

MOUTH CARE - PAEDIATRIC ONCOLOGY

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QUESTION

Evidence to assist with reviewing paediatric mouth care guidelines (for PROMPT)

SEARCH LIMITS

English-language, last 3 - 5 years.

SEARCH METHODOLOGY

A systematic search was conducted for literature. See the Appendix for the PRISMA chart and Medline search strategy.

DATABASES SEARCHED

- Medline – index of peer reviewed articles across health sciences and medicine.
- Embase – index of biomed and pharmacological peer reviewed journal articles.
- Emcare – index of nursing, allied health, critical-care medicine and more.

LITERATURE RESULTS

All articles can be provided in full text - email library@monashhealth.org a list of articles you require.

PEER-REVIEWED LITERATURE - IN REVERSE CHRONOLOGICAL ORDER

Articles are grouped by theme:

- Guidelines
- Standards
- Dental Care
- Education
- Risk Factors & Prevention
- Therapies
 - Chewing Gum
 - Low Level Laser
 - Mouth Rinses
 - Pain Medications
 - Supplements
 - Honey
 - Other Biological Agents

Each article summary contains excerpts from the abstract and an online link.

GUIDELINES

Miranda-Silva. W, et al. (2021). **MASCC/ISOO clinical practice guidelines for the management of mucositis: sub-analysis of current interventions for the management of oral mucositis in pediatric cancer patients**, *Supportive Care in Cancer*, 29 (7), 3539-3562. [Web Link](#)

There is limited or conflicting evidence about interventions for the management of OM in pediatric cancer patients, except for chewing gum which was ineffective for prevention. In conclusion, currently, data from adult studies may need to be extrapolated for the management of pediatric patients. Honey and photobiomodulation therapy in this patient population had encouraging potential. Implementation of a basic oral care protocol is advised amid lack of high level of evidence studies.

Patel. P, et al. (2021). **Clinical practice guideline for the prevention of oral and oropharyngeal mucositis in pediatric cancer and hematopoietic stem cell transplant patients: 2021 update**, *European Journal of Cancer*, 154, 92-101. [Web Link](#)

Cryotherapy should be used for older cooperative pediatric patients who receive short infusions of melphalan or 5-fluorouracil. Intraoral photobiomodulation therapy (620-750 nm spectrum) should be used in pediatric patients undergoing autologous or allogeneic HSCT and for pediatric head and neck carcinoma patients undergoing radiotherapy. Palifermin should not be used routinely in pediatric cancer or HSCT patients.

Carvalho. C.G, et al. (2018). **Guide for health professionals addressing oral care for individuals in oncological treatment based on scientific evidence**, *Supportive Care in Cancer*, 26 (8), 2651-2661. [Web Link](#)

A systematic search of the literature was performed for articles published between 2000 and April 2017 The studies stress the need for oral assessments as well as preventive and curative actions prior to oncological treatment. To minimize the severity of oral problems, the studies emphasize daily oral care, the treatment of xerostomia with saliva substitute and hydration, and low-level laser therapy, nystatin, acyclovir, respectively, for the prevention and treatment of oral mucositis, oral candidiasis, and infection by herpes simplex virus. The guide drafted has the function of assisting health professionals involved in the oral care of patients with cancer, enabling the prevention or treatment of oral complications stemming from oncological treatment.

STANDARDS

Potocki. R, et al. (2019) **Creating a standard of care: Oral health in children receiving chemotherapy**, *Pediatrics*, 144 (2). [Web Link](#)

Oral health is very important in children undergoing chemotherapy, however it can be forgotten in the anxiety of a life-threatening diagnosis. Establishing a standard oral health regimen and educational materials for patients and families is an important first step in improving the oral health of our oncology patients and therefore decreasing the incidence of severe mucositis and associated complications. If successful, the program will be expanded to include patients being admitted for all types of chemotherapy.

Hartnett. E, et al. (2018). **Development of interprofessional evidence based standard of care for prevention and treatment of mucositis, both inpatient and outpatient, adult and pediatric**, *Supportive Care in Cancer*, 26, 39-364. [Web Link](#)

This project suggests that interprofessional collaboration is an effective strategy for development

and implementation of a standardized guideline for both pediatric and adult inpatients and outpatients.

