expected to have a significant lifespan post-RT, a

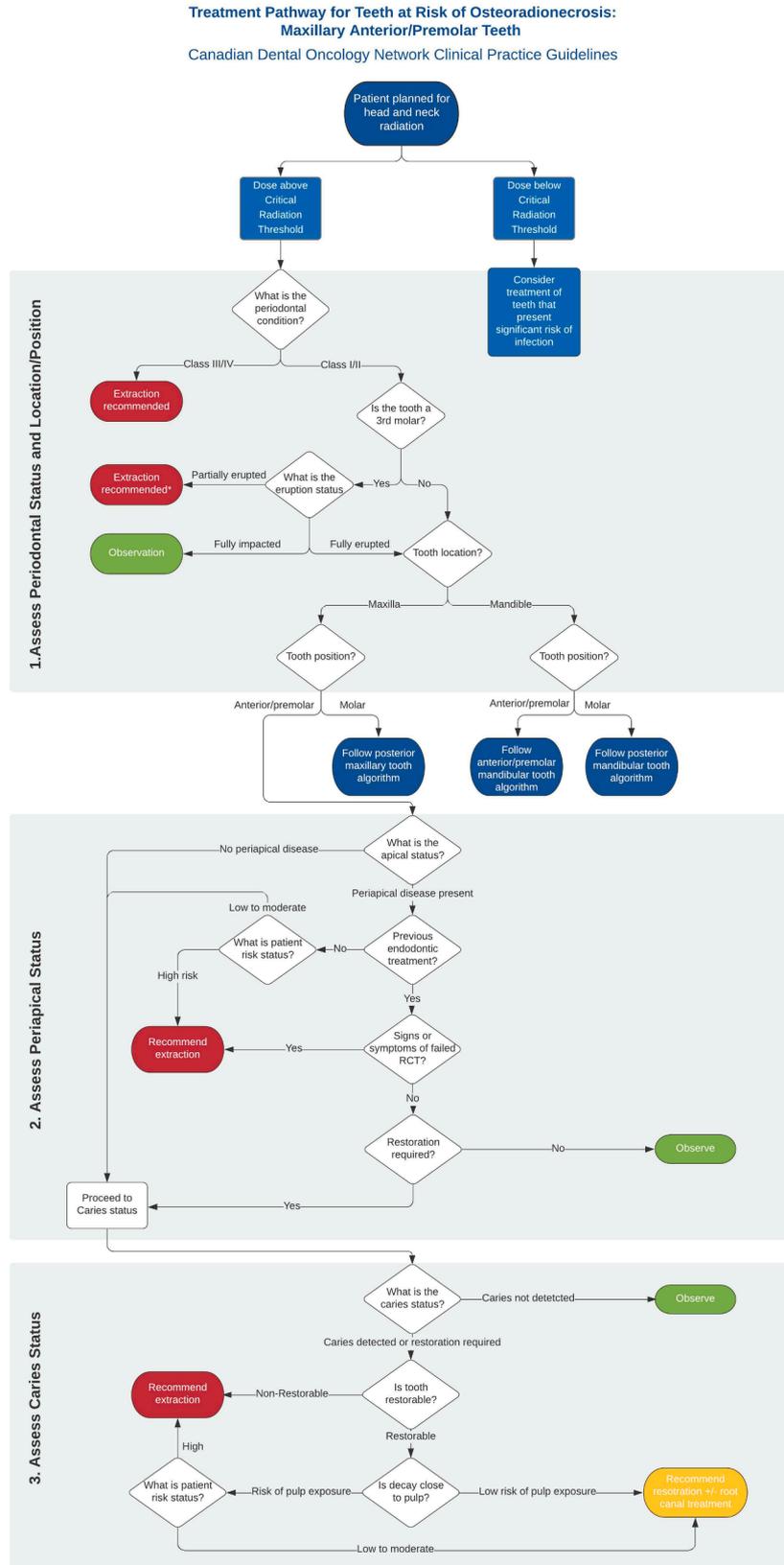


Figure 3. Treatment Pathways for Anterior/Premolar Teeth in the Maxilla (Colour to be Used in Print).

patient with poor previous compliance with oral care, or a patient with poor oral hygiene. Time available between extraction and commencement of RT was considered as a separate question (see radiation dose and timing above).

