

**Supplementary Table 1: Population, Intervention, Comparison, Outcome & Study Design (PICOS) for assessing the efficacy of oral LLLT**

<b>Population</b>	CYP less than 18 years old with a diagnosis of any form of cancer <sup>1</sup>
<b>Intervention</b>	Any form of oral LLLT or photobiomodulation as prevention or treatment for oral mucositis.
<b>Comparison</b>	No oral LLLT
<b>Outcome</b>	<p>May consider outcomes such as (but not restricted to) oral mucositis, oral pain, adverse events, etc.</p> <p><b>Primary outcomes:</b>  Severity of oral mucositis  Timing and intensity of oral pain and ChIMES<sup>2</sup> score  Acceptability, effectiveness, and adherence to oral low-level laser therapy  Symptoms, other than pain, considered important to the paediatric population  Duration of action of oral low-level laser therapy  Oral temperature  Any adverse events.</p> <p><b>Additional outcomes:</b>  Interruptions to cancer treatment  Oral pain on a 0 (no pain) to 10 (maximum pain) scale  Quality of life  Normalcy of diet (days of total parenteral nutrition)  Duration of hospitalisation (days).</p>
<b>Study design</b>	Must be an RCT

<sup>1</sup> Where studies included any CYP less than 18 years old, they were eligible for inclusion. See Supplementary Table 6 for a breakdown of the number of children in each study, including where the number is unknown.

<sup>2</sup> Jacobs S, Baggott C, Agarwal R, et al. Validation of the Children's International Mucositis Evaluation Scale (ChIMES) in paediatric cancer and SCT. *Br J Cancer* 2013;109:2515-22. <https://doi.org/10.1038/bjc.2013.618>

**Supplementary Table 2: PICOS for assessing the safety of oral LLLT**

<b>Population</b>	People of any age with a diagnosis of any form of cancer
<b>Intervention</b>	Any form of oral LLLT or photobiomodulation as prevention or treatment for oral mucositis.
<b>Comparison</b>	No oral LLLT
<b>Outcome</b>	May consider outcomes such as (but not restricted to) oral mucositis, oral pain, adverse events, etc.  <b>Primary outcome:</b> Adverse events
<b>Study design</b>	Any study

**Supplementary Table 3: Databases and sources searched**

Databases and sources searched
EMBASE, MEDLINE®, Allied and Complementary Medicine Database (AMED), Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effects, International Society of Paediatric Oncology, American Society of Clinical Oncology, Multinational Association of Supportive Care in Cancer, International Cancer Research Portfolio, National Cancer Research Institute, National Cancer Institute Clinical Trials, ISRCTN registry, Web of Science, ClinicalTrials.gov, Centerwatch

**Supplementary Table 4: The search strategy used for identifying studies through MEDLINE**

MEDLINE search strategy
<ol style="list-style-type: none"> <li>1. exp NEOPLASMS/</li> <li>2. exp LEUKEMIA/</li> <li>3. exp LYMPHOMA/</li> <li>4. exp RADIOTHERAPY/</li> <li>5. exp Antineoplastic agents/</li> <li>6. Bone Marrow Transplantation/</li> <li>7. neoplasm\$.mp.</li> <li>8. cancer\$.mp.</li> <li>9. (leukaemi\$ or leukemi\$).mp.</li> </ol>

10. (tumour\$ or tumor\$).mp.
11. malignan\$.mp.
12. neutropeni\$.mp.
13. carcino\$.mp.
14. adenocarcinoma\$.mp.
15. lymphoma\$.mp.
16. (radioth\$ or radiat\$ or irradiat\$).mp.
17. (bone adj marrow adj5 transplant\$).mp.
18. chemo\$.mp.
19. or/1-18
20. exp STOMATITIS/
21. Candidiasis, Oral/
22. stomatitis.mp.
23. mucositis.mp.
24. (oral adj6 mucos\$).mp.
25. (mycosis or mycotic).mp.
26. mIAS.ti.ab.
27. or/20-26
- 28 . laser/
29. laser\$.mp.
30. (diode\$ or photobiomodulat \$ or light \$ or infrared or cold-laser or phototherapy).mp.
31. or/28-30
32. 19 and 27 and 31

### Supplementary Table 5: List of included studies for considering safety of LLLT

Reference	Country
Luna Oliva I, Robles García M, López Serrano B, Pérez BP, Sáez de la Fuente I, Torres Lagares D, et al. 980nm diode laser effectiveness in induced oral mucositis treatment. <i>Med Oral Patol Oral Cir Bucal</i> . 2012 May 1;17(Supplement1):S260. doi:10.4317/medoral.17643760	Spain
Jéandet I, Martignoles JA, Tronchon S, Brouillat C, Filiol S, Villemagne C, et al. A cohort pilot study on the use of a preventive treatment of oral mucositis using low-level laser therapy on patients undergoing a haematopoietic stem cell transplantation <i>Bone Marrow Transplant</i> . 2016;51(1):S232.	France
Treister NS, London WB, Guo D, Malsch M, Verrill K, Brewer J, et al. A feasibility study evaluating extraoral photobiomodulation therapy for prevention of mucositis in pediatric hematopoietic cell transplantation. <i>Photomed Laser Surg</i> . 2016 Apr;34(4):178-84. doi: 10.1089/pho.2015.4021.	USA
Schubert MM, Eduardo FP, Guthrie KA, Franquin JC, Bensadoun RJ, Migliorati CA, et al. A phase III randomized double-blind placebo-controlled clinical trial to determine the efficacy of low level laser therapy for the prevention of oral mucositis in patients undergoing hematopoietic cell transplantation. <i>Support Care Cancer</i> . 2007 Oct;15(10):1145-54. doi: 10.1007/s00520-007-0238-7.	USA
Elad S, Luboshitz-Shon N, Cohen T, Wainchwaig E, Shapira MY, Resnick IB, et al. A randomized controlled trial of visible-light therapy for the prevention of oral mucositis. <i>Oral Oncol</i> . 2011 Feb;47(2):125-30. doi: 10.1016/j.oraloncology.2010.11.013.	Israel