DENTAL CARE

Ribeiro I.L.A, et al. (2021). **Integrated oral care contributes positively to the course of treatment of oncopediatric patients**, *European Journal of Pediatrics*, 180 (9), 2757-2764. [Web Link](#)

This study describes the benefits of permanent oral care with daily oral surveillance for pediatric patients, which reduced the duration of severe oral mucositis, increased surveillance and the efficiency in diagnostic for signs of oral mucositis, enabling early intervention, and decreased chemotherapy interruptions, contributing positively to the course of treatment.

Ritwik. P , et al. (2020). **Oral and dental considerations in pediatric cancers**, *Cancer metastasis reviews*, 39, 43-53. [Web link](#)

As the survival rates of childhood cancers improve, it is essential for the dental profession to provide the individualized care necessary for this vulnerable population. The oral health profession also reinforces health practices congruent with cancer prevention and cancer screening.

Chettata. S, (2019). **Implementation of a standardized oral care program in paediatric haematology-oncology patients-a single center experience**, *Bone Marrow Transplantation*, 53, 819–833. [Web Link](#)

Implementation of an oral care program improved mouth care of patients in the short term. We observed some decrease in adherence over time, underlying the necessity of repeated inputs from the oncological team to maintain a high level of motivation and adherence to basic oral care. Further investigations are necessary to study middle and long-term adherence as well as its effect on oral complications.

Ritwik. P. (2018). **Dental care for patients with childhood cancers**, *Ochsner Journal*, 18 (4), 351-357. [Web Link](#)

Childhood cancer survivors present with unique challenges for dental management because of dental anomalies caused by cancer therapy. Interprofessional collaborative care between the pediatric dentist and the oncologist during and after cancer therapy will enable best outcomes for the pediatric patient. In addition, dental professionals must be prepared to meet the unique needs of long-term cancer survivors because of the increasing survival rates of childhood cancers.

EDUCATION

Bezerra P.M.M, et al. (2022). **The impact of oral health education on the incidence and severity of oral mucositis in pediatric cancer patients: a systematic review and meta-analysis**, *Supportive Care in Cancer*, 30 (11), 8819-8829. [Web Link](#)

This systematic review aimed to determine the impact of oral health education interventions on the incidence and severity of OM. While data analysis of the selected studies was heterogeneous, the implementation of oral health education strategies was found to reduce the incidence and severity of OM during the follow-up period. To conclude, oral health education interventions improved OM outcomes in pediatric oncology patients with a low quality of evidence.

Bezerra P.M.M, et al. (2021). **The effectiveness of an oral health education and prevention program on the incidence and severity of oral mucositis in pediatric cancer patients: a non-randomized controlled study**, *Supportive Care in Cancer*, 29 (12), 7877-7885. [Web Link](#)

To investigate the effectiveness of an Oral Health Education and Prevention Program (OHEPP) on the incidence and severity of oral mucositis (OM) in pediatric cancer patients. The OHEPP was a ludic strategy for promoting oral health and monitoring the oral health condition. There was a higher incidence of OM in patients who did not attend the OHEPP, and the relative risk of developing OM was significantly lower in OHEPP attendants. No difference in the occurrence of severe OM was observed. OHEPP reduced the risk of developing OM by 1.4-fold, with an effectiveness of 27%. Participation in OHEPP was an effective measure to reduce the incidence of OM in pediatric cancer patients.

Kostak M.A, et al. (2020). **Effects of oral health care education on the severity of oral mucositis in pediatric oncology patients**, *Turkish Journal of Oncology*, 35 (4), 422-429. [Web Link](#)

The findings obtained in this study suggest that oral health care education is an effective method to reduce the severity of oral mucositis in pediatric oncology patients. Oral mucositis's degree and scores were lower in the intervention groups than the control group on the 7th day of chemotherapy. It is recommended that oral health care education should be given to children and their parents from the beginning of hospitalization.

RISK FACTORS & PREVENTION

de Farias Gabriel. A, (2022). **Risk factors associated with the development of oral mucositis in pediatric oncology patients: Systematic review and meta-analysis**, *Oral Diseases*, 28 (4), 1068-1084. [Web Link](#)

This systematic review aimed to identify potential risk factors associated with the development of OM in pediatric cancer patients. Meta-analysis showed that groups submitted to high-risk chemotherapy for OM had a 2.79-fold increased risk of OM. In conclusion, identifying risk factors for OM is essential in order to allow individualized and early prevention treatment.

