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Long-term cost-effectiveness of screening for fracture risk in a UK primary care setting: the SCOOP study

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Abstract

Summary Community-based screening and treatment of women age 70–85 years at high fracture risk reduced fractures; moreover, the screening programme of fracture risk in older women had an effect that was cost-saving. The results support a case for a screening programme of fracture risk in older women in the UK.

Purpose The SCOOP (screening for prevention of fractures in older women) randomised controlled trial investigated whether community-based screening could reduce fractures in women age 70–85 years. The objective of this study was to estimate the long-term cost-effectiveness of screening for fracture risk in a UK primary care setting compared with usual management, based on the SCOOP study.

Methods A health economic Markov model was used to predict the life-time consequences in terms of costs and quality of life of the screening programme compared with the control arm. The model was populated with costs related to drugs, administration and screening intervention derived from the SCOOP study. Fracture risk reduction in the screening arm compared with the usual management arm was derived from SCOOP. Modelled fracture risk corresponded to the risk observed in SCOOP.

Results Screening saved 9 hip fractures and 20 non-hip fractures over the remaining lifetime (mean 14 years) of 1,000 patients compared with usual management. In total, the screening arm saved costs (£286) and gained 0.015 QALYs/patient in comparison with usual management arm.

Conclusions This analysis suggests that a screening programme of fracture risk in older women in the UK would gain quality of life and life years, and reduce fracture costs to more than offset the cost of running the programme.

Key words Fracture risk assessment · Cost-effectiveness · United Kingdom · FRAX · Randomized controlled trial

Introduction

It is estimated that over 500,000 fragility fractures were sustained in the UK in 2010 [1]. Fragility fractures are associated with major societal costs and individual suffering. In 2010, the monetary burden of osteoporosis was £4,397 million in the UK, the majority of which was costs related to treating fractures. In addition, approximately 160,000 QALYs were lost in the same year due to incident and previous fractures. Although many available treatments for fracture prevention have been shown to be cost-effective in patients at high risk of fracture [2], there is a large “treatment gap”, in that a minority of individuals at high fracture risk are identified and receive appropriate treatment [3].

Historically, fracture risk has been assessed mainly by the use of bone mineral density (BMD) measurement alone. BMD has been shown, however, to have low sensitivity for fracture risk in that most fragility fractures arise in individuals without densitometric osteoporosis [4]. FRAX® is a tool freely accessible on the web (www.shef.ac.uk/FRAX), which was developed to improve the prediction of fracture risk [5]. FRAX calculates the 10-year hip and major osteoporotic fracture probabilities based on a set of clinical risk factors and is recommended, for example, by the National Institute for Health and Care Excellence (NICE) and the National Osteoporosis Guidelines Group (NOGG) for the assessment of patients in the UK [6, 7]. NOGG also uses FRAX probabilities as the basis for intervention thresholds.

Despite effective assessment tools and medications for osteoporosis, screening for fracture risk is not currently advocated in many countries, including the UK, although NICE recommends assessment of fracture risk in all women aged 65 years and older. A recent randomised controlled trial, the SCOOP study, investigated whether community-based screening could reduce fractures in women age 70 to 85 years [8]. Fracture risk was evaluated for patients randomised to the screening arm using the FRAX tool. If hip fracture probability was high, the patient was invited to undergo a dual energy X-ray absorptiometry scan (DXA) to measure BMD at the femoral neck. There was no evidence that screening reduced the incidence of all osteoporosis-related fractures (HR: 0.94, 95% CI: 0.85 to 1.03) but there was strong evidence of a reduction in the risk of hip fractures (HR: 0.72, 95% CI: 0.59 to 0.89). A cost-effectiveness analysis based on the SCOOP study, using a within-trial design limited to the time frame of the trial (5 years), provided evidence that screening was likely cost-effective and an efficient use of health care resources [9].

It is important to analyse the long-term consequences of screening for fracture risk in terms of costs and health-related outcomes to inform future decisions about such clinical strategies. The objective of this study was to estimate the long-term cost-effectiveness of screening for fracture risk in a UK primary care setting compared with usual management, based on the SCOOP study.

