



Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER322
Topic:	Photobiomodulation for the prevention and treatment of oral mucositis and radiation dermatitis associated with cancer treatment
Summary of findings:	<p>Health Technology Wales researchers identified a number of systematic review and meta-analyses that examined the clinical and cost-effectiveness of photobiomodulation for oral mucositis and radiation dermatitis.</p> <p>For oral mucositis, there appears to be evidence that photobiomodulation can reduce the severity of symptoms. However, there are uncertainties around whether this translate into improvements in quality of life for patients, the generalisability of evidence to Wales, and the cost-effectiveness of the intervention for this setting. For radiation dermatitis, evidence appears to be less well developed, although there is some evidence that photobiomodulation also reduces the severity for patients with breast cancer.</p> <p>It is unclear to what extent photobiomodulation is already used in Wales or whether particular treatment protocols or novel technologies (i.e. CareMin650) are more beneficial. An evidence appraisal report (EAR) is likely to be able to provide additional information that would reduce these uncertainties.</p>

Introduction and aims

Oral mucositis and radiation dermatitis are common side effects of cancer treatment. Oral mucositis can occur after chemotherapy or radiotherapy for head and neck cancer or before bone marrow transplantation and symptoms usually start within 10 days. Radiation dermatitis can occur after radiotherapy for a range of cancers and symptoms can occur within 90 days of radiation exposure. Both side effects are characterised by damage to tissue and can be graded from symptoms that cause minor discomfort to ulceration and skin necrosis. Photobiomodulation or low-level laser therapy aims to treat or prevent these side effects by promoting healing, reducing inflammation and increasing cellular metabolism through the delivery of light in the red or near-infrared spectrum. The topic proposer highlighted CareMin650 system which uses a novel method to deliver photobiomodulation that may have benefits compared to conventional methods of delivery.

Health Technology Wales (HTW) researchers searched for evidence on the clinical and cost-effectiveness of photobiomodulation for the prevention and treatment of chemotherapy or radiotherapy-induced oral mucositis and radiation dermatitis.

Evidence overview

Technology Assessment/Guidance

HTW researchers identified a National Institute for Health And Care Excellence (NICE) Interventional Procedures Guidance on low-level laser therapy for preventing or treating oral mucositis caused by radiotherapy or chemotherapy (IPG615). The guidance outlines that evidence suggests there are no major safety concerns and efficacy is adequate to support use under standard arrangements for clinical governance, consent, and audit.

Secondary Evidence

HTW researchers also identified several systematic reviews and meta-analysis on the effectiveness of photobiomodulation for oral mucositis or radiation dermatitis.

Al-Rudayni et al. (2021) evaluated the efficacy of photobiomodulation for treatment of chemotherapy-induced oral mucositis. They included six randomised controlled trials (n=398) that compared photobiomodulation to a sham control and report that photobiomodulation was associated with a reduction in severe oral mucositis (RR 0.43, 95% CI 0.20 to 0.93; $p < 0.05$). An analysis on a subset of these trials suggest the intervention led to reduce duration of mucositis but results for reduction in pain were mixed. None of the included trials reported any significant adverse events associated with photobiomodulation. Another systematic review and meta-analysis evaluated the efficacy of photobiomodulation for oral mucositis in patients with head and neck cancer (Campos et al. 2020) and included several studies not included by Al-Rudayni et al. (2021). They report that photobiomodulation was associated with a decreased risk of debilitation lesions (RR = 0.36, 95% CI = 0.29 to 0.44) and pain reduction. A systematic review that focused on outcomes for children undergoing chemotherapy was also identified (Redman et al. 2021). They report that intervention may reduce the severity of oral mucositis. However, they note that there was wide variation in trial protocols and risk of bias related to blinding and that further evidence of efficacy for children is needed.