Michailidou. A, et al. (2021). **Nursing interventions for the prevention and management of stomatitis in children with leukemia undergoing chemotherapy**, *Perioperative Nursing*, 10 (4), 276-293. [Web Link](#)

The purpose of this systematic review was to investigate nursing therapeutic interventions for the prevention and management of chemotherapy induced stomatitis (CIS) in children with leukemia. Despite the many treatments suggested, none are effective and safe in all cases for use in clinical practice. Overall, based on the findings of these studies, the most effective and safe treatments for stomatitis are low intensity laser therapy, combination of low intensity laser therapy with photo dynamic therapy (PDT), palifermin and topical application of honey and other bee products. CIS can be prevented and managed with pharmacological and non-pharmacological methods with encouraging results. But better scientific documentation of their action is required.

Michailidou. A, et al. (2021). **Chemotherapy-induced stomatitis: Prevention and care**, *Perioperative Nursing*, 10 (2), 148-158. [Web Link](#)

The aim of the study was to summarize the nursing interventions for the prevention and care of chemotherapy-induced stomatitis in children with leukemia. From the literature review, nursing assessment of stomatitis and concomitant pain is a prerequisite for successful care. Its prevention and treatment can be done with the administration of drugs (chlor-hexidine gluconate, palifermin), with other technologies (use of lasers) and without the administration of drugs (bee products), cryotherapy, mastic chewing, glutamine administration). The serious effects of chemotherapy-

induced stomatitis in children with leukemia strongly create the need to find and implement effective nursing interventions to care it.

Mazhari. F, et al. (2019). **Management of oral mucositis in pediatric patients receiving cancer therapy: A systematic review and meta-analysis**, *Pediatric Blood and Cancer*, 66 (3). [Web Link](#)
We performed a systematic review and meta-analysis of published studies to investigate the effects of agents and techniques in reducing OM. This review provided a comprehensive examination of available options for children who have OM. The results support the possibility of a positive effect of palifermin on reducing OM in children receiving cancer therapy.

THERAPIES

CHEWING GUM

Semerci. R, et al. (2022). **Effect of chewing gum on the management of chemotherapy-induced oral mucositis in children: Systematic review of experimental studies**, *European journal of cancer care*, 31 (6). [Web Link](#)

Experimental studies particularly randomised controlled trials using rigorous designs, consistent outcome measures, and larger sample sizes are required to determine the efficacy of chewing gum in reducing chemotherapy-induced oral mucositis in paediatric oncology patients.

Utami K.C, et al. (2018). **Chewing gum is more effective than saline-solution gargling for reducing oral mucositis**, *Enfermeria Clinica*, 28. [Web Link](#)

This quasi-experimental study compared the effectiveness of chewing gum and gargling with a saline solution as two types of intervention to reduce oral mucositis scores. The data showed that chewing gum is more effective than gargling with a saline solution, and it can be incorporated into the nursing protocol for treating pediatric cancer patients.

LOW LEVEL LASER

Reyad. F.A, et al. (2022). **Photobiomodulation for chemotherapy-induced oral mucositis in leukemic children: A randomized controlled clinical trial**, *Oral Diseases*, [web link](#)

The use of PBM along with the conventional treatment was effective in reducing pain and in the recovery of OM lesions in children receiving chemotherapy for the treatment of ALL. It was also safe and applicable to children.

Karaman. K, et al. (2022). **Is Low-level Laser Therapy a Candidate to Be a Good Alternative in the Treatment of Mucositis in Childhood Leukemia?**, *Journal of Pediatric Hematology/Oncology*, 44 (1), 199-203. [Web link](#)

The aim was to evaluate the effect of low-level laser therapy (LLLT) for the treatment of CT-induced OM children. In the treatment of oral OM that occurs in children after CT, both standard care and LLLT treatment improve the grade and pain of OM.

