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Analyses of cost-effective BMD scanning and treatment strategies for generic alendronate, and the cost-effectiveness of risedronate and strontium ranelate in those people who would be treated with generic alendronate

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Introduction

This report is an addendum to previous results presented to the Appraisal Committee that estimated the impact of lowering the efficacy of bisphosphonate treatment in fracture risks associated with the following clinical risk factors (glucocorticoids use, rheumatoid arthritis, smoking, alcohol consumption and parental history of hip fracture) – henceforth referred to as Type B clinical risk factors. (November 2006[1])

In this report we predominantly focus on generic alendronate, as it has been shown in earlier work to be the most cost-effective first-line treatment option. Sensitivity analyses have been conducted on the price of alendronate treatment (£53.56 per year for the once weekly preparation and £108.20 for the daily preparation, as provided by NICE) and also on the efficacy of alendronate were it is assumed to be affected by the use of acid-suppressant medication.

Additional analyses have been undertaken for risedronate and strontium ranelate, and provide the incremental cost-effectiveness ratio for these interventions for combinations of age, number of clinical risk factors and T-Score, for which strategies with generic weekly alendronate led to a cost of less than £20,000 per QALY in women who are found by opportunistic assessment and £30,000 per QALY for those who self identify..

The full model description has been provided in other reports [2] and will not be re-stated, however key variables in the base-case for our analyses, are provided in Table 1.

A key definition that will be re-stated is the distinction between women who need to opportunistically assessed and those that self-identify. Women who self-identify are those that present to a clinician with a clinical risk factor, with no need to find this woman from a multitude of women with the majority having no risk factors. Women could self-identify by having a previous fracture, or reporting one to a clinician, being prescribed glucocorticoids, having a diagnosis of rheumatoid arthritis or consulting a GP concerned about osteoporosis.
Women who are opportunistically assessed have not presented to a clinician and resources have to be consumed in order to find whether the woman would be a candidate for BMD scanning or treatment.

The maximum cost per QALY was assumed to be £20,000 per QALY for women who are opportunistically assessed and £30,000 for women who self-identify with a previous fracture.

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[1] Stevenson M. Analyses of cost-effective BMD scanning and treatment strategies for generic alendronate, risedronate, strontium ranelate, raloxifene and teriparatide following corrections to the methodology associated with lower efficacy in some risk factors. http://www.nice.org.uk/nicemedia/pdf/OsteoAddAnalyses.pdf

[2] Stevenson MD, Lloyd-Jones M, De Negris E, Brewer N, Davis S, Oakley J. *A systematic review and economic evaluation of interventions for the Prevention and Treatment of Postmenopausal Osteoporosis*. Health Technol Assess. 2005 (9) 22 pp 1 -160

Additional analyses look at the effect that would be caused were there to be a proven link between acid-suppressant medication and increased fracture rates. Whilst an accompanying report concludes that the evidence base is poor [3] we have conducted analyses assuming that the midpoint of data provided by Servier to NICE on the effects of concomitant use of acid suppressant medication was the correct value, in order to provide additional data to the NICE appraisal committee. It is noted that were this true, then the underlying efficacy in patients not on acid suppressant medication would be slightly improved than that used in the base case, although additional analyses investigating this have not been conducted.

[3] Lloyd Jones M. (2008) Critique of evidence put forward by Servier suggesting an association between acid-suppressive medication and fracture risk

Table 1: The base-case scenario.

Parameter	Value	Source
Persistence at 5-years	50%	Estimated from the results of the accompanying literature review
The assumed relative risk of bisphosphonates on fracture risks caused by factors other than age, BMD and previous fracture status.	0.50	Appraisal committee Estimation
The assumed relative risk of bisphosphonates on fracture risks caused age, BMD and previous fracture status	Age dependent, due to the proportion of fractures associated with other risk factors.	Author's calculation based on meta-analysed RCTs and the WHO data-set. (Academic in confidence)
Costs set to HRG values including estimate of home-help costs	Age dependent, see previous report	HRG fracture costs including estimate of home-help costs.
Utility multiplier associated with vertebral fracture.	Year 1 0.792 Year 2+ 0.909	On the request of the appraisal commitee these values were modified from Kanis et al. *Osteoporosis International* 2004; 15 20-26, which was used for all other fracture types. Here the impact of vertebral fracture in year 1 was lessened so that it was equal to that of hip fracture.
Costs incurred over 5-years via side effects associated with bisphosphonate	£4.50 per patient that is compliant (costs for non-compliant patients are included in our analyses)	See earlier text
Utility multiplier associated with bisphosphonate related GI symptoms	Age dependent, see previous report, but 10 times that estimated by ScHARR	On the request of the appraisal committee this value in a cohort of women is 10 times that which would be estimated in the ScHARR base case. (see previous reports)
Cost of bisphosphonate	£53.56 and £108.20 per annum	Price of once weekly generic alendronate and daily generic alendronate.

