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

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Corrigendum notice

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

Sarah Davis, Marrissa Martyn-St James, Jean Sanderson, John Stevens, Edward Goka, Andrew Rawdin, Susi Sadler, Ruth Wong, Fiona Campbell, Matt Stevenson, Mark Strong, Peter Selby and Neil Gittoes

This paper[1] is corrected as follows.

Introduction

During the course of providing additional analyses for the National Institute for Health and Care Excellence Technology Appraisal Committee, two errors were identified in the data entered in the network meta-analysis that informed the cost-effectiveness analysis described in the original report.[1] This corrigendum notice describes the errors identified and the impact of correcting these errors on the main analyses presented in the original report.[1]

Description of the error identified

The number of hip fractures for patients receiving zoledronic acid in the Health Outcomes and Related Incidence with Zoledronic acid Once Yearly-Recurrent Fracture Trial (HORIZON-RFT)[2] had been incorrectly entered in the data sheet used for the network meta-analysis as 79, which was in fact the number of non-vertebral fractures, instead of 23. As this error had been introduced after the original data extraction sheet had been quality assured by a second reviewer, the other data used in the network meta-analysis for all four fracture outcomes were double-checked against the quality assured data extraction sheet. One other discrepancy was identified, which was that for the non-vertebral fracture outcome in the Fracture Intervention Trial (FIT) II,[3] the number at risk of vertebral fractures ($n = 2077$ for placebo and $n = 2057$ for alendronic acid) had been used instead of the number at risk of non-vertebral fractures ($n = 2218$ for placebo and $n = 2214$ for alendronic acid). Both of these errors were corrected and the network meta-analyses for hip fracture and non-vertebral fractures were re-run.

Corrected treatment effectiveness estimates

For the non-vertebral fracture outcome, the correction to the numbers at risk in the FIT II study had minimal impact on the efficacy, as can be seen in *Table 1*. However, for the hip fracture outcome, the impact on the efficacy estimates was substatial, as can be seen in *Table 1*. This was because in the original analysis the incorrect data inputted for the HORIZON-RFT study had estimated an increased rather than a decreased risk of hip fracture for zoledronic acid. This had affected the hazard ratio for zoledronic acid, but it had also affected the estimates of the hazard ratio for the other bisphosphonates as the network meta-analysis assumed a class effect.

TABLE 1 Efficacy estimates for hip fracture and non-vertebral fracture [hazard ratios, median (95% predictive intervals)] before and after correcting the errors in the network meta-analysis data inputs

	Hip fracture		Non-vertebral fracture	
	Original analysis containing error	Corrected analysis	Original analysis containing error	Corrected analysis
Alendronic acid	0.78 (0.26 to 2.28)	0.66 (0.41 to 1.05)	0.80 (0.54 to 1.07)	0.80 (0.55 to 1.07)
Risedronic acid	0.82 (0.28 to 2.37)	0.69 (0.44 to 1.10)	0.71 (0.49 to 1.02)	0.71 (0.49 to 1.01)
Ibandronic acid (oral)	0.87 (0.27 to 2.92)	0.68 (0.37 to 1.38)	0.80 (0.49 to 1.43)	0.81 (0.49 to 1.44)
Ibandronic acid (i.v.)	0.87 (0.27 to 2.92)	0.68 (0.37 to 1.38)	0.92 (0.59 to 1.43)	0.92 (0.59 to 1.43)
Zoledronic acid (i.v.)	0.94 (0.32 to 2.72)	0.65 (0.42 to 1.02)	0.75 (0.53 to 1.05)	0.75 (0.53 to 1.05)

i.v., intravenous.

Corrected base-case cost-effectiveness analyses

The results were re-run for the base-case scenario presented in the original publication using the corrected efficacy data shown in *Table 1*. In the base-case scenario, the full data from the probablistic sensitivity analysis (PSA) for the whole population (2 million patients with one set of parameter samples per patient) were used to calculate average costs and quality-adjusted life-years (QALYs) for each of the 10 risk categories for both Qfracture and FRAX and an incremental analysis was conducted for each risk category. The original publication also explored the uncertainty around the base-case analysis by reporting cost-effectiveness acceptability curves for each risk category and structural sensitivity analyses using mid-point parameter estimates, but this corrigendum notice focuses only on the key base-case results.

