Institution: University of Sheffield

Unit of Assessment: 2 - Public Health, Health Services and Primary Care

Title of case study: Informing guidance for treatment of women with osteoporosis

1. Summary of the impact

Research at the University of Sheffield to evaluate the cost-effectiveness of different treatments for women with osteoporosis was used by the National Institute of Health and Care Excellence (NICE) to develop their guidance on the condition. The evaluation model was the first to combine cost-effectiveness of both treatment and screening and to include more detailed categorisation of patients. The model was used by NICE in their 2005, 2008 and 2011 guidance, which is mandatory for the NHS in England and Wales, and, therefore, since 2008 has influenced the treatment of over two million women with osteoporosis.

2. Underpinning research

The School of Health and Related Research (ScHARR) at the University of Sheffield was contracted by NICE in 2003 to develop a model which could assess the cost-effectiveness of available treatment options for post-menopausal women with osteoporosis.

Between 2003 and 2004, a systematic review was carried out of all the evidence on the then available treatments – alendronate, etidronate, risedronate, raloxifene and teriparatide – to assess effectiveness in terms of reduction in fractures and risk of side effects. (R1)

Professor Stevenson developed a new model, which was the first to combine screening and treatment within one algorithm and provided a much more granular categorisation of the population than had been attempted before, incorporating: eight separate age bands (range 50-85 years); 13 classifications of a measure of bone fragility, (T-Score- ranging from 0 to -5 standard SD) and four classifications of number of risk factors (range 0-3).

The aim was to develop a model which would not only identify which risk factors made which treatments cost-effective, but to determine the cost-effectiveness of screening for those risk factors. In order to create a model which was able to deal with the complexity of so many different factors, Professor Stevenson applied a Gaussian process technique which had not been used previously in health economics. (R2, R3)

Prior to this research, there were few treatment algorithms and few screening algorithms for people suspected of being osteoporotic. Where algorithms did exist, they were simplistic, broad in nature and none had been formulated explicitly within the context of a cost-effectiveness framework.

For each combination of age, bone fragility measurements (T-Score) and number of risk factors, Professor Stevenson's mathematical model was able to assess the likelihood of hip, vertebral, wrist, and proximal humerus fractures, nursing home admission and death. These data were combined with cost and utility values derived from literature reviews to determine the costs and benefits of treatment. From this, the model could estimate the cost per quality adjusted life year in each of the age, T-Score and risk factor combinations.

For each age and number of risk factor combination, the additional expected costs of screening using a bone mineral density scan were included to estimate if a combined policy of screening and treatment was cost-effective. This step is required as it may be cost-effective to treat a woman in isolation, but the costs of identifying the individual within a group of seemingly homogeneous

women may be prohibitive.

Between 2006 and 2007, Professor Stevenson updated his model to take into account a new treatment, strontium ranelate whilst also updating, as appropriate, the data within the model. (R4)

All of the research to develop the model was undertaken by the University of Sheffield. The team are listed below, with the dates they joined and left Sheffield, where applicable:

Professor Matt Stevenson, 1996– current; Professor John Brazier, 1989- current; Professor John Kanis, 1979 – current (emeritus); Dr Myfanwy Lloyd Jones 1996 - 2012; Sarah Davis, 2004-2006 / 2011 - current; Dr Jeremy Oakley, 1999-current; and Enrico De Negris, 2002-2006.

3. References to the research

Authors employed by the University of Sheffield during the period of the research are highlighted in bold.

R1. **Stevenson M, Lloyd Jones M, De Nigris E, Brewer N, Davis S and Oakley J**. A systematic review and economic evaluation of alendronate, etidronate, risedronate, raloxifene and teriparatide for the prevention and treatment of postmenopausal osteoporosis. Health Technol Assess 2005a; 9 (22) pp1-160

R2. **Stevenson MD**, **Oakley J, Chilcott JB**. Gaussian process modelling in conjunction with individual patient simulation modelling. A case study describing the calculation of cost-effectiveness ratios for the treatment of osteoporosis. Med Decis Making 24 (2004) 89-100 doi: 10.1177/0272989X03261561

R3. **Stevenson MD**, **Brazier JE, Calvert NW, Lloyd-Jones M, Oakley J, Kanis JA**. Description of an individual patient methodology for calculating the cost-effectiveness of treatments for osteoporosis in women. Journal of Operational Research Society. 2005b; 56 (2): 214-221

R4. **Stevenson M**, **Davis S, Lloyd Jones M, Beverley C.** The clinical and cost-effectiveness of strontium ranelate for the prevention of osteoporotic fragility fractures in post-menopausal women. Health Technol Assess 2007; 11 (4) pp1-134

4. Details of the impact

The research has had an impact on health and welfare, by informing NICE guidance on treatment to prevent fractures due to osteoporosis in post-menopausal women and thereby influencing treatment for this patient group.

Process to impact:

The model, developed by the University of Sheffield researchers, was used to draw up the NICE guidance TA87, released in 2005. Prior to this, prescribing patterns and the use of bone mineral density tests were not standardised across the country and had not been subjected to cost-effectiveness analyses. In 2008, NICE released new guidance, TA160 and TA161 [S1 and S2], which used the same cost-effectiveness model developed in Sheffield, updated by the Sheffield team to include the new treatment, strontium ranelate.

In 2009, the guidance was taken to judicial review following complaints by a number of stakeholders, and NICE was asked to review the model on which their decisions had been based. NICE concluded that the model was sound and so it remains the basis for their current guidance, updated in 2011.

Impact on health and welfare:

The research has had impact on health and welfare by informing the decisions made by a regulatory authority, namely NICE.

The NICE guidance (TA160 and TA161) says: 'The Committee concluded that the Assessment Group [named as ScHARR in para 1.4.1 p14] had provided an executable economic model … The Committee confirmed that the model provided a suitable framework to allow it to make recommendations on the cost-effective use of treatment for women at risk of fracture… Therefore the Committee concluded that the recommendations based on the Assessment Group's model were appropriate, and that the recommendations should remain unchanged.' (TA160, para 4.3.65 pp78-9; TA161, para 4.3.66 pp83-4) [S1, S2].

NICE estimate that there are more than 2 million women with osteoporosis in England and Wales (TA161 amended, p9). As NICE guidance is mandatory, the research – through TA160 and TA161 – has influenced the treatment of all post-menopausal women with osteoporosis in England and Wales since the initial guidance was released in October 2008.

NICE guidance identifies which women should be offered a bone mineral density scan, and based on the result of the scan, which women should be offered treatment with alendronate. Where women are unable to take alendronate, the guidance specifies whether alternative treatments can be prescribed based on age, clinical risk factor and bone mineral density characteristics (T-Score). Without the algorithm developed through the Sheffield research, it would not be possible for NICE to issue guidance to this level of granularity in terms of age, T-Score and clinical risk factor combinations.

5. Sources to corroborate the impact

S1. Alendronate, etidronate, risedronate, raloxifene and strontium ranelate for the primary prevention of osteoporotic fragility fractures in postmenopausal women (amended). NICE technology appraisal guidance Issued: October 2008 (last modified: January 2011). http://guidance.nice.org.uk/TA160 (primary prevention).

S2. Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (amended). NICE technology appraisal guidance Issued: October 2008 (last modified: January 2011). http://guidance.nice.org.uk/TA161 (secondary prevention).

Relevant sections referencing the ScHARR reports are given in the text in the section above.