Summarised results for women identified through opportunistic assessment who will be treated with generic alendronate

	How scenario is different from the base-case.	Identification strategies potentially[4] cost-effective from what age (years)?	Percentage of women age 50 or older that were opportunistically assessed that would be offered a BMD scan (%)	Percentage of women age 50 or older that were opportunistically assessed that would be treated (%)
1	Price of generic alendronate set to £53.56	65	38.2	12.2
2	Price of generic alendronate set to £108.20	70	33.7	9.0

Summarised results for self-identifying women

	How scenario is different from the base-case.	Identification strategies potentially[5] cost-effective from what age (years)?	Percentage of women age 50 or older that were opportunistically assessed that would be offered a BMD scan (%)	Percentage of women age 50 or older that were opportunistically assessed that would be treated (%)
1	Price of generic alendronate set to £53.56	50	85.1	27.5
2	Price of generic alendronate set to £108.20	55	72.3	23.0

[4] Assuming a cost per QALY of £20,000
[5] Assuming a cost per QALY of £30,000

Detailed results for women found through opportunistic assessment. [6]

Scenario 1 (£53.56 per year for the once weekly preparation)

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
65-69 years	Do not BMD	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£18,391
70-74 years	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.0 SD	BMD and treat where T-Score <-0.5 SD	£9,290
75 years and over	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	BMD and treat where T-Score <-0.5 SD	BMD and treat where T-Score < 0.5 SD	£1,060

Scenario 2 (£108.20 per year for the once daily preparation)

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
70-74 years	BMD and treat where T-Score <-3.0 SD	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£11,333
75 years and over	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.0 SD	BMD and treat where T-Score <-0.5 SD	£5,651

[6] Assuming a cost per QALY of £20,000

Detailed results for self-identifying women. [7]

Note that the number of clinical risk factors are in addition to the presenting risk factor (such as a fracture)

Scenario Base-case 1 (once weekly alendronate at £53.56 per annum)

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
50-54 years	Do not BMD	Do not BMD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£25,570
55-59 years	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.5 SD	£19,732
60-64 years	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	£15,231
65-70 years	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	BMD and treat where T-Score <-0.5 SD	£7,525
70-74 years	BMD and treat where T-Score <-1.0 SD	BMD and treat where T-Score <-0.5 SD	BMD and treat where T-Score < 0.5 SD	BMD and treat where T-Score < 1.0 SD	£2,826
75 years and over	BMD and treat where T-Score < 0.0 SD	BMD and treat where T-Score < 0.5 SD	BMD and treat where T-Score < 1.0 SD	BMD and treat where T-Score <1.0 SD	Dominating

Note that as a sensitivity analyses these analyses have been re-calculated using a cost per QALY threshold of £20,000. These results are presented later in the report.

[7] Assuming a cost per QALY of £30,000

Scenario Base-case 2 (£108.20 per year for the daily preparation) [8]

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
55-59 years	Do not BMD	Do not BMD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£20,200
60-64 years	Do not BMD	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£17,826
65-70 years	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	£13,929
70-74 years	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	BMD and treat where T-Score < -0.5 SD	BMD and treat where T-Score < 0.0 SD	£8,991
75 years and over	BMD and treat where T-Score < -1.0 SD	BMD and treat where T-Score < -0.5 SD	BMD and treat where T-Score < 0.5 SD	BMD and treat where T-Score <1.0 SD	£3,286

Comment on the use of DXA scanning in elderly patients with clinical risk factors.

This report has given the T-Score thresholds at which treatment with bisphosphonate becomes cost-effective.

What has not been considered is the use of treatment without DXA scanning. However it is noted that this may be applicable when it is highly likely that a woman would be at the T-Score threshold or lower, when the patient is elderly and when there is a shortage of DXA machines.

For example in base case 2 (page 10) women aged 75 years and only would need a T-Score of –0.5SD or lower to receive treatment. The average T-Score for women of this age is –1.94SD [9] and thus a decision may be made to treat without DXA. These decisions have not been evaluated in this report.

[8] Assuming a cost per QALY of £30,000

[9] Stevenson MD, Lloyd-Jones M, De Negris E, Brewer N, Davis S, Oakley J. *A systematic review and economic evaluation of interventions for the Prevention and Treatment of Postmenopausal Osteoporosis*. Health Technol Assess. 2005 (9) 22 pp 1 -160

The cost per QALY for generic alendronate (priced at £53.56 for once weekly and £108.20 for once daily), risedronate (£264) and strontium ranelate (£334) for combinations of age, number of clinical risk factors and T-Score.

