Randomised Evaluation of COVID-19 Therapy (RECOVERY)

Data Monitoring Committee Charter

Version 1.1

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Version History

Version	Date	Summary
1.0	15-Apr-2020	Approved by DMC
1.1	21-Dec-2021	Updated membership

1 Study Details

Title:	Randomised Evaluation of COVID-19 Therapy (RECOVERY)
EUDRACT number:	2020-001113-21
Sponsor:	University of Oxford
Funder:	UK Research & Innovation / National Institute for Health Research
Principal Investigators	Prof Peter Horby & Prof Martin Landray (University of Oxford)

2 Background

RECOVERY is a randomised controlled trial among hospitalised adults hospitalised investigating the effects of different therapies for COVID-19 disease. To facilitate collaboration, even in hospitals that suddenly become overloaded, patient enrolment, follow-up, and all other trial procedures are greatly streamlined.

It is anticipated that many thousands of individuals will be randomly allocated between several treatment arms, each to be given in addition to the usual standard of care in the participating hospital. Initially, these treatment arms will be: No additional treatment *vs* Lopinavir-Ritonavir *vs* low-dose corticosteroids (dexamethasone) *vs* Hydroxychloroquine. (An additional arm of nebulised interferon has provisional approval but is not active at present.) For patients for whom not all the trial arms are appropriate or at locations where not all are available, randomisation will be between fewer arms. New trial arms may be added as evidence emerges that other candidate therapeutics should be evaluated. The main outcomes are in-hospital death, discharge, use of ventilation and use of renal dialysis or haemofiltration.

This document describes the roles and responsibilities of the independent Data Monitoring Committee (DMC) and provides guidelines for their decision-making.

3 Roles and Responsibilities

The independent DMC will act in an advisory capacity to the Steering Committee. Responsibilities of the DMC are:

(i) to provide an independent overview of the safety of trial participants; and
(ii) to make recommendations about continuation, termination or other modifications to the trial protocol (in particular for individual arms) based on their unblinded review of the study clinical outcome data.

The DMC will function independently of all other individuals and bodies associated with the RECOVERY trial, including the Investigators, the Steering Committee, and the Funder.

4 Appointment and Membership

4.1 DMC Members

On the invitation of the Steering Committee Chair and the Principal Investigators, the following have agreed to serve as members of the DMC:

Name	Role	Location	Expertise
Peter Sandercock	Chair	Edinburgh, UK	Clinical trials in stroke medicine
Janet Darbyshire	Member	London, UK	Clinical trials in infectious disease
Robert Fowler	Member	Toronto, Canada	Clinical trials in critical care
David Lalloo	Member	Liverpool, UK	Clinical trials in infectious disease
David DeMets	Member	Wisconsin, USA	Clinical trial statistician
Mohammed Munavvar	Member	Preston, UK	Respiratory medicine
Adilia Warris	Member	Exeter, UK	Paediatrics
Janet Wittes	Member	Washington DC, USA	Clinical trial statistician

Prof Jonathan Emberson and Dr Natalie Staplin (Nuffield Department of Population Health, University of Oxford) are the statisticians to the DMC. They will be responsible for providing the unblinded report to the DMC and for drafting the minutes of its meetings.

4.2 Ad Hoc DMC Advisors

If required by the DMC Chair, after discussion with other members of the DMC, experts in a particular field (e.g. ventilation, infectious disease) may be asked to provide additional advice in confidence on specific aspects of the unblinded data. Not only would the content of such discussions with DMC Advisors be confidential, but every effort should be made to ensure that the fact that their advice has been sought also remains confidential.

4.3 Modifications to DMC Membership

Further DMC Members may be appointed if members resign or are unable to attend for a prolonged period (e.g. because of illness), or at the request of the DMC Chair. All such appointments must be agreed by the Principal Investigators.

4.4 Conflicts of Interest

The DMC Members and Advisors must not otherwise be involved in the conduct of the RECOVERY trial and must have no significant financial or other conflicts of interest with the Sponsor. In particular, no DMC Member or Advisor should have a financial investment in the manufacturers of any of the study treatments that would result in questions regarding his/her independence.

All DMC Members and Advisors should disclose any conflict of interest to the DMC Chair at the start of each meeting thereafter.

5 Review of emerging information

5.1 Frequency of reviews

During the study, interim analyses of all study data will be supplied in strict confidence to the independent DMC. The DMC will request such analyses at a frequency relevant to the emerging data from this and other studies (typically every 2-4 weeks). Additional meetings of the DMC may be called at any time by the Chair or at the request of the Principal Investigators.

5.2 Guidelines for recommending changes to the protocol

At each review, the DMC will independently evaluate the study data and any other information considered relevant.

The DMC will determine if, in their view, the randomised comparisons in the study have provided evidence on mortality that is strong enough (with a range of uncertainty around the results that is narrow enough) to affect national and global treatment strategies.