Methods

The SCOOP study

SCOOP ('screening for prevention of fractures in older women') was a pragmatic, unblinded, two parallel group randomised controlled trial to assess the effectiveness and cost-effectiveness of screening to prevent fractures in older women [8]. The primary endpoint was the proportion of participants experiencing at least one osteoporosis-related fracture over the 5-year follow-up. Women age 70–85 years were recruited from primary care in seven regions in England (Norwich, Southampton, Bristol, Birmingham, Manchester, York and Sheffield). Consenting participants were randomised to either a screening arm (n=6,233) or the control arm (n=6,250).

Using a baseline risk factor questionnaire, 10-year hip fracture probability with FRAX was calculated for participants randomised to the screening arm. The risk factors included in the questionnaire and used to calculate fracture probability were age, sex, height, weight, prior fragility fracture, parental history of hip fracture, current smoking, use of oral glucocorticoids, rheumatoid arthritis, other causes of secondary osteoporosis and high daily alcohol consumption (≥ 3 units/day). If the hip fracture probability was high (5.2–8.5%, depending on age), the participant was invited to undergo a DXA measurement at the femoral neck. Fracture probability was then re-calculated with the inclusion of the BMD result, and individuals with a fracture risk above the intervention threshold (hip fracture probability between 5.24% and 8.99% depending on age) were advised to make an appointment with their General Practitioner (GP) to discuss potential treatment. The GP was also informed directly of the screening result.

For the participants randomised to the control arm, a letter was sent to the GP informing them of their patient's participation in the study. No additional information was provided to these women or their GP and they received standard management. The 10-year fracture probability using FRAX was calculated for the control arm participants at the end of the study.

Characteristics were similar across groups: the mean age was 75.4 years (SD 4.2) in the screening arm, and in control arm was 75.5 years (SD 4.1); FRAX 10-year hip fracture probability in the screening arm was 8.5% (SD 7.4) and in the control arm was 8.5% (SD 7.3); the 10-year probability of a major osteoporotic fracture (distal forearm, clinical spine, proximal humerus or hip fracture) was 19.3% in the screening arm (SD 8.9) and 19.3% (SD 8.8) in the control arm.

Screening led to a relative reduction in hip fractures of 28% compared with the control arm (HR=0.72, 95% CI 0.59 to 0.89, $p=0.002$). The proportion of women who experienced an osteoporosis-related fracture was similar in the screening arm to the control arm (12.9% vs. 13.6%, HR 0.94, 95% CI 0.85 to 1.03, $p=0.178$).

Health economic model

A health economic Markov model was used to predict the life-time consequences in terms of costs and quality of life of the screening programme compared with the control arm (hereafter termed usual management). The model was adapted based on previously published models of osteoporosis interventions [10-12]. The model used a six-month cycle length and the cohort was followed from study participation until death or an age of 100 years. The model consisted of eight health states, including: wrist fracture, vertebral fracture, hip fracture, other osteoporotic fracture, post-vertebral fracture, post-hip fracture, dead and well (i.e. without fracture). "Other osteoporotic fracture" was a composite health state comprising

pelvis, rib, humerus, tibia, clavicle, scapula, sternum and other femoral fractures. Patients who sustained a hip/vertebral fracture transitioned to the post hip/vertebral fracture state in the cycle following the fracture and remained there until sustaining a new vertebral or hip/vertebral fracture or death occurred. All patients began in the “well” health state. In each cycle, an individual was at risk of sustaining a fracture or death (Figure 1).

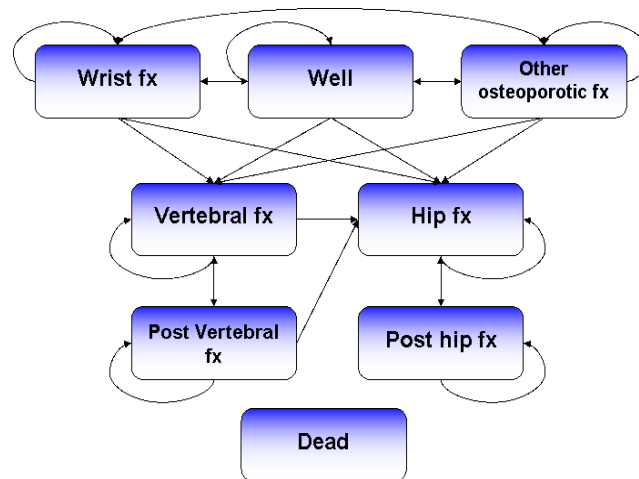


Fig.1 Model structure. Fx = fracture

Data

The model was populated with costs related to drugs, administration and screening intervention derived from the SCOOP data. Fracture risk reduction in the screening arm compared with the usual management arm was derived from SCOOP data. Modelled fracture risk corresponded to the risk observed in SCOOP.