Genot M, Awada A, Awada F, Jaivenois MF, Crombez P, Delmelle M, et al. A randomized study testing the efficacy of low-energy laser irradiation for treatment of oral mucositis in patients with haematological malignancy treated with intensive chemotherapy with or without radiotherapy and bone marrow transplant. <i>Support Care Cancer</i> . 2007;15:707-8.	Belgium
Hodgson BD, Margolis DM, Salzman DE, Eastwood D, Tarima S, Williams LD, et al. Amelioration of oral mucositis pain by NASA near-infrared light-emitting diodes in bone marrow transplant patients. <i>Support Care Cancer</i> . 2012 Jul;20(7):1405-15. doi: 10.1007/s00520-011-1223-8.	USA
Simões A, Benites BM, Benassi C, Torres-Schroter G, de Castro JR, Campos L. Antimicrobial photodynamic therapy on treatment of infected radiation-induced oral mucositis: Report of two cases. <i>Photodiagnosis Photodyn Ther</i> . 2017 Dec;20:18-20. doi: 10.1016/j.pdpdt.2017.08.007.	Brazil
Freitas AC, Campos L, Brandão TB, Cristóforo M, Eduardo Fde P, Luiz AC, et al. Chemotherapy-induced oral mucositis: effect of LED and laser phototherapy treatment protocols. <i>Photomed Laser Surg</i> . 2014 Feb;32(2):81-7. doi: 10.1089/pho.2013.3576.	Brazil
Sharon-Buller A, Sela M. CO2-laser treatment of ulcerative lesions. <i>Oral Surg Oral Med Oral Pathol Oral Radiol Endod</i> . 2004 Mar;97(3):332-4. doi: 10.1016/j.tripleo.2003.11.012	Israel
Oton-Leite AF, Corrêa de Castro AC, Morais MO, Pinezi JC, Leles CR, Mendonça EF. Effect of intraoral low-level laser therapy on quality of life of patients with head and neck cancer undergoing radiotherapy. <i>Head Neck</i> . 2012 Mar;34(3):398-404. doi: 10.1002/hed.21737.	Brazil
Arun Maiya G, Sagar MS, Fernandes D. Effect of low level helium-neon (He-Ne) laser therapy in the prevention & treatment of radiation induced mucositis in head & neck cancer patients. <i>Indian J Med Res</i> . 2006 Oct;124(4):399-402.	India
Oton-Leite AF, Silva GB, Morais MO, Silva TA, Leles CR, Valadares MC, et al. Effect of low-level laser therapy on chemoradiotherapy-induced oral mucositis and salivary inflammatory mediators in head and neck cancer patients. <i>Lasers Surg Med</i> . 2015 Apr;47(4):296-305. doi: 10.1002/lsm.22349.	Brazil
Gautam AP, Fernandes DJ, Vidyasagar MS, Maiya AG, Nigudgi S. Effect of low-level laser therapy on patient reported measures of oral mucositis and quality of life in head and neck cancer patients receiving chemoradiotherapy--a randomized controlled trial. <i>Support Care Cancer</i> . 2013 May;21(5):1421-8. doi: 10.1007/s00520-012-1684-4.	India
Salvador DRN, Soave DF, Sacono NT, de Castro EF, Silva GBL, E Silva LP, et al. Effect of photobiomodulation therapy on reducing the chemo-induced oral mucositis severity and on salivary levels of CXCL8/interleukin 8, nitrite, and myeloperoxidase in patients undergoing hematopoietic stem cell transplantation: a randomized clinical trial. <i>Lasers Med Sci</i> . 2017 Nov;32(8):1801-1810. doi: 10.1007/s10103-017-2263-1.	Brazil
Amadori F, Bardellini E, Majorana A. Effectiveness of lllt in the prevention and treatment of chemotherapy-induced oral mucositis in children. <i>Support Care Cancer</i> . 2018;26(2 Suppl 1):S139.	Italy
de Paula Eduardo F, Bezinelli LM, da Graça Lopes RM, Nascimento Sobrinho JJ, Hamerschlak N, Correa L. Efficacy of cryotherapy associated with laser therapy for decreasing severity of melphalan-induced oral mucositis during hematological stem-cell transplantation: a prospective clinical study. <i>Hematol Oncol</i> . 2015 Sep;33(3):152-8. doi: 10.1002/hon.2133.	Brazil
Arora H, Pai KM, Maiya A, Vidyasagar MS, Rajeev A. Efficacy of He-Ne Laser in the prevention and treatment of radiotherapy-induced oral mucositis in oral cancer patients. <i>Oral Surg Oral Med Oral Pathol Oral Radiol Endod</i> . 2008 Feb;105(2):180-6. doi: 10.1016/j.tripleo.2007.07.043.	India
Lima AG, Antequera R, Peres MP, Snitcosky IM, Federico MH, Villar RC. Efficacy of low-level laser therapy and aluminum hydroxide in patients with chemotherapy and radiotherapy-induced oral mucositis. <i>Braz Dent J</i> . 2010;21(3):186-92. doi: 10.1590/s0103-64402010000300002.	Brazil
González-Arriagada WA, Ramos LMA, Andrade MAC, Lopes MA. Efficacy of low-level laser therapy as an auxiliary tool for management of acute side effects of head and neck radiotherapy. <i>J Cosmet Laser Ther</i> . 2018 Apr;20(2):117-122. doi: 10.1080/14764172.2017.1376097.	Brazil
Carvalho PA, Lessa RC, Guollo A, Carraro DM, Lopes RN. Evaluation of laser therapy in the prevention of oral mucositis related to radiotherapy: Comparison among the effects of three different low-power laser protocols. <i>Head Neck</i> . 2015;37(Suppl 1):E187-8.	Brazil
Ahmed KM, Hussein SA, Noori AJ, Abdulateef SN, Abdulla BK. Evaluation of Low Level Laser Therapy in the management of chemotherapy-induced oral mucositis in pediatric and young cancer patients: a randomized clinical trial. <i>Eur Sci J</i> . 2015;11(27):209-22.	Iraq
Leite Cavalcanti A, José de Macêdo D, Suelly Barros Dantas F, Dos Santos Menezes K, Filipe Bezerra Silva D, Alves de Melo Junior W, et al. Evaluation of oral mucositis occurrence in oncologic patients under antineoplastic therapy submitted to the low-level laser coadjuvant therapy. <i>J Clin Med</i> . 2018 Apr 24;7(5):90. doi: 10.3390/jcm7050090.	Brazil
Barasch A, Peterson DE, Tanzer JM, D'Ambrosio JA, Nuki K, Schubert MM, et al. Helium-neon laser effects on conditioning-induced oral mucositis in bone marrow transplantation patients. <i>Cancer</i> . 1995 Dec 15;76(12):2550-6. doi: 10.1002/1097-0142(19951215)76:12<2550::aid-cnrc2820761222>3.0.co;2-x.	USA
Cruz LB, Ribeiro AS, Rech A, Rosa LG, Castro CG Jr, Brunetto AL. Influence of low-energy laser in the prevention of oral mucositis in children with cancer receiving chemotherapy. <i>Pediatr Blood Cancer</i> . 2007 Apr;48(4):435-40. doi: 10.1002/pbc.20943.	Brazil
Lino MD, Carvalho FB, Oliveira LR, Magalhães EB, Pinheiro AL, Ramalho LM. Laser phototherapy as a treatment for radiotherapy-induced oral mucositis. <i>Braz Dent J</i> . 2011;22(2):162-5. doi: 10.1590/s0103-64402011000200013.	Brazil