The base-case results when estimating fracture risk using Qfracture and FRAX are summarised in *Figures 1* and *2*, respectively (these replace *Figures 89* and *102* in the original publication). Each point

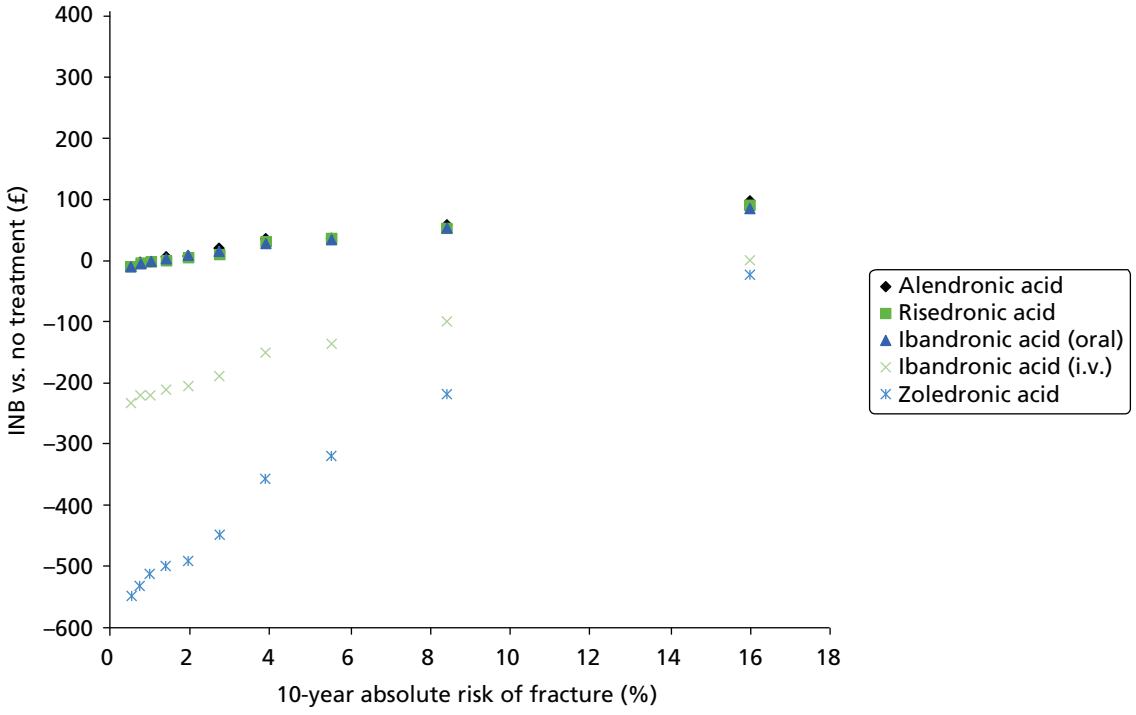

FIGURE 1 Incremental net benefit (when valuing a QALY at £20,000) compared with no treatment against the 10-year fracture risk from QFracture. i.v., intravenous.

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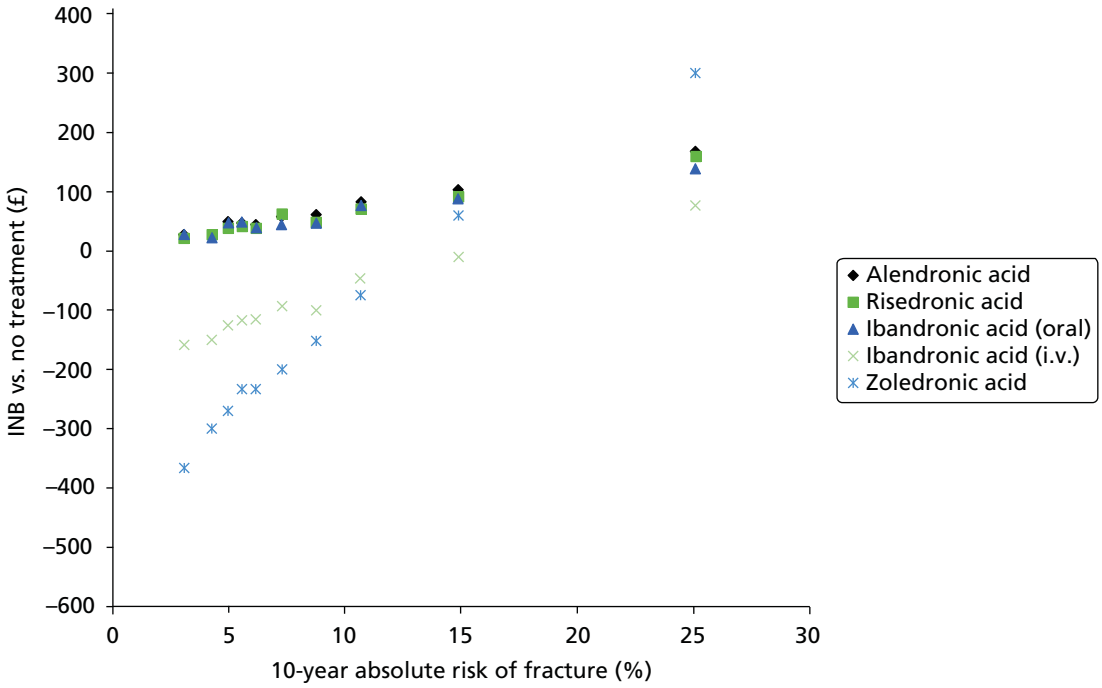

