NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **IP408/4 Extracorporeal carbon dioxide removal for acute respiratory failure**

Your information

Name:	Mark Griffiths
Job title:	Consultant
Organisation:	BartsHealth
Email address:	[redacted]
Professional organisation or society membership/affiliation:	FRCP
Nominated/ratified by (if applicable):	Click here to enter text.
Registration number (e.g. GMC, NMC, HCPC)	3258356

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

☐ Please tick this box if you would like to receive information about other NICE topics.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice.

☒ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? – Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? – Is this procedure/technology performed/used by clinicians in specialities other than your own? – If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	Previously highly experienced, lately I have not use ECCOR specifically I don't think that it is being used widely in the NHS I believe very rarely NA
2	– Please indicate your research experience relating to this procedure	I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers.

	(please choose one or more if relevant):	I have published this research.
3	Does the title adequately reflect the procedure? Is the proposed indication appropriate? If not, please explain. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Yes Yes Established practice and no longer new.
4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	Highly unlikely
5	Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure? Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?	No REST study: *JAMA.* 2021;326(11):1013-1023. doi:10.1001/jama.2021.13374 **Conclusions and Relevance** Among patients with acute hypoxemic respiratory failure, the use of extracorporeal carbon dioxide removal to facilitate lower tidal volume mechanical ventilation, compared with conventional low tidal volume mechanical ventilation, did not significantly reduce 90-day mortality. However, due to early termination, the study may have been underpowered to detect a clinically important difference. **Trial Registration** ClinicalTrials.gov Identifier: NCT02654327

Current management

6	Please describe the current standard of care that is used in the NHS.	ECCOR has not found a place between conventional management and the use of ECMO
7	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	No

Potential patient benefits and impact on the health system

8	What do you consider to be the potential benefits to patients from using this procedure/technology?	See above, otherwise there have been no changes of which I am aware
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	
10	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	

Safety and efficacy of the procedure/technology

13	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:	No change

	Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	
14	Please list the key efficacy outcomes for this procedure/technology?	
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Cannot predict at present.

Abstracts and ongoing studies

18	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help	*JAMA*. 2021;326(11):1013-1023. doi:10.1001/jama.2021.13374

	us if you list any that you think are particularly important.	
19	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Not that I know of
20	Please list any other data (published and/or unpublished) that you would like to share.	NA

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	Hundreds but I don't think that it will be used
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured:	No change Beneficial outcome measures: Adverse outcome measures:

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	I don’t know whether specific devices are still being marketed in the UK. I think that largely the technology has been superseded by ECMO.

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Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.			
Choose an item.			
Choose an item.			

☐ I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Click here to enter text.**
Dated:	**Click here to enter text.**

View results

Respondent

2 Anonymous

138:31
Time to complete

Your information

1. Name: *

Nicholas Barrett

2. Job title: *

Consultant in Critical Care Medicine

3. Organisation: *

Guy's and St Thomas' NHS Foundation Trust

4. Email address: *

[redacted]

5. Professional organisation or society membership/affiliation: *

Faculty of Intensive Care Medicine

6. Nominated/ratified by (if applicable):

FICM - Dale Gardiner, Chair FICM Professional Affairs and Safety Committee

7. Registration number (e.g. GMC, NMC, HCPC) *

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How NICE will use this information:

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For more information about how we process your data please see our privacy notice: https://www.nice.org.uk/privacy-notice

8. I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. *

- (●) I agree
- ( ) I disagree

The procedure/technology

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

9. Please describe your level of experience with the procedure/technology, for example:

   Are you familiar with the procedure/technology?

I have used extracorporeal CO2 removal (ECCO2R) in clinical practice for 10 years. I have used both the arterio-venous and venovenous devices. I have been part of the steering committees for trials of this technology and have published/spoken widely on its use.

10. Have you used it or are you currently using it?

    - Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?

    - Is this procedure/technology performed/used by clinicians in specialities other than your own?

    - If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.

I have used ECCO2R for the last 10 years. Over this time the technology has migrated from arteriovenous, pumpless devices to veno-venous pumped devices. ECCO2R is part of a spectrum of extracorporeal devices with can facilitate CO2 clearance at low blood flows (0.5-1L/minute), whilst devices at higher blood flows (3-5L/minute) are referred to as extracorporeal membrane oxygenation (ECMO) and are able to provide oxygenation and CO2 clearance.

