O3_A2_A_Scientific Evidence
ORAL CARE

Q1	**What is the most appropriate therapy for the treatment of Xerostomia in patients hospitalized in a palliative settings/facility? Treatment indications?**
Patients	Patients elderly and/or frail and/or end of life indications in a palliative facility Oncology patients that have undergone radiation therapy Frail, aged, end of life adults Children in a palliative facility
Intervention	Xerostomia treatments: Topic agents: gels (Biotene), aerosols (Glandosome spray), lozenges (Saliva Orthana lozenges), oral rinses and chewing gums Systemic agents pilocarpine hydrochloride, cevimaline, Transcutaneous electrical nerve stimulation Acupuncture
Comparator	Conservative care of any kind
Outcome	Efficacy (Mucosal status, saliva secretion, by questionnaire or the visual analogue scale) measured in response rate and clinical benefit. Side effects to therapy Quality of life.
Methodology	Systematic reviews Randomized controlled trials Meta-analysis
Extra	none

Studies:
The literature search resulted in 5 reviews and several randomized controlled trials that assessed the use of

Indications:
- Oncology patients diagnosed with xerostomia after radiation therapy and patients with xerostomia due to various diseases or medications.
- Pilocarpine is contraindicated in patients with respiratory disorders such as asthma or COPD, glaucoma, or liver disease.
- Cevimeline may have a lower adverse side effect profile and has demonstrated a similar effectiveness in increasing unstimulated salivary flow.

Discussion:
One review (1) on the use of pilocarpine hydrochloride suggests that pilocarpine hydrochloride is more effective than placebo and at least as effective as artificial saliva, providing response rate of 42% to 51%. However, the dose-dependent side-effects resulted in 15-29% of patient withdraw (1).
There is limited evidence to support the use of pilocarpine hydrochloride or other parasympathomimetic drugs in the treatment of radiation-induced xerostomia. Available studies suggest that approximately half of patients will respond, but side effects can be problematic (1).
Evidence was found for the use of acupuncture for various treatment-related or cancer-related symptoms including xerostomia, without any difference between the two groups. Currently, there is no quality literature data to recommend acupuncture in clinical practice in patients with xerostomia (8).

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Oxygenated glycerol trimester (OGT) saliva substitute spray shows evidence of effectiveness compared to an electrolyte spray (standardized mean difference (SMD) 0.77, 95% confidence interval (CI) 0.38 to 1.15) (5).

Both integrated mouth care systems (toothpaste + gel + mouthwash) and oral reservoir devices show promising results but there is insufficient evidence at present to recommend their use (5).

Although chewing gum is associated with increased saliva production in the majority of those with residual capacity, there is no evidence that gum is more or less effective than saliva substitutes (5).

Conclusions:

Apart from the conservative approach, alternative oral or topic agents can be used in patients with xerostomia, especially after radiation therapy. According to the literature, there is a clinical benefit and an improved response rate of pilocarpine compared to placebo or any other intervention, but it remains unclear the duration of the treatment and the patients' selection criteria.

Currently, there is no evidence to recommend acupuncture as management technique for xerostomia.

Other treatments (chewing gum, the use of gel and mouth was or OGT) are not generally recommended as there is no available scientific evidence.

References:

