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Appendices

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Randomised controlled trial and parallel economic evaluation of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR)

GJ Peek, D Elbourne, M Mugford, R Tiruvoipati, A Wilson, E Allen, F Clemens, R Firmin, P Hardy, C Hibbert, N Jones, H Killer, M Thalanany and A Truesdale

July 2010
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Appendix 1
CESAR trial letters

Letter to GPs to allow data access including invoice

Access to GP records letter 2

Follow-up letter to patients

Follow-up letter to GPs

Letter of thanks to patients

Letter to patients allocated to treatment group who did not receive ECMO

Patient reminder letter 1

Patient reminder letter 2

Confirmation letter for patient 6-month follow-up

Information letter for carers

Letter to carer

Reminder letter to carer

Requesting 6-month follow-up appointment letter

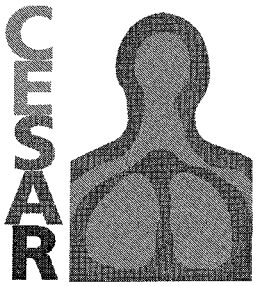
Researcher GP fax 1

Researcher GP fax 2

Letter to GPs to allow data access including invoice

CESAR Data Co-ordinating Centre
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT

tel: 020 7927 2376/2075 fax: 020 7637 2853 website: www.cesar-trial.org



ISRCTN47279827

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

address

date

Dear Dr ....

Re XXX (include nhs number if we have it)

As you may remember, the above patient is enrolled in the CESAR trial which aims to compare extra-corporeal membrane oxygenation (ECMO) with conventional treatment in severe respiratory failure. The trial includes follow up at 6 months. Xxxx advised us that he/she does not wish to be interviewed by a researcher but has agreed to us obtaining information from you. I enclose a copy of the signed consent form.

I would be grateful if you or one of your staff could help us by completing the enclosed questionnaire and returning it in the enclosed freepost envelope. Please note we are only interested in health service usage between the dates inserted at the beginning of the questionnaire.

We will pay your practice £40 as an acknowledgement of the work involved on receipt of the completed questionnaire. We will send your practice a proforma invoice to be used on your headed paper.

Yours sincerely

Koro Diallo

Data Management Co-ordinator

steve.robertson@lshtm.ac.uk

Enc: GP questionnaire

Copy of patient consent form

Freepost envelope
Proforma invoice

INVOICE

Reference Number: study number	
CESAR Trial administrative costs	£40.00

Please make the cheque payable to:-

_____

And send to (address):-

_____

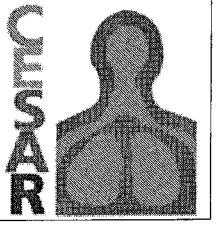
_____

_____

_____

Please return to :-

CESAR Trial Data Co-ordinating Centre
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street
FREEPOST LON20255
London
WC1 7BR

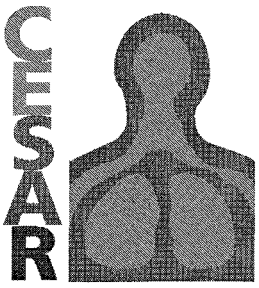


ISRCTN47279827

Access to GP records letter 2

CESAR Data Co-ordinating Centre
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT

tel: 020 7927 2376/2075 fax: 020 7637 2853 website: www.cesar-trial.org



ISRCTN47279827

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure

address

date

Dear Dr ....

Re XXX (include nhs number if we have it)

As you may remember, the above patient is enrolled in the CESAR trial which aims to compare extra-corporeal membrane oxygenation (ECMO) with conventional treatment in severe respiratory failure. The trial includes follow up at 6 months. Xxxx advised us that he/she does not wish to be interviewed by a researcher but has agreed to us obtaining information from you. I enclose a copy of the signed consent form.

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We will pay your practice £40 as an acknowledgement of the work involved on receipt of the completed questionnaire. We will send your practice a proforma invoice to be used on your headed paper.

Yours sincerely

Koro Diallo
Data Management Co-ordinator

steve.robertson@lshtm.ac.uk

Enc: GP questionnaire
Copy of patient consent form
Freepost envelope
Proforma invoice

Follow-up letter to patients

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Medical Statistics Unit
London School of Hygiene & Tropical Medicine
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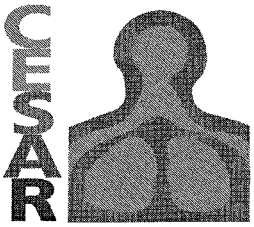


Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

ISRCTN47279827

[patient's address]

date

Dear [name of patient]

I am very pleased that you have been discharged home from hospital following your very serious illness. You may know from discussions with the doctors and nurses and from conversations with family and friends that you were enrolled in the CESAR study when in intensive care. I am now writing to give you more information about CESAR. As it is important that we consider how you are in the longer term, not just while you were in hospital, I am also asking if you will agree to have a follow-up assessment in [month that is 6 months on from date of randomisation]. This assessment is being carried out as patients and researchers feel strongly that it is very important not just to look at the short-term, but also to compare the longer-term health of people who had conventional treatment with those who had ECMO. It is very important that we follow up as many patients as possible as it is only by doing this that we will be able to tell which method of treatment is better.

Information about the study is set out below.

Why are you in the CESAR study?

As you were so seriously ill with breathing problems, the doctors were concerned that you might not survive. In cases such as yours it is not clear what the best treatment should have been. There are two possible treatments that could have been used, conventional ventilation and ECMO. There is an urgent need for new treatments. These have to be compared with the treatment that is normally used to make sure we only introduce new treatments that are a real improvement. Since we did not really know which of these two treatments would be better for you we asked permission from your relatives to include you in a study to try to find the answer.

What is the study trying to find out?

The study is comparing two ways of looking after patients with serious breathing problems.

- One way uses a ventilator to push oxygen into the lungs. We call this conventional ventilation, as it is the most common method.
- The other way uses a system called ECMO to by-pass the lungs. This is only available in one place (Leicester), and only available for the study.

At this time, we do not know if conventional ventilation is better or worse than ECMO for patients with serious breathing problems. This study is designed to help decide the best way of caring for patients with these problems so that more patients survive.

Patients from many hospitals in the UK are taking part in this NHS study which has been given research ethics committee approval. The introductory information sheet which was given to your relatives is in the pack with this letter for your information.

What happened to you as a result of being in the study?

Since we do not know which treatment is the better:

- Half the patients in the study were treated on a ventilator.
- The other half were transferred to Glenfield Hospital, Leicester to be considered for ECMO.

Once you were included in the study, neither you nor the doctors were able to choose which of these two methods was offered. Instead, this decision was made randomly and depended on chance (so-called random assignment). This element of chance is important so that the two methods can be tested fairly. Following entry into the study you were allocated [allocation]. Further information about [allocated treatment] is in the pack with this letter.

What happens now?

We plan to follow-up all patients at about six months following their entry into the study. If you agree, we will contact you again to make an appointment for a researcher working with this study to find out about your state of health. The researcher will not be medically qualified, but is professionally qualified to undertake the assessment. This assessment will take about an hour and will take place at your home (or elsewhere if this is more convenient for you).

I hope that you will agree to continue in the study. If you do not wish to be visited at home, we could arrange a telephone interview, or send the questionnaires through the post. These methods would provide us with less information, especially about your physical state, so I very much hope that you will agree to be interviewed 'face to face' at home. We would also like to obtain information about your care from your GP, and we need your permission to do this.

It is possible that we will be funded to conduct additional, longer term follow-up assessments. So that we do not lose contact with you we are asking for your agreement to send your name to an organisation called the NHS Central Register (based at the General Register Office) that holds the name of the area where you are registered with a GP. This will help us to keep in contact with you in the future. If you agree, you will not need to do anything except to tick the appropriate box on the enclosed reply slip.

In addition to all the other issues you have had to face, we are aware that illness may lead people to have extra costs. We want to understand how much your illness cost you and your family, so the researcher will also ask you about this. As an aid to your memory we have included an Events Diary which you might like to complete from the time of discharge from hospital until the assessment. Of course, all information that we collect from health service notes and directly from you and the people caring for you will be treated in the strictest confidence.

I should be very pleased if you would return the enclosed reply slip (in the freepost envelope) letting me know whether you wish or do not wish to have a follow-up visit. If you agree, the researcher will contact you in [2 months prior to visit] to arrange a time that is mutually convenient for your assessment.

We will keep you informed about the progress of the study each year unless you say that you do not want this information. When the study finishes we will ask if you would like to have a summary of the study results.

If you have any questions about CESAR or the NHS Central Register please do not hesitate to contact me.

Yours sincerely

Steven Robertson

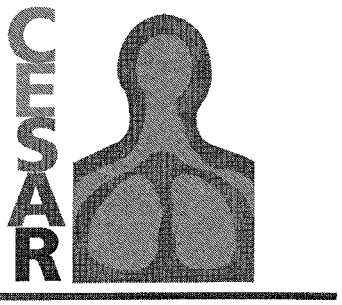
Data Management Co-ordinator

Enc: reply slip

freepost envelope

CESAR Information Pack (Events Diary, Introductory information, Information for relatives if allocation is to (allocated treatment)

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure



Agreement to participation in follow-up and access to information from your GP and the Central Register

Please complete and return this reply slip in the freepost envelope provided

Please amend or add to these details if they are wrong or incomplete

Name:	**GP's name:**
Address: (including postcode)	**GP's Address:** (including postcode)
Tel. number:	**GP's tel. number:**
NHS number: (if known)	

(Please tick appropriate box)	YES	NO
I agree to be visited at home	☐	☐
I do not wish to be assessed at home but agree to the following:	☐	☐
• A telephone interview	☐	☐
• A postal questionnaire	☐	☐
I agree to information being obtained from my GP records		
I agree for CESAR to request details from the NHS Central Register in order to keep in touch with me at a later date and to follow-up my health status	☐	☐
I would like to receive annual updates about the study	☐	☐

I would like to be asked at the end of the study whether I wish to see the results ☐ ☐

If you have agreed to any part of the follow-up please let us know how you would like us to contact you to make arrangements in the future (please tick as appropriate):

Post ☐

Telephone ☐

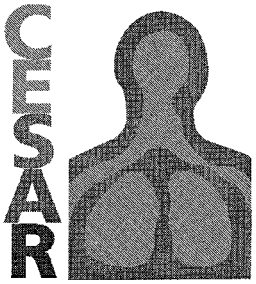
Email (please provide address) _____ ☐

Signature:_____ Date: ☐☐ ☐☐ ☐☐☐☐ dd/mm/yyyy

Follow-up letter to GPs

CESAR Data Co-ordinating Centre
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT

tel: 020 7927 2376/2075 fax: 020 7637 2853 website: www.cesar-trial.org



ISRCTN47279827

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure

[GP address]

Date

Dear [name will be personalised]

Re: [patient's name, dob: dd/mm/yyyy , CESAR study number]

[Patients's name] was recruited into The CESAR Trial on [date of randomisation at hospital]. Copies of the information leaflets which were given to [*patient's name*] relative prior to trial entry are enclosed as well as a copy of the letter which has been sent to [*patient's name]* following his/her discharge home on [*date of discharge*]. The patient's relative's assent included agreement to random allocation, access to records and follow-up at six months. However, we will only make further contact with [*patient's name*] when she/he has returned the reply slip with permission to follow-up.

All of the patients recruited into the trial were severely ill, and we will not necessarily know about their health status after they leave hospital. We will therefore want to check first that the six-month follow up is appropriate for the family at any particular time before arranging for a researcher to assess [*patient's name]* at home. The researcher is not medically qualified, but is professionally qualified to undertake the assessment. The researcher will therefore contact you shortly before this assessment is due to ask if there are any reasons why he/she should not contact [*patient's name*] to make arrangements for the assessment. Please would you check that we have the correct contact details. If the patient has directly contacted the CESAR trial office shortly before the follow-up assessment is due, the GP will not be contacted.

Please return the reply slip using the enclosed freepost envelope. Alternatively you can fax it on 020 7637 2853, or send an email message to steve.robertson@lshtm.ac.uk.

We will also be registering [*patient's name*] on the NHS central register for possible later follow-up providing she/he gives us permission to do so. We will be asking [*patient's name*] for his/her NHS number to facilitate this, but it would be very helpful if you would provide this on the reply slip in case he/she cannot easily find it.

If you wish, we will send you the results of the trial when it is completed – please indicate on the reply slip if this would be of interest to you.

If you have any questions about the enclosed, or would like any further information, please do not hesitate to get in touch with us.

With many thanks for your time and assistance.

Yours sincerely

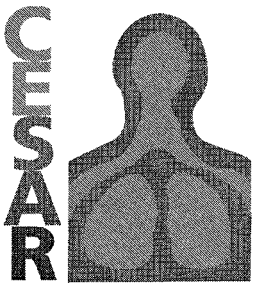
Steven Robertson

Data Management Co-ordinator

Enc: Reply slip
Copy of letter to patient

Information for relatives (introductory and allocation)
Freepost envelope

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure



GP's name: Add details
Address: Add details

Patient's name, dob: dd/mm/yyyy, CESAR study number

1. I am the GP for the above named patient.

   Yes ☐ (go to question 3)

   No ☐ (go to question 2)

2. The GP responsible for this patient is:

   Name: _____

   Address: _____

   Postcode: _____ Telephone: _____

   Thank you. Please now return this slip in the enclosed envelope

3. The following contact information for [patient's name] is correct/incorrect (please delete as applicable and amend the information below if required).

   Name: Add details
   Address: Add details

4 [Patient's name] NHS number is:_____

5. I would like to receive a copy of the CESAR Trial report when it is available

Yes ☐ No ☐

6. I would like to receive copies of the CESAR newsletter Yes ☐ No ☐

Thank you. Please now return this slip in the enclosed envelope to:

The CESAR Trial Data Co-ordinating Centre, Medical Statistics Unit

London School of Hygiene and Tropical Medicine

Keppel Street LONDON WC1E 7HT

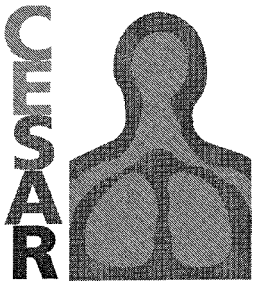
Or fax 020 7637 2853

www. cesar-trial.org

Letter of thanks to patients

CESAR Data Co-ordinating Centre
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT

tel: 020 7927 2376/2075 fax: 020 7637 2853 website: www.cesar-trial.org



ISRCTN47279827

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure

Name

Address

Date

Dear [patient's name]

Many thanks for participating in the follow-up assessment of the CESAR study on [date of visit] with [researcher name], our study researcher. Information obtained will be very helpful in determining which treatment for respiratory failure is better.

Now that you have had your follow-up assessment we would like to know if you are interested in receiving an annual update on the study and its final results. Although we asked you this in the letter we sent when you were discharged home from hospital we felt we should ask you again now that your assessment has taken place.

I am enclosing a reply slip for you to let us know whether you wish to continue receiving information about CESAR, and would be grateful if you could complete this and return it to our Data Co-ordinating Centre in London in the enclosed freepost envelope.

Once again many thanks for your help, and best wishes for the future.

Yours sincerely

Steven Robertson

Data Management Co-ordinator

Tel: 020 7927 2075

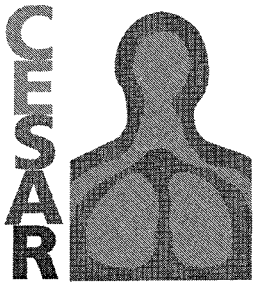
Fax: 020 7637 2853

steve.robertson@lshtm.ac.uk

Enc: Reply slip

Freepost envelope

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure



Please complete/amend if necessary

Patients name
Address
Postcode
Phone
CESAR study number

I would like to receive annual updates on CESAR Yes ☐ No ☐

I would like to be asked if I want to see the final results when they are available Yes ☐ No ☐

Signature:_____

Date: ☐☐ ☐☐ ☐☐☐☐

Please complete this reply slip and return in the freepost envelope to:

CESAR Data Co-ordinating Centre, Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

Telephone: 020 7927 2376/2075

Letter to patients allocated to treatment group who did not receive ECMO

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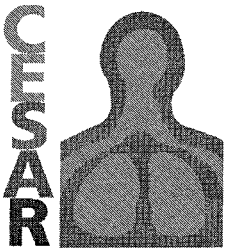
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT

tel: 020 7927 2376/2075 fax: 020 7637 2853 website: www.cesar-trial.org



Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure

[name/address]

[date]

Dear [patient name]

I am very pleased that you have been discharged home from hospital following your very serious illness. You may know from discussions with the doctors and nurses and from conversations with family and friends that you were enrolled in the CESAR study when in intensive care. I am now writing to give you more information about CESAR. As it is important that we consider how you are in the longer term, not just while you were in hospital, I am also asking if you will agree to have a follow-up assessment in [date 6 months post randomisation]. This assessment is being carried out as patients and researchers feel strongly that it is very important not just to look at the short-term, but also to compare the longer-term health of people who had conventional treatment with those who had ECMO. It is very important that we follow up as many patients as possible as it is only by doing this that we will be able to tell which method of treatment is better.

Information about the study is set out below.

Why are you in the CESAR study?

As you were so seriously ill with breathing problems, the doctors were concerned that you might not survive. In cases such as yours it is not clear what the best treatment should have been. There are two possible treatments that could have been used, conventional ventilation and ECMO. There is an urgent need for new treatments. These have to be compared with the treatment that is normally used to make sure we only introduce new treatments that are a real improvement. Since we did not really know which of these two treatments would be better for you we asked permission from your relatives to include you in a study to try to find the answer.

What is the study trying to find out?

The study is comparing two ways of looking after patients with serious breathing problems.

- One way uses a ventilator to push oxygen into the lungs. We call this conventional ventilation, as it is the most common method.
- The other way uses a system called ECMO to by-pass the lungs. This is only available in one place (Leicester), and only available for the study.

At this time, we do not know if conventional ventilation is better or worse than ECMO for patients with serious breathing problems. This study is designed to help decide the best way of caring for patients with these problems so that more patients survive.

Patients from many hospitals in the UK are taking part in this NHS study which has been given research ethics committee approval. The introductory information sheet which was given to your relatives is in the pack with this letter for your information.

What happened to you as a result of being in the study?

Since we do not know which treatment is the better:

- Half the patients in the study were treated on a ventilator.
- The other half were transferred to Glenfield Hospital, Leicester to be considered for ECMO.

Once you were included in the study, neither you nor the doctors were able to choose which of these two methods was offered. Instead, this decision was made randomly and depended on chance (so-called random assignment). This element of chance is important so that the two methods can be tested fairly. Following entry into the study you were allocated to consideration for ECMO. Further information about ECMO was given to your relatives at the time you were entered into the trial, and a copy is included in the pack with this letter. However, due to your condition improving when you arrived in Leicester it was decided not to start ECMO treatment, and conventional ventilatory management was continued. I have also enclosed information about this treatment.

What happens now?

We plan to follow-up all patients at about six months following their entry into the study. If you agree, we will contact you again to make an appointment for a researcher working with this study to find out about your state of health. The researcher will not be medically qualified, but is professionally qualified to undertake the assessment. This assessment will take about an hour and will take place at your home (or elsewhere if this is more convenient for you).

I hope that you will agree to continue in the study. If you do not wish to be visited at home, we could arrange a telephone interview, or send the questionnaires through the post. These methods would provide us with less information, especially about your physical state, so I very much hope that you will agree to be interviewed 'face to face' at home. We would also like to obtain information about your care from your GP, and we need your permission to do this.

It is possible that we will be funded to conduct additional, longer term follow-up assessments. So that we do not lose contact with you we are asking for your agreement to send your name to an organisation called the NHS Central Register (based at the General Register Office) that holds the name of the area where you are registered with a GP. This will help us to keep in contact with you in the future. If you agree, you will not need to do anything except to tick the appropriate box on the enclosed reply slip.

In addition to all the other issues you have had to face, we are aware that illness may lead people to have extra costs. We want to understand how much your illness cost you and your family, so the researcher will also ask you about this. As an aid to your memory we have included an Events Diary which you might like to complete from the time of discharge from hospital until the assessment. Of course, all information that we collect from health service notes and directly from you and the people caring for you will be treated in the strictest confidence.

I should be very pleased if you would return the enclosed reply slip (in the freepost envelope) letting me know whether you wish or do not wish to have a follow-up visit. If you agree, the researcher will contact you in [date 2 months before assessment date] to arrange a time that is mutually convenient for your assessment.

We will keep you informed about the progress of the study each year unless you say that you do not want this information. When the study finishes we will ask if you would like to have a summary of the study results.

If you have any questions about CESAR or the NHS Central Register please do not hesitate to contact me.

Yours sincerely

Steven Robertson

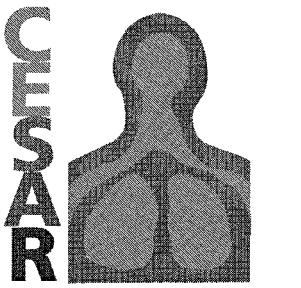
Data Management Co-ordinator

Enc: reply slip

freepost envelope

CESAR Information Pack (Events Diary, Introductory information, Information for relatives if allocation is to ECMO, Information for relatives if allocation is to conventional ventilation)

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure



Agreement to participation in follow-up and access to information from your GP and the Central Register

Please complete and return this reply slip in the freepost envelope provided

Please amend or add to these details if they are wrong or incomplete

Name:	**GP's name:**
Address: (including postcode)	**GP's Address:** (including postcode)
Tel. number:	**GP's tel. number:**
NHS number: (if known)	

(Please tick appropriate box)	Yes	No
I agree to be visited at home	☐	☐
I do not wish to be assessed at home but agree to the following:		
• A telephone interview	☐	☐
• A postal questionnaire	☐	☐
I agree to information being obtained from my GP records	☐	☐
I agree for CESAR to request details from the NHS Central Register in order to keep in touch with me at a later date and to follow-up my health status	☐	☐
I would like to receive annual updates about the study	☐	☐
I would like to be asked at the end of the study whether I wish to see the results	☐	☐

If you have agreed to any part of the follow-up please let us know how you would like us to contact you to make arrangements in the future (please tick as appropriate): ☐ ☐

Post ☐

Telephone ☐

Email (please provide address) _____ ☐

Signature:_____ Date: ☐☐ ☐☐ ☐☐☐☐ dd/mm/yyyy

Patient reminder letter 1

CESAR Data Co-ordinating Centre
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT

tel: 020 7927 2376/2075 fax: 020 7637 2853 website: www.cesar-trial.org

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

ISRCTN47279827

[address]

[date]

Dear [patient name]

Re: 6-month follow up

You may remember that I wrote to you following your discharge from hospital to see whether you would be willing to be assessed 6 months after you were enrolled in the CESAR study. I enclose a copy of my original letter.

As I have not received a reply and the time for your assessment is getting close, I am writing again to see if you are willing to take part. This assessment is being carried out as patients and researchers feel strongly that it is very important not just to look at the short-term, but also to compare the longer-term health of people who had conventional treatment with those who had ECMO. It is very important that we follow up as many patients as possible as it is only by doing this that we will be able to tell which method of treatment is better.

The assessment would take place in your home. It includes questions about your general health and quality of life, a 'blowing test' to examine your lung function, and an examination of your arm movement. It would take approximately one hour, and can be arranged at a time and date convenient to you.

If you do not wish to be assessed at home, we could arrange a telephone interview, or send the questionnaires through the post. We would also like to obtain information from your GP, and need your permission to do this.

These methods would provide us with less information, especially about your physical state, so I very much hope that you will agree to be interviewed at home, and enclose a reply slip to be returned in the enclosed freepost envelope. If you have any questions please do not hesitate to contact me.

It is possible that we will be funded to conduct additional, longer term follow-up assessments. So that we do not lose contact with you we are asking for your agreement to send your name to an organisation called the NHS Central Register (based at the General Register Office) that holds the name of the area where you are registered with a GP. This will help us to keep in contact with you in the future. If you agree, you will not need to do anything except to tick the appropriate box on the enclosed reply slip.

Yours sincerely

Steven Robertson

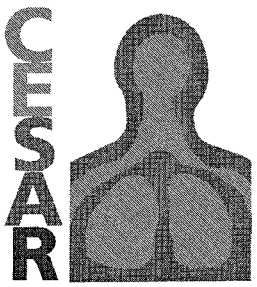
Data Management Co-ordinator

Enc: Reply slip

Copy of letter sent at discharge

Freepost envelope

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure



Agreement to participation in follow-up and access to information from your GP and the Central Register

Please complete and return this reply slip in the freepost envelope provided

Please amend or add to these details if they are wrong or incomplete

Name:	**GP's name:**
Address: (including postcode)	**GP's Address:** (including postcode)
Tel. number:	**GP's tel. number:**
NHS number: (if known)	

(Please tick appropriate box)

	Yes	No
I agree to be visited at home	☐	☐
I do not wish to be assessed at home but agree to the following:		
• A telephone interview	☐	☐
• A postal questionnaire	☐	☐
I agree to information being obtained from my GP records	☐	☐
I agree for CESAR to request details from the NHS Central Register in order to keep in touch with me at a later date and to follow-up my health status	☐	☐

	YES	NO
I would like to receive annual updates about the study	☐	☐
I would like to be asked at the end of the study whether I wish to see the results	☐	☐

If you have agreed to any part of the follow-up please let us know how you would like us to contact you to make arrangements in the future (please tick as appropriate):

Post ☐

Telephone ☐

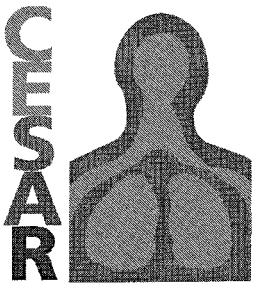
Email (please provide address) _____ ☐

Signature:_____ Date: ☐☐ ☐☐ ☐☐☐☐ dd/mm/yyyy

Patient reminder letter 2

CESAR Data Co-ordinating Centre
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street
London WC1E 7HT

tel: 020 7927 2376/2075 fax: 020 7637 2853 website: www.cesar-trial.org



ISRCTN47279827

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

address

date

Dear [patient name]

You may recall that I wrote to you recently regarding the follow-up at 6 months for the CESAR study. I have not yet received a reply from you and I appreciate that you may not wish to think about this at the present time. However, the follow-up is a very important part of the study and information obtained from it will help us to determine which treatment is better.

This assessment is being carried out as patients and researchers feel strongly that it is very important not just to look at the short-term, but also to compare the longer-term health of people who had conventional treatment with those who had ECMO. I am therefore writing to ask if you are prepared to have a follow-up visit and also to ask for your permission to obtain information about your health from your GP records.

It is possible that we will be funded to conduct additional, longer term follow-up assessments. So that we do not lose contact with you we are asking for your agreement to send your name to an organisation called the NHS Central Register (based at the General Register Office) that holds the name of the area where you are registered with a GP. This will help us to keep in contact with you in the future. If you agree, you will not need to do anything except to tick the appropriate box on the enclosed reply slip.

I would be very grateful if you could complete the enclosed reply slip and return it to me in the freepost envelope as soon as possible.

If you have any queries about CESAR or the NHS Central Register please do not hesitate to contact me.

Yours sincerely

Steven Robertson

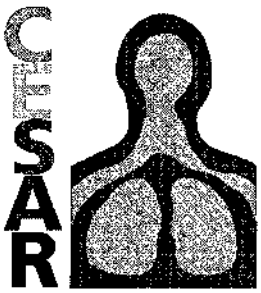
Data Management Co-ordinator

steve.robertson@lshtm.ac.uk

Enc: reply slip

freepost envelope

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure



Agreement to participation in follow-up and access to information from your GP and the Central Register

Please complete and return this reply slip in the freepost envelope provided

Name:	**GP's name:**
Address: (including postcode)	**GP's Address:** (including postcode)
Tel. number:	**GP's tel. number:**
NHS number: (if known)	

Please amend or add to these details if they are wrong or incomplete

(Please tick appropriate box)	Yes	No
I agree to be visited at home	☐	☐
I do not wish to be assessed at home but agree to the following:		
• A telephone interview	☐	☐
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I agree to information being obtained from my GP records	☐	☐
I agree for CESAR to request details from the NHS Central Register in order to keep in touch with me at a later date and to follow-up my health status.	☐	☐
I would like to receive annual updates about the study	☐	☐
I would like to be asked at the end of the study whether I wish to see the results	☐	☐

If you have agreed to any part of the follow-up please let us know how you would like us to contact you to make arrangements in the future (please tick as appropriate):

Post ☐

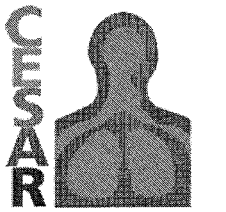
Telephone ☐

Email (please provide address) _____ ☐

Signature:_____ Date: ☐☐ ☐☐ ☐☐☐☐ dd/mm/y

Confirmation letter for patient 6-month follow-up

CESAR General Practice Advisory Group
Department of General Practice and Primary Health Care
University of Leicester
Leicester General Hospital



ISRCTN47279827

[Patient's address]

[date]

Dear [patient name]

Re: 6-month follow up

Thank you for telephoning me to discuss your CESAR follow-up visit. Thank you for agreeing to this assessment. This is being carried out as patients and researchers feel strongly that it is very important not just to look at the short-term, but also to compare the longer-term health of people who had conventional treatment with those who had ECMO.

The assessment will include questions about your general health and quality of life, a 'blowing test' to examine your lung function, and an examination of your arm movements. It is important that I do not know which treatment you received when you were in hospital. Some treatments can leave scars in the neck, and so I would like you to wear the enclosed neck scarf for the duration of the assessment when we meet.

There will also be some questions about any costs incurred by you and your family as a result of your health care since discharge. You may find it useful to refer to the Events Diary that we sent to you after discharge when answering these questions. The whole assessment will take approximately 1 hour.

I enclose two questionnaires for you to complete beforehand which I will collect at my visit. If you have any difficulties completing these we can go through them when I arrive.

I confirm that the date and time of the visit is [e.g. Tuesday 12th June 2002] at ** : ** 24 hours. Please do not hesitate to call me if you need to change this.

Yours sincerely

[research assistant's name]

CESAR Trial Research Assistant

Tel: 0116 258 4367

Fax: 0116 258 4982

email

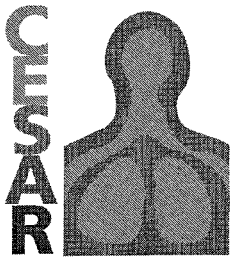
Enc: Quality of Life Questionnaire

St George's Hospital Respiratory Questionnaire

CESAR neck scarf (to be worn during assessment)

Information letter for carers

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure



INFORMATION ABOUT CESAR

[patient's name] was enrolled in the CESAR study when he/she was in intensive care with serious breathing problems. Further information about CESAR is set out below.

What is the study trying to find out?

This study is comparing two ways of looking after patients with serious breathing problems. One way uses a ventilator to push oxygen into the lungs. We call this conventional ventilation as it is the most common method. The other way uses a system called ECMO to by-pass the lungs. This is only available in one place (Leicester), and only available for this study. At this time, we do not know if conventional ventilation is better or worse than ECMO for patients with serious breathing problems. This study is designed to help decide the best way of caring for patients with these problems so that more patients survive. It involves the co-operation of many doctors and nurses in hospitals throughout the UK.

What is already known about treatments for patients with severe breathing problems?

Conventional ventilation

One advantage of staying on this method is that there is usually no need to move very ill patients out of their local intensive care unit. This form of care is currently considered the best standard care, and has been used for many years. This means that the staff are very experienced in using it. However, using a ventilator to give oxygen at high pressure over a long period of time causes some lung damage to patients who already have breathing problems.

ECMO (extra-corporeal membrane oxygenation)

ECMO involves an operation (under anaesthetic) to set up a temporary by-pass for the patient's lungs. While on ECMO, patients stay on very gentle ventilation which may

help the lungs recover. Glenfield Hospital in Leicester is the only UK hospital with a reasonable length of experience in using ECMO for adults, so patients may have to be transferred some distance. Transferring very ill patients may be risky, but despite this ECMO may well be helpful. The early results of using ECMO appear promising. However, we are not yet sure whether ECMO is better or worse than conventional ventilation. So while it is being investigated, ECMO is only available in this study.

What does being in the study involve?

- Half the patients in the study will continue to be treated on a ventilator.
- The other half will be transferred to Glenfield Hospital, Leicester to be considered for ECMO.

Once in the study, the patient's treatment is decided by chance, rather like the toss of a coin. This element of chance is important so that the two methods can be tested fairly. The doctor calls a central office and is told which of the two treatments will be given. If the patient is assigned to have ECMO, then transfer to Leicester will be required. An experienced transport team comes from the ECMO Unit to transfer the patient. The quickest and safest type of transport will be arranged. This is usually either an ambulance or a helicopter.

We send written information to patients when they are discharged home.

CESAR Data Co-ordinating Centre

Medical Statistics Unit

London School of Hygiene and Tropical Medicine

Keppel Street

London WC1E 7HT

Tel: 020 7927 2376/2075

Fax: 020 7637 2853

Website: www . c e s a r- t r i a l . o r g

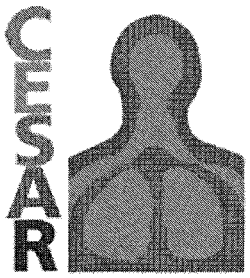
Letter to carer

CESAR General Practice Advisory Group

Department of General Practice and Primary Health Care

University of Leicester

Leicester General Hospital



ISRCTN47279827

Name

Address

Date

Dear [carer's name]

[patient's name] is enrolled in the CESAR study which aims to compare a new technique (extra-corporeal membrane oxygenation, known as ECMO) with usual treatment in patients with severe respiratory failure. The study includes a follow-up visit 6 months after the start of treatment. This assessment is conducted by a researcher at the patient's home.

The follow-up is being carried out as patients and researchers feel strongly that it is very important not just to look at the short-term, but also to compare the longer-term health of people who had conventional treatment with those who had ECMO.

When [patient's name] was assessed at home 6 months after joining the study he/she named you as his/her carer. We are interested in the impact the care you are providing is having on you, and so would be very grateful if you could complete the enclosed questionnaire and return it in the freepost envelope provided. The information you provide will be treated with the strictest confidence and will not be made available to the person you care for.

I enclose for your interest a short description of the study. Many thanks for your help.

Yours sincerely

[research assistant's name]

CESAR Study Research Assistant

Tel: 0116 258 4367

Fax: 0116 258 4982

email

Enc: Caregiver Strain Index (CSI) questionnaire

Freepost envelope

Information about CESAR

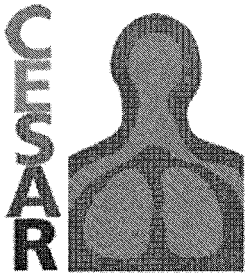
Reminder letter to carer

CESAR General Practice Advisory Group

Department of General Practice and Primary Health Care

University of Leicester

Leicester General Hospital



ISRCTN47279827

Name

Address

Date

Dear [carer's name]

You may remember a few weeks ago we asked for your help in completing a short questionnaire on your role as carer.

We have not yet received a reply, and would be very grateful if you could find the time to complete the questionnaire. A further copy is also enclosed.

We think it is very important to assess the impact of treatments on carers, and hope you will be able to help us in this way.