ECCO2R has been widely used in a recent research trial (REST) but is not used widely outside of the research setting at this point. Use of ECCO2R is a little more common in ECMO centres where it can be used as additional device to aid in weaning.

ECCO2R is only used in ICUs by intensivists

11. Please indicate your research experience relating to this procedure (please choose one or more if relevant):

- [x] I have done bibliographic research on this procedure.
- [x] I have done research on this procedure in laboratory settings (e.g. device-related research).
- [x] I have done clinical research on this procedure involving patients or healthy volunteers.
- [x] I have published this research.
- [ ] I have had no involvement in research on this procedure.
- [ ] Other

12. Does the title adequately reflect the procedure?

- (•) Yes
- ( ) Other

13. Is the proposed indication appropriate? If not, please explain

no - the proposed description indicates the role is in patients with acute respiratory failure to reduce injurious ventilation. At this stage, ECCO2R really remains in the research domain. Additionally there are other indications in patients with hypercapnic respiratory failure (eg exacerbations of COPD), but again this really sits in the research domain at this stage

14. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?

The approach is part of a continuum of extracorporeal support. At the blood flows used by ECCO2R there is minimal contribution to oxygenation but significant CO2 clearance - as blood flows increase the technique is termed ECMO and both O2 and CO2 are impacted. The current standard of care for patients who could receive ECCO2R is either invasive or non-invasive mechanical ventilation. At this stage the approach needs further research

15. Which of the following best describes the procedure:

- ( ) Established practice and no longer new.
- ( ) A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.
- (•) Definitely novel and of uncertain safety and efficacy.
- ( ) The first in a new class of procedure.

16. Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?

From the available data it is unlikely to replace current standard care. If it has a role then this is likely to be as an adjunct to current care

17. Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure?

There are a number of devices available on the market with considerable industry interest in this approach. There is currently a lack of research demonstrating efficacy of the devices in improving outcomes. There are also concerns around harm from the approach.

18. Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?

Yes - two bodies of work have been published. The first was the REST trial which explored the role of ECCO2R in improving outcomes for patients with moderate to severe respiratory failure by adding ECCO2R to mechanical ventilation and reducing mechanical ventilation intensity. This approach provided no significant benefit to patients and there was a signal (though not statistically significant) for harm with a numerically higher incidence of itnracranial haemorrhage. A small pilot study of ECCO2R in exacerbations of COPD has also been recently published and has demonstrated a faster resolution of arterial CO2 and pH with a reduced time on NIV but no significant improvement in other outcomes and a longer length of stay in the ECCO2R group.

Current management

19. Please describe the current standard of care that is used in the NHS.

Patients with acute hypoxaemic respiratory failure receive nasal oxygen (increasingly via high flow devices) and when this fails would be offered mechanical ventilation, usually invasive via an endotracheal tube but at times using non-invasive ventilation. Patients with acute hypercapnic respiratory failure receive non-invasive ventilation or invasive mechanical ventilation via an endotracheal tube.

20. Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?

    If so, how do these differ from the procedure/technology described in the briefing?

Yes. ECMO works in a similar way. Both devices pump blood through the device, adding oxygen and removing carbon dioxide. The difference is the rate of flow through the device - at higher flows the physical properties of oxygen carriage in blood mean that oxygen delivery is greater and consequently ECMO can support patients with severe hypoxic respiratory failure whilst ECCO2R cannot. Both ECCO2R and ECMO are highly efficient at removing CO2. The ECMO network is well-established in the Uk and centrally commissioned by NHSE Highly Specialised Services.

Potential patient benefits and impact on the health system

21. What do you consider to be the potential benefits to patients from using this procedure/technology?

At this stage the benefits are uncertain. Hypothetical benefits for patients with acute hypoxaemic respiratory failure are that the technique may improve the intensity of ventilation and that this in turn may improve the outcomes for patients. At this stage this remains unproven and the largest trial which has reported to date demonstrated no benefit.

Potential benefits for patients with COPD include intubation avoidance and faster resolution of respiratory acidosis along with reduced sensations of breathlessness and distress. At this stage ECCO2R is likely to be an adjunctive tool to NIV in this population but again trial data demonstrating benefit is lacking.

