

# A systematic review and economic evaluation of bisphosphonates for the prevention of fragility fractures

Sarah Davis,<sup>1\*</sup> Marrison Martyn-St James,<sup>1</sup>  
Jean Sanderson,<sup>1</sup> John Stevens,<sup>1</sup> Edward Goka,<sup>1</sup>  
Andrew Rawdin,<sup>1</sup> Susi Sadler,<sup>1</sup> Ruth Wong,<sup>1</sup>  
Fiona Campbell,<sup>1</sup> Matt Stevenson,<sup>1</sup> Mark Strong,<sup>1</sup>  
Peter Selby<sup>2</sup> and Neil Gittoes<sup>3</sup>

<sup>1</sup>Health Economics and Decision Science, School of Health and Related Research, University of Sheffield, Sheffield, UK

<sup>2</sup>Department of Medicine, University of Manchester, Manchester Royal Infirmary, Manchester, UK

<sup>3</sup>Centre for Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, University Hospitals Birmingham, Birmingham, UK

\*Corresponding author

**Declared competing interests of authors:** Peter Selby reports personal fees from Internis Pharma and non-financial support from AMGen, outside the submitted work. Neil Gittoes reports personal fees from the advisory board at Eli Lilly and Company, personal fees from the advisory board at AMGen, personal fees from speaker fees at AMGen, personal fees from speaker fees at GlaxoSmithKline, personal fees from the advisory board at ProStrakan, personal fees from advisory board at Shire, personal fees from the advisory board at Internis Pharma, personal fees from the advisory board at Consilient Health and personal fees from the advisory board at NPS Pharmaceuticals, outside the submitted work.

Published October 2016

DOI: 10.3310/hta20780

## Plain English summary

### Bisphosphonates for the prevention of fragility fractures

Health Technology Assessment 2016; Vol. 20: No. 78

DOI: 10.3310/hta20780

NIHR Journals Library [www.journalslibrary.nihr.ac.uk](http://www.journalslibrary.nihr.ac.uk)

# Plain English summary

## Background

Fragility fractures are fractures that result from mechanical forces that would not ordinarily result in fracture, known as low-level (or 'low-energy') trauma. Some patients are at a particularly high risk of fragility fractures.

## Aims

We aimed to determine how effective bisphosphonates [alendronic acid (Fosamax® and Fosamax® Once Weekly, Merck Sharp & Dohme Ltd), risedronic acid (Actonel® and Actonel Once a Week®, Warner Chilcott UK Ltd), ibandronic acid (Bonviva®, Roche Products Ltd) and zoledronic acid (Aclasta®, Novartis Pharmaceuticals UK Ltd)] are at preventing fractures, whether or not treatment has any risks for patients and whether or not the clinical benefits are achieved at a reasonable cost.

## Methods

We have systematically identified and examined trials that assessed the clinical effects of bisphosphonates. For each clinical outcome, we have combined data from multiple trials to estimate the clinical effectiveness of each bisphosphonate treatment.

We combined data from published sources in an economic model to estimate lifetime costs and clinical benefits for each bisphosphonate and compared these to the estimated costs and clinical outcomes for untreated patients.

## Results

All bisphosphonates reduced the risk of vertebral fractures compared with no treatment. For fractures at other sites (e.g. hip and wrist), all of the bisphosphonates reduced the average number of fractures, but for some bisphosphonates we could not exclude the possibility that this was a chance finding. No bisphosphonate was found to be superior to any other at preventing fractures.

Patients taking oral bisphosphonates may experience side effects affecting the stomach and gullet. Patients treated with zoledronic acid may experience flu-like symptoms.

Bisphosphonates taken orally provide greater value for money than those delivered through intravenous infusion. The benefits of bisphosphonate treatment may not outweigh the costs in those with the lowest risk of fracture.

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.058

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

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

Editorial contact: [nhredit@southampton.ac.uk](mailto:nhredit@southampton.ac.uk)

The full HTA archive is freely available to view online at [www.journalslibrary.nihr.ac.uk/hta](http://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](http://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 commissioned and funded by the HTA programme on behalf of NICE as project number 13/04/001. The protocol was agreed in September 2014. The assessment report began editorial review in May 2015 and was accepted for publication in October 2015. 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. 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.

© Queen's Printer and Controller of HMSO 2016. This work was produced by Davis *et al.* under the terms of a commissioning contract issued by the Secretary of State for Health. 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](http://www.journalslibrary.nihr.ac.uk)), produced by Prepress Projects Ltd, Perth, Scotland ([www.prepress-projects.co.uk](http://www.prepress-projects.co.uk)).

## **Health Technology Assessment Editor-in-Chief**

**Professor Hywel Williams** Director, HTA Programme, UK and Foundation Professor and Co-Director of the Centre of Evidence-Based Dermatology, University of Nottingham, UK

## **NIHR Journals Library Editor-in-Chief**

**Professor Tom Walley** Director, NIHR Evaluation, Trials and Studies and Director of the EME Programme, UK

## **NIHR Journals Library Editors**

**Professor Ken Stein** Chair of HTA Editorial Board and Professor of Public Health, University of Exeter Medical School, UK

**Professor Andree Le May** Chair of NIHR Journals Library Editorial Group (EME, HS&DR, PGfAR, PHR journals)

**Dr Martin Ashton-Key** Consultant in Public Health Medicine/Consultant Advisor, NETSCC, UK

**Professor Matthias Beck** Chair in Public Sector Management and Subject Leader (Management Group), Queen's University Management School, Queen's University Belfast, UK

**Professor Aileen Clarke** Professor of Public Health and Health Services Research, Warwick Medical School, University of Warwick, UK

**Dr Tessa Crilly** Director, Crystal Blue Consulting Ltd, UK

**Dr Eugenia Cronin** Senior Scientific Advisor, Wessex Institute, UK

**Ms Tara Lamont** Scientific Advisor, NETSCC, UK

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

**Professor Geoffrey Meads** Professor of Health Sciences Research, Health and Wellbeing Research and Development Group, University of Winchester, UK

**Professor John Norrie** Health Services Research Unit, University of Aberdeen, UK

**Professor John Powell** Consultant Clinical Adviser, National Institute for Health and Care Excellence (NICE), 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 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 Jim Thornton** Professor of Obstetrics and Gynaecology, Faculty of Medicine and Health Sciences, University of Nottingham, UK

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

Please visit the website for a list of members of the NIHR Journals Library Board:  
[www.journalslibrary.nihr.ac.uk/about/editors](http://www.journalslibrary.nihr.ac.uk/about/editors)

**Editorial contact:** [nihredit@southampton.ac.uk](mailto:nihredit@southampton.ac.uk)