Protocolised non-invasive compared with invasive weaning from mechanical ventilation for adults in intensive care: the Breathe RCT

Gavin D Perkins,^{1,2*} Dipesh Mistry,¹ Ranjit Lall,¹ Fang Gao-Smith,² Catherine Snelson,³ Nicholas Hart,^{4,5} Luigi Camporota,⁵ James Varley,⁶ Coralie Carle,⁷ Elankumaran Paramasivam,⁸ Beverly Hoddell,¹ Adam de Paeztron,¹ Sukhdeep Dosanjh,¹ Julia Sampson,^{1,2} Laura Blair,¹ Keith Couper,^{1,2} Daniel McAuley,⁹ J Duncan Young,¹⁰ Tim Walsh,¹¹ Bronagh Blackwood,⁹ Louise Rose,¹² Sarah E Lamb,¹ Melina Dritsaki,¹ Mandy Maredza,¹ Iftekhar Khan,^{1,13} Stavros Petrou¹ and Simon Gates¹ on behalf of Breathe collaborators

- ¹Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, Coventry, UK
- ²Critical Care Unit, Heartlands Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
- ³Department of Critical Care, Queen Elizabeth Hospital, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK
- ⁴Division of Asthma, Allergy and Lung Biology, King's College London, London, UK ⁵Guy's and St Thomas' Foundation Trust, King's College London, London, UK
- ⁶Department of Critical Care, Addenbrooke's Hospital, Cambridge University Hospitals, Cambridge, UK
- ⁷Department of Critical Care, Peterborough City Hospital, Peterborough, UK ⁸Department of Critical Care, Leeds Teaching Hospitals, Leeds, UK
- ⁹School of Medicine, Dentistry and Biomedical Sciences, Centre for Experimental Medicine Institute for Health Sciences, Queen's University Belfast, Belfast, UK
- ¹⁰Nuffield Department of Clinical Neurosciences, Medical Sciences Division, University of Oxford, Oxford, UK
- ¹¹Anaesthesia, Critical Care and Pain Medicine, Division of Health Sciences, The University of Edinburgh, Edinburgh, UK
- ¹²Faculty of Nursing, University of Toronto, Toronto, ON, Canada
- ¹³Population and Patient Health, King's College London, London, UK

*Corresponding author G.D.Perkins@warwick.ac.uk

Declared competing interests of authors: Gavin D Perkins reports grants and non-financial support from the Intensive Care Foundation during the conduct of the study. Daniel McAuley reports personal fees from consultancy for GlaxoSmithKline (London, UK), SOBI (Swedish Orphan Biovitum; Stockholm, Sweden), Peptinnovate Ltd (Stevenage, UK), Boehringer Ingelheim (Ingelheim am Rhein, Germany) and Bayer AG (Leverkusen, Germany). Outside the submitted work, his institution has received funds from grants from the UK National Institute for Health Research (NIHR), the Wellcome Trust and others, and from GlaxoSmithKline for Daniel McAuley undertaking bronchoscopy as part of a clinical trial. In addition, Daniel McAuley is one of four named inventors on a patent US8962032 covering the use of sialic acid-bearing nanoparticles as anti-inflammatory agents issued to his institution, Queen's University Belfast (www.google. com/patents/US8962032). Daniel McAuley is a member of the Health Technology Assessment (HTA) General Board. James Varley reports non-financial support from La Jolla Pharmaceutical Company (San Diego, CA, USA) and personal fees from Emas Pharma (Hitchin, UK) outside the submitted work. Nicholas Hart reports grants from Guy's and St Thomas' Charity during the conduct of the study, grants from Philips Respironics (Murraysville, PA, USA), non-financial support from Philips Respironics RT Meeting (Myotrace), personal fees from Fisher & Paykel Healthcare (Auckland, New Zealand), grants from ResMed (San Diego, CA, USA), grants from B & D Electromedical (Stratford-upon-Avon, UK), grants from Fisher & Paykel Healthcare. In addition, Nicholas Hart has a patent, Myotrace, pending and he is on the Pulmonary Research Advisory Board for Philips. Nicholas Hart's Lane Fox Clinical Respiratory Physiology Research Group has received unrestricted grants (managed by Guy's and St Thomas' Foundation Trust) from Philips Respironics, Philips, ResMed, Fisher & Paykel Healthcare, and B & D Electromedical. Philips Respironics and Philips Research are contributing to the development of the Myotrace technology.