When considering teeth with periodontal disease that will receive a dose at or above the CRT, the risk factors that should be considered, in order of importance, are the following:

1. Periodontal disease progression
2. Dental assessment/oral health status
3. Compliance with dental treatment
4. Cancer type and prognosis
5. Patient's overall health status
6. Patient's wants and desires

Here, a patient at low risk of complications from periodontal disease post-RT would be a patient with slow or no periodontal disease progression, good oral health status, good previous compliance with dental treatment, a patient with good systemic health, a patient highly motivated to maintain their dentition, or who has a poor long-term prognosis and is unlikely to experience late effects.

Treatment Pathways:

Once the general recommendations and risk factors have been taken into consideration, a clinician should apply their own CRT when utilizing the treatment pathways. Ideally, the CRT should be consistent across an institution. Then, individual teeth that will receive a radiation dose at or above the CRT should be assessed using the appropriate treatment pathways depending on their location (maxilla or mandible) and position (molar or anterior/premolar).

All pathways begin with the same recommendations, regardless of tooth location or position in the patient mouth. In general:

1. Patients who will be receiving a palliative dose of RT or a dose below the CRT should have only those teeth which are symptomatic and/or that present a risk of infection during RT addressed prior to radiation.
2. All teeth with moderate-severe periodontal involvement that will fall within the radiation volume at or above a the CRT should be considered for extraction.
3. Other than mandibular molar teeth, (consensus not reached) teeth with previous endodontic therapy where an asymptomatic periapical lesion is present may be observed provided the tooth is adequately obturated and has been stable since treatment.
4. Healthy unopposed teeth that may cause trauma to soft tissues within the radiation field should be smoothed or reduced.

Figures 3 and 4 are the treatment pathways for anterior/premolar teeth in the maxilla and mandible, respectively. In general:

1. Prophylactic extraction of heavily restored and asymptomatic premolars is not recommended even in patients with questionable long-term compliance.
2. Clinicians are more likely to recommend restorations, and endodontic therapy if needed, over extractions in the maxilla than in the mandible, and in patients who are considered low risk.

Figures 5 and 6 summarize the recommendations for molar teeth in the maxilla and mandible, respectively. In general:

1. It is recommended to consider prophylactic extraction of heavily restored molar teeth, even if they are asymptomatic, in patients with questionable long-term compliance.
2. Asymptomatic molars that cannot be easily accessed for cleaning and extraction in the future as a result of trismus should be considered for extraction.

3. Clinicians are more likely to recommend extraction of mandibular teeth than maxillary teeth, particularly in moderate- to high-risk patients.

Prevention:

The following prophylactic treatments should be considered to prevent the occurrence of post-radiation caries:

1. Full dental assessment
2. Home care instructions
3. Diet counselling
4. Daily fluoride application
5. Regular dental visits
6. Oral hygiene
7. Regular cleaning
8. Management of xerostomia
9. Counseling on complications from RT
10. Smoking cessation

The following prophylactic treatments should be considered to prevent further tooth loss and ORN in a patient with periodontal disease:

1. Oral hygiene instruction
2. Frequent follow-up/regular cleanings every 3 months
3. Daily fluoride application
4. Management of xerostomia
5. Smoking cessation

The following prophylactic treatments should be considered to prevent the occurrence of oral mucositis:

1. Oral rinses
2. Suitable hygiene materials
3. Elimination of potential irritants

Discussion

It is well established that patients undergoing RT for HNC should be assessed by a dentist prior to starting RT [30]. However, there are few prospective studies that precisely describe the nature of the complete dental assessment, the prophylactic dental treatments that should be performed prior to RT, the timing of said interventions, and most importantly, the outcomes associated with these dental treatments [17]. These guidelines will act as a starting point as we systematically go about determining the outcome of our dental interventions prior to RT for HNC. While we cannot be certain that the treatment recommendations provided will result in the most ideal outcome for patients, this cannot be known without establishing a clear and consistent treatment strategy and evaluating it prospectively. Treatment pathways such as the CDON Head and Neck Guidelines make it possible to identify opportunities for future improvement and facilitate enacting these improvements [31].

