National Institute for Health and Care Excellence

IP408/3 – Extracorporeal carbon dioxide removal for acute respiratory failure
Consultation Comments table

IPAC date: 13 May 2016

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Company	**General**	As a manufacture of devices for providing extracorporeal CO2 removal, ALung Technologies is pleased to see NICE continue to evolve its guidance on the use of this life-saving technology. We appreciate the opportunity to provide comments on the proposed guidance for this procedure. Our feedback on this guidance is focused on three areas: indications, complications, and efficacy measures.	Thank you for your comment.

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2	Consultee 1 Company	**2**	<u>Indications</u> Section 2 of the proposed guidance lists acute respiratory failure, and specifically ARDS as the primary indication for ECCO2R. Ventilator weaning, and bridge to transplant are also listed as indications. We wish to inform NICE that in addition to these indications, there is substantial interest and ongoing clinical use of ECCO2R in patients with acute exacerbation of COPD, both to prevent intubation when non-invasive ventilation (NIV) is failing, and as a supplement to mechanical ventilation to facilitate protective ventilation and rapid extubation. In fact, ALung's Hemolung RAS has an approved indication (CE mark) in severe COPD when NIV has failed and mechanical ventilation is deemed undesirable. We believe that the guidance document would benefit from a more thorough consideration of the applications of ECCO2R technology in COPD patients. Missing from the literature review was a key paper on this indication: "Extracorporeal Co2 Removal in Hypercapnic Patients At Risk of Noninvasive Ventilation Failure: A Matched Cohort Study With Historical Control" by Del Sorbo et al (Critical Care Medicine, January 2015 - Volume 43 - Issue 1 - p 120–127). We encourage the committee to review this, and other papers on ECCO2R in COPD, and incorporate this indication into the guidance document.	Thank you for your comment. The Del Sorbo (2015) paper has been identified by the post-consultation updated literature search alongside 3 other papers on the use of $ECCO_2R$ in chronic obstructive pulmonary disease (COPD). They have all been included in Appendix A. This guidance is on the use of $ECCO_2R$ in acute respiratory failure. COPD is a different indication. The potential for $ECCO_2R$ to be used for COPD is mentioned in section 6.1 of the guidance: '' *The committee noted that there are several ongoing studies using extracorporeal carbon dioxide ($ECCO_2R$) removal in patients with acute exacerbation of chronic obstructive pulmonary disease."* NICE will consider whether to develop guidance on $ECCO_2R$ for COPD when we receive a notification for it and when more evidence is available.

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3	Consultee 1 Company	**5**	<u>Complications</u> The review and guidance thoroughly explored the complications of ECCO2R, which clinicians must balance against the potential injurious effects of invasive mechanical ventilation. Of concern however is that complications can vary widely from device to device. For instance, patients receiving VV-ECCO2R with a device like the Hemolung RAS which utilizes a single 15.5 Fr dual lumen venous cannula are very unlikely to experience limb ischemia or compartment syndrome as there is no arterial cannulation.	Thank you for your comment. The IP programme issues guidance on procedures rather than individual devices.

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4	Consultee 1 Company	**5**	While it is noted in the review that these are complications of arterial access, the technique is generally described as "ECCO2R" when these complications are presented. Thus a reader may miss the distinction of AV-ECCO2R vs VV-ECCO2R in terms of complications. We suggest that a stronger distinction of potential complications, as they are related to particular devices/techniques, be made in the guidance.	Thank you for your comment. Section 3.2 of the guidance has been changed and we have clarified the text where possible in sections 4 and 5 to indicate whether AV- or VV-$ECCO_2R$ was used. Safety events are not usually mentioned in section 3. Therefore the following sentence has been removed from section 3.2: ''Cannulation of the femoral artery may be associated with leg ischaemia.'' Section 3.2 now states: ''*There are 2 main types of $ECCO_2R$: venovenous (VV) and arteriovenous (AV). In both types, cannulae are connected to a low-resistance synthetic membrane device where exchange of CO_2 occurs. In VV-$ECCO_2R$, either a single-access double lumen catheter or a dual-access system using 2 venous catheters is inserted into a large vein or veins (typically the femoral or internal jugular veins) and connected to a venovenous circuit. Flow across the membrane is maintained using a pump. In AV-$ECCO_2R$, an artery and a vein are cannulated (typically the femoral artery and femoral vein). Arterial blood pressure drives blood continuously through the device and it is returned through the vein.''*