Redman. M.G, et al. (2022). **Low-level laser therapy for oral mucositis in children with cancer**, *Archives of Disease in Childhood*, 107 (2), 128-133. [Web Link](#)

There is vast variation in different trial protocols. Insufficient blinding between LLLT or sham therapy/control led to a strong risk of performance bias. 75 studies (encompassing 2712 patients of all ages who had undergone LLLT) demonstrated minor and infrequent adverse reactions, but most studies had significant areas of weakness in quality. Conclusion LLLT appears to be a safe

therapy, but further evidence is needed to assess its efficacy as a prevention or treatment tool for oral mucositis in children with cancer.

Anschau. F, et al. (2020). **Efficacy of low-level laser for treatment of cancer oral mucositis: a systematic review and meta-analysis**, *Lasers in Medical Science*, 34 (6). 1053-1062. [Web Link](#)

There is moderate evidence that LLLT is effective in resolving OM lesions in adult patients undergoing cancer therapy. LLLT demonstrates potential for decreasing the resolution time of OM lesions by approximately 4.21 days.

MOUTH RINSES

Grover. P, et al. (2022). **A two phase audit investigating the benefit of additional 0.5% cocaine mouthwash to institutional standard of care Mucositis management**, *Supportive Care in Cancer*, 30, 1-207. [Web Link](#)

To assess the benefit of the use of 0.5% cocaine mouth wash (CMW) to institutional standard of care (SOC) management of mucositis-related pain in head and neck cancer (HNC) patients undergoing radiotherapy/ chemoradiotherapy. Addition of CMW to SOC guidelines for mucositis management suggests no clear benefit or harm on clinical assessment or patient reported outcomes.

Malek. F, et al. (2021). **A Prospective Multicentric Randomized Double-Blind Trial on the Safety and Efficacy of Ketamine Mouthwash in Control of Pediatric Chemotherapy-Induced Mucositis**, *Pediatric Blood and Cancer*, 68. [Web Link](#)

Differences were detected between the two groups' reduction of Mucositis pain intensity. Oral tolerance improved significantly on the second and third day among the Ketamine group compared with the placebo group. Noticeable statistical differences were seen for the onset of effect and duration of effect in the Ketamine group in all three study days. Ketamine mouthwashes caused a clinically significant decrease in the pain scores and revealed an acceptable safety profile. Hence it could be an initiator of a new era in the treatment of severe mucositis.

Amadori. F, et al. (2021). **Ozonized water for treatment of oral mucositis in children: A pilot study**, *Supportive Care in Cancer*, 29. [Web Link](#)

The aim of this pilot study was to investigate the effectiveness of ozonized water in the treatment of OM in childhood. Ozonized water treatment seems to be effective in reducing OM-related pain in children.

Immonen. E, et al. (2020). **Randomized controlled and double-blinded study of Caphosol versus saline oral rinses in pediatric patients with cancer**, *Pediatric Blood and Cancer*, 67 (10). [Web Link](#)

The purpose of this study was to compare topically administered Caphosol to saline rinses in the prevention of mucositis in pediatric cancer patients. No difference in prevention of oral mucositis was observed between the use of Caphosol or saline rinses.

Prakash. S, et al. (2020). **Ketamine mouthwash versus placebo in the treatment of severe oral mucositis pain in children with cancer: A randomized double-blind placebo-controlled trial**, *Pediatric Blood and Cancer*, 67 (9). [Web Link](#)

Among children on cancer chemotherapy with severe OM, ketamine mouthwash at a dose of 1 mg/kg did not significantly reduce OM pain. It did not decrease the need for rescue pain

medications. Further research is warranted to test higher doses of ketamine for a clinically significant effect.

Bahrololoomi. Z, et al. (2020). **Evaluating the additive effect of Persica and chlorhexidine mouthwashes on oral health status of children receiving chemotherapy for their hematolignancy: A randomized clinical trial**, *Journal of clinical and experimental dentistry*, 12 (6), 574-580. [Web Link](#)

Both mouth-rinse combinations were effective on mucositis, plaque and gingival status of children receiving chemotherapy. However, Persica does not seem to pose additional effect on chlorhexidine in decreasing severity of chemotherapy induced mucositis. Key words: Mucositis, chemotherapy, children, chlorhexidine, Persica.

PAIN MEDICATIONS

Walker S.M, et al. (2022). **Intravenous opioids for chemotherapy-induced severe mucositis pain in children: Systematic review and single-center case series of management with patient- or nurse-controlled analgesia (PCA/NCA)**, *Paediatric Anaesthesia*, 32 (1), 17-34. [Web Link](#)

Management of severe mucositis pain can require prolonged IV opioid therapy. Individual and treatment-related variability in analgesic requirements highlight the need for regular review, titration, and management by specialist services.