Yours sincerely

[research assistant's name]

CESAR Study Research Assistant

Tel: 0116 258 4367

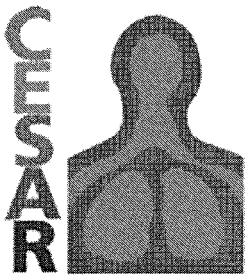
Fax: 0116 258 4982

email

Enc: Caregivers Strain Index (CSI) questionnaire

Freepost envelope

Requesting 6-month follow-up appointment confirmation letter



CESAR General Practice Advisory Group

Department of General Practice and Primary Health Care

University of Leicester

Leicester General Hospital

ISRCTN47279827

[Patient's address]

[date]

Dear [patient name]

Re: 6-month follow up

Thank you for agreeing to this assessment. This is being carried out as patients and researchers feel strongly that it is very important not just to look at the short-term, but also to compare the longer-term health of people who had conventional treatment with those who had ECMO.

The assessment will include questions about your general health and quality of life, a 'blowing test' to examine your lung function, and an examination of your arm movements. It is important that I do not know which treatment you received when you were in hospital. Some treatments can leave scars in the neck, and so I would like you to wear the enclosed neck scarf for the duration of the assessment when we meet.

There will also be some questions about any costs incurred by you and your family as a result of your health care since discharge. You may find it useful to refer to the Events Diary that we sent to you after discharge when answering these questions. The whole assessment will take approximately 1 hour.

The proposed date and time of the visit is [e.g. Tuesday 12th June 2002] at ** : ** 24 hours. Please contact me on the telephone number below to confirm this suits you, or to rearrange the visit if the proposed date and time is not convenient. When we have arranged a convenient time I will send an appointment confirmation letter to you with further details about the visit.

Yours sincerely

[research assistant's name]

CESAR Trial Research Assistant

Tel: 0116 258 4367

Fax: 0116 258 4982
email

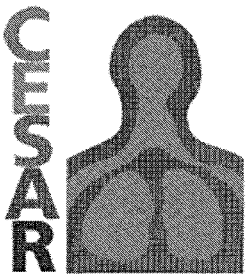
Researcher GP fax 1

CESAR General Practice Advisory Group

Department of General Practice and Primary Health Care

University of Leicester

Leicester General Hospital



ISRCTN47279827

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

FACSIMILE COVER SHEET

Date:

To: [patient's GP]

From:

Fax Number: [GP's fax number]

Subject: [patient's name, DoB and CESAR study number]

.....

Dear Dr ----------

As you may remember, the above patient is enrolled in the CESAR trial which aims to compare extra-corporeal membrane oxygenation (ECMO) with conventional treatment in severe respiratory failure. The trial includes follow up at 6 months post-randomisation with an assessment conducted by a researcher at the patient's home. [patient's name] is due to be assessed very soon. I have the following details for [patient's name]:

[address and telephone number]

I will be ringing the surgery in the next couple of days to check these are correct and that [patient's name] is still registered with you.

I would also be grateful if you could let me know of any reason you think it might be inappropriate to contact [patient's name] regarding the follow-up assessment, and whether there is any contraindication for spirometry (as listed below).

The patient has consented to the CESAR study obtaining information from GP records and a signed copy is held at the CESAR office. Thank you in advance for your help.

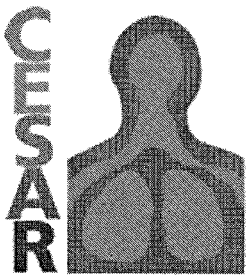
Sincerely

[researcher's name]

CONTRAINDICATIONS FOR SPIROMETRY

- Angina
- MI in last 6 weeks
- Poorly controlled hypertension
- Aortic aneurysm
- Surgery in last 6 weeks

Researcher GP fax 2



FACSIMILE COVER SHEET

CESAR General Practice Advisory Group

Department of General Practice and Primary Health Care

University of Leicester

Leicester General Hospital

ISRCTN47279827

Date:

To: [patient's GP]

From:

Fax Number: [GP's fax number]

Subject: [patient's name, DoB and CESAR study number]

.....

Dear Dr ---------

As you may remember, the above patient is enrolled in the CESAR trial which aims to compare extra-corporeal membrane oxygenation (ECMO) with conventional treatment in severe respiratory failure. The trial includes follow up at 6 months post-randomisation with an assessment conducted by a researcher at the patient's home. [patient's name] is due to be assessed very soon. I have the following details for [patient's name]:

[address and telephone number]

I will be ringing the surgery in the next couple of days to check these are correct and that [patient's name] is still registered with you.

I would also be grateful if you could let me know of any reason you think it might be inappropriate to contact [patient's name] regarding the follow-up assessment, and whether there is any contraindication for spirometry (as listed below).

The patient has consented to the CESAR study obtaining information from GP records and a signed copy is attached for your information. Thank you in advance for your help.

Sincerely

[researcher's name]

CONTRAINDICATIONS FOR SPIROMETRY

- Angina
- MI in last 6 weeks
- Poorly controlled hypertension
- Aortic aneurysm
- Surgery in last 6 weeks

Appendix 2
CESAR trial datasheets

Guidelines for interviewing a patient in hospital at 6 months

Guidelines for conducting 6-month follow-up

Patient summary sheet

EQ-5D Health Questionnaire

HAD Scale

St George's Hospital Respiratory Questionnaire

SF-36 v2 Health Survey

Additional questions and examination

Assent form (Leicester 2003)

Assent form

Registration form A

Registration form – Clinical Advisory Team (form B)

Entry form C

Glenfield Transport Team form A

Transfer outcome sheet

Level of organ support

Events diary

Events diary additional information

Patient costs questionnaire

Economic questions if visited in hospital

Caregiver strain index

6-month follow-up assessment checklist

Health service use of patients in CESAR trial

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure

ISRCTN47279827

Guidelines for interviewing a patient in hospital at 6 months

Questionnaire order for people in hospital - advice on specific questions

1. EQ-5D

Question 3, page 1: Usual activities: ask this question, expect patient to answer
"I am unable to perform my usual activities"

2. Physical examination

Arm movements, Spirometer
Ask how tall they are if they are unable to stand – Spirometer measurements are every 5cm anyway, so does not have to be 100% accurate

3. Additional questions

Sleep questions – as normal

4. SGRQ

Part 1
Replace "Since returning home" with "since leaving intensive care".

Part 2
Section 2, 4, 6 and 7– try to relate activities to what they may be doing in hospital e.g. walking about ward, walking up stairs in ward.

5. SF-36

Question 3 apply to hospital situation, as for SGRQ
Question 4, 5 and 10 expect patient to say "all of time". Question 6 "extremely"

6. HAD

As normal

7. MMSE

As normal

8. Economic questions

2 page questionnaire replacing patient costs questionnaire

9. Carer questionnaire

Does not apply

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

ISRCTN47279827

Guidelines for researchers conducting a 6 month follow-up assessment

Outline

Survivors at 6 months post randomisation will be assessed and examined at home by a researcher. In cases where this is not possible a telephone interview will be attempted. When a patient has agreed to the 6 month follow-up an assessment pack is sent to the researcher in Leicester by the Data Co-ordinating Centre in London. The patient's GP should be contacted by the researcher, on receipt of the assessment pack, to check that the patient is still alive, registered with that GP and that there are no reasons why it would be inappropriate to contact the patient. The researcher is then responsible for (in liaison with Hillary Watkinson):

- arranging the appointment with the patient (using the method indicated on the patient summary sheet)
- sending the confirmation letter (with the EQ-5D and SGHRQ to be completed and collected at the visit)
- notifying Steven Robertson at the Data Co-ordinating Centre of the appointment details.

In order to avoid researchers accidentally finding out patient allocation, all appointment arrangements will be made by Hillary Watkinson, in liaison with Steven Robertson and the assessment researchers.

The patient will also be sent a scarf to conceal any scars, so the researcher remains blinded to allocation. The patient will be asked to return the scarf in a freepost envelope after the researcher has left. During the visit the researcher will assess whether the patient has a carer and, if relevant, details will be collected on the 6 month follow-up assessment checklist. If a carer has been identified, and is present, a Caregiver Strain Index questionnaire will be given and the carer will be asked to complete this and return either before the researcher leaves or at a later date in a freepost envelope. If the carer is not present the researcher will write to the carer asking him/her to complete and return the questionnaire. When the interview has been conducted the researcher should photocopy all of the documents, complete the 6 month follow-up assessment checklist, and send the copies in the envelope provided to:

Steven Robertson

CESAR Data Co-ordinating Centre

Medical Statistics Unit

London School of Hygiene & Tropical Medicine

Keppel Street

London WC1E 7HT

The originals of <u>all</u> documents should be kept in the CESAR folder at the Department of General Practice and Primary Health Care at the University of Leicester.

Interview pack contents:

- Guidelines for conducting a 6 month follow-up
- Guidelines for researchers
- Patient summary sheet
- EQ-5D (send with confirmation letter)
- St George's Hospital Respiratory Questionnaire (send with confirmation letter)
- The SF-36v2™ Health Survey
- HAD Scale
- Patient Costs Questionnaire
- Additional questions and examination (including spirometry)
- Caregiver Strain Index
- 6 month follow-up assessment checklist
- Copy of signed patient agreement to CESAR accessing patient data from GP records

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

ISRCTN47279827

CESAR 6-month follow-up: Guidelines for researchers

1. Introduction to patients

- Reinforce purpose of assessment – to assess long term outcomes for two different ways of treating respiratory failure.
- Recognise that patient has been very ill and they should say if they are feeling too tired to continue or would like to take a break.
- Emphasise the need not to know where or how patient was treated so researcher cannot be biased, hence the need for scarf to be worn for the duration of the assessment.
- Tell patient that interview will include a series of questions about specific aspects of their health and an assessment of their breathing. Some questions may not seem relevant to them but important all are answered so we can compare patients in the trial.
- If the patient is followed up in hospital please refer to ***Guidelines for interviewing a patient in hospital at 6 months July 2004*** for specific guidelines

2. Questionnaires sent to patients (if patient is in hospital these may not be posted but completed at interview instead)

- Check EQ-5D and SGRQ received.
- Ask if any problems completing and check responses.
- Ask patient to fill in any incomplete responses.

3. SF-36

- Explain this is a questionnaire designed to measure general health and whether there are any problems with activities, and that it was designed for self-completion.
- If patient asks for clarification re-read the question and response options but do not reword question (see detailed guidance in photocopy of chapter 4 from SF-36 manual).
- Check for completeness of responses and draw attention of patient to any omissions.

4. HAD Scale

- Explain that treatment in intensive care may affect the way people feel and that this self-completed questionnaire is designed to detect them.
- Respond to queries in same way as for SF-36.
- Please calculate the HAD score and enter onto the datasheet

5. Additional questions and examination

5.1 Sleep questions

- Explain sleep problems can occur after intensive care and that these questions are designed to detect them.
- Read questions and record responses.

5.2, 5.3 Examination

- Explain that you would now like to make a brief examination. Arm movement can be affected by intensive care treatments, so you would like to check this (no need for patient to undress). Secondly, you would like to test breathing, and finally measure height, as this determines their breathing scores.
- Show card to check no contraindications to spirometry.
- Repeat test until 3 readings which differ <10% obtained.
- Circle best of three for each variable.
- Calculate and record predicted values.

5.4 MMSE (use pad version)

- Explain some patients experience confusion after intensive care and that this is a standard questionnaire to detect it. Some of the questions may seem inappropriate but it is important that all are answered.
- Some of the questions are very easy, some are not so easy. Don't worry if you think you have "got any wrong".
- It is important to reassure the patient, as anxiety can affect performance.
- Aim to be neutral in feedback e.g. "thank you" not "yes that's right", or "no, that's wrong".
- If the patient gets distressed at being asked the questions, it is up to the interviewer's discretion whether you stop or not.

Guide to completing MMSE

Question 1	Season – use discretion e.g. different cultures have different seasons, may not know exactly when spring ends and summer begins.
Question 2	"Building/floor" – asking address is OK.
Question 3	"Apple, table penny", the order in which the patient repeats them is irrelevant.
Question 4	Ask the patient to spell "world" forwards If they don't understand the word describe it. If OK, then ask them to spell it backwards.
Question 8	Read out instruction all in one go, no prompts
Questions 9 and 10	If physically unable to write, read or is illiterate, then score out of 29 or 28.

6. Patient costs questionnaire

- Read out interviewer script on front page.
- Ask patient if they would prefer you to read out questions or complete it themselves.
- Note whether Events Diary was used on the checklist
- If patient fatigued offer later telephone administration and note on checklist.

7. Identifying carers

- Identify if patient has a carer, if yes record details on checklist
- If carer is present give them a Caregiver Strain Index questionnaire and ask to complete during visit.
- Give carer a freepost envelope in case they prefer to return at a later date
- If carer identified but not present collect details on checklist and write to them asking to complete the Caregiver Strain Index questionnaire.
- The patient should not see or be given a copy of the Caregiver Strain Index.

8. Finishing the interview

- Thank patient for their time and attention.
- Remind them that they will receive a copy of the trial results if requested.
- Remind the patient to keep the scarf on until after you have left and give the patient the freepost envelope to return it in.
- Note duration of interview on the checklist.
- Complete checklist and return a copy to DCC in London with copies of all other documents.

9. Potential problems

- Patient cannot read but is not mentally impaired. Administer all questionnaires orally.
- Patient appears too frail/unco-operative – restrict interview to EQ-5D, physical examination and SF-36 in that order.

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

ISRCTN47279827

Patient summary sheet

CESAR study number: **Date of birth:** ☐☐ ☐☐ ☐☐☐☐ dd/mm/yyyy

Surname:
First name:

Date of randomisation: ☐☐ ☐☐ ☐☐☐☐ dd/mm/yyyy

Date of discharge: ☐☐ ☐☐ ☐☐☐☐ dd/mm/yyyy

Address: **Postcode:** **Telephone number:** **NHS number:** **GP's name:** **GP's address:** **Postcode:** **GP's telephone number:** **GP's fax number:**	

Method by which patient has requested contact:

Date 6 month assessment due: ☐☐ ☐☐ ☐☐☐☐ dd/mm/yyyy
(approximately 6 months post randomisation)

Date researcher should contact patient to make appointment: ☐☐ ☐☐ ☐☐☐☐ dd/mm/yyyy
(approximately 2 months before assessment is due)

Please contact GP before making direct contact with patient

EQ-5D Health Questionnaire

CESAR study number ☐☐☐☐☐☐

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ☐
I have some problems in walking about ☐
I am confined to bed ☐

Self-care

I have no problems with self-care ☐
I have some problems washing or dressing myself ☐
I am unable to wash or dress myself ☐

Usual Activities *(e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ☐
I have some problems with performing my usual activities ☐
I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐
I have moderate pain or discomfort ☐
I have extreme pain or discomfort ☐

Anxiety/Depression

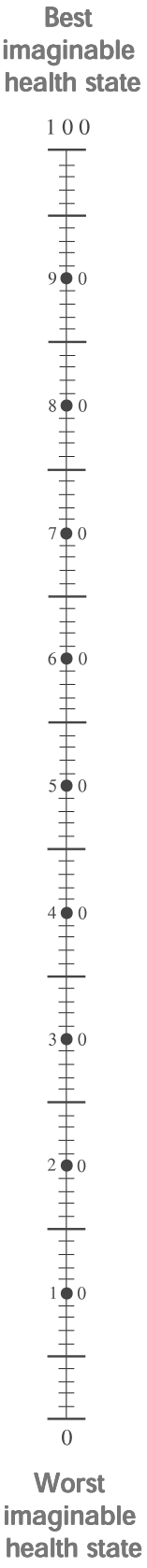
I am not anxious or depressed ☐
I am moderately anxious or depressed ☐
I am extremely anxious or depressed ☐

CESAR study number ☐☐☐☐☐☐

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by marking a point on the scale which indicates how good or bad your health state is today.

Your own health state today



CESAR study number ☐☐☐☐☐☐

Background Information

1. Are you

a current smoker	☐
an ex smoker	☐
a never smoker	☐

2. Which of the following best describes your main activity?

in employment or self employment	☐
retired	☐
housework	☐
student	☐
seeking work	☐
other (please specify) _____	☐

	Yes	No
3. Did your education continue after the minimum school leaving age?	☐	☐
4. If Yes, do you have a degree or equivalent qualification?	☐	☐

Please complete this form and return it to the researcher when you have your assessment visit.

HAD Scale

CESAR study number ☐☐☐☐☐

Tick only one box for each question

I feel tense or 'wound up':

- Most of the time ☐
- A lot of the time ☐
- Time to time, occasionally ☐
- Not at all ☐

I still enjoy the things I used to enjoy:

- Definitely as much ☐
- Not quite so much ☐
- Only a little ☐
- Hardly at all ☐

I get a sort of frightened feeling as if something awful is about to happen:

- Very definitely and quite badly ☐
- Yes, but not too badly ☐
- A little, but it doesn't worry me ☐
- Not at all ☐

I can laugh and see the funny side of things:

- As much as I always could ☐
- Not quite so much now ☐
- Definitely not so much now ☐
- Not at all ☐

Worrying thoughts go through my mind:

- A great deal of the time ☐
- A lot of the time ☐
- From time to time but not too often ☐
- Only occasionally ☐

I feel cheerful:

- Not at all ☐
- Not often ☐
- Sometimes ☐
- Most of the time ☐

I can sit at ease and feel relaxed:

- Definitely ☐
- Usually ☐
- Not often ☐
- Not at all ☐

I feel as if I am slowed down:

- Nearly all the time ☐
- Very often ☐
- Sometimes ☐
- Not at all ☐

I get a sort of frightened feeling like 'butterflies' in the stomach:

- Not at all ☐
- Occasionally ☐
- Quite often ☐
- Very often ☐

I have lost interest in my appearance:

- Definitely ☐
- I don't take so much care as I should ☐
- I may not take quite as much care ☐
- I take just as much care as ever ☐

I feel restless as if I have to be on the move:

- Very much indeed ☐
- Quite a lot ☐
- Not very much ☐
- Not at all ☐

I look forward with enjoyment to things:

- As much as ever I did ☐
- Rather less than I used to ☐
- Definitely less than I used to ☐
- Hardly at all ☐

I get sudden feelings of panic:

- Very often indeed ☐
- Quite often ☐
- Not very often ☐
- Not at all ☐

I can enjoy a good book or radio or TV programme:

- Often ☐
- Sometimes ☐
- Not often ☐
- Very seldom ☐

For office use only: D (8-10)_ _ _ _ _ _ _ A (8-10)_ _ _ _ _ _ _

The St George's Hospital Respiratory Questionnaire (SGHRQ)

This questionnaire is designed to help us learn much more about how your breathing is troubling you and how it affects your life. We are using it to find out which aspects of your illness cause you most problems rather than what doctors and nurses think your problems are. Please read the instructions carefully but do not spend too long deciding about your answers. If there is anything you do not understand please ask the researcher at the time of the interview.

CESAR study number ☐☐☐☐☐☐

CESAR study number ☐☐☐☐☐☐

PART 1

Questions about how much chest trouble you have had since returning home.
Please put a cross in one bubble for each question.

	most days a week	several days a week	a few days a month	only with chest infections	not at all
1) Since returning home, I have coughed	◯	◯	◯	◯	◯
2) Since returning home, I have brought up phlegm (sputum)	◯	◯	◯	◯	◯
3) Since returning home, I have had shortness of breath	◯	◯	◯	◯	◯
4) Since returning home, I have had attacks of wheezing	◯	◯	◯	◯	◯

5) Since returning home, how many severe or very unpleasant attacks of chest trouble have you had?

a) More than 3 attacks ◯
b) 3 attacks ◯
c) 2 attacks ◯
d) 1 attack ◯
e) No attacks ◯ (please go to question 7)

6) How long did the worst attack of chest trouble last?

a) A week or more ◯
b) 3 or more days ◯
c) 1 or 2 days ◯
d) Less than a day ◯

7) Since returning home, in an average week, how many good days (with little chest trouble) have you had?

a) None ◯
b) 1 or 2 ◯
c) 3 or 4 ◯
d) Nearly every day ◯

CESAR study number ☐☐☐☐☐☐

8) If you have a wheeze, is it worse in the morning?

No ◯ Yes ◯ Not applicable ◯

.....

PART 2

The questions in this section relate to your current state of health and should reflect how you are these days.

Section 1

1) How would you describe your chest condition (please put a cross in 1 box)?

a) The most important problem I have ◯
b) Causes me quite a lot of problems ◯
c) Causes me a few problems ◯
d) Causes no problems ◯

2) If you were in paid employment around the time you were entered into the CESAR trial, please put a cross in one of the boxes below to tell us about the effect on your current situation.

a) My chest trouble made me stop paid work altogether ◯
b) My chest trouble interfered with my work or made me change my work ◯
c) My chest trouble does not affect my work ◯
d) Not applicable as I was not in paid work at the time ◯

Section 2

Questions about what activities usually make you feel breathless. Please put a cross in each box **that applies to you** these days.

a) Sitting or lying still ◯
b) Getting washed or dressed ◯
c) Walking around the home ◯
d) Walking outside on the level ◯
e) Walking up a flight of stairs ◯
f) Walking up hills ◯
g) Playing sports or games ◯

Section 3

Some more questions about your cough and breathlessness. Please put a cross in each box that applies to you these days.

a) My cough hurts ◯
b) My cough makes me tired ◯
c) I am breathless when I talk ◯
d) I am breathless when I bend over ◯
e) My cough or my breathing disturbs my sleep ◯
f) I get exhausted easily ◯

CESAR study number ☐☐☐☐☐☐

Section 4

Questions about other effects that your chest trouble may have on you.
Please put a cross in each box that applies to you these days.

a) My cough or breathing is embarrassing in public ◯
b) My chest trouble is a nuisance to my family, friends and neighbours ◯
c) I get afraid or panic when I cannot get my breath ◯
d) I feel that I am not in control of my chest problem ◯
e) I do not expect my chest to get any better ◯
f) I have become frail or an invalid because of my chest problem ◯
g) Exercise is not safe for me ◯
h) Everything seems too much of an effort ◯

Section 5

Questions about your medication for your chest trouble. Please put a cross in each box that applies to you.

a) My medication does not help me very much ◯
b) I get embarrassed using my medication in public ◯
c) I have unpleasant side effects from my medication ◯
d) My medication interferes with my life a lot ◯
e) I am receiving no medication for my chest trouble ◯

Section 6

These are questions about how your activities might be affected by your breathing trouble. Please put a cross in each box which you think applies to you because of your breathing trouble.

a) I take a long time to get washed or dressed ◯
b) I cannot take a bath or shower or I take a long time ◯
c) I walk slower than other people or I stop for rests ◯
d) Jobs such as housework take a long time or I have to stop for rests ◯
e) If I walk up one flight of stairs I have to go slowly or stop ◯
f) If I hurry or walk fast I have to stop or slow down ◯
g) My breathing makes it difficult to do things such as walking up hills, carrying things upstairs, light gardening such as weeding, dance, play bowls or play golf ◯
h) My breathing makes it difficult to do things such as carrying heavy loads, dig the garden or shovelling snow, jog or walk at 5 miles per hour, play tennis or swim ◯
i) My breathing makes it difficult to do things such as very heavy manual work, run, cycle, swim fast or play competitive sports ◯

CESAR study number ☐☐☐☐☐☐

Section 7

We would like to know how your chest trouble usually affects your daily life.
Please put a cross in each box that applies to you because of your chest trouble.

a) I cannot play sports or games ◯
b) I cannot go out for entertainment or recreation ◯
c) I cannot go out of the house to do the shopping ◯
d) I cannot do housework ◯
e) I cannot move far from my bed or chair ◯

Now please put a cross in the box next to the statement which best describes how your chest trouble affects you.

a) It does not stop me doing anything I would like to do ◯
b) It stops me doing one or two things I would like to do ◯
c) It stops me doing most of the things I would like to do ◯
d) It stops me doing everything I would like to do ◯

Please complete this form and return it to the researcher when you have your assessment visit.

The SF-36v2™ Health Survey

Instructions for completing the questionnaire

Please answer every question. Some questions may look like others, but each one is different. Please take time to read and answer each question carefully by putting a cross in the bubble that best represents your response.

EXAMPLE

This is an example. Do not answer this question. The questionnaire begins with the section *Your Health in General* on the next page.

For each question you will be asked to place a cross in a bubble on each line:

1. How strongly do you agree or disagree with each of the following statements?

	Strongly agree	Agree	Uncertain	Disagree	Strongly Disagree
a) I enjoy listening to music	○	⊗	○	○	○
b) I enjoy reading magazines	⊗	○	○	○	○

CESAR study number ☐☐☐☐☐☐

CESAR study number ☐☐☐☐☐☐

Your Health in General

1. In general, would you say your health is:

Excellent	Very Good	Good	Fair	Poor
○	○	○	○	○

2. **Compared to one year ago**, how would you rate your health in general **now**?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
○	○	○	○	○

3. The following questions are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

		Yes, limited a lot	Yes, limited a little	No, not limited at all
a)	**Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	○	○	○
b)	**Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	○	○	○
c)	Lifting or carrying groceries	○	○	○
d)	Climbing **several** flights of stairs	○	○	○
e)	Climbing **one** flight of stairs	○	○	○
f)	Bending, kneeling or stooping	○	○	○
g)	Walking more than a **mile**	○	○	○
h)	Walking **several** hundred yards	○	○	○
i)	Walking **one** hundred yards	○	○	○
j)	Bathing or dressing yourself	○	○	○

CESAR study number ☐☐☐☐☐☐

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Cut down on the amount of time you spent on work or other activities	○	○	○	○	○
b) Accomplished less than you would like	○	○	○	○	○
c) Limited in the kind of work or other activities	○	○	○	○	○
d) Had difficulty performing the work or other activities (e.g. it took extra effort)	○	○	○	○	○

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Cut down on the **amount of time** you spent on work or other activities	○	○	○	○	○
b) **Accomplished less** than you would like	○	○	○	○	○
c) Did work or other activities **less carefully than usual**	○	○	○	○	○

6. During the past 4 weeks, to what extent have your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or groups?

Not at all ○ Slightly ○ Moderately ○ Quite a bit ○ Extremely ○

7. How much bodily pain have you had during the past 4 weeks?

None ○ Very mild ○ Mild ○ Moderate ○ Severe ○ Very severe ○

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all ○ A little bit ○ Moderately ○ Quite a bit ○ Extremely ○

CESAR study number ☐☐☐☐☐☐

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) did you feel full of life?	○	○	○	○	○
b) have you been very nervous?	○	○	○	○	○
c) have you felt so down in the dumps nothing could cheer you up?	○	○	○	○	○
d) have you felt calm and peaceful?	○	○	○	○	○
e) did you have a lot of energy?	○	○	○	○	○
f) have you felt downheartened and depressed?	○	○	○	○	○
g) did you feel worn out?	○	○	○	○	○
h) have you been happy?	○	○	○	○	○
i) did you feel tired?	○	○	○	○	○

10. During the past 4 weeks, how much of the time have your physical or emotional problems interfered with your social activities (like visiting friends, relatives etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
○	○	○	○	○

11. How TRUE or FALSE is each of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a) I seem to get sick a little easier than other people	○	○	○	○	○
b) I am as healthy as anybody I know	○	○	○	○	○
c) I expect my health to get worse	○	○	○	○	○
d) My health is excellent	○	○	○	○	○

Thank you for taking time to complete this questionnaire, please now return it to the researcher.

Additional Questions and Examination

CESAR study number ☐☐☐☐☐☐

1. Sleep Questions (FLP)

These statements describe your sleep and rest activities today.
If **AGREE, PROBE - "Is this due to your health?"**

		Yes	No	If yes, is this due to your health? Yes	No
a)	I spend much of the day lying down to rest	☐	☐	☐	☐
b)	I sit for much of the day	☐	☐	☐	☐
c)	I sleep or doze most of the time, day and night	☐	☐	☐	☐
d)	I lie down to rest more often during the day	☐	☐	☐	☐
e)	I sit around half asleep	☐	☐	☐	☐
f)	I sleep less at night; for example I wake up easily, I don't fall asleep for a long time or I keep waking up	☐	☐	☐	☐
g)	I sleep or doze more during the day	☐	☐	☐	☐

2. Upper Limb Movement

			Yes	No
Is there a history of trauma to or pre-existing restriction of upper limbs?			☐	☐
If No:	a)	Can patient join hands behind back?	☐	☐
	b)	Can patient join hands behind head?	☐	☐
	c)	Can patient fully extend both arms?	☐	☐

CESAR study number ☐☐☐☐☐☐

3. Lung Capacity

Please allow the patient **3** attempts using the spirometer and record all 3 values for FEV_1, FVC, FER and PEF. Please then circle the **best** score for each.

	Predicted values				
FEV_1	☐.☐☐	☐.☐☐	☐.☐☐	☐.☐☐	litres
FVC	☐.☐☐	☐.☐☐	☐.☐☐	☐.☐☐	litres
FER	☐☐☐	☐☐☐	☐☐☐	☐☐☐	%
PEF	☐☐☐	☐☐☐	☐☐☐	☐☐☐	litres/min
Height of patient		☐☐☐ cms			

Was new spirometer used? ☐ Yes ☐ No

4. Mini-Mental State Examination (MMSE) score

(please refer to the MMSE handout for details) ☐☐

University Hospitals of Leicester NHS
NHS Trust

ASSENT FORM

Assent by relative to participation in a clinical trial

Title of Project:
CESAR: Conventional ventilation or ECMO for Severe Adult Respiratory failure: A Collaborative Randomised Controlled Trial

PATIENT NAME: _____ Please initial the boxes

1. I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions. ☐
2. I understand that my relative's participation in this trial is voluntary and that he/she is free to withdraw at any time, without giving any reason, without his/her medical care or legal rights being affected. ☐
3. I understand that sections of my relative's medical notes may be looked at by responsible individuals from The CESAR Trial or from regulatory authorities where it is relevant to my relative's participation in research. I give permission for these individuals to have access to my relative's records. ☐
4. I understand and acknowledge that the investigation is designed to add to medical knowledge. I acknowledge that the purpose of the investigation, the risks involved from drugs or other procedures, and the nature and purpose of such procedures have been explained to me by discussion with the doctor caring for my relative. I have had the opportunity to discuss these matters with them. ☐
5. I have received a written explanation of these matters. ☐
6. I agree for my relative to take part in the above study and believe that my relative would not object to taking part in the study. ☐

Name of relative/next of kin who is giving assent	Date	Signature
_____	_____	_____
Name of assenting doctor	Date	Signature
_____	_____	_____
Name of assenting nurse	Date	Signature
_____	_____	_____

Please make 2 copies of this form. Send 1 copy to the CESAR Data Co-ordinating Centre, file 1 copy in the CESAR folder and keep the original with the patient's note.

Conventional Ventilation or
ECMO for
Severe
Adult
Respiratory Failure

ASSENT FORM

Assent by relative to participation in a clinical trial

Title of Project:

CESAR: Conventional ventilation or ECMO for Severe Adult Respiratory failure: A Collaborative Randomised Controlled Trial

PATIENT NAME: _____ Please initial the boxes

1. I confirm that I have read and understand the information sheet for the above study and have had the opportunity to ask questions. ☐
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5. I have received a written explanation of these matters. ☐
6. I agree for my relative to take part in the above study and believe that my relative would not object to taking part in the study. ☐

Name of relative/next of kin who is giving assent	Date	Signature
_____	_____	_____
Name of assenting doctor	Date	Signature
_____	_____	_____
Name of assenting nurse	Date	Signature
_____	_____	_____

Please make 2 copies of this form. Send 1 copy to the CESAR Data Co-ordinating Centre, file 1 copy in the CESAR folder and keep the original with the patient's note.

FORM A

Registration form

This form should be completed by a member of the intensive care team at the participating hospital.

STEP 1 - Collect registration data

Data necessary in order to register a patient for trial entry (please print clearly and be ready to give the information over the telephone).

1. CESAR hospital code: ☐☐☐☐

2. CESAR hospital categorisation:

3. Hospital name:

4. Contact telephone number:_____

Please complete patient details or affix addressograph

5. Patient's first name:_____

6. Patient's surname: _____

7. Patient's date of birth: ☐☐ ☐☐ 1 9 ☐☐ (dd / mm / yyyy)

8. Patient's gender: Male ☐ Female ☐

Please complete questions i-vii and go to Step 2 on the next page.

For each attempted registration, please record the recruiting doctor's name, the date and the time.

Doctor	_____	_____	_____	_____	_____
Date	_____	_____	_____	_____	_____
Time	_____	_____	_____	_____	_____

i.(a)	Duration of IPPV?	_____ (hrs)	_____ (hrs)	_____ (hrs)	_____ (hrs)	_____ (hrs)
i.(b)	Duration of high pressure (>30cmH_20) and/or high FiO_2 (>80% oxygen)?	_____ (hrs)	_____ (hrs)	_____ (hrs)	_____ (hrs)	_____ (hrs)
ii.	Is there intra-cranial bleeding? (If yes, patient is not eligible for trial entry, at this time)	Yes No ☐☐	Yes No ☐☐	Yes No ☐☐	Yes No ☐☐	Yes No ☐☐
iii.	Is there any other contra-indication to limited heparinisation? (If yes, patient is not eligible for trial entry)	☐☐	☐☐	☐☐	☐☐	☐☐
iv.	Is there any contra-indication to continuation of active treatment? (If yes, patient is not eligible for trial entry)	☐☐	☐☐	☐☐	☐☐	☐☐
v.(a)	PaO_2 on 100% Oxygen (mmHg)	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
v.(b)	PEEP (cmH_2O)	☐☐	☐☐	☐☐	☐☐	☐☐
v.(c)	Lung compliance (ml/cmH_2O)	☐☐	☐☐	☐☐	☐☐	☐☐
v.(d)	Number of quadrants with infiltration seen on chest x-ray?	☐	☐	☐	☐	☐
vi.	pH (uncompensated hypercapnoea)	☐.☐☐	☐.☐☐	☐.☐☐	☐.☐☐	☐.☐☐

vii. Diagnostic category:

1. Pneumonia ☐
2. Obstetric acute respiratory distress syndrome (ARDS) ☐
3. Other ARDS ☐
4. Trauma including surgery within 24 hours ☐
5. Other (please specify) _____ ☐

FORM A

STEP 5 - Randomisation

Please telephone 0116 287 1471 and ask the switchboard for the CESAR Trial Clinical Advisor. You will then be transferred to the CAT who will ask for confirmation that assent has been obtained. They will ask you for the information provided in STEP 4. The CAT will then telephone the randomisation service to enter the patient into the trial.

Name of recruiting doctor: _____ Contact telephone number:_____

Apache II Score * ☐☐

* Within 24 hours of admission to ICU, or at time of randomisation if this is less than 24 hours.

STEP 6 - Allocation

The CAT will then telephone you to inform you of:
(please write these in the appropriate spaces below)

Study number ☐☐☐☐☐☐ Allocation 1. Transfer for consideration of ECMO ☐
2. Conventional ventilation ☐

Date of randomisation ☐☐ ☐☐ 20☐☐
dd / mm / yyyy

Time of randomisation ☐☐ : ☐☐ 24 hour

If this hospital is a CTC and the patient is assigned to Conventional Ventilation please take a *'Level of Care and Organ Support'* datasheet from the CESAR trial folder and collect the data on a daily basis. In all other cases the patient is being transferred and the CAT will give an estimated time of arrival of the transport team.