Simões A, Eduardo FP, Luiz AC, Campos L, Sá PH, Cristóforo M, et al. Laser phototherapy as topical prophylaxis against head and neck cancer radiotherapy-induced oral mucositis: comparison between low and high/low power lasers. <i>Lasers Surg Med</i> . 2009 Apr;41(4):264-70. doi: 10.1002/lsm.20758.	Brazil
Schulze Selting K, Dittus D, Döring M, Handgretinger R, Barth M. Laser therapy - a new treatment option on oral mucositis. <i>Bone Marrow Transplant</i> . 2014;49(Suppl 1):S399.	Germany
Lang-Bicudo L, Eduardo Fde P, Eduardo Cde P, Zezell DM. LED phototherapy to prevent mucositis: a case report. <i>Photomed Laser Surg</i> . 2008 Dec;26(6):609-13. doi: 10.1089/pho.2007.2228.	Brazil
Quinn A, Holeva K, Clump D. Light years ahead: Use of low level laser therapy for oral mucositis. <i>Oncol Nurs Forum</i> . 2015;42(2):E173.	USA
Gautam AP, Fernandes DJ, Vidyasagar MS, Maiya GA. Low level helium neon laser therapy for chemoradiotherapy induced oral mucositis in oral cancer patients - a randomized controlled trial. <i>Oral Oncol</i> . 2012 Sep;48(9):893-7. doi: 10.1016/j.oraloncology.2012.03.008.	India
Gautam AP, Fernandes DJ, Vidyasagar MS, Maiya AG, Vadhira BM. Low level laser therapy for concurrent chemoradiotherapy induced oral mucositis in head and neck cancer patients - a triple blinded randomized controlled trial. <i>Radiother Oncol</i> . 2012 Sep;104(3):349-54. doi: 10.1016/j.radonc.2012.06.011.	India
Pereira EM, De Almeida Lawall M, Vieira CL, Veras GR. Low level laser therapy in oral mucositis: A case report. <i>Head Neck</i> . 2015;37(Suppl 1):E142.	Brazil
Cauwels RGEC, Martens LC. Low level laser therapy in oral mucositis: a pilot study. <i>Eur Arch Paediatr Dent</i> . 2011;12(2):118-23.	Belgium
Bensadoun RJ, Franquin JC, Ciais G, Darcourt V, Schubert MM, Viot M, et al. Low-energy He/Ne laser in the prevention of radiation-induced mucositis: A multicenter phase III randomized study in patients with head and neck cancer. <i>Support Care Cancer</i> . 1999 Jul;7(4):244-52. doi: 10.1007/s005200050256.	France
Jaguar GC, Prado JD, Nishimoto IN, Pinheiro MC, de Castro DO Jr, da Cruz Perez DE, et al. Low-energy laser therapy for prevention of oral mucositis in hematopoietic stem cell transplantation. <i>Oral Dis</i> . 2007 Nov;13(6):538-43. doi: 10.1111/j.1601-0825.2006.01330.x.	Brazil
Kuhn A, Porto FA, Miraglia P, Brunetto AL. Low-level infrared laser therapy in chemotherapy-induced oral mucositis: a randomized placebo-controlled trial in children. <i>J Pediatr Hematol Oncol</i> . 2009 Jan;31(1):33-7. doi: 10.1097/MPH.0b013e318192cb8e.	Brazil
Kuhn A, Vacaro G, Almeida D, Machado A, Braghini PB, Shilling MA, et al. Low-level infrared laser therapy for chemo- or radiotherapy-induced oral mucositis: a randomized, placebo-controlled study. <i>J Oral Laser Applications</i> . 2007;7:175-81.	Brazil
Amadori F, Bardellini E, Conti G, Pedrini N, Schumacher RF, Majorana A. Low-level laser therapy for treatment of chemotherapy-induced oral mucositis in childhood: a randomized double-blind controlled study. <i>Lasers Med Sci</i> . 2016 Aug;31(6):1231-6. doi: 10.1007/s10103-016-1975-y.	Italy
Abramoff MM, Lopes NN, Lopes LA, Dib LL, Guilherme A, Caran EM, et al. Low-level laser therapy in the prevention and treatment of chemotherapy-induced oral mucositis in young patients. <i>Photomed Laser Surg</i> . 2008 Aug;26(4):393-400. doi: 10.1089/pho.2007.2144.	Brazil
Antunes HS, de Azevedo AM, da Silva Bouzas LF, Adão CA, Pinheiro CT, Mayhe R, et al. Low-power laser in the prevention of induced oral mucositis in bone marrow transplantation patients: a randomized trial. <i>Blood</i> . 2007 Mar 1;109(5):2250-5. doi: 10.1182/blood-2006-07-035022.	Brazil
Medeiros NJ, Medeiros NF, Santos CC, Parente GV, Carvalho JN. Low-power laser therapy in chemical-induced oral mucositis: a case study. <i>Braz J Otorhinolaryngol</i> . 2013 Nov-Dec;79(6):792. English, Portuguese. doi: 10.5935/1808-8694.20130143.	Brazil
Libik TV, Gileva OS, Danilov KV, Grigorev SS, Pozdnyakova AA. Management of cancer therapy-induced oral mucositis pain and xerostomia with extra- and intra oral laser irradiation. <i>AIP Conference Proceedings</i> . 2017;1882:020044. doi: 10.1063/1.5001623.	Russia
Gobbo M, Verzegnassi F, Ronfani L, Zanon D, Melchionda F, Bagattoni S, et al. Multicenter randomized, double-blind controlled trial to evaluate the efficacy of laser therapy for the treatment of severe oral mucositis induced by chemotherapy in children: laMPO RCT. <i>Pediatr Blood Cancer</i> . 2018 Aug;65(8):e27098. doi: 10.1002/pbc.27098.	Italy
Whelan HT, Connelly JF, Hodgson BD, Barbeau L, Post AC, Bullard G, et al. NASA light-emitting diodes for the prevention of oral mucositis in pediatric bone marrow transplant patients. <i>J Clin Laser Med Surg</i> . 2002 Dec;20(6):319-24. doi: 10.1089/104454702320901107.	USA
Eduardo Fde P, Bezinelli LM, de Carvalho DL, Lopes RM, Fernandes JF, Brumatti M, et al. Oral mucositis in pediatric patients undergoing hematopoietic stem cell transplantation: clinical outcomes in a context of specialized oral care using low-level laser therapy. <i>Pediatr Transplant</i> . 2015 May;19(3):316-25. doi: 10.1111/ptr.12440.	Brazil
Montmaneix N, Chausset A, Sozeau C, Merlin E, Duclos C. Paediatric experience in low-level laser therapy in the prevention of oral mucositis. <i>Bone Marrow Transplant</i> . 2011;46(1):S417.	France
Ribeiro da Silva VC, da Motta Silveira FM, Barbosa Monteiro MG, da Cruz MMD, Caldas Júnior AF, Pina Godoy G. Photodynamic therapy for treatment of oral mucositis: Pilot study with pediatric patients undergoing chemotherapy. <i>Photodiagnosis Photodyn Ther</i> . 2018 Mar;21:115-120. doi: 10.1016/j.pdpdt.2017.11.010.	Brazil
Wong SF, Wilder-Smith P. Pilot study of laser effects on oral mucositis in patients receiving chemotherapy. <i>Cancer J</i> . 2002 May-Jun;8(3):247-54. doi: 10.1097/00130404-200205000-00008.	USA
Soto M, Lalla RV, Gouveia RV, Zecchin VG, Seber A, Lopes NN. Pilot study on the efficacy of combined intraoral and extraoral low-level laser therapy for prevention of oral mucositis in pediatric patients undergoing hematopoietic stem cell transplantation. <i>Photomed Laser Surg</i> . 2015 Nov;33(11):540-6. doi: 10.1089/pho.2015.3954.	Brazil