22. Are there any groups of patients who would particularly benefit from using this procedure/technology?

Two potential groups - the COPD group with exacerbations which do not respond to NIV may benefit. Less certain are patients with hypoxic respiratoryfailure.

23. Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system?

Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

For COPD it could lead to improved patient satisfaction, improved comfort, improved ability to eat and drink during an exacerbation and improved ability to communicate their views about their healthcare needs. Although yet to be proven a potential benefot for patients with COPD includes intubation avoidance. As intubation is associated with significant morbidity and mortality this approach may lead to benefit for patients

24. What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?

This technique needs to be managed in an ICU. Given the lack of certainty about outcomes ideally this should be managed in a centre where research can be undertaken and who have experience with other forms of extracorporeal therapy.

25. Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?

There is specific training required for medical and nursing staff in managing the devices and their potential complications including haemolysis, bleeding and vascular access problems. Training also needs to be undertaken to understand the interaction between the native lungs and the device.

Safety and efficacy of the procedure/technology

26. What are the potential harms of the procedure/technology?

Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:

- Adverse events reported in the literature (if possible, please cite literature)
- Anecdotal adverse events (known from experience)
- Theoretical adverse events

Key adverse events relate to haemorrhage (including intracranial haemorrhage), thrombosis and haemolysis.

Arterial insufficiency for the arteriovenous device

REST trial: doi: 10.1001/jama.2021.13374
AECOPD trial: DOI: 10.1186/s13613-022-01006-8
doi: 10.1136/thoraxjnl-2019-213591

27. Please list the key efficacy outcomes for this procedure/technology?

improved survival at 180 days, reduction in resource utilisation overall (eg reduction in mechanically ventilated days, reduction in ICU and hospital LOS), complications from the device (failure, thrombosis, need for change of circuit)

28. Please list any uncertainties or concerns about the efficacy and safety of this procedure/technology?

The trial data to date has demonstrated considerable potential harm. This is particuarly problematic for the arteriovenous device where limb threatening ischaemia has been reported. Bleeding and thrombosis remain the most likely areas of concern

29. Is there controversy, or important uncertainty, about any aspect of the procedure/technology?

Yes, there is no clear evidence of benefit in either key patient group

30. If it is safe and efficacious, in your opinion, will this procedure be carried out in:

- (●) Most or all district general hospitals.
- ( ) A minority of hospitals, but at least 10 in the UK.
- ( ) Fewer than 10 specialist centres in the UK.
- ( ) Cannot predict at present.

Abstracts and ongoing studies

31. Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work).

    Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

DOI: 10.1186/s13613-022-01006-8
DOI: 10.1001/jama.2021.13374

32. Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.

Yes - from clinicaltrials.gov

1 Recruiting Effects of Blood Pulsatility on Von Willebrand Factor During ECCO2R
Hôpital européen Georges Pompidou
Paris, France

2 Terminated Flow-flow ECCO2-R and 4 ml/kg Tidal Volume vs. 6 ml/kg Tidal Volume to Enhance Protection From VILI in Acute Lung Injury
University of Turin - Department of Anesthesia and Intensive Care Medicine
Turin, Italy

3 Not yet recruiting Novel ECCO2R Device for Hypercapnic Respiratory Failure

4 Not yet recruiting ecco2R to facilitatE earLy libEration From mechanicAl Ventilation inpatientS With Copd Acute Exacerbation

5 Recruiting ECCO2R in the Treatment of Acute Exacerbation of COPD With Severe Hypercapnia

Lung Diseases, Obstructive

Beijing Institute of Respiratory Medicine, Beijing Chao-yang Hospital, Capital Medical University
Beijing, China

6 Terminated Ultra-protective Pulmonary Ventilation Supported by Low Flow ECCO2R for Severe ARDS

National University Hospital
Singapore, Singapore
Ng Teng Fong General Hospital
Singapore, Singapore

7 Withdrawn The PALP™-COPD Trial (Low-Flow CO2-Removal (ECCO2-R) in Exacerbated COPD)

MAQUET Cardiopulmonary AG
Rastatt, Germany

8 Completed Correction by ECCO2-R of Hypercapnia in Patients With DVP in Moderate to Severe ARDS Under Protective Ventilation.
Henri Mondor Hospital
Creteil, France

