



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:

1. Determine the quantity and quality of evidence available for a technology of interest.
2. Identify any gaps in the evidence/ongoing evidence collection.
3. Inform decisions on topics that warrant fuller assessment by Health Technology Wales.

Topic:	Automated oxygen titration (FreeO2 system)
Topic exploration report number:	TER248

Introduction and aims

Precise control of oxygen flows can be difficult to achieve in clinical practice and can be time-consuming. Closed-loop automatic control systems adjust the oxygen flow administered to spontaneously breathing patients in order to maintain a predefined pulsed oxygen saturation. Optimising the oxygen therapy can improve adequate oxygenation by shortening the time spent either in hyperoxia or hypoxemia as well as automatically wean patients from oxygen.

Health Technology Wales researchers searched for evidence on closed loop automated oxygen titration/administration systems.

Summary of evidence

Primary evidence

A randomised controlled trial (RCT) by Lellouche et al. (2016) evaluated the feasibility of using the FreeO₂ system in comparison to manual oxygen titration in a cohort of 50 patients with chronic obstructive pulmonary disease (COPD) hospitalised in the respiratory ward for an acute exacerbation. Nurses and physicians carrying out oxygen adjustment and monitoring asked to rate the appropriateness and acceptability of each intervention (924 evaluations conducted by nurses and 96 by physicians) felt that the FreeO₂ system was at least as appropriate and acceptable as manual oxygen management. The percentage of time within oxygen saturation (SpO₂) target was significantly higher with FreeO₂ and the time with severe desaturation and hyperoxia was significantly reduced with FreeO₂. Time from study inclusion to hospital discharge was also reduced in the FreeO₂ group, however, the difference was not statistically significant.

l'Her et al. (2017) conducted a multicentre RCT in patients admitted to the emergency department for acute respiratory disorder (n=187) in order to compare automated closed-loop or manual oxygen titration for three hours. The authors report that the time within SpO₂ target was higher under automated titration. Additionally, automated titration significantly reduced

time with hypoxemia and hyperoxia as well as oxygen weaning and the duration of hospital stay.

The study by Ouanes et al. (2021) is a prospective crossover cohort study evaluating the efficacy of FreeO₂ in 51 patients admitted to intensive care units after mechanical ventilation. The authors concluded that for the purpose of oxygen weaning in patients recovering from mechanical ventilation, automated oxygen titration was associated with a substantial reduction in oxygen delivery and better oxygenation parameters (time in target oxygen saturation, time with hyperoxia/hypoxemia or severe desaturation) in comparison with constant oxygen flow.

Economic evidence

A study by Poder et al. (2018) evaluated the cost-effectiveness of FreeO₂ system in comparison to manual oxygen titration in a cohort of 47 patients with COPD. The authors reported that the intervention with FreeO₂ generated savings at 180 days but the decrease was not deemed statistically significant. Nevertheless, an improvement was reported in the time spent at the target oxygen saturation. The incremental cost-effectiveness ratio (ICER) indicated that the FreeO₂ system is more cost-effective than manual oxygen titration, generating savings per percentage point of time spent at the target oxygen saturation.

Ongoing trials

We identified four relevant ongoing randomised controlled trials of automated oxygen titration/administration systems. These compare the effectiveness of interventions with automated oxygen titration in comparison to manual titration. The trials cover spontaneously breathing participants, including patients with COPD, COVID-19 or acute respiratory distress that are admitted to the hospital. Three of the four trials are scheduled for completion in 2021. Details of the studies are included in the Brief Literature Results section.

Areas of uncertainty

Closed-loop automatic control oxygen titration systems have been evaluated in a number of randomised controlled, but these were often pilot studies and all included different patient populations. It is therefore difficult to determine in what populations this intervention is likely to be most effective. However, ongoing evidence collection might address this question. From a different perspective, it is unclear if the technology has an appropriate CE mark and if the algorithms embedded in the technology for the automatic adjustment of oxygen flow constitute a digital health application that require additional regulatory scrutiny.

Conclusions

From the evidence identified, interventions with closed-loop automatic control of oxygen titration appear to have some benefits in comparison to manual adjustment of oxygen. However, the evidence base is limited in any particular population which makes it difficult to assess where it might deliver most benefit. Clinical trials addressing such interventions in relevant populations have been identified and could potentially enable a fuller health technology assessment in the future.

Brief literature search results

Resource	Results
HTA organisations	
Healthcare Improvement Scotland	We did not identify any relevant guidance from this source.
Health Technology Assessment Group	We did not identify any relevant guidance from this source.
Health Information and Quality Authority	We did not identify any relevant guidance from this source.
EUnetHTA	We did not identify any relevant guidance from this source.
International HTA Database	We did not identify any relevant guidance from this source.
UK guidelines and guidance	
SIGN	We did not identify any relevant guidance from this source.
NICE	We did not identify any relevant guidance from this source.
Secondary literature and economic evaluations	
https://www.epistemonikos.org/en/	We did not identify any relevant evidence from this source.
https://www.tripdatabase.com/	We did not identify any relevant evidence from this source.
Cochrane library	We did not identify any relevant evidence from this source.
Medline	We did not identify any relevant evidence from this source.
Primary studies	
https://www.epistemonikos.org/en/	We did not identify any relevant evidence from this source.
https://www.tripdatabase.com/	Lellouche F, Bouchard P-A, Roberge M, et al. (2016). Automated oxygen titration and weaning with FreeO2 in patients with acute exacerbation of COPD: a pilot randomized trial. <i>International journal of chronic obstructive pulmonary disease</i> . 11: 1983.
Cochrane library	We did not identify any relevant evidence from this source.
Medline	l'Her E, Dias P, Gouillou M, et al. (2017). Automatic versus manual oxygen administration in the emergency department. <i>European Respiratory Journal</i> . 50(1). Ouanes I, Bouhaouala F, Maatouk S, et al. (2021). Automatic oxygen administration and weaning in patients following mechanical ventilation. <i>Journal of Critical Care</i> . 61: 45-51. Poder TG, Kouakou CR, Bouchard P-A, et al. (2018). Cost-effectiveness of FreeO2 in patients with chronic obstructive pulmonary disease hospitalised for acute exacerbations: analysis of a pilot study in Quebec. <i>BMJ open</i> . 8(1).
Ongoing primary or secondary research	
PROSPERO database	We did not identify any relevant evidence from this source.
Clinicaltrials.gov	NCT03835741 - Automated Adjustment of Oxygen on Patient With Acute COPD Exacerbation - FreeO2 HypHop (FreeO2 HypHop). Randomised, parallel clinical trial. Estimated study completion date: June 2022. NCT04320056 - Closed-Loop Oxygen to Verify That Healthcare Workers Interventions Decrease During SARS-CoV-2 Pneumonia (COVID-19). Randomised, parallel clinical trial. Estimated study completion date: October 2021.

	NCT03661086 - Oxygen Control and Weaning by O2matic to Patients Admitted With an Exacerbation of COPD (O2MATIC-WEAN). Randomised, parallel clinical trial. Estimated study completion date: December 2021. NCT04079465 - Automated Oxygen Control by O2matic to Patients Admitted With Acute Hypoxemia (O2MATIC-ACUT). Randomised, parallel clinical trial. Estimated study completion date: December 2021.
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Other	
Evidence provided by topic proposer	The evidence identified from the searches conducted matched the evidence provided by the topic proposer.

Date of search:	<i>April 2021</i>
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Concepts used:	Closed loop automatic control of oxygen, automated oxygen titration, automated oxygen administration, FreeO ₂
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