In such a circumstance, the DMC will inform the Trial Steering Committee who will make the results available to the public and amend the trial arms accordingly.

Unless this happens, the Steering Committee, study staff, investigators, study participants, funders and other partners will remain blind to the interim results on study outcomes until 28 days after the last patient has been randomised for a particular intervention arm (at which point analyses may be conducted comparing that arm with the no additional treatment arm).

5.3 Ad Hoc Review of Suspected Serious Adverse Reactions

Individual unblinded reports of each Suspected Serious Adverse Reaction (SSAR) will be provided to the DMC Chair by Central Coordinating Office clinicians. These may be provided at the time of the next meeting, or sooner if deemed clinically necessary.

5.4 Review of Information from External Sources

During the RECOVERY trial, there may be new information pertaining to the safety and efficacy of the study treatments, including results from other trials of similar or related treatments. The Principal Investigators will review any such information and make a written assessment for consideration by the DMC of whether, in its view: (i) any changes should be made to the trial protocol; and/or (ii) further information should be provided to investigators.

It may be desirable during the RECOVERY trial to combine or compare its results with those of other similar ongoing trials. If the DMC Chair wishes the interim data from RECOVERY to be shared with another trial they will first discuss this with the Steering Committee chair and Principal Investigators. Any sharing of data will be done in a way which minimises any risk to the integrity of the RECOVERY trial.

5.5 Decision making

In general, DMC decisions should be made by consensus, but where this is not possible, decisions will require a simple majority of the voting members of the DMC present at the meeting. For the avoidance of doubt, the DMC Statisticians and any ad hoc advisors are non-voting.

6 Publications

The Steering Committee will be responsible for drafting the main reports from the study and for review of any other reports. DMC Members will be given the opportunity to provide comments on the main results manuscript prior to its submission for publication.

7 Indemnity

The University of Oxford will indemnify the DMC members against any claims or legal actions for performing the role outlined in the DMC Charter. The details of the indemnity will be outlined in detail in the agreements between the University and the DMC Member (or their institution).

8 Conduct of meetings

8.1 Agenda

Session	Present	Content
Open*	DMC members DMC statistician Principal Investigators Study statisticians	Principal Investigators to report on: • Data quality, and completeness of follow-up and adjudication • Any relevant new external evidence (especially results from other relevant ongoing trials) • Any proposals for changes in the study protocol
Closed	DMC members DMC statisticians	• DMC Chair to review conflict of interest statements from all DMC members • DMC statistician to report on unblinded data • DMC to formulate recommendations
Open*	DMC members DMC statistician Principal Investigators Study statisticians	• Principal Investigators to clarify any issues raised • Discussion of any action items • Set date of next meeting

* No unblinded information is to be presented or discussed during the Open sessions.

8.2 Minutes and Archiving

Unless otherwise determined by the DMC Chair, minutes for the Open and Closed sessions will be taken by the DMC Statistician. The DMC Chair will be responsible for the accuracy of the minutes, and for their secure storage until the end of the trial.

Meeting documents (including closed session minutes) will only be distributed by secure means (e.g. encrypted and password-protected electronic files). These will remain confidential until the end of the trial, at which time they will be archived by the Sponsor and may be made available for public scrutiny (e.g. by regulatory authorities). Any hard copy meeting documents or closed session minutes must be disposed of securely after each meeting.

8.3 Communication of DMC Meeting outcome

Within 1 week after each meeting, the DMC Chair will provide the Chief Investigator with a letter stating the general outcome of the meeting and any recommendations. For example, this letter may simply contain the statement that the trial should continue as planned and give the planned date for the next DMC meeting. Unless indicated otherwise by the DMC Chair, this letter will not be considered confidential.

9 APPENDIX: Key contact details [CONFIDENTIAL]

9.1 Data Monitoring Committee

Role	Name	Contact details
Chair	Peter Sandercock	
Members	Janet Darbyshire	
	Robert Fowler	
	David Lalloo	
	David DeMets	
	Mohammed Munavvar	
	Adilia Warris	
	Janet Wittes	
Unblinded statisticians	Jonathan Emberson	
	Natalie Staplin	

9.2 Steering Committee

Role	Name	Address
Principal Investigators (blinded)	Peter Horby	
	Martin Landray	
Study Statisticians (blinded)	Enti Spata	

RECOVERY Central Coordinating Office
Nuffield Department of Population Health (NDPH)
Richard Doll Building
University of Oxford
Old Road Campus
Roosevelt Drive
Oxford OX3 7LF
United Kingdom
recoverytrial@ndph.ox.ac.uk

10Signature log

I confirm that I have read and approved this Charter, and that I have no conflicts of interest (as described in Section 4.4 above). Only the Chair signature is required for minor changes to the DMC charter (e.g. updated contact details)

Name	Signature	Date
Peter Sandercock		
Janet Darbyshire		
Robert Fowler		
David Lalloo		
David DeMets		
Mohammed Munavvar		
Adilia Warris		
Janet Wittes		