Many of the recommendations from the CDON Head and Neck Guidelines are well supported by evidence in the literature. The general recommendation that all patients, both dentate and edentulous, be referred to a dentist is supported by evidence that denture trauma can induce ORN [32]. The recommendation that 7–14 days of healing be available between dental extractions and the start of RT recognizes the evidence for 2 weeks of healing and the necessity to avoid delays to commencement of RT which can negatively impact prognosis [32,33,34]. All treatment pathways begin with the recommendation that moderate to severely periodontally involved teeth within the CRT be extracted, a well-supported indication for pre-RT extractions [35]. It has been shown that when moderate-severely periodontally involved teeth are not extracted, 33% of patients will go on to develop ORN [16,36]. Not surprisingly, mandibular molar teeth were most frequently

**Treatment Pathway for Teeth at Risk of Osteoradionecrosis:
Mandibular Anterior/Premolar Teeth**
Canadian Dental Oncology Network Clinical Practice Guidelines

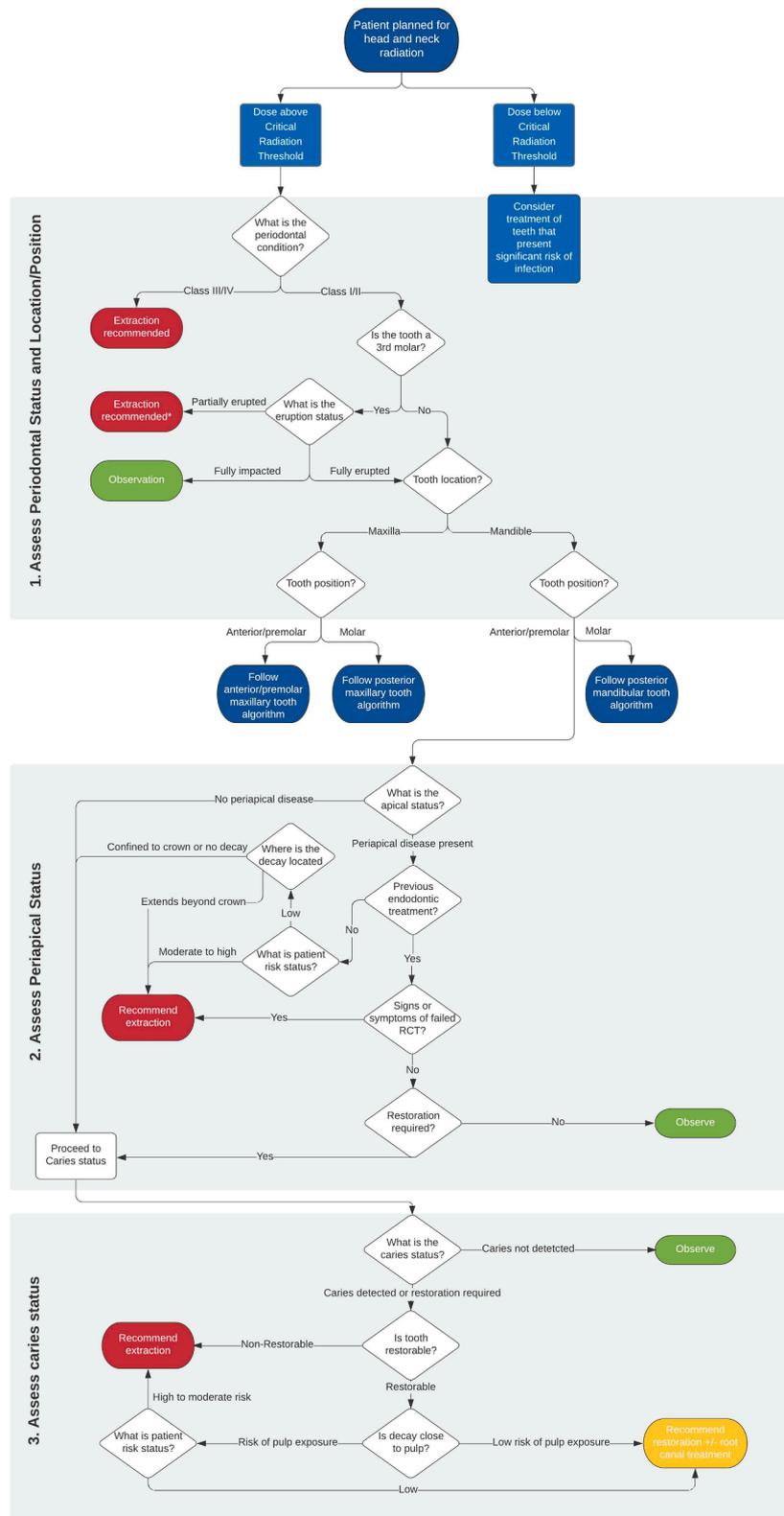


Figure 4. Treatment Pathways for Anterior/Premolar Teeth in the Mandible (Colour to be Used in Print).

**Treatment Pathway for Teeth at Risk of Osteoradionecrosis:
Maxillary Molar Teeth**
Canadian Dental Oncology Network Clinical Practice Guidelines

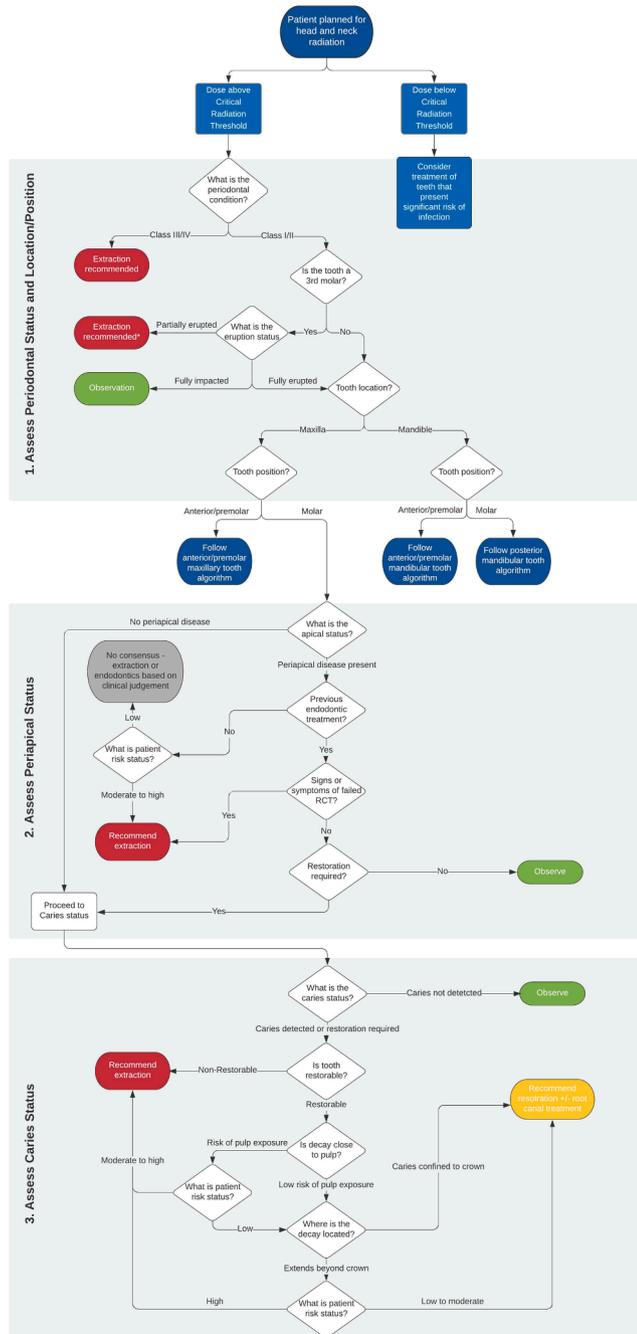


Figure 5. Summary Recommendations for Molar Teeth in the Maxilla (Colour to be Used in Print). Can you change the figure title to Treatment Pathways for Maxillary Molar Teeth

recommended for extraction over other teeth, consistent with the finding that ORN most frequently occurs following extractions in the posterior mandible [12,37].