Please ensure the relative has a copy of the further information about the allocated treatment.

If randomisation has been successfully achieved please complete the details on Page 4. Make 2 copies and return 1 copy of the completed form to the CESAR Data Co-ordinating Centre and file 1 copy in the CESAR folder. Please keep the original with the patient's notes.

If the patient has not been randomised please keep this form in the patient's notes.

For the purpose of CESAR, the following definitions are being used.

An organ can be considered to have failed if it meets the criteria set out below as defined by Moreno, R et al, Intensive Care Medicine 1999; 25:686-96:

		Criteria met? Yes	No
Respiratory:	PaO_2/FIO_2 < 200 mmhg with ventilatory support	☐	☐
Coagulation:	Platelet count < 50 x 10^3 / mm^3	☐	☐
Liver:	Bilirubin > 102 mmol/l	☐	☐
Cardiovascular:	Dopamine > 5 mcg/kg/min (or adrenaline/noradrenaline any dose)	☐	☐
Central Nervous System:	GCS (Glasgow Coma Score) ≤ 9	☐	☐
Renal:	Creatinine > 300 mmol/l or urine output < 500ml / day	☐	☐

Please complete this page only if a patient has been randomised to the CESAR Study.

FORM A

Identifying details

PATIENT

Surname: _____

Forename: _____

NHS number: _____
(if available)

Telephone no: _____

Home address: _____

_____

_____

Postcode: _____

NEXT OF KIN

Surname: _____

Forename: _____

Relationship to patient: _____

Telephone no: _____

Home address: _____
(if different to patient's address): _____

_____

Postcode: _____

FAMILY DOCTOR

Full name: _____

Telephone no: _____

Address: _____

_____

_____

Postcode: _____

Please remember to post a copy of the assent form completed by the patient's relative when returning this form.

Please post a copy of this form to:
CESAR Trial Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT using the freepost envelope which is provided in the CESAR trial folder.

STEP 2 - Patient eligibility and bed availability

FORM A

Please now telephone 0116 287 1471 and ask the switchboard for the CESAR Trial Clinical Advisor. You will then be transferred to the CAT (Clinical Advisory Team). You will be asked to provide the information from Step 1. They will then call you back to let you know whether the patient is eligible and beds are available.

Date	_____	_____	_____	_____	_____
Time	_____	_____	_____	_____	_____
	Yes No	Yes No	Yes No	Yes No	Yes No
Is the patient eligible?	☐☐	☐☐	☐☐	☐☐	☐☐
Are beds available?	☐☐	☐☐	☐☐	☐☐	☐☐
Enter date and time beds are held until:					
Date	_____	_____	_____	_____	_____
Time	_____	_____	_____	_____	_____

If the answer to both of these questions is **Yes**, please continue with STEP 3, the assent procedure.

STEP 3 - Obtain assent

Please now talk to the relative(s) to tell them about CESAR and to seek their assent. Please give them a CESAR information pack* so that they have time to read the written information before being asked to sign the assent form.

* The CESAR information pack for relatives is kept in the CESAR trial folder.

Has assent been obtained? **Yes** ☐ **No** ☐

If **Yes**, from whom? (name) _____ Relationship to patient?_____

If NO: please telephone 0116 287 1471 and ask the switchboard for the CESAR Trial Clinical Advisor. You will then be transferred to the CAT. They will then remove the reserve on the beds. You are not required to continue with this form. Please keep this form with the patient's notes.

If YES: please proceed to STEP 4.

STEP 4 - Collect randomisation data

Randomisation will be based on the current condition of the patient, therefore we will be repeating some of the questions from STEP 1.

i.(a) **Total** duration of IPPV? _____ (hrs)

i.(b) **Total** duration of high pressure (>30cmH_20) and/or high FiO_2 (>80% oxygen)? _____ (hrs)

ii. Is there intra cranial bleeding Yes ☐ No ☐
(If yes, patient is not eligible for trial entry, at this time)

iii. Is there any other contra-indication to limited heparinisation? Yes ☐ No ☐
(If yes, patient is not eligible for trial entry)

iv. Is there any contra-indication to continuation of active treatment? Yes ☐ No ☐
(If yes, patient is not eligible for trial entry)

v.(a) PaO_2 on 100% Oxygen ☐☐☐ (mmHg) v.(b) PEEP ☐☐ (cmH_20)

v.(c) Lung compliance ☐☐ (ml/cmH_20) v.(d) Number of quadrants with infiltration seen on chest x-ray ☐

vi. pH (uncompensated hypercapnoea) ☐.☐☐

vii. Diagnostic category:
1. Pneumonia ☐
2. Obstetric acute respiratory distress syndrome (ARDS) ☐
3. Other ARDS ☐
4. Trauma including surgery within 24 hours ☐
5. Other (please specify) _____ ☐

viii. Number of organs failed? ☐
An organ can be considered to have failed if it meets the criteria set out on page 3, as defined by Moreno, R et al, Intensive Care Medicine 1999; 25:686-96.

FORM B

Registration form – Clinical Advisory Team (CAT)

This form should be completed by a member of the CAT in Leicester **prior** to completing a trial entry form.

Please complete this form using information provided during the telephone conversation with the doctor at the participating hospital.

1. CESAR hospital code: ☐☐☐☐☐
2. CESAR hospital categorisation: _____
3. Hospital name:_____
4. Contact telephone number: _____

Please complete patient details:

5. Patient's first name:_____
6. Patient's surname: _____
7. Patient's date of birth: ☐☐ / ☐☐ / 1 9 ☐☐ (dd / mm / yyyy)
8. Patient's gender: Male ☐ Female ☐

Note for CAT advisor

Please inform the recruiting doctor that you will be asking for answers to questions i-vii from *their* registration form (FORM A), and you will then call them back as soon as possible to confirm patient eligibility and bed availability.

STEP 1 - Collect registration data

For each attempted registration, please record the recruiting doctor's name, the date and the time.

	Doctor	_____	_____	_____	_____	_____
	Date	_____	_____	_____	_____	_____
	Time (24hr)	_____	_____	_____	_____	_____
i.(a)	Duration of IPPV?	____ (hrs)	____ (hrs)	____ (hrs)	____ (hrs)	____ (hrs)
i.(b)	Duration of high pressure (>30cm$H_2$0) and/or high FiO_2 (>80% oxygen)?	____ (hrs)	____ (hrs)	____ (hrs)	____ (hrs)	____ (hrs)
ii.	Is there intra cranial-bleeding? (If yes, patient is not eligible for trial entry, at this time)	Yes No	Yes No	Yes No	Yes No	Yes No
iii.	Is there any other contra-indication to limited heparinisation? (If yes, patient is not eligible for trial entry)	☐☐	☐☐	☐☐	☐☐	☐☐
iv.	Is there any contra-indication to continuation of active treatment? (If yes, patient is not eligible for trial entry)	☐☐	☐☐	☐☐	☐☐	☐☐
v.(a)	PaO_2 on 100% Oxygen (mmHg)	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
v.(b)	PEEP (cm$H_2$0)	☐☐	☐☐	☐☐	☐☐	☐☐
v.(c)	Lung compliance (ml/cm$H_2$0)	☐☐	☐☐	☐☐	☐☐	☐☐
v.(d)	Number of quadrants with infiltration seen on chest x-ray?	☐	☐	☐	☐	☐
vi.	pH (uncompensated hypercapnoea)	☐.☐☐	☐.☐☐	☐.☐☐	☐.☐☐	☐.☐☐
vii.	Diagnostic category:					

1. Pneumonia ☐
2. Obstetric acute respiratory distress syndrome (ARDS) ☐
3. Other ARDS ☐
4. Trauma including surgery within 24 hrs ☐
5. Other (please specify) _____ ☐

Please calculate the patient's Murray Score for each attempted registration.

FORM B

Murray Score	☐.☐	☐.☐	☐.☐	☐.☐	☐.☐
Is the patient eligible?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐

STEP 2 - Bed availability

If the call is from a CTC please check the availability of an ECMO bed. If the call is from an RH you will also need to check the availability of CTC beds in the transfer hospitals. Please consult the list of CTC hospitals in your CAT folder or the ECMO office and record the name in the box below.

Are beds available?	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
Enter date and time beds are held until: (please record the minimum date and time of bed availability)	Date _____	_____	_____	_____	_____
	Time _____	_____	_____	_____	_____
	Hospital _____	_____	_____	_____	_____

If **No**, you do not need to continue with this form at this point.

In both circumstances, you must now contact the participating hospital to inform the recruiting doctor about eligibility, bed availability and to instruct the recruiting doctor to obtain assent (where appropriate).

If the patient is eligible and beds are available, please continue with STEP 3, the assent procedure.

If appropriate, please give reason why referred patient was not accepted and randomised :

_____

STEP 3 - Assent procedure

The recruiting doctor at the participating hospital will now ask the patient's relative(s) for permission to enter the patient into the trial and will then telephone the CAT to confirm. If there has been no contact from the participating hospital by the end of the period for which beds are being held please call the recruiting doctor to find out the current status of the patient.

Has assent been obtained? Yes ☐ No ☐

If YES, please proceed to STEP 4.
If NO, please give reason and remove the reserve on beds for ECMO and CTC.

Reason assent not obtained: _____

Please keep this form in the CESAR box file in the ECMO office. Information collected on this form will be used to complete the log of eligible patients.

STEP 4 - Collect randomisation data

FORM B

The doctor at the participating hospital will telephone the CAT and provide the randomisation data which is based on the current condition of the patient.

i.(a) **Total** duration of IPPV? _____ (hrs)

i.(b) **Total** duration of high pressure (>30cmH_20) and/or high FiO_2 (>80% oxygen)? _____ (hrs)

ii. Is there intra cranial bleeding? Yes ☐ No ☐
(If yes, patient is not eligible for trial entry, at this time)

iii. Is there any other contra-indication to limited heparinisation? Yes ☐ No ☐
(If yes, patient is not eligible for trial entry)

iv. Is there any contra-indication to continuation of active treatment? Yes ☐ No ☐
(If yes, patient is not eligible for trial entry)

v.(a) PaO_2 on 100% Oxygen ☐☐☐ (mmHg) v.(b) PEEP ☐☐ (cmH_2O)

v.(c) Lung compliance ☐☐ (ml/cmH_2O) v.(d) Number of quadrants with infiltration seen on chest x-ray ☐

vi. pH (uncompensated hypercapnoea) ☐.☐☐

vii. Diagnostic category:

1. Pneumonia ☐
2. Obstetric acute respiratory distress syndrome (ARDS) ☐
3. Other ARDS ☐
4. Trauma including surgery within 24 hrs ☐
5. Other (please specify) _____ ☐

viii. Number of organs failed? (please see page 4 for definitions) ☐

Please use question V parts a-d to calculate the patient's Murray Score. ☐☐

After completing STEP 4 please inform the doctor at the recruiting hospital that you will phone back in a few minutes. Please ask the recruiting doctor to complete the Apache II score on page 3 of their registration form in the meantime.

STEP 5 - Randomisation

Please complete a CESAR Trial ENTRY form (FORM C) and telephone 0800 387 444 to randomise the patient.

After the randomisation process is complete please do the following:

1. Phone the recruiting hospital to inform them of the patient's study number, allocation and estimated time of arrival of the transport team if relevant, and remember to note the Appache II score ☐☐

2. If the recruiting hospital is a CTC and the allocation is to Conventional Ventilation please remind the recruiting doctor to take a *Level of Care and Organ Support* datasheet from their trial folder

3. Give the entry form (FORM C) to Janice to fax to the DCC on 020 7637 2853 and then file in the CESAR CAT Entry Form folder

4. File the registration form in the CESAR box file in the ECMO office

5. Alert transport team if necessary and ensure you give them a transfer recruitment pack which is kept in the CAT folder

Definitions of failed organs

FORM B

For the purpose of CESAR, the following definitions are being used.

An organ can be considered to have failed if it meets the criteria set out below as defined by Moreno, R et al, Intensive Care Medicine 1999; 25:686-96:

		Tick if appropriate Yes
Respiratory:	PaO_2/FIO_2 < 200 mmhg with ventilatory support	☐
Coagulation:	Platelet count < 50 x 10^3 / mm^3	☐
Liver:	Bilirubin > 102 mmol/l	☐
Cardiovascular:	Dopamine > 5 mcg/kg/min (or adrenaline/noradrenaline any dose)	☐
Central Nervous System:	GCS (Glasgow Coma Score) ≤ 9	☐
Renal:	Creatinine > 300 mmol/l or urine output < 500ml / day	☐

FORM C

ENTRY FORM

Please complete this form **after** a CAT Registration form (FORM **B**) has been completed and the patient has satisfied all the trial entry criteria. When you have completed this form please telephone **0800 387444** and you will be taken through the randomisation process using a touchtone telephone system. This form must be completed by a member of the Clinical Advisory Team (CAT) in Leicester.

1. **CESAR** trial hospital code: ☐☐☐☐

2. Hospital name:_____

(the randomisation service will confirm this automatically)

3. Your advisory code number: ☐☐☐☐

You will now be asked for the first name initial then second name initial.

4. Patient's first name: _____

5. Patient's surname: _____

6. Patient's date of birth: ☐☐ / ☐☐ / 19☐☐ (dd / mm / yyyy)

7. Has assent been obtained from the patient's relative(s)? Yes ☐ No ☐

i. **Total** duration of high pressure (>30cmH_20) and/or high FiO_2 (>80% oxygen)? ____ **(hrs)**

ii. Is there intra-cranial bleeding (If yes, patient is not eligible for trial entry, at this time) Yes ☐ No ☐

iii. Is there any other contra-indication to limited heparinisation? (If yes, patient is not eligible for trial entry) Yes ☐ No ☐

iv. Is there any contra-indication to continuation of active treatment? (If yes, patient is not eligible for trial entry) Yes ☐ No ☐

v. Murray score (if ≥ 3, go to **vii**, if < 3 go to **vi**) ☐.☐

vi. pH (uncompensated hypercapnoea) ☐.☐☐

vii. Diagnostic category (tick one box only):

1. Pneumonia ☐
2. Obstetric acute respiratory distress syndrome (ARDS) ☐
3. Other ARDS ☐
4. Trauma including surgery within 24 hours ☐
5. Other (please specify) _____ ☐

viii. Number of organs failed? ☐

Study number: ☐☐☐☐☐☐ **Allocation:**

1. Transfer for consideration of ECMO ☐
2. Conventional ventilation ☐

Date of randomisation: ☐☐ / ☐☐ / 20☐☐ (dd / mm / yyyy) Time of randomisation: ☐☐:☐☐ 24 hour

Additional Information **(these questions will not be asked by the automated randomisation service):**

1. Name of recruiting doctor: _____
2. Contact number (inc. code): _____
3. Patient's gender: Male ☐ Female ☐
4. **Total** duration of IPPV? ____ **(hrs)**
5. If patient is randomised at an RH and is allocated Conventional ventilation, please give name of CTC transferred to: _____
6. Signature: .....

Please fax a copy of this form to: **CESAR Data Co-ordinating Centre on 020 7637 2853** and file the original in the CESAR CAT Entry Form folder.

FORM A

Registration form

This form should be completed by a member of the intensive care team at the participating hospital.

STEP 1 - Collect registration data

Data necessary in order to register a patient for trial entry (please print clearly and be ready to give the information over the telephone).

1. CESAR hospital code: 8 3 1 6
2. CESAR hospital categorisation: RH
3. Hospital name: Glenfield Transport Team
4. Contact telephone number:_____

Please complete patient details or affix addressograph

5. Patient's first name:_____
6. Patient's surname: _____
7. Patient's date of birth: ☐☐ ☐☐ 1 9 ☐☐ (dd / mm / yyyy)
8. Patient's gender: Male ☐ Female ☐

Please complete questions i-vii and go to Step 2 on the next page.

For each attempted registration, please record the recruiting doctor's name, the date and the time.

		Doctor	_____	_____	_____	_____	_____
		Date	_____	_____	_____	_____	_____
		Time	_____	_____	_____	_____	_____
i.(a)	Duration of IPPV?		____ (hrs)	____ (hrs)	____ (hrs)	____ (hrs)	____ (hrs)
i.(b)	Duration of high pressure (>30cmH_2O) and/or high FiO_2 (>80% oxygen)?		____ (hrs)	____ (hrs)	____ (hrs)	____ (hrs)	____ (hrs)
ii.	Is there intra-cranial bleeding? (If yes, patient is not eligible for trial entry, at this time)		Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐	Yes ☐ No ☐
iii.	Is there any other contra-indication to limited heparinisation? (If yes, patient is not eligible for trial entry)		☐☐	☐☐	☐☐	☐☐	☐☐
iv.	Is there any contra-indication to continuation of active treatment? (If yes, patient is not eligible for trial entry)		☐☐	☐☐	☐☐	☐☐	☐☐
v.(a)	PaO_2 on 100% Oxygen	(mmHg)	☐☐☐	☐☐☐	☐☐☐	☐☐☐	☐☐☐
v.(b)	PEEP	(cmH_2O)	☐☐	☐☐	☐☐	☐☐	☐☐
v.(c)	Lung compliance	(ml/cmH_2O)	☐☐	☐☐	☐☐	☐☐	☐☐
v.(d)	Number of quadrants with infiltration seen on chest x-ray?		☐	☐	☐	☐	☐
vi.	pH (uncompensated hypercapnoea)		☐.☐☐	☐.☐☐	☐.☐☐	☐.☐☐	☐.☐☐

vii. Diagnostic category:

1. Pneumonia ☐
2. Obstetric acute respiratory distress syndrome (ARDS) ☐
3. Other ARDS ☐
4. Trauma including surgery within 24 hours ☐
5. Other (please specify) _____ ☐

STEP 2 - Patient eligibility and bed availability

FORM A

Please now telephone 0116 287 1471 and ask the switchboard for the CESAR Trial Clinical Advisor. You will then be transferred to the CAT (Clinical Advisory Team). You will be asked to provide the information from Step 1. They will then call you back to let you know whether the patient is eligible and beds are available.

Date	_____	_____	_____	_____	_____
Time	_____	_____	_____	_____	_____
Is the patient eligible?	Yes No	Yes No	Yes No	Yes No	Yes No
Are beds available?	☐☐	☐☐	☐☐	☐☐	☐☐
Enter date and time beds are held until:	☐☐	☐☐	☐☐	☐☐	☐☐
Date	_____	_____	_____	_____	_____
Time	_____	_____	_____	_____	_____

If the answer to both of these questions is **Yes**, please continue with STEP 3, the assent procedure.

STEP 3 - Obtain assent

Please now talk to the relative(s) to tell them about CESAR and to seek their assent. Please give them a CESAR information pack* so that they have time to read the written information before being asked to sign the assent form.

* The CESAR information pack for relatives is kept in the CESAR trial folder.

Has assent been obtained? **Yes** ☐ **No** ☐

If **Yes**, from whom? (name) _____ Relationship to patient?_____

If NO: please telephone 0116 287 1471 and ask the switchboard for the CESAR Trial Clinical Advisor. You will then be transferred to the CAT. They will then remove the reserve on the beds. You are not required to continue with this form. Please keep this form with the patient's notes.

If YES: please proceed to STEP 4.

STEP 4 - Collect randomisation data

Randomisation will be based on the current condition of the patient, therefore we will be repeating some of the questions from STEP 1.

i.(a) **Total** duration of IPPV? _____ (hrs)

i.(b) **Total** duration of high pressure (>30cm$H_2$0) and/or high FiO_2 (>80% oxygen)? _____ (hrs)

ii. Is there intra cranial bleeding (Yes ☐ No ☐)
(If yes, patient is not eligible for trial entry, at this time)

iii. Is there any other contra-indication to limited heparinisation? (Yes ☐ No ☐)
(If yes, patient is not eligible for trial entry)

iv. Is there any contra-indication to continuation of active treatment? (Yes ☐ No ☐)
(If yes, patient is not eligible for trial entry)

v.(a) PaO_2 on 100% Oxygen ☐☐☐ (mmHg)

v.(b) PEEP ☐☐ (cm$H_2$0)

v.(c) Lung compliance ☐☐ (ml/cm$H_2$0)

v.(d) Number of quadrants with infiltration seen on chest x-ray ☐

vi. pH (uncompensated hypercapnoea) ☐.☐☐

vii. Diagnostic category:
1. Pneumonia ☐
2. Obstetric acute respiratory distress syndrome (ARDS) ☐
3. Other ARDS ☐
4. Trauma including surgery within 24 hours ☐
5. Other (please specify) _____ ☐

viii. Number of organs failed? ☐
An organ can be considered to have failed if it meets the criteria set out on page 3, as defined by Moreno, R et al, Intensive Care Medicine 1999; 25:686-96.

FORM A

STEP 5 - Randomisation

Please telephone 0116 287 1471 and ask the switchboard for the CESAR Trial Clinical Advisor. You will then be transferred to the CAT who will ask for confirmation that assent has been obtained. They will ask you for the information provided in STEP 4. The CAT will then telephone the randomisation service to enter the patient into the trial.

Name of recruiting doctor: _____ Contact telephone number:_____

Apache II Score * ☐☐

* Within 24 hours of admission to ICU, or at time of randomisation if this is less than 24 hours.

STEP 6 - Allocation

The CAT will then telephone you to inform you of:
(please write these in the appropriate spaces below)

Study number ☐☐☐☐☐☐ Allocation 1. Transfer for consideration of ECMO ☐
2. Conventional ventilation ☐

Date of randomisation ☐☐ / ☐☐ / 20☐☐ (dd / mm / yyyy)

Time of randomisation ☐☐ : ☐☐ 24 hour

If this hospital is a CTC and the patient is assigned to Conventional Ventilation please take a *'Level of Care and Organ Support'* datasheet from the CESAR trial folder and collect the data on a daily basis. In all other cases the patient is being transferred and the CAT will give an estimated time of arrival of the transport team.

Please ensure the relative has a copy of the further information about the allocated treatment.

If randomisation has been successfully achieved please complete the details on Page 4. Make 2 copies and return 1 copy of the completed form to the CESAR Data Co-ordinating Centre and file 1 copy in the CESAR folder. Please keep the original with the patient's notes.

If the patient has not been randomised please keep this form in the patient's notes.

For the purpose of CESAR, the following definitions are being used.

An organ can be considered to have failed if it meets the criteria set out below as defined by Moreno, R et al, Intensive Care Medicine 1999; 25:686-96:

		Criteria met? Yes	No
Respiratory:	PaO_2/FIO_2 < 200 mmhg with ventilatory support	☐	☐
Coagulation:	Platelet count < 50 x 10^3 / mm^3	☐	☐
Liver:	Bilirubin > 102 mmol/l	☐	☐
Cardiovascular:	Dopamine > 5 mcg/kg/min (or adrenaline/noradrenaline any dose)	☐	☐
Central Nervous System:	GCS (Glasgow Coma Score) ≤ 9	☐	☐
Renal:	Creatinine > 300 mmol/l or urine output < 500ml / day	☐	☐

Please complete this page only if a patient has been randomised to the CESAR Study.

FORM A

Identifying details

PATIENT

Surname: _____

Forename: _____

NHS number: _____
(if available)

Telephone no: _____

Home address: _____

_____

_____

Postcode: _____

NEXT OF KIN

Surname: _____

Forename: _____

Relationship to patient: _____

Telephone no: _____

Home address: _____
(if different to patient's address): _____

_____

Postcode: _____

FAMILY DOCTOR

Full name: _____

Telephone no: _____

Address: _____

_____

_____

Postcode: _____

Please remember to post a copy of the assent form completed by the patient's relative when returning this form.

Please post a copy of this form to:
CESAR Trial Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT using the freepost envelope which is provided in the CESAR trial folder.

Transfer Outcome Datasheet

Patient Initials ☐☐ CESAR study number ☐☐☐☐☐☐

Patient name:_____

Name of this hospital: _____

Name of unit/ward: _____ Unit/ward specialty: _____

Contact name: _____ Contact tel. number: _____

Date of admission to this unit: ☐☐☐☐☐☐☐☐ dd/mm/yyyy

Details in the section above to be completed by the CESAR Data Co-ordinating Centre. Please amend or complete any information that is incorrect or missing.

During the period of admission to this unit has the patient been readmitted to any critical care unit and then returned to this unit? Yes ☐ No ☐

If YES, please give the following details:

Name of unit:_____ Contact doctor:_____

Tel. number:_____

Date of admission to critical care: ☐☐☐☐☐☐☐☐ dd/mm/yyyy

Date of return to this unit/ward: ☐☐☐☐☐☐☐☐ dd/mm/yyyy

Please complete the following when the patient is transferred, discharged or has died

Date patient left this unit: ☐☐☐☐☐☐☐☐ dd/mm/yyyy

1. Has the patient been transferred to a department other than critical care in this hospital? Yes ☐ No ☐

If NO, please go to Q2. If YES, please give the following details:

Name of unit:_____

Tel. number:_____ Contact doctor:_____

2. Has the patient been transferred to an intensive care or high dependency unit in this hospital? Yes ☐ No ☐

If NO, please go to Q3. If YES, please give the following details:

Name of unit:_____

Tel. number:_____ Contact doctor:_____

3. Has the patient been transferred to a critical care unit in another hospital? Yes ☐ No ☐

If NO, please go to Q4. If YES, please give the following details:

Name of unit:_____

Name of hospital:_____

Tel. number:_____ Contact doctor (if known):_____

Name of Ambulance Trust:_____

Name of contact person to collect transport details: _____

Contact telephone number for the above named person :_____

4. **Has the patient been discharged to a department other than critical care in a different hospital to continue their treatment?** Yes ☐ No ☐
If **NO**, please go to Q5. If **YES**, please give details:

Name of hospital:_____ Tel. number:_____
Contact doctor (if known):_____ Name of ambulance trust:_____
Name of contact person to collect transport details: _____
Contact telephone number for the above named person :_____

5. **Has the patient been discharged from hospital?** Yes ☐ No ☐
If **NO**, please go to Q6. If **YES**, was the patient discharged

a) Home ☐
b) To any type of residential care ☐

If the patient has been dischared to residential care please give the following:

Name of care organisation: _____
Address: _____
_____
Contact person: _____
Telephone number: _____

If the patient has been discharged, was hospital transport used? Yes ☐ No ☐
If **YES**, please give the following details:

Name of Ambulance Trust:_____
Name of contact person to collect transport details: _____
Contact telephone number for the above named person :_____

6. **Has the patient died?** Yes ☐ No ☐
If **NO**, please go to Q7. If **YES**, please give the following details:

Date of death: ☐☐☐☐☐☐☐☐ dd/mm/yyyy

Cause of death: _____ Was a post mortem carried out? Yes ☐ No ☐

7. **Name of person completing this form:** _____
Tel. number: _____ **Fax number:** _____
Email: _____

If you have any queries regarding this form please contact:
Steven Robertson, CESAR Data Co-ordinating Centre
Medical Statistics Unit
London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT
Telephone 020 7927 2075 Fax 020 7637 2853 Email steve.robertson@lshtm.ac.uk

On completion of this outcome page, please either return a copy in the freepost envelope or fax to :
CESAR Data Co-ordinating Centre on **020 7637 2853.**
Please file the original with the patient's notes.

Level of Care and Organ Support Data Collection Sheet Days 1-7

1. Hospital name:

2a. Patient 's surname:_____

2b. Patient's first name:_____

3. Patient's initials: ☐☐

4. CESAR study number: ☐☐☐☐☐☐

5. Date of birth: ☐☐ / ☐☐ / 1 9 ☐☐ (dd / mm / yyyy)

6. Date of randomisation: ☐☐ / ☐☐ / 2 0 ☐☐ (dd / mm / yyyy)

7. Time of randomisation: ☐☐ : ☐☐ 24 hour

N.B. Data collection must begin on the day that the patient is randomised **irrespective of the time of randomisation.**

Please record the following data on a daily basis until the patient is discharged from the critical care unit

Day number / Date	1 / /	2 / /	3 / /	4 / /	5 / /	6 / /	7 / /
Level of care: only 1 box should be ticked for each day of stay, and the highest level of care within a day should be recorded:							
Level 3: Intensive Care[1*]	☐	☐	☐	☐	☐	☐	☐
Level 2: High Dependency Care[2*]	☐	☐	☐	☐	☐	☐	☐
Organ system support: more than one organ system support can be recorded:							
1. Basic respiratory support	☐	☐	☐	☐	☐	☐	☐
2. Advanced respiratory support	☐	☐	☐	☐	☐	☐	☐
3. Circulatory support	☐	☐	☐	☐	☐	☐	☐
4. Neurological support	☐	☐	☐	☐	☐	☐	☐
5. Renal Support	☐	☐	☐	☐	☐	☐	☐
6. ECMO	☐	☐	☐	☐	☐	☐	☐
7. Liver support	☐	☐	☐	☐	☐	☐	☐
8. No organ support	☐	☐	☐	☐	☐	☐	☐
9. Other (specify).....	☐	☐	☐	☐	☐	☐	☐
Location of care: only one box should be ticked for each day of stay. If a patient moves location (e.g. from the ICU to the HDU) please tick the box for the location where the patient has spent ≥ 50% of the day:							
Intensive Care Unit (ICU)	☐	☐	☐	☐	☐	☐	☐
High Dependency Unit (HDU)	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU/Coronary Care Unit	☐	☐	☐	☐	☐	☐	☐
Cardiothoracic ICU	☐	☐	☐	☐	☐	☐	☐
Neurological ICU	☐	☐	☐	☐	☐	☐	☐
Theatre recovery area	☐	☐	☐	☐	☐	☐	☐
Other (please state).....	☐	☐	☐	☐	☐	☐	☐
Has plateau airway pressure exceeded 30 cmH_20 for more than 4 hours in last 24 hour period*? (If plateau not recorded has peak inspiratory pressure exceeded 30 cmH_20)[3]	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A

*The first 24 hour period is defined as the time from trial entry until the following morning. Thereafter each 24 hour period starts from the beginning of each morning/day shift. If you answer N/A please indicate reason e.g. patient not ventilated.

Primary diagnosis: _____

During days 1-7 in critical care has the patient required any of the following:

	Yes	No
1. Use of high frequency/oscillation/jet ventilation	☐	☐
2. Use of nitric oxide	☐	☐
3. Use of prone position	☐	☐
4. Use of steroids	☐	☐

NB: Level of care is not the same as the location of care. For definitions *1-3 and organ support please see Page 14.

If the patient is still receiving critical care **after day 7** please return the pages for Days 1-7 by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** and continue recording data on page 3, Critical Care – Days 8-14.

If the patient has been transferred, has died or has been discharged during Days 1-7, please complete the outcome page (page 13) and return this datasheet in full by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** with the **Days 1-7 page**.

Please keep the original form in the patient's notes and make a copy for your files.

N.B. If it is easier for you to post a copy of this datasheet back to the CESAR Data Co-ordinating Centre please use the freepost envelope which is in the trial folder. Please remember to make **2** copies of this form, send **1** copy to the CESAR Data Co-ordinating Centre, keep **1** copy in your trial folder and file the original in the patient's notes.

CESAR Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT
Telephone: 020 7927 2376/2075
Fax: 020 7637 2853

Level of Care and Organ Support Data Collection Sheet Days 8-14

1. Hospital name:

2. CESAR Study number: ☐☐☐☐☐☐ 3. Patient's initials: ☐☐

Please record the following data on a daily basis until the patient is discharged from the critical care unit

Day number / Date	8 / /	9 / /	10 / /	11 / /	12 / /	13 / /	14 / /
Level of care: only 1 box should be ticked for each day of stay, and the highest level of care within a day should be recorded:							
Level 3: Intensive Care[1*]	☐	☐	☐	☐	☐	☐	☐
Level 2: High Dependency Care[2*]	☐	☐	☐	☐	☐	☐	☐
Organ system support: more than one organ system support can be recorded:							
1. Basic respiratory support	☐	☐	☐	☐	☐	☐	☐
2. Advanced respiratory support	☐	☐	☐	☐	☐	☐	☐
3. Circulatory support	☐	☐	☐	☐	☐	☐	☐
4. Neurological support	☐	☐	☐	☐	☐	☐	☐
5. Renal Support	☐	☐	☐	☐	☐	☐	☐
6. ECMO	☐	☐	☐	☐	☐	☐	☐
7. Liver support	☐	☐	☐	☐	☐	☐	☐
8. No organ support	☐	☐	☐	☐	☐	☐	☐
9. Other (specify).....	☐	☐	☐	☐	☐	☐	☐
Location of care: only one box should be ticked for each day of stay. If a patient moves location (e.g. from the ICU to the HDU) please tick the box for the location where the patient has spent ≥ 50% of the day:							
Intensive Care Unit (ICU)	☐	☐	☐	☐	☐	☐	☐
High Dependency Unit (HDU)	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU/Coronary Care Unit	☐	☐	☐	☐	☐	☐	☐
Cardiothoracic ICU	☐	☐	☐	☐	☐	☐	☐
Neurological ICU	☐	☐	☐	☐	☐	☐	☐
Theatre recovery area	☐	☐	☐	☐	☐	☐	☐
Other (please state).....	☐	☐	☐	☐	☐	☐	☐
Has plateau airway pressure exceeded 30 cmH_20 for more than 4 hours in last 24 hour period*? (If plateau not recorded has peak inspiratory pressure exceeded 30 cmH_20)[3]	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A

*The first 24 hour period is defined as the time from trial entry until the following morning. Thereafter each 24 hour period starts from the beginning of each morning/day shift. If you answer N/A please indicate reason e.g. patient not ventilated.

During days 8-14 in critical care has the patient required any of the following:

	Yes	No
1. Use of high frequency/oscillation/jet ventilation	☐	☐
2. Use of nitric oxide	☐	☐
3. Use of prone position	☐	☐
4. Use of steroids	☐	☐

NB: Level of care is not the same as the location of care.

For definitions *1-3 and organ support please see Page 14.

If the patient is still receiving critical care **after day 14** please return the pages for Days 8-14 by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** and continue recording data on page 5, Critical Care – Days 15-21.

If the patient has been transferred, has died or has been discharged during Days 8-14, please complete the outcome page (page 13) and return this datasheet in full by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** with the **Days 8-14 page**.

Please keep the original form in the patient's notes and make a copy for your files.

N.B. If it is easier for you to post a copy of this datasheet back to the CESAR Data Co-ordinating Centre please use the freepost envelope which is in the trial folder. Please remember to make **2** copies of this form, send **1** copy to the CESAR Data Co-ordinating Centre, keep **1** copy in your trial folder and file the original in the patient's notes.