FIGURE 2 Incremental net benefit (when valuing a QALY at £20,000) compared with no treatment against the 10-year fracture risk from FRAX.

shows the mean incremental net benefit (INB) (relative to no treatment and when valuing a QALY at £20,000) and the mean 10-year absolute risk of fracture for one risk category for a particular bisphosphonate treatment.

A fully incremental analysis for each risk category is provided in *Appendices 1* and *2* for QFracture and FRAX, respectively (these replace *Appendices 9* and *10* in the original publication).

When using QFracture to estimate fracture risk, and valuing a QALY at £20,000, no treatment has the highest INB for patients in the first 3 risk categories (average risk scores of 0.5%, 0.7% and 1.0%, respectively). For all of the other risk categories, one of the oral bisphosphonates has the highest INB, although the oral bisphosphonate with maximum INB varies across the risk categories. For the intravenous (i.v.) bisphosphonates, i.v. ibandronic acid has an incremental cost-effectiveness ratio (ICER) of £20,160 versus no treatment in the 10th risk category (average risk score of 16.0%) but is either dominated or extendedly dominated in all risk categories. Zoledronic acid has an ICER of £22,213 versus no treatment in the highest risk category, but has an ICER above £30,000 versus the optimal oral bisphosphonate.

When using FRAX to estimate fracture risk, and valuing a QALY at £20,000, the oral bisphosphonates have positive INBs versus no treatment across all risk categories. The optimal treatment based on maximum INB varies across the risk categories but one of the oral bisphosphonates is optimal from the lowest risk category (average risk of 3.1%) to the ninth risk category (average risk of 14.9%). For the i.v. bisphosphonates, i.v. ibandronic acid has an ICER of £21,693 in the ninth risk category (average risk of 14.9%) and an ICER of £9461 in the 10th risk category (average risk of 25.1%), but it is extendedly dominated in all risk categories. Zoledronic acid has an ICER of £16,614 versus no treatment in the ninth risk category but an ICER of £23,252 versus the optimal oral bisphosphonate. However, in the 10th risk category, zoledronic acid has an ICER of £4453 versus no treatment and an ICER of £11,216 versus the optimal bisphosphonate, making it the optimal treatment in the highest risk category when valuing a QALY at £20,000.

To estimate treatment thresholds for cost-effective intervention, the full data from the PSA for the whole population (2 million patients with one parameter sample per patient) were used in a non-parametric regression. The regression was used to estimate the relationship between INB and absolute fracture risk. The mean INB predicted by the regression across the range of risk scores represented in the simulated population are plotted in *Figures 3* and *4* when estimating fracture risk using QFracture and FRAX respectively (these replace *Figures 90* and *103* in the original publication). The results here differ from those presented in *Figures 1* and *2* because non-parametric regression is able to average over the stochastic uncertainty associated with the individual patient trajectories while simultaneously estimating a smooth relationship between INB and absolute risk.

The risk level at which each treatment achieves a positive INB and the range over which each treatment is optimal (has a maximum INB based on the mean regression estimate) are summarised in *Table 2* for QFracture and *Table 3* for FRAX (these replace *Tables 38* and *39*, respectively).

