ISOO/MASCC/ASCO Guideline: Salivary Gland Hypofunction and/or Xerostomia Induced by Nonsurgical Cancer Therapies

ORAL CARE STUDY GROUP
Citation

## Grading of Recommendations and Levels of Evidence

<table>
<thead>
<tr>
<th>Types of recommendations</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence - based</td>
<td>There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.</td>
</tr>
<tr>
<td>Formal consensus</td>
<td>The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement.</td>
</tr>
<tr>
<td>Informal consensus</td>
<td>The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion.</td>
</tr>
<tr>
<td>No recommendation</td>
<td>There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.</td>
</tr>
</tbody>
</table>
## Grading of Recommendations and Levels of Evidence

<table>
<thead>
<tr>
<th>Quality of the evidence</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits v harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.</td>
</tr>
<tr>
<td>Low</td>
<td>Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.</td>
</tr>
<tr>
<td>Insufficient</td>
<td>Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.</td>
</tr>
</tbody>
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Grading of Recommendations and Levels of Evidence

<table>
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<tr>
<th>Strength of the recommendation</th>
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<tr>
<td>Strong</td>
<td>There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists’ agreement.</td>
</tr>
<tr>
<td>Moderate</td>
<td>There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists’ agreement.</td>
</tr>
<tr>
<td>Weak</td>
<td>There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists’ agreement.</td>
</tr>
</tbody>
</table>
Guideline Question

“What are the most effective interventions to prevent, minimize, and manage salivary gland hypofunction and xerostomia in the oncology patient receiving nonsurgical cancer therapy?”
Target Population

Adult patients with cancer who are scheduled to receive or who have received nonsurgical cancer therapy. Cancer diagnoses included head and neck cancer (radiation therapy in the head and neck region, chemotherapy, and chemoradiotherapy); hematologic malignancies (hematopoietic stem cell therapy, systemic chemotherapy, and total body irradiation); thyroid cancer (radioactive iodine); other solid cancer (systemic cancer chemotherapy); and all cancers treated by biologic cancer therapy including targeted therapies.
Target Audience

Oncologists and other physicians, dentists, dental specialists, dental hygienists, oncology nurses, clinical researchers, advanced practitioners, and patients with cancer, with particular emphasis on those individuals with head and neck cancer.
Methods

A multidisciplinary Expert Panel was convened by MASCC/ISOO and ASCO to develop clinical practice guideline recommendations based on a systematic review of the medical literature.
Clinical Question 1

“What is the efficacy of available pharmacologic and nonpharmacologic interventions (including the effects of radiation dose, type, and regimen) for the prevention of salivary gland hypofunction and/or xerostomia induced by nonsurgical cancer therapies?”
Recommendation 1.1.

“Intensity-modulated radiation therapy should be used to spare major and minor salivary glands from a higher dose of radiation to reduce the risk of salivary gland hypofunction and xerostomia in patients with head and neck cancer”

• Type: evidence-based

• Evidence quality: high

• Strength of recommendation: strong
Recommendation 1.2.

“Other radiation modalities that limit cumulative dose to and irradiated volume of major and minor salivary glands as or more effectively than intensity-modulated radiation therapy may be offered to reduce salivary gland hypofunction and xerostomia”

- Type: informal consensus
- Evidence quality: low
- Strength of recommendation: strong
Recommendation 1.3.

“Acupuncture may be offered during radiation therapy for head and neck cancer to reduce the risk of developing xerostomia”

- Type: evidence-based
- Evidence quality: intermediate
- Strength of recommendation: moderate
Recommendation 1.4.

“Systemic administration of the sialogogue bethanechol may be offered during radiation therapy for head and neck cancer to reduce the risk of salivary gland hypofunction and xerostomia”

• Type: evidence-based
• Evidence quality: low
• Strength of recommendation: weak
Recommendation 1.5.

“Vitamin E or other antioxidants should not be used to reduce the risk of radiation-induced salivary gland hypofunction and xerostomia because of the potential adverse impact on cancer-related outcomes and the lack of evidence of benefit”

• Type: informal consensus

• Evidence quality: low

• Strength of recommendation: weak
Recommendation 1.6.

“Evidence remains insufficient for a recommendation for or against the use of submandibular gland transfer administered before head and neck cancer treatment to reduce the risk of salivary gland hypofunction and xerostomia because of insufficient evidence with contemporary radiation modalities.”
Recommendation 1.7.

“Evidence remains insufficient for a recommendation for or against the use of the following interventions during radiation therapy for head and neck cancer: Oral pilocarpine, amifostine (with contemporary radiation modalities), or low-level laser therapy.”
Recommendation 1.8.

“Evidence remains insufficient for a recommendation for or against the use of the following interventions to reduce the risk of salivary gland hypofunction or xerostomia in patients with head and neck cancer: n-acetylcysteine oral rinse, traditional Chinese medicine–based herbal mouthwash, local clonidine, concurrent chemotherapy with nedaplatin, boost radiation therapy, hyperfractionated or hypofractionated radiation therapy, intra-arterial chemoradiation, minocycline, melatonin, nimotuzumab, zinc sulfate, propolis, viscosity-reducing mouth spray, transcutaneous electrical nerve stimulation (TENS), parotid gland massage, thyme honey, and human epidermal growth factor.”
Clinical Question 2

“What is the efficacy of available pharmacologic and nonpharmacologic interventions for the management of salivary gland hypofunction and/or xerostomia induced by nonsurgical cancer therapies?”
Recommendation 2.1.

“Topical mucosal lubricants or saliva substitutes (agents directed at ameliorating xerostomia and other salivary gland hypofunction-related symptoms) may be offered to improve xerostomia induced by nonsurgical cancer therapies.”

- Type: evidence-based
- Evidence quality: intermediate
- Strength of recommendation: strong
Recommendation 2.2.

“Gustatory and masticatory salivary reflex stimulation by sugar-free lozenges, acidic (nonerosive and sugar-free special preparation if dentate patients) candies, or sugar-free, nonacidic chewing gum may be offered to produce transitory increased saliva flow rate and transitory relief from xerostomia by stimulating residual capacity of salivary gland tissue.”

• Type: evidence-based

• Evidence quality: intermediate

• Strength of recommendation: moderate
Recommendation 2.3.

“Oral pilocarpine, and cevimeline where available, may be offered after radiation therapy in patients with head and neck cancer for transitory improvement of xerostomia and salivary gland hypofunction by stimulating residual capacity of salivary gland tissue. However, improvement of salivary gland hypofunction may be limited.”

• Type: evidence-based

• Evidence quality: high

• Strength of recommendation: strong
Recommendation 2.4.

“Acupuncture may be offered after radiation therapy in patients with head and neck cancer for improvement of xerostomia.”

• Type: evidence-based
• Evidence quality: low
• Strength of recommendation: weak
Recommendation 2.5.

“Transcutaneous electrostimulation or acupuncture-like transcutaneous electrostimulation of the salivary glands may be offered after radiation therapy in patients with head and neck cancer for improvement of salivary gland hypofunction and xerostomia.”

- Type: evidence-based
- Evidence quality: low
- Strength of recommendation: weak
Recommendation 2.6.

“Evidence remains insufficient for a recommendation for or against the use of the following interventions for improvement of salivary gland hypofunction and xerostomia: Extract of ginger and mesenchymal stem cell therapy.”
Other References


