Blinded randomised controlled trial of low-dose Adjuvant Steroids in Adults admitted to hospital with Pandemic influenza (ASAP): a trial 'in hibernation', ready for rapid activation

Wei Shen Lim,[1*] Clare Brittain,[2] Lelia Duley,[2] Sheila Edwards,[3] Stephen Gordon,[4] Alan Montgomery,[2] Jonathan Nguyen-Van-Tam,[5] Robert Read,[6] Diane Whitham,[2] David Whynes,[7] Mark Woodhead[8] and Dan Wootton[9]

[1]Respiratory Medicine, Nottingham University Hospitals NHS Trust, Nottingham, UK
[2]Nottingham Clinical Trials Unit, University of Nottingham, Nottingham, UK
[3]British Thoracic Society, London, UK
[4]School of Tropical Medicine, Liverpool School of Tropical Medicine, Liverpool, UK
[5]Division of Epidemiology and Public Health, University of Nottingham, Nottingham, UK
[6]Faculty of Medicine, University of Southampton, Southampton, UK
[7]School of Economics, University of Nottingham, Nottingham, UK
[8]Respiratory Medicine, Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK
[9]Institute of Infection and Global Health, University of Liverpool, Liverpool, UK

*Corresponding author

Declared competing interests of authors: WSL reports an unrestricted, independent, investigator-initiated research grant from Pfizer, outside the field of influenza. JSN-V-T reports grants from GlaxoSmithKline, grants from F Hoffmann–La Roche, and non-financial support from European Scientific Working Group of Influenza, outside the submitted work. In addition, JN-V-T was employed by SmithKline Beecham (now a part of GlaxoSmithKline – manufacturer of zanamivir and influenza vaccines) from 2000 to 2001, and by Roche Products Ltd (manufacturer of oseltamivir) from 2001 to 2002; he has held no shares, share options or pension rights in either company since 2004. He performed paid consultancy for both companies and several other influenza vaccine manufacturers in the period 2008–10 (all of these lying outside the ICJME 36-month official window of declaration but declared here for completeness). JN-V-T's brother is a current employee of GlaxoSmithKline but does not work in an influenza-related field.

Published February 2015
DOI: 10.3310/hta19160

Plain English summary

Adjuvant Steroids in Adults admitted to hospital with Pandemic influenza

Health Technology Assessment 2015; Vol. 19: No. 16
DOI: 10.3310/hta19160

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

Plain English summary

The aims of this study are to (1) find out whether a commonly used steroid (a medicine that reduces inflammation) called dexamethasone, given in addition to the normal treatment for flu, will benefit patients admitted to hospital with flu during a pandemic and (2) set up a trial in advance of a pandemic, which can be put into 'hibernation' for rapid activation when required.

The trial will be conducted at approximately 40 hospitals in the UK. Adults admitted with flu in a pandemic will be asked to take part. Participants will be randomly given either a 5-day course of dexamethasone or a matching placebo (dummy medicine without any active ingredients). Information recorded routinely in patients' medical notes will be used to determine whether or not treatment with dexamethasone reduces the number of patients who die or are admitted to intensive care within 30 days of hospital admission.

The challenges encountered during set-up included:

(a) planning for a period when health-care resources will be exceptionally stretched
(b) ensuring geographical spread of participating hospitals
(c) addressing future training needs of investigators
(d) resilience planning of trial management.

Patients and the public were found to prefer arrangements for giving their consent which current regulations do not permit. Whether or not this will create difficulties in future remains to be determined.

This study demonstrates that advance set-up of a trial with full regulatory approvals in place, is possible; it serves as a model for the development of other 'off-the-shelf' trials in public health emergencies.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 5.116

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index and is assessed for inclusion in the Database of Abstracts of Reviews of Effects.

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

Editorial contact: nihredit@southampton.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 11/46/14. The contractual start date was in December 2012. The report detailing the set up phase and initial outcomes began editorial review in November 2014 and was accepted for publication in January 2015. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and production house have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report. Should the study progress further, the full report will be published in the HTA journal.

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. 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.

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