It can be seen from *Table 2* that for the revised analysis a strategy of no treatment with bisphosphonates is the optimal strategy (when valuing a QALY at £20,000) for patients with a QFracture score of < 1.2%. Alendronic acid is optimal from 1.2% to 20.8% and risedronic acid is optimal for patients with QFracture score of between 20.8% and 26.0%. In the original analysis, zoledronic acid was not optimal at any level of fracture risk but now it is optimal for QFracture scores of ≥ 26%. Oral and i.v. ibandronic acid are not optimal at any level of absolute fracture risk, but the INBs for oral ibandronic acid are close to those for the other oral bisphosphonates. In patients unable to take an oral medication, i.v. ibandronate would be optimal between 15.8% and 16.6% but i.v. zoledronate would be optimal > 16.6%.

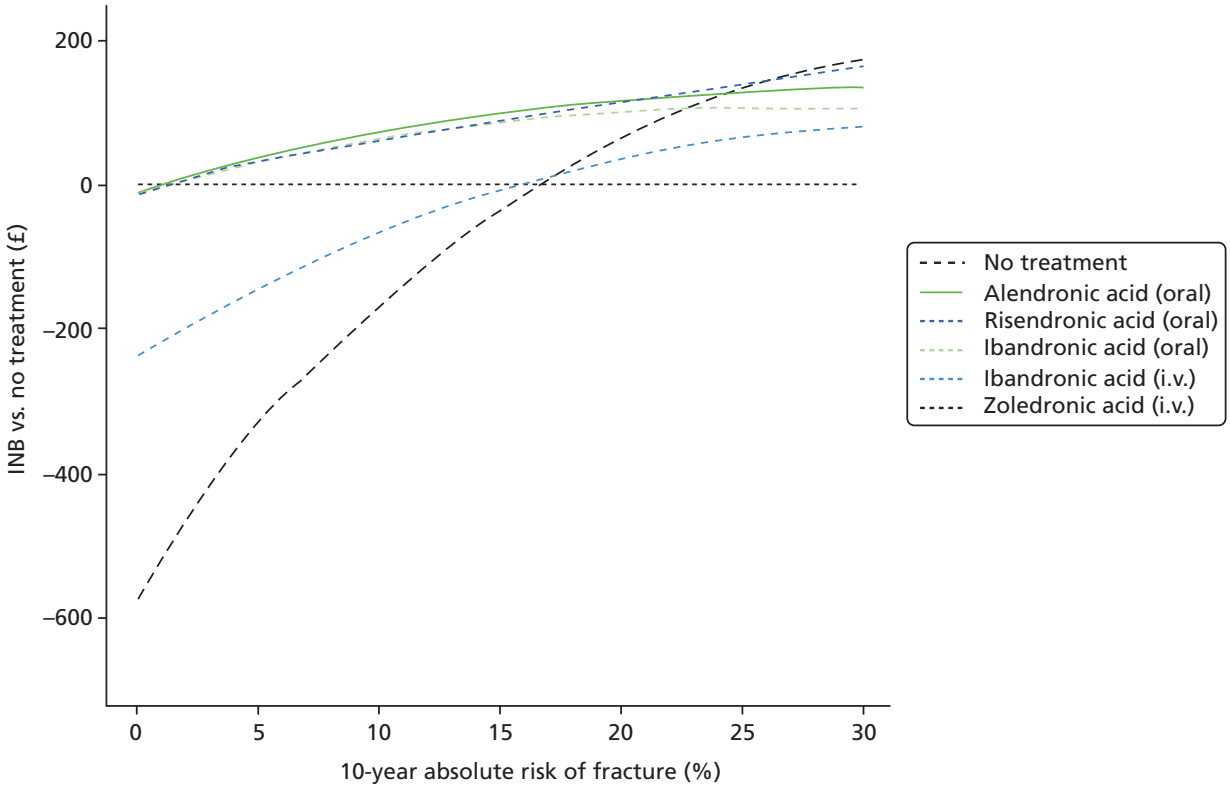

FIGURE 3 Regression for INB (when valuing a QALY at £20,000) compared with no treatment against 10-year fracture risk from QFracture.