Clinical costs in the first and subsequent years after fracture were collected from two retrospective cohort studies that estimated fracture costs in postmenopausal women in the UK [13, 14]. In the “Well” health state, quality of life based on EQ-5D-3L was assumed to be equal to the age and gender matched general UK population taken from a study by Szende et al. [15]. Wrist, hip, vertebral and other fractures were assumed to have an impact on quality of life during the first year after fracture (weights 0.82, 0.55, 0.68 and 0.86, respectively). Hip and vertebral fractures were assumed to also have an impact on quality of life in subsequent years (weights 0.82 and 0.84, respectively). Quality of life weights, in the first year after fracture and subsequent years respectively, were collected from the International Costs and Utilities Related to Osteoporotic fractures Study (ICUROS) [16]. Annual mortality in the general female population was obtained from the Office for National Statistics dataset [17]. The relative risks of death in patients who had sustained a fracture compared with the general population were derived from a study by Jönsson et al. [12]. In agreement with previous health economic studies of osteoporotic treatments it was assumed that 30% of the excess mortality after a hip, vertebral, wrist and other osteoporotic fracture was related to the fracture event [10]. The remaining excess mortality was assumed to be related to other concomitant diseases [18, 19].

Analysis

The outcome measures were life years, quality-adjusted life years (QALYs), costs and incremental cost per QALY (ICER). Costs and effects were discounted by 3.5% annually in accordance with NICE guidelines [20]. The intervention was assumed to be cost-effective if the ICER lay at or below NICE's willingness-to-pay (WTP) threshold for recommending new treatment of £20,000–30,000 per QALY gained [20].

A probabilistic sensitivity analysis (PSA) was conducted by simultaneously sampling from estimated probability distributions of treatment effect of screening vs. usual management to obtain 1,000 sets of model input estimates. For each simulation, expected costs and QALYs were calculated for the screening arm and the usual management arm, respectively, along with the difference between comparators. Acceptability curves were constructed for the pairwise comparison.

Since the SCOOP study only provided evidence of an effect of screening compared with usual management for hip fracture risk reduction, a deterministic sensitivity analysis was conducted assuming that screening had an effect only on this risk.

Other deterministic sensitivity analyses were conducted to estimate the impact on the results of changing the discount rate, modelling time horizon, and assuming that 100% of the excess mortality of fracture was related to the fracture event.

Results

Base case scenario

Over the remaining lifetime (mean 14 years) of 1,000 women, screening saved 9 hip fractures and 20 non-hip fractures compared with usual management. Fracture-related costs were £551 lower per patient in the screening arm compared with the usual management arm (Table 1). Drug and intervention costs were £265 higher in the screening arm. In total, the screening arm was cost-saving (£286) and gained 0.015 QALYs/patient in comparison with usual management arm.

Table 1 Base case cost-effectiveness results

	Usual management	Screening	Screening vs. usual management
Mean costs, per patient (£)			
Hospitalisations	3,059	2,934	-125
Nursing home	6,056	5,645	-410
Outpatient	378	363	-15
Total morbidity cost	9,493	8,942	-551
Drugs	12	43	31
Treatment management	92	326	234
Total intervention cost	104	369	265

Total cost	9,596	9,310	-286
Effects, per patient			
Life years	10.485	10.487	0.002
QALYs	7.359	7.374	0.015
Cost-effectiveness ratios			
Cost/Life year			Cost-saving
Cost/QALY			Cost-saving

Probabilistic sensitivity analysis (PSA)

The PSA showed that the probability of screening being cost-effective at a willingness-to-pay (WTP) of £20,000 was 97% and 98% at a WTP of £30,000. In 87% of the PSA simulations, screening was cost-saving, i.e. saved costs and gained QALYs, compared with usual management. Mean difference in QALYs (screening vs. usual management) was 0.015 (95% CI 0.007, 0.023). Mean difference in costs was £-281 (95% CI -579, -77).

