Technoleg Iechyd Cymru
Health Technology Wales

HEALTH TECHNOLOGY WALES (HTW) GUIDANCE 043 (September 2022)

Continuous topical oxygen therapy to treat people with chronic non-healing and complex diabetic foot ulcers

HTW Guidance:

The evidence supports the routine adoption of continuous topical oxygen therapy to treat patients with chronic non-healing and complex diabetic foot ulcers. The use of continuous topical oxygen therapy, in addition to standard of care, increases the number of wounds with complete wound healing and reduces the wound area and time to healing, as compared with standard of care alone.

Economic analysis indicates that the use of continuous topical oxygen therapy results in a greater benefit to patients at lower cost compared with standard of care. Cost savings of £211 per patient are estimated. When considering the projected prevalence of chronic non-healing and complex diabetic foot ulcers over the next 5 years in Wales, this could translate to total cost-savings of £8,637.

Why did Health Technology Wales (HTW) appraise this topic?

Diabetic foot ulcers are the largest single reason for hospital admission in people with diabetes. They can lead to significant morbidity and mortality and can have a large detrimental impact on quality of life. In people with diabetes, the circulation to the legs is often impaired due to the development of occlusive disease in the large and small blood vessels that supply blood and oxygen to the lower limbs. Continuous topical oxygen therapy has therefore been proposed as a means of improving wound healing through continuously supplying an external flow of pure oxygen through small tubes directly into the wounds themselves.

This topic was submitted by Inotec AMD Limited, manufacturers of a continuous topical oxygen therapy device called NATROX.

The status of HTW guidance is that NHS Wales should adopt this guidance or justify why it has not been followed. HTW will evaluate the impact of its guidance.

Evidence Summary

Refer to Evidence Appraisal Report 043 (EAR043) for a full report of the evidence supporting this Guidance.

EAR043 aimed to identify and summarise evidence that addresses the following question: what is the clinical and cost effectiveness of continuous topical oxygen therapy (TOT) in addition to standard of care (SOC) for the treatment of chronic non-healing and complex wounds in comparison to SOC alone? The majority of the evidence, and the evidence of highest certainty, we identified was for DFUs, and we have therefore focused on this wound type (evidence on other wound types is reported in Appendix 1 of the EAR).

Standard of care usually comprises cleaning and dressing the wound. Debridement, offloading or compression therapy may also be used in the treatment of DFUs. When the wound is infected, antibiotics are prescribed. Continuous TOT devices supply a constant flow of pure oxygen through small tubes to the wound for 24 hours per day. This allows an oxygen gradient to develop between the overlying dressing and the wound bed, facilitating oxygen diffusion into the wound to promote healing.

We identified one meta-analysis, one systematic review, three additional randomised controlled trials and one study reporting longer-term follow up from one of the included randomised controlled trials.

Continuous TOT plus standard of care significantly increased complete DFU healing compared to standard of care alone, after up to 12 weeks of follow-up. Continuous TOT, in combination with standard of care, also reduced the time to DFU wound closure and reduced the wound size compared to standard of care alone. The risk of amputation at one-year was significantly lower in those DFUs treated with a combination of continuous TOT, moist wound therapy and standard of care, compared to continuous TOT plus standard of care or moist wound therapy plus standard of care. The evidence suggests that one-year wound recurrence rates are lower in people treated with continuous TOT plus standard of care, compared with standard of care alone. The evidence reports that continuous TOT devices are well-tolerated by people with DFUs. The evidence showed no significant reduction in pain, the number of infections/incidents of cellulitis, 12-week wound recurrence rates or 12-week amputation rates following continuous TOT and standard of care, versus standard of care alone. Additionally, there were no significant differences between the treatment groups in the number of adverse events or serious adverse events.

A de-novo cost-utility analysis was conducted to evaluate the cost effectiveness of treating patients with DFUs with continuous TOT in addition to standard of care, compared with standard of care alone, from the perspective of treatment in NHS Wales. Due to a higher wound healing rate with continuous TOT in addition to standard of care, as well as a reduction in amputation events and infection, there was greater benefit to patients at a lower cost compared to standard care alone. Treatment with continuous TOT in addition to standard of care is therefore dominant, when compared to standard of care alone.

The appropriate mechanism for patient engagement was determined and the patient perspective was considered where possible.