In the tables on the following pages the cost per QALY for each treatment compared with no treatment (without any identification costs) has been listed. Only those combinations of age, T score and number of clinical risk factors at which treatment with generic alendronate leads to a strategy with a cost-effectiveness of less than £20,000 per QALY for women identified by opportunistic assessment and £30,000 for self identifying women have been included. The values have been curtailed at T-Scores of –1.0 SD (which is the beginning of osteopenia) and at a –5.0 SD. Because these values excludes identification, the costs per QALY for generic alendronate are lower than in the tables shown for the entire prevention strategies on the previous pages. These tables illustrate the difference in the cost effectiveness between the interventions for a given combinations of age, T score and number of clinical risk factors.

The base-case scenario for generic alendronate has also been used for all other drugs with the exception of disutility associated with strontium ranelate, which was assumed to have only 10% the disutility of generic alendronate.

In the tables, A1 denotes alendronate priced at £53.56, A2 denotes alendronate priced at £108.20, R denotes risedronate and SR denotes strontium ranelate. Domin equals dominated, where both cost savings and health benefits are accrued.

Note that for risedronate the disutility of side-effects for risedronate has been set equal to that for alendronate as both are bisphosphonates. This value is set to 10-times of that based on the patient event monitoring study identified by ScHARR at the request of the Appraisal Committee. The disutility of side-effects for strontium ranelate has been set to the level of disutility for bisphosphonates recommended by ScHARR. These assumptions have been used at the request of the appraisal committee.

Note also that the incremental cost-effectiveness ratios for risedronate and strontium ranelate cross as the T-Score of a patient changes. This is due to the relative weight of side-effect disutility and fracture prevention: the impact of side-effects remain constant regardless of T-Score, and the disutility associated with risedronate has been assumed to be 10 times that of strontium ranelate, whereas the benefits from fracture prevention become more pronounced as the T-Score decreases, and pooled bisphosphonates have a better efficacy than strontium ranelate. As the T-Score decreases the relative benefit of risedronate increases compared with strontium ranelate.

Additionally note that the results for very low T-Scores at age 55-59 years are slightly better for strontium ranelate than those at 60-64 years. This is due to the greater underlying risk of vertebral fracture in the younger age group as reported in epidemiological data and the greater z-score required to reach a defined T-Score (such as –4.5) for women at a younger age. Refer to an earlier report for more detail.[10]

[10] Stevenson MD, Lloyd-Jones M, De Negris E, Brewer N, Davis S, Oakley J. *A systematic review and economic evaluation of interventions for the Prevention and Treatment of Postmenopausal Osteoporosis*. Health Technol Assess. 2005 (9) 22 pp 1 -160

Cost per QALY ratios for interventions compared with no treatment for opportunistically assessed women

Age 65-69 years

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors								
1 Clinical Risk Factor				A1 £9,824 A2 £33,177 R £99,407 SR £93,944	A1 £3,855 A2 £10,781 R £43,862 SR £65,335	A1 Domin A2 £1,191 R £19,174 SR £42,050	A1 Domin A2 Domin R £6,603 SR £24,250	A1 Domin A2 Domin R Domin SR £11,679
2 Clinical Risk Factors			A1 £12,667 A2 £35,249 R £99,640 SR £50,728	A1 £2,043 A2 £14,840 R £50,704 SR £37,025	A1 Domin A2 £3,952 R £25,153 SR £25,724	A1 Domin A2 Domin R £10,447 SR £16,400	A1 Domin A2 Domin R £1,364 SR £8,533	A1 Domin A2 Domin R Domin SR £2,462
3 Clinical Risk Factors		A1 £15,647 A2 £42,161 R £117,762 SR £96,370	A1 £3,234 A2 £17,059 R £56,481 SR £69,394	A1 Domin A2 £5,251 R £28,034 SR £47,649	A1 Domin A2 Domin R £12,348 SR £30,537	A1 Domin A2 Domin R £2,987 SR £17,473	A1 Domin A2 Domin R Domin SR £7,779	A1 Domin A2 Domin R Domin SR £877