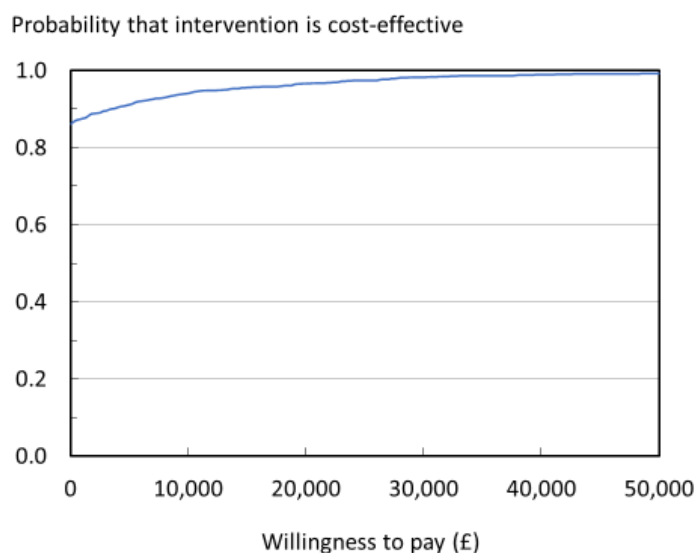


Fig. 2 Cost-effectiveness acceptability curve for pairwise comparison of screening vs. no screening.

Deterministic sensitivity analyses

When it was assumed that screening had an effect only on the risk of hip fracture, the QALY gained and cost-savings were lower compared with the base case scenario. However, the results showed that screening would still be cost-saving if the programme had an effect on hip fractures alone (Table 2).

Table 2 Results of deterministic sensitivity analysis assuming screening had an effect only on the risk of hip fracture

	Usual management	Screening	Screening vs. usual management
Total cost (£), per patient	9,596	9,355	-241
QALYs, per patient	7.359	7.369	0.011
Cost/QALY			Cost-saving

Other sensitivity analyses

The impact of changing modelling assumptions on the QALY gained of screening compared with usual management is shown in Table 3. In all scenarios, screening was cost-saving (not shown in table). The results were most sensitive to assuming a 0% discount rate on effects and costs. Results were also rather sensitive to assuming that 100% of excess mortality was attributable to fractures. Applying a 10-year time horizon had a small negative impact in this population of older women.

Table 3 Other sensitivity analyses

Scenario	QALY difference per patient, screening vs. usual management
Base case	0.015
5% discount rates	0.014
0% discount rates	0.020
10-year modelling time horizon	0.012
100% of excess mortality attributable to fractures	0.019

Discussion

Osteoporosis is a silent disease that tends to go underdiagnosed and undertreated despite the availability of effective assessment tools and medications. This study estimated the cost-effectiveness of screening for hip fracture risk with the FRAX tool compared with usual management in UK primary care setting, using a health economic Markov model to estimate the life-time consequences of screening. The population modelled and fracture risks were based on to the SCOOP study. We found that screening gained 0.015 QALYs and saved £286 per patient because of fracture risk reduction compared with usual management; the conclusions were robust across a number of sensitivity analyses. This study indicates that screening for fracture risk in elderly women is an efficient means to identify high risk patients, improve treatment uptake in these patients, and ultimately improve health outcomes.

Our study has a number of strengths and limitations. A major strength is the use of fracture risk data and costs as observed in the SCOOP pragmatic trial, permitting an accurate depiction

of the relative effect of screening based in a real-world setting. The structure of the Markov model used in this study is validated and adapted based on a model used in previously published studies [12]. A limitation of the model is that it has a hierarchical structure that causes a slight underestimation of the number of less severe fractures, as patients suffering a hip or vertebral fracture cannot subsequently sustain wrist or other fractures in following cycles (i.e. remain in post hip/vertebral state). Some other assumptions were necessary to estimate the life-time consequences of screening and usual management. The most conservative assumption was that the effect of screening was only modelled for a maximum of 5 years, - the follow-up time in the SCOOP study, and thereafter women in the screening arm were assumed to be at the same fracture risk as the usual management arm. This assumption sets a ceiling on the potential gains as it ignores the fact that many high-risk women would continue on treatment for longer than 5 years and that the offset of treatment effects is not immediate. Population-based studies show long term reductions in hip fractures risk during longer exposures to anti-resorptive medications similar to those used in SCOOP [21]. The assumption that the protective effect on fracture risk ceases on the day of medication discontinuation is very conservative and further contributes to the ceiling effect. Oral bisphosphonates, the predominant treatment prescribed for high risk patients in SCOOP, are known to at least partially reduce bone turnover and bone mineral density for several months or years following discontinuation [22, 23], with likely persisting fracture protection. These observations underpin recent suggestions that patients could undertake a break from bisphosphonate therapy without immediately losing fracture protection [24-27]. An assumption of a linear offset of the fracture protective effect over a few years has been built into previous models of oral bisphosphonate and has a significant impact on improving cost-effectiveness [28].