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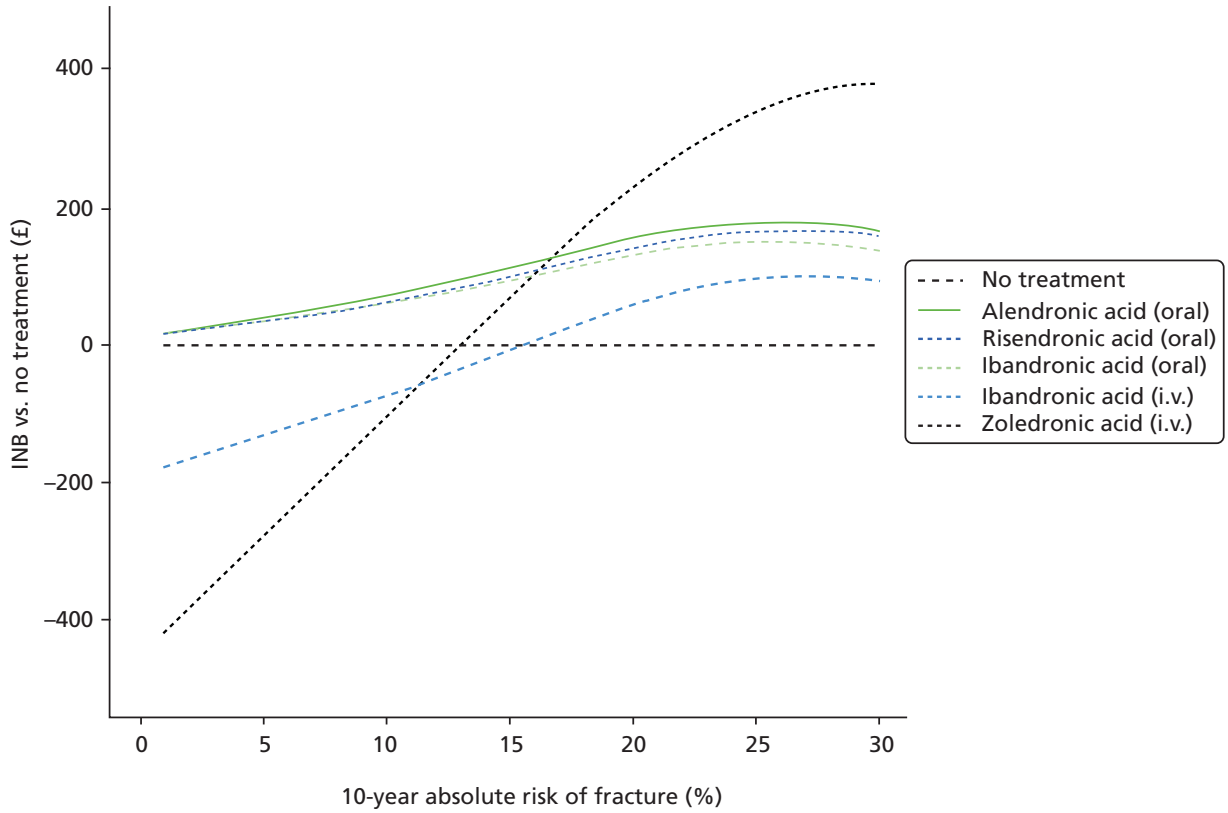

FIGURE 4 Regression for INB (when valuing a QALY at £20,000) compared with no treatment against 10-year fracture risk from FRAX.

TABLE 2 Thresholds at which INB becomes positive and INB becomes maximum as predicted by non-parametric regression of INB against risk predicted by QFracture

Treatment	Range over which INB is positive compared with no treatment (%)	Range over which INB is greater than for all over treatments (%)
No treatment	NA	< 1.2
Alendronic acid	≥ 1.2	≥ 1.2 and < 20.8
Risedronic acid	≥ 1.4	≥ 20.8 and < 26.0
Ibandronic acid (oral)	≥ 1.2	Never
Ibandronic acid (i.v.)	≥ 15.8	Never
Zoledronic acid	≥ 16.6	≥ 26.0

NA, not applicable.

TABLE 3 Thresholds at which INB becomes positive and INB becomes maximum as predicted by non-parametric regression of INB against risk predicted FRAX

Treatment	Range over which INB is positive compared with no treatment (%)	Range over which INB is greater than for all over treatments (%)
No treatment	NA	Never
Alendronic acid	Whole range observed in modelled population	> 2.5 and ≤ 16.7
Risedronic acid	Whole range observed in modelled population	Never
Ibandronic acid (oral)	Whole range observed in modelled population	≤ 2.5
Ibandronic acid (i.v.)	≥ 15.4	Never
Zoledronic acid	> 13.0	>16.7

NA, not applicable.