9 Completed ECCO2R as an Adjunct to NIV in AECOPD

Guy's and St Thomas' NHS Foundation Trust
London, United Kingdom

10 Recruiting ECCO2R - Mechanical Power Study

ASST-Santi Paolo e Carlo, San Paolo Hospital
Milan, Italy

11 Unknown † Extracorporeal Carbon Dioxide Removal in Severe Chronic Obstructive Pulmonary Disease Exacerbation
China-Japan Friendship hospital
Beijing, Beijing, China

12 Recruiting Post-Market Study of Low-flow ECCO2R Using PrismaLung+

13 Recruiting Enhanced Lung Protective Ventilation With ECCO2R During ARDS

Service de REANIMATION, HOPITAL EUROPEEN MARSEILLE
Marseille, France

14 Recruiting Early Extubation by ECCO2R Compared to IMV in Patients With Severe Acute Exacerbation of COPD

Kliniken der Stadt Köln gGmbH, ARDS and ECMO Zentrum Köln-Merheim
Köln, Germany

15 Completed Low-Flow CO2 Removal for Mild to Moderate ARDS With PRISMALUNG

CHU AMIENS, Département Anesthésie Réanimation
Amiens, France
CHU Besançon, Réanimation
Besançon, France
CHU CLERMONT FERRAND, Département Anesthésie Réanimation
Clermont Ferrand, France
(and 2 more...)

17 Not yet recruiting CO2 Removal in Severe Acute exacerbatIons of Chronic Obstructive Lung Diseases

CHU Angers
Angers, France
CHU Besançon
Besançon, France
Hôpital Avicennes, AP-HP
Bobigny, France
(and 17 more...)

18 Not yet recruiting Extracorporeal CO2 Removal for Acute Decompensation of COPD

19 Completed Extracorporeal CO2 Removal in Acute Exacerbation of COPD Not Responding to Non-Invasive Ventilation

20 Recruiting Use of Extracorporeal CO2 Removal in Case of Moderate to Severe ARDS to

Apply an Ultraprotective Mechanical Ventilation Strategy

University Hospital of Montpellier
Montpellier, France

33. Please list any other data (published and/or unpublished) that you would like to share.

Other considerations

34. Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?

If eficacious in exacerbations of COPD, it is likely to be around 10-30% of all exacerbations as this is the proportion who currently get intubated. If efficatious in moderate to severe hypoxic respiratory failure it is likely to be around 10-15% of patients with hypoxic respiratory failure

35. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Beneficial outcome measures.

These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.

Physiological outcomes
• Impact on ABG parameters (PaO2, SpO2, PaCO2, HCO3, pH, lactate)
• Impact on basic physiology Respiratory rate, heart rate, blood pressure, temperature
• impact on work of breathing

Mortality/length of stay
• Mortality – ICU, hospital, 3 month
• Length of stay – ICU, hospital
• Three-month readmission rate
• Need for intubation
• Duration of mechanical ventilation
• Need for tracheostomy

Patient centred outcomes (measured daily)
• Dyspnoea score – using a dyspnoea visual analogue scale and numerical rating scale
• Patient tolerance – using a tolerability visual analogue scale
• Ability of the patient to maintain an oral diet with food chart and standardised nutrient tables ("GSTT Ready Reckoner")
• Calculated daily caloric intake and predicted daily calorie deficit (ACCP guidelines)
• NIV related side effects
• EuroQoL 5D survey
• Time to mobilisation
o time to sitting out of bed
o time to stand with assist
o time to walk with assist

Patient centred outcomes (measured at 3 months following discharge)
• COPD assessment test
• Occurrences of readmission to hospital
• St George Respiratory Questionnaire
• EuroQoL 5D survey

Economic outcomes
• Consumables cost
• ICU bed stay cost

36. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Adverse outcome measures.

These should include early and late complications. Please state the post procedure timescales over which these should be measured:

Haematological/biochemical outcomes
• plasma free Hb and other markers of haemolysis.
• Significant bleeding episodes using the ISTH-SCC bleeding score
• Incidence of deep vein thrombosis and pulmonary embolism following decannulation.