The cost-effectiveness analysis based on the SCOOP study by Turner et al. [9] used, in contrast to the analysis in this paper, a within-trial design limited to the time frame of the trial (5 years). Additionally, it used questionnaires (EQ-5D) to document self-reported quality of life (QoL) at typically annual intervals to derive QALYs. The results showed that the QALYs per person gained with screening was 0.0237 (95% CI: -0.0034 to 0.0508) with an incremental total health care cost of £66 (95% CI -21.7, 153) compared with usual management, providing a cost per QALY gained of £2,772. This compares with the longer-term gains of 0.015 QALYs (95% CI 0.007, 0.023) per person and a £241 (95% CI -579, -77) lower cost yielding a cost-saving result in the present analysis. The expectation, given the different study designs, would be that modelling over a longer time period (remaining lifetime) would provide larger cost-savings [29]. While we might also expect a larger average QALY gain over a longer timeframe, the within-trial analysis showed a larger apparent gain (0.0237 vs. 0.015), despite the QoL questionnaires not being administered at the time of the incident fracture events. The reason for the difference is not entirely clear. One potential explanation, besides the inherent differences in study design between modelling and within-trial analysis, could be that the within-trial study design captured an additional element of quality of life improvement resulting from screening, an improvement that hasn't been noted in screening studies in other diseases [30, 31]. Alternatively, it could be an effect related to pharmaceutical treatment or fracture prevention, but this seems unlikely given the small proportion of patients on treatment in the screening arm (approximately 14%). It remains possible that the measured

larger gain in QALYs occurred by chance, given that SCOOP was not primarily powered to detect a statistical difference in QALYs between arms, and indeed there was no evidence of such a difference as displayed in the confidence interval around the mean [9]. Disregarding the unexpected difference in QALYs gained between the two studies, it is clear that both studies used well accepted health economic methods, and both consistently indicate that a screening programme of fracture risk is a cost-effective intervention.

A small number of randomised studies have now addressed the potential benefit of population screening for fracture prevention. In the Aberdeen Prospective Osteoporosis Screening Study (APOSS), 4,800 women aged 45–54 years were screened by BMD. Osteoporosis treatment, predominantly hormone replacement therapy (HRT) was recommended to those women with BMD in the lowest quartile of the screening arm. The study showed an increase in HRT uptake in those so identified [32], and a parallel increase in uptake of other osteoporosis therapies [33]. After a follow-up of 9 years, the study reported weak evidence of a decrease in fracture rates in the screened arm, but this did not alter the UK National Screening Committee's position of not recommending screening in osteoporosis [34]. The latter decision was underpinned by the conclusion that there was no randomised controlled trial assessing the clinical and cost-effectiveness of any current approach to screening for osteoporosis. The SCOOP study has now addressed this, and recently another study of screening using the FRAX tool has been published from Denmark [35-37]. While no formal cost-effectiveness analysis has yet been published from the latter study, the FRAX approach in both studies avoids the use of bone mineral density measurements in all participants, thus reducing this contribution to screening costs. A systematic review found that screen-and-treat strategies based on FRAX and similar tools were more cost-effective compared with selecting patients based solely on age, gender and BMD [38]. This may be explained by lower screening costs due to avoided BMD measurements, but also that FRAX and similar tools enables finding patients where it is cost-effective to treat even at lower ages (e.g. 50–60 years).

Conclusion

The burden of fragility fractures in ageing populations is high and increasing. There is a substantial treatment gap so that most women at high risk of fracture are neither identified nor treated. This analysis suggests that a screening programme for fracture risk in older women in the UK could gain quality of life and life years, and reduce fracture costs so as to more than offset the cost of running the programme.

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S Clarke, R Fong, N Gittoes, I Harvey, R Holland, A Howe, H Johansson, E Lenaghan, T Marshall, T Peters, N Redmond, L Shepstone have nothing to disclose.