Age 70-75 years

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors			A1 £17,239 A2 £43,453 R £118,198 SR £87,900	A1 £5,496 A2 £20,262 R £62,367 SR £66,293	A1 Domin A2 £8,545 R £34,537 SR £48,600	A1 Domin A2 £1,581 R £18,311 SR £34,188	A1 Domin A2 Domin R £7,911 SR £22,375	A1 Domin A2 Domin R £1,069 SR £13,048
1 Clinical Risk Factor			A1 £9,887 A2 £28,352 R £81,004 SR £73,905	A1 £1,567 A2 £13,363 R £45,323 SR £55,367	A1 Domin A2 £4,063 R £24,989 SR £40,130	A1 Domin A2 Domin R £11,763 SR £27,687	A1 Domin A2 Domin R £3,296 SR £17,068	A1 Domin A2 Domin R Domin SR £8,544
2 Clinical Risk Factors	A1 £17,058 A2 £41,277 R £113,253 SR £87,936	A1 £8,182 A2 £24,208 R £69,905 SR £69,638	A1 £1,406 A2 £11,782 R £40,619 SR £50,728	A1 Domin A2 £3,911 R £23,200 SR £37,025	A1 Domin A2 Domin R £11,463 SR £25,724	A1 Domin A2 Domin R £3,654 SR £16,400	A1 Domin A2 Domin R Domin SR £8,533	A1 Domin A2 Domin R Domin SR £2,463
3 Clinical Risk Factors	A1 £6,846 A2 £22,661 R £67,754 SR £67,666	A1 £876 A2 £11,431 R £41,525 SR £53,329	A1 Domin A2 £3,256 R £22,309 SR £37,844	A1 Domin A2 Domin R £10,509 SR £25,378	A1 Domin A2 Domin R £2,825 SR £15,476	A1 Domin A2 Domin R Domin SR £7,740	A1 Domin A2 Domin R Domin SR £1,740	A1 Domin A2 Domin R Domin SR Domin

Age 75 years and older

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors		A1 £13,974 A2 £42,758 R £124,831 SR £90,077	A1 £4,166 A2 £9,268 R £69,619 SR £70,332	A1 Domin A2 £2,378 R £39,362 SR £52,311	A1 Domin A2 Domin R £22,136 SR £37,880	A1 Domin A2 Domin R £11,291 SR £26,342	A1 Domin A2 Domin R £3,902 SR £16,921	A1 Domin A2 Domin R Domin SR £9,524
1 Clinical Risk Factor	A1 £17,020 A2 £48,165 R £136,971 SR £91,247	A1 £7,251 A2 £27,243 R £84,252 SR £75,657	A1 £242 A2 £13,665 R £49,953 SR £58,746	A1 Domin A2 £4,543 R £28,746 SR £43,295	A1 Domin A2 Domin R £14,923 SR £30,883	A1 Domin A2 Domin R £6,091 SR £20,935	A1 Domin A2 Domin R £76 SR £12,277	A1 Domin A2 Domin R Domin SR £5,576
2 Clinical Risk Factors	A1 £4,090 A2 £19,148 R £62,087 SR £63,417	A1 £623 A2 £10,670 R £41,403 SR £51,787	A1 Domin A2 £3,714 R £25,229 SR £39,334	A1 Domin A2 Domin R £13,380 SR £28,005	A1 Domin A2 Domin R £5,458 SR £18,778	A1 Domin A2 Domin R £3 SR £11,308	A1 Domin A2 Domin R Domin SR £5,128	A1 Domin A2 Domin R Domin SR £348
3 Clinical Risk Factors	A1 £1,106 A2 £6,036 R £32,315 SR £47,002	A1 Domin A2 £648 R £19,171 SR £35,563	A1 Domin A2 Domin R £9,220 SR £24,512	A1 Domin A2 Domin R £2,216 SR £15,117	A1 Domin A2 Domin R Domin SR £7,860	A1 Domin A2 Domin R Domin SR £2,290	A1 Domin A2 Domin R Domin SR Domin	A1 Domin A2 Domin R Domin SR Domin

Cost per QALY ratios for interventions compared with no treatment for self-identifying women

Age 50-54 years

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors								
1 Clinical Risk Factor								
2 Clinical Risk Factors			A1 £20,593 A2 £48,557 R £128,283 SR £93,142	A1 £1,428 A2 £13,447 R £48,605 SR £63,887	A1 Domin A2 £856 R £15,779 SR £37,582	A1 Domin A2 Domin R £3,085 SR £391,217	A1 Domin A2 Domin R Domin SR £17,236	A1 Domin A2 Domin R Domin SR £5,503
3 Clinical Risk Factors		A1 £28,285 A2 £65,080 R £169,996 SR £101,782	A1 £5,731 A2 £20,209 R £61,488 SR £70,213	A1 Domin A2 £4,838 R £24,852 SR £44,069	A1 Domin A2 Domin R £7,883 SR £24,133	A1 Domin A2 Domin R Domin SR £10,219	A1 Domin A2 Domin R Domin SR £1,263	A1 Domin A2 Domin R Domin SR Domin