Bezinelli LM, Eduardo FP, Neves VD, Correa L, Lopes RM, Michel-Crosato E, et al. Quality of life related to oral mucositis of patients undergoing haematopoietic stem cell transplantation and receiving specialised oral care with low-level laser therapy: A prospective observational study. <i>Eur J Cancer Care (Engl)</i> . 2016 Jul;25(4):668-74. doi: 10.1111/ecc.12344.	Brazil
Eduardo FP, Bezinelli L, Luiz AC, Correa L, Vogel C, Eduardo CP. Severity of oral mucositis in patients undergoing hematopoietic cell transplantation and an oral laser phototherapy protocol: a survey of 30 patients. <i>Photomed Laser Surg</i> . 2009 Feb;27(1):137-44. doi: 10.1089/pho.2007.2225.	Brazil
Curra M, De Campos Baldin JJCM, Carvalho ALH, Martins MAT, Daudt LE, Gaio EJ, et al. Severity of oral mucositis in patients undergoing hematopoietic stem cell transplantation and correlation with oral status. <i>Head Neck</i> . 2015;37(Suppl 1):E157.	Brazil
Chor A, de Azevedo AM, Maiolino A, Nucci M. Successful treatment of oral lesions of chronic lichenoid graft-vs.-host disease by the addition of low-level laser therapy to systemic immunosuppression. <i>Eur J Haematol</i> . 2004 Mar;72(3):222-4. doi: 10.1046/j.0902-4441.2003.00202.x.	Brazil
Silva GB, Mendonça EF, Bariani C, Antunes HS, Silva MA. The prevention of induced oral mucositis with low-level laser therapy in bone marrow transplantation patients: a randomized clinical trial. <i>Photomed Laser Surg</i> . 2011 Jan;29(1):27-31. doi: 10.1089/pho.2009.2699.	Brazil
Genot-Klastersky MT, Klastersky J, Awada F, Awada A, Crombez P, Martinez MD, Jaivenois MF, Delmelle M, Vogt G, Meuleman N, Paesmans M. The use of low-energy laser (LEL) for the prevention of chemotherapy- and/or radiotherapy-induced oral mucositis in cancer patients: results from two prospective studies. <i>Support Care Cancer</i> . 2008 Dec;16(12):1381-7. doi: 10.1007/s00520-008-0439-8.	Belgium
Corti L, Chiarion-Sileni V, Aversa S, Ponzoni A, D'Arcais R, Pagnutti S, et al. Treatment of chemotherapy-induced oral mucositis with light-emitting diode. <i>Photomed Laser Surg</i> . 2006 Apr;24(2):207-13. doi: 10.1089/pho.2006.24.207.	
de Fátima Lima Ferreira M, de Carvalho FB, de Oliveira SCPS, Monteiro JSC, Santos GMP, Gesteira MFM, et al. Use of laser photomodulation in the evolution of oral mucositis associated to cyclophosphamide, methotrexate, 5-fluorouracil - CMF in 5 fluorouracil + adriamycin + cyclophosphamide - FAC chemotherapy protocols in patients with breast cancer. <i>Proc SPIE 8569, Mechanisms for Low-Light Therapy VIII, 85690O</i> . 2013. doi: 10.1117/12.2005274	Brazil
Khourī VY, Stracieri ABPL, Rodrigues MC, de Moraes DA, Pieroni F, Simões BP, et al. Use of therapeutic laser for prevention and treatment of oral mucositis. <i>Braz Dent J</i> . 2009;20(3):215-20. doi: 10.1590/S0103-64402009000300008.	Brazil
Guedes CDCFV, de Freitas Filho SAJ, de Faria PR, Loyola AM, Sabino-Silva R, Cardoso SV. Variation of Energy in Photobiomodulation for the Control of Radiotherapy-Induced Oral Mucositis: A Clinical Study in Head and Neck Cancer Patients. <i>Int J Dent</i> . 2018 Feb 22;2018:4579279. doi: 10.1155/2018/4579279.	Brazil
Moskvin S, Pritiko D, Sergeenko E, Lukash E, Gusev L. A brief literature review and own clinical experience in prophylaxis of oral mucositis in children using low level laser therapy. <i>Biomedicine (Taipei)</i> . 2019 Mar;9(1):1. doi: 10.1051/bmdcn/2019090101.	Russia
Rezk-Allah SS, Abd Elshaf HM, Farid RJ, Hassan MAE, Alsirafy SA. Effect of Low-Level Laser Therapy in Treatment of Chemotherapy Induced Oral Mucositis. <i>J Lasers Med Sci</i> . 2019 Spring;10(2):125-130. doi: 10.15171/jlms.2019.20.	Egypt
Giacco CA, Castro S, Fluck V, Martinez JE, Higuera J. Evaluation of patients with oral mucositis following oncological treatment and treated with low intensity laser. <i>Biocell</i> . 2019;43(Suppl 3):A91.	Argentina
Lavaee F, Amanati A, Ramzi M, Naseri S, Shakiba Sefat H. Evaluation of the effect of photodynamic therapy on chemotherapy induced oral mucositis. <i>Photodiagnosis Photodyn Ther</i> . 2020 Jun;30:101653. doi: 10.1016/j.pdpdt.2020.101653.	Iran
Legouté F, Bensadoun RJ, Seegers V, Pointreau Y, Caron D, Lang P, et al. Low-level laser therapy in treatment of chemoradiotherapy-induced mucositis in head and neck cancer: Results of a randomised, triple blind, multicentre phase III trial. <i>Radiat Oncol</i> . 2019 May 22;14(1):83. doi: 10.1186/s13014-019-1292-2.	France
Pires Marques EC, Piccolo Lopes F, Nascimento IC, Morelli J, Pereira MV, Machado Meiken VM, et al. Photobiomodulation and photodynamic therapy for the treatment of oral mucositis in patients with cancer. <i>Photodiagnosis Photodyn Ther</i> . 2020 Mar;29:101621. doi: 10.1016/j.pdpdt.2019.101621.	Brazil
Rupel K, Zupin L, Colliva A, Kamada A, Poropat A, Ottaviani G, et al. Photobiomodulation at multiple wavelengths differentially modulates oxidative stress in vitro and in vivo. <i>Oxid Med Cell Longev</i> . 2018 Nov 11;2018:6510159. doi: 10.1155/2018/6510159.	
Pinheiro SL, Bonadiman AC, Borges Lemos ALDA, Annicchino BM, Segatti B, Pucca DS, et al. Photobiomodulation therapy in cancer patients with mucositis: a clinical evaluation. <i>Photobiomodul Photomed Laser Surg</i> . 2019 Mar;37(3):142-150. doi: 10.1089/photob.2018.4526.	Brazil
El Mobadder M, Farhat F, El Mobadder W, Nammour S. Photobiomodulation Therapy in the Treatment of Oral Mucositis, Dysphagia, Oral Dryness, Taste Alteration, and Burning Mouth Sensation Due to Cancer Therapy: A Case Series. <i>Int J Environ Res Public Health</i> . 2019 Nov 15;16(22):4505. doi: 10.3390/ijerph16224505.	Lebanon
Noirrit-Esclassan E, Valera MC, Vignes E, Munzer C, Bonal S, Daries M, et al. Photobiomodulation with a combination of two wavelengths in the treatment of oral mucositis in children: The PEDIALASE feasibility study. <i>Arch Pediatr</i> . 2019 Jul;26(5):268-274. doi: 10.1016/j.arcped.2019.05.012.	France
Nunes LFM, de Arruda JAA, Souza AF, Silva RCC, Lanza CRM, Kakehasi FM, et al. Prophylactic photobiomodulation therapy using 660 nm diode laser for oral mucositis in paediatric patients under chemotherapy: 5-year experience from a Brazilian referral service. <i>Lasers Med Sci</i> . 2020 Oct;35(8):1857-1866. doi: 10.1007/s10103-020-03060-9.	Brazil

Minicucci EM, Cruz AR, Simoes CC, Gomes DO, Felipe DF. Protocol and preliminary results of symptoms and control of mucositis in patients submitted to autologous stem cell transplantation. <i>Support Care Cancer</i> . 2019;27(Suppl 1):S128.	Brazil
Bourbonne V, Otz J, Bensadoun RJ, Dissaux G, Lucia F, Leclere JC, et al. Radiotherapy mucositis in head and neck cancer: prevention by low-energy surface laser. <i>BMJ Support Palliat Care</i> . 2019 Sep 16;bmjspcare-2019-001851. doi: 10.1136/bmjspcare-2019-001851.	France
Soares RG, Farias LC, da Silva Menezes AS, de Oliveira E Silva CS, Tabosa ATL, Chagas PVF, et al. Treatment of mucositis with combined 660- and 808-nm-wavelength low-level laser therapy reduced mucositis grade, pain, and use of analgesics: a parallel, single-blind, two-arm controlled study. <i>Lasers Med Sci</i> . 2018 Nov;33(8):1813-1819. doi: 10.1007/s10103-018-2549-y.	Brazil
Genot-Klastersky MT, Paesmans M, Ameye L, Kayumba A, Beauvois S, Dragan T, et al. Retrospective evaluation of the safety of low-level laser therapy/photobiomodulation in patients with head/neck cancer. <i>Support Care Cancer</i> . 2020 Jul;28(7):3015-3022. doi: 10.1007/s00520-019-05041-3.	Belgium