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Telephone: 020 7927 2376/2075
Fax: 020 7637 2853

Level of Care and Organ Support Data Collection Sheet Days 15-21

1. Hospital name:

2. CESAR Study number: ☐☐☐☐☐☐ 3. Patient's initials: ☐☐

Please record the following data on a daily basis until the patient is discharged from the critical care unit

Day number / Date	15 / /	16 / /	17 / /	18 / /	19 / /	20 / /	21 / /
Level of care: only 1 box should be ticked for each day of stay, and the highest level of care within a day should be recorded:							
Level 3: Intensive Care[1*]	☐	☐	☐	☐	☐	☐	☐
Level 2: High Dependency Care[2*]	☐	☐	☐	☐	☐	☐	☐
Organ system support: more than one organ system support can be recorded:							
1. Basic respiratory support	☐	☐	☐	☐	☐	☐	☐
2. Advanced respiratory support	☐	☐	☐	☐	☐	☐	☐
3. Circulatory support	☐	☐	☐	☐	☐	☐	☐
4. Neurological support	☐	☐	☐	☐	☐	☐	☐
5. Renal Support	☐	☐	☐	☐	☐	☐	☐
6. ECMO	☐	☐	☐	☐	☐	☐	☐
7. Liver support	☐	☐	☐	☐	☐	☐	☐
8. No organ support	☐	☐	☐	☐	☐	☐	☐
9. Other (specify).....	☐	☐	☐	☐	☐	☐	☐
Location of care: only one box should be ticked for each day of stay. If a patient moves location (e.g. from the ICU to the HDU) please tick the box for the location where the patient has spent ≥ 50% of the day:							
Intensive Care Unit (ICU)	☐	☐	☐	☐	☐	☐	☐
High Dependency Unit (HDU)	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU/Coronary Care Unit	☐	☐	☐	☐	☐	☐	☐
Cardiothoracic ICU	☐	☐	☐	☐	☐	☐	☐
Neurological ICU	☐	☐	☐	☐	☐	☐	☐
Theatre recovery area	☐	☐	☐	☐	☐	☐	☐
Other (please state).....	☐	☐	☐	☐	☐	☐	☐
Has plateau airway pressure exceeded 30 cmH_20 for more than 4 hours in last 24 hour period*? (If plateau not recorded has peak inspiratory pressure exceeded 30 cmH_20)[3]	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A

*The first 24 hour period is defined as the time from trial entry until the following morning. Thereafter each 24 hour period starts from the beginning of each morning/day shift. If you answer N/A please indicate reason e.g. patient not ventilated.

During days 15-21 in critical care has the patient required any of the following:

	Yes	No
1. Use of high frequency/oscillation/jet ventilation	☐	☐
2. Use of nitric oxide	☐	☐
3. Use of prone position	☐	☐
4. Use of steroids	☐	☐

NB: Level of care is not the same as the location of care.

For definitions *1-3 and organ support please see Page 14.

If the patient is still receiving critical care **after day 21** please return the pages for Days 15-21 by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** and continue recording data on page 7, Critical Care – Days 22-28.

If the patient has been transferred, has died or has been discharged during Days 15-21, please complete the outcome page (page 13) and return this datasheet in full by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** with the **Days 15-21 page**.

Please keep the original form in the patient's notes and make a copy for your files.

N.B. If it is easier for you to post a copy of this datasheet back to the CESAR Data Co-ordinating Centre please use the freepost envelope which is in the trial folder. Please remember to make **2** copies of this form, send **1** copy to the CESAR Data Co-ordinating Centre, keep **1** copy in your trial folder and file the original in the patient's notes.

CESAR Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT
Telephone: 020 7927 2376/2075
Fax: 020 7637 2853

Level of Care and Organ Support Data Collection Sheet Days 22-28

1. Hospital name:
2. CESAR Study number: ☐☐☐☐☐☐ 3. Patient's initials: ☐☐

Please record the following data on a daily basis until the patient is discharged from the critical care unit

Day number / Date	22 / /	23 / /	24 / /	25 / /	26 / /	27 / /	28 / /
Level of care: only 1 box should be ticked for each day of stay, and the highest level of care within a day should be recorded:							
Level 3: Intensive Care[1*]	☐	☐	☐	☐	☐	☐	☐
Level 2: High Dependency Care[2*]	☐	☐	☐	☐	☐	☐	☐
Organ system support: more than one organ system support can be recorded:							
1. Basic respiratory support	☐	☐	☐	☐	☐	☐	☐
2. Advanced respiratory support	☐	☐	☐	☐	☐	☐	☐
3. Circulatory support	☐	☐	☐	☐	☐	☐	☐
4. Neurological support	☐	☐	☐	☐	☐	☐	☐
5. Renal Support	☐	☐	☐	☐	☐	☐	☐
6. ECMO	☐	☐	☐	☐	☐	☐	☐
7. Liver support	☐	☐	☐	☐	☐	☐	☐
8. No organ support	☐	☐	☐	☐	☐	☐	☐
9. Other (specify).....	☐	☐	☐	☐	☐	☐	☐
Location of care: only one box should be ticked for each day of stay. If a patient moves location (e.g. from the ICU to the HDU) please tick the box for the location where the patient has spent ≥ 50% of the day:							
Intensive Care Unit (ICU)	☐	☐	☐	☐	☐	☐	☐
High Dependency Unit (HDU)	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU/Coronary Care Unit	☐	☐	☐	☐	☐	☐	☐
Cardiothoracic ICU	☐	☐	☐	☐	☐	☐	☐
Neurological ICU	☐	☐	☐	☐	☐	☐	☐
Theatre recovery area	☐	☐	☐	☐	☐	☐	☐
Other (please state).....	☐	☐	☐	☐	☐	☐	☐
Has plateau airway pressure exceeded 30 cmH_20 for more than 4 hours in last 24 hour period*? (If plateau not recorded has peak inspiratory pressure exceeded 30 cmH_20)[3]	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A

*The first 24 hour period is defined as the time from trial entry until the following morning. Thereafter each 24 hour period starts from the beginning of each morning/day shift. If you answer N/A please indicate reason e.g. patient not ventilated.

During days 22-28 in critical care has the patient required any of the following:

	Yes	No
1. Use of high frequency/oscillation/jet ventilation	☐	☐
2. Use of nitric oxide	☐	☐
3. Use of prone position	☐	☐
4. Use of steroids	☐	☐

NB: Level of care is not the same as the location of care.
For definitions *1-3 and organ support please see Page 14.

If the patient is still receiving critical care **after day 28** please return the pages for Days 22-28 by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** and continue recording data on page 9, Critical Care – Days 29-35.

If the patient has been transferred, has died or has been discharged during Days 22-28, please complete the outcome page (page 13) and return this datasheet in full by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** with the **Days 22-28 page**.

Please keep the original form in the patient's notes and make a copy for your files.

N.B. If it is easier for you to post a copy of this datasheet back to the CESAR Data Co-ordinating Centre please use the freepost envelope which is in the trial folder. Please remember to make **2** copies of this form, send **1** copy to the CESAR Data Co-ordinating Centre, keep **1** copy in your trial folder and file the original in the patient's notes.

CESAR Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT
Telephone: 020 7927 2376/2075
Fax: 020 7637 2853

Level of Care and Organ Support Data Collection Sheet Days 29-35

1. Hospital name:
2. CESAR Study number: ☐☐☐☐☐☐ 3. Patient's initials: ☐☐

Please record the following data on a daily basis until the patient is discharged from the critical care unit

Day number / Date	29 / /	30 / /	31 / /	32 / /	33 / /	34 / /	35 / /
Level of care: only 1 box should be ticked for each day of stay, and the highest level of care within a day should be recorded:							
Level 3: Intensive Care[1*]	☐	☐	☐	☐	☐	☐	☐
Level 2: High Dependency Care[2*]	☐	☐	☐	☐	☐	☐	☐
Organ system support: more than one organ system support can be recorded:							
1. Basic respiratory support	☐	☐	☐	☐	☐	☐	☐
2. Advanced respiratory support	☐	☐	☐	☐	☐	☐	☐
3. Circulatory support	☐	☐	☐	☐	☐	☐	☐
4. Neurological support	☐	☐	☐	☐	☐	☐	☐
5. Renal Support	☐	☐	☐	☐	☐	☐	☐
6. ECMO	☐	☐	☐	☐	☐	☐	☐
7. Liver support	☐	☐	☐	☐	☐	☐	☐
8. No organ support	☐	☐	☐	☐	☐	☐	☐
9. Other (specify).....	☐	☐	☐	☐	☐	☐	☐
Location of care: only one box should be ticked for each day of stay. If a patient moves location (e.g. from the ICU to the HDU) please tick the box for the location where the patient has spent ≥ 50% of the day:							
Intensive Care Unit (ICU)	☐	☐	☐	☐	☐	☐	☐
High Dependency Unit (HDU)	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU/Coronary Care Unit	☐	☐	☐	☐	☐	☐	☐
Cardiothoracic ICU	☐	☐	☐	☐	☐	☐	☐
Neurological ICU	☐	☐	☐	☐	☐	☐	☐
Theatre recovery area	☐	☐	☐	☐	☐	☐	☐
Other (please state).....	☐	☐	☐	☐	☐	☐	☐
Has plateau airway pressure exceeded 30 cmH_20 for more than 4 hours in last 24 hour period*? (If plateau not recorded has peak inspiratory pressure exceeded 30 cmH_20)[3]	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A

*The first 24 hour period is defined as the time from trial entry until the following morning. Thereafter each 24 hour period starts from the beginning of each morning/day shift. If you answer N/A please indicate reason e.g. patient not ventilated.

During days 29-35 in critical care has the patient required any of the following:

	Yes	No
1. Use of high frequency/oscillation/jet ventilation	☐	☐
2. Use of nitric oxide	☐	☐
3. Use of prone position	☐	☐
4. Use of steroids	☐	☐

NB: Level of care is not the same as the location of care.
For definitions *1-3 and organ support please see Page 14.

If the patient is still receiving critical care **after day 35** please return the pages for Days 29-35 by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** and continue recording data on page 11, Critical Care – Days 36-42.

If the patient has been transferred, has died or has been discharged during Days 29-35, please complete the outcome page (page 13) and return this datasheet in full by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** with the **Days 29-35 page**.

Please keep the original form in the patient's notes and make a copy for your files.

N.B. If it is easier for you to post a copy of this datasheet back to the CESAR Data Co-ordinating Centre please use the freepost envelope which is in the trial folder. Please remember to make **2** copies of this form, send **1** copy to the CESAR Data Co-ordinating Centre, keep **1** copy in your trial folder and file the original in the patient's notes.

CESAR Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT
Telephone: 020 7927 2376/2075
Fax: 020 7637 2853

Level of Care and Organ Support Data Collection Sheet Days 36-42

N.B. If the patient is still receiving critical care after day 42 the CESAR Data Co-ordinating Centre will send additional data collection sheets as necessary.

1. Hospital name:

2. CESAR Study number: ☐☐☐☐☐☐ 3. Patient's initials: ☐☐

Please record the following data on a daily basis until the patient is discharged from the critical care unit

Day number / Date	36 / /	37 / /	38 / /	39 / /	40 / /	41 / /	42 / /
Level of care: only 1 box should be ticked for each day of stay, and the highest level of care within a day should be recorded:							
Level 3: Intensive Care[1*]	☐	☐	☐	☐	☐	☐	☐
Level 2: High Dependency Care[2*]	☐	☐	☐	☐	☐	☐	☐
Organ system support: more than one organ system support can be recorded:							
1. Basic respiratory support	☐	☐	☐	☐	☐	☐	☐
2. Advanced respiratory support	☐	☐	☐	☐	☐	☐	☐
3. Circulatory support	☐	☐	☐	☐	☐	☐	☐
4. Neurological support	☐	☐	☐	☐	☐	☐	☐
5. Renal Support	☐	☐	☐	☐	☐	☐	☐
6. ECMO	☐	☐	☐	☐	☐	☐	☐
7. Liver support	☐	☐	☐	☐	☐	☐	☐
8. No organ support	☐	☐	☐	☐	☐	☐	☐
9. Other (specify).....	☐	☐	☐	☐	☐	☐	☐
Location of care: only one box should be ticked for each day of stay. If a patient moves location (e.g. from the ICU to the HDU) please tick the box for the location where the patient has spent ≥ 50% of the day:							
Intensive Care Unit (ICU)	☐	☐	☐	☐	☐	☐	☐
High Dependency Unit (HDU)	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU	☐	☐	☐	☐	☐	☐	☐
Combined ICU/HDU/Coronary Care Unit	☐	☐	☐	☐	☐	☐	☐
Cardiothoracic ICU	☐	☐	☐	☐	☐	☐	☐
Neurological ICU	☐	☐	☐	☐	☐	☐	☐
Theatre recovery area	☐	☐	☐	☐	☐	☐	☐
Other (please state).....	☐	☐	☐	☐	☐	☐	☐
Has plateau airway pressure exceeded 30 cmH_20 for more than 4 hours in last 24 hour period*? (If plateau not recorded has peak inspiratory pressure exceeded 30 cmH_20)[3]	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A	☐ Yes ☐ No ☐ N/A

*The first 24 hour period is defined as the time from trial entry until the following morning. Thereafter each 24 hour period starts from the beginning of each morning/day shift. If you answer N/A please indicate reason e.g. patient not ventilated.

During days 36-42 in critical care has the patient required any of the following:

	Yes	No
1. Use of high frequency/oscillation/jet ventilation	☐	☐
2. Use of nitric oxide	☐	☐
3. Use of prone position	☐	☐
4. Use of steroids	☐	☐

NB: Level of care is not the same as the location of care.

For definitions *1-3 and organ support please see Page 14.

If the patient is still receiving critical care **after day 42** please return the pages for Days 36-42 by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** and continue recording data on the new datasheet pages which have been sent to you.

If the patient has been transferred, has died or has been discharged during Days 36-42, please complete the outcome page (page 13) and return this datasheet in full by fax to the CESAR Data Co-ordinating Centre on **020 7637 2853** with the **Days 36-42 page**.

Please keep the original form in the patient's notes and make a copy for your files.

N.B. If it is easier for you to post a copy of this datasheet back to the CESAR Data Co-ordinating Centre please use the freepost envelope which is in the trial folder. Please remember to make **2** copies of this form, send **1** copy to the CESAR Data Co-ordinating Centre, keep **1** copy in your trial folder and file the original in the patient's notes.

CESAR Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT
Telephone: 020 7927 2376/2075
Fax: 020 7637 2853

1. Hospital name:
2. CESAR Study number: ☐☐☐☐☐☐
3. Patient's initials: ☐☐

Outcome Page

Date of admission to this unit: ☐☐ ☐☐ 2 0 ☐☐ dd / mm / yyyy

1. Is the patient alive? Yes ☐ No ☐ If **YES**, go to Q.2. If **NO**, please give the following:

   Date of death: ☐☐ ☐☐ 2 0 ☐☐ dd / mm / yyyy Cause of death:_____

   Was a Post Mortem carried out? Yes ☐ No ☐

   Please now go to the bottom of this page for instructions on returning this form.

2. Date patient left this unit: ☐☐ ☐☐ 2 0 ☐☐ dd / mm / yyyy

3. Has the patient been discharged to a department other than intensive care or high dependency in this hospital? Yes ☐ No ☐ If **YES**, please give the following, if **NO**, go to Q4:

   Name of unit :_____ Tel. number:_____

   Contact doctor :_____

   Please now go to Q6

4. Has the patient been transferred to a different critical care unit in this or another hospital? Yes ☐ No ☐

   If **YES**, please give the following details, if **NO** go to Q5:

   Name of unit :_____ Tel. number:_____

   Hospital:_____ Contact doctor (if known):_____

   Name of Ambulance Trust:_____

   Name of contact person to collect full details of transport arrangements:_____

   Contact telephone number for the above named person :_____

   Please now go to Q6

5. Has the patient been discharged to a department other than intensive care or high dependency in a different hospital, to continue their treatment? Yes ☐ No ☐

   If **YES**, please give the following details, if **NO** go to Q6:

   Name of unit :_____ Tel. number:_____

   Hospital:_____ Contact doctor (if known):_____

   Name of Ambulance Trust:_____

   Name of contact person to collect full details of transport arrangements:_____

   Contact telephone number for the above named person :_____

   Please now go to Q6

6. If the patient has been transferred please describe the reason for the transfer (please tick one box only):
   Clinical ☐
   Non-clinical (e.g. due to bed pressures in existing critical care unit) ☐

7. Ambulance booking reference number (if known): _____

On completion of this outcome page, please fax a copy to: CESAR Data Co-ordinating Centre on 020 7637 2853, keep 1 copy in your trial folder and file the original with the patient's notes.

Definitions

Level of care

1 **Level 3 care** is for patients requiring one or more of the following:
- Advanced respiratory system monitoring and support alone
- Two or more organ systems being monitored and supported, one of which may be advanced respiratory support
- Patients with chronic impairment of one or more organ systems sufficient to restrict daily activity (co-morbidity) and who require support for an acute reversible failure of another organ.

2 **Level 2** care is for patients requiring one or more of the following:
- Single organ system monitoring and support, excluding advanced respiratory support
- General observation and monitoring: more detailed observation and the use of monitoring equipment that cannot safely be provided on a general ward. This may include extended post-operative monitoring for high-risk patients
- Step-down care: patients who no longer need intensive care but who are not well enough to be returned to a general ward.

Ventilation strategy

3 It is recommended that intensivists adopt the low volume and low pressure ventilation strategy as defined in the NIH ARDS Network Study. Adherence to this strategy is defined as a plateau pressure <30 cm H_2O (or, if plateau pressure is not measured, then use peak inspiratory pressure <30 cm H_2O). This will usually mean a tidal volume of 4-8ml/kg body weight as defined in the low tidal volume ventilation strategy according to the ARDS Network group.

Organ support

* For the purposes of this data collection sheet Organ Support will be defined using the Department of Health's Augmented Care Period (ACP) set of definitions as follows:

1. Basic respiratory system monitoring/support (indicated by one or more of the following)
   - More than 50% oxygen by fixed performance mask
   - The potential for deterioration to the point of needing advanced respiratory support
   - Physiotherapy to clear secretions at least two hourly, whether via tracheostomy, minitracheostomy, or in the absence of an artificial airway
   - Patients recently extubated after a prolonged period of intubation and mechanical ventilation
   - Mask CPAP or non-invasive ventilation
   - Patients who are intubated to protect the airway but needing no ventilatory support and who are otherwise stable

2. Advanced respiratory system monitoring/support (indicated by one or more of the following)
   - Mechanical ventilatory support (excluding mask (CPAP) by non-invasive methods e.g. mask ventilation)

3. Circulatory system monitoring/support (indicated by one or more of the following)
   - Vasoactive drugs used to support arterial pressure or cardiac output
   - Circulatory instability due to hypovolaemia from any cause
   - Patients resuscitated following cardiac arrest where intensive care is considered clinically appropriate
   - Intra aortic balloon pumping

4. Neurological system monitoring/support (indicated by one or more of the following)
   - Central nervous system depression, from whatever cause, sufficient to prejudice the airway and protective reflexes
   - Invasive neurological monitoring e.g. ICP, jugular bulb sampling

5. Renal system monitoring/support (indicated by)
   - Acute renal replacement therapy (haemodialysis, haemofiltration etc.)

6. ECMO
   - Extra-corporeal Membrane Oxygenation (Glenfield Hospital Only)

7. Liver support (indicated by)
   - Extra-corporeal liver replacement device i.e. MARS (Teraklin, Rostock, Germany), bioartificial liver or charcoal haemoperfusion

Other personal costs relating to your illness

Please note details of date and personal costs relating to your illness since you came home, and what they were for (see example in bold below).

Drugs or equipment costs	Travel/fares or mileage costs for health care	Childcare costs when needing health care	Private consultation	Home help, private nurse etc.	Other
e.g. £6 for prescription of antibiotics March 1-8					

Days off from work

If you have returned to work, please enter the date ☐☐☐☐☐☐☐☐ dd/mm/yyyy

If you have taken time off work due to illness since then, please complete the table below:

Please enter the start and stop dates for any period of absence from work	Number of days off sick	Reason for absence from work

Please keep this diary at home until you are visited 6 months after joining the study. If you have any queries please contact:

CESAR Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT

Tel: 020 7927 2376/2075

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure

EVENTS DIARY

This *Events Diary* is for you to keep, in order that you may have a record of events related to your health from the time of your discharge from hospital.

In addition, as you may be aware, a study researcher will visit you at home about 6 months after you joined the study to ask you about events related to your health.

To keep track of these events you may find this *Events Diary* will help you answer the questions. This is partly so that we can estimate how much your illness cost in terms of time off work, personal expenses and cost of continuing care. Please have this *Diary* available when the researcher visits you.

If you require additional space to record details of health service use, please use the sheet entitled *Events Diary - additional information* which is included with this booklet.

Date of discharge from hospital ☐☐☐☐☐☐☐☐ dd/mm/yyyy

On the day you were discharged from hospital please tell us how you travelled home:

_____

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General Practice

If you see the doctor, nurse, physiotherapist or occupational therapist from your general practice, please write the date of each visit, whom you see and where. Use one box for each visit.

Date of visit	Whom did you see (i.e. doctor, nurse, physiotherapist, occupational therapist, counselling or psychological treatments)	Where did you see them (practice or home visit, please specify)

Telephone Advice

If you have contacted any of the following for advice about your health by phone please give dates. Please exclude calls for arranging appointments and repeat prescriptions.

Date of phone advice	Whom did you call (e.g. NHS Direct, your GP, nurse etc.)

Hospital Admissions

If you are admitted to hospital, please write the name of the hospital and the dates of each admission and discharge. Use one box for each admission.

Name of hospital	Date of admission	Date of discharge

Hospital Visits (not inpatient)

If you have visited hospital as an **outpatient** or in an emergency (i.e. casualty/A&E), please write the name of the hospital or outpatient clinic with the date of each visit. Use one box for each visit.

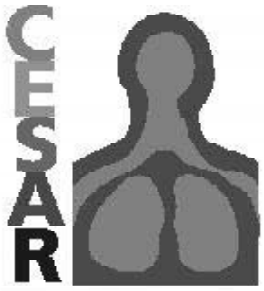
Date	Name of outpatient clinic and hospital	Emergency or routine?

Community and Social Services

If you have any visits from community or social service staff please give the date of each visit.

Date of visit	Who visited you (e.g. social worker, homecare worker or care attendant, health visitor)

Conventional Ventilation or ECMO for Severe Adult Respiratory Failure



EVENTS DIARY

Additional information

Please use this sheet to record details of health service use if there is not enough space on the *Events Diary*.

Please continue on the next page if necessary.

Please keep this additional sheet with your *Events Diary* until you are visited 6 months after joining the study. If you have any queries please contact:

CESAR Data Co-ordinating Centre, Medical Statistics Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT

Tel: 020 7927 2376/2075

DOI: 10.3310/hta14350

Health Technology Assessment 2010; Vol. 14: No. 35

Patient Costs Questionnaire

Interviewer: The following explains the purpose of this interview and in particular the reasons for economic questions. You may either read out the following or use your own words to convey to the patient the reasons for the interview. The same questionnaire can be used for all patients whether they are living at home or in residential/nursing home care.

- I'm sure that the time you were ill was very difficult for you and the people close to you in many ways.
- This questionnaire will help us to understand how much your illness, following your time in intensive care, has cost you and your family financially.
- We are also interested in whether your treatment affected your use of other health and community services.
- We are also interested to know about any health, community or voluntary services that you may have used since your discharge from hospital.
- If you cannot remember the exact details please give your best estimates.
- When you came home from hospital you were sent an Events Diary to help you to record details of health-related events and personal costs.
- Did you use this?
- Have you got it handy as it may help in completing this questionnaire?
- The information provided will be confidential to the researchers and used only to contribute to overall study results.

CESAR study number ☐☐☐☐☐☐

CESAR study number ☐☐☐☐☐☐

Part One: Healthcare and Community Services

1. Transport

On the day you returned home after your stay in hospital, how did you travel home?

Ambulance ☐ Voluntary car services ☐ Taxi ☐
Own/family car ☐ Other (please specify) ☐ .....

Approximate distance (one-way): .....miles. If you used a taxi please give the fare you paid: £.....

2. General Practitioners

Since returning home from your time in hospital, have you consulted your GP? YES ☐ NO ☐

If NO, please go to QUESTION 3. If YES, please give details of the number of consultations you have had with your GP:

At the surgery ☐☐ At home ☐☐ By telephone* ☐☐ **Please exclude calls for arranging appointments and repeat prescriptions.*

How do you normally travel to see your GP? (e.g. Own car, taxi etc) .....

If you usually travel by car or ambulance, please give approximate return mileage to your GP surgery: .....miles

If you usually travel by public transport or taxi please give the usual return fare per visit: £.....

3. Other telephone advice

Since returning home from your time in hospital have you contacted any of the following by phone for advice about your health?

	Contact by telephone	If YES, how many times?
NHS Direct	YES ☐ NO ☐	
Other (please specify)	YES ☐ NO ☐	

CESAR study number ☐☐☐☐☐☐

4. Nursing, Therapy and Social Services

Since returning home from your time in hospital, have you received any of the following services? YES ☐ NO ☐

If NO, please go to QUESTION 5. If YES, please give further details below.

	Approx. number of visits	Location of visit (home, hospital, clinic etc)	Did you have to pay?	If yes, approx. cost per visit	Did you have private medical insurance to cover this cost?	If this invloved travelling, please give type of transport used (own car, ambulance etc.) or write N/A	If travelled by car / ambulance please give approx. return mileage	If you travelled by public transport / taxi please give return fare per visit
			Yes No		Yes No N/A			
Nurse			☐ ☐	£	☐ ☐ ☐			£
Physiotherapist			☐ ☐	£	☐ ☐ ☐			£
Occupational therapist			☐ ☐	£	☐ ☐ ☐			£
Counselling or psychological treatments			☐ ☐	£	☐ ☐ ☐			£
Social worker			☐ ☐	£	☐ ☐ ☐			£
Home care worker or care attendant			☐ ☐	£	☐ ☐ ☐			£
Health visitor			☐ ☐	£	☐ ☐ ☐			£
Other (please specify)			☐ ☐	£	☐ ☐ ☐			£

Interviewer: Please use this space to record any other services which could not be listed above .

CESAR study number ☐☐☐☐☐☐

5. Hospital care

Since returning home from your time in hospital:

Part A Have you been admitted to hospital? YES ☐ NO ☐ *If NO, please go to QUESTION 5 PART B.*

If YES, how many times? ☐☐

Please complete the following table as far as you are able to (for day procedures give the same date for admission and discharge).

	Date admitted	Date discharged	Name of hospital and town	Please describe how you travelled to the hospital (car, ambulance etc.)	If you travelled by car / ambulance please give approx. return mileage	If you travelled by public transport or taxi please give return fare	Did you have private medical insurance to cover this stay?
							Yes No N/A
Stay 1						£	☐ ☐ ☐
Stay 2						£	☐ ☐ ☐
Stay 3						£	☐ ☐ ☐
Stay 4						£	☐ ☐ ☐
Stay 5						£	☐ ☐ ☐

Part B Have you visited a hospital as an outpatient? YES ☐ NO ☐

If NO, please go to QUESTION 6. If YES, please give further details below.

	Approx. number of visits	Did you have to pay?	If Yes, approx. how much per visit	Did you have private medical insurance to cover this cost?	Please describe how you travelled for these visits (own car, ambulance etc.)	If you travelled by car or ambulance please give approx. return mileage	If you travelled by public transport or taxi please give return fare per visit
		Yes No		Yes No N/A			
Consultant clinic (with any doctor)		☐ ☐	£	☐ ☐ ☐			£
Visits to A & E		☐ ☐	£	☐ ☐ ☐			£
Day care/day hospital (e.g. for rehabilitation)		☐ ☐	£	☐ ☐ ☐			£
Other (please specify)		☐ ☐	£	☐ ☐ ☐			£

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6. Nursing home or residential care

Since returning home from your time in hospital, have you been admitted to a nursing home or residential care? YES ☐ NO ☐

If NO, please go to QUESTION 7. If YES, please give further details below.

	Date admitted	Date discharged	Please tick type of care	Did you have to pay?	If yes, approx. cost per stay	Did you have private insurance to cover this cost?	Please describe how you travelled (taxi, ambulance etc.)	If you travelled by car / ambulance please give approx. return mileage	If you travelled by public transport or taxi please give return fare
				Yes No		Yes No N/A			
Stay 1			Nursing home ☐ Residential care ☐	☐ ☐	£	☐ ☐ ☐			£
Stay 2			Nursing home ☐ Residential care ☐	☐ ☐	£	☐ ☐ ☐			£
Stay 3			Nursing home ☐ Residential care ☐	☐ ☐	£	☐ ☐ ☐			£
Stay 4			Nursing home ☐ Residential care ☐	☐ ☐	£	☐ ☐ ☐			£

Interviewer: Please use separate sheet if there are more than 4 stays.

Part Two: Patient's Personal Costs

7. Personal expenditure on medication

Part A Since returning home from hospital, have you taken any medication? YES ☐ NO ☐

If NO, please go to QUESTION 8. If YES, go to PART B

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Part B Was the medication provided by the hospital when you were discharged?

YES ☐ Please give details of any repeat prescriptions and any new medication in the tables below

NO ☐ Please give details of all medication taken in the tables below

Table 1

Prescription drugs from GP	Was the prescription NHS or private?	Approximately how long did you take this medication?	Approximate cost if paid for your medication including prescription charges	Are you currently taking this medication?
e.g. Ampicillin		e.g. Twice daily for a month	e.g. £5.50	

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Table 2

Non-prescription drugs i.e. over the counter medication	Approximately how long did you take this medication?	Approximate cost if paid for your medication including prescription charges
e.g. Aspirin	e.g. Twice daily for a month	e.g. £3.00

8. Personal expenditure on healthcare

Since returning home from your time in hospital, have you used any of the following services or items? YES ☐ NO ☐

(Interviewer: please read out list of items from the table below. Also include any item/adaptation that has been ordered/arranged but not yet received by patient.)

If NO, please go to QUESTION 9. If YES, please provide as many details as you can in the table on page 8.

CESAR study number ☐☐☐☐☐☐

Personal expenditure on healthcare

Please give details of each item under each heading	Did you have to pay anything?	Approximate cost if known	Did you have private medical insurance to cover this cost?
A) Private medical care (e.g. any private treatment not included in Question 5B). Please specify:	Yes ☐ No ☐ N/A ☐		Yes ☐ No ☐ N/A ☐
B) Equipment (e.g. wheelchair). Please specify: N.B. If you used any equipment but did not pay for it please specify who arranged this for you (e.g. hospital, social services, voluntary sector etc.)	Yes ☐ No ☐ N/A ☐ Equipment was provided by :		Yes ☐ No ☐ N/A ☐
C) Childcare (any childcare arrangements you had to make due to your illness). Please specify:	Yes ☐ No ☐ N/A ☐		Yes ☐ No ☐ N/A ☐
D) Any adaptations to your home such as a ramp, stair lift, changes to the bathroom etc. Please specify: If you had any adaptations done to your home but did not pay for it please specify who provided this for you?	Yes ☐ No ☐ N/A ☐ Adaptations provided by:		Yes ☐ No ☐ N/A ☐
E) Any other items of health care. Please specify.	Yes ☐ No ☐ N/A ☐		Yes ☐ No ☐ N/A ☐

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Part Three: Employment

9. Employment before hospitalisation

Were you in employment before you were admitted to intensive care? Yes ☐ No ☐

If YES, was this:

Paid employment	Full time ☐	Part-time ☐
Unpaid employment (e.g. volunteer)	Full time ☐	Part-time ☐

If NO, please choose one or more of the following categories that best described your status before your time in hospital and go to QUESTION 12.

Retired ☐	Retired on medical grounds ☐	Unemployed ☐
Student ☐	Housewife/househusband ☐	Other (*please specify*) ..... ☐

10. Employment after discharge

Part A **Please tell us your current employment status by ticking one of the following boxes.**

Returned to paid work	☐	Date returned to work _ _ / _ _ / _ _ *(dd/mm/yy)*
Returned to unpaid work (volunteer)	☐	Date returned to work _ _ / _ _ / _ _ *(dd/mm/yy)*
Paid sick leave	☐	Please go to Q.12
Unpaid sick leave	☐	Please go to Q.12
Retired on medical grounds after discharge	☐	Please go to Q.12
Unemployed	☐	Please go to Q.12
Other (please specify)	☐	Please go to Q.12

_____

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Part B If you returned to work:

Is this job: Full time ☐ Part-time ☐

Is it the same employment that you had before your illness? YES ☐ NO ☐

11. Time off work

If you have returned to work since returning home, have you had to take any time off work because of further illness?

YES ☐ **NO** ☐ **Not Applicable** ☐

If NO, please go to question 12. If YES, how many days? ☐☐☐

12. Benefits and allowances

(Interviewer: please remind and reassure patient that all data will be kept confidential)

Are you currently receiving any government benefits or allowances? YES ☐ NO ☐

If YES, please give approximate date when you became eligible. _ _ / _ _ / _ _ *(dd/mm/yy)*

If NO, have you applied for any benefits or allowances since your discharge from hospital? YES ☐ NO ☐

(Interviewer: The following list of benefits/allowances might help remind the patient/carer about any benefits they might have applied for: housing benefit, incapacity benefit, severe disablement allowance, invalid care allowance, attendance allowance and disability allowance)

DOI: 10.3310/hta14350

CESAR study number ☐☐☐☐☐☐

13. Employment - additional information

Please give any comments on income, work etc. that were not covered in questions 9-12.

_____

_____

_____

14. Healthcare from family and friends

Since returning home from your time in hospital, have you received care from family members, relatives or friends as a result of illness? YES ☐ NO ☐

If NO, please go to QUESTION 15. If YES, please complete the following:

1) Was this help from an unpaid carer? YES ☐ NO ☐
2) Did your carer have to take this time off work? YES ☐ NO ☐
3) Did your carer have to give up his/her employment? YES ☐ NO ☐
4) Did your carer have to take up a different job or switch to a part-time job to care for you? YES ☐ NO ☐

Please describe the frequency of involvement by carers since discharge in the table below:

Total weekly hours of help (e.g. 2 hours help twice a week, total is 2x2 = 4)	Over what period did you receive this help? (e.g. 1 week)	Total hours of help
Any comments		

CESAR study number ☐☐☐☐☐☐

5) Do you need regular daily help with things that fit and healthy people would normally do for themselves? YES ☐ NO ☐

(Interviewer: if YES please record carer details on checklist and issue a CSI if carer present)

15. Changes to family circumstances

Since you were admitted to intensive care, have there been any significant changes in your family circumstances? YES ☐ NO ☐

If NO, please go to QUESTION 16. If YES, please provide (approximate) costs for the following:
(Interviewer: Please try to establish any major changes and express costs as per month if possible, giving comments to explain if necessary. If patient is only able to give a total cost please make a note of this in the 'comments' column)

Description	Approximate monthly additional cost, if known	Comments
Change in residence (e.g. had to move to a different but own house, move to a relative's house etc.)		
Any other such as lost employment income through illness (please specify)		

DOI: 10.3310/hta14350

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16. Do you have any health related insurance policy/plan? YES ☐ NO ☐

If No please go to QUESTION 17, if YES, please tell us what it covers by ticking one or more of the following options:

1) Health care costs ☐ 2) Income protection ☐

3) Any other (please specify) …….. ☐

17. Do you have any other comments about the cost of your health care that you'd like me to record? YES ☐ NO ☐

(*Interviewer: Please record any comments made by the patient or carer)*

_____

_____

_____

_____

_____

_____

_____

_____

_____

Economic questions if visited in hospital

CESAR study number ☐☐☐☐☐☐

In addition to all the other issues you have had to face, we are aware that illness may lead people to have extra costs. We want to understand how much your illness cost you and your family, so the following questions will address this.

