



Topic Exploration Report ¹

Cyclically pressurised topical wound oxygen therapy for hard-to-heal wounds

What is a Topic Exploration Report?

Topic Exploration Reports are not health technology assessments. These reports provide a high-level briefing on new topics submitted to Health Technology Wales and are not based on exhaustive or systematic literature searches. Instead, they rely on a focussed scan of key resources.

What evidence is used in a Topic Exploration Report?

Priority is given to summarising the most relevant or useful evidence, rather than covering all possible evidence. Information reported is typically based on abstracts and study authors' own conclusions, rather than detailed scrutiny of full texts.

What are the aims of a Topic Exploration Report?

Topic Exploration Reports offer an overview of the available evidence on a topic and aim to highlight any uncertainties or gaps in the evidence. These reports outline the quantity and type of evidence found, but no critical appraisal or formal evidence synthesis is conducted.

How should a Topic Exploration Report be used?

Topic Exploration Reports can be used to indicate what evidence may be available for a topic, and do not provide definitive guidance on how a technology should be used. The evidence presented within the reports should be interpreted with caution.

¹ [Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg](#)
Translation of published technical HTW documents from English into Welsh

Topic exploration report number	TER624
Topic	Cyclically pressurised topical wound oxygen therapy for hard-to-heal wounds
Summary of findings	<p>Topical oxygen therapy is a treatment for chronic, hard-to-heal wounds that aims to provide more oxygen locally to a wound site. Cyclically pressurised topical wound oxygen therapy delivers humidified oxygen at higher pressure and provides non-contact compression of the wound, with the aim to increase oxygen perfusion and reduce oedema. It is intended as an adjunct to standard care for chronic wounds.</p> <p>A NICE guideline on the treatment and management of diabetic foot problems was identified and an update from July 2025 states NICE will update the guideline to add consideration for topical oxygen therapy as an adjunctive treatment for those people with diabetic foot ulcers (in addition to standard care, if healing is not progressing). One systematic review that discussed cyclically pressurised topical wound oxygen therapy separately from continuously diffused oxygen (CDO) therapy was identified. It included 18 studies and concluded that cyclically pressurised topical wound oxygen therapy appears to have positive effects on wound healing but there were limitations to the available evidence.</p> <p>A randomised controlled trial and a retrospective cohort analysis were identified. Both studies found that cyclically pressurised topical wound oxygen therapy with the TWO2 device in addition to standard care led to statistically significantly improved diabetic foot ulcer healing compared with standard care alone or with placebo control up to 12 months after treatment. An economic analysis from a UK perspective predicted cyclically pressurised topical wound oxygen therapy had an 81% likelihood of being cost effective at a willingness-to-pay threshold of £25,000 per quality-adjusted life year.</p> <p>Areas of uncertainty include several studies/reviews being identified that did not distinguish between cyclically pressurised topical wound oxygen therapy and CDO, whether there is more evidence for different populations and whether the scope should be narrowed for a full appraisal, and which devices have been used in older studies.</p>

Introduction and aims

Chronic, hard-to-heal wounds, such as diabetic foot ulcers and venous leg ulcers, can pose a significant burden to health services. They may be resistant to standard care treatments and are associated with significant complications, morbidity and mortality. Diabetic foot ulcers can lead to amputations and are associated with poor clinical outcomes.

Topical oxygen therapy is a treatment that aims to provide more oxygen locally to a wound site, as systemic oxygen circulation is often impaired, and oxygen is required for normal wound healing. Topical oxygen therapy can be split into two interventions: continuously diffused oxygen (CDO) therapy/topical continuous oxygen therapy (TCOT) and cyclically pressurised topical wound oxygen therapy. Cyclically pressurised topical wound oxygen therapy delivers humidified oxygen at higher pressure and provides non-contact compression of the wound, with the aim to increase oxygen perfusion and reduce oedema. It is delivered intermittently and is intended as an adjunct to standard care. TWO2 (AOTI) is Class IIa, CE-marked medical device that delivers cyclical pressurised oxygen, non-contact compression and humidification to wounds through an extremity chamber and can be used by patients at home.

Health Technology Wales researchers searched for evidence on the clinical and cost effectiveness of cyclically pressurised topical wound oxygen therapy for hard-to-heal wounds.