**Supplementary Table 6: Trials to consider for future systematic reviews/meta-analyses**

Title	Contact	URL	Date of registration/start	Reason for consideration
Divergent Low Level Laser Therapy as novel treatment for oral mucositis in pediatric cancer patients	Tissing, WJE	<a href="https://apps.who.int/trialsearch/Trial2.aspx?TrialID=NTR5659">https://apps.who.int/trialsearch/Trial2.aspx?TrialID=NTR5659</a>	2016-01-19	Children, RCT
Low-level Laser Therapy in the Prevention of Chemotherapy-induced Mucositis in Children and Young Adults Treated for a Tumoral Disease (MUCILA)	Roussy, G	<a href="https://clinicaltrials.gov/ct2/show/NCT03983369">https://clinicaltrials.gov/ct2/show/NCT03983369</a>	2018-09-12	Children and young adults, multicenter RCT
Oral Manifestations in Children With Cancer	Gurgel, BCV	<a href="https://clinicaltrials.gov/ct2/show/NCT02662465">https://clinicaltrials.gov/ct2/show/NCT02662465</a>	2016-01-25	RCT including age 1-25
Effectiveness of Diode low-level laser therapy on treatment of mucositis induced by chemoradiotherapy in H&N cancer patients referring to Guilan(Rasht) dental college:A single- blind randomized clinical trial	Barati, S	<a href="http://en.irct.ir/trial/33928">http://en.irct.ir/trial/33928</a>	2018-12-03	Any age, single blind randomised trial
Prevention of Oral Mucositis Using Photobiomodulation Therapy	Mandrell, B	<a href="https://clinicaltrials.gov/ct2/show/NCT04227340">https://clinicaltrials.gov/ct2/show/NCT04227340</a>	2020-01-13	Feasibility study, children. May provide further safety information.
Low-Level Laser Therapy for Prevention of Oral Mucositis	Clump, DA	<a href="https://clinicaltrials.gov/ct2/show/NCT02682992">https://clinicaltrials.gov/ct2/show/NCT02682992</a>	2016-02-17	Adults only – safety information
LITEFORM. Lite Therapy Effectiveness For ORal Mucositis Trial. A randomised controlled trial of the clinical and cost effectiveness of Low Level Laser in the management of Oral Mucositis in Head and Neck cancer irradiation	Nugent, M	<a href="https://www.icrpartnership.org/project/114786">https://www.icrpartnership.org/project/114786</a>	2017-01-01	Adults only – safety information
Effectiveness of Low Energy Laser Treatment in Oral Mucositis Induced by Chemotherapy and Radiotherapy in Head and Neck Cancer	Lagares, D	<a href="https://clinicaltrials.gov/ct2/show/NCT01876407">https://clinicaltrials.gov/ct2/show/NCT01876407</a>	2013-06-12	Adults only – safety information



Low-Level Laser Therapy for Prevention of Oral Mucositis	Kim, H	<a href="https://clinicaltrials.gov/ct2/show/NCT02723604">https://clinicaltrials.gov/ct2/show/NCT02723604</a>	2016-03-30	Adults only – safety information
Photobiomodulation to Demonstrate Safety and Reduce the Incidence of Oral Mucositis in Adult Head & Neck Cancer Patients	Kothari, V	<a href="https://clinicaltrials.gov/ct2/show/NCT03972527">https://clinicaltrials.gov/ct2/show/NCT03972527</a>	2019-06-03	Adults only – safety information
Head and neck cancer/Oral Mucositis	Unknown	<a href="https://www.centerwatch.com/clinical-trials/listings/221549/head-and-neck-canceroral-mucositis-4/?section=elg">https://www.centerwatch.com/clinical-trials/listings/221549/head-and-neck-canceroral-mucositis-4/?section=elg</a>	Unknown	Adults only – safety information
Evaluation of Low-Level Laser Therapy Efficacy in Pain Management of Grade 2 Oral Mucositis Induced by Radiotherapy or Chemoradiotherapy: a Study in Patients With Upper Aerodigestive Tract Cancer (ESMULLLAT)	Vigarios, E	<a href="https://clinicaltrials.gov/show/NCT03955224">https://clinicaltrials.gov/show/NCT03955224</a>	2019-05-20	Adults only – safety information
Effect of photobiomodulation on the severity of oral mucositis and molecular changes in head and neck cancer patients undergoing radiotherapy: a study protocol for a cost-effectiveness randomized clinical trial	Martins, AFL	<a href="https://doi.org/10.1186/s13063-019-3196-8">https://doi.org/10.1186/s13063-019-3196-8</a>	2017-08	Adults only – safety information

**Supplementary Table 7: Protocols used by the studies included in the efficacy comparison (Empty fields indicate information not available)**

Author & Year	Hodgson 2012	Salvador 2017	Amadori 2018	Ahmed 2015	Cruz 2007	Kuhn 2009	Amadori 2016	Abramoff 2008	Gobbo 2018	Cowen 1997	Fani 2013	Silva 2015	Silva 2011	Khoury 2009
<b>Study</b>	Amelioration of oral mucositis pain by NASA near-infrared light-emitting diodes in bone marrow transplant patients	Effect of photobiomodulation therapy on reducing the chemo-induced oral mucositis severity and on salivary levels of CXCL8/interleukin 8, nitrite, and myeloperoxidase in patients undergoing hematopoietic stem cell transplantation: a randomized clinical trial	Effectiveness of low-level laser therapy in the prevention and treatment of chemotherapy-induced oral mucositis in children	Evaluation of Low Level Laser Therapy in the Management of Chemotherapy-Induced Oral Mucositis in Pediatric and Young Cancer Patients : a Randomized Clinical Trial	Influence of low-energy laser in the prevention of oral mucositis in children with cancer receiving chemotherapy	Low-level infrared laser therapy in chemotherapy-induced oral mucositis: a randomized placebo-controlled trial in children.	Low-level laser therapy for treatment of chemotherapy-induced oral mucositis in childhood: a randomized double-blind controlled study.	Low-level laser therapy in the prevention and treatment of chemotherapy-induced oral mucositis in young patients	Multicenter randomized, double-blind controlled trial to evaluate the efficacy of laser therapy for the treatment of severe oral mucositis induced by chemotherapy in children : laMPO RCT.	Low energy Helium-Neon laser in the prevention of oral mucositis in patients undergoing bone marrow transplant: results of a double blind randomized trial.	The effect of the low-level laser on prevention of chemotherapy-induced oral mucositis in patients with acute leukemia	The Impact of Low-Level Laser Therapy on Oral Mucositis and Quality of Life in Patients Undergoing Hematopoietic Stem Cell Transplantation Using the Oral Health Impact Profile and the Functional Assessment of Cancer Therapy-Bone Marrow Transplantation Questionnaire	The Prevention of Induced Oral Mucositis with Low-Level Laser Therapy in Bone Marrow Transplantation Patients: A Randomized Clinical Trial	Use of therapeutic laser for prevention and treatment of oral mucositis
<b>No of children</b>	29	<i>unknown</i>	<i>unknown</i>	<i>unknown</i>	60	21	123	13	101	2	<i>unknown</i>	<i>unknown</i>	<i>unknown</i>	<i>unknown</i>

Prevention and or Treatment	Prevention/treatment	Prevention/treatment	Prevention/treatment	Prevention/treatment	Prevention	Treatment	Treatment	Prevention/treatment	Treatment	Prevention	Prevention	Prevention	Prevention	Prevention/treatment
Intraoral or extraoral	Extraoral	Intraoral	Intraoral	intraoral	intraoral	intraoral	intraoral	intraoral	intraoral	intraoral	intraoral	intraoral	intraoral	intraoral
Country	USA	Brazil	Italy	Iraq	Brazil	Brazil	Italy	Brazil	Italy	France	Iran	Brazil	Brazil	Brazil
<b>Laser details</b>														
Laser used	LED device (Warp 75, Quantum Devices, Barneveld, WI)	InGaAlP laser diode (Twin laser, MMOptics Ltda., São Carlos, SP, Brazil)	diode laser	iLase™ (BIOLASE, Inc., Irvine, CA92618 USA, continuous infrared AlGaInAs diode)	MMOptics laser	GaAlAs laser [Dental Manufactory Company (DMC) Equipment (Sao Carlos, SP, Brazil)]	diode laser (DioBeam 830, CMS Dental, Copenhagen, Denmark).	AsGaAl diode laser (THERA LASER; DMC Equipments Ltda. São Carlos, Brazil)	diode laser device (class IV, K-Laser Cube series, Eltech K-Laser, Via Castagnole 20/H, Treviso, Italy)	He-Ne laser. prototype purchased from Fradema S.A., Geneva, Switzerland.	A diode laser (Aluminum Gallium Indium; Azor-2k-02, Russia)	InGaAlP diode laser	InGaAlP diode laser	indium gallium aluminum phosphide (InGaAlP) AND and gallium aluminum arsenide (GaAlAs) lasers
Wavelength	670 (±10)nm	660 nm	830nm	940±15nm	780nm	830nm	830nm	685nm	660 and 970nm combined wavelengths	632.8nm	660nm	660nm	660nm	660nm and 780 nm
Fluence								72 J/cm <sup>2</sup>	36.8 J/cm <sup>2</sup>					
Energy delivery (density)	4 J/cm <sup>2</sup>	4 J/cm <sup>2</sup>	Prophylactic - 2.2 J/cm <sup>2</sup> ; Therapeutic - 4.5 J/cm <sup>2</sup>	4.2 J/cm <sup>2</sup>	4J/cm <sup>2</sup>	4 J/cm <sup>2</sup>	4.5 J/cm <sup>2</sup>		8 J/cm <sup>2</sup>	1.5 J/cm <sup>2</sup>	1.5 J per point	4 J/cm <sup>2</sup>	4 J/cm <sup>2</sup>	6.3 J/cm <sup>2</sup>