Age 55-59 years

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors				A1 £11,230 A2 £33,296 R £96,288 SR £86,755	A1 Domin A2 £9,853 R £39,037 SR £57,486	A1 Domin A2 Domin R £14,926 SR £34,485	A1 Domin A2 Domin R £2,847 SR £17,617	A1 Domin A2 Domin R Domin SR £6,137
1 Clinical Risk Factor			A1 £26,211 A2 £62,662 R £166,600 SR £101,921	A1 £4,990 A2 £20,039 R £64,593 SR £72,019	A1 Domin A2 £4,991 R £27,028 SR £46,786	A1 Domin A2 Domin R £9,234 SR £26,700	A1 Domin A2 Domin R Domin SR £12,497	A1 Domin A2 Domin R Domin SR £2,859
2 Clinical Risk Factors		A1 £27,498 A2 £64,017 R £168,771 SR £98,390	A1 £9,581 A2 £25,866 R £72,302 SR £72,252	A1 £65 A2 £10,880 R £38,623 SR £49,718	A1 Domin A2 £554 R £16,019 SR £34,013	A1 Domin A2 Domin R £3,848 SR £18,558	A1 Domin A2 Domin R Domin SR £6,950	A1 Domin A2 Domin R Domin SR Domin
3 Clinical Risk Factors		A1 £12,120 A2 £31,718 R £87,599 SR £75,128	A1 £2,396 A2 £13,067 R £43,492 SR £54,590	A1 Domin A2 £3,252 R £20,728 SR £36,759	A1 Domin A2 Domin R £7,596 SR £22,050	A1 Domin A2 Domin R Domin SR £10,671	A1 Domin A2 Domin R Domin SR £2,438	A1 Domin A2 Domin R Domin SR Domin

Age 60 - 64 years

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors				A1 £9,005 A2 £27,739 R £81,155 SR £80,020	A1 Domin A2 £9,039 R £35,753 SR £53,964	A1 Domin A2 £388 R £15,014 SR £33,633	A1 Domin A2 Domin R £3,987 SR £18,523	A1 Domin A2 Domin R Domin SR £7,874
1 Clinical Risk Factor			A1 £19,590 A2 £48,317 R £130,266 SR £93,726	A1 £3,969 A2 £16,753 R £55,205 SR £66,389	A1 Domin A2 £4,617 R £24,774 SR £43,998	A1 Domin A2 Domin R £9,518 SR £25,858	A1 Domin A2 Domin R £953 SR £13,473	A1 Domin A2 Domin R Domin SR £4,478
2 Clinical Risk Factors		A1 £20,479 A2 £48,359 R £127,855 SR £91,189	A1 £7,753 A2 £21,788 R £61,810 SR £65,764	A1 Domin A2 £9,059 R £33,994 SR £46,093	A1 Domin A2 £529 R £14,895 SR £31,919	A1 Domin A2 Domin R £4,201 SR £18,513	A1 Domin A2 Domin R Domin SR £7,791	A1 Domin A2 Domin R Domin SR £1,147
3 Clinical Risk Factors	A1 £26,824 A2 £60,054 R £154,805 SR £91,670	A1 £9,065 A2 £25,250 R £71,399 SR £69,143	A1 £1,395 A2 £10,588 R £56,761 SR £49,886	A1 Domin A2 £2,538 R £18,141 SR £33,752	A1 Domin A2 Domin R £7,070 SR £20,753	A1 Domin A2 Domin R £213 SR £10,722	A1 Domin A2 Domin R Domin SR £3,312	A1 Domin A2 Domin R Domin SR Domin

Age 65-69 years

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors			A1 £14,860 A2 £39,524 R £109,853 SR £91,716	A1 £3,538 A2 £17,111 R £55,680 SR £67,144	A1 Domin A2 £5,778 R £28,648 SR £44,963	A1 Domin A2 Domin R £13,186 SR £30,748	A1 Domin A2 Domin R £3,694 SR £18,022	A1 Domin A2 Domin R Domin SR £8,455
1 Clinical Risk Factor		A1 £24,507 A2 £58,092 R £153,857 SR £102,178	A1 £8,381 A2 £26,086 R £76,505 SR £76,913	A1 Domin A2 £10,489 R £40,678 SR £55,814	A1 Domin A2 £1,618 R £19,480 SR £38,449	A1 Domin A2 Domin R £7,258 SR £23,879	A1 Domin A2 Domin R £362 SR £12,412	A1 Domin A2 Domin R Domin SR £4,334
2 Clinical Risk Factors	A1 £21,315 A2 £51,152 R £291,716 SR £95,926	A1 £8,525 A2 £25,465 R £127,855 SR £75,060	A1 £1,790 A2 £12,037 R £61,810 SR £54,562	A1 Domin A2 £3,967 R £33,994 SR £38,087	A1 Domin A2 Domin R £14,895 SR £25,480	A1 Domin A2 Domin R £4,201 SR £15,296	A1 Domin A2 Domin R Domin SR £7,000	A1 Domin A2 Domin R Domin SR £501
3 Clinical Risk Factors	A1 £9,910 A2 £27,762 R £154,805 SR £74,198	A1 £2,651 A2 £13,919 R £71,359 SR £57,083	A1 Domin A2 £4,986 R £36,761 SR £40,886	A1 Domin A2 Domin R £18,141 SR £27,473	A1 Domin A2 Domin R £7,070 SR £16,635	A1 Domin A2 Domin R £214 SR £8,146	A1 Domin A2 Domin R Domin SR £1,693	A1 Domin A2 Domin R Domin SR Domin