Nielsen B.N, et al. (2021). **Evaluation of topical morphine for treatment of oral mucositis in cancer patients**, *British Journal of Pain*, 15 (4), 411-419. [Web Link](#)

Orally applied opioids may offer analgesia with fewer side effects than systemic opioids. The findings indicate that the analgesic effect of peripherally applied morphine is not significantly different from placebo, and parenteral opioids should continue to be the standard of care.

SUPPLEMENTS

Hassan. H, et al. (2022). **Mucositis reduction with probiotics in children with cancer: A randomised-controlled feasibility study**, *Archives of Disease in Childhood*, 107 (3), 259-264. [Web Link](#)

Whilst this study did not achieve all intended outcomes, it demonstrated that randomisation and implementation of this study are feasible. Barriers identified included recruitment, the capture of data and adherence with the probiotic or placebo. Findings from this study have been used to develop a parallel biological sub-study that can be undertaken in a future RCT.

Widjaja. N. A, et al. (2020). **Efficacy Oral Glutamine to Prevent Oral Mucositis and Reduce Hospital Costs During Chemotherapy in Children with Acute Lymphoblastic Leukemia**, *Asian Pacific journal of cancer prevention : APJCP*, 21 (7), 2117-2121. [Web Link](#)

To investigate the use of glutamine administered orally during Methotrexate chemotherapy to prevent oral mucositis and reduce hospital costs in children with acute lymphoblastic leukemia (ALL). There was significant difference in the prevention of oral mucositis by oral glutamine vs placebo. The hospital cost for glutamine supplementation was lower than control group.

Gutierrez-Vargas. R, et al. (2020). **Effect of zinc on oropharyngeal mucositis in children with acute leukemia undergoing chemotherapy**, *Medicina oral, patologia oral y cirugia bucal*, 25(6), 791-798. [Web link](#)

The objective of this study was to determine the effect of zinc in OM in children with acute

leukemia in the early stages of oncological treatment. Zinc facilitated a reduction in the severity and duration of OM; further studies focusing on children are needed to confirm the effects of this trace element.

Pico-Monllor. M, et al. (2019). **Search and Selection of Probiotics That Improve Mucositis Symptoms in Oncologic Patients. A Systematic Review**, *Nutrients*, 11 (10). [Web Link](#)

Our analysis suggests that a combination of Bifidobacterium longum, Lactobacillus acidophilus, Bifidobacterium breve, Bifidobacterium infantis, and Saccharomyces boulardii could be a good combination of probiotics to reduce incident rates of mucositis or ameliorate its symptoms in chemo or radiotherapy treated patients.

HONEY

Badr. L, et al. (2023). **The efficacy of honey or olive oil on the severity of oral mucositis and pain compared to placebo (standard care) in children with leukemia receiving intensive chemotherapy: A randomized controlled trial (RCT)**. *Journal of pediatric nursing, in press*, [web link](#)
Manuka honey or olive oil can be used as alternative therapies by nurses to children with leukemia and suffering from OM, especially in low and middle-income countries where more expensive therapies may not be available or economical. Pediatric nurses may recommend Manuka honey to treat OM in children with leukemia as it is safe and inexpensive compared to other treatment modalities.

Zhang. L, et al. (2022). **Use of Honey in the Management of Chemotherapy-Associated Oral Mucositis in Paediatric Patients**. *Cancer Management and Research*, 14, 2773-2783. [web link](#)
Honey not only has been shown to have the capability for healing injured tissues but it is also a more economical treatment, and it has fewer side effects compared to synthetic drugs. Honey or honey products can prevent chemotherapy-induced OM (CIOM) and be the best treatment to grade I, II and III CIOM. However, it is disappointing that studies involving children as patients were few, and limited data available so far.