<b>Number of irradiated points</b>	2	10		10	5		5	18	9	15	12	10	10	
<b>Energy delivered</b>	12 J/cm <sup>2</sup> /treatment	12.8 J/day						2 J per point of application	8J/ area	54 J/session		12.8 J/day	12.8 J/day	
<b>Spot size</b>		0.04 cm <sup>2</sup>	1 cm <sup>2</sup>				1 cm <sup>2</sup>	600 micrometer spot	1 cm <sup>2</sup>		2mm	0.04 cm <sup>2</sup>	0.04 cm <sup>3</sup>	
<b>Time spent at each point (seconds)</b>	80 s	4s	Prophylactic - 15s; Therapeutic - 30s	30s			30s	54 s	25 s	10s	60s	4s	4s	10s
<b>Power density</b>	~50 mW/cm <sup>2</sup>													
<b>Power</b>		40mw	150mW	0.3mW 'output power' (sounds wrong??)	60mW	100mW	150mW	35mW	3.2W Peak	60mW	25 mW	40mW	40mW	25 mW
<b>Frequency of LLLT</b>	daily	daily	daily	daily	daily	daily	daily	alternate days	daily	daily	twice weekly	daily	daily	daily (different laser on alternate days)

<b>Durati on of LLLT</b>	15 days	from the first day of the conditioning regimen and continued every day until the seventh post-transplant day (D+7)	5 days	3 weeks	5 days	5 days	4 days	5 days (prophylactic); 5 days MINIMUM (therapeutic)	4 days	5 days (d-5 to d-1)	1 month	1st day of the conditioning regimen through to the 7th day after transplantation (D + 7)	Daily sessions began on D-4 and continued through to D+4.	Prevention: 1st day of conditioning until clinical manifestation of oral mucositis.  Treatment: started from initial clinical manifestations of mucositis with follow-up until D+15 after transplantation
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**Supplementary Table 8: Merging WHO and NCI CTC grading systems**

<b>Merging of WHO and NCI CTC grades</b>
<p>Different authors used different grading scales for the severity of oral mucositis. Hodgson et al<sup>1</sup> provided us with unpublished baseline data for their patients, including each time WHO &amp; NCI CTC grades measured. This gave us 157 NCI CTC measurements to compare with 157 WHO measurements in our population of children with cancer. Comparing the frequency of measurements of different grades, we used Spearman's rank correlation co-efficient. This demonstrated Spearman's <math>\rho = 0.7</math> [95% CI -0.477, 0.978], <math>p</math> value = 0.233<sup>2</sup>. There is a strong correlation between these results – even though the description of the grades has some differences, operationally they are similar, with no statistically significant difference between them. Therefore, we chose to combine WHO &amp; NCI CTC grades for the meta-analysis. Both WHO &amp; NCI CTC grades define grade 3 as severe.<sup>3</sup> For the meta-analysis, we compared those with grade <math>\geq 3</math> (severe to life-threatening) mucositis with grade <math>\leq 2</math> (none to moderate) mucositis to enable exploration of the outcome measure of severity of oral mucositis.</p> <p>1 - Hodgson BD, Margolis DM, Salzman DE, et al. Amelioration of oral mucositis pain by NASA near-infrared light-emitting diodes in bone marrow transplant patients. <i>Support Care Cancer</i>. 2012;20(7):1405-1415. doi:10.1007/s00520-011-1223-8.</p> <p>2 - Statistical software used: Correlation test. Langtest web application. Available from: <a href="http://langtest.ip/shiny/cor/">http://langtest.ip/shiny/cor/</a> [cited 25<sup>th</sup> August 2020].</p> <p>3 - National Institute for Health and Care Excellence. IP overview: Low-level laser therapy for preventing or treating oral mucositis caused by radiotherapy or chemotherapy. Available from: <a href="https://www.nice.org.uk/guidance/ipq615/documents/overview">https://www.nice.org.uk/guidance/ipq615/documents/overview</a> [cited 14<sup>th</sup> Feb 2021].</p>

**Supplementary Table 9: Narrative synthesis considering effect of LLLT on oral pain**

<b>RCT</b>	<b>Effect of LLLT on oral pain</b>
Abramoff 2008	Authors state pain relief in the group receiving therapeutic laser, but statistical analysis is not performed.
Ahmed 2015	(Note: Some patients were adults). Prophylactic laser reduced oral pain on day 12 (laser median = 2.5, sham median = 4, $p=0.032$ ), 14 (laser median = 0, sham median = 3, $p=0.008$ ), and 16 (laser median = 0, sham median = 2, $p=0.001$ ) of treatment. At days 6, 18 and 20 of treatment, the median score of pain for both groups was 0. At days 8 (laser median = 1.5, sham median = 2, $p=0.458$ ) and 10 (laser median = 2, sham median = 4, $p=0.051$ ), there was no statistically significant difference in scores.
Amadori 2016	Median Visual Analogue Scale scores of oral pain lower in the laser group at day 4 (laser group = 1, sham group = 2, $p=0.002$ ) and day 7 (laser group median = 0, sham group median = 1, $p=0.0005$ ). No difference at day 1 (laser group median = 4, sham group median = 4, $p = 0.9$ )
Amadori 2018	Abstract reports reduction in OM pain in groups receiving LLLT as treatment of OM. Further details not yet published or available.

Cowen 1997	Only 2 patients aged 17 - unable to distil results. Laser application had reduced pain scores on the threshold of statistical significance: mean pain score $12.7 \pm 1.3$ for laser patients; $20.3 \pm 2.5$ for control patients ( $p=0.05$ ).
Gobbo 2018	No reduction in self-reported pain at day 4: laser group median = 4, IQR 2-6; control group median 5, IQR 3-7 ( $p=0.07$ ). Statistically significant reduction in self-reported pain score at day 7: laser group median = 1, IQR 0-3; control group median 2.5 IQR 1-5 ( $p=0.006$ ). and day 11: laser group median = 0, IQR 0-1; control group median 1, IQR 0-3 ( $p=0.01$ ).
Hodgson 2012	Unpublished data used as in meta-analysis. No statistically significant difference. Standardised mean difference 0.50 (95% CI of -0.38 to 1.38) on days 3-5, 0.02 (95% CI of -0.80 to 0.84) on days 8 to 10, and -0.06 (95% CI of -0.88 to 0.76) on days 11-14.

#### Supplementary Table 10: Effect of LLLT on use of analgesia

RCT	Effect of LLLT on use of analgesia
Amadori 2016]	Children treated with LLLT requested less additional analgesia (morphine, tramadol or paracetamol) than those receiving the sham protocol ( $p<0.05$ ).
Cruz 2007	No statistically significant difference between the mean amount of days where 'painkillers' were used in the laser group compared to the control group.
Gobbo 2018	No statistically significant difference between the use of analgesics in the laser group compared to the control group.