References

1. Svedbom, A, Hernlund, E, Ivergard, M, Compston, J, Cooper, C, Stenmark, J, McCloskey, EV, Jonsson, B, Kanis, JA, and IOF, EURPo (2013) Osteoporosis in the European Union: a compendium of country-specific reports. *Arch Osteoporos* 8: 137. doi: 10.1007/s11657-013-0137-0
2. Kanis, JA, Cooper, C, Rizzoli, R, Reginster, JY, on behalf of the Scientific Advisory Board of the European Society for, C, Economic Aspects of, O, the Committees of Scientific, A, and National Societies of the International Osteoporosis, F (2019) European guidance for the diagnosis and management of osteoporosis in postmenopausal women. *Osteoporosis International* 30(1): 3-44. doi: 10.1007/s00198-018-4704-5
3. Kanis, JA, Borgstrom, F, Compston, J, Dreinhofer, K, Nolte, E, Jonsson, L, Lems, WF, McCloskey, EV, Rizzoli, R, and Stenmark, J (2013) SCOPE: a scorecard for osteoporosis in Europe. *Arch Osteoporos* 8: 144. doi: 10.1007/s11657-013-0144-1
4. Kanis, JA, Johnell, O, Oden, A, Johansson, H, and McCloskey, E (2008) FRAX and the assessment of fracture probability in men and women from the UK. *Osteoporos Int* 19(4): 385-97. doi: 10.1007/s00198-007-0543-5
5. Kanis, JA, Oden, A, Johnell, O, Johansson, H, De Laet, C, Brown, J, Burckhardt, P, Cooper, C, Christiansen, C, Cummings, S, Eisman, JA, Fujiwara, S, Gluer, C, Goltzman, D, Hans, D, Krieg, MA, La Croix, A, McCloskey, E, Mellstrom, D, Melton, LJ, 3rd, Pols, H, Reeve, J, Sanders, K, Schott, AM, Silman, A, Torgerson, D, van Staa, T, Watts, NB, and Yoshimura, N (2007) The use of clinical risk factors enhances the performance of BMD in the prediction of hip and osteoporotic fractures in men and women. *Osteoporos Int* 18(8): 1033-46. doi: 10.1007/s00198-007-0343-y
6. National Institute for Health and Care Excellence (NICE). NICE clinical guideline 146. Osteoporosis: assessing the risk of fragility fracture. . of Medium] 2014 Last Update [cited Access 2014.
7. Compston, J, Cooper, A, Cooper, C, Gittoes, N, Gregson, C, Harvey, N, Hope, S, Kanis, JA, McCloskey, EV, Poole, KES, Reid, DM, Selby, P, Thompson, F, Thurston, A, Vine, N, and National Osteoporosis Guideline, G (2017) UK clinical guideline for the prevention and treatment of osteoporosis. *Arch Osteoporos* 12(1): 43. doi: 10.1007/s11657-017-0324-5