When using FRAX to predict absolute risk in the revised analysis (see *Table 3*), it can be seen that oral ibandronic acid is optimal for patients with a FRAX score of ≤ 2.5%, and alendronic acid is optimal treatment for patients with a risk level between 2.5% and 16.7%. Zoledronic acid is optimal for FRAX scores > 16.7%. In patients unable to take an oral medication, i.v. zoledronate would be optimal > 13.0% but i.v. ibandronic acid is never the optimal treatment.

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Appendix 1

Base-case results from the probabilistic sensitivity analysis for QFracture

TABLE 4 Base-case results from 200,000 PSA samples for QFracture risk category 1 (average 10-year fracture risk of 0.5%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
No treatment	820.88	15.89373	0.00	0.00000	NA	317,054	475,991	NA
Ibandronic acid (oral)	828.64	15.89362	7.76	–0.00011	–68,054	317,044	475,980	Dominated
Alendronic acid	829.19	15.89361	8.31	–0.00013	–65,953	317,043	475,979	Dominated
Risedronic acid	829.96	15.89363	9.08	–0.00011	–85,649	317,043	475,979	Dominated
Ibandronic acid (i.v.)	1046.32	15.89336	225.44	–0.00038	–597,986	316,821	475,754	Dominated
Zoledronic acid (i.v.)	1377.34	15.89410	556.46	0.00037	1,512,115	316,505	475,446	1,512,115

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

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TABLE 5 Base-case results from 200,000 PSA samples for QFracture risk category 2 (average 10-year fracture risk of 0.7%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
No treatment	1479.03	14.74397	0.00	0.00000	NA	293,400	440,840	NA
Alendronic acid	1486.19	14.74411	7.16	0.00014	50,815	293,396	440,837	Extendedly dominated
Ibandronic acid (oral)	1486.28	14.74407	7.25	0.00011	68,423	293,395	440,836	Dominated
Risedronic acid	1488.35	14.74417	9.32	0.00020	46,596	293,395	440,837	46,596
Ibandronic acid (i.v.)	1703.30	14.74409	224.28	0.00012	1,823,389	293,178	440,619	Dominated
Zoledronic acid (i.v.)	2032.62	14.74503	553.59	0.00107	519,802	292,868	440,318	629,213

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 6 Base-case results from 200,000 PSA samples for QFracture risk category 3 (average 10-year fracture risk of 1.0%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
No treatment	2970.36	13.54164	0.00	0.00000	NA	267,862	403,279	NA
Ibandronic acid (oral)	2976.64	13.54189	6.28	0.00025	25,030	267,861	403,280	25,030
Alendronic acid	2977.40	13.54183	7.04	0.00019	37,855	267,859	403,277	Dominated
Risedronic acid	2978.41	13.54187	8.05	0.00023	34,256	267,859	403,278	Dominated
Ibandronic acid (i.v.)	3193.86	13.54182	223.51	0.00018	1,269,942	267,642	403,061	Dominated
Zoledronic acid (i.v.)	3514.87	13.54317	544.51	0.00153	356,124	267,348	402,780	421,151

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 7 Base-case results from 200,000 PSA samples for QFracture risk category 4 (average 10-year fracture risk of 1.4%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
No treatment	3610.90	12.31686	0.00	0.00000	NA	242,726	365,895	NA
Ibandronic acid (oral)	3614.48	12.31721	3.58	0.00035	10,241	242,730	365,902	Extendedly dominated
Alendronic acid	3614.63	12.31724	3.73	0.00038	9868	242,730	365,903	9868
Risedronic acid	3618.35	12.31721	7.45	0.00035	21,521	242,726	365,898	Dominated
Ibandronic acid (i.v.)	3831.35	12.31728	220.45	0.00042	524,886	242,514	365,687	Extendedly dominated
Zoledronic acid (i.v.)	4149.41	12.31886	538.52	0.00200	269,797	242,228	365,416	330,522

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 8 Base-case results from 200,000 PSA samples for QFracture risk category 5 (average 10-year fracture risk of 2.0%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
No treatment	4149.72	11.41659	0.00	0.00000	NA	224,182	338,348	NA
Ibandronic acid (oral)	4151.38	11.41713	1.66	0.00055	3048	224,191	338,363	3048
Alendronic acid	4151.49	11.41702	1.78	0.00044	4072	224,189	338,359	Dominated
Risedronic acid	4154.82	11.41708	5.10	0.00049	10,320	224,187	338,358	Dominated
Ibandronic acid (i.v.)	4364.19	11.41700	214.48	0.00042	516,811	223,976	338,146	Extendedly dominated
Zoledronic acid (i.v.)	4680.93	11.41859	531.21	0.00200	265,872	223,691	337,877	364,453