Evidence overview

Guidance

HTW has previously issued guidance on topical oxygen therapy (GUI043), however, this was specifically for CDO and does not cover cyclically pressurised topical wound oxygen therapy (HTW 2022).

A NICE guideline is available on the treatment and management of diabetic foot problems (NICE 2019). The guideline recommends offering one or more of the following treatment options as standard of care: offloading, control of foot infection, control of ischaemia, wound debridement, and wound dressings. In July 2025, NICE stated they 'will update the guideline to add consideration for topical oxygen therapy as an adjunctive treatment for those people with diabetic foot ulcers (in addition to standard care, if healing is not progressing)'.

Secondary evidence

High-level searches identified a rapid review by the Canadian Agency for Drugs and Technologies in Health (CADTH) on topical oxygen therapy (CADTH 2020). This only covered CDO and, so, is not included in this TER. However, they identified one systematic review that considered cyclically pressurised topical wound oxygen therapy and CDO separately (Sayadi et al. 2018). As our searches did not identify any secondary evidence on cyclically pressurised topical wound oxygen therapy only or that evaluated it separately from CDO, we sourced the review identified by CADTH and have discussed its findings on cyclically pressurised topical wound oxygen therapy below.

Sayadi et al. (2018) included 18 clinical studies on cyclically pressurised topical wound oxygen therapy in their systematic review. These covered various wound types and study designs, with comparative and non-comparative evidence identified. The number of patients/wounds included ranged from two in a case study report to 3,462 in a retrospective study. The review authors concluded that cyclically pressurised topical wound oxygen therapy appears to have positive effects on wound healing but highlighted issues with variable treatment protocols in studies and most of the evidence being case reports or small non-randomised trials, with limits to the generalisability of the evidence.

Evidence overview

Primary evidence

We searched for primary evidence published after the search date of the review by Sayadi (June 2017). One randomised controlled trial (RCT) and one retrospective cohort analysis were identified.

In a multicentre, double-blind RCT, patients with diabetic foot ulcers that had not healed with standard care alone were randomised to either the active treatment group with TWO2 or a placebo control group (Frykberg et al. 2020). Both groups continued to receive standard care as well. TWO2 use led to a superior closure rate at the first analysis point (unspecified in the abstract) compared to the control group (odds ratio [OR] 4.57, $p = 0.01$; OR 6.00, $p = 0.004$ when adjusted for University of Texas Classification ulcer grade). Using Cox proportional hazards modelling, diabetic foot ulcers were found to be 4.66 times more likely to heal after 12 weeks of TWO2 treatment compared to placebo. At 12 months, 56% of ulcers in the TWO2 group were closed compared with 27% in the control group ($p = 0.013$).

Real-world evidence from a retrospective review of medical records of patients with diabetic foot ulcers from two US Veterans Affairs hospitals found significant reductions in hospitalisations and amputations within 360 days of initial wound documentation after treatment with TWO2 (Yellin et al. 2022). In the unmatched cohorts of patients with diabetic foot ulcers (TWO2 $n = 91$, no TWO2 $n = 111$), significantly fewer patients had hospitalisations (6.6% vs. 54.1%, $p < 0.0001$) and amputations (12.1% vs. 41.4%, $p < 0.0001$) in the TWO2 cohort compared with the no TWO2 cohort. Significantly lower proportions of hospitalisations and amputations in the TWO2 cohort were maintained in the propensity-score matched cohorts (TWO2 $n = 70$, No TWO2 $n = 70$; $p < 0.0001$ and $p = 0.0007$, respectively).

Economic evidence

One economic evaluation from a UK perspective was identified. Using clinical outcomes from the RCT by Frykberg et al. (2020) outlined above and costs from NHS England, the cost effectiveness of TWO2 over two years was modelled (Kerr et al. 2025). Base case results indicated that diabetic footcare costs are £5,038 lower with TWO2 than standard care alone over two years, based on a weekly TWO2 price of £650. An increase in quality-adjusted life years (QALYs) of 0.07 was also found. Probabilistic sensitivity analyses estimated TWO2 had an 81% likelihood of being cost effective at a willingness-to-pay threshold of £25,000 per QALY.