Hao. S, et al. (2022). **Effect of Honey on Pediatric Radio/Chemotherapy-Induced Oral Mucositis (R/CIOM): A Systematic Review and Meta-Analysis**, *Evidence-based Complementary and Alternative Medicine*. [Web Link](#)

Honey has been recommended for adults with radio/chemotherapy-induced oral mucositis (R/CIOM), but its effect for pediatric patients has not been systematically evaluated. Totally, five studies containing 316 patients were included in our systematic review and meta-analysis. The result indicated that honey intervention significantly reduced the recovery time in pediatric patients and also reduced the occurrence of all grades of R/CIOM and the occurrence of grade III and grade IV R/CIOM. Therefore, honey could be a competent candidate for the complementary treatment of pediatric R/CIOM.

Yang. C, et al. (2019). **Topical application of honey in the management of chemo/radiotherapy-induced oral mucositis: A systematic review and network meta-analysis**, *International journal of nursing studies*, 89, 80-87. [Web Link](#)

The aim of this review was to assess the comparative efficacy of honey for patients with cancer undergoing chemo/radiotherapy-induced oral mucositis through a systematic review and network meta-analysis. From the results, Honey treatment significantly increased the therapeutic effect of chemo/radiotherapy-induced moderate-severe oral mucositis The adjuvant treatment honey is effective and safe for patients with cancer undergoing chemo/radiotherapy-induced oral

mucositis, especially applied pure natural local honey can be invoked as a first-line adjuvant therapy agent.

OTHER BIOLOGICAL AGENTS (EG. ALOE, OILS)

Massano. D, et al. (2022). **Administration of Samital in children with oral mucositis: a feasibility study**, *European review for medical and pharmacological sciences*, 26 (22), 8576-8581. [Web link](#)
SAMITAL administration appears to be safe in the pediatric population, as it is not absorbed in the bloodstream and does not cause any local or systemic side effects. However, the current formulation is only partially suitable for children, and future studies on SAMITAL in children would need an adapted formulation to increase compliance.

Alkhouli. M, et al. (2021). **Efficacy of Aloe-Vera Use for Prevention of Chemotherapy-Induced Oral Mucositis in Children with Acute Lymphoblastic Leukemia: A Randomized Controlled Clinical Trial**, *Comprehensive child and adolescent nursing*, 44 (1), 49-62. [Web Link](#)

According to the observed findings, CIOM degrees were less severe in the aloe-vera group than in the sodium bicarbonate group. Statistically significant difference of occurrence of different CIOM degrees between groups was recorded in the 2nd, 3rd, 4th, and 7th weeks of follow-up period. Moreover, Mann-Whitney U test indicated that patients in the sodium bicarbonate group began CIOM sooner than those in the aloe-vera group with a statistically significant difference ($p = .001$). These findings show that topical application of aloe-vera solution is effective in the prevention of CIOM in ALL children.

Alkhouli. M, et al. (2021). **Assessing the topical application efficiency of two biological agents in managing chemotherapy-induced oral mucositis in children: A randomized clinical trial**, *Journal of oral biology and craniofacial research*, 11 (3), 373-378. [Web Link](#)

This randomized clinical trial aimed to assess the efficiency of Aloe Vera and Olive Oil in managing chemotherapy-induced oral mucositis. Both Aloe Vera and Olive Oil significant differences in the management of chemotherapy-induced oral mucositis compared to sodium bicarbonate treatments. However, olive Oil is effective in managing CIOM.

Alkhouli. M, (2019). **Evaluation of the effectiveness of olive oil to prevent chemotherapy induced oral mucositis: A randomized controlled clinical trial**, *Pediatric Dental Journal*, 29 (3), 123-131. [Web Link](#)

Based on the observed results, (OM) grades were with less severity in olive oil group than in sodium bicarbonate group with statistically significant difference reported from the 2 nd week of study phase. As a result, olive oil retarded the beginning of oral mucositis (OM) compared with sodium bicarbonate. From this study, olive oil can be used topically on oral tissues to prevent chemotherapy induced (OM) in acute lymphoblastic leukemia children.

