Methenamine hippurate compared with antibiotic prophylaxis to prevent recurrent urinary tract infections in women: the ALTAR non-inferiority RCT

Chris Harding,[1,2*] Thomas Chadwick,[3] Tara Homer,[3] Jan Lecouturier,[3] Helen Mossop,[3] Sonya Carnell,[4] Will King,[3] Alaa Abouhajar,[4] Luke Vale,[3] Gillian Watson,[4] Rebecca Forbes,[4] Stephanie Currer,[4] Robert Pickard,[5†] Ian Eardley,[6] Ian Pearce,[7] Nikesh Thiruchelvam,[8] Karen Guerrero,[9] Katherine Walton,[10] Zahid Hussain,[11] Henry Lazarowicz[12] and Ased Ali[13]

[1]Department of Urology, Freeman Hospital, Newcastle upon Tyne, UK
[2]Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK
[3]Population Health Sciences Institute, Newcastle University, Newcastle upon Tyne, UK
[4]Newcastle Clinical Trials Unit, Newcastle University, Newcastle upon Tyne, UK
[5]Institute of Cellular Medicine, The Medical School, Newcastle upon Tyne, UK
[6]Leeds Teaching Hospitals NHS Trust, Leeds, UK
[7]Manchester University NHS Foundation Trust, Manchester, UK
[8]Addenbrooke's Hospital, Cambridge, UK
[9]Queen Elizabeth University Hospital, Glasgow, UK
[10]Department of Microbiology, Freeman Hospital, Newcastle upon Tyne, UK
[11]The Royal Oldham Hospital, Oldham, UK
[12]Liverpool University Hospitals NHS Foundation Trust, formerly The Royal Liverpool University Hospital, Liverpool, UK
[13]Urology Department, Pinderfields Hospital, Wakefield, UK

*Corresponding author C.Harding@nhs.net
†In memoriam

Declared competing interests of authors: Chris Harding reports personal fees from Astellas Pharma (Tokyo, Japan), Medtronic plc (Dublin, Ireland), Allergan Ltd (Dublin, Ireland), GlaxoSmithKline plc (Brentford, UK), Teleflex Medical Inc. (Temecula, CA, USA) and grants from Medtronic plc, the National Institute for Health and Care Research (NIHR) Health Technology Assessment (HTA) programme (HTA 15/40/05) and The Urology Foundation (London, UK) outside the submitted work. Karen Guerrero reports grants from the NIHR HTA programme (HTA 16/82/01 and HTA 15/150/05) and the NIHR Health and Social Care Delivery Research (HSDR) programme (HSDR 14/04/02), and a Contura International Ltd (London, UK)

Departmental Education Grant to support national training courses to her department. Luke Vale reports being co-ordinating editor of *Cochrane Incontinence* (from 2016) and being a member of NIHR HTA, Clinical Evaluation and Trials Panel from 2015 to 2018. Thomas Chadwick reports grants from the NIHR HTA programme (HTA 16/154/01, HTA 15/130/94 and HTA 11/72/01) during the conduct of the study.

Published May 2022
DOI: 10.3310/QOIZ6538

Plain English summary

The ALTAR non-inferiority RCT

Health Technology Assessment 2022; Vol. 26: No. 23
DOI: 10.3310/QOIZ6538

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

Plain English summary

Women with recurrent urine infections often require preventative treatment to reduce the frequency of infection episodes. Daily low-dose antibiotic medication is a guideline-recommended treatment option for these women. There is increasing concern globally regarding antibiotic-resistant infections, which has led researchers to look at alternative treatments. This trial was conducted to find out whether or not taking an alternative treatment that is not an antibiotic [i.e. methenamine hippurate (Hiprex®; Mylan NV, Canonsburg, PA, USA)] was as effective as the standard daily low-dose antibiotics.

A total of 240 women from across the UK took part in the trial. They were divided equally into two groups; half of the women were given methenamine hippurate and the other half were given standard low-dose antibiotics. Both treatments were prescribed to be taken every day for 1 year. To make a fair comparison, people were put into the two groups at random using a computer program.

Aspects of the trial that could be improved were identified through telephone interviews with patients and recruiting staff. Feedback from these telephone interviews helped to ensure the successful conduct of the trial.

Patients were followed up for 18 months, comprising the 12 months when they were taking treatment and a 6-month follow-up phase after they had finished treatment. We found that the non-antibiotic option of methenamine hippurate was no worse than the current standard treatment of daily antibiotics in preventing urinary tract infection episodes in adult women. For both treatments, patients expressed high levels of satisfaction. One advantage of the methenamine hippurate treatment was that infecting bacteria were slightly less likely to develop resistance to antibiotics. We also evaluated health-care costs of both treatments and found that methenamine hippurate seemed worthwhile to the NHS in the short term, but there was uncertainty over longer-term costs and benefits. These results will help patients with repeated urinary tract infections to decide on treatment options, particularly if they want to avoid prolonged courses of preventative antibiotics.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.014

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, the Cochrane Library and 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

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

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.

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 13/88/21. The contractual start date was in February 2016. The draft report began editorial review in November 2020 and was accepted for publication in May 2021. 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 and Care 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, 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, the HTA programme or the Department of Health and Social Care.

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