Cannulation-related outcomes
• Arterial cannulation/injury
• Cannulation site bleeding
• Cannulation site infection – idivided into clinically apparent (erythematous, oedematous, or purulent discharge) and microbiologically proven (swabs of site demonstrating growth of a pathogenic bacteria)
• Deep vein thrombosis and pulmonary embolism following decannulation

Further comments

37. If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe *

There is a need for further research. A number of trials outside the UK are in progress. Health economic data should be undertaken using UK benchmarking

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

38. Type of interest: *

- [ ] Direct: financial
- [x] Non-financial: professional
- [x] Non-financial: personal
- [ ] Indirect
- [ ] No interests to declare

39. Description of interests, including relevant dates of when the interest arose and ceased. *

I am on the data safety monitoring committee for the VentAvoid trial which is a trial using the ALung device in the USA (ongoing)

I sit on an expert advisory board to ALung and Baxter (ongoing) - my employer receives remuneration for this role. My Trust receives remuneration to act as a reference centre for Getinge (ongoing). I do not receive any monies from any company directly or indirectly.

I am the Chair of EuroELSO, the organisation seeking to advance education and research into extracorporeal life support techniques across Europe (ongoing)

I have previously led or co-led trials of ECCO2R which have received industry and research body funding, although all monies were paid to the Trust. Ceased 2020

40. I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

    Please note, all declarations of interest will be made publicly available on the NICE website. *

    - (●) I agree
    - ( ) I disagree

Signature

41. Name: *

    nicholas barrett

42. Date: *

    16/03/2023

View results

Respondent

1 Anonymous

28:45
Time to complete

Your information

1. Name: *

Olusegun Olusanya

2. Job title: *

Consultant in Intensive Care Medicine

3. Organisation: *

St Bartholomew's Hospital

4. Email address: *

[redacted]

5. Professional organisation or society membership/affiliation: *

Intensive Care Society

6. Nominated/ratified by (if applicable):

Dr Steve Mathieu, ICS President

7. Registration number (e.g. GMC, NMC, HCPC) *

6100365

How NICE will use this information:

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8. I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. *

- (●) I agree
- ( ) I disagree

The procedure/technology

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

9. Please describe your level of experience with the procedure/technology, for example:

   Are you familiar with the procedure/technology?

   Yes- I am an ECMO consultant in training working in a tertiary cardiothoracic unit. I am familiar with VA ECMO/VV ECMO/ECCO2R.

10. Have you used it or are you currently using it?

    - Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake?

    - Is this procedure/technology performed/used by clinicians in specialities other than your own?

    - If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.

    I have used it before and am involved in decisions regarding its use. I use it very infrequently now.

11. Please indicate your research experience relating to this procedure (please choose one or more if relevant):

- [x] I have done bibliographic research on this procedure.
- [ ] I have done research on this procedure in laboratory settings (e.g. device-related research).
- [ ] I have done clinical research on this procedure involving patients or healthy volunteers.
- [ ] I have published this research.
- [ ] I have had no involvement in research on this procedure.
- [ ] Other

12. Does the title adequately reflect the procedure?

- (•) Yes
- ( ) Other

13. Is the proposed indication appropriate? If not, please explain

Strictly speaking this procedure should be for acute hypercapnoeic respiratory failure, not just "acute respiratory failure".

14. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design?

This is a challenging question to answer. It is technically not new- VV ECMO and the concept of CO2 dialysis has existed since the 1970s. The modern ECCO2R circuits that can be inserted and managed outside of a cardiothoracic centre are the real innovation- and these have also been in existence for more than 10 years.

15. Which of the following best describes the procedure:

- (●) Established practice and no longer new.
- ( ) A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.
- ( ) Definitely novel and of uncertain safety and efficacy.
- ( ) The first in a new class of procedure.

16. Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?

Currently the flows are too low to replace standard ventilation or ECMO, so it would be an addition to existing standard of care.

17. Have there been any substantial modifications to the procedure technique or, if applicable, to devices involved in the procedure?

No

18. Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?

Yes. The REST trial has since been published (https://jamanetwork.com/journals/jama/article-abstract/2783809) which showed no significant mortality benefit, and a possible signal for harm- albeit the trial was terminated early.

Current management

19. Please describe the current standard of care that is used in the NHS.

The current standard of care for acute respiratory failure involves treating the underlying cause, and then a stepwise escalation in support from facemask therapies--> High flow oxygen--> Noninvasive ventilation-->Invasive mechanical ventilation-->Neuromuscular blockade and PEEP titration-->prone ventilation-->VV ECMO support.

20. Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this?

    If so, how do these differ from the procedure/technology described in the briefing?

VV ECMO is the closest therapy, which involves full support for both CO2 clearance and oxygenation, using larger circuits and requiring anticoagulation. This is delivered in 8 centres in the UK currently.

Potential patient benefits and impact on the health system

21. What do you consider to be the potential benefits to patients from using this procedure/technology?

The main benefits would be to provide a reduction in mechanical ventilation, therefore potentially reducing ventilator induced lung injury. This was shown to be the case in the REST trial.

22. Are there any groups of patients who would particularly benefit from using this procedure/technology?

Yes- patients with hypercarbic respiratory failure who are unable to be safely mechanical ventilated.

23. Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system?

    Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?

    I don't think so. At the moment, following the REST trial, ECCO2R can really only be recommended for use within a clinical trial setting or in specialist centres. Unless there is a major change eg. ECCO2R devices that can be used without anticoagulation, I don't see this changing.

24. What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?

    ECCO2R can be run safely in non-expert centres (according to REST)- so nothing.

25. Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?

    Yes- training regarding insertion and management of the devices is essential. This was demonstrated in the REST trial.

Safety and efficacy of the procedure/technology

26. What are the potential harms of the procedure/technology?

    Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:

    - Adverse events reported in the literature (if possible, please cite literature)
    - Anecdotal adverse events (known from experience)
    - Theoretical adverse events

    there are harms related to the device insertion and harms related to the therapy:
    Device insertion- bleeding, infection, pneumothorax, failure
    Therapy- anticoagulation can result in significant bleeds, particularly intracranial haemorrhage. This was demonstrated in REST where 52% of ECCO2R patients experienced an adverse event as opposed to 23% of controls

27. Please list the key efficacy outcomes for this procedure/technology?

    They should be CO2 control and mechanical power on the ventilator- which REST demonstrated some efficacy for. The ideal efficacy outcome is of course mortality, however REST did not show that.

28. Please list any uncertainties or concerns about the efficacy and safety of this procedure/technology?

    REST confirmed that the potential improvements in ventilator driving pressure came at a cost of increased complications. Based on this, the place of ECCO2R remains uncertain in my opinion.

29. Is there controversy, or important uncertainty, about any aspect of the procedure/technology?

    The theory is sound. Its clinical effectiveness is the question.

30. If it is safe and efficacious, in your opinion, will this procedure be carried out in:

- ( ) Most or all district general hospitals.
- (•) A minority of hospitals, but at least 10 in the UK.
- ( ) Fewer than 10 specialist centres in the UK.
- ( ) Cannot predict at present.

Abstracts and ongoing studies

31. Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work).

    Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.

REST recently published long term outcomes which showed no mortality benefit from the therapy https://thorax.bmj.com/content/early/2022/10/05/thorax-2022-218874

A systematic review/Bayesian analysis was also pessimistic about its future https://err.ersjournals.com/content/31/166/220030

32. Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.

ESLO collects some data on ECCO2R https://www.elso.org/registry/elsoliveregistrydashboard.aspx

33. Please list any other data (published and/or unpublished) that you would like to share.

Other considerations

34. Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?

Between 200 and 300 nationally (REST recruited 412 over 3 years)

35. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Beneficial outcome measures.

These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured.

Tidal volumes and driving pressure
Ventilator free days
ICU mortality
Hospital mortality
90 day and 180 day mortality
SF-36 of survivors
Hospital Anxiety/Depression scale of survivors and their families
6 minute walk test of survivors
Lung injury based on imaging (CT/CXR/Lung ultrasound)

36. Please suggest potential audit criteria for this procedure/technology. If known, please describe:

Adverse outcome measures.

These should include early and late complications. Please state the post procedure timescales over which these should be measured:

Procedural complications
Infection
Haemorrhage (in particular intracranial haemorrhage)

Further comments

37. If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe *

I personally think that REST has put widespread use of ECCO2R for severe acute respiratory failure to bed. It may have a place in a selected group of hypercarbic patients, and in some patients (eg COPD patients) it may avoid intubation altogether- however I think this is a very select group https://thorax.bmj.com/content/75/10/897

Declarations of interests

Please state any potential conflicts of interest relevant to the procedure/technology (or competitor technologies) on which you are providing advice, or any involvements in disputes or complaints, in the previous **12 months** or likely to exist in the future. Please use the NICE policy on declaring and managing interests as a guide when declaring any interests. Further advice can be obtained from the NICE team.