MEDLINE SEARCH STRATEGY

Database: Ovid MEDLINE(R) ALL <1946 to February 24, 2023>

Search Strategy:

-
- 1 exp Neoplasms/ or Medical Oncology/ or Oncology nursing/ (3807748)
 - 2 (cancer* or tumor* or neo*plasm* or oncolog*).tw. (3423196)
 - 3 Chemoradiotherapy/ or Chemotherapy, Adjuvant/ or Consolidation Chemotherapy/ or Chemoprevention/ or Induction Chemotherapy/ or Maintenance Chemotherapy/ or Electrochemotherapy/ (72658)
 - 4 (chemo* adj3 (induce* or cause* or related)).tw. (39807)
 - 5 1 or 2 or 3 or 4 (4856054)
 - 6 (child* or pediatric* or paediatric*).tw. (1785554)
 - 7 adolescent/ or exp child/ or exp infant/ or Pediatrics/ or Hospitals, Pediatric/ (3948896)
 - 8 6 or 7 (4379978)
 - 9 Oral hygiene/ or Mouth diseases/ or Mucositis/ or mucositis.tw. (42756)
 - 10 ((oral or mouth or dental) adj2 (hygiene or care or health)).tw. (66123)
 - 11 Dental Care/ or Dental Care for Children/ (26684)
 - 12 9 or 10 (97647)
 - 13 5 and 8 and 12 (3126)
 - 14 exp consensus/ or exp consensus development conference/ or exp consensus development conferences as topic/ or critical pathways/ or exp guideline/ or guidelines as topic/ or exp practice guideline/ or practice guidelines as topic/ or health planning guidelines/ or (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt. or (position statement* or policy statement* or practice parameter* or best practice* or gold standard).ti,ab,kf,kw. or (standards or guideline or guidelines or guidance or recommendat*).ti,ab,kf,kw. or ((practice or treatment* or clinical) adj guideline*).ab. or (CPG or CPGs).ti. or consensus*.ti,kf,kw. or

consensus*.ab. /freq=2 or ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*).ti,ab,kf,kw. or (care adj2 (standard or path or paths or pathway or pathways or map or maps or plan or plans)).ti,ab,kf,kw. (1317407)

15 (systematic review or meta-analysis).pt. or meta-analysis/ or systematic review/ or systematic reviews as topic/ or meta-analysis as topic/ or exp technology assessment, biomedical/ or network meta-analysis/ or ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf. or ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf. or ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*).ti,ab,kf. or (data synthes* or data extraction* or data abstraction*).ti,ab,kf. or (handsearch* or hand search*).ti,ab,kf. or (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf. or (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf. or (meta regression* or metaregression*).ti,ab,kf. or (meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw. or (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw. or (cochrane or (health adj2 technology assessment) or evidence report).jw. or (comparative adj3 (efficacy or effectiveness)).ti,ab,kf. or (outcomes research or relative effectiveness).ti,ab,kf. or ((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf. or (meta-analysis or systematic review).mp. or (multi* adj3 treatment adj3 comparison*).ti,ab,kf. or (mixed adj3 treatment adj3 (meta-analy* or metaanaly*).ti,ab,kf. or umbrella review*.ti,ab,kf. or (multi* adj2 paramet* adj2 evidence adj2 synthesis).ti,ab,kf. or (multiparamet* adj2 evidence adj2 synthesis).ti,ab,kf. or (multi-paramet* adj2 evidence adj2 synthesis).ti,ab,kf. (657983)

16 (Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or Clinical Trial, Phase III).pt. or Randomized Controlled Trial/ or exp Randomized Controlled Trials as Topic/ or Controlled Clinical Trial/ or exp Controlled Clinical Trials as Topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or Placebos/ or Control Groups/ or (random* or sham or placebo*).ti,ab,hw,kf. or ((singl* or doubl*) adj (blind* or dumm* or mask*).ti,ab,hw,kf. or ((tripl* or trebl*) adj (blind* or dumm* or mask*).ti,ab,hw,kf. or (control* adj3 (study or studies or trial* or group*).ti,ab,kf. or (Nonrandom* or non random* or non-random* or quasi-random* or quasirandom*).ti,ab,hw,kf. or allocated.ti,ab,hw. or ((open label or open-label) adj5 (study or studies or trial*).ti,ab,hw,kf. or ((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*).ti,ab,hw,kf. or (pragmatic study or pragmatic studies).ti,ab,hw,kf. or ((pragmatic or practical) adj3 trial*).ti,ab,hw,kf. or ((quasiexperimental or quasi-experimental) adj3 (study or studies or trial*).ti,ab,hw,kf. or (phase adj3 (III or "3") adj3 (study or studies or trial*).ti,hw,kf. (2549166)