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

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TABLE 9 Base-case results from 200,000 PSA samples for QFracture risk category 6 (average 10-year fracture risk of 2.7%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	4259.84	10.39853	–5.11	0.00071	–7196	203,711	307,696	NA
Ibandronic acid (oral)	4262.50	10.39842	–2.44	0.00060	–4053	203,706	307,690	Dominated
No treatment	4264.95	10.39782	0.00	0.00000	NA	203,691	307,670	Dominated
Risedronic acid	4266.70	10.39839	1.76	0.00057	3082	203,701	307,685	Dominated
Ibandronic acid (i.v.)	4474.45	10.39877	209.50	0.00095	221,226	203,501	307,489	Extendedly dominated
Zoledronic acid (i.v.)	4777.98	10.40100	513.04	0.00318	161,434	203,242	307,252	209,945

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 10 Base-case results from 200,000 PSA samples for QFracture risk category 7 (average 10-year fracture risk of 3.9%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Risedronic acid	4715.58	9.38372	–6.95	0.00119	–5838	182,959	276,796	NA
Alendronic acid	4716.22	9.38395	–6.32	0.00142	–4462	182,963	276,802	2854
Ibandronic acid (oral)	4717.33	9.38362	–5.20	0.00109	–4777	182,955	276,791	Dominated
No treatment	4722.53	9.38253	0.00	0.00000	NA	182,928	276,753	Dominated
Ibandronic acid (i.v.)	4914.94	9.38456	192.41	0.00203	94,780	182,776	276,622	Dominated
Zoledronic acid (i.v.)	5194.98	9.38829	472.45	0.00576	82,030	182,571	276,454	110,208

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 11 Base-case results from 200,000 PSA samples for QFracture risk category 8 (average 10-year fracture risk of 5.5%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	5474.70	8.32505	–12.15	0.00117	–10,381	161,026	244,277	NA
Ibandronic acid (oral)	5475.02	8.32501	–11.82	0.00113	–10,425	161,025	244,275	Dominated
Risedronic acid	5476.08	8.32510	–10.77	0.00123	–8762	161,026	244,277	23,683
No treatment	5486.85	8.32388	0.00	0.00000	NA	160,991	244,229	Dominated
Ibandronic acid (i.v.)	5669.06	8.32613	182.21	0.00226	80,792	160,854	244,115	Extendedly dominated
Zoledronic acid (i.v.)	5948.50	8.33096	461.66	0.00708	65,180	160,671	243,980	80,701

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 12 Base-case results from 200,000 PSA samples for QFracture risk category 9 (average 10-year fracture risk of 8.4%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	8927.82	6.52781	–25.76	0.00166	–15,515	121,628	186,906	NA
Ibandronic acid (oral)	8931.78	6.52766	–21.81	0.00151	–14,403	121,621	186,898	Dominated
Risedronic acid	8933.73	6.52770	–19.86	0.00155	–12,823	121,620	186,897	Dominated
No treatment	8953.58	6.52615	0.00	0.00000	NA	121,569	186,831	Dominated
Ibandronic acid (i.v.)	9118.31	6.52949	164.73	0.00334	49,260	121,472	186,766	Extendedly dominated
Zoledronic acid (i.v.)	9357.47	6.53539	403.89	0.00924	43,689	121,350	186,704	56,651

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

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TABLE 13 Base-case results from 200,000 PSA samples for QFracture risk category 10 (average 10-year fracture risk of 16.0%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	19,603.27	4.01625	–47.44	0.00247	–19,211	60,722	100,884	NA
Risedronic acid	19,607.90	4.01618	–42.80	0.00240	–17,857	60,716	100,878	Dominated
Ibandronic acid (oral)	19,611.94	4.01607	–38.76	0.00228	–16,985	60,709	100,870	Dominated
No treatment	19,650.70	4.01378	0.00	0.00000	NA	60,625	100,763	Dominated
Ibandronic acid (i.v.)	19,742.32	4.01833	91.61	0.00454	20,160	60,624	100,808	Extendedly dominated
Zoledronic acid (i.v.)	19,887.32	4.02439	236.61	0.01060	22,312	60,600	100,844	34,915