38. Type of interest: *

- [ ] Direct: financial
- [ ] Non-financial: professional
- [ ] Non-financial: personal
- [ ] Indirect
- [x] No interests to declare

39. Description of interests, including relevant dates of when the interest arose and ceased. *

N/A

40. I confirm that the information provided above is complete and correct. I acknowledge that any changes in these declarations during the course of my work with NICE, must be notified to NICE as soon as practicable and no later than 28 days after the interest arises. I am aware that if I do not make full, accurate and timely declarations then my advice may be excluded from being considered by the NICE committee.

Please note, all declarations of interest will be made publicly available on the NICE website. *

- (●) I agree
- ( ) I disagree

Signature

41. Name: *

Olusegun Olusanya

42. Date: *

10/03/2023

NICE National Institute for Health and Care Excellence

Professional Expert Questionnaire

Technology/Procedure name & indication: **IP408/4 Extracorporeal carbon dioxide removal for acute respiratory failure**

Your information

Name:	Zudin Puthucheary
Job title:	Clinical Senior Lecturer and Consultant in Intensive Care
Organisation:	Queen Mary University of London and Barts Health NHS Trust
Email address:	[redacted]
Professional organisation or society membership/affiliation:	FRCP, FFICM
Nominated/ratified by (if applicable):	The Intensive Care Society
Registration number (e.g. GMC, NMC, HCPC)	4430519

How NICE will use this information:

The information that you provide on this form will be used to develop guidance on this procedure.

☐ Please tick this box if you would like to receive information about other NICE topics.

Your advice and views represent your individual opinion and not that of your employer, professional society or a consensus view. Your name, job title, organisation and your responses, along with your declared interests will also be published online on the NICE website as part of public consultation on the draft guidance, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate.

For more information about how we process your data please see our privacy notice.

☒ I give my consent for the information in this questionnaire to be used and may be published on the NICE website as outlined above. If consent is NOT given, please state reasons below:

Click here to enter text.

Please answer the following questions as fully as possible to provide further information about the procedure/technology and/or your experience.

1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? – Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? – Is this procedure/technology performed/used by clinicians in specialities other than your own? – If your specialty is involved in patient selection or referral to another specialty for this	I am familiar with the technology and concept and have seen a patient started on ECCOR about 10 years ago. I helped design a trial in Singapore in 2014, however the protocol we agreed on began with optimisation of conventional ARDS management, and we were therefore unable to recruit patients to this trial. The procedure is not used in the UK widely, though I am aware that it is used in Germany for type II respiratory failure. There remains (in my understanding) no good evidence for its use either this setting or in Type I respiratory failure, and therefore this in not used widely in intensive care, and especially not in the UK. If new evidence of guidance were to suggest it should be used, then it would be applied by Intensive Care Physicians working in hub/spoke networks, as opposed to being exclusively used by the Severe Acute Respiratory Failure centres. I work in such a hub hospital, and therefore would be one of those physicians that would use it.

	procedure/technology, please indicate your experience with it.	
2	– Please indicate your research experience relating to this procedure (please choose one or more if relevant):	My only involvement was in optimising an ARDS protocol for an ECCOR trial that failed to recruit 10 years ago in Singapore.
3	Does the title adequately reflect the procedure? Is the proposed indication appropriate? If not, please explain. How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	The two types of acute respiratory failure have different indications and pathogenesis. I would propose that the title reflect either “hypoxic” respiratory failure or “hypercarbic” respiratory failure. Alternatively, it may be the intention for the review to provide guidance on both. The procedure is novel and of uncertain safety and efficacy. Aside from the actual procedure itself, concerns lie with the adherence to complex interventions and treatments for respiratory failure (of either type) that should precede its use. For example, in acute hypoxic respiratory failure in COVID-19, our UK national service evaluation (https://pubmed.ncbi.nlm.nih.gov/33974106/) demonstrated many missed opportunities to optimise treatment using conventional techniques. This is important as there is higher level of invasiveness and therefore risk of complications to ECCOR use compared to ventilator optimisation, appropriate fluid management, cardiac function optimisation, and prone positioning. In regard to hypercarbic respiratory failure, the NCEPOD report suggests there is high level of misunderstanding of the current methods, indications, and monitoring that could be applied, and when to do so. This is likely to be the case for ECCOR too, which would seem best applied once conventional therapy is optimised.
4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	It would be used in addition to existing standard of care.
5	Have there been any substantial modifications to the procedure technique or,	YES, newer systems have been developed and there are several trials including the UK based REST trial