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5	Consultee 1 Company	**6**	It is also very important to note that ECCO2R technology has rapidly evolved over the last several years, and many of the complications from previous studies are much less common (e.g. the Morris study in which large bore catheters, high flows, and two 2.5 m2 oxygenators, without membrane coatings, were used). We suggest that the guidance more strongly note this.	Thank you for your comment. Section 6.2 of the guidance states: '' *The committee noted that the technology for this procedure is evolving.*''
6	Consultee 1 Company	**4**	<u>Measure of efficacy</u> Many of the papers reviewed cite changes in oxygenation index (P/F ratio) as measurements of ECCO2R effectiveness, with an implication in some cases that such changes are a result of the small amount of oxygenation done by the device. While improving oxygenation is important, it should not be construed that such effect is a result of the ECCO2R device itself. In fact, much of the oxygenation improvement may come from optimization of mechanical ventilation as facilitated for ECCO2R (e.g. being able to safely increase PEEP). The amount of oxygen actually provided by an ECCO2R device is likely not clinically relevant. In terms of clinical endpoints, mortality must not be assumed to be the only measure of utility for ECCO2R devices. Particularly in COPD patients, ventilator-free days, ICU/hospital length of stay, and patient quality of life measures (e.g. as improved by avoiding intubation) are key measures of clinical utility. We believe this should be noted in the review and guidance.	Thank you for your comment. The efficacy outcomes reported are those which are described in the available evidence. Additionally, section 4.6 of the guidance states: '' *The specialist advisers listed the following key efficacy outcomes: mortality, ventilator-free days, length of stay in intensive care, intubation avoidance and lowering of CO_2 in the blood*.''
7	Consultee 1 Company	**General**	Again, we would like to thank the committee for the opportunity to review this proposed guidance. We look forward to continued collaboration in this area, and welcome the opportunity to discuss further our comments.	Thank you for your comment.

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8	Consultee 2 Professional organisation The Royal College of Anaesthetists on behalf of the Faculty of intensive care medicine/ Intensive care society Joint Standards Committee	**General**	The FICM/ICS Joint Standards Committee have reviewed this consultation. The Committee had no specific comments but asked me to feedback that they thought this was a good document and agreed with your approach.	Thank you for your comment.
9	Consultee 3 Professional organisation Guy's and St Thomas' NHS Foundation Trust	**General**	We agree that extracorporeal carbon dioxide removal for acute respiratory failure is an intervention with limited evidence. We also agree with the proposed recommendation that this should only be carried out in line with the commissioned severe respiratory failure service with expertise and clear governance arrangements in place and that ideally centres should contribute to current or planned research trials. We suggest given the clear difference between the complications of the arteriovenous and venovenous technique that NICE recommend that the venovenous technique appears safer for patients on the current available evidence.	Thank you for your comment.

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10	Consultee 4 Company	**1.4**	Baxter Healthcare is in agreement with encouraging clinicians to enter patients into clinical trials and registries. However if the guidelines are to refer to specific studies (the REST study) then we believe that it should also point clinicians towards the international SUPERNOVA study (Strategy of UltraProtective Lung Ventilation With Extracorporeal CO2 Removal for New-Onset Moderate to seVere ARDS) - ClinicalTrials.gov Identifier:NCT02282657. Although the study is in the pilot stages at the moment it is likely that the full study, including sites within the UK, will commence during the time between the publication of the updated guidance and its next review.	Thank you for your comment. The committee considered your comment and decided not to change the guidance. Section 1.4 of the guidance states: '' *NICE encourages clinicians to enter patients into ongoing trials such as the protective ventilation with veno-venous lung assist in respiratory failure (REST) trial, and to collaborate in data collection initiatives such as the Extracorporeal Life Support Organization register. Data collected should include information on patient selection criteria, thresholds for intervention, the type of $ECCO_2R$ technique being used and clinical outcomes. NICE may update the guidance on publication of further evidence.''* The SUPERNOVA is currently only a pilot study and the RCT has not commenced. NICE does not normally recommend entering patients into trials that are not currently recruiting. However, this recommendation does not exclude the option of entering patients in the SUPERNOVA study once the RCT commences.

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11	Consultee 4 Company	**2**	Acute respiratory failure is an under recognised condition and adherence to Lung Protective Ventilation (LPV) is not widely achieved in practice. We therefore feel that it would be informative within the introduction to the guidelines to refer to the recently published multinational observational study the LUNG SAFE study (reference 1) as this provides robust data to describe this level of unmet need. We also feel that it would be of value to further illustrate the clinical rationale for the use of ECCO2R by noting that there is evidence (e.g. reference 2) that the low adherence to LPV could be due to concerns relating to hypercapnia and acidosis. ECCO2R removes CO2 thereby correcting for acidosis. (Reference 1: Bellani, G. et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. JAMA February 23, 2016 Volume 315, Number 8) (Reference 2: Rubenfeld G.D. et al. MD Barriers to providing lung-protective ventilation to patients with acute lung injury. Crit Care Med 2004 Vol. 32, No. 6)	Thank you for your comment. This section of the guidance is intended to be a brief summary of the indications and current treatments for this specific procedure. Furthermore, we do not usually reference the overview.
12	Consultee 5 Professional organisation British Thoracic Society	**General**	The British Thoracic Society (BTS) recognises that there are emerging data regarding the use of extracorporeal carbon dioxide removal to treat acute respiratory failure and supports further work to define its role. It is a high-risk intervention due to the nature of the procedure itself and the critically-ill population in which it may be indicated. As such, BTS reinforces the importance of robust clinical governance around its use. There is also a need for transparent and comprehensive outcome data collection, ideally through research.	Thank you for your comment. The consultee agrees with main recommendation.

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