1. Davies AN, Shorthose K, Thompson J. Parasympathomimetic drugs for the treatment of salivary gland dysfunction due to radiotherapy. CochraneDatabase of Systematic Reviews 2007, Issue 3. Art.No.:CD003782. DOI: 10.1002/14651858.CD003782.pub2
2. Spivakovsky S, Spivakovsky Y. Parasympathomimetic drugs for dry mouth due to radiotherapy. Evid Based Dent. 2016 Sep;17(3):79. doi: 10.1038/sj.ebd.6401185. PubMed PMID: 27767109.
3. Johnson JT, Ferretti GA, Nethery WJ, Valdez IH, Fox PC, Ng D, Muscoplat CC, Gallagher SC. Oral pilocarpine for post-irradiation xerostomia in patients with head and neck cancer. The New England journal of medicine. 1993;329(6):390-5. doi: 10.1056/NEJM199308053290603. PubMed PMID: 8326972.
4. Hawthorne M, Sullivan K. Pilocarpine for radiation-induced xerostomia in head and neck cancer. Int J Palliat Nurs. 2000 May;6(5):228-32. Review. PubMed PMID: 12419994.
5. Furness S, Bryan G, McMillan R, Worthington HV. Interventions for the management of dry mouth: non-pharmacological interventions. Cochrane Database Syst Rev. 2013 Aug 30;(8):CD009603. doi: 10.1002/14651858.CD009603.pub2. Review. Update in: Cochrane Database Syst Rev. 2013;(9):CD009603. PubMed PMID: 23996155.
6. Lakshman AR , Subhas Babu G and Rao S. Evaluation of effect of transcutaneous electrical nerve stimulation on salivary flow rate in radiation induced xerostomia patients: A pilot study. Journal of cancer research and therapeutics, 2015, 11(1), 229
7. Johnstone PA , Peng YP , May BC , Inouye WS and Niemtzow RC. Acupuncture for pilocarpine-resistant xerostomia following radiotherapy for head and neck malignancies. International journal of radiation oncology, biology, physics, 2001, 50(2), 353
8. Towler P, Molassiotis A, Brearley SG. What is the evidence for the use of acupuncture as an intervention for symptom management in cancer supportive and palliative care: an integrative overview of reviews. Support Care Cancer. 2013 Oct;21(10):2913-23. doi: 10.1007/s00520-013-1882-8. Review.
9. Wong RK, James JL, Sagar S, Wyatt G, Nguyen-Tân PF, Singh AK, Lukaszczyk B, Cardinale F, Yeh AM, Berk L. Phase 2 results from Radiation Therapy Oncology Group Study 0537: a phase 2/3 study comparing acupuncture-like transcutaneous electrical nerve stimulation versus pilocarpine in treating early radiation-induced xerostomia. Cancer. 2012 Sep 1;118(17):4244-52. doi: 10.1002/cncr.27382. Epub 2012 Jan 17.)
10. Chibly AM, Nguyen T, Limesand KH. Palliative Care for Salivary Gland Dysfunction Highlights the Need for Regenerative Therapies: A Review on Radiation and Salivary Gland Stem Cells. J Palliat Care Med. 2014 Aug 6;4(4). pii: 1000180.

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11. Fogh S, Yom SS. Symptom management during the radiation oncology treatment course: a practical guide for the oncology clinician. Semin Oncol. 2014 Dec;41(6):764-75. doi: 10.1053/j.seminoncol.2014.09.020. Review.
12. Stein P, Aalboe J. Dental Care in the Frail Older Adult: Special Considerations and Recommendations. J Calif Dent Assoc. 2015 Jul;43(7):363-8

Q2	**Thrush (oropharyngeal candidiasis) is a superficial yeast infection that may involve the tongue, inner cheek (buccal mucosa), inner lip region, and occasionally the gums (gingiva): it is very frequent in palliative care patients; can oral hygiene reduce the rate of oral complications from oral candidiasis?**
Patients	Patients elderly and/or frail and/or end of life indications in a palliative facility Frail, aged, end of life adults Children in a palliative facility
Intervention	Oral care
Comparator	No oral care
Outcome	Efficacy outcomes as response rates, clinical benefit rates Quality of life.
Methodology	Systematic reviews Randomized controlled trials Guidelines
Extra	none

Studies:
Two systematic reviews, MASCC clinical practice guidelines and several randomized trials were included.

Indications:
- Cancer patients receiving specialist palliative care. Oral candidosis was associated with a poor performance status, the presence of xerostomia, and the presence of dentures; oral candidosis was not associated with the use of oral/parenteral antibiotics, or the use of oral/parenteral corticosteroids
- Palliative care patients require special dental attention, ranging from operative and preventive care to support for emotional needs.
- terminally ill cancer patients admitted over the past 2 years
- Oral candidiasis is one of the most common clinical features of those patients infected with the human immunodeficiency virus [HIV], this manifestation was seen in up to 90% of individuals infected with HIV
- Patients with mucositis secondary to cancer therapy.

Discussions:
Oral problems, such as dry mouth and candidiasis are highly prevalent and occur in the terminal stage of cancer, for which oral care is useful to improve the oral cavity condition.
Accurate diagnosis of oral problems and corresponding appropriate administration of interventions may be important for improving QOL care for these patients (1). As some hygiene products can be more difficult to tolerate by some patients, their choice is important [2].
Prevention is important in oral candidiasis and the use of anti- Candida rinses such as Chlorhexidine or Hexetidine can be taken into account, especially to prevent treatment-induced mucositis [4, 6].

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Moreover, limited literature data show that a decreased oral intake may reduce the incidences of dry mouth, stomatitis, and oral candidiasis (good oral intake group vs poor oral intake group) were 38.3% (44 cases) versus 81.0% (128 cases; P < .0001), 10.4% (12cases) versus 16.5% (26 cases; P ¼ .15), and 6.6% (7 cases) versus 22.8% (36 cases; P ¼ .0002), respectively in terminally ill patients [3].
The use of oral care can lower the incidence of candidiasis [4] and a combination of tooth-brushing, flossing and mouth rinses is recommended by the MASCC international guidelines [5].

