Recommendations and Reviews

The efficacy and benefits of Continuous Diffusion of Oxygen (CDO) therapy using the OxyGeni® (CDO®) System are supported not only by multiple studies in various wound types, yet have also been analyzed and recommended in several meta-analyses and systematic reviews, and most recently recommended as a Standard of Care by multiple respected organizations conveying treatment guidelines to physicians. CDO is a continuously applied form of topical oxygen therapy (TOT), together referred to simply as CDO herein. Below are references and links for the supporting material, beginning with recommendations as standard of care, followed by systematic reviews and meta-analyses. Aside from our website (eo2.com), you can learn more about CDO therapy on our YouTube educational channel (youtube.com/eo2concepts) where there are application videos, testimonials from doctors, nurses and patients, webinars, and expert advice.

Standard of Care Recommendations

- Health Canada - Canadian Agency for Drugs and Technologies in Health (CADTH) [1]
  - Recommended CDO for implementation nationwide, September 2024
  - "CDO appears to be clinically effective and cost-effective for hard-to-heal diabetic foot ulcers, and has been recommended as an adjunct treatment for patients with diabetic foot ulcers that have not responded to standard care"
  - "CDO may also be effective for treating other types of hard-to-heal wounds like venous leg ulcers and pressure ulcers"
- Wound Healing Society DFU Treatment Guidelines [2]
  - Recommended CDO as a Level 1 treatment recommendation, January 2024
  - "(CDO) has been shown to increase the incidence of healing and decrease the time to heal"
- Journal of Wound Care (JWC) International Consensus Document [3]
  - JWC Consensus Document added CDO as a Standard of Care, August 2023
  - Recommends CDO therapy with "broad access to therapy with appropriate reimbursement by Payers and health systems"
  - References recent recommendations, including IWGDF Guidelines, ADA Standards of Care and JWC Delphi Consensus Guidance as well as the multiple meta-analysis & systematic reviews
- International Working Group for the Diabetic Foot (IWGDF) [4]
  - IWGDF recommended CDO in 2023 Guidelines for Wound Care, July 2023
  - Received highest ranking possible and one of only 6 therapies out of 29 listed that are recommended (most are Do Not Use or Not Recommended)
- Alliance for Wound Care Stakeholders [5]
  - AWCS issued an open letter to CMS recommending review and approval of CDO, May 2023
  - "Evidence supporting (CDO's) efficacy in healing chronic DFUs can no longer be disputed"
  - Supported the inclusion of CDO in clinical practice guidelines for chronic DFUs
- American Diabetes Association (ADA) [6]
  - ADA added CDO as a recommended Standard of Care with Grade A evidence, January 2023
  - "(CDO) therapy has been studied rather vigorously in recent years with several high-quality RCT's and at least five systematic reviews and meta-analyses all supporting its efficacy in healing"
  - "Importantly, topical oxygen therapy devices provide for home-based therapy rather than the need for daily visits to specialized centers (such as Hyperbaric Oxygen treatments). Very high participation with very few reported adverse events combined with improved healing rates makes this therapy another attractive option for advanced wound care."
- JWC Delphi Consensus Guidance [7]
  - Eighteen experts with experience using topically applied oxygen published a consensus guidance document recommending use of CDO in wounds that are delayed in healing, have failed prior therapies or are ischemic
  - The consensus states that wounds likely to benefit include diabetic foot ulcers, venous leg ulcers and ischemic ulcers
  - "The growing body of clinical trial and real-world evidence demonstrating the effectiveness of (CDO) in diabetic foot and other wounds supports its incorporation into clinical practice"

Meta-Analyses & Systematic Reviews

There are multiple systematic reviews and meta-analyses all finding statistically significant efficacy leading them to recommend the application of CDO and topically applied oxygen in healing chronic wounds. These peer-reviewed journals have found CDO to be safe and efficacious, delivering significantly improved clinical outcomes.

- International Wound Journal: Efficacy of Topical Oxygen Therapy for Wound Healing - Meta-Analysis of RCT & Observational Studies. July 2024 [8]
  - "Topical oxygen therapy is considered a great adjuvant therapy for chronic wound healing, particularly wounds with vascular compromise such as diabetic ulcers and pressure ulcers"
  - "These findings provide further evidence for the generally known hypothesis that oxygen is crucial for the healing of different types of wounds"
  - EO2's study demonstrates "superior methodological quality"
- Advances in Wound Care (Wound Healing Society): Efficacy of Topical Wound Oxygen Therapy in Healing Chronic Diabetic Foot Ulcers: Systematic Review and Meta-Analysis. April 2023 [9]
  - "Our study shows that (CDO) is a viable diabetic foot ulcer therapy"
  - "It is interesting to note that if the (disposable EpiFlo) study is removed from meta-analysis, there is no heterogeneity, and a fixed-effects model is possible with extremely statistically significant results"
- American Diabetes Association: New Evidence-Based Therapies for Complex Diabetic Foot Wounds. May 2022 [10]
  - CDO "has come of age and the evidence supporting its efficacy in healing chronic DFUs can no longer be disputed"
  - "Oxygen is obviously essential for life itself, and it is no less essential for wound repair, being a necessary co-factor for several oxygen-dependent enzymes that are crucial in the wound healing cascade"
- International Wound Journal: Efficacy and safety of topical oxygen therapy for diabetic foot ulcers: an updated systematic review and meta-analysis. May 2022 [11]
  - "Oxygen is a crucial element in the wound healing process, and topical oxygen therapy (CDO) can ameliorate oxygen deficiency"
  - "The existing evidence suggests that (CDO) is effective and safe"
- Health Sciences Review: Topical oxygen therapy for healing diabetic foot ulcers: a systematic review and meta-analysis of randomised control trials. March 2022 [12]
  - "safe and associated with a higher rate of complete wound healing"
  - "represents an appealing therapy prospect in individuals with DFU not improving with SC, and given their simplicity of use"
- Diabetic Medicine: Topical oxygen therapy for diabetes-related foot ulcers: A systematic review and meta-analysis. August 2021 [13]
  - "This systematic review and meta-analysis suggested that topical oxygen therapy improved the healing of DFUs, as evidenced by an approximate two-fold increased likelihood of ulcer healing"
  - "Sensitivity analyses suggested the findings were robust"

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