The guidelines established here must also take into consideration evidence from prospective studies. Brennan et al have undertaken a prospective observational study of 756 HNC patients undergoing RT with the goal of identifying risk factors associated with tooth loss and ORN post-RT [38,39]. The results of this study should be used to amend the guidelines as necessary, as the evidence becomes available. Several of the authors of this manuscript are in the process of collecting tooth-level data in nearly 3000 patients at risk of ORN. The intent is to

analyze how extraction or observation of these teeth can contribute to ORN. The results of this analysis, once complete, should be used to update the guidelines as needed.

The treatment pathways in these clinical guidelines are not intended to apply to all patients. Rather, guidelines are intended to reduce unwarranted practice variation, the type of variation that occurs when patients with similar diagnoses, prognoses and demographic status receive different care depending on where, when or by whom they are treated [40]. Desired or wanted variation is the type that occurs when the patient, both in terms of their entire being and preferences, are taken into consideration [41]. A patient with a limited prognosis and few remaining teeth acting as abutments for a denture will surely have an improved quality of life if those teeth are maintained, rather than extracted solely because each tooth meets the requirements for extraction in the treatment pathways (15). A well-informed and motivated young patient with HPV-related HNC may elect to prophylactically remove their third molars prior to RT, particularly if there is adequate time for healing [37].

Finally, we would like to emphasize that the CRT established in this study reflects the radiation dose at which dental oncologists would be concerned about ORN were they to extract a tooth in this region after RT. The radiation dose delivered to each patient should always be determined as a function of the oncologic situation to maximize tumor control while respecting normal tissue limits.

Limitations

This study is limited in that only a single nationality is represented in participants. It is possible that the results may not be applicable in another country, particularly where the dental needs or scope of government funded dental services differs significantly from that of the study participants. However, providing practitioners with clinical pathways that are locally developed and consensus driven are more likely to improve the quality of care [31]. By engaging clinicians working in the nation where the practice guidelines are to be applied, this increases their likelihood of success [42].

While we met our goal of 70% participant retention between rounds, of the initial 32 participants, only 18 were still engaged by the time of the in-person meeting. This may be attributed to the participant fatigue effect, a known weakness of the Delphi method [22]. It is possible that the opinions of these other clinicians may have altered the consensus level of certain decisions. Despite this, participants who did complete the in-person meeting had a high degree of confidence in the results of the process, with all participants answering at least a 7 on the 9-point Likert scale.

Future directions

The treatment pathways and recommendations from the CDON Head and Neck guidelines will be prospectively tested in a national, multi-centre study. While this is a significant undertaking, we have already demonstrated a willingness as a group to work collaboratively on this project. The planned study is to include a step-wedge design. First, the typical practice of a centre will be observed prospectively over a time period. This will be followed by application of the clinical practice guidelines and observation of their impact on patient care, along with close monitoring of complications post-RT and the impact on unwanted variation in practice.

Conclusion

The CDON Head and Neck Guidelines represent the culmination of a yearlong modified Delphi process that engaged dental oncologists across the country. To our knowledge, these are the first clinical practice guidelines for the prophylactic dental care provided prior to head and neck RT. These guidelines will be applied prospectively across the nation

**Treatment Pathway for Teeth at Risk of Osteoradionecrosis:
Mandibular Molar Teeth**
Canadian Dental Oncology Network Clinical Practice Guidelines