Published September 2019 DOI: 10.3310/hta23480

Plain English summary

The Breathe RCT

Health Technology Assessment 2019; Vol. 23: No. 48 DOI: 10.3310/hta23480

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Plain English summary

Patients who become very unwell may require help from a breathing machine. This requires the patient to be given drugs to put them to sleep (sedation) and have a tube placed through their mouth directly into the windpipe (tube ventilation). This can be life-saving, but may cause harm if used for long periods of time. Non-invasive ventilation (mask ventilation) provides breathing support through a mask that covers the face. Mask ventilation has several advantages over tube ventilation, such as less need for sedation, and it enables the patient to cough and communicate. In previous studies, switching patients from tube to mask ventilation when they start to get better seemed to improve survival rates and reduce complications. The Breathe trial tested if using a protocol to remove tube ventilation and replace it with mask ventilation is better than continuing with tube ventilation until the patient no longer needs breathing machine support.

The trial recruited 364 patients. Half of these patients were randomly selected to have the tube removed and replaced with mask ventilation and half were randomly selected to continue with tube ventilation until they no longer needed breathing machine support. The mask group spent 3 fewer days receiving tube ventilation, although the overall time needing breathing machine help (mask and tube) did not change. Fewer patients in the mask group needed antibiotics for chest infections. After removing the tube, twice as many patients needed the tube again in the mask group as in the tube group. There were no differences between the groups in the number of adverse (harm) events or the number of patients who survived to leave hospital. Mask ventilation was no more expensive than tube ventilation.

In conclusion, mask ventilation may be an effective alternative to continued tube ventilation when patients start to get better in intensive care.

© Queen's Printer and Controller of HMSO 2019. This work was produced by Perkins et al. under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.819

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the Health Technology Assessment journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: http://www.nets.nihr.ac.uk/programmes/hta

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 10/134/06. The contractual start date was in January 2013. The draft report began editorial review in September 2017 and was accepted for publication in June 2018. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care.

© Queen's Printer and Controller of HMSO 2019. This work was produced by Perkins *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health and Social Care. This issue may be freely reproduced for the purposes of private research and study and extracts (or indeed, the full report) may be included in professional journals provided that suitable acknowledgement is made and the reproduction is not associated with any form of advertising. Applications for commercial reproduction should be addressed to: NIHR Journals Library, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, Alpha House, University of Southampton Science Park, Southampton SO16 7NS, UK.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).

NIHR Journals Library Editor-in-Chief

Professor Ken Stein Professor of Public Health, University of Exeter Medical School, UK

NIHR Journals Library Editors

Professor John Powell Chair of HTA and EME Editorial Board and Editor-in-Chief of HTA and EME journals. Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), UK, and Honorary Professor, University of Manchester, and Senior Clinical Researcher and Associate Professor, Nuffield Department of Primary Care Health Sciences, University of Oxford, UK

Professor Andrée Le May Chair of NIHR Journals Library Editorial Group (HS&DR, PGfAR, PHR journals) and Editor-in-Chief of HS&DR, PGfAR, PHR journals

Professor Matthias Beck Professor of Management, Cork University Business School, Department of Management and Marketing, University College Cork, Ireland

Dr Tessa Crilly Director, Crystal Blue Consulting Ltd, UK

Dr Eugenia Cronin Senior Scientific Advisor, Wessex Institute, UK

Dr Peter Davidson Consultant Advisor, Wessex Institute, University of Southampton, UK

Ms Tara Lamont Director, NIHR Dissemination Centre, UK

Dr Catriona McDaid Senior Research Fellow, York Trials Unit, Department of Health Sciences, University of York, UK

Professor William McGuire Professor of Child Health, Hull York Medical School, University of York, UK

Professor Geoffrey Meads Professor of Wellbeing Research, University of Winchester, UK

Professor John Norrie Chair in Medical Statistics, University of Edinburgh, UK

Professor James Raftery Professor of Health Technology Assessment, Wessex Institute, Faculty of Medicine, University of Southampton, UK

Dr Rob Riemsma Reviews Manager, Kleijnen Systematic Reviews Ltd, UK

Professor Helen Roberts Professor of Child Health Research, UCL Great Ormond Street Institute of Child Health, UK

Professor Jonathan Ross Professor of Sexual Health and HIV, University Hospital Birmingham, UK

Professor Helen Snooks Professor of Health Services Research, Institute of Life Science, College of Medicine, Swansea University, UK

Professor Ken Stein Professor of Public Health, University of Exeter Medical School, UK

Professor Jim Thornton Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

Professor Martin Underwood Warwick Clinical Trials Unit, Warwick Medical School, University of Warwick, UK

Please visit the website for a list of editors: www.journalslibrary.nihr.ac.uk/about/editors

Editorial contact: journals.library@nihr.ac.uk