#### Supplementary Table 11: Effect of LLLT on nutrition

RCT	Effect of LLLT on diet
Cowen 1997	There was no significant difference between the laser and control group of mean duration of parenteral nutrition (p value not provided; only 2 of 30 patients were children)
Cruz 2007	There was no significant difference between the laser and control group of food intake (kcal) at Day 1 ( $p=0.207$ ), 8 ( $p=0.522$ ), or 15 ( $p=0.876$ ).
Hodgson 2012	This RCT compared patients' ability to tolerate normal/soft/liquid/no diet. Using unpublished data provided by the author and comparing each of the 7 time-points of measurement, there was no significant difference between the laser and control groups ( $p=0.3239$ ).

**Supplementary Table 12: Outcome measures considered where not covered elsewhere**

Study	Outcome measure
<b>Hodgson 2012</b>	Incidence and duration of erythema and ulceration, WHO pain assessment
<b>Salvador 2017</b>	Salivary samples
<b>Cruz 2007</b>	Drugs used (antibiotics/antivirals/antifungals) White cell count Buccal health Tooth brushes sessions Nutritional status
<b>Kuhn 2009</b>	Mean duration of OM
<b>Abramoff 2008</b>	changes in granulocyte levels; oesophagitis (NCI criteria)
<b>Gobbo 2018</b>	White cell count/neutrophil count Admission to hospital because of OM alone
<b>Cowen 1997</b>	Use of narcotics, daily scores of saliva production
<b>Silva 2017</b>	Progression of oral mucositis

**Supplementary Figure 1: Data extraction form****Laser Therapy in Children with Cancer: Data Extraction Form****Protocol**

Melody Redman, Katherine Harris, Bob Phillips. Low level laser therapy to prevent or treat oral mucositis in children with cancer. PROSPERO 2018 CRD42018099772 Available from: [http://www.crd.york.ac.uk/PROSPERO/display\\_record.php?ID=CRD42018099772](http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018099772)

**Source**

First Author/Editor	Title	Year	Source (e.g. Journal, Trial Registry)



## Eligibility for Efficacy/Safety

Criteria		Yes/No/Unclear	Comments
Received laser therapy as an intervention			
<i>For efficacy:</i> Patients <18 with any form of cancer			
<i>For efficacy:</i> Randomised Control Trial (RCT)			
Outcome(s)	oral mucositis, oral pain, etc		
	adverse events		

IF YES TO ALL THE ABOVE, PROCEED.

IF NO TO RCT OR AGE<18, BUT OUTCOMES INCLUDE ADVERSE EVENTS, PROCEED BUT STATE TYPE OF TRIAL IN COMMENTS SECTION.

IF UNCLEAR, AWAIT DISCUSSION WITH SECOND REVIEWER.

IF STUDY IS TO BE EXCLUDED, PLEASE RECORD WHY:

## References to this data

If this source has been identified through other methods or the data has been used in other studies, please link the papers in *RevMan 5.3* and list below:

Code	First Author/Editor	Year		Source (e.g. Journal, Trial Registry)

### Quality Assessment

If RCT, use Cochrane Risk of Bias tool (Higgins J Green S Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration 2011 [https://handbook-5-1.cochrane.org/chapter\\_8/8\\_assessing\\_risk\\_of\\_bias\\_in\\_included\\_studies.htm](https://handbook-5-1.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm)).

If other, use BMC Medical Research Methodology (Loke Y, Price D, Herxheimer A, the Cochrane Adverse Effects Methods Group. Systematic reviews of adverse effects: framework for a structured approach. BMC Medical Research Methodology. 2007 Jul 5;7(1):32.)

### Trial demographics

	Comments
<b>Number of participants</b>	
<b>Age of participants</b> (average and range e.g. median = 7 years; range = ages 3-17)	
<b>Gender distribution</b> (% , raw numbers e.g. 70 males (50%), 70 females (50%))	
<b>Cancer details</b> (e.g. type: leukaemia, staging)	
<b>Country of study</b>	
<b>Other information</b>	

### Trial characteristics

Characteristic	Comments (state if unclear)

<b>Single centre or multi-centre</b>	
<b>Eligibility criteria (include definition)</b>	
<b>Method of randomization and how many participants randomized</b>	
<b>Distribution of participants across intervention groups (e.g. Group A = 20, Group B = 22)</b>	
<b>Number of participants who received intended treatment</b>	
<b>Number of participants who were analysed</b>	
<b>Number of participants who experienced an adverse effect</b>	
<b>Form of laser therapy used</b>	
<b>Single or multi-therapy</b>	
<b>Frequency and method of administration (including duration of each session of oral laser therapy)</b>	

<b>Overall duration of treatment</b>	
<b>Setting in which laser therapy administered (e.g. hospital, home)</b>	
<b>Comparator (e.g. nothing, other treatment)</b>	
<b>Median/mean (range) length of follow-up reported in this paper</b>	
<b>Statistical technique used</b>	
<b>Time-points when outcomes were measured during the study (e.g. 3 days, 5 days, 10 days...)</b>	
<b>Time-points reported in the study (e.g. &lt;1 week, &lt;2weeks)</b>	
<b>Type of analysis in study (e.g. intention to treat)</b>	
<b>Other</b>	

### Primary outcomes for the review

<b>Outcome</b>	<b>Reported</b>	<b>Comments</b>
<b>Severity of oral mucositis</b>	<b>Yes / No</b>	
<b>Timing and intensity of oral pain (+/-ChIMES score)</b>	<b>Yes / No</b>	

<b>Acceptability / adherence to oral low level laser therapy</b>	<b>Yes / No</b>	
<b>Symptoms, other than pain, considered important to the paedialow level laser therapytric population</b>	<b>Yes / No</b>	
<b>Duration of action of oral low level laser therapy</b>	<b>Yes / No</b>	
<b>Oral temperature</b>	<b>Yes / No</b>	
<b>Adverse events or reactions</b>	<b>Yes / No</b>	

### Secondary outcomes for the review

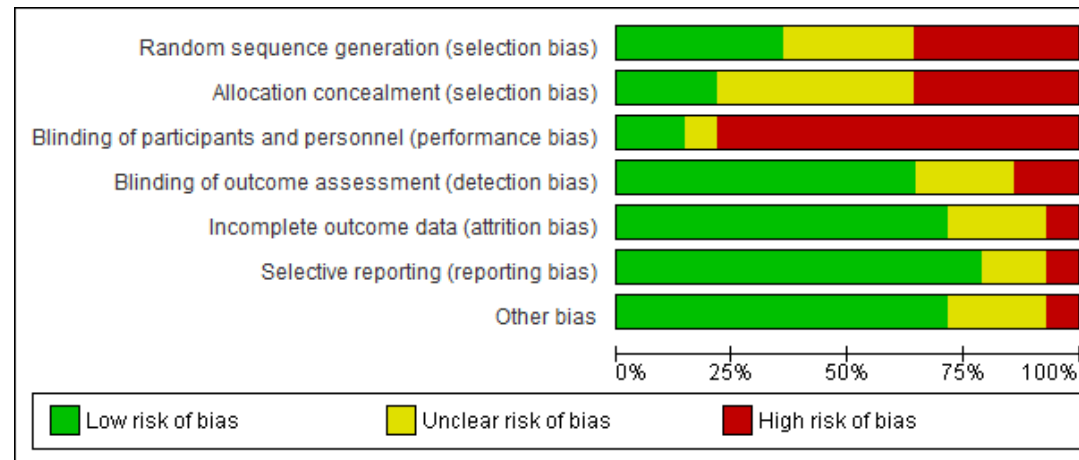
<b>Outcome</b>	<b>Reported</b>	<b>Comments</b>
<b>Interruptions to cancer treatment</b>	<b>Yes / No</b>	
<b>Oral pain on a 0 (no pain) to 10 (maximum pain) scale</b>	<b>Yes / No</b>	
<b>Quality of life</b>	<b>Yes / No</b>	
<b>Normalcy of diet (days of total parenteral nutrition - TPN)</b>	<b>Yes / No</b>	
<b>Duration of hospitalisation (days)</b>	<b>Yes / No</b>	
<b>Other</b>	<b>Yes / No</b>	