Age 70-75 years

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors	A1 £18,334 A2 £42,224 R £110,346 SR £391,217	A1 £10,043 A2 £26,676 R £74,105 SR £391,217	A1 £3,468 A2 £14,248 R £44,985 SR £391,217	A1 Domin A2 £6,520 R £27,208 SR £391,217	A1 Domin A2 £1,274 R £15,436 SR £391,217	A1 Domin A2 £1,581 R £7,259 SR £391,217	A1 Domin A2 Domin R £1,353 SR £391,217	A1 Domin A2 Domin R Domin SR £391,217
1 Clinical Risk Factor	A1 £11,665 A2 £29,020 R £78,506 SR £391,217	A1 £6,009 A2 £18,637 R £54,644 SR £391,217	A1 £965 A2 £9,669 R £33,898 SR £391,217	A1 Domin A2 £3,401 R £20,351 SR £391,217	A1 Domin A2 Domin R £10,629 SR £391,217	A1 Domin A2 Domin R £3,471 SR £391,217	A1 Domin A2 Domin R Domin SR £391,217	A1 Domin A2 Domin R Domin SR £391,217
2 Clinical Risk Factors	A1 £3,962 A2 £13,985 R £43,630 SR £391,217	A1 £664 A2 £8,360 R £30,100 SR £391,217	A1 Domin A2 £3,029 R £18,383 SR £391,217	A1 Domin A2 Domin R £9,942 SR £391,217	A1 Domin A2 Domin R £3,491 SR £391,217	A1 Domin A2 Domin R Domin SR £391,217	A1 Domin A2 Domin R Domin SR Domin	A1 Domin A2 Domin R Domin SR Domin
3 Clinical Risk Factors	A1 Domin A2 £7,346 R £28,875 SR £391,217	A1 Domin A2 £2,534 R £18,384 SR £391,217	A1 Domin A2 Domin R £9,236 SR £391,217	A1 Domin A2 Domin R £2,788 SR £391,217	A1 Domin A2 Domin R Domin SR £391,217	A1 Domin A2 Domin R Domin SR £391,217	A1 Domin A2 Domin R Domin SR Domin	A1 Domin A2 Domin R Domin SR Domin

Age 75 years and older

	-1.0 to –1.5	-1.5 to –2.0	-2.0 to –2.5	-2.5 to –3.0	-3.0 to –3.5	-3.5 to –4.0	-4.0 to –4.5	-4.5 to –5.0
0 Clinical Risk Factors	A1 £6,807 A2 £23,494 R £71,075 SR £65,436	A1 £2,363 A2 £14,572 R £49,384 SR £54,706	A1 Domin A2 £7,312 R £31,668 SR £42,742	A1 Domin A2 £2,019 R £18,860 SR £31,567	A1 Domin A2 Domin R £10,157 SR £22,432	A1 Domin A2 Domin R £3,986 SR £14,972	A1 Domin A2 Domin R Domin SR £8,746	A1 Domin A2 Domin R Domin SR £3,741
1 Clinical Risk Factor	A1 £3,494 A2 £16,186 R £52,377 SR £55,217	A1 Domin A2 £9,711 R £36,917 SR £45,893	A1 Domin A2 £3,979 R £23,660 SR £35,530	A1 Domin A2 Domin R £13,598 SR £25,852	A1 Domin A2 Domin R £6,015 SR £17,917	A1 Domin A2 Domin R £673 SR £11,421	A1 Domin A2 Domin R Domin SR £5,549	A1 Domin A2 Domin R Domin SR £918
2 Clinical Risk Factors	A1 Domin A2 £6,771 R £28,666 SR £38,247	A1 Domin A2 £2,796 R £19,841 SR £31,113	A1 Domin A2 Domin R £11,861 SR £23,302	A1 Domin A2 Domin R £5,228 SR £16,045	A1 Domin A2 Domin R £399 SR £10,075	A1 Domin A2 Domin R Domin SR £4,945	A1 Domin A2 Domin R Domin SR £690	A1 Domin A2 Domin R Domin SR Domin
3 Clinical Risk Factors	A1 Domin A2 Domin R £14,943 SR £28,236	A1 Domin A2 Domin R £8,108 SR £20,906	A1 Domin A2 Domin R £2,390 SR £13,660	A1 Domin A2 Domin R Domin SR £7,366	A1 Domin A2 Domin R Domin SR £2,394	A1 Domin A2 Domin R Domin SR Domin	A1 Domin A2 Domin R Domin SR Domin	A1 Domin A2 Domin R Domin SR Domin