1. Employment before hospitalisation

	Yes	No
Were you in employment before you were admitted to intensive care?	☐	☐

If YES, was this:

a) Paid employment — Full time ☐ Part time ☐

b) Unpaid employment (e.g. volunteer) — Full time ☐ Part time ☐

If NO, please choose one or more of the following categories that best described your status before your time in hospital.

1. Retired ☐
2. Retired from work on medical grounds ☐
3. Student ☐
4. Housewife/househusband ☐
5. Unemployed ☐
6. Other (please specify) ..... ☐

2. Benefits and allowances

(Interviewer: please remind and reassure patient that all data will be kept confidential)

	Yes	No
Are you currently receiving any government benefits or allowances?	☐	☐

If YES, please give the approximate date you became eligible. ☐☐☐☐☐☐☐☐ dd/mm/yyyy

	Yes	No
If NO, have you applied for any benefits or allowances since you were admitted to hospital?	☐	☐

(Interviewer: The following list of benefits/allowances might help remind the patient/carer about any benefits they might have applied for: housing benefit, incapacity benefit, severe disablement allowance, invalid care allowance, attendance allowance and disability allowance)

3. Changes to family circumstances

Since you were admitted to intensive care, have there been any significant changes in your family circumstances? Yes ☐ No ☐

If NO, please go to Question 4.

If YES, please provide (approximate) costs for the following:

(Interviewer: Please try to establish any major changes and express costs as per month if possible, giving comments to explain if necessary. If patient is only able to give a total cost please make a note of this in the comments column)

Description	Approximate monthly additional cost if known	Comments
Any adaptations to the home		
Any other (e.g.lost employment income through illness, please specify)		

4. Health Insurance

Do you have any health related insurance policy/plan? Yes ☐ No ☐

If YES, please tell us what it covers by ticking one or more of the following options:

1. Health care costs ☐ 2. Income protection ☐

3. Any other (please specify) ☐ .....

Caregiver Strain Index

The following questions have been designed to find out how carers are affected by looking after someone who has been discharged from hospital or who has an illness.

Name of carer: _____

Age: ☐☐

Sex: Male ☐ Female ☐

CESAR study number ☐☐☐☐☐☐

CESAR study number ☐☐☐☐☐☐

Please answer every question. If any of the questions do not seem appropriate to your own personal circumstances, please respond by ticking the NO box.

	YES	NO
1. Sleep is disturbed (e.g. because care is needed at night or because the patient is in and out of bed or wanders around at night).	☐	☐
2. It is inconvenient (e.g. because helping takes so much time or it's a long way over to help).	☐	☐
3. It is a physical strain (e.g. because of lifting in and out of a chair; effort or concentration is required).	☐	☐
4. It is confining (e.g. helping restricts free time, or cannot go visiting).	☐	☐
5. There have been family adjustments (e.g. because helping has disrupted routine; there has been no privacy).	☐	☐
6. There have been changes in personal plans (e.g. had to turn down a job; could not go on holiday).	☐	☐
7. There have been other demands on my time (e.g. from other family members).	☐	☐
8. There have been emotional adjustments (e.g. severe argument; relationship with other family members).	☐	☐
9. Some behaviour is upsetting (e.g. due to incontinence and need for intimate personal care; memory problems; accusations of stealing).	☐	☐
10. It is upsetting to find that the patient has changed so much from his/her former self (e.g. is a different person than they used to be).	☐	☐
11. There have been work adjustments (e.g. because of having to take time off).	☐	☐
12. It is a financial strain.	☐	☐
13. Feeling completely overwhelmed (e.g. because of worry about the patient; concern about how you will manage).	☐	☐

Thank you for taking time to complete this questionnaire

Please give the completed form directly to the researcher or use the stamped addressed envelope (S.A.E.) and return to:

Dr Andy Wilson
Senior Lecturer
Department of GP and PHC
University of Leicester
Gwendoline Rd
Leicester LE5 4PW

6 Month Follow-Up Assessment Checklist

This checklist should be completed by the Follow-up Assessment Researcher

Patient Initials ☐☐ CESAR study number ☐☐☐☐☐☐

Date of follow-up appointment: ☐☐/☐☐/☐☐☐☐ dd/mm/yyyy

How was the appointment conducted? ☐ Home visit ☐ Telephone ☐ Postal

Does the patient have a carer? ☐ Yes ☐ No

If Yes, please give:

Name: _____ Address: _____

_____

Tel. number: _____ _____

If the patient has a carer, has a CSI been completed and returned? ☐ Yes, completed at assessment ☐ Yes, returned by post ☐ No, carer refused ☐ No, form not returned

Was the events diary used? ☐ Yes ☐ No

Duration of interview? _____

Was the interview completed? ☐ Yes ☐ No

If No, please give the following details:

1) Reason interview not completed? _____

	Yes	No
2) Were any arrangements made for a telephone follow-up?	☐	☐

If Yes, please give details: _____

Please indicate which follow-up forms have been completed and returned with this checklist:

	Yes	No	If not returned please give reason
1. EQ-5D	☐	☐	_____
2. SGHRQ	☐	☐	_____
3. SF-36v2	☐	☐	_____
4. HAD	☐	☐	_____
5. Patient Costs Questionnaire	☐	☐	_____
6. Additional Questions and Examination	☐	☐	_____

Was the researcher blind to the patient's allocation up to the PCQ? YES ☐ NO ☐

Was the researcher blind to the patient's allocation at the end of the interview YES ☐ NO ☐

If you have answered NO to either (or both) questions about allocation, please record what you think the patient's allocation is:

ECMO ☐ Conventional ☐ No idea ☐

Is there evidence of post illness hearing impairments? YES ☐ NO ☐

Date checklist completed: ☐☐/☐☐/☐☐☐☐ dd/mm/yyyy

Researcher's name: _____ Researcher's signature: _____

Please photocopy this form and all the follow-up documents, send the copies to:

Steven Robertson, CESAR Data Co-ordinating Centre
Medical Statistics Unit, London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

and file the originals in the CESAR folder.

Health Service Use of Patients in CESAR Trial

Patient Initials ☐☐ CESAR study number ☐☐☐☐☐☐

Name of GP surgery: .....

Name of patient: .....

Date of birth: ☐☐☐☐☐☐☐☐ dd/mm/yyyy

Data required from: start date ☐☐☐☐☐☐☐☐ dd/mm/yyyy
to
finish date ☐☐☐☐☐☐☐☐ dd/mm/yyyy (6 months after entry into trial)

We would be grateful if you are able to provide the following details for the above patient. Information collected from questions 1-2 below form part of the primary outcome for the clinical aspect of the study. Information collected on pages 2-4 will be used as part of the CESAR economic evaluation.

1. Was the patient alive at ☐☐☐☐☐☐☐☐ dd/mm/yyyy

   YES ☐ If YES, please go to Question 2.
   NO ☐ If NO, please complete the following and go to page 2:

   Date of death: ☐☐☐☐☐☐☐☐ dd/mm/yyyy

   Cause of death:_____

2. If YES, please select the option which best describes the patient's mobility and self-care status on ☐☐☐☐☐☐☐☐ dd/mm/yyyy

   Mobility

   Patient has no problems in walking about ☐
   Patient has some problems in walking about ☐
   Patient is confined to bed ☐
   Patient's mobility status not known ☐

   Self-care

   Patient has no problems with self-care ☐
   Patient has some problems washing or dressing ☐
   Patient is unable to wash or dress ☐
   Patient's self-care status not known ☐

Patient Initials ☐☐ CESAR study number ☐☐☐☐☐☐

Instructions for table 1: Please enter '0' in the appropriate column if no visits or telephone contacts were made by the above patient to any particular professional group. Please put a tick (✔) in the fourth column if data on visits and telephone contact to some professionals is not available from your records.

Table 1: Consultations at GP surgery and community clinics			
Professional consulted	Number of consultations at surgery/clinic	Number of telephone contacts	Data for this not available from GP records
GP			
Nurse			
Physiotherapist			
Occupational therapist			
Provider of counselling or psychological treatments			
Any other (please specify)			

Instructions for table 2: Please enter '0' if no visits were made by any particular professional group. Please put a tick (✔) in the third column if data on visits by some professionals is not available from your records.

Table 2: Home visits by the following professionals		
	Number of home visits	Data for this not available from GP records
GP		
Nurse		
Physiotherapist		
Occupational therapist		
Provider of counselling or psychological treatments		
Any other (please specify)		

Table 3: Outpatient clinic visits. If no visits tick box ☐	
Specialty	Number of visits
....	....

Patient Initials ☐☐ CESAR study number ☐☐☐☐☐☐

Table 4: Other hospital visits by patient including investigations etc.		
	Number of visits	If none tick box
A & E		☐
Day care / day hospital		☐
Investigations, physio, occupational therapy etc.		☐
Any other (please specify)		☐

Table 5: Hospital admissions.		
	Specialty	Dates admitted and discharged
Inpatient admission If none tick box ☐	....	dd / mm / yy Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐ Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐ Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐ Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐ Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐
Day case procedures If none tick box ☐	....	dd / mm / yy Date ☐☐ ☐☐ ☐☐ Date ☐☐ ☐☐ ☐☐ Date ☐☐ ☐☐ ☐☐ Date ☐☐ ☐☐ ☐☐

Table 6: Nursing home or residential care admissions. If none tick box ☐		
Type of home		Dates admitted and discharged
Nursing home ☐	Residential care ☐	dd / mm / yy Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐
Nursing home ☐	Residential care ☐	Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐
Nursing home ☐	Residential care ☐	Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐
Nursing home ☐	Residential care ☐	Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐
Nursing home ☐	Residential care ☐	Admitted ☐☐ ☐☐ ☐☐ Discharged ☐☐ ☐☐ ☐☐

Patient Initials ☐☐ CESAR study number ☐☐☐☐☐☐

Table 7: Other health related referrals.		
	If none tick box	Date of referral
Social services referral by GP	☐	dd / mm / yy ☐☐ ☐☐ ☐☐
Any other referral by GP for services not provided within this surgery e.g. physiotherapy, occupational therapy (please specify)	☐	☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐ ☐☐

If possible please send a printout of all medication prescribed between the **start** and **finish** dates as listed on page 1. If this is not possible please complete table 8.

Please tick box if printout is enclosed ☐

Table 8: Prescriptions		
Date prescribed	Name of medication	Period for which the medication was prescribed (e.g. 2 weeks)

Thank you for completing this form. Please return it in the enclosed freepost envelope to:

CESAR Trial Data Co-ordinating Centre
Medical Statistics Unit, London School of Hygiene & Tropical Medicine
Keppel Street, London WC1E 7HT

Appendix 3

Study protocol

CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure

Giles J Peek,[1*] Felicity Clemens,[2] Diana Elbourne,[2] Richard Firmin,[1] Pollyanna Hardy,[2,3] Clare Hibbert,[5] Hilliary Killer,[1] Miranda Mugford,[4] Mariamma Thalanany,[4] Ravin Tiruvoipati,[1] Ann Truesdale[2] and Andrew Wilson[6]

Address: [1]Department of Cardiothoracic Surgery, Glenfield Hospital, Groby Road, Leicester, LE3 9QP, UK; [2]Medical Statistics Unit, London School of Hygiene and Tropical Medicine, Keppel St, London WC1E 7HT, UK; [3]Clinical Epidemiology and Biostatistics Unit, Royal Children's Hospital, Melbourne, Australia; [4]School of Medicine Health Policy and Practice, University of East Anglia, Norwich, NR4 7TJ, UK; [5]School of Health and Related Research, University of Sheffield and RTI Health Solutions, Williams House Manchester Science Park, Manchester ME15 6SE, UK; and [6]Department of Health Sciences, University of Leicester, Leicester General Hospital, Leicester, LE5 4PW, UK

Email: Giles J Peek* - giles.peek@uhl-tr.nhs.uk; Felicity Clemens - Felicity.clemens@lshtm.ac.uk; Diana Elbourne - diana.elbourne@lshtm.ac.uk; Richard Firmin - richard.firmin@uhl-tr.nhs.uk; Pollyanna Hardy - polly.hardy@mcri.edu.au; Clare Hibbert - chibbert@rti.org; Hilliary Killer - hilliary.killer@uhl-tr.nhs.uk; Miranda Mugford - m.mugford@uea.ac.uk; Mariamma Thalanany - M.Thalanany@uea.ac.uk; Ravin Tiruvoipati - rt67@leicester.ac.uk; Ann Truesdale - ann.truesdale@lshtm.ac.uk; Andrew Wilson - aw7@le.ac.uk

* Corresponding author

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Abstract

Background: An estimated 350 adults develop severe, but potentially reversible respiratory failure in the UK annually. Current management uses intermittent positive pressure ventilation, but barotrauma, volutrauma and oxygen toxicity can prevent lung recovery. An alternative treatment, extracorporeal membrane oxygenation, uses cardio-pulmonary bypass technology to temporarily provide gas exchange, allowing ventilator settings to be reduced. While extracorporeal membrane oxygenation is proven to result in improved outcome when compared to conventional ventilation in neonates with severe respiratory failure, there is currently no good evidence from randomised controlled trials to compare these managements for important clinical outcomes in adults, although evidence from case series is promising.

Methods/Design: The aim of the randomised controlled trial of Conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR) is to assess whether, for patients with severe, but potentially reversible, respiratory failure, extracorporeal membrane oxygenation will increase the rate of survival without severe disability ('confined to bed' and 'unable to wash or dress') by six months post-randomisation, and be cost effective from the viewpoints of the NHS and society, compared to conventional ventilatory support. Following assent from a relative, adults (18–65 years) with severe, but potentially reversible, respiratory failure (Murray score ≥ 3.0 or hypercapnea with pH < 7.2) will be randomised for consideration of extracorporeal membrane oxygenation at Glenfield Hospital, Leicester or continuing conventional care in a centre providing a high standard of conventional treatment. The central randomisation service will minimise by type of conventional treatment centre, age, duration of high pressure ventilation, hypoxia/hypercapnea, diagnosis and number of organs failed, to ensure balance in key prognostic variables. Extracorporeal membrane oxygenation will not be available for patients meeting entry criteria outside the trial. 180 patients will be recruited to have 80% power

to be able to detect a one third reduction in the primary outcome from 65% at 5% level of statistical significance (2-sided test). Secondary outcomes include patient morbidity and health status at 6 months.

Discussion: Analysis will be based on intention to treat. A concurrent economic evaluation will also be performed to compare the costs and outcomes of both treatments.

Background

It is estimated that over 350 adult patients suffer from severe, but potentially reversible, respiratory failure in the UK each year. The mortality rate for such patients is very high and has only improved marginally in the majority of centres over the last 20 years[1,2] Current management uses intermittent positive pressure ventilation (IPPV). The airway pressures and oxygen concentrations required to maintain adequate blood gases are often very high in patients with severe respiratory failure, and this combination of barotrauma, volutrauma and oxygen toxicity can prevent lung recovery. An alternative treatment, extracorporeal membrane oxygenation (ECMO), uses cardio-pulmonary bypass technology to temporarily provide gas exchange to patients with severe, but potentially reversible, respiratory failure. During ECMO, ventilator settings can be reduced, and such 'lung-rest' allows the lungs to recover. There is currently no good evidence from randomised controlled trials (RCTs) to compare ECMO against conventional management for important clinical outcomes.

Patients are usually considered for ECMO when they have such severe disease that they continue to deteriorate despite maximal optimum 'conventional' treatment. For the purposes of this protocol, conventional will be defined as any treatment which relies on the patient's lungs to provide gas exchange. Conventional treatment may therefore include inhaled nitric oxide and prone ventilation[3–5], as well as the more usual types of positive pressure ventilation. The use of ECMO to support neonatal patients with severe respiratory failure has been rigorously evaluated in an RCT[6,7]. The *neonatal* ECMO RCT convincingly demonstrated the effectiveness of ECMO in improving patient survival without severe disability. Neonatal ECMO in the UK is now a supra-regional service receiving central funding. The use of ECMO as it is currently practised in older children[8], and adults[9] is more controversial, and has yet to be evaluated in an RCT in the UK.

Previous studies

A review of the literature was carried out to identify all studies relevant to adult ECMO. Only two RCTs have been reported[1,10], both in the United States but they used such different approaches that they have not been combined as a formal meta-analysis. Each is detailed below, followed by the recent non-experimental evidence.

An RCT of adult ECMO was conducted by the US National Institutes of Health (NIH)[1], in the early days of extracorporeal support in the 1970s. Survival in both groups was very poor (around 10%), and no difference was shown in survival between the conventional and ECMO treated groups. There were a number of important differences in the perfusion and ventilation techniques used during this trial compared to those used today. Firstly, veno-arterial (VA) rather than veno-venous (VV) perfusion was used, and this was thought to be responsible for the high incidence of pulmonary micro-thrombosis and fibrosis seen in the lungs of the ECMO patients (due to reduced pulmonary blood flow). Secondly, patients were anti-coagulated to such a degree that severe bleeding occurred. Thirdly, high pressure ventilation was continued during ECMO resulting in continued barotrauma and volutrauma[11,12]. Finally, the mean duration of ventilation prior to ECMO in the NIH ECMO trial was over 9 days, whereas it is now well-recognised that after 7 days of high pressure ventilation with high fraction of inspired oxygen (FIO_2) the lungs only have limited powers of recovery[13].

More recently there has been an RCT of the related technique of extra-corporeal carbon dioxide removal ($ECCO_2R$)[10]. This showed no difference between $ECCO_2R$ and conventional treatment. Again there were numerous differences in the clinical and perfusion protocols between this trial and those in widespread use in the majority of centres currently[14]. Firstly, the experimental arm of the trial used low flow $ECCO_2R$ in a group of patients who had severe lung disease, which warranted higher flow ECMO with full support of oxygenation and carbon-dioxide removal. This was demonstrated by the need to increase the airway pressure in the $ECCO_2R$ group half-way through the study. The reliance on the patient's lungs to provide oxygenation, especially at such high airway pressures, also eliminated any possibility for lung rest. Also, despite the involvement of one of the team in the 1970s NIH ECMO trial, in which VA ECMO was used with very small numbers in each centre (< 5), the $ECCO_2R$ programme in this trial was not well developed prior to the

study (as the team had only provided $ECCO_2R$ to sheep and one patient prior to starting the trial). The high incidence of bleeding and thrombotic complications reported in this study may attest to this inexperience. In addition, the conventional treatment used in the trial was Pressure Controlled Inverse Ratio Ventilation (PCIRV) using a computer controlled algorithm. The results of this treatment showed 44% survival compared to expected survivals of < 20% in other similar series of patients[2]. Despite this, survival in the $ECCO_2R$ group was the same as the 'conventional' group. The success of the PCIRV protocol in this study has led to the wide adoption of the technique within 'conventional' ventilatory management with survival of 66% for patients with *moderate to severe* respiratory failure (mean Murray score 2.8, mean ratio between the oxygen tension in the arterial blood and the fraction of inspired oxygen (PaO_2/FIO_2) 88 mmHg)[15]. Unfortunately no other authors have been able to duplicate the PCIRV results of Morris et al. for patients with *severe progressive* respiratory failure.

Because the two trials described above have little relevance to the ECMO regimens used in the majority of centres worldwide, the only relevant evidence consists of observational studies. By the nature of their design, the information they provide is potentially biased, and must therefore be viewed with caution.

Recent case series of patients with similar degrees of respiratory failure to the eligibility criteria for the second trial suggest survival rates without ECMO of 18% to 44%[1,10]. compared to rates of up to 66% with high flow ECMO (including full support of oxygenation and lung rest), provided by experienced teams principally in the USA, UK and Germany[9,13,14].

In a cohort study of the first 50 adult patients to receive ECMO for respiratory support at Glenfield Hospital, Leicester, UK, patients had severe respiratory failure as shown by the mean pre-ECMO Murray Lung Injury Score of 3.4 (SD 0.5) and PaO_2/FIO_2 ratio of 65 mmHg (SD 36.9). They were referred for ECMO with severe respiratory failure caused by either the Acute Respiratory Distress Syndrome (ARDS) or with pneumonia. The overall survival rate was 66%[9].

For the reasons outlined above, it is impossible to reach firm conclusions from the above experimental and observational data regarding the clinical effectiveness or costeffectiveness of VV high flow ECMO for respiratory failure in adults. The recent evidence from observational studies does, however, suggest that ECMO could potentially be a highly useful treatment in these patients. The case selection and treatment protocols used during ECMO are now well defined by the international Extracorporeal Life Support Organization (ELSO), and the only team using ECMO in adults consistently in the UK has built up clinical expertise[9].

It is not possible to further define the safety and efficacy of ECMO as a treatment without a rigorous trial. The procedure has received a Cii categorisation (safety and/or efficacy not yet fully established; procedure requires a fully controlled evaluation) from the UK Safety and Efficacy Register of the New Interventional Procedures of the Medical Royal Colleges (SERNIP). Additionally a situation of equipoise currently exists, whereby clinicians can see the potential benefits of ECMO, but do not have enough evidence to make an informed choice as to the best treatment for their patient.

The aim of the present trial is therefore to assess whether for patients with severe, but potentially reversible, respiratory failure, ECMO will increase the rate of survival without severe disability by six months post randomisation and will be cost effective from the viewpoints of the NHS and society, compared to conventional ventilatory support.

Methods/Design

Design

The most scientifically rigorous design to assess effects of health interventions is that of an RCT. The design will be similar to the highly successful UK neonatal ECMO RCT[6] suitably adapted for the adult population. The design will be 'pragmatic' ie it will, as far as possible, mirror usual practice in the UK. The procedures are illustrated schematically in *Figure 1* below, and detailed in the text.

Primary hypotheses

The primary hypotheses are that, for patients with severe, but potentially reversible, respiratory failure, ECMO:

(a) Will increase the rate of survival without severe disability by six months post-randomisation.
(b) Will be cost effective from the viewpoints of the NHS and society, compared to conventional ventilatory support.

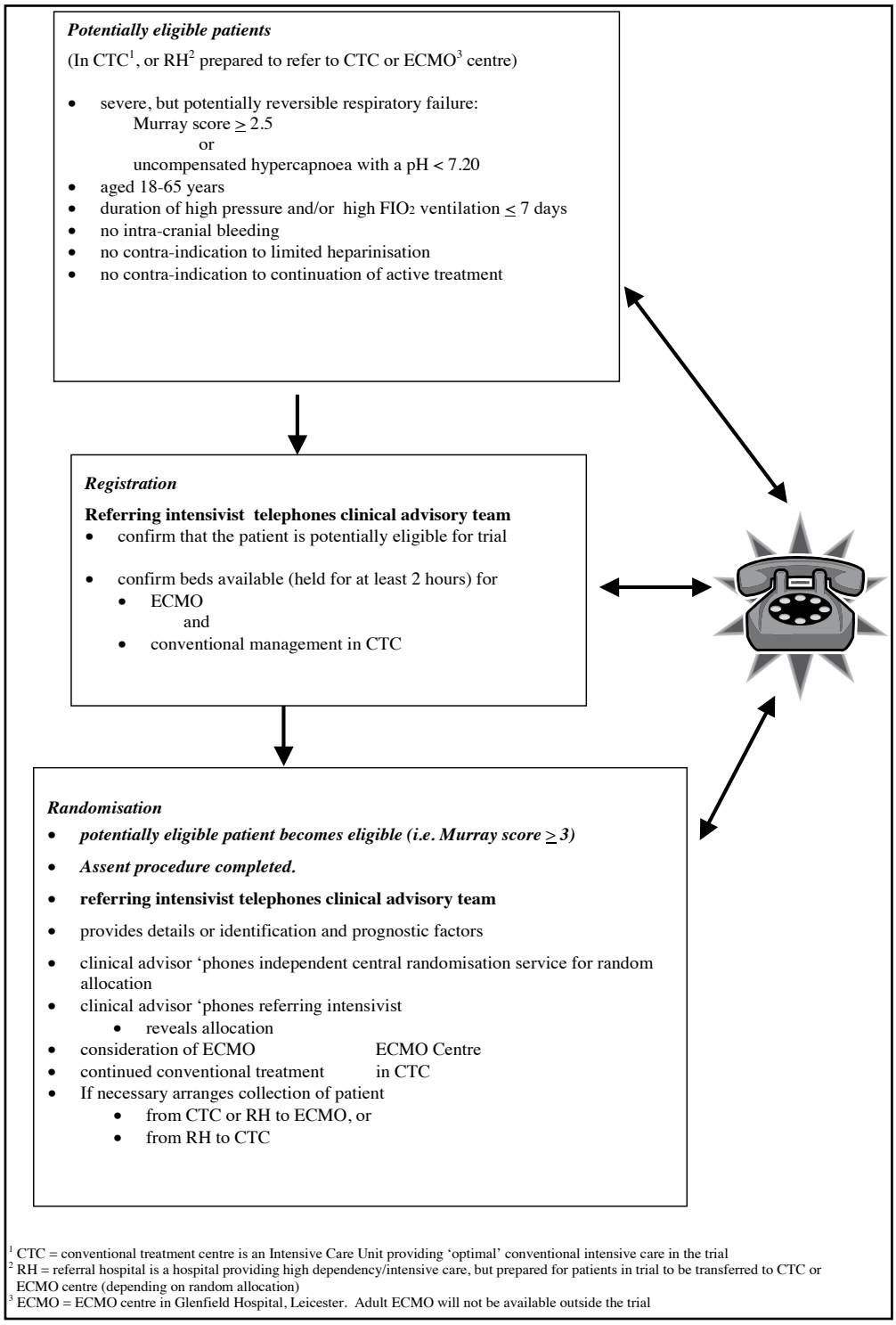

FIGURE 1 *Organisation of the trial.*

Inclusion criteria

i) Centres

(a) ECMO: This will be provided in the Glenfield Hospital, Leicester, which has 17 years of experience and is the only ELSO-recognised adult ECMO centre in the UK.

(b) Conventional treatment centres (CTC): These are either centres acknowledged by Critical

Care Network leads (where established) to provide an appropriately high standard of conventional care for ECMO-eligible patients, or they are units which treat ≥ 350 patients per year, and can provide pressure controlled ventilation and veno-venous haemofiltration.

(c) Referral hospitals (RH): In addition to the centres described under (b) above, patients meeting ECMO entry criteria may be entered into the trial from other hospitals, if these hospitals are prepared to transfer the patient to a designated CTC should the allocation be to conventional management.

ii) Patients

Adult patients (18–65 years) with severe, but *potentially reversible* respiratory failure. Severe respiratory failure will be defined as a Murray score (appendix 1)[16] ≥ 3.0, or uncompensated hypercapnea with a pH < 7.20. This level of hypercapnea was selected to reflect common intensive care clinical practice. The Murray score must be calculated using all 4 parameters (PaO_2/FIO_2, Positive End Expiratory Pressure (PEEP), Lung compliance and Chest X-ray appearance). The Murray score of 3.0 is a MINIMUM entry criterion. Since patients may deteriorate quickly and conventional treatment must be optimised prior to referral into the trial, intensivists will also have the option to discuss registration of the patient for the trial as soon as the Murray score exceeds 2.5. If the patient then continues to deteriorate, prior identification of available beds, and discussion of the trial with the relatives, will allow rapid randomisation and trial entry.

Exclusion criteria prior to trial entry

- Duration of high pressure (> 30 cmH_2O of peak inspiratory pressure) and/or high FIO_2 (> 0.8) ventilation > 7 days[13].
- Intra-cranial bleeding.
- Any other contra-indication to limited heparinisation.
- Patients who are moribund and have any contra-indication to continuation of active treatment.

Moribund patients are those who the duty ECMO consultant feels have a very low chance of meaningful survival with ECMO treatment.

Allocation of patients

Selection bias at entry will be minimised by the procedures described below and shown schematically in *Figure 1*. Potentially eligible patients may be entered into the trial from any participating intensive care unit in the UK. [If a hospital has not yet received ethics committee approval, patients can be entered under an Emergency Inclusion Protocol (EIP)]. The referring intensivist will contact a member of the clinical advisory team to confirm that the patient is eligible for the trial, and that beds for ECMO and conventional management are available. These beds will then be 'held' for at least two hours. If these conditions are met, the referring intensivist will discuss the trial with the patient's relative(s), give written information, and ask for agreement to trial entry. The relative will be asked to sign the assent form indicating that he/she believes his/her relative would not object to taking part in the study. The intensivist will then speak to the advisory team and, if the assent procedure has been completed, the advisor will telephone the independent central randomisation service to register the identifying details, and to give information about key prognostic factors. Randomisation will then be to conventional management or to consideration of ECMO support.

Minimization criteria will be used to ensure a balance of key prognostic factors between groups using the following criteria:

Type of centre (CTC or RH)

Age (18–30, 31–45, 46–65)

Hours of high pressure and/or high FIO_2 ventilation (0–48, 49–168)

Mode of trial entry (i.e. hypoxic/hypercarbic)

Diagnostic group (pneumonia, obstetric acute respiratory distress syndrome (ARDS), trauma including surgery within previous 24 hours, other ARDS, and other)

Numbers of organs failed 1–2 or 3 or more, failure being defined as an individual SOFA score for that organ of ≥ 2)[17,18].

If a patient is referred into the trial when there is no intensive care unit (ICU) or ECMO bed available that patient will not be entered. If beds become available subsequently, the patient is still suitable and the referring intensivist still wants to enter the patient then they will be randomised in the normal fashion. The fact that these patients were referred but were unable to be entered will be recorded.

Referrals for trial entry from hospitals not registered as trial centres; Emergency Inclusion Protocol (EIP)

During the study period ECMO will not be offered outside the framework of the trial to patients eligible for trial entry. If, exceptionally, a UK hospital from outside the study wishes to refer a patient, the transport team from the ECMO centre will go to the hospital and assess the patient. If the patient is suitable then they will call the central randomisation service and the patient will be randomised in the normal fashion. If the patient draws conventional treatment, the ECMO team will transport the patient to the nearest available CTC, and if selected for ECMO they will transport the patient back to Glenfield hospital.

Interventions

1. Conventional management

Patients randomised to conventional ventilatory support will receive the intensive care provided as standard in one of a number of participating CTCs. This may occasionally involve transfer (see Transport, below) from an RH. Conventional ventilatory support can include any treatment modality thought appropriate by the patient's intensivist (excluding ECMO or other extracorporeal techniques). Intensivists will have full discretion to treat patients as they think appropriate. It will be recommended that intensivists adopt the low volume ventilation strategy. Adherence to this strategy is defined for the purposes of CESAR as a plateau pressure $< 30\,cmH_2O$ (or if plateau pressure is not measured the peak inspiratory pressure). This will usually mean a tidal volume of 4–8 ml/kg body weight as defined in the low tidal volume ventilation strategy according to the ARDS Network group[19].

Each CTC will produce their own statement of the general philosophy of treatment. This will be based on a pro-forma, which will detail their approach to ventilation, nutrition, antibiotics and other treatment issues. This pro-forma will also collect basic data regarding the size of unit, number of staff, cases treated per year etc.

2. ECMO

Patients randomised to ECMO will be transferred (see Transport, below) to the ECMO centre for consideration of ECMO support. During the trial, adult ECMO will only be available as part of the trial. There will be no crossover to ECMO for patients allocated to conventional management. ECMO will be provided according to published Glenfield Hospital treatment protocols[9]. This protocol is very similar to those used in other ELSO recognised adult ECMO centres[14], and is summarised below:

Veno-venous ECMO via percutaneous cannulation is used if the patient's haemodynamic status is sufficiently stable to make cardiac assist (via veno-arterial access) unnecessary. Blood is drained from the right atrium through a cannula introduced via the right jugular or femoral veins, and is returned via the contra-lateral femoral vein. Circuits are designed to allow full support of gas exchange i.e. blood flow of 120 ml/kg/min. One or two (depending on body weight) Medos Hi-Lite 7000LT poly-methyl pentene lungs with heat exchangers are arranged in parallel with counter current gas flow, 100% oxygen is used as the sweep gas. Stockert (Sorin Biomedical) roller pumps with bladder box servo control or venous pressure servo-regulation are used. Blood raceway tubing is Tygon S-65-HL (Norton Performance Plastics). Normothermia is maintained. The circuit and patient are managed 24 hours per day by a trained 'ECMO Specialist' capable of performing surveillance and emergency repairs to the circuit.

During ECMO, ventilator settings are gradually reduced to allow lung rest, i.e. peak inspiratory pressure 20 cmH_2O, end expiratory pressure $10\,cmH_2O$, rate 10 breaths per minute and FIO_2 30%. Anticoagulation is maintained with heparin to keep the activated clotting time (ACT) between 160 and 220 seconds. Patients are fed enterally or parenterally into the circuit, as indicated. Invasive procedures are avoided to reduce the risk of haemorrhage, and therefore any additional venous access necessary, e.g. for haemofiltration, is achieved via the circuit. Patients are diuresed to dry weight. Haemoglobin concentrations are maintained at 14 g/dl, and platelet counts are kept > 100,000 per ml. Patients are weaned from ECMO and decannulated when chest X-ray appearance and lung compliance have improved, and adequate gas exchange without excessive ventilation (peak pressure less than 30 cmH_2O, and FIO_2 less than 60%) can be demonstrated during a 'trial-off' ECMO.

Patients developing liver failure either during or after ECMO (defined as a serum bilirubin > 200 uMol/L) are supported with MARS (Molecular Absorbent Recirculating System, Teraklin GMBH, Rostock, Germany).

If the patient's condition alters such that ECMO is no longer possible or appropriate then ECMO will

not be initiated. However such a patient's outcome will be analysed as part of the ECMO group (intention to treat).

3. Transport
Patients who are in a designated CTC will not need to be transported if they are randomised to conventional management. All other trial patients will need transport, which will be provided by a team from the ECMO centre. If the transport team decides that it is not safe to move the patient then s/he will remain in the original unit until s/he is considered safe to transfer, or recovers or dies. Such outcomes will also be analysed as part of the treatment option to which the patient was randomised i.e. analysis is by intention to treat.

Outcome measures
Primary
Death or severe disability at six months (defined as death by 6 months or before discharge from hospital at any time to end of data collection, or where the answer to the first two questions of the Euroqol questionnaire (EQ5D) are 'confined to bed' and 'unable to wash or dress yourself').

Secondary
1. Hospital indices: duration of ventilation, use of high frequency/oscillation/jet ventilation, use of nitric oxide, prone positioning, use of steroids, length of ICU stay, length of hospital stay. Some data will be recorded daily (see 'Economic issues', below). For ECMO patients only, data will be collected on mode (VV/VA), duration of ECMO, blood flow and sweep flow.
2. Health status 6 months after randomisation. This will include activities of daily living, quality of life, respiratory symptoms, cognitive psychological state and lung function. Where applicable carer strain will also be assessed. (See also 'economic issues' below.)
3. Surviving patients will be asked to give agreement for information to be held by the NHS Central Register if appropriate, further funding may be requested later for longer-term follow-up including lung function tests.

Six month follow-up
Assessment of outcome at the 6 month follow-up will be performed by trained researchers who will interview and examine patients in their homes. Patients and their relatives will be instructed not to reveal which treatment was used. Patients will wear a special scarf to cover the neck, masking the presence or absence of cannulation wounds. The assessment will include a generic measure of health status (SF36[20]) and quality of life (Euroqol EQ5D[21]), respiratory related quality of life (St George's Hospital Respiratory Questionnaire[22]), psychological state (Hospital Anxiety and Depression Scale[23]) and cognitive function (Mini-Mental State Examination[24]). The interview will also include specific questions on sleep (from the Functional limitation profile[25]). Lung function will be assessed by spirometry. Where applicable, effects on the carer will be measured using the carer strain index[26]. If a home visit is unacceptable, patients will be offered a telephone interview or postal questionnaire. For those unwilling to be assessed by interview or questionnaire, permission will be requested for information to be sought from the patient's general practitioner.