A further systematic review and meta-analysis evaluated the effectiveness of photobiomodulation for radiation dermatitis (de Aguiar et al. 2021). They identified seven studies and highlight that the majority of patients in these studies were receiving treatment for breast cancer. They report that patients receiving photobiomodulation had a reduced risk of grade 3 symptoms (RR 0.21, 95 % CI 0.05 to 0.94) and more lower severity symptoms (grade 1, RR 1.55, 95 % CI 1.14 to 2.10; grade 2, RR 0.33, 95 % CI 0.09 to 1.23). However, it is noted that further randomised controlled trials are needed to confirm these effects.

Two studies that reported findings for cost-effectiveness were identified. Alongside their evaluation of efficacy, Campos et al. (2020) used a decision-tree to explore cost-effectiveness within the Brazilian healthcare system and report an incremental cost-effectiveness ratio (ICER) of US\$7.22 per case of oral mucositis avoided. Kauark-Fontes et al. (2021) conducted a systematic review to address the cost-effectiveness of photobiomodulation for both oral mucositis and radiation dermatitis, in particular lymphedema for breast cancer. They included four studies and report that ICERs ranged from US\$ 3050.75 USD to 5592.10 USD per grade 3 and 4 case of oral mucositis prevented and a cost of US\$21.47 per percentage point reduction in lymphedema compared to US\$80.51 for manual lymph drainage and physical therapy.

The topic proposer highlighted the CareMin650 system that may have benefits to conventional methods of delivery. It is unclear from initial review of the studies described above whether this technology was included.

Areas of uncertainty

There appear to be a number of sham-controlled randomised controlled trials that suggest photobiomodulation is effective in reducing the severity of oral mucositis. However, evidence on its effectiveness for radiation dermatitis appears more limited, with fewer high quality randomised controlled trials, and appears to focus largely on outcomes of patients with breast cancer. Across the evidence, there appears to be variation in protocols for use of photobiomodulation and the topic proposer highlighted potential benefits of a novel approach compared to conventional methodologies. It is unclear what the comparative effectiveness of these protocols.

Identified systematic reviews and meta-analyses either did not report the countries where studies were conducted or they appeared to be conducted outside of the UK so it is unclear where this may sit in the treatment pathway in Wales and whether evidence is generalisable to current practice. There is also uncertainty around whether a reduction in symptom severity translates into improvement in health-related quality of life and whether an ICER for cost per quality-adjusted life year (QALY) would be considered cost-effective.

Literature search results

Health technology assessments and guidance

NICE. (2018). Low-level laser therapy for preventing or treating oral mucositis caused by radiotherapy or chemotherapy [IPG615]. National Institute for Health and Care Excellence. Available at: <https://www.nice.org.uk/guidance/ipg615> [Accessed 03.12.2021].

Evidence reviews and economic evaluations

Al-Rudayni AHM, Gopinath D, Maharajan MK, et al. (2021). Efficacy of Photobiomodulation in the Treatment of Cancer Chemotherapy-Induced Oral Mucositis: A Meta-Analysis with Trial Sequential Analysis. *International journal of environmental research and public health*. 18(14). doi: 10.3390/ijerph18147418

Campos TM, do Prado Tavares Silva CA, Sobral APT, et al. (2020). Photobiomodulation in oral mucositis in patients with head and neck cancer: a systematic review and meta-analysis followed by a cost-effectiveness analysis. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. 28(12): 5649-59. doi: 10.1007/s00520-020-05613-8

de Aguiar BRL, Silva Guerra EN, Costa Normando AG, et al. (2021). Effectiveness of photobiomodulation therapy in radiation dermatitis: a systematic review and meta-analysis. *Critical reviews in oncology/hematology*. 162: 103349. doi: 10.1016/j.critrevonc.2021.103349

Kauark-Fontes E, Rodrigues-Oliveira L, Epstein JB, et al. (2021). Cost-effectiveness of photobiomodulation therapy for the prevention and management of cancer treatment toxicities: a systematic review. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. doi: 10.1007/s00520-020-05949-1

Redman MG, Harris K, Phillips BS. (2021). Low-level laser therapy for oral mucositis in children with cancer. *Archives of disease in childhood*. doi: 10.1136/archdischild-2020-321216

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Concepts used:

photobiomodulation; mucositis; dermatitis; cancer