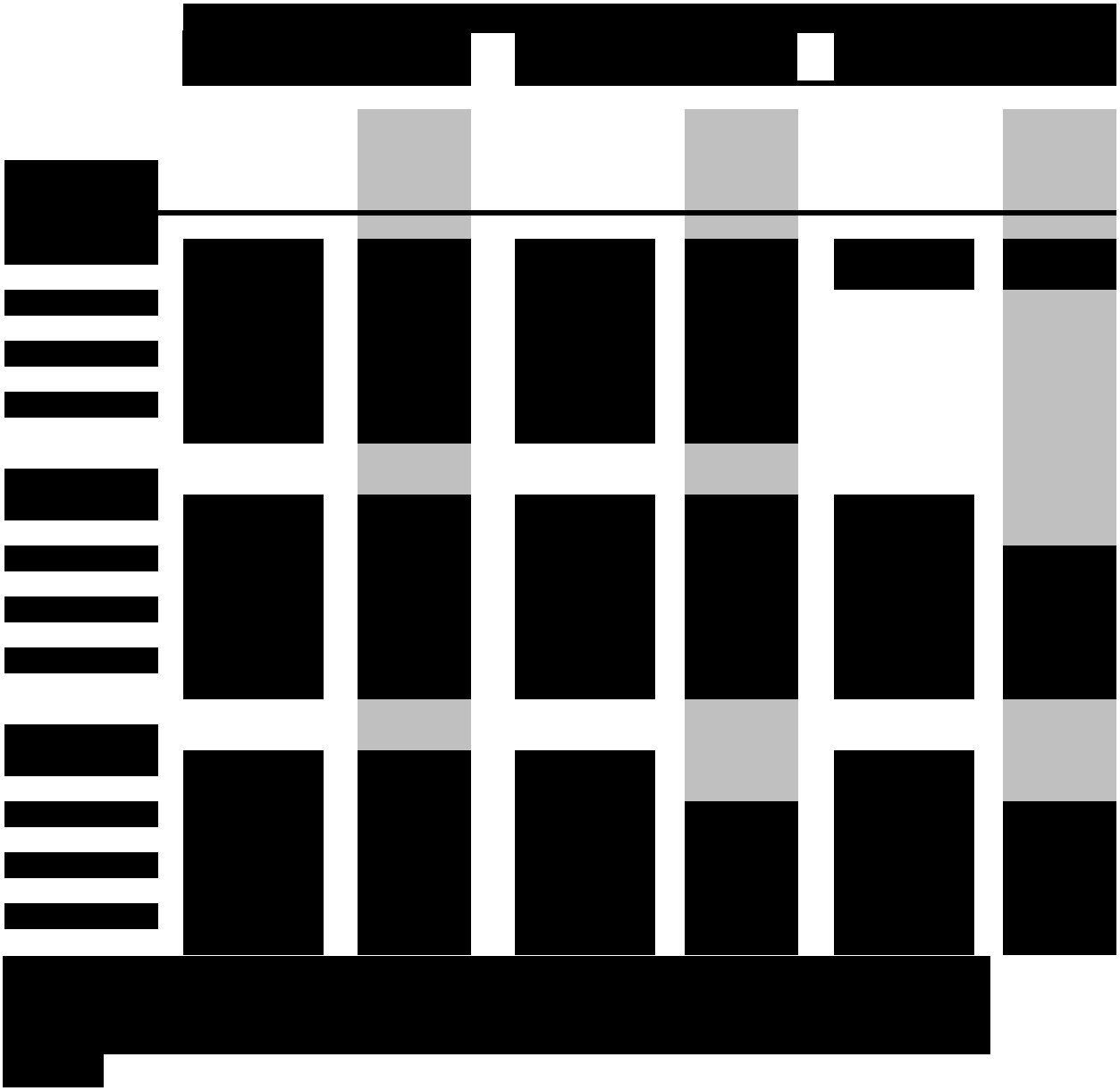
Results assuming that patients taking acid-suppressant medication have a greater risk of fracture than those who do not.

In an accompanying document we discuss whether there is sufficient evidence to believe that the use of acid-suppressant medication increases the risk of fracture. We have undertaken some analyses assuming that the risks of fracture are increased by [redacted]% [in confidence, Servier] at the hip and spine, but reduced by [redacted]% [in confidence, Servier] at the wrist and proximal humerus. These values have been taken from data provided by Servier and are the midpoint values for patients using concomitant acid suppressant medication, with adjustment for confounders (although these confounders were not detailed in the document submitted by Servier.) This table is reproduced below.

The effect of PPIs specifically was requested, however it is believed that the pooled estimate from all acid suppressant medication is the best estimate of this effect. This is due to the overlapping confidence intervals between the effects of PPI and the effects of h2receptor antagonists and the fact that neither intervention systematically produced a greater effect on fracture rate. The combined data additionally has a smaller confidence interval with the midpoint value similar to the midpoint value for PPIs alone.