Longer term follow-up
Further follow up will be the subject of a separate protocol. So that the study organisers do not lose contact with patients should they move addresses, and also to follow up on health status, patients are being asked to give their agreement for their contact details to be sent to the NHS Central Register.

Economic issues
The primary objective of the economic evaluation is to assess incremental cost-effectiveness of ECMO in terms of additional survival with and without disability at six months post-randomisation. This will be done by determining the costs to health services and households, assessing cost-effectiveness from the viewpoint of the NHS and also from the societal viewpoint. The overall approach will be to describe the care received by patients in both arms of the trial, identifying use of health services with potentially important costs or changes in household resources.

The trial will assess the cost of treatment to the health and social services and to patients and their families in each treatment group. An incremental cost-effectiveness ratio will be calculated and compared to that for similar life-extending treatments. Information for the costs of inpatient and domiciliary care will be collected using methods adapted from the neonatal ECMO trial [21–23].

Costs of care will be estimated by recording use of key health care services as part of the data set for each person in the trial, and separately estimating costs associated with each item of health care use. Service use will be measured as daily level

of intensive care support, until discharge to an ordinary ward. Subsequent health care costs will be based on days of inpatient care, and use of transport, outpatient and primary care services. Resource use after discharge from hospital will be collected by questionnaire at 6 month follow up. After discharge home, trial participants will be sent an 'aide memoire' to record health service contacts.

Societal costs will be estimated for this trial as the net total costs to health services and to patients. Societal costs of illness can also include the costs borne by relatives and friends of visiting, supporting and caring for the patient. It is likely that visiting costs will differ between trial arms. A literature review found no studies of visiting costs for adult patients. A pilot study conducted outside the CESAR trial has established a survey method for measuring costs[24] and will be conducted in a sub-sample of ICUs taking part in the trial and willing to do the additional research, in order to describe typical visiting costs for patients in ECMO and conventional centres.

To estimate levels of intensive care, data will be collected within the trial about the nature and duration of organ system support for individual patients. Data will be collected at the same time as the trial from participating intensive care centres and the ECMO centre to estimate costs of each level of care using a standard methodology [25,26]. Health care service use after discharge will be derived from a questionnaire to patients at 6 months. Patients agreeing to participate will be invited to complete a simple diary as a memory aid to assist completion of the 6-month questionnaire. Household costs will be determined according to any changes the patients may have experienced in household circumstances (including major costs related to the illness and changes in economic activities).

Cost-effectiveness in terms of disability free survival and quality-adjusted life years gained will be estimated based on 6-month responses to the Euroqol EQ5D questionnaire.

Finally, the implications of the trial for efficient provision of ECMO services in the UK will be considered. Until the end of the trial, ECMO will only be available in one centre. Cost analysis will be done to assess sensitivity of cost-effectiveness ratios to transport and local volume of service in the ICU and ECMO unit in order to predict the best configuration of ECMO services, if the treatment is effective.

Data collection instruments for economic evaluation

1. For trial patients and relatives

(a) Daily organ support chart to be completed by caregivers in intensive care units for each patient in the trial
(b) Patient's diary of events after discharge – to be completed and kept by patient to help answer questions at 6 months.
(c) EQ5D health related quality of life questionnaire
(d) Patient's and relative's costs questionnaire: versions for survivors, and for relatives of patients who die (self completed)

2. For participating centres

(a) ICU cost estimates derived from a national DH funded study conducted by one of the trial investigators [27,28] for each ICU (and equivalent for ECMO centre during final year of trial)
(b) Daily ward costs from participating hospitals (based on finance data)
(c) Transport costs

Other health and social care unit costs will be based on nationally available data (e.g. Netten and Dennett, PSSRU, University of Kent 1999 or NHS reference costs) or special costing exercises by researchers.

Sample size

A 70% mortality in the control group is anticipated, based on the NIH ARDS network database. Cross-referencing with the Case Mix Programme Database, which is the national comparative audit of patient outcomes co-ordinated by the Intensive Care National Audit & Research Centre (ICNARC) confirms that this estimated mortality is approximately correct. The mortality of the 1,506 patients with a PaO_2/FIO_2 ratio of ≤ 100 mmHg in this database was 61.6%. The mean PaO_2/FIO_2 ratio in the ECMO patients was 65 mmHg with an SD of 37. Thus the selection criteria of a Murray score of = 3.0 should successfully identify patients with an expected mortality of = 70%. In addition this is also the patient group that is currently receiving ECMO. Assuming a 10% risk of severe disability among survivors in both trial arms, an alpha = 0.05 (2 sided test) and beta = 0.2, a sample size of 120 patients in each group (i.e. a total sample size of 240) would be required to detect a reduction in the rate of primary outcome from 73% to the 55% which is a conservative estimate based on the descriptive studies of adult ECMO already

discussed. As there is some controversy about the estimated mortality in the control group, a power calculation grid is included for a range of estimated mortalities (*Table 1*), should data from the on-going trial suggest a different level. The sample size was reviewed June 2003 when the Principal Investigators made anapplication for an extension of funding to the Health Technology Assessment Programme (HTA). In the original application, they provided a grid showing the implications of different estimates for the primary outcome in the control group and for the size of difference. This showed, for instance, that with a sample size of about 240 if the primary outcome rate in the control group was about 57% or more they would be able to detect a reduction by a third OR if the primary outcome rate in the control group was about 73% or more, they would be able to detect a reduction by a quarter. If the primary outcome rate in the control group was around 65% or more, a sample size of about 180 would allow them to detect a reduction by a third (all estimates based on 5% statistical significance (2-sided test) and 80% power). The HTA agreed an extension of recruitment by which time CESAR is likely to recruit about 180 patients.

Recruitment rate

Glenfield ECMO unit treated 40–50 adults per year (prior to 2001). In 1997, 28 hospitals referred 44 patients for ECMO. If all 224 Intensive Care Units (ICUs) in the UK hospitals were to refer patients for ECMO at the same rate as the 28, a total of around 350 patients might be eligible for trial entry in the UK per annum. It is unlikely that all 224 centres will participate, so some patients will be treated in hospitals not participating in the trial and some will not be asked for nor give assent for the trial. If 100 centres do wish to take part, it should be possible to recruit sufficient patients over the recruitment period.

Statistical analysis

Type of analysis

Analysis will be by intention to treat, with sub-group analyses based on the minimisation criteria at trial entry.

Frequency of analysis

An independent Data Monitoring Committee (DMC) will review, in strict confidence, data from the trial approximately half way through the recruitment period. The Chair of the DMC may also request additional meetings/ analyses. In the light of these data, and other evidence from relevant studies, the DMC will inform the Steering Committee, if in their view:

i. there is proof beyond reasonable doubt that the data indicate that any part of the protocol under investigation is either clearly indicated or contra-indicated, either for all patients or for a particular subgroup, or
ii. it is evident that no clear outcome will be obtained with the current trial design.

Unless modification or cessation of the protocol is recommended by the DMC, the Steering Committee, collaborators and administrative staff (except those who supply the confidential information) will remain ignorant of the results of the interim analysis.

TABLE 1 *Power calculation grid*

		Mortality in Control Group											
		70%			60%			50%			45%		
% of survivors severely disabled		15%	10%	5%	15%	10%	5%	15%	10%	5%	15%	10%	5%
Primary adverse outcome %		74.5	73	71.5	66	64	62	57.5	55	52.5	53.25	50.5	47.75
Relative risk	0.5	64	66	70	82	86	92	104	112	122	118	128	140
	0.67	136	142	150	180	192	204	236	256	278	270	296	326
	0.75	224	236	250	302	324	348	404	440	480	468	514	566
	0.8	336	356	378	462	496	532	624	682	746	726	800	62

Sample size calculation for different assumptions about mortality, disability and relative risk (Beta = 0.2, Alpha = 0.05, 2 sided)

Membership of Data Monitoring Committee

Professor Sir Richard Doll (Chair until 2005), Professor Douglas Altman (Chair from 2005), Professor Tim Evans and Dr Duncan Macrae.

Ethical considerations

Since the patients in this trial will all be sedated and ventilated the patient's next of kin will be asked to give assent for the patient's inclusion in the trial. There will be information booklets for the patient's relatives which will include information about the trial, conventional treatment and ECMO. This may raise some ethical issues since strictly speaking the patient's next of kin can only assent for treatment of an incompetent adult, and cannot give true consent on their behalf. However, there is a duty of care to act in the patient's best interests and apply whatever treatment is believed to be the most effective. Since in this case it is not yet clear which treatment is most effective there is a larger duty of care to the community as a whole to determine which treatment is most effective by means of an RCT. When patients have recovered and been discharged home they will be informed that they have been part of a clinical trial and given a copy of the information leaflet. During the trial period patients who would be eligible for the trial will not be able to get ECMO in the UK except as part of the trial.

The trial has been approved by the Trent Multicentre Research Ethics Committee (REC) as well as relevant Local RECs,

Ancillary studies

In addition to addressing the main aims of the study, some collaborators may wish to conduct other more detailed or complementary ancillary studies. The principal investigators welcome this provided that proposals are discussed in advance with the Trial Steering Committee.

Publication policy

To safeguard the scientific integrity of the trial, data from this study should not be presented in public or submitted for publication without requesting comments and receiving agreement from the Trial Steering Committee. The primary results of the trial will be published by the group as a whole although the paper will be written by a smaller writing committee, and a table of contributors will delineate individual investigators' personal contributions to the study. The success of the trial depends on the collaboration of many people.

Organisation

Principal investigators

i. *Giles Peek:* Will co-ordinate the activities of the collaborators at all clinical centres and the project staff at Glenfield Hospital Leicester, the Clinical Co-ordinating Centre, will organise the clinical advisory service and in conjunction with the clinical research fellow will promote the trial to encourage participation of referring centres. Will be closely involved in data analysis and a key member of the writing committee.
ii. *Diana Elbourne:* Will co-ordinate activity at the London School of Hygiene and Tropical Medicine (LSHTM), the Data Co-ordinating Centre with particular responsibility for data collection, management and statistics. Key member of writing committee, senior statistician.
iii. *Richard Firmin:* Will work closely with Giles Peek and will be head of the clinical advisory service.
iv. *Ann Truesdale:* Will work closely with Diana Elbourne as Study Co-ordinator working with staff at the LSHTM and form part of the writing committee.
v. *Miranda Mugford:* Will co-ordinate the economic study team and work closely with Clare Hibbert, and form part of the writing committee.
vi. *Hilliary Killer:* Will assist in the day to day management of the trial at the ECMO centre and will work closely with the economic study team. Will form part of the clinical advisory team. Will provide a nursing and technical viewpoint.
vii. *Clare Hibbert:* Will be a member of the economic study team with Miranda Mugford.
viii. *Andy Wilson:* Will co-ordinate the activities of the GP Advisory Group and take responsibility for the follow-up assessment at six months and form part of the writing committee.

Trial Steering Committee

The Steering Committee will approve the main study protocol, monitor and supervise the trial towards its interim and overall objectives, review relevant information from other sources, consider the recommendations of the DMC, and resolve problems brought by the trial co-ordinating centres. The committee will comprise an independent chairperson, Professor David Field, independent members, Ms Jayne Fawcett(University of York), Dr David Goldhill (Consultant Anaesthetist, Royal National Orthopaedic Hospital), Mrs Silvia Holden (Cruse Bereavement Care), Mrs Wendy Nganasurian (Patients Association), Professor Anne Tattersfield (Professor of Respiratory Medicine,

Nottingham City Hospital), Dr John Scott (East Anglian Ambulance Trust) Professor Nigel Webster (Professor of Anaesthesia and Intensive Care, Aberdeen Royal Infirmary)as well as the members of the project management group. This represents all the different disciplines involved in the trial. Specialist working groups will advise the Steering Committee.

Project Management Group (PMG)

A project management group will be established and will be responsible for the day to day management of the trial. The group will comprise the principal investigators and project staff from the Clinical Co-ordinating Centre at Leicester and the Data Co-ordinating Centre at the LSHTM and from the health economics group based at UEA Norwich and School of Health and Related Research (ScHARR) in Sheffield. The group will meet regularly in person and by telephone.

The responsibilities of the PMG include:

(a) Establishing and monitoring recruitment of participating centres
(b) Distribution and supply of data collection forms and other appropriate documentation for the trial
(c) Data collection and management
(d) Data entry and cleaning
(e) Data analysis
(f) Organising and servicing the Data Monitoring Committee.

Local co-ordination

Each participating centre will identify an intensivist as a local co-ordinator and two intensive care nurses (one primary and one as backup).

The responsibility of the local co-ordinators will be to:

(a) Ensure local research ethics approval is obtained
(b) Be familiar with the trial and consider recruitment of potentially eligible patients
(c) Liaise with the Clinical Co-ordinating Centre to register eligible patients
(d) Liaise with the transport team when relevant
(e) Liaise with the Data Co-ordinating Centre
(f) Ensure that relevant medical and nursing staff are informed about the trial
(g) Ensure that mechanisms for recruitment are in place
(h) Ensure that data collection forms are completed and returned to the Data Co-ordinating Centre promptly and to deal with any queries
(i) Facilitate other aspects of co-ordination as relevant
(j) Make data available for verification, audit and inspection purposes as necessary
(k) Liaise with the economics team
(l) Ensure that the confidentiality of all information about trial participants is respected by all persons.

Confidentiality

Patients will be identified by their trial number to ensure confidentiality. However, as the patients in the trial will be followed up to 6 months following randomisation, it is essential that the team at the Data Co-ordinating Centre has the names and addresses of the trial participants recorded on the data collection forms in addition to the allocated trial number. Stringent precautions will be taken to ensure confidentiality of names and addresses at the Data Co-ordinating Centre. The investigators and local coordinators will ensure conservation of records in areas to which access is restricted.

Discussion

The CESAR trial should define the appropriate use of extra-corporeal life support for adults with severe potentially reversible respiratory failure. It will also determine the cost efficacy of such treatment. CESAR will also provide profound insight into the conventional treatment of such patients in the UK.

Abbreviations

ARDS	Acute Respiratory Distress Syndrome
CESAR	Conventional Ventilation or ECMO for Severe Adult Respiratory Failure
cmH_2O	Centimetre of water
CTC	Conventional Treatment Centre
CXR	Chest X-ray
DH	Department of Health
DMC	Data Monitoring Committee
$ECCO_2R$	Extracorporeal Carbon Dioxide Removal
ECMO	Extracorporeal membrane oxygenation
EIP	Emergency Inclusion Protocol
ELSO	Extracorporeal Life Support Organization
EQ5D	Euroqol questionnaire
FIO_2	Fraction of inspired oxygen
ICNARC	Intensive Care National Audit and Research Centre

ICU	Intensive Care Unit
IPPV	Intermittent Positive Pressure Ventilation
kpa	Kilopascals
LSHTM	London School of Hygiene & Tropical Medicine
MARS	Molecular adsorbent recirculating system
mmHg	Millimetres of mercury
NIH	National Institute of Health
NSCAG	National Specialist Commissioning Advisory Group
PaO_2	Partial pressure of oxygen in arterial blood
PCIRV	Pressure Controlled Inverse Ratio Ventilation
PEEP	Positive End Expiratory Pressure
pH	negative base 10 logarithm of the hydrogen ion concentration in millimoles per litre
PIP	Peak Inspiratory Pressure
RCT	Randomised Controlled Trial
RH	Referral Hospital
ScHARR	School of Health and Related Research
SERNIP	Safety & efficacy register of new interventional procedures
SF36	Short form 36 questionnaire
SOFA	Sequential Organ Failure Assessment
TV	Tidal Volume
UEA	University of East Anglia
UK	The United Kingdom of Great Britain and Northern Ireland
VA	Veno-Arterial
VV	Veno-Venous

Competing interests

GJP, RKF, HMK and RT are all clinicians involved in ECMO.

Authors' contributions

GJP conceived the study. GJP, DE, RKF, CH, HMK, MM and AT were applicants for the funding. All authors were involved in designing the study and drafting the protocol. All authors read and approved the final protocol.

Appendix 1: Murray score

The Murray score is a grading system for ARDS which uses 4 pieces of information graded 0–4 to give a severity index for ARDS. The data required are:

- PaO_2/FIO_2 in mmHg (multiply Kpa result $\times 7.5$): this must be taken with the FIO_2 at 1 for at least 20 minutes
- PEEP in CMH_2O
- Lung Compliance in ml/CMH_2O
- Number of quadrants with infiltration seen on chest X-ray.

Patients can be registered for the trial when the Murray Score exceeds 2.5, and are eligible to enter and be randomised when it exceeds 3.0. Patients who are hypercarbic, but not hypoxic and therefore have a low Murray score may enter the trial and be randomised once the arterial pH falls below 7.2. The Murray score is calculated by taking the score for each variable and dividing by 4, for the purposes of the CESAR trial all 4 variables must be used to calculate the score.

Score values

- PaO_2/FIO_2: $\geq 300 = 0$, 225–299 = 1, 175–224 = 2, 100– 174 = 3, $< 100 = 4$.
- CXR: normal = 0, 1 point per quadrant infiltrated.
- PEEP: $\leq 5 = 0$, 6–8 = 1, 9–11 = 2, 12–14 = 3, $\geq 15 = 4$.
- Compliance (ml/cmH_2O): $\geq 80 = 0$, 60–79 = 1, 40–59 = 2, 20–39 = 3, and $\leq 19 = 4$.

The compliance may be calculated as follows:

$$\frac{\text{TV}}{\text{PIP-PEEP}}$$

where TV is Tidal Volume, and PIP is Peak Inspiratory Pressure.

Example

- A patient has a PaO_2 of 6.6 Kpa on 100% oxygen: To convert KPa to mmHg = $6.6 \times 7.5 = 49.5$ mmHg, divide by the FIO_2 (= 1), the PaO2/FIO2 is 49.5, as this is less than 100, **score 4**
- The Chest X-ray has consolidation and infiltration in 3 out of 4 quadrants, **score 3**
- The PEEP is set at 10 cmH_2O, **score 2**
- The Peak airway pressure is 38 cmH_20, and the tidal volume is 420 ml, PIP-PEEP = 28, compliance is 420/28 = 15, **score 4**.

The Murray score is (to one decimal place):

$4 + 3 + 2 + 4 = 13$,
$13/4 =$ **3.3**

The Murray score is high enough for trial entry (> 3).

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Glenfield ECMO Unit

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Economics Group

Elizabeth Coates

GP Advisory Group University of Leicester

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Appendix 4

Economics protocol

Methods of data collection and analysis for the economic evaluation alongside a national, multi-centre trial in the UK: Conventional ventilation or ECMO for Severe Adult Respiratory failure (CESAR)

Mariamma M Thalanany,[1] Miranda Mugford,[1*] Clare Hibbert,[2] Nicola J Cooper,[3] Ann Truesdale,[4] Steven Robinson,[4] Ravindranath Tiruvoipati,[5,6] Diana R Elbourne,[4] Giles J Peek,[5] Felicity Clemens,[4] Polly Hardy[4,7] and Andrew Wilson[3] on behalf of the CESAR Trial Group

[1]School of Medicine, Health Policy and Practice, University of East Anglia, Norwich NR4 7TJ, UK
[2]Health Economics & Decision Science, School of Health & Related Research, University of Sheffield S1 4DA, UK
[3]Department of Health Sciences, University of Leicester LE1 7RH, UK
[4]London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK
[5]Glenfield Hospital, Leicester,UK, LE3 9QP, UK,
[6]Frankston Hospital, Victoria, Australia 3199
[7]Clinical Epidemiology and Biostatistics Unit, Royal Children's Hospital, Melbourne, Australia

Email: MMT: m.thalanany@uea.ac.uk
MM: m.mugford@uea.ac.uk*
CH: Clare.Hibbert@astrazeneca.com
NJC: njc21@le.ac.uk
AT: ann.truesdale@lshtm.ac.uk
SR: steven.robertson@sgul.ac.uk
RT: travindranath@hotmail.com
ERD: diana.elbourne@lshtm.ac.uk
GJP: giles.peek@uhl-tr.nhs.uk
FC: Felicity.clemens@lshtm.ac.uk
PH: polly.hardy@mcri.edu.au
AW: aw7@le.ac.uk

* Corresponding author

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Abstract

Background: Extracorporeal Membrane Oxygenation (ECMO) is a technology used in treatment of patients with severe but potentially reversible respiratory failure. A multi-centre randomised controlled trial (CESAR) was funded in the UK to compare care including ECMO with conventional intensive care management. The protocol and funding for the CESAR trial included plans for economic data collection and analysis. Given the high cost of treatment, ECMO is considered an expensive technology for many funding systems. However, conventional treatment for severe respiratory failure is also one of the more costly forms of care in any health system.

Methods/design: The objectives of the economic evaluation are to compare the costs of a policy of referral for ECMO with those of conventional treatment; to assess cost-effectiveness and the cost-utility at 6 months follow-up; and to assess the cost-utility over a predicted lifetime. Resources used by patients in the trial are identified. Resource use data are collected from clinical report forms and through follow up interviews with patients. Unit costs of hospital intensive care resources are based on parallel research on cost functions in UK NHS intensive care units. Other unit costs are based on published NHS tariffs. Cost-effectiveness analysis uses the outcome: survival without severe disability. Cost-utility analysis is based on quality-adjusted life-years gained based on the Euroqol EQ-5D at 6 months. Sensitivity analysis is planned to vary assumptions about transport costs and method of costing intensive care. Uncertainty will also be expressed in analysis of individual patient data. Probabilities of cost-effectiveness given different funding thresholds will be estimated.

Discussion: In our view it is important to record our methods in detail and present them before publication of the results of the trial so that a record of detail not normally found in the final trial reports can be made available in the public domain.

The CESAR trial registration number is ISRCTN47279827.

Background

Extracorporeal Membrane Oxygenation (ECMO) was introduced into treatment of severe but potentially reversible respiratory failure in the 1970s. The technique involves placing patients on a life support circuit with a membrane oxygenator to temporarily take over the gas exchange function of the lung thereby allowing the lungs to rest and recover [1,2]. The early reports of the use of ECMO in adult with severe respiratory failure were enthusiastic [3]. It soon became clear however, that although ECMO was effective and cost effective compared to conventional ventilation in newborns [4], the evidence was much less clear for the adult population. Many centres in the world use ECMO technology and have reported survival rates in excess of 50% in uncontrolled observational studies of patient outcomes [5,6]. However, considerable improvements have also been reported in survival rates of conventionally treated patients with severe respiratory failure [7-9].

Given the high cost of treatment, ECMO is considered an expensive technology for many funding systems. However, conventional treatment for severe respiratory failure is also one of the more costly forms of care in any health system [10]. Differences in lengths of stay and types of care received by patients following either clinical pathway may result in different statistical distributions of cost for inpatient care. In addition, because appropriate care is provided in relatively few centres, the location of care and need for specialist transport for patients also affects the costs of care. Finally, if there is increased survival to discharge from hospital, then there will be more use of services in primary and community care, and requirement for help for recovering people at home. Thus the health service costs and the household costs might fall at any stage of the treatment and recovery, and in many different forms.

In addition to the costs of alternative forms of care, the economic choice depends on the value of the outcome gained. Uncertainty about the effectiveness of referral to an ECMO centre led to a trial to assess the costs and effectiveness of the new form of care funded by the NHS Health Technology Assessment programme. The protocol for the 'Conventional ventilation or ECMO for Severe Adult Respiratory failure (CESAR) Trial was published in 2006 [11]. This paper provides details of the methods used for the economic evaluation, mentioned in the protocol and conducted as an integral part of the CESAR trial.

Previous economic evaluations

A literature search failed to find any economic evaluation studies of adult ECMO. However, there have been a series of economic evaluations of ECMO in babies alongside the UK collaborative randomised trial of neonatal ECMO [12] which reported the estimated additional cost (UK 1994-95 price) of ECMO per additional surviving infant with no disability as £75,327 at one year of age. Follow-up at 4 and 7 years for the same study shows the incremental cost (UK 2001 & 2003 price) of neonatal ECMO to be £24,775 & £23,566 per disability-free life-year gained [13,14]. Similarly a retrospective cost-utility analysis [15] reports costs of USD 24,386 per quality-adjusted life-year saved for 'salvage ECMO' in children. In all cases, in spite of the high cost of neonatal ECMO, the incremental cost per QALY was within health care funders' range of acceptable value for money. This remains a question in the case of adult ECMO.

The CESAR trial

The CESAR trial [11] was designed to compare two alternative strategies for treating severe but potentially reversible respiratory failure: conventional ventilation, and transfer to a centre providing ECMO. In the UK, during the CESAR trial, ECMO is provided by Glenfield Hospital, Leicester, and conventional treatment by other UK hospitals capable of providing a high standard of care for ECMO eligible patients.

The primary outcome measure for the clinical evaluation is increase in survival at 6 months without severe disability ('confined to bed' and 'unable to wash or dress') at six months. Power calculations based on estimates of these outcomes from severe adult respiratory distress syndrome (ARDS) suggested a sample size of 180 would have sufficient power to detect a reduction in primary outcome by a third (based on 5% statistical significance, 2-sided test and 80% power). All ICUs in the UK were invited to take part in the trial and 148 units referred patients for consideration for entry to the trial. The participation of so many ICUs is necessary due to the small numbers of adults who suffer from the condition annually.

Methods

Economic questions about treatment of severe respiratory failure

The economic evaluation addresses the question of value for money of the alternative treatment options. The economic question asks 'for patients with severe but potentially reversible respiratory failure, is ECMO cost-effective from the viewpoints of the NHS and society?'. This question can be rephrased 'is the additional cost of achieving an important gain in outcome within the range that the health funding system, or society, is willing to pay'?

The objectives of the economic evaluation are:

- To compare the costs of a policy of referral for ECMO with those of conventional treatment.
- To assess the cost-effectiveness of referral for ECMO compared with conventional treatment in terms of additional survival with and without disability at six months post-randomisation.
- To assess the cost-utility of referral for ECMO compared with conventional treatment in terms of utility gain as measured by EQ-5D at 6 months follow-up.
- To assess the cost-utility of referral for ECMO compared with conventional treatment in terms of utility gain as measured by EQ-5D, and other sources, over a predicted lifetime.

Design of the economic evaluation alongside the CESAR trial

The design of this economic evaluation alongside the CESAR trial is based on published recommendations [for example, 16]. This involves defining: the type of economic evaluation to be conducted; the comparator form of care; the perspective and time horizon for costs and outcomes; appropriate outcome measures for each perspective and type of evaluation; identification, measurement and valuation of resources; estimation of unit costs; and a plan for economic analysis, which includes decisions on discounting future costs and consequences, tackling uncertainties and presentation of results.

Type of economic evaluation

The first planned analysis is a cost effectiveness analysis (CEA) with increase in survival without severe disability at six months (the primary outcome in the CESAR trial) as the main outcome measure. A short term cost-utility analysis (CUA) was also planned in which health benefits are quantified in terms of quality-adjusted life-years (QALYs), and measured using the instrument EQ-5D at 6 months. Lifetime CUA is planned using a decision model based on CESAR trial results and including additional data for predicted lifetime QALYs and health care costs.

Comparator

The ideal comparator for any economic evaluation designed to assess the cost effectiveness in a particular context is the most commonly used treatment for the condition in that context. The CESAR trial was designed as a pragmatic comparison, where patients allocated to conventional care were receiving treatment that would be the normal form of care in the NHS. To ensure that the patients in the control group received as near as possible the best practice of care, the CESAR trial protocol specified aspects of service provision that must be considered, including facilities available at the participating ICUs, experience of treating such patients, and certain aspects of the clinical treatment protocol for ventilated patients. Full details are given in the CESAR trial protocol [11]. In general, however, the comparator group was intended to be representative of NHS care provision (in qualifying ICUs) for acute respiratory failure during the period of the trial.

Perspective or viewpoint for analyses

In the UK, the National Institute for Health and Clinical Excellence (NICE) proposes that applicants presenting economic analyses for NICE appraisals should take a NHS perspective [17]. However, there are aspects of public patient choice and valuation that may not be considered in such an analysis. Economic evaluators are guided to take a societal viewpoint if possible [16]. As the ECMO technology may be adopted for review by NICE or a similar agency in the UK, it was decided that the perspective for the CESAR trial should include both the NHS and societal perspectives. The latter viewpoint is important, as the results of this study are likely to have economic impacts other than through health care requirements if there is significantly increased survival of either able bodied or disabled adults. It is also anticipated that the results of the trial may provide useful information for a wider international audience where different ranges of services are provided within the health system.

Time horizon for economic evaluation

The follow-up duration for the CESAR trial is 6 months. This does not allow the full long term cost and benefits to be measured. However, it satisfies the recommendation of the American Thoracic

Society for cost-effectiveness analyses of ICU therapies to have a minimum follow-up period of 6 months [10]. However, to meet our fourth objective, prediction and modelling longterm (lifetime) costs and benefits are also planned.

Outcome measures for economic evaluation

Survival without severe disability

Death of patients in the trial was recorded during the period of follow up whenever it occurred. Staff at the CESAR trial data management centre maintained contact with all centres with patients being treated within the CESAR trial ensuring complete reporting. For those discharged from hospital, contact was sought either through their home, or through their family doctors, if patients consented to be approached in either of these ways. Any further deaths would be reported in this way. Severe disability in survivors at six months was defined as those who were unable to care for themselves and were confined to bed: that is who had worst possible scores for the Euroqol EQ-5D domains for self care and for mobility.

Quality-adjusted life-years (QALYs)

The calculation of QALYs was planned to be based on assessment of health related quality of life at six months from randomisation. The EQ-5D is a standardised instrument used for measuring health outcomes. Quality-adjusted health utility weights for each patient are calculated for the CESAR trial using UK specific utility values for each patient's response to the EQ-5D at 6 months. We could find no previous models for estimation of QALYs gained at 6 months in similar patients, and so they are estimated assuming that the value of the health state at trial entry was zero, and that over the months of survival, patients have experienced linearly increasing quality of life up to the level at 6 months.

Estimates of lifetime QALYs are predicted based on assumptions of gradual improvement of quality of life up to 2 years from randomization [18-22], and of predicted life expectancy based on age specific rates for the population of England and Wales. Age and sex specific life expectancy is calculated for each surviving patient in the trial using UK life tables [23]. It is assumed that, at 24 months post randomization, all surviving trial patients attained the same average life expectancy and health state as adults of similar age in the UK population. It is assumed that average health states for different age groups would be the same as those obtained from the 1996 Health survey for England [24].

Cost estimation

Identifying resource use

For the CESAR trial relevant aspects of resource use were identified using expert advice (managers, medical, nursing and patient representatives all commented on the draft lists) and also considering the items included in the economic evaluation of neonatal ECMO [12]. A list of resource items important from one or more viewpoints is given in *Table 1*. This includes resource use associated with initial stay in intensive and high dependency care units at different levels of care (measured by number of organs supported – see below), use of ambulance transport, stays in other hospital wards before discharge, costs of visiting incurred by relatives whilst patients are in hospital, resource use after discharge up to six months, major changes in household, out-of-pocket expenses of patient and family, loss of paid and unpaid working time, changes in working time, and informal care.

Measuring resource use

Resource use data are collected prospectively for every trial participant at various points of his/her progress from recruitment to follow-up using a series of data forms and questionnaires. Some, but not all, of these are additional to the instruments planned for the CESAR trial management and clinical outcome data collection [11]. These instruments are:

(a) Daily organ support form – completed by intensive care staff for each trial participant on a daily basis, and used to classify intensity of resources used during the intensive care ECMO/conventional treatment period.
(b) Transport form (a) at trial entry – completed by Glenfield Hospital transport team to record transfer of trial participants to ECMO centre or conventional treatment centres.
(c) Transport form (b) – completed by Glenfield transport team to record ambulance journey of participants returning either to the original recruiting hospital or another intensive care unit after ECMO.
(d) Outcomes data sheet – completed by medical staff and records date on death of patient (if applicable), date of discharge, date of transfer to another hospital/home, use of ambulance for transfer etc.
(e) Events Diary – to be completed and kept by every participant to document all services used from discharge to follow-up as an *aide memoire* to help them to answer questions at 6 months. This included information about informal help received as well as formal services.

(f) Patient cost questionnaire at 6-month follow up – administered by trained interviewer at patient's home or by telephone to collect resource use data from discharge to follow-up, covering items recorded in (e) above.
(g) GP proforma – completed by GPs to collect medication use of those patients who refuse the 6-month follow-up but give permission for use of GP records.

The Events Diary (e) and the Patient cost questionnaire (f) were piloted with five patients discharged from Glenfield Hospital ICU, and the GP proforma (g) piloted with 5 general practitioners. Interviewers were trained in the administration of the patient cost questionnaire (f). As it was anticipated that many Ambulance Trusts across UK may become involved in transporting trial patients, all ambulance trusts were contacted and agreement obtained to provide costs of patient journeys (including overhead & running costs) as and when it took place during the trial.

Two items of resource use not collected alongside the trial are: resource use associated with and following a patient's death in ICU, and cost incurred by relatives whilst visiting patients in intensive care/ hospital stay. These items were excluded from the data collection from CESAR trial patients due to the practical difficulty of collecting data and due to the lack of a well-defined methodology available at the early stages of planning the CESAR trial. However, the cost of visiting patients in intensive care was thought likely to be an important social cost, and is being estimated by a separate study in a sample of CESAR centres and is described in more detail under 'Estimating unit costs' below.

Resource data collection for the economic evaluation

Following recruitment, the progress of all participants is tracked initially until their discharge from hospital so that resource use, and clinical progress, can be accurately measured and collected at each stage. During the intensive treatment period (ECMO or conventional ventilation) data are collected on number of days spent in each treatment mode, including daily information on number of organs supported and the level of critical care (ICU or HDU). After transfer to another hospital or another ward within the same hospital after the acute phase of the illness, resource use is measured as number of in-patient days up to discharge.

Details of all ambulance use related to transferring trial patients at recruitment are collected by the Glenfield transport team and details of all other ambulance journeys (for example transfer between hospitals) are collected by the relevant hospitals and sent to the research team. Data collected include date, time, origin and destination of journey, mode of transport (road ambulance, fixed wing aircraft, or helicopter), duration of journey, and distance travelled by patient.

After discharge from hospital, each participant is sent details of the forthcoming interview and the 'events diary' to record resource use. The patient is asked to give permission for one of a series of options to take place 6 months after trial entry: (1) face-to-face interview, (2) telephone interview, (3) postal questionnaire and (4) collection of resource use from GP records. Those patients still in hospital at six months if fit enough are asked to give permission to be interviewed at their hospital bedside using a very short resource use questionnaire.