Conclusions:
We endorse the recommendations of the MASCC guidelines of using oral care for prevention of oral mucositis and candidiasis.

References:
1.Andrew N. Davies, Susan R. Brailsford, David Beighton, Oral candidosis in patients with advanced cancer, August 2006, Volume 42, Issue 7, Pages 698–702 Oral Oncology
2. Dr. Wiseman, The Treatment of Oral Problems in the Palliative Patient Michael Wiseman, BSc, DDS, M SND RCS (Edin), FASGD J Can Dent Assoc 2006; 72(5):453–8
3. Nobuhisa Nakajima, Characteristics of Oral Problems and Effects of Oral Care in Terminally Ill Patients With Cancer, American Journal of Hospice & Palliative Medicine® 2016 :1-5
4. Carla Garcia-Cuesta **1**, Maria-Gracia Sarrion-Pérez **2**, Jose V. Bagán **3** Current treatment of oral candidiasis: A literature review J Clin Exp Dent. 2014;6(5):e576-82.
5. Rajesh V. Lalla, Joanne Bowen, Andrei Barasch, Linda Elting, Joel Epstein, Dorothy M. Keefe, Deborah B. McGuire, Cesar Migliorati, Ourania Nicolatou-Galitis, Douglas E. Peterson, Judith E. Raber-Durlacher, Stephen T. Sonis, Sharon Elad, The Mucositis Guidelines Leadership Group of the Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC=ISOO). MASCC=ISOO Clinical Practice Guidelines for the Management of Mucositis Secondary to Cancer Therapy Review Article Cancer May 15, 2014
6. Deborah B. McGuire & Janet S. Fulton & Jumin Park & Carlton G. Brown & M. Elvira P. Correa & June Eilers & Sharon Elad & Faith Gibson & Loree K. Oberle-Edwards & Joanne Bowen & Rajesh V. Lalla & On behalf of the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) Systematic review of basic oral care for the management of oral mucositis in cancer patients Support Care Cancer (2013) 21:3165–3177.

Q3	**Mouth pain, in different oral cavity diseases, could become an obstacle both for clinical assessment and for patient's wellbeing, especially for palliative care patients; what are the most functional strategies, adoptable by both healthcare professionals and patients, which could front this frequent problem?**
Patients	Patients elderly and/or frail and/or end of life indications in a palliative facility Frail, aged, end of life adults Children in a palliative facility
Intervention	Topical treatments
Comparator	No treatment
Outcome	Efficacy measured as response rate, relative risk or clinical benefit Side effects to therapy Quality of life.
Methodology	Systematic reviews Randomized controlled trials Meta-analysis

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Extra	none

Studies:
Three systematic reviews, international clinical guidelines and one randomized trial were included.

Indications:
- children treated with chemoradiotherapy for cancer
- patients with radiation-induced salivary gland dysfunction
- patients with mucositis secondary to cancer therapy

Discussions:
Oral mucositis has an increased prevalence, especially in cancer patients that undergo various cancer treatments. We have identified, through a comprehensive literature various pharmacological and non-pharmacological approaches that have been used to prevent and treat oral mucositis.
Current international guidelines recommend various intervention in preventing and treating mucositis [3], such as proper oral care, growth factors, anti-inflammatory agents, antimicrobials and analgesics, cryotherapy or laser therapy [1,3].
Other forms of therapy have also been investigated in a systematic review [4], suggesting a relative risk [RR]=0.66 (p=.002) for allopurinol vs. placebo , a RR=0.74 (p=.02) for aloe vera vs. placebo, a RR= 0.36-0.74 for cryotherapy in various grades of mucositis and a RR=0.2 for polymixin, tobramycin, and amphotoricin (PTA), suggesting that for some patients, these types of interventions can be beneficial.

Conclusions:
Although the current literature research is more applicable to cancer patients, it is our opinion that the current guideline recommendations can be applied to both oncology and non-oncology

References:
1. El Bousaadani A, Eljahd L, Abada R, Rouadi S, Roubal M, Mahtar M, Prevention and treatment of mucositis in children with oral cancers: Practical recommendations. Cancer Radiother. 2016 May;20(3):226-30. doi: 10.1016/j.canrad.2015.11.006. Epub 2016 Mar 28.
2. Davies AN1, Shorthose K. Parasympathomimetic drugs for the treatment of salivary gland dysfunction due to radiotherapy (Review) Cochrane Database Syst Rev. 2007 Jul 18;(3):CD003782
3. Lalla RV, Bowen J, Barasch A, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*. 2014;120(10):1453-1461. doi:10.1002/cncr.28592.
4. Andrew N Davies1 , Jo Thompson1, Parasympathomimetic drugs for the treatment of salivary gland dysfunction due to radiotherapy, 2015 The Cochrane Collaboration

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