	if applicable, to devices involved in the procedure? Has the evidence base on the efficacy and safety of this procedure changed substantially since publication of the guidance?	

Current management

6	Please describe the current standard of care that is used in the NHS.	Hypoxic Resp failure: Without intubation, there are various indications for HFNO, CPAP for patients with pneumonia (COVID/not-COVID), immunocompromised, and from pulmonary oedema. With intubation, management is an escalation across processes: low tidal volume ventilation, PEEP ladders/high PEEP, NMBAs, proning and a variety of views in regards to alveolar recruitment and ECMO. Unfortunately RV/LV optimisation is patchy as bedside echocardiography is not standard in UK ICUs unlike in Europe/USA There are joint ICS/BTS guidance that exist Hypercarbic Resp failure from COPD: Is managed as per BTS COPD guidelines (nebulised bronchodilators, steroids, antibiotics if necessary, cardiac optimisation, and bilevel ventilation)

7	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	NO, though one would have thought that conventional VV-ECMO would be an alternative in the setting of refractory respiratory failure, despite the limited evidence

Potential patient benefits and impact on the health system

8	What do you consider to be the potential benefits to patients from using this procedure/technology?	IF efficacious, may prevent intubation in patients who would not survive intubation. Much easier to set up than ECMO, so could be rolled out of SARF centres, and therefore potentially more equitable and cheaper.
9	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Not clear
10	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Only if future research proves this to be true
11	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Increased ICU staffing
12	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Yes

Safety and efficacy of the procedure/technology

13	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence:	Risks are directly related to instrumentation of large vessels, or anticoagulation related

	Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	
14	Please list the key efficacy outcomes for this procedure/technology?	Mortality, cost-effectiveness
15	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	As far as I am aware there are no good data on its efficacy, and some data on safety from randomised controlled trials
16	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	The indication for use is controversial
17	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Cannot predict at present, based on staffing, but at least 10 in the UK

Abstracts and ongoing studies

18	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help	https://pubmed.ncbi.nlm.nih.gov/35445986/ https://pubmed.ncbi.nlm.nih.gov/34666820/ https://err.ersjournals.com/content/31/166/220030 would be the most informative https://thorax.bmj.com/content/early/2022/10/05/thorax-2022-218874

	us if you list any that you think are particularly important.	
19	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	The ORION trial is ongoing but I would personally struggle to see an efficacy signal being developed
20	Please list any other data (published and/or unpublished) that you would like to share.	

Other considerations

21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	Not clear to me- the incidence of ARDS is fluctuating with the current COVID-19 problems, but the ICNARC 2021 report states that 2380 patients were admitted with respiratory failure to ICUS in England, Wales and Northern Ireland (https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports/Summary-Statistics) The BTS audit report of NIV would be a key document for COPD: https://www.brit-thoracic.org.uk/quality-improvement/clinical-audit/national-adult-non-invasive-ventilation-audit-2019/
22	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post	Beneficial outcome measures: Mortality at various time points Length of Stay Delirium and Sedation use Ventilator free days Adverse outcome measures: General or Intracranial Haemorrhage Complications from cannulation

	procedure timescales over which these should be measured:	

Further comments

23	If you have any further comments (e.g. issues with usability or implementation, the need for further research), please describe.	As previously stated, I have approached this as someone who does not use ECCOR, but is a Respiratory Intensivist

NICE National Institute for Health and Care Excellence

Declarations of interests

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Type of interest *	Description of interest	Relevant dates	
		Interest arose	Interest ceased
Choose an item.			
Choose an item.			
Choose an item.			

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Please note, all declarations of interest will be made publicly available on the NICE website.

Print name:	**Zudin Puthucheary**
Dated:	**17/03/2023**