8. Shepstone, L, Lenaghan, E, Cooper, C, Clarke, S, Fong-Soe-Khioe, R, Fordham, R, Gittoes, N, Harvey, I, Harvey, N, Heawood, A, Holland, R, Howe, A, Kanis, J, Marshall, T, O'Neill, T, Peters, T, Redmond, N, Torgerson, D, Turner, D, McCloskey, E, and Team, SS (2018) Screening in the community to reduce fractures in older women (SCOOP): a randomised controlled trial. *Lancet* 391(10122): 741-747. doi: 10.1016/S0140-6736(17)32640-5
9. Turner, DA, Khioe, RFS, Shepstone, L, Lenaghan, E, Cooper, C, Gittoes, N, Harvey, NC, Holland, R, Howe, A, McCloskey, E, O'Neill, TW, Torgerson, D, Fordham, R, and Team, SS (2018) The Cost-Effectiveness of Screening in the Community to Reduce Osteoporotic Fractures in Older Women in the UK: Economic Evaluation of the SCOOP Study. *J Bone Miner Res* 33(5): 845-851. doi: 10.1002/jbmr.3381
10. Strom, O, Borgstrom, F, Sen, SS, Boonen, S, Haentjens, P, Johnell, O, and Kanis, JA (2007) Cost-effectiveness of alendronate in the treatment of postmenopausal women in 9 European countries--an economic evaluation based on the fracture intervention trial. *Osteoporos Int* 18(8): 1047-61. doi: 10.1007/s00198-007-0349-5
11. Borgstrom, F, Jonsson, B, Strom, O, and Kanis, JA (2006) An economic evaluation of strontium ranelate in the treatment of osteoporosis in a Swedish setting: based on the results of the SOTI and TROPOS trials. *Osteoporos Int* 17(12): 1781-93. doi: 10.1007/s00198-006-0193-z
12. Jonsson, B, Strom, O, Eisman, JA, Papaioannou, A, Siris, ES, Tosteson, A, and Kanis, JA (2011) Cost-effectiveness of Denosumab for the treatment of postmenopausal osteoporosis. *Osteoporos Int* 22(3): 967-82. doi: 10.1007/s00198-010-1424-x
13. Gutierrez, L, Roskell, N, Castellsague, J, Beard, S, Rycroft, C, Abeyasinghe, S, Shannon, P, Gitlin, M, and Robbins, S (2012) Clinical burden and incremental cost of fractures in postmenopausal women in the United Kingdom. *Bone* 51(3): 324-31. doi: 10.1016/j.bone.2012.05.020
14. Gutierrez, L, Roskell, N, Castellsague, J, Beard, S, Rycroft, C, Abeyasinghe, S, Shannon, P, Robbins, S, and Gitlin, M (2011) Study of the incremental cost and clinical burden of hip fractures in postmenopausal women in the United Kingdom. *J Med Econ* 14(1): 99-107. doi: 10.3111/13696998.2010.547967
15. Szende, A, Janssen, B, and Cabases, J, Self-Reported Population Health: An International Perspective based on EQ-5D. 2014: Springer Netherlands.
16. Kanis, JA, Johansson, H, Oden, A, Harvey, NC, Gudnason, V, Sanders, KM, Sigurdsson, G, Siggeirsdottir, K, Fitzpatrick, LA, Borgstrom, F, and McCloskey, EV (2018) Characteristics of recurrent fractures. *Osteoporos Int* 29(8): 1747-1757. doi: 10.1007/s00198-018-4502-0
17. Dataset: National life tables: Great Britain (2014-2016). Accessed 2018-11-27]; Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/nationallifetablesgreatbritainreferencetables>.
18. Parker, MJ and Anand, JK (1991) What is the true mortality of hip fractures? *Public Health* 105(6): 443-6.
19. Kanis, JA, Oden, A, Johnell, O, De Laet, C, Jonsson, B, and Oglesby, AK (2003) The components of excess mortality after hip fracture. *Bone* 32(5): 468-73.
20. National Institute for Health and Care Excellence (NICE), Guide to the methods of technology appraisal 2013: <https://www.nice.org.uk/process/pmg9/chapter/foreword>.