				<b>Code of paper</b>		
				<b>Outcome(s) of interest and definition in study</b>		
				<b>Measurement tool</b>		
				BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)		
				n	<b>Continuous data</b>	<b>Intervention group</b>
				Mean (SD)		
				Events/number	<b>Dichotomous data</b>	
				n	<b>Continuous data</b>	<b>Control group</b>
				Mean (SD)		
				Episodes or people	<b>Dichotomous data</b>	
				<i>SD or SE</i>	<b>Details if outcome only described in text</b>	
				<b>Length of follow up</b>		
				<b>Yes/No/Unclear</b>	<b>Participants blinded</b>	<b>Assessing risk of bias</b>
				<b>Yes/No/Unclear</b>	<b>Assessor blinded</b>	
				<b>Yes/No/Unclear</b>	<b>Blinding of researcher</b>	
				<b>Other comments</b>		

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On assessment of the reference list, are there any potentially relevant studies that haven't been included from the search strategy? Or are there any sources of unpublished data mentioned? If so, list below.			
<b>First Author/Editor</b>	<b>Title</b>	<b>Year</b>	<b>Source (e.g. Journal, Trial Registry)</b>
Contact details for unpublished data			
Any other comments			

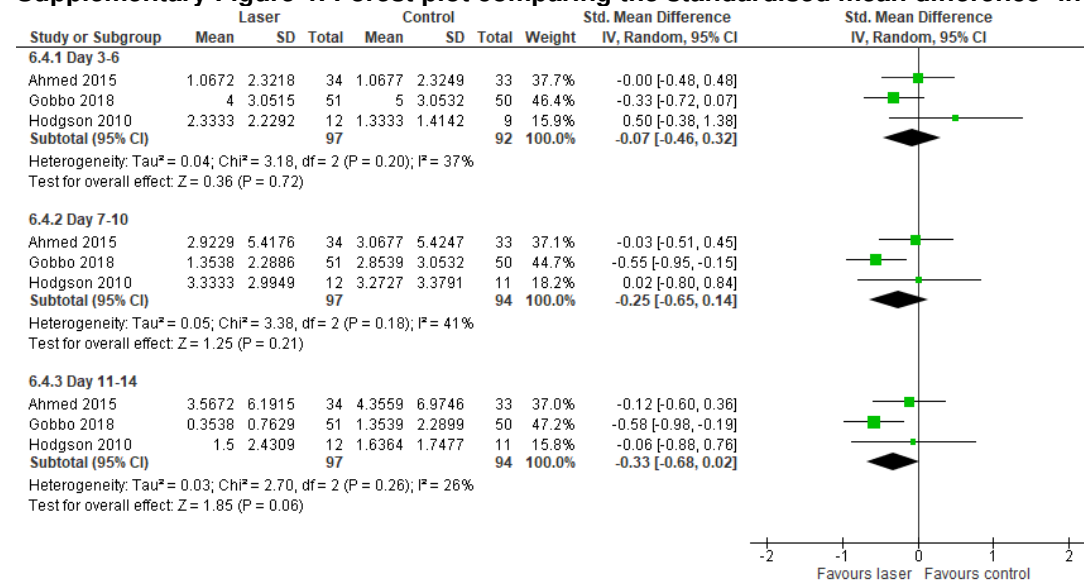
**Supplementary Figure 2: Risk of bias graph: assessment of each risk of bias item presented as percentages across all included studies**





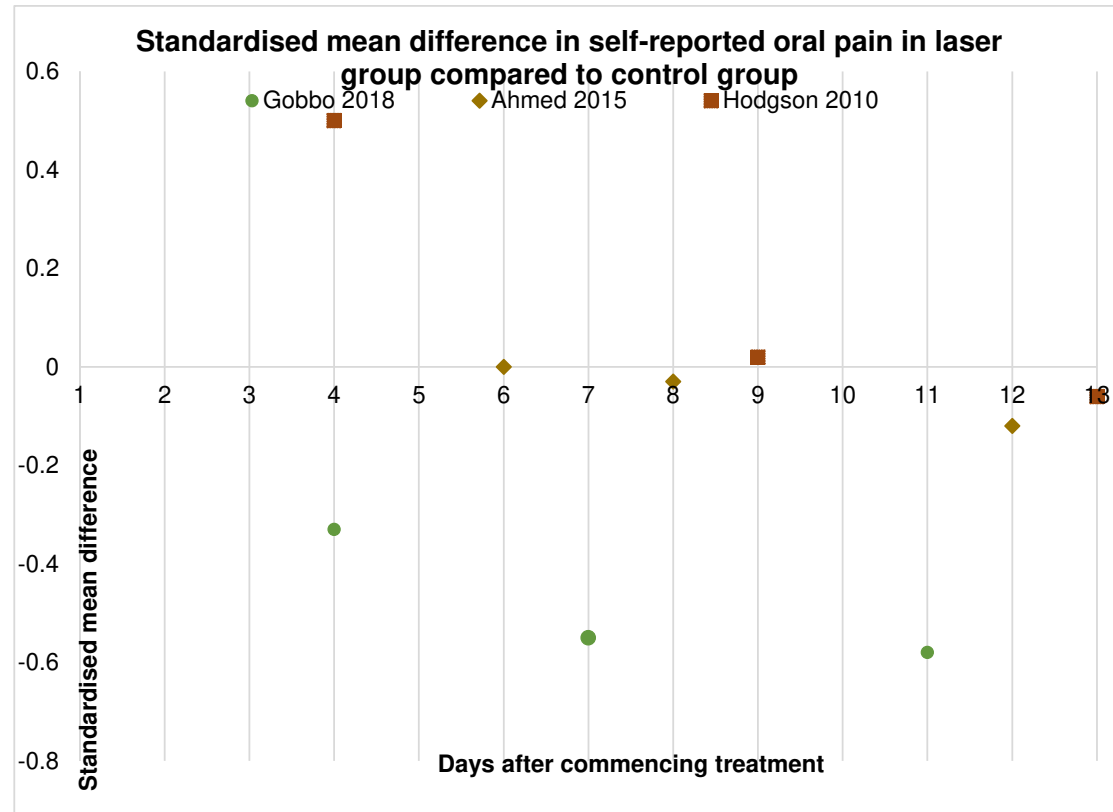
**Supplementary Figure 3: Risk of bias summary: assessment of each risk of bias item for each included study. (? = unclear; + = low risk, - = high risk)**

Abramoff 2008	?	?	-	?	?	+	
Ahmed 2015	-	?	-	+	+	+	
Amadori 2016	+	?	-	+	+	+	
Amadori 2018	+	?	?	?	?	?	
Cowen 1997	+	+	+	+	+	+	
Cruz 2007	?	-	-	-	+	+	
Fani 2013	?	-	-	?	+	+	
Gobbò 2018	+	+	-	+	+	+	
Hodgson 2010	-	+	+	+	+	+	
Khouri 2009	-	?	-	-	?	?	
Kuhn 2008	?	?	-	+	+	-	
Salvador 2017	-	-	-	+	-	?	
Silva 2011	+	-	-	+	+	+	
Silva 2015	-	-	-	+	+	+	
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias

**Supplementary Figure 4: Forest plot comparing the standardised mean difference<sup>3</sup> in oral pain out of a 10 point scale**

<sup>3</sup> Standardised mean differences were used to allow comparison between different pain scales (some pain scales allowed responses up to 5 and some allowed responses up to 10).

**Supplementary Figure 5: Graph comparing standardised mean difference<sup>4</sup> in self-reported oral pain in laser group compared to control group**



<sup>4</sup> Standardised mean differences were used to allow comparison between different pain scales (some pain scales allowed responses up to 5 and some allowed responses up to 10).