Areas of uncertainty

- Several studies and systematic reviews were identified that either did not distinguish between CDO/TCOT and cyclically pressurised topical wound oxygen therapy or were unclear whether they had examined the interventions separately.
- It is not clear which devices were used in the studies included in the systematic review by Sayadi et al. and, given the age of many of the studies, it is unknown whether these devices are still available or match performance standards of currently available devices.
- There are various types of chronic hard-to-heal wounds and consideration may need to be given as to which populations to include in an appraisal, dependent on the amount of evidence for different indications.
- The two identified primary studies and the economic study were sponsored or funded by AOTI, the manufacturer of TWO2.

Literature search results

Health technology assessments and guidance	
<p>HTW. (2022). Continuous topical oxygen therapy. Guidance GUI043. Health Technology Wales. Available at: https://healthtechnology.wales/reports-guidance/topical-oxygen-therapy-natrox/ [Accessed 01 October 2025].</p> <p>NICE. (2019). Diabetic foot problems: prevention and management. NICE guideline NG19. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng19 [Accessed 01 October 2025].</p>	
Evidence reviews and economic evaluations	
<p>CADTH. (2020). Topical Wound Oxygen Therapy for Wound Healing: A Review of Clinical Effectiveness, Cost-Effectiveness and Guidelines. Summary with critical appraisal. Canadian Agency for Drugs and Technologies in Health. Available at: https://www.cda-amc.ca/topical-wound-oxygen-therapy-wound-healing-review-clinical-effectiveness-cost-effectiveness-and [Accessed 01 October 2025].</p> <p>Kerr M, Wild D, Edmonds M, et al. (2025). Cost effectiveness of topical wound oxygen therapy for chronic diabetic foot ulcers. <i>J Diabetes Complications</i>. 39(5): 109016. doi: https://doi.org/10.1016/j.jdiacomp.2025.109016</p>	
Individual studies	
<p>Frykberg RG, Franks PJ, Edmonds M, et al. (2020). A Multinational, Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy of Cyclical Topical Wound Oxygen (TW02) Therapy in the Treatment of Chronic Diabetic Foot Ulcers: The TW02 Study. <i>Diabetes Care</i>. 43(3): 616-24. doi: https://doi.org/10.2337/dc19-0476</p> <p>Yellin JI, Gaebler JA, Zhou FF, et al. (2022). Reduced Hospitalizations and Amputations in Patients with Diabetic Foot Ulcers Treated with Cyclical Pressurized Topical Wound Oxygen Therapy: Real-World Outcomes. <i>Adv Wound Care (New Rochelle)</i>. 11(12): 657-65. doi: https://doi.org/10.1089/wound.2021.0118</p>	
Identified from review of CDO by CADTH	
<p>Sayadi LR, Banyard DA, Ziegler ME, et al. (2018). Topical oxygen therapy & micro/nanobubbles: a new modality for tissue oxygen delivery. <i>International Wound Journal</i>. 15(3): 363-74. doi: https://doi.org/10.1111/iwj.12873</p>	

Date of search	01 October 2025
Concepts used	TW02, cyclical topical wound oxygen therapy, topical pressurised oxygen therapy, non-contact cyclical compression, wounds, hard-to-heal, diabetic foot ulcer, venous leg ulcer

Proposed research question and evidence selection criteria (if selected)

Proposed Research question	What is the clinical and cost effectiveness of cyclically pressurised topical wound oxygen therapy, in addition to standard care, to treat hard-to-heal wounds compared to standard care alone?
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	Inclusion criteria	Exclusion criteria
Population	People with chronic, hard-to-heal wounds, including but not limited to diabetic foot ulcers and venous leg ulcers	
Intervention	Cyclically pressurised topical wound oxygen therapy in addition to standard care	Continuously diffused oxygen therapy, topical continuous oxygen therapy
Comparison/ Comparators	Standard care alone: <ul style="list-style-type: none"> • Offloading • Control of foot infection • Control of ischaemia • Wound debridement • Wound dressings Continuously diffused oxygen therapy	
Outcome measures	Wound reduction (in size and time taken to reduce) Wound recurrence or exacerbation Wounds remaining healed Need for further treatment Number of appointments needed to attend (GP/home visits/outpatient) Hospitalisations Risk of amputation Risk of infection Mortality Compliance Health related QoL Resource use Economic outcomes	

Proposed speciality	Injuries, accidents and wounds
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