Estimating unit costs

In order to estimate total cost of treatment for each trial participant, the respective quantities of resource use are multiplied by their corresponding unit costs. Some resources used by participants are in the form of actual costs (not charges) and do not need any valuation. For example, cost of ambulance journeys are obtained directly from the relevant ambulance service providers and incorporate all overhead and running costs. The unit costs of most items of resource use are obtained from nationally available sources [25,26]. Use of medication is valued using the price of drugs listed in the *British National Formulary* [27]. Informal care is valued by the opportunity cost method suggested by Posnett & Jan [28]. Average cost per day of ICU and ECMO is obtained from a separate study and weighted/adjusted for each centre in the CESAR trial (see 'Cost/day of ICU including ECMO unit care' below). Cost of visiting is also derived from a separate study (see 'Costs of visiting patients in intensive care' below). Costs of private travel will be estimated using Automobile Association (AA) [28] motoring costs.

Valuation of informal care time

Informal time will be valued using weights suggested for Posnett & Jan's [29] scenarios: working time were output is replaced; working time where output is not replaced; non-work time of those in paid employment and those not in

paid employment; and finally time for those not in paid employment where unpaid housework is not replaced. Average wage rates of men and women in the United Kingdom needed for estimating time costs is obtained from Office of National Statistics (ONS) [30].

Predicted future costs of lifetime care

It was assumed that survivors at 6 months would continue to have similar average daily costs of care as at the 6 months follow up point, until 24 months post randomization. At 24 months, the average health service expenditure for the surviving patients in the CESAR trial was assumed to be the same as that of similar age groups in the UK. The age groups used in predicting future costs and benefits were: 16-44 years, 45-64 years, 65-74 years and 75-84 years. Data on health services costs for these age groups have been published in the proceedings of Parliament [31]. The same age groups were used as the basis for estimating both patients' long-term costs and their benefits.

Price year, inflation, currency and discounting

Resources and costs will be measured in the year in which they occur using appropriate unit costs for each year of resource use. All costs are then revalued for analysis and reporting to 2005 UK values using health care inflation estimates.

The follow-up duration for the short term analyses is 6 months and therefore discounting is not necessary. For the lifetime estimates, costs and QALYs were discounted at 3.5%, based on UK Treasury guidelines [32].

Cost per day of ICU including ECMO unit care

The task of achieving a case-mix adjusted daily costs of ICU care was achieved through a prospective, observational, longitudinal multi-centre study (the 'Critical Care HRG study'), concurrent with the CESAR trial, involving a volunteer sample of 70 critical care units, where monthly data on critical care unit expenditure together with daily data on patients' organ support were collected for a two/three-month period [33]. The sample of participating critical care units had good geographical coverage in England with smaller numbers from Scotland and Northern Ireland, but none from Wales. An average daily cost of ICU was estimated by collecting data on the monthly expenditure of intensive care units and apportioning this sum by their monthly throughput of patients. Case-mix adjustment of this average daily cost was achieved by a weighting based on the number of organs supported on that day.

Data collection: Data on patients' organ support requirements were collected on a daily basis by the critical care unit staff using specially designed data collection booklets. These data were collected for consecutive admissions during the study period. At the same time, the intensive care units and hospital finance departments were sent questionnaires to document their monthly expenditure on consumables (drugs and fluids, disposable equipment, nutritional products and blood and blood products), staff (consultant medical staff and other medical staff), clinical support services (radiology tests and laboratory services), professionals allied to medicine (physiotherapists, clinical pharmacists, dieticians, medical technical officers, information technologists, clinical and biomedical scientists, speech and language therapists, clinical psychologists and occupational therapists), support staff (personnel officers and directorate accountants) and specialised bed therapy. Data were also collected on the organizational characteristics of the intensive care units and the monthly number of patient days, number of staffed beds, number of patient admissions etc. An average daily cost was calculated using the following formula:

$$\frac{\sum(\text{Monthly expenditure on staff + consumables + clinical support services})}{\text{Monthly number of total patient days}}$$

The average daily cost in critical care ICU had to be adjusted to reflect the severity of illness or degree of organ support required by patients. For this purpose, data provided by 46 critical care units in the Critical Care ICU HRG study [34] were used. Only those critical care units that supplied data on their expenditure, organ support and unit characteristics were included in this analysis. The aim was to develop an appropriate model from which estimates of daily case-mix adjusted costs could be determined.

Different ways of modelling the organ support and expenditure data were explored. The model of choice was informed by the Breusch-Pagan and Hausman specification tests [35] that favoured a random-effects model based on the number of organs supported on a daily basis; clustered to include 0-1 organ, 2 organs and ≥ 3 organs. This model offered a simple and reproducible system of estimating case-mix adjusted costs of care.

Daily organ support weights were 0.577 for 0-1 organ supported, 1.137 for 2 organs supported and 1.156 for ≥ 3 organs supported [36]. These weights will be applied to average daily costs of patients participating in the CESAR trial. A total cost per patient of their ICU stay was calculated by weighting patients' average daily cost according to the number of organs supported on a daily basis and summing these daily costs for each patient.

Internal validation of the average daily cost data collected was not performed, however external validation was possible using data collected by the Critical Care National Cost Block Programme [37]. Twenty-one intensive care units in this study (30%) contributed data to the Cost Block Programme for the financial year 2000-2001. Although the Cost Block Programme collected data for a different time period and using a different configuration of units, the similarity between the mean costs per patient day is striking, in particular, the costs of consumables and clinical support services. The study by Hibbert et al [33] had wider coverage of resources with respect to professionals allied to medicine and an in-built allowance for capital equipment, which may be responsible for a slightly higher mean costs per day (£1302, 2003 price year) compared to £1028 (2001 price year, £1119 inflated to 2003 price year) for the Cost Block Programme.

The completeness of the returned data was investigated by each resource item and expressed as a percentage of the number of responses divided by the total number of 18 possible responses which reflected the quantity of data sought from participating centres. Data on nursing and administrative staff together with drugs and fluids yielded the highest number of responses (77%). Data on clinical and biomedical scientists and clinical psychologists yielded the lowest number of responses at 14%.

Not all CESAR centres participated in the Critical Care HRG study. Separate visits or contacts by correspondence were made with all CESAR centres that did not participate in the ICU HRG costing study, including the ECMO centre, to collect the same expenditure data in order to estimate the daily cost in the same way. Forty hospitals recruited patients up until the 31st March 2005. Given that more than one hospital recruited, in some cases, more than one patient during each financial year and patients could have received treatment in both an ICU and an HDU, one hundred and sixteen cost questionnaires were sent out in total to account for this (58 for the ICU and combined ICU / High Dependency Units (HDUs) and 58 for the separate HDUs – where provided). The types of critical care units i.e. which of the participating critical care units had both an ICU and an HDU or operated as a combined ICU / HDU, were not known, so each critical care unit was sent two cost questionnaires for each financial year when a patient was recruited to the trial. Thirteen hospitals completed the expenditure questionnaires however, only 11 hospitals returned data on both their unit characteristics and expenditure, which were needed in order to apportion the expenditure data correctly (i.e. down to an average daily cost). In order to estimate average daily costs for each CESAR hospital for the financial year in which a patient/ patients were treated, missing data were substituted with mean estimates obtained from the responding hospitals by financial year.

Figure 1 shows the whole process of estimating unit costs of ICU stay, derivation of weights for number of organs supported and how this feeds into the cost estimation in the trial. A fuller description of this part of the research is included in Clare Hibbert's PhD thesis [36].

Costs of visiting patients in intensive care

A pilot study of the costs of visiting [38] was carried out in December 2001 at an ICU in the UK. The daily costs per visit estimated in the pilot study are shown in *Table 2*. The pilot study informed the methods for a multi-centre study in six intensive care units in the UK which are registered with the CESAR trial. The aim was to estimate the average cost of visiting patients in intensive care. All adults including primary carers visiting the intensive care units during a three week duration were requested to complete a questionnaire that asked them about their time spent in visiting and travel, out-of-pocket expenses, employment status, loss of income etc. Data from this study will be used to estimate the average cost of visiting per day.

Analysis and reporting of costs and economic evaluation

Estimation of costs for each patient

Costs falling upon the health sector (health & social services), upon patients or their families, and other costs such as help from friends will be presented in total and disaggregated form. Resource use and unit costs described above will be used for to estimate mean, medians, standard deviations and ranges of costs for each patient in the CESAR trial.

Cost effectiveness analysis
Incremental cost-effectiveness ratio (ICER)

With the availability of patient level data on costs and effects it is possible to summarize uncertainty in the ICER as a confidence interval. As cost data are typically not normally distributed, non-parametric bootstrapping will be used to generate confidence intervals.

Cost-utility analysis

Lifetime incremental cost-utility ratios will be estimated using bootstrap estimation methods [39,40], and using data and simplifying assumptions described in previous paragraphs.

Sensitivity analysis and uncertainty

Sensitivity analysis based on testing specific assumptions and probabilistic analysis will be used to explore the uncertainty in the results [41,42]. Items to be tested in sensitivity analyses are listed in *Table 3*. Primary analysis will be on complete case basis, where a complete case is defined as cases meeting the CESAR trial clinical effectiveness data analysis. Estimation of the key cost variables is based on between 40 and 50 data items representing different aspects of resource use from each participant. If any single item is missing, the cost variable will also be incomplete. We predict that the complete case analysis will contain a small proportion of the total number of trial participants and thus have a high potential for bias and imprecision. Any missing resource item values will be replaced with imputed values and re-analysed as part of the sensitivity analysis. Missing data will be imputed using Rubin's multiple imputation method [43] with SOLAS v3.20 (Statistical Solutions Inc, Co Cork, Eire).

Generalising the results to different settings

It would be beneficial to health care decision makers if economic study results could be generalised from one setting to another as this would avoid having to repeat every study in every setting. Factors which may vary in different settings are: unit costs of resources, geographical variations in demography or epidemiology of disease, clinical practice patterns, incentives to health care professionals and availability of resources. To facilitate estimation of the transferability of economic data from the CESAR trial to other health care setting, such factors in the study population will be described, and resource use and prices reported separately.

Discussion

The CESAR trial is the first RCT of adult ECMO with an economic evaluation incorporated into the design of the trial. The CESAR trial was funded with full economic support from the design stages of the trial with funding for two part-time health economists which helped the economic research team to tackle many challenges in the design, methods, data collection, developing and piloting the economic questionnaire and planning the analysis. The trial protocol was developed in collaboration with health economists, who are members of the Trial Steering Committee, and an economics working group oversees the economic data collection and analysis.

Incorporation of economic evaluations within randomised controlled trials of medical therapies has been a growing trend in the past decade. Many health care systems in developed countries now use economic evaluations as a formal input to decisions about whether to fund new technologies. In the UK, economic evaluations play a key role in the technology appraisal process at the National Institute of Clinical Excellence (NICE) which makes decisions about a range of health technologies (NICE 2004).

Economic evaluations conducted alongside randomised trials are meant to inform decision-makers about the economic benefit of the technology under investigation. The information will shed the most light on the question of 'value for money' if the trial and the evaluation are properly designed, if appropriate data are collected and correctly analysed, and if the many sources of uncertainly surrounding these evaluations are adequately addressed. The past decade has seen a large increase in the number of published economic evaluations as well as improvements in economic evaluation techniques. However, much debate and confusion still persist among analysts, readers, and policy-makers concerning methods and the overall usefulness of CEA in resource allocation decision making. A number of potential reasons may account for this, among them political expediency, social preferences and systemic barriers to implementation. In addition, there are a number of more technical shortcomings associated with the generation of economic evidence including methodological inconsistency across completed economic evaluations and the limited generalisability or transferability of findings or settings beyond the location of the original study.

The economic evaluation methodology described in this paper aims to address these issues and guidelines and recommendations from more recent publications in methods for economics and trials [44] were used in the design and conduct of the evaluation and the planned analysis.

The CESAR trial was funded with full economic support from the design stages of the trial with funding for three part-time health economists which helped the economic research team to tackle many challenges in the design, methods, data collection, developing and piloting the economic questionnaire and planning the analysis. The trial protocol was developed in collaboration with health economists, who were members of the trial steering group, and an economics working group including the trial manager and leaders have overseen the economic evaluation.

The strengths of the trial on which this economic evaluation was based are that it was randomised and controlled, pragmatic in design, and provided a vehicle for collecting a comprehensive set of data on resource use and clinical effectiveness. These provide a reliable basis for estimating the economic efficiency of ECMO for adults with severe respiratory failure. The study cost accounting was comprehensive and included most major health service cost items. Most unit costs used for valuation of reported resources used were from published national sources and where unit costs were unavailable rigorous methods were used for their estimation and the methods used clearly described. Unit costs for ICU stays were estimated for every centre that recruited a patient which was then weighted for each patient to reflect the level of care and number of organs supported during the acute phase of the illness. Very few resource items were excluded from the data collection process alongside the trial.

Presenting this methodology paper before the end of the trial is an attempt to make transparent the methods used for the evaluation, and to allay concern of manipulation of economics results. In our view it is important to record our methods in detail and present before publication of the results of the trial so that a record of detail not normally found in the final trial reports can be made available in the public domain.

There are aspects of the planned methods that may be seen as idealistic. In particular, our estimation of resource use after hospital discharge is based on patients' reports after a traumatic period in their lives of many different aspects of service use and personal costs. The aggregate cost variables are made up from a combination of this large number of reported items, many of which may be missing. Although complete case analysis is our primary method of analysis, we are conscious that this might be quite unrepresentative of the CESAR trial population. Our planned secondary approach is to use imputation of missing values to increase the numbers of patients for whom we can estimate costs. However, this also raises the question about how much detail we actually needed to collect from patients (or other sources). Previous researchers have attempted to establish reduced form resource use data for costing [45,46] but have not arrived at any general rules for doing this. Subject to Steering Group approval, the data from this trial will be available for further analysis of this problem.

Conclusions

As a result of this publication of the methods for the economic evaluation in the CESAR trial prior to publication of the results, we shall be open to scrutiny for any changes to protocol in our reported data collection and analysis. By this means we hope to increase confidence in the results of the economic evaluation.

Abbreviations

CEA: Cost Effectiveness Analysis; CESAR: Conventional Ventilation or ECMO for Severe Adult Respiratory Failure; CUA: Cost-utility Analysis; ECMO : Extracorporeal membrane oxygenation; ICER: Incremental Cost Effectiveness Ratio; ICU:Intensive care unit; NHS: National Health Service; ONS: Office of National Statistics; PSSRU: Personal Social Services Research Unit; RCT; Randomized controlled trial; UK:United Kingdom.

Competing interests

The authors declare that they have no competing interests

Authors' contributions

Thalanany MM – made substantial contributions to 1) conception and design of the economic evaluation in the CESAR trial, 2) design of all economic questionnaires, 3) transport data collection, 4) design and analysis of the cost of

visiting study; 5) was involved in drafting the manuscript; and 6) has given the final approval of the version to be published.

Mugford M – 1) responsibility for leading and co-ordinating all activities of the economic group; 2) made substantial contributions to conception and design; 3) was involved in revising the manuscript critically for important intellectual content; and 4) has given final approval of the version to be published.

Truesdale A, Elbourne D, Peek G, Clemens F, Cooper N, Hibbert C, Wilson A – 1) made substantial contributions to conception and design; 2) were involved in revising the manuscript critically for important intellectual content; and 3) have given final approval of the version to be published.

Robertson S, Hardy P – 1) were involved in revising the manuscript critically for important intellectual content; 2) took part in data collection and analysis; and 3) have given final approval of the version to be published.

Tiruvoipati R – 1) was involved in revising the manuscript critically for important intellectual content; 2) took part in data collection; and 3) has given final approval of the version to be published.

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CESAR is a collaborative study between the Glenfield Hospital, Leicester; Medical Statistics Unit, London School of Hygiene and Tropical Medicine; University of East Anglia, Norwich, University of Sheffield, and University of Leicester.

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The economic evaluation team comprises Miranda Mugford (Professor of Health Economics), researchers Mariamma M Thalanany, Clare Hibbert, Lizzie Coates (2002-2004), Nicola Cooper, and Ann Raven (independent researcher 2000 - 2001), Diana Elbourne, Ann Truesdale, Steven Robertson (2001-2005) and Val Knights (clerical support 2001-2005).

Clinical Co-ordinating Centre at Glenfield Hospital organises the clinical advisory service, coordinates the activities of all clinical centres in the trial and comprises Giles Peek (cardio-thoracic surgeon), Richard Firmin (consultant surgeon), Ravindranath Tiruvoipati (CESAR clinical research fellow), Hilliary Killer (General Manager), and Nikki Jones (CESAR clinical research fellow 2001-2003).

Samantha Harris (research nurse, Glenfield Hospital) helped with piloting the memory aid and resource use questionnaire. Transport of patients at trial recruitment is organised by Gail Faulkner, Corrine McCullough (2001-2004), Jackie Redfern (2004-2005), Alan Sheward (2004-2005) and Megan Gratrix (2005-2006).

Data Co-ordination and statistical support is provided by Medical Statistics Unit, London School of Hygiene and Tropical Medicine under the direction of Diana Elbourne, and includes Ann Truesdale (Trial advisor), Pollyanna Hardy (Statistician 2001-2005), Felicity Clemens (statistician), Korotimi Diallo (Data Manager), Steven Robertson (Data Manager to 2005), Keith Tomlin (Database manager to 2004) and Andy King (programmer), Debbie Piercy (Clerical assistant and data entry clerk).

The 6-month follow-up team is co-ordinated by Dr Andy Wilson (University of Leicester) and interviewers Jo Sanderson (2002-2006) Paul Sinfield and Carolyn Tarrant.

The Trial Steering Committee meets every year and is responsible for approving any changes to protocol and monitors and supervises the trial towards achieving its objectives. Members include an independent chairperson, Professor David Field (Professor of Neonatal Medicine, Leicester Royal Infirmary), independent members Professor Nigel Webster (Professor of Anaesthesia and Intensive Care, Aberdeen Royal Infirmary), Professor Anne Tattersfield (Professor of Respiratory Medicine, Nottingham City Hospital), Wendy Nganasurian (lay member), Silvia Holden (lay member), and Dr John Scott (East Anglian Ambulance Trust).

Members of the project management group are ex-officio. This represents all the different disciplines involved in the trial. Specialist working groups will advise the Steering Committee.

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TABLE 1 *Items of resource use in the CESAR trial*

Resource items	Instrument for data collection within CESAR trial	Source of unit cost data	References to sources
From trail entry to discharge from hospital			
Days of organ support	Daily organ support form	ICU costing study	[36,37]
Days on ECMO	Daily organ support form	ICU costing study	[36,37]
Days on conventional ventilation	Daily organ support form	ICU costing study	[36,37]
Days in intensive care	Daily organ support form	ICU costing study	[36,37]
Days of other hospital stay before discharge	Outcomes data sheet	PSSRU – http://www.pssru.ac.uk/uc/uc2005contents.htm	[25]
Miles transported by air ambulance	Transport forms (a) and (b)	cost provided by transport provider	
Miles transported by land ambulance	Transport forms (a) and (b)	cost provided by ambulance trusts	
From discharge to follow-up at 6 months			
Telephone contacts with GP	Events diary and patient cost questionnaire	PSSRU	[25]
Contacts with NHS direct	Events diary and patient cost questionnaire	NHS direct personal communication	
Visits to GP	Events diary and patient cost questionnaire	PSSRU	[25]
Home visits by nurse	Events diary and patient cost questionnaire	PSSRU	[25]
Visits to counsellor	Events diary and patient cost questionnaire	PSSRU	[25]
Visits to physiotherapist	Events diary and patient cost questionnaire	PSSRU	[25]
Visits to occupational therapist	Events diary and patient cost questionnaire	PSSRU	[25]
Visits by health visitor	Events diary and patient cost questionnaire	PSSRU	[25]
Days of inpatient stay	Events diary and patient cost questionnaire	PSSRU	[25]
Outpatient visits	Events diary and patient cost questionnaire	PSSRU	[25]
A&E visits	Events diary and patient cost questionnaire	PSSRU	[25]
Visits to day hospital/ day care	Events diary and patient cost questionnaire	PSSRU	[25]
Days in residential care	Events diary and patient cost questionnaire	PSSRU	[25]
Days in nursing home	Events diary and patient cost questionnaire	PSSRU	[25]
Medication	Events diary and patient cost questionnaire		
PSSRU	[25]		
Visits by social worker	Events diary and patient cost questionnaire	PSSRU	[25]
Visits by homecare worker	Events diary and patient cost questionnaire	PSSRU	[25]
Aids & adaptations	Events diary and patient cost questionnaire	Reported by participants and some estimated from personal enquiries by researcher to equipment suppliers	
Value of hours of informal care	Events diary and patient cost questionnaire	ONS	[30]
Miles of private car use for health care	Events diary and patient cost questionnaire	Automobile Association (AA)	[28]
Out-of-pocket expenses	Events diary and patient cost questionnaire	Reported by CESAR trial patients	
Major changes in household	Events diary and patient cost questionnaire	Reported by CESAR trial patients	
Childcare costs	Events diary and patient cost questionnaire	Reported by CESAR trial patients	

continued

TABLE 1 *Continued*

Resource items	Instrument for data collection within CESAR trial	Source of unit cost data	References to sources
Change in employment	Events diary and patient cost questionnaire	Reported by CESAR trial patients	
Change in benefits or allowances	Events diary and patient cost questionnaire	Reported by CESAR trial patients	
Loss of income from employment	Events diary and patient cost questionnaire	Reported by CESAR trial patients	
Other costs	Events diary and patient cost questionnaire	Reported by CESAR trial patients	
Other changes	Events diary and patient cost questionnaire	Reported by CESAR trial patients	

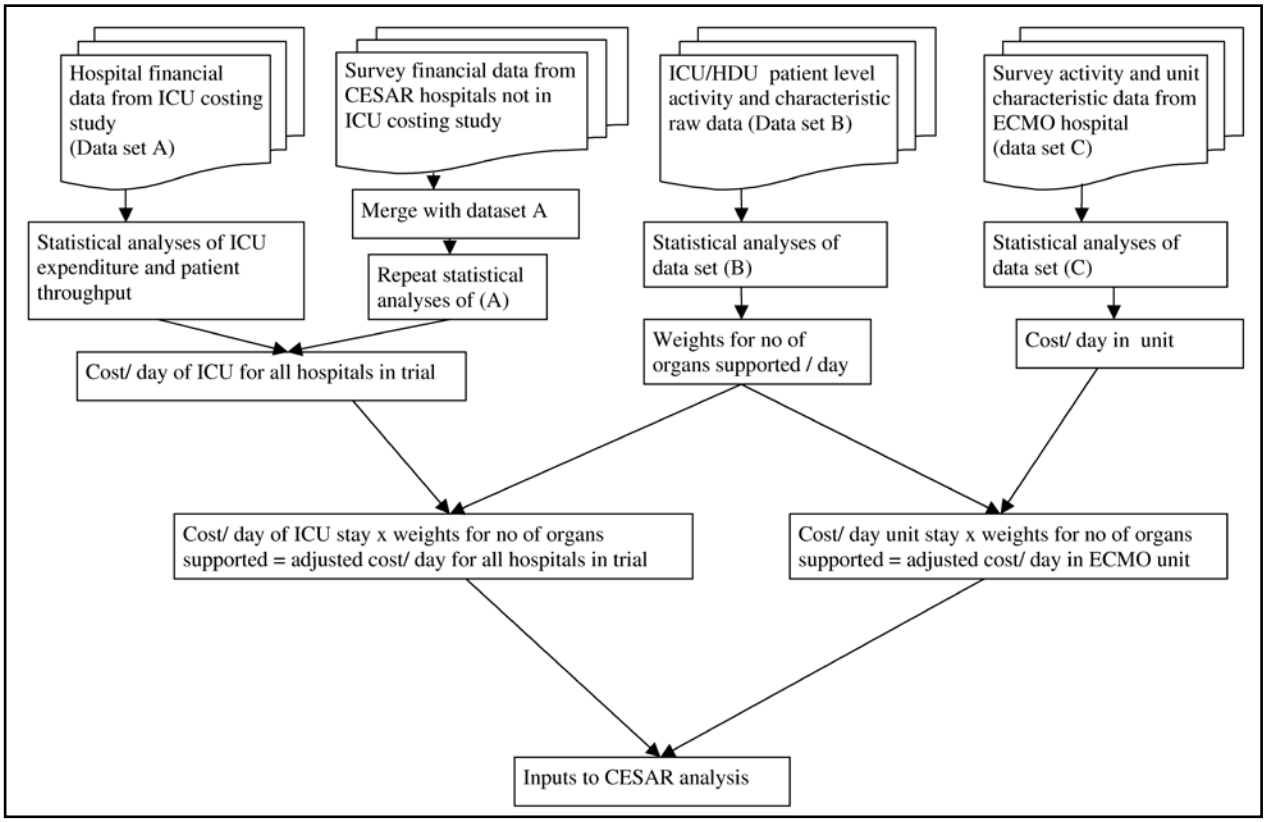

FIGURE 1 *Unit cost flowchart for hospital critical care.*

TABLE 2 *Cost of time forgone, lost pay, out-of-pocket expenses per visit to ICU at UK 2005 prices (source: Thalanany et al [38])*

Daily costs	Range (£)	Mean (£)	Median (£)
Lost pay ($n = 5$)*	17.36–65.10	50.72	54.72
Cost of time forgone ($n = 54$)	5.04–208.32	46.21	24.06
Out-of-pocket expenses	0.00–509.54	29.30	9.39

TABLE 3 *Items to test during sensitivity analysis*

	Ranges and thresholds
Days on ECMO	Highest & lowest observations
Length of stay in Critical Care Unit (ICU & HDU)	Highest & lowest calculated costs
Total length of stay in hospital	Highest & lowest calculated costs
Cost per day on organ support	Highest & lowest calculated costs
Distance from ECMO centre (cost of transport)	Replacing air with road transport
Change in difference in survival	Upper & lower CI of the attributable benefit
Other items with significant cost difference	Highest & lowest observations
Assumption of linear increasing utility for survivors over first 6 months	Assume constant utility at 6 month reported rate

Appendix 5

ECMO protocols

The Heart Link / ECMO Programme

ECMO Protocols

The Heart Link / ECMO Programme

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Page

The Heart Link / ECMO Programme

Title: **Admission Of Patients For ECMO (Specialist Action)**

Description: To ensure the smooth running and efficient admission & cannulation of a patient onto ECMO

Personnel:

ECMO Specialist	Perfusionist
ECMO Co-ordinator	Nurse
ECMO Director	Theatre Team
Transfer Team	Anaesthetist
Paediatric / Cardio-Thoracic SHO	ECMO Fellow
On-call MLSO	Haematologist On-call

Equipment: ECMO Cart
ECMO Trolley

ECMO Specialist Action:

1) Collect information on patient from ECMO Co-ordinator prior to patient admission - age, weight, condition, referral hospital, estimated time of arrival (ETA).

2) Liaise with ECMO Co-ordinator for updated information.

3) Check and prepare essential equipment & ECMO cart.

4) Prepare ACT Heparin infusion:-
5,000iu Heparin in 50mls 5% Dextrose for Neonates / Small Paeds
10,000iu Heparin in 50mls 5% Dextrose for Larger Paeds
25,000iu Heparin in 50mls 5% Dextrose / Normal Saline for Adults

Prepare bolus dose Heparin to administer during cannulation:-
75iu Heparin/kg administered as directed by RKF/AWS/GJP

Prepare infusions as prescribed with Bedside Nurse / prescribed by ECMO Fellow.

5) Prepare all necessary documentation:-
   - Admission Form
   - ECMO Specialist Evaluation Form
   - ELSO Form
   - Parameter Sheet
   - ECMO Chart

NB: Be aware of documentation for any research studies.

The Heart Link / ECMO Programme

6) Prepare all necessary equipment for ACT monitoring.

7) Assist Perfusionist, as per Perfusionist's instructions.

8) When patient arrives, ensure unit of X-matched blood is available and checked with Perfusionist.

9) Ensure Nurse takes patient's blood for analysis.

10) Order appropriate blood products and ensure X-matching is performed.

11) Assist Nursing / Theatre / Medical / Perfusion Staff where needed, document time of cannulation / type of cannulas used and handover from Perfusion.

12) Following cannulation, ensure antibiotic cover at cannulation is administered, as prescribed.

13) ACTs need to be monitored every 15 minutes for 2 hours, then every 30 minutes for 1 hour and every hour thereafter if ACTs are stable.

    Commence Heparin between 20 – 60iu/kg/hr until within the desired range, then titrate accordingly.

    Commence Heparin infusion once ACT is <250 secs

14) Ensure ECMO Co-ordinator completes Parameter Sheet & it is signed by ECMO Consultant.

15) Ensure ECMO Fellow documents procedure in the patient's notes.

16) Perform a complete circuit check and document accordingly.

17) Monitor blood gases as required and maintain within prescribed parameters by adjustments to flows / sweep.

18) Ensure all necessary documentation is completed.

The Heart Link / ECMO Programme

Title: **Admission Of Patients For ECMO (Nurse Action)**

Description: To ensure the smooth running and efficient admission & cannulation of a patient onto ECMO

Personnel: Nurse allocated to patient referred for ECMO

Nurse Action:

1) Bed
Ensure appropriately-sized bed for patient is functioning for elevation to maximum height.

2) Ventilator
Ensure appropriate ventilator is in position & ready for use and emergency re-intubation equipment is available.

3) Suction
Ensure that all suction equipment is set up and functioning.

4) Monitoring
Ensure GE PRN 50-M monitor is in situ and set up.

5) Drugs
Ensure emergency drugs are available (Crash Sheet for neonatal / paediatric patients) and assist ECMO Specialist with all necessary infusions prior to arrival of the patient.

6) Documentation
Ensure all necessary documentation is ready, as per documentation protocol.

7) Patient Arrival
Assist in the safe transfer of the patient from a Patient Safety Transporting Bed to an ITU bed / cot and ensure ventilation is continued until ECMO has commenced.

8) Connect to appropriate monitoring.

9) Record baseline observations.

10) Send blood samples for ABGs, clotting screen, U&Es, CRP, cross matching, LFTs, Amylase, Cortisol levels etc.

11) Assist in positioning the patient for cannulation.

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MRSA & MC&S

Ensure full MRSA and MC&S screens are performed & blood cultures taken within the first 24 hours of a patient's arrival.

Monday:
Blood Cultures – from patient and circuit – MC&S
All MRSA to include wound sites and ECMO cannulae.
Also swab the ECMO cannulae for MC&S.

Only swab wounds and other invasive sites if they look infected.
Compulsory - Send urine, sputum and swabs for MC&S.

Thursday:
Urine, blood CULTURES FROM CIRCUIT AND PATIENT & sputum for MC&S only.
Collect MC&S swabs if any wound or invasive site looks infective (WCC & Differential)

The Heart Link / ECMO Programme

Title: Documentation Protocol

Description: To ensure all Specialists are familiar with and know how to complete the ECMO Specialist Documentation

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Document:

ECMO Patient Admission Form

To be used for each patient on admission for ECMO.
All appropriate sections to be completed by the Specialist on duty at the time of admission or the Specialist retrieving the patient at referral centre (as some details need to be gained from staff at the referral centre).

The family details section should be completed in order that relatives can be contacted quickly in an emergency.

The reverse of the form is to document existing IV lines or skin damage etc that the patient arrives with, any IV lines that remain in once cannulated and any other relevant information.

ECMO Specialist Evaluation Form

One form to be completed by the Specialist for the shift worked.
Pages 1 & 2 should be completed at the beginning of the shift, following the initial circuit check.
Page 3 is to document any changes or problems during the shift.
Page 4 is an hourly checklist to document the circuit checks performed throughout the shift and any problems encountered with the circuit.

ECMO Chart

This is for hourly recording of patient and circuit observations.
Details concerning cannulation should be completed at the time of cannulation and transferred to each chart appropriately.
ECMO hours and arterial blood results should be written in red ink.
Mixed venous gas should be written in black ink.
Post oxygenator gases must always be performed each shift (or more frequently if required).
Results must be documented on the ECMO Chart.

The Heart Link / ECMO Programme

Parameters Form / Physicians Orders

To be completed daily by the ECMO Co-ordinator.

Trial Off Form

This form documents each trial off ECMO and is completed by the Specialist during and after each trial off.
Page 2 is to be used as a reminder of when procedures need to be completed for VA ECMO and a tick box provided to note when the task has been completed.
Page 3 is to note all the blood gas results.

ELSO Registry Form

Should be completed for each ECMO patient by the ECMO Co-ordinator.

The Heart Link / ECMO Programme

Title: **ECMO Emergency Cart Supply**

Description: Check list for Specialist

Personnel: ECMO Specialist

Equipment:

Raceway (Super Tygon 1/4", 3/8",1/2")	Cable Tie-Gun
Sterile Scissors	Tie-Straps
500ml bag of 0.9% Saline	Spare Pigtails
Perfusion: Rapid Access IV Giving Set	Three-way Taps
Small Sterile Towel	Sterile Gloves
50ml Luer Lock Syringes	Betadine Solution
Connectors appropriate to tubing in use	Pink Spray

ECMO Specialist Action:

Action:	**Rationale:**
Ensure supplies are checked at the beginning of shift	To ensure cart supply is ready in case of an emergency
Ensure above supplies are available and at hand at all times in case of circuit emergency	For immediate use in circuit emergency
Ensure absent items are replaced	To minimise delay in an emergency

The Heart Link / ECMO Programme

Title: **Performing The Activated Clotting Time (ACT)**

Description: To perform the ACT test each hour or as required

Personnel: ECMO Specialist

Equipment:

ACT Test Tube (White Cap)	1ml Syringe
2ml Syringe	Actylyte
Steret	Gloves

ECMO Specialist Action:

Action:	**Rationale:**
Gather equipment	
Wash hands	
Clean sample port using street	
Attach a 2ml syringe to the three-way tap	
Turn tap on & aspirate 2mls, turn tap off	The pigtail contains dead-space
Set aside this syringe and replace with 1ml syringe. Turn tap on and withdraw 0.5ml, then remove & replace with original 2ml syringe	
Take sample to Actylyte machine & tap test tub on solid surface	
Simultaneously place 0.5ml of blood into test tube whilst pressing 'start' on machine	To start timing immediately blood starts to clot
Flick the base of the tube	To ensure blood mixes with activator

The Heart Link / ECMO Programme

Place the bottle into the Actylyte machine and twist clockwise until a green light comes on	To ensure detector is functioning
Return to sample port and return 2mls of dead-space, ensuring no air is injected	Reduces the need for blood transfusions
Dispose of equipment properly	Health & safety
When machine bleeps, the test is complete – record result on the ECMO Chart	

The Heart Link / ECMO Programme

Title: **Heparin Management**

Description: To ensure safe & smooth running management of continuous Heparin infusion into the ECMO circuit

Personnel: ECMO Specialist

Equipment:

Heparin (Non-Bactericide)	1,000iu/ml
Syringe Pump	50ml Syringe & Infusion Line
Blue / Green Needle	Actylyte Machine
ACT Bottles (0.5mls)	

ECMO Specialist Action:

Action:	Rationale:
Ensure designated port for administration of Heparin is labelled & dated at all times (2nd pigtail)	Designated port post sample port to prevent it affecting the ACT result
Ensure Heparin infusion is being delivered according to ACTs and concentrations, as detailed below:-	To ensure correct dose & strength of Heparin is being administered, as prescribed

Heparin Concentrations

5,000iu in 50mls 5% Dextrose for Neonates
10,000iu in 50mls 5% Dextrose for Paeds
25,000iu in 50mls 5% Dextrose or 0.9% Normal Saline for Adults

NB: Above concentrations may need to be revised for patients with severe coagulopathies and therefore management is dependent upon the individual ACT results and written parameters – as directed by the ECMO Director / ECMO Co-ordinator / ECMO Fellow

The Heart Link / ECMO Programme

Ensure Heparin is being delivered at all times *NB: normal rang is 20iu → 60iu/kg/hr*	To prevent coagulation of the circuit
ACTs need to be monitored every 15 minutes for 2 hours, then every 30 minutes for 1 hour and every hour thereafter if ACTs are stable. *NB: Never discontinue a Heparin infusion – this is a Consultant only decision and must be documented in the patient's notes*	To prevent clot formation in the circuit
Ensure aware of written ACT parameters	Changes may be made, depending on the patient's status
Ensure aware of compatibility / reaction of other drugs, when used in associated with Heparin infusion	
If ACTs fall below the prescribed parameters, Bolus should be given as well as an increase in dose and ACTs checked at least ¼ hourly until within parameters	Prevent clots forming
Any concerns, contact the ECMO Co-ordinator	For Senior Specialist advice and instruction

Minimum Bolus

0.5ml plus an increased Heparin infusion rate for Neonates / Small Paeds

1ml plus an increased Heparin infusion rate for Larger Paeds / Adults

The Heart Link / ECMO Programme

Title: **Emergency Communication Protocol**

Description: To ensure the Specialist is aware of the procedure for obtaining assistance if an ECMO emergency occurs

Personnel: ECMO Specialist
Nurse
On-call ECMO Team
- ECMO Director
- ECMO Co-ordinator
- Perfusionist
- ECMO Fellow

ECMO Specialist Action (in the event of an ECMO emergency):

1) Call for assistance.
At least three people are required:-
- One Nurse to hand ventilate & monitor the patient
- One person to telephone for support / instructions
- One person to assist the Specialist

Each person should be aware of his / her responsibilities and directed by the Specialist.