Concomitant use of bisphosphonates and acid suppressants versus current use of bisphosphonates without acid suppressant use and risk of fracture. Extract from Servier submission to NICE

[Contents of table in confidence, Servier]



Summarised results for women taking acid suppressant medication identified through opportunistic assessment who will be treated with generic alendronate

	How scenario is different from the base-case.	Identification strategies potentially[11] cost-effective from what age (years)?	Percentage of women age 50 or older that were opportunistically assessed that would be offered a BMD scan (%)	Percentage of women age 50 or older that were opportunistically assessed that would be treated (%)
1	Price of generic alendronate set to £53.56	70	33.7	8.9
2	Price of generic alendronate set to £108.20	70	25.6	5.4

Summarised results for self-identifying women taking acid suppressant medication

	How scenario is different from the base-case.	Identification strategies potentially[12] cost-effective from what age (years)?	Percentage of women age 50 or older that were opportunistically assessed that would be offered a BMD scan (%)	Percentage of women age 50 or older that were opportunistically assessed that would be treated (%)
1	Price of generic alendronate set to £53.56	55	64.1	25.0
2	Price of generic alendronate set to £108.20	60	60.5	18.8

[11] Assuming a cost per QALY of £20,000
[12] Assuming a cost per QALY of £30,000

Detailed results for women found through opportunistic assessment. [13]

Scenario 1 (once weekly alendronate at £53.56 per annum)

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
70-74 years	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	£11,081
75 years and over	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-0.5 SD	BMD and treat where T-Score < 0.0SD	£5,010

Scenario 2 (daily alendronate at £108.20 per annum)

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
70-74 years	Do Not BMD	BMD and treat where T-Score <-3.0 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-2.0 SD	£18,419
75 years and over	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	£11,777

[13] Assuming a cost per QALY of £20,000

Detailed results for self-identifying women. [14]

Scenario Base-case 1 (once weekly alendronate at £53.56 per annum)

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
55-59 years	Do not BMD	Do not BMD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£21,593
60-64 years	Do not BMD	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£19,210
65-70 years	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	£14,505
70-74 years	BMD and treat where T-Score <-1.0 SD	BMD and treat where T-Score <-0.5 SD	BMD and treat where T-Score < 0.0 SD	BMD and treat where T-Score < 0.5 SD	£7,456
75 years and over	BMD and treat where T-Score < -0.5 SD	BMD and treat where T-Score < 0.0 SD	BMD and treat where T-Score < 0.5 SD	BMD and treat where T-Score <1.0 SD	£632

[14] Assuming a cost per QALY of £30,000

Scenario Base-case 2 (daily alendronate at £108.20 per annum)

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
60-64 years	Do not BMD	Do not BMD	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	£20,879
65-70 years	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.5 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£22,367
70-74 years	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score < -1.0 SD	BMD and treat where T-Score < 0.0 SD	£12,252
75 years and over	BMD and treat where T-Score < -1.5 SD	BMD and treat where T-Score < -1.0 SD	BMD and treat where T-Score < 0.0 SD	BMD and treat where T-Score <0.5 SD	£6,635

Results using a £20,000 cost per QALY threshold for self-identifying women.

Detailed results for self-identifying women. [15]

Note that the number of clinical risk factors are in addition to the presenting risk factor (such as a fracture)

Scenario Base-case 1 (once weekly alendronate at £53.56 per annum)

Age (years)	0 Clinical Risk Factors	1 Clinical Risk Factor	2 Clinical Risk Factors	3 Clinical Risk Factors	Cost Per QALY of strategy
55-59 years	Do Not BMD	Do Not BMD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£11,666
60-64 years	Do Not BMD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	£15,042
65-70 years	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-2.0 SD	BMD and treat where T-Score <-1.5 SD	BMD and treat where T-Score <-1.0 SD	£6,970
70-74 years	BMD and treat where T-Score <-1.0 SD	BMD and treat where T-Score <-0.5 SD	BMD and treat where T-Score < 0.0 SD	BMD and treat where T-Score < 0.5 SD	£2,664
75 years and over	BMD and treat where T-Score < -0.5 SD	BMD and treat where T-Score < 0.0 SD	BMD and treat where T-Score < 1.0 SD	BMD and treat where T-Score <1.0 SD	Dominating

It is seen that compared with using a £30,000 threshold (p7), it is now not worth undertaking BMD scans in women aged 50-54 years, and that the T-Score required for treatment in some combinations is lower. For example, for women aged 60-64 years with 2 additional risk factors to the self-identifying factor, a T-Score of –2.0 SD is needed when using a £20,000 cost per QALY threshold, but only –1.5SD when using a £30,000 threshold.

[15] Assuming a cost per QALY of £20,000