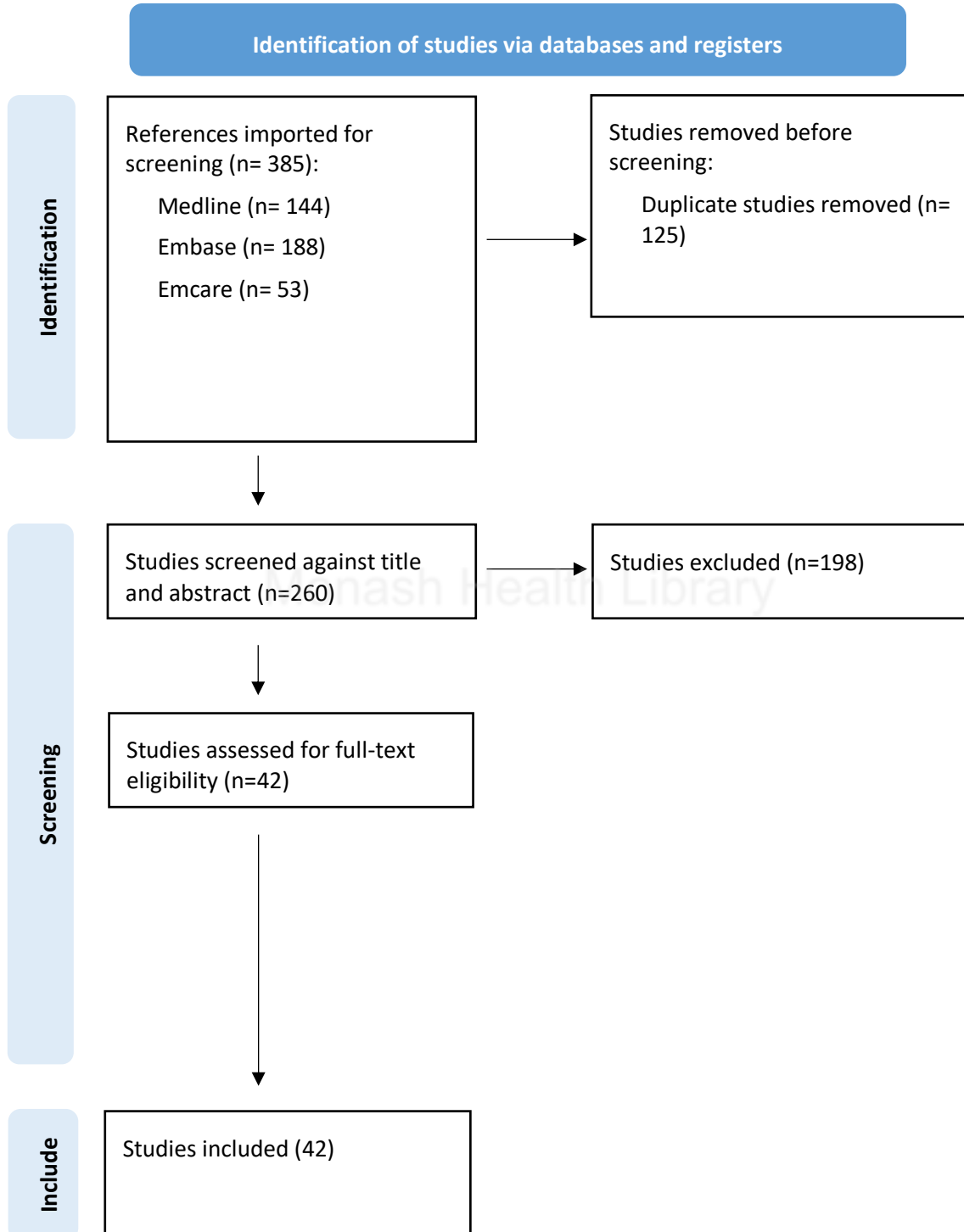
- 17 14 or 15 or 16 (4038300)
- 18 5 and 8 and 12 and 17 (698)
- 19 limit 18 to yr="2018 -Current" (144)

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APPENDIX

PRISMA CHART



This report contains curated literature results against a unique set of criteria at a particular point in time. Users of this service are responsible for independently appraising the quality, reliability, and applicability of the evidence cited. We strongly recommend consulting the original sources and seeking further expert advice.