Appraisal Panel considerations

- The Appraisal Panel considered the circumstances under which continuous TOT may be used for the treatment of DFUs and were informed by the clinical experts that this would be in patients with chronic non-healing and complex DFUs in whom standard treatment had failed. The experts emphasised the importance of limiting the use of continuous TOT as an advanced therapy in this group of patients, and not considering its use as an alternative to standard treatment at an earlier stage in the care pathway.
- The experts explained that other advanced wound therapies are available to treat patients with chronic non-healing and complex DFUs, including advanced dressings and negative pressure wound therapy. The Appraisal Panel noted that the comparison of continuous TOT with these advanced therapies is beyond the scope of this appraisal, and experts commented that there is a lack of evidence to compare each of them directly anyway. It was emphasised, however, that the use of continuous TOT would not necessarily be regarded as a displacement of other advanced therapies but rather as an additional therapeutic option.
- The Appraisal Panel explored with the experts some potential limitations of the evidence available. The experts explained that people recruited into clinical trials usually have well-controlled diabetes, with fewer complications, and tend not to have wound infections. This means that the studied population may not necessarily be analogous to the population treated in routine clinical practice, where uncontrolled diabetes and infected wounds are more likely to be encountered. It was also noted that the studies considered were not undertaken in the UK and that devices, other than the one approved for use in the UK, were usually used. Nonetheless, the Appraisal Panel deemed it reasonable to conclude that wound care is relatively uniform internationally and that the results of the published studies are relevant to the treatment of patients in NHS Wales.
- The Appraisal Panel concluded that the published evidence of clinical effectiveness is robust, both in terms of quantity and quality. It concluded that the evidence shows that the use of continuous TOT in addition to standard therapy leads to a higher rate of complete wound healing and a reduced wound area and time to healing, as compared with standard treatment alone. It also noted that, while limited evidence of patient experience is available, it appears to be well-tolerated and associated with high patient satisfaction.
- The Appraisal Panel noted from the de novo economic analysis that had been undertaken by the HTW health economists, that the use of continuous TOT in addition to standard therapy leads to clinical benefit at lower cost than standard therapy alone and is therefore a dominant and cost-effective treatment for patients with chronic non-healing and complex DFUs.
- The Appraisal Panel concluded that the evidence supports the routine adoption of continuous TOT in addition to standard of care for the treatment of patients with chronic non-healing and complex DFUs.
- The Appraisal Panel would welcome further research into the comparative effectiveness of continuous TOT and other advanced therapies for the treatment of DFUs. Furthermore, research to determine the effectiveness of continuous TOT on wound healing in DFUs of different grades is also recommended.

Responsibilities for consideration of this Guidance

Health Technology Wales (HTW) was established by Ministerial recommendation[1,2] to support a strategic, national approach to the identification, appraisal and adoption of non-medicine health technologies into health and care settings. The HTW Appraisal Panel comprises senior representation from all Welsh boards with delegated authority to produce guidance 'from NHS Wales, for NHS Wales'. The status of HTW guidance is 'adopt or justify'. There is an expectation from Welsh Government that HTW guidance is implemented with adoption regularly audited by HTW.[3]

The guidance in this document is intended to assist Welsh care system decision makers to make evidence-informed decisions when determining the place of health technologies and thereby improve the quality of care services.

The content of this HTW guidance was based upon the evidence and factors available at the time of publication. An international evidence base was reviewed and external topic experts and HTW committee members consulted to contextualise available evidence to Wales. Readers are asked to consider the generalisability of the evidence reviewed to NHS Wales and that new trials and technologies may have emerged since first publication and the evidence presented may no longer be current. It is acknowledged that evidence constitutes only one of the sources needed for decision making and planning.

This guidance does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgment in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

No part of this guidance may be used without the whole of the guidance being quoted in full. This guidance represents the view of HTW at the date noted. HTW guidance is not routinely updated. It may, however, be considered for review if requested by stakeholders, based upon the availability of new published evidence which is likely to materially change the guidance given.

Standard operating procedures outlining HTW's evidence review methods and framework for producing its guidance are available from the HTW website.

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Declarations of interest were sought from all reviewers. All contributions from reviewers were considered by HTW's Assessment Group. However, reviewers had no role in authorship or editorial control and the views expressed are those of Health Technology Wales.

Chair, Health Technology Wales Appraisal Panel

1. National Assembly for Wales, Health and Social Care Committee. Access to medical technologies in Wales. December 2014.
2. Response to Recommendations from the Health & Social Care Committee: Inquiry into Access to Medical Technologies in Wales. February 2015.
3. Gething, V. Letter to all Health Board Chairs re Funding for Sacral Nerve Stimulation in Wales. VG_01655_17. September 2017.