21. Abrahamsen, B, Eiken, P, Prieto-Alhambra, D, and Eastell, R (2016) Risk of hip, subtrochanteric, and femoral shaft fractures among mid and long term users of alendronate: nationwide cohort and nested case-control study. *BMJ* 353: i3365. doi: 10.1136/bmj.i3365
22. Black, DM, Schwartz, AV, Ensrud, KE, Cauley, JA, Levis, S, Quandt, SA, Satterfield, S, Wallace, RB, Bauer, DC, Palermo, L, Wehren, LE, Lombardi, A, Santora, AC, Cummings, SR, and Group, FR (2006) Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. *JAMA* 296(24): 2927-38. doi: 10.1001/jama.296.24.2927
23. Ensrud, KE, Barrett-Connor, EL, Schwartz, A, Santora, AC, Bauer, DC, Suryawanshi, S, Feldstein, A, Haskell, WL, Hochberg, MC, Torner, JC, Lombardi, A, Black, DM, and Fracture Intervention Trial Long-Term Extension Research, G (2004) Randomized trial of effect of alendronate continuation versus discontinuation in women with low BMD: results from the Fracture Intervention Trial long-term extension. *J Bone Miner Res* 19(8): 1259-69. doi: 10.1359/JBMR.040326
24. Adams, AL, Adams, JL, Raebel, MA, Tang, BT, Kuntz, JL, Vijayadeva, V, McGlynn, EA, and Gozansky, WS (2018) Bisphosphonate Drug Holiday and Fracture Risk: A Population-Based Cohort Study. *J Bone Miner Res* 33(7): 1252-1259. doi: 10.1002/jbmr.3420
25. Adler, RA, El-Hajj Fuleihan, G, Bauer, DC, Camacho, PM, Clarke, BL, Clines, GA, Compston, JE, Drake, MT, Edwards, BJ, Favus, MJ, Greenspan, SL, McKinney, R, Jr., Pignolo, RJ, and Sellmeyer, DE (2016) Managing Osteoporosis in Patients on Long-Term Bisphosphonate Treatment: Report of a Task Force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 31(1): 16-35. doi: 10.1002/jbmr.2708
26. McClung, M, Harris, ST, Miller, PD, Bauer, DC, Davison, KS, Dian, L, Hanley, DA, Kendler, DL, Yuen, CK, and Lewiecki, EM (2013) Bisphosphonate therapy for osteoporosis: benefits, risks, and drug holiday. *Am J Med* 126(1): 13-20. doi: 10.1016/j.amjmed.2012.06.023
27. Curtis, JR, Westfall, AO, Cheng, H, Delzell, E, and Saag, KG (2008) Risk of hip fracture after bisphosphonate discontinuation: implications for a drug holiday. *Osteoporos Int* 19(11): 1613-20. doi: 10.1007/s00198-008-0604-4
28. Jonsson, B, Kanis, J, Dawson, A, Oden, A, and Johnell, O (1999) Effect and offset of effect of treatments for hip fracture on health outcomes. *Osteoporos Int* 10(3): 193-9. doi: 10.1007/s001980050215
29. Kanis, JA, Adams, J, Borgstrom, F, Cooper, C, Jonsson, B, Preedy, D, Selby, P, and Compston, J (2008) The cost-effectiveness of alendronate in the management of osteoporosis. *Bone* 42(1): 4-15. doi: 10.1016/j.bone.2007.10.019
30. Edelman, D, Olsen, MK, Dudley, TK, Harris, AC, and Oddone, EZ (2002) Impact of diabetes screening on quality of life. *Diabetes Care* 25(6): 1022-6. doi: 10.2337/diacare.25.6.1022
31. Collins, RE, Lopez, LM, and Marteau, TM (2011) Emotional impact of screening: a systematic review and meta-analysis. *BMC Public Health* 11: 603. doi: 10.1186/1471-2458-11-603
32. Torgerson, DJ, Thomas, RE, Campbell, MK, and Reid, DM (1997) Randomized trial of osteoporosis screening. Use of hormone replacement therapy and quality-of-life results. *Arch Intern Med* 157(18): 2121-5. doi: 10.1001/archinte.157.18.2121
33. Barr, RJ, Stewart, A, Torgerson, DJ, and Reid, DM (2010) Population screening for osteoporosis risk: a randomised control trial of medication use and fracture risk. *Osteoporos Int* 21(4): 561-8. doi: 10.1007/s00198-009-1007-x

34. Peto L. and Allaby M. Screening for osteoporosis in postmenopausal women. A report for the UK National Screening Committee. of Medium] 2013 Last Update [cited Access 2013; Available from: https://legacyscreening.phe.org.uk/policydb_download.php?doc=270.
35. Hoiberg, MP, Rubin, KH, Holmberg, T, Rothmann, MJ, Moller, S, Gram, J, Bech, M, Brixen, K, and Hermann, AP (2019) Use of antiosteoporotic medication in the Danish ROSE population-based screening study. *Osteoporos Int* 30(6): 1223-1233. doi: 10.1007/s00198-019-04934-7
36. Rubin, KH, Rothmann, MJ, Holmberg, T, Hoiberg, M, Moller, S, Barkmann, R, Gluer, CC, Hermann, AP, Bech, M, Gram, J, and Brixen, K (2018) Effectiveness of a two-step population-based osteoporosis screening program using FRAX: the randomized Risk-stratified Osteoporosis Strategy Evaluation (ROSE) study. *Osteoporos Int* 29(3): 567-578. doi: 10.1007/s00198-017-4326-3
37. Rothmann, MJ, Moller, S, Holmberg, T, Hojberg, M, Gram, J, Bech, M, Brixen, K, Hermann, AP, Gluer, CC, Barkmann, R, and Rubin, KH (2017) Non-participation in systematic screening for osteoporosis-the ROSE trial. *Osteoporos Int* 28(12): 3389-3399. doi: 10.1007/s00198-017-4205-y
38. Muller, D, Pulm, J, and Gandjour, A (2012) Cost-effectiveness of different strategies for selecting and treating individuals at increased risk of osteoporosis or osteopenia: a systematic review. *Value Health* 15(2): 284-98. doi: 10.1016/j.jval.2011.11.030