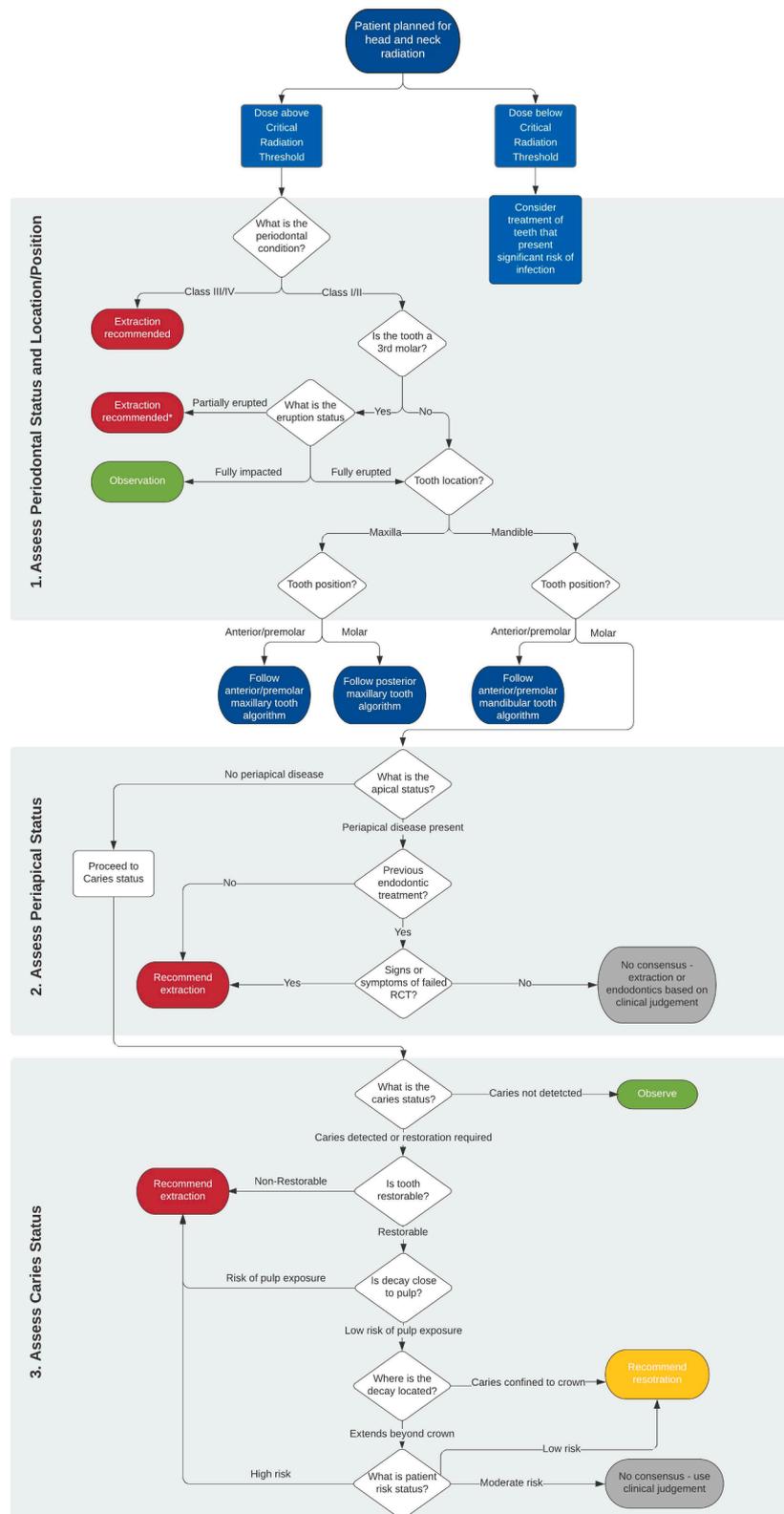


Figure 6. Summary Recommendations for Molar Teeth in the Mandible (Colour to be Used in Print). Can you change the figure title to Treatment Pathways for Mandibular Molar Teeth

to form the first step towards evidence-based treatment guidelines. This represents a small, but important step towards determining how we can help to reduce the risk of long-term complications post-RT in our collective patients.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.oraloncology.2021.105604>.

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