2) The Specialist should attempt to deal with the cause of the emergency immediately wherever possible e.g. commence repair of the circuit in the event of a ruptured raceway.
If a problem cannot be resolved without help from members of the ECMO Team, all attempts should be made to maintain the circuit whilst waiting for backup.

3) Telephone numbers and on-call rotas are held at Switchboard.
In the event of circuit failure, call 2222 and ask for the ECMO Team to be called.
State “ECMO emergency”.

The Heart Link / ECMO Programme

Title: **Fire & Explosion Risk**

Description: To prevent fire or explosion in the event of surgical procedures where diathermy apparatus is used

Personnel: ECMO Co-ordinator
ECMO Specialist
Nurse
Anaesthetist
ECMO Fellow

ECMO Specialist Action:

Action:	**Rationale:**
During cannulation, decannulation or surgical procedures there should be no source of free flowing oxygen, other than that minimally required to maintain patient oxygenation	Oxygen is flammable in the presence of Betadine skin prep & diathermy and may cause an explosion
Bag / mask should be labelled “No oxygen flow during surgery”	To ensure all staff involved are aware of risks
Anaesthetic presence should ensure safe placement of the oxygen administration equipment away from diathermy and related electrical apparatus	The Anaesthetist would be the main user of such equipment during surgical procedures

The Heart Link / ECMO Programme

Title: **Dressing Cannulation Site**

Description: To apply dressing to cannula site following cannulation & redress PRN

Personnel: ECMO Specialist
Nurse

Equipment: Dressing Pack
Clear Occlusive Dressing
Betadine
Normasol

ECMO Specialist Action:

Action:	**Rationale:**
Clean trolley with water & detergent, wash hands and set up trolley as per UHL policy	Observe universal precautions
Remove existing dressing	
Observe cannula site	
Ensure cannula sites are sutured securely	
Clean wound with Normasol, observing asepsis	As above
If cannula site is oozing, apply pressure with small folded gauze & call the ECMO Fellow for further assessment regarding potential surgical intervention	To try to reduce oozing
Apply tegaderm dressing using a piece large enough to ensure the cannula is secure	Clean dressing to enable observation of site

The Heart Link / ECMO Programme

Dispose of waste & ensure patient comfort	
If there is excessive bleeding from the cannula site, perform a clotting screen and inform Surgeon	Surgical / medical intervention may be required
If cannula site is red or infected, take a swab – see Infection Screen Protocol	

The Heart Link / ECMO Programme

Title: **Flushing The Patient Bridge**

Description: Releasing the Bridge Clamp to maintain patency of the Patient Bridge

Personnel: ECMO Specialist

Equipment: Bridge Clamp

ECMO Specialist Action:

Action:	**Rationale:**
Every 10 – 15 minutes the bridge clamp should be opened for approximately 5 seconds, then re-clamped in a different position on the bridge. *NB: More often if separation is occurring* This action must be documented on the Observation Chart / Hourly Checklist Chart	To prevent clot formation in the bridge and undue pressure on one part of tubing
Each time the clamp is released, the bridge tubing should be inspected for clots or marks on the tubing	Ensure the clamp is fully closed and prevent damage to tubing

The Heart Link / ECMO Programme

Title: **Clamping On & Off ECMO**

Description: Clamping patients onto and off ECMO in the event of an emergency situation or an elective period off ECMO

Personnel: ECMO Co-ordinator
ECMO Specialist
Nurse
ECMO Fellow

Equipment: Clamp
Hand Ventilation Equipment
Emergency Drugs (as required)

ECMO Specialist Action (for elective period off ECMO):

Action:	**Rationale:**
Ensure relatives have been informed of procedure	To avoid undue anxiety
Ensure Nurse is aware of procedure and is able to hand ventilate the patient throughout or mechanical ventilation is increased appropriately	To maintain patient oxygenation off ECMO
Ensure any emergency drugs (which may be required) are available and that IV lines are accessible	To maintain patient stability throughout the procedure
If the procedure is to be performed, gather all supplies in advance	To minimise time off ECMO
<u>Clamp off</u> Venous – Bridge – Arterial Clamp the venous drainage tubing above the patient bridge, release the bridge clamp and use it to clamp the arterial return tubing again above the patient bridge	To prevent blood draining out of the patient and allow a little to return

The Heart Link / ECMO Programme

<u>Clamp on</u> Arterial – Bridge – Venous Release the clamp on the arterial tubing, clamp the patient bridge and release the clamp on the venous tubing	To avoid a sudden drainage of blood with no return
<u>Routine procedures:</u> Routine procedures e.g. walking the raceway & a routine pigtail change require Venous – Bridge – Arterial	

ECMO Specialist Action (in an emergency):

Action:	**Rationale:**
<u>In an emergency</u> Arterial – Bridge – Venous The tubing should be clamped immediately and then help called for Hand ventilate the patient and give emergency drugs etc The order is always A-B-V *NB: The Bedside Nurse must always be taught to clamp off Arterial – Bridge – Venous in an emergency situation*	To avoid blood loss or air to the patient

The Heart Link / ECMO Programme

Title: **Trans-membrane Pressure Monitoring**

Description: To replace Transducer Lines, flush Transducer Lines, recalibrate and set alarms / alarm limits on Stockert Box / Monitor

Personnel: ECMO Specialist

Equipment: 2 x 50ml, 20ml or 30ml Luer Lock Syringes for each oxygenator
Flush Bag
2 x Steret

ECMO Specialist Action:

Action:	**Rationale:**
Gather supplies	To prevent unnecessary anxiety
<u>To replace transducer sets</u> • Ensure that the transducer lines are primed. • Turn off the three-way tap at the oxygenator and attached primed transducer set to three-way tap • Ensure that three-way tap is cleaned with steret prior to attachment of transducer set	
<u>To recalibrate the Stockert Box</u> • Turn the transducer 'off' to the oxygenator and open the line to air • Press the 'zero' button on the Stockert Box and allow the box to zero • Once calibrated, turn the transducer to the 'on' position • Change the transducer lines every seven days	To calibrate

The Heart Link / ECMO Programme

<u>To reset the alarm limits</u> • Reset the alarm to read 50mmhg greater than the reading, by using the 'yellow' Stockert adjustment tool to adjust the alarm limits on the Stockert Box	To set alarms
<u>To flush the transducer lines</u> • Switch the three-way tap off to oxygenator • Remove the white cap off the three-way tap and clean site with steret • Place luer lock syringe onto the cleaned part of the three-way tap • Flush the line via use of the transducer to clear the line • Ensure to flush until the line is fully clear • Switch three-way tap back on to oxygenator • Clean empty port with steret and replace white bung • Dispose of waste safely • Repeat on all transducer lines (pre / post oxygenator)	To be carried out each shift and prn
<u>To zero lines and adjust alarms</u> • Set alarms as already mentioned above	

The Heart Link / ECMO Programme

Title: **Administration Of Drugs & Blood Products**

Description: The safe & appropriate administration of prescribed drugs & blood products and the use of UHL policy

Personnel: ECMO Specialist
Nurse
Member of the ECMO Medical Team
Paediatrician / Surgical SHO or Registrar

Equipment:

Drug	Filter
Dilutant	Giving Set / Syringe
Needle / Syringe / Giving Set	Three-way Tap Connector
Blood Product	

ECMO Specialist Action:

Action:	**Rationale:**
Check prescription chart	For correct patient, correct date & time, correct dose, any allergies and signed by doctor
Check product	For correct dose, correct dilution, expiry date, correct blood product & correct blood group
<u>Prepare drugs</u> As per UHL policy <u>Prepare blood products</u> Using appropriate filter and giving set	
Use a suitable port on the ECMO circuit to administer drugs / blood products i.e. Blood into bladder ports (HAS 4.5% + 20% Albumin) All clotting factors post-oxygenator	To infuse as quickly as is required To prevent destruction in oxygenator

The Heart Link / ECMO Programme

Bolus drugs into drug port and infusions pre-bladder (except TPN) TPN must be administered post bladder c/o a designated pigtail Trasylol to be administered post bladder or directly to patient's central access	To reduce the risk of air embolus
Use a suitable technique to administer bolus or continuous infusion and ensure infusion pumps are checked hourly and administering correctly. *NB: Ensure strict hand hygiene and non-touch technique*	For patient safety
Observe for side effects & reactions and stop infusions / inform Medical Staff as necessary	For patient safety

The Heart Link / ECMO Programme

Title: **Procedure For Applying & Removal Of Tie-straps**

Description: Apply initial Tie-straps post cannulation, assess Tie-strap security at prescribed intervals and remove & replace as required (in the event of Tie-straps becoming loose, falling off or not being present)

Personnel: ECMO Specialist

Equipment: Tie-straps
Tie-strap Gun

ECMO Specialist Action:

Action:	**Rationale:**
All tie-straps are to be checked at the beginning of each shift and at appropriate intervals thereafter during the shift (i.e. Specialist's Hourly Checklist)	To check the security of each tie-strap regularly
Check tie-straps by supporting tubing using both hands and examine each tie-strap by twisting gently with thumb & finger to see if secure	
If tie-strap is loose, prepare for replacement	
Gather supplies	To prevent undue anxiety
Place tie-strap in gun, support the connector & tubing and secure a tie-strap with the gun *NB: Do not use scissors in tie-strap removal – seek assistance from the ECMO Co-ordinator*	For a tight & secure fit

The Heart Link / ECMO Programme

Title: **Walking The Raceway**

Description: Prevent any one segment of ECMO tubing from prolonged exposure to compression in the Roller Head / to prevent rupture of the tubing

Personnel: ECMO Specialist
Bedside Nurse
ECMO Fellow
ECMO Co-ordinator

Equipment: 2 x Clamps (3 x if a third cannula is inserted)
Marker Pen
Emergency Drugs

ECMO Specialist Action:

Action:	**Rationale:**
Ensure the ECMO Team is present and gather equipment needed	To ensure the Specialist is prepared and has adequate support, if needed
Inform relatives of the procedure	To avoid undue anxiety
Mark the tubing close to where it enters the pump raceway (left-hand side of the pump)	To show the length of tubing needed to be walked through the raceway
Ventilation is increased or patient is hand-ventilated by the Nurse or Doctor in 100% oxygen	To pre-oxygenate the patient and obtain good SaO_2 prior to procedure
Take the patient off ECMO (clamping V-B-A) and turn off the pump	Unable to perform the procedure with the pump rotating
• Open the boot lid • Place pump head in 12 o'clock position • Undo the gates, holding the tubing securely	To ensure a completely new piece of tubing is now positioned in the raceway

The Heart Link / ECMO Programme

Remove & advance the tubing (in the same direction as pump flow) through the pump head until the marked tubing is out of the boot	*NB The identification mark will always be on the right-hand side of the pump*
Ensure the tubing is well-positioned in the boot of the pump and is securely held by the gate clamps	To ensure correct positioning and even occlusion of the tubing
Check the circuit is correctly configured and there is no air or kinks in the circuit	For patient safety prior to returning to ECMO support
Turn on the pump to previous settings and unclamp A-B-V	
Recommence IPPV at previous settings	
Record the date, time, personnel involved, HR, BP, SaO_2 & any problems in the patient's notes and also document & sign the Parameter Sheet	

Comments

Each circuit should be assessed and the raceway checked hourly & under constant supervision by the ECMO Specialist. Any concerns about the raceway should be discussed immediately with the ECMO Co-ordinator & Perfusionist and action taken if needed. In the event of an emergency, the 2222 ECMO Crash Call must be instigated.

One clear length of raceway tubing (approx' 40" in length) must always be left at the end of the raceway, to be used in the event of a raceway rupture. This nominated length of tubing will be marked clearly with white tape indicating the nominated line and must not be walked beyond this line in any circumstances, apart from rupture. This enables one single straight connector to be used - allowing the ECMO Specialist to perform the procedure quickly, safely & efficiently with minimal instability to the patient.

The Heart Link / ECMO Programme

Frequency Guides To Walking The Raceway:

The frequency the raceway needs to be walked depends on the patient – please see rough guides below:-

Adult Raceway:

NB: Adult patients need the raceway walking more frequently than Paediatrics or Neonates, due to the increased number of revolutions per minute (RPM).

RPM	Frequency the raceway needs walking
< 80	Every five days
> 80	Every three days
> 90	Alternate days
> 100	Daily

Paediatrics (3/8" Raceway):

Flows (ml/min)	Frequency the raceway needs walking
< 1400	Every five days
1400 - 1600	Every three days
>1600	Daily

Neonates (1/4" Raceway):

Flows (ml/min)	Frequency the raceway needs walking
< 400	Every five days
400 - 500	Every three days
>500	Daily

The Heart Link / ECMO Programme

Title: **Use Of The Hand Crank**

Description: To use the Hand Crank to continue ECMO flow in the event of pump or power failure or if transferring a patient short distances / for transfer to the Catheter Suite, Theatre, CT Scan or within ITU

Personnel: ECMO Specialist
Nurse
ECMO Fellow

Equipment: Hand Crank

ECMO Specialist Action:

Action:	**Rationale:**
Always check a hand crank is present on the cart at the beginning of a shift	To ensure one is available in an emergency
Always note the direction the pump is rotating and the revolutions per minute (RPM)	To ensure a quick response and avoid incorrect direction of hand cranking
<u>If power supply fails:</u> • Turn off the pump • Lift lid to roller pump & insert the hand crank in one of the holes on the roller • Immediately start to turn the roller in the direction of flow and maintain previous patient flow rates *NB: Bladder / circuit pressures (pre / post oxygenator) must be observed at all times throughout this procedure*	To maintain patients stability / safety and circuit flow To prevent clotting of the circuit & cannulae

The Heart Link / ECMO Programme

<u>If power is off for more than a few seconds:</u> • Call in the ECMO Team • Dial 2222: stating 'ECMO emergency'	For medical support / backup
<u>If the pump fails:</u> • Proceed as per 'If the power supply fails' & 'If the power is off for more than a few seconds' • Assist the Perfusionist in changing the pump *NB: The ECMO Specialist role is only to <u>assist</u> Perfusionist*	
Ensure you are aware of the patient's condition at all times – ask the Nurse to tell you what the oxygen saturations, blood pressure, heart rate etc are *NB: Ensure the duration of the event is noted*	To recognise whether adequate support is being maintained

The Heart Link / ECMO Programme

Title: **Changing A Pigtail "Two Man Technique" (Pre-Pump Only)**

Description: To replace an ECMO circuit Pigtail

Personnel: ECMO Specialist
Nurse
ECMO Fellow
ECMO Co-ordinator (if required)

Equipment: 3 x Clamps
1 x Pigtail
1 x Three-way Tap
5mls Syringe Flush
Gloves

ECMO Specialist Action:

Action:	**Rationale:**
Gather supplies and inform Nurse & relatives	To have everything at hand for quickness
Wash hands and put on gloves	To observe universal precautions
Attach three-way tap to the pigtail and flush, leaving the syringe on the three-way tap	To prevent air embolus
Turn pump off	Clamping tubing whilst the pump is on may cause the circuit to rupture
Instruct the Nurse to clamp tubing on either side of the pigtail (keeping hold of the clamps to steady tubing)	To prevent blood loss when the old pigtail is removed
Disconnect the old pigtail and connect the new pigtail with the three-way tap & syringe attached	
Instruct Nurse to remove the clamp nearest the bladder, draw back to de-bubble, turn tap off to circuit & release second clamp	

The Heart Link / ECMO Programme

Check circuit for air, ensure no clamps are on the tubing, then restart pump	To ensure it is safe to return the patient to ECMO

Comments

1) There are two types of Pigtails:

- Normal-sized (thin bore) Pigtails
- Haemofiltration (large bore) Pigtails

Haemofiltration Pigtails are only to be used in the event of haemofiltration

2) Do not tighten three-way taps with a clamp - they need to be hand tight only

3) Do not loosen affected Pigtails prior to removal

4) If clamping a Pigtail post-pump, please follow protocol for one man Pigtail technique

The Heart Link / ECMO Programme

Title: **Changing A Pigtail "One Man Technique"**

Description: To replace an ECMO circuit Pigtail

Personnel: ECMO Specialist
Nurse
ECMO Fellow
ECMO Co-ordinator

Equipment: 5 x Clamps
1 x Pigtail
1 x Three-way Tap
5mls Syringe Flush
Gloves

ECMO Specialist Action:

Action:	**Rationale:**
Gather supplies and inform Nurse & relatives	To have everything at hand for quickness
Wash hands and put on gloves	To observe universal precautions
Attach three-way tap to the pigtail and flush, leaving the 5ml syringe on the three-way tap	To prevent air embolus
Ensure ECMO Team are present	
Turn pump off	To ensure patient safety
Ensure Nurse / Co-ordinator clamps the patient off (V-B-A) *NB: In the event of an emergency, the Nurse must clamp the patient off A-B-V*	To ensure patient safety
Clamp tubing either side of the pigtail	To prevent blood loss when the old pigtail is removed

The Heart Link / ECMO Programme

Disconnect the old pigtail and connect the new pigtail with the three-way tap & syringe attached	
Remove the clamp nearest to the bladder (in order to de-bubble), turn tap off to circuit and release the second clamp	
Turn the pump back on, check the circuit for air and ensure no clamps are left on the circuit tubing	To ensure safe return of the patient back onto ECMO
Instruct the Nurse to remove the patient's clamps A-V-B	

Comments

1) Do not loosen affected Pigtails prior to removal

The Heart Link / ECMO Programme

Title: **Changing An ECMO Circuit Three-way Tap**

Description: To replace an ECMO circuit tap at prescribed intervals and in the event of cracking / clotting

Personnel: ECMO Specialist

Equipment:

1 x Sterile Three-way Tap	Padded Clamps
2 x Sterets	3mls Flush
Gloves	5ml Syringe

ECMO Specialist Action:

Action:	**Rationale:**
Gather supplies	
Wash hands and put gloves on	Observe universal precautions
Attach tap to syringe and flush through all the ports	To remove air from the tap
Place steret package around the pigtail, then clamp the pigtail over the packet	To protect the pigtail from damage by the clamp
Whilst holding the pigtail, remove the old tap	
Wipe lightly with steret, then attach new tap to the pigtail	Substances in plastic may be degraded by excessive exposure to alcohol
<u>If pre-pump:</u> Remove the clamp, draw back on the syringe to aspirate air, close the tap off to circuit and replace syringe with the luer lock cap	

The Heart Link / ECMO Programme

<u>If post-pump:</u> Turn the tap on to circuit, loosen the clamp whist aspirating air & immediately re-clamp, close tap off to circuit, replace syringe with luer lock cap, then unclamp	Pigtails and taps post-pump are exposed to high pressures - the use of the clamp controls the backflow of blood into the syringe

<u>Comments</u>

1) Notify the Nurse prior to change, particularly if IV infusions will be affected

2) All taps must be turned off to the circuit when not in use

3) Taps located at the bladder stems should be changed every <u>72 hours</u>

The Heart Link / ECMO Programme

Title: **Air Bubble Removal**

Description: To remove air from the circuit

Personnel: ECMO Co-ordinator
ECMO Specialist
Nurse
Perfusionist

Equipment: Syringe (appropriately-sized to aspirate air)
Gloves

ECMO Specialist Action:

Action:	**Rationale:**
<u>If air is in bladder or bladder stems</u> • Apply gloves • Attach syringe to port with air in, turn three-way tap onto bladder & syringe and slowly aspirate air • Turn tap off to bladder, remove syringe and replace cap	
<u>If air is moving through tubing on venous side:</u> • Have a clamp at hand to clamp A-B-V whilst watching the bubble • If it settles in the bladder, do not clamp off and proceed as per 'If air in bladder or bladder stems'	Air on the venous side pre-bladder should get trapped and settle in the bladder
<u>If air is moving through tubing on arterial side:</u> • Clamp patient off A-B-V, contact the ECMO Team on 2222, time the clamp off period, hand bag the patient and de-air the circuit	Patients require isolation from the ECMO circuit due to the risk of air – a prolonged period of time off ECMO will cause the ECMO circuit to clot

The Heart Link / ECMO Programme

<u>If air embolus settles at highest point in the circuit:</u> • Aspirate air from the nearest pigtail port • Increase pump flow, work the air through the bridge & into the bladder and aspirate out of the bladder stem three-way tap	Air rises to the highest point - this is usually post-oxygenator, near the platelet pigtail intended for platelet administration
Once air is removed and no active source of air entering circuit found, return the patient to ECMO (A-B-V)	
Return to previous IPPV	

<u>Comments</u>

1) If there a large amount of air in the circuit, clamp the patient off immediately as per the emergency procedure (A-B-V), circulate through the bridge, disconnect sweep gas and call the Perfusionist.

2) Please be aware emergency fluid may need to be administered to maintain pump flow using rapid access line

3) Once the emergency procedure has been initiated, hand bag the patient in 100% oxygen.

4) Whilst waiting for the Perfusionist, attempt to find the source of air entry & rectify

5) Once the problem has been rectified, please ensure that the sweep gas is reconnected

The Heart Link / ECMO Programme

Title: **Inserting A Connector In The Event Of A Raceway Rupture**

Description: Insertion of a connector

Personnel:
ECMO Director
ECMO Co-ordinator
ECMO Specialist
Nurse
ECMO Fellow
Perfusionist

Equipment:
Replacement Raceway
Sterile Field
9 x Clamps
Drizzle Fluid
50ml Syringe
Appropriate Connectors
Perfusion Scissors

ECMO Specialist Action:

Action:	**Rationale:**
When rupture is identified, clamp the patient off ECMO immediately (A-B-V)	To minimise blood loss and ensure no air emboli reach the patient
Alert Nurse to the problem and ensure hand ventilation is commenced or mechanical ventilation adjusted accordingly	Maintain patient oxygenation
Allocate one person to alert Switchboard of the ECMO emergency (call 2222) and obtain any equipment / drugs needed	To avoid duplication and ensure speed & efficiency
Clamp tubing at entry & exit points of the roller pump, inspect tubing and prepare to insert a straight connector into the tubing	To ensure the quickest & safest procedure is performed until backup from Perfusion is available

The Heart Link / ECMO Programme

Ask assisting Nurse / ECMO Specialist to draw up drizzle solution into the 50ml syringe and open sterile pack & gloves	To prime the new connector – asepsis is required at all times
Apply three clamps at each point either side of the rupture, where tubing is to be cut	To prevent excess blood spillage
Swab the tubing where the cut is to be made with Betadine solution and cut the tubing closest to the end that will be discarded	To maintain asepsis and ensure sufficient tubing is available to securely fit the connector
Insert connector & drizzle solution in whilst connecting the other end	To prevent air emboli
Remove clamps and place the raceway back into the pump *NB: The raceway to be placed in the pump will be walked past the nominated white mark (white tape on raceway tubing) – this is the only occasion where the raceway will be walked past the nominated white mark*	
Start the pump slowly and circulate through the patient bridge	To ensure no air is in the circuit and allow for its removal before the patient is returned to ECMO
Return the patient to ECMO support by releasing the clamp on the arterial tubing first and using it to clamp the patient bridge, then release the clamp on the venous side of the tubing	To prevent sudden venous drainage with no return

The Heart Link / ECMO Programme

Connect the tie straps to the inserted connector *NB: Once Perfusion arrive, elective raceway & pump change-out must be performed*	To ensure circuit and patient safety
Prepare for elective change-out of the pump / raceway in accordance with the Perfusionist's instructions	To ensure circuit and patient safety

The Heart Link / ECMO Programme

Title: **Conversion From VV – VA ECMO Or VA – VV ECMO**

Description: To ensure the safe and efficient conversation from VV to VA ECMO / VA to VV ECMO

Personnel: ECMO Co-ordinator
ECMO Specialist
Nurse
Perfusionist
ECMO Director
Theatre Team
Anaesthetist
ECMO Fellow

ECMO Specialist Action:

Action:	**Rationale:**
Ensure all members of the team (stated above) are fully aware of the planned conversion	To ensure effective communication and an efficient procedure
Ensure relatives are fully informed of the procedure	To reduce stress / anxiety
Assist the Perfusion Team, as required	To help in the event of an emergency
Ensure all necessary equipment is at hand - ready for immediate use	To reduce delay if an emergency arises
Ensure the emergency box is checked & correct	For use in an emergency
Ensure the patient is fully sedated and anaesthetised prior to conversion	To ensure patient comfort and safety
Monitor patient status throughout the procedure - informing medical staff / Perfusionist of any relevant changes	To ensure patient safety

The Heart Link / ECMO Programme

Monitor the circuit throughout the procedure	To maintain a functioning circuit
Ensure major structural changes to the circuit (e.g. two patient bridges) are documented on the Specialist Evaluation Form and verbally handed over to the next Specialist	To ensure efficient communication
Post procedure, perform a full circuit check / handover from the Perfusionist	To ensure circuit and patient safety
Post-procedure, ensure the circuit is clean & tidy	To ensure a clean & safe circuit

The Heart Link / ECMO Programme

Title: **Weaning From VA Or VV ECMO**

Description: To wean to minimal levels of ECMO support

Personnel: ECMO Co-ordinator
ECMO Specialist
ECMO Fellow

ECMO Specialist Action:

Action:	**Rationale:**
Maintain frequent arterial / mixed venous blood gases - keeping within written parameters	In order to recognise any trends present and keep the levels within written parameters
If the patient is ready to wean, reduce the ECMO flows gradually - checking saturations & gases with each reduction in flow and adjusting sweep gas accordingly	
If the arterial or mixed venous blood gases remain within their set parameters whilst on minimal support, then a trial off could be discussed with the on-call ECMO Consultant and arrangements made for a trial off to take place	

Minimum Weaning Parameters:

	VA ECMO	**VV ECMO**
Neonate / Small Paed	30 (mls/kg)	50 (mls/kg)
Adult	1000 (mls/min)	1000 (mls/min)

NB: The weaning parameter of a Neonate / small Paed should be no less than 10 revolutions per minute (RPM)

The Heart Link / ECMO Programme

Title: **Trial Off Veno-Venous ECMO**

Description: To manage and monitor a trial off VV ECMO, maintaining the function of the ECMO circuit and the safety of the patient

Personnel: ECMO Director
ECMO Co-ordinator
ECMO Specialist
Nurse
ECMO Fellow

ECMO Specialist Action:

Action:	**Rationale:**
Ensure ECMO Co-ordinator is aware of decision to trial off *NB: Co-ordinator must be present for trial off period, unless in the event of an overnight trial off*	
Check that any pre-decannulation ETT change is performed	It is easier to make changes to the ETT whilst the patient is not dependant on the ventilator
Ensure ventilator is changed prior to commencement of trial off, not during or immediately after	
Check that new IV / arterial access is gained	
Check the patency of the existing IV access	To assess the need for further IV access
Ventilation will be increased by the ECMO Fellow	To ensure oxygenation after membrane gas supply
Disconnect sweep gas supply to the oxygenator – documenting the time	

The Heart Link / ECMO Programme

Increase pump flow *NB: The first ABG should be taken 30mins – 40mins post disconnection of the sweep gas, to allow for efficient mixing*	To prevent areas of stasis
Check ABGs every 20 mins for two hours and every 30 mins thereafter Ventilation to be altered according to parameters set by the ECMO Fellow	
Continue maintenance of the circuit, as per protocol	The circuit may still be needed
If ABGs are satisfactory after a prescribed amount of time - the ECMO Co-ordinator will discuss decannulation with the on-call ECMO Consultant	
Maintain the circuit without sweep gas supply until decannulation	
Keep relatives & staff informed accordingly throughout *NB: The minimum trial off period is two hours*	To reduce anxiety, ensure patient safety and make sure the patient is suitable to remove from ECMO support
Document the trial off on appropriate Trial Off Forms & ECMO Chart	

The Heart Link / ECMO Programme

Title: **Trial Off Veno-Arterial ECMO**

Description: To manage and monitor a trial off VA ECMO, maintaining the function of the ECMO circuit and the safety of the patient

Personnel:
ECMO Consultant (on-call)
ECMO Co-ordinator
ECMO Specialist
Nurse
ECMO Fellow

Equipment:
VA Trial Off Documentation
9 x Clamps (at least)
Clock
Emergency Drugs
2 x Actylyte Machines

ECMO Specialist Action:

Action:	**Rationale:**
Ensure ECMO Co-ordinator is aware of decision to trial off *NB: Co-ordinator must be present for trial off period, unless in the event of an overnight trial off*	
Check that any pre-decannulation ETT change is performed	It is easier to make changes to the ETT whilst the patient is not dependant on the ventilator
Ensure ventilator is change prior to commencement of trial off, not during or immediately after	
Check that new IV / arterial access is gained	
Check the patency of the existing IV access	To assess the need for further IV access

The Heart Link / ECMO Programme

Prepare a new Heparin infusion (at the same concentration as the circuit Heparin) and connect to the patient's IV line - this infusion will be commenced with trial off at ½ rate of the current circuit Heparin	Need to maintain heparinisation of the patient & patency of cannulae
Transfer necessary infusions from the circuit to the patient	To keep essential drug infusions maintained
Ventilator settings will be increased by the ECMO Fellow	To ensure adequate oxygenation when off ECMO
Clamp the patient off ECMO by clamping the venous drainage tubing as near to the cannula as possible	To remove the patient from ECLS, whilst ensuring they have sufficient blood volume for their own circulation
Release the bridge clamp and use it to clamp off the arterial return tubing (V-B-A), as close to the cannula as possible	
Turn sweep gas flow off	To prevent a possible build-up of gas pressure and thus emboli
Decrease the circuit Heparin to half its original rate	This is still needed in the circuit, but at a reduced rate due to the break in patient consumption
Start patient Heparin at half the original dose	Need to maintain heparinisation of the patient & patency of cannulae
Document the time trial off commenced using the VA ECMO Trial Off Record Sheet	An accurate note of the commencement of trial off is required
Release clamps (V-B-A / A-B-V) every 10 minutes	To prevent clot formation in the cannulae and to maintain patency of cannulae & the ECMO circuit

The Heart Link / ECMO Programme

Perform circuit and patient ACT's every 10 minutes prior to flushing the cannulaes.	
Perform arterial blood gases every 20 minutes.	
Maintain the circuit without sweep gas supply until decannulation or re-commencement of ECMO	
Keep relatives / all team members informed accordingly throughout *NB: The minimum trial off period is two hours*	To reduce anxiety, ensure patient safety and make sure the patient is suitable to remove from ECMO support
Document the trial off on designated Trial Off Form & ECMO Chart	

The Heart Link / ECMO Programme

Title: **Decannulation Protocol**

Description: To assist in the decannulation of an ECMO patient following a successful trial off

Personnel:
ECMO Director
ECMO Consultant
ECMO Fellow
ECMO Co-ordinator
ECMO Specialist
Nurse
Theatre Team (for VA or cut-down cannulation site)

Equipment:
Theatre Tray / Diathermy (if VA)
Yellow Perfusion Bin
Dressings (for Cannulae sites)
Dressing Pack (for each site)
2 x Sterile Pots (Cannula Tips)
Clamps
2 x Sutures
Stitch Cutter
Betadine Solution

ECMO Specialist Action:

Action:	**Rationale:**
Gather all supplies • If decannulating from VV ECMO, notify appropriate staff • If decannulating from VA ECMO or cut down site, the Theatre Team is also required	To ensure an efficient procedure
Ensure venous access to the patient is secure & patent and the necessary drugs are transferred to the patient & running as per prescription	To ensure satisfactory patient status & safety
Ensure emergency drugs are drawn up and at hand for immediate use	To prevent complications or patient deterioration
Ensure ventilation is correct and re-intubation equipment is ready at hand for immediate use	To ensure patient safety

The Heart Link / ECMO Programme

Assist Surgeon with the procedure, as required	For a quick, efficient & safe procedure
Ensure cannulae tips are sent for culture	For research & awareness of sepsis
Monitor patient's status throughout the procedure	For patient safety
Dispose of the circuit, as per the ECMO equipment clean-up protocol	To maintain a clean & safe environment
Ensure all documentation is completed	For future records
Any concerns post-decannulation, contact the ECMO Fellow	To gain advice / further instructions and to make them aware of the patient's status
Seek medical advice regarding the necessity for administration of antibiotics	To reduce the risk of decannulation bactraemia

The Heart Link / ECMO Programme

Title: **Equipment Clean-up Procedure**

Description: To maintain the ECMO circuit components, day to day running of the circuit and decannulation & disposal of equipment

Personnel: ECMO Specialist

Equipment:
- Soap & Water
- Infusion Devices
- Bladder Box
- Emergency Cart
- ECMO Cart
- Stockert Roller Pump
- Actylyte Machine

ECMO Specialist Action:

Action:	**Rationale:**
Ensure the ECMO cart is cleaned on a daily basis with water / detergent (or as often as required)	To maintain a clean & safe environment
Ensure all components are in good working order – inform the ECMO Co-ordinator / Perfusion Department of any defects	To ensure the circuit is functioning properly
In the event of decannulation, all disposable components should be put into the yellow Perfusion Bin (from the ECMO Store Room) - place lid on the yellow bin & ensure it is securely sealed (dated / timed / location noted & signed)	To ensure safe disposal of the circuit
Clean all equipment & store in the ECMO Store Room	To ensure safe disposal of the circuit
Dispose of the Emergency Cart items to the allocated area	

Feedback

The HTA programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

NETSCC, Health Technology Assessment
Alpha House
University of Southampton Science Park
Southampton SO16 7NS, UK
Email: hta@hta.ac.uk
www.hta.ac.uk

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