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

Appendix 2

Base-case results from the probabilistic sensitivity analysis for FRAX

TABLE 14 Base-case results from 200,000 PSA samples for FRAX risk category 1 (average 10-year fracture risk of 3.1%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
No treatment	5893.14	13.55153	0.00	0.00000	NA	265,137	400,653	NA
Ibandronic acid (oral)	5893.89	13.55297	0.75	0.00144	522	265,165	400,695	522
Alendronic acid	5897.29	13.55316	4.15	0.00163	2542	265,166	400,697	17,536
Risedronic acid	5898.82	13.55291	5.69	0.00138	4118	265,159	400,688	Dominated
Ibandronic acid (i.v.)	6101.11	13.55401	207.98	0.00249	83,694	264,979	400,519	Extendedly dominated
Zoledronic acid (i.v.)	6402.23	13.55864	509.10	0.00712	71,522	264,771	400,357	92,075

NA, not applicable
a ICER vs. next least costly non-dominated strategy.

TABLE 15 Base-case results from 200,000 PSA samples for FRAX risk category 2 (average 10-year fracture risk of 4.3%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
No treatment	5965.88	13.22114	0.00	0.00000	NA	258,457	390,668	NA
Risedronic acid	5969.60	13.22271	3.72	0.00157	2369	258,485	390,712	2369
Alendronic acid	5971.73	13.22273	5.85	0.00159	3677	258,483	390,710	Extendedly dominated
Ibandronic acid (oral)	5972.83	13.22262	6.95	0.00148	4688	258,480	390,706	Dominated
Ibandronic acid (i.v.)	6183.45	13.22451	217.57	0.00337	64,542	258,307	390,552	Extendedly dominated
Zoledronic acid (i.v.)	6462.06	13.23096	496.18	0.00982	50,528	258,157	390,467	59,693

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 16 Base-case results from 200,000 PSA samples for FRAX risk category 3 (average 10-year fracture risk of 5.0%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Ibandronic acid (oral)	6547.48	13.34036	–4.96	0.00212	–2338	260,260	393,663	NA
Alendronic acid	6547.75	13.34048	–4.69	0.00224	–2093	260,262	393,667	2285
Risedronic acid	6551.40	13.34010	–1.04	0.00186	–561	260,251	393,652	Dominated
No treatment	6552.45	13.33824	0.00	0.00000	NA	260,212	393,595	Dominated
Ibandronic acid (i.v.)	6754.53	13.34202	202.09	0.00378	53,434	260,086	393,506	Extendedly dominated
Zoledronic acid (i.v.)	7031.62	13.34874	479.17	0.01050	45,649	259,943	393,430	58,615

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

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TABLE 17 Base-case results from 200,000 PSA samples for FRAX risk category 4 (average 10-year fracture risk of 5.6%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	6860.42	13.60355	–0.41	0.00241	–170	265,211	401,246	NA
Ibandronic acid (oral)	6860.63	13.60358	–0.21	0.00244	–84	265,211	401,247	8172
No treatment	6860.83	13.60114	0.00	0.00000	NA	265,162	401,173	Dominated
Risedronic acid	6864.22	13.60338	3.38	0.00224	1511	265,203	401,237	Dominated
Ibandronic acid (i.v.)	7070.60	13.60573	209.77	0.00459	45,721	265,044	401,101	Extendedly dominated
Zoledronic acid (i.v.)	7347.85	13.61379	487.02	0.01265	38,499	264,928	401,066	47,701

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 18 Base-case results from 200,000 PSA samples for FRAX risk category 5 (average 10-year fracture risk of 6.2%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	7415.93	12.31142	–8.46	0.00182	–4647	238,812	361,927	NA
Risedronic acid	7418.89	12.31127	–5.50	0.00167	–3298	238,806	361,919	Dominated
Ibandronic acid (oral)	7421.94	12.31140	–2.45	0.00180	–1361	238,806	361,920	Dominated
No treatment	7424.39	12.30960	0.00	0.00000	NA	238,768	361,864	Dominated
Ibandronic acid (i.v.)	7622.75	12.31372	198.36	0.00412	48,191	238,652	361,789	Extendedly dominated
Zoledronic acid (i.v.)	7894.97	12.32140	470.58	0.01180	39,890	238,533	361,747	48,019

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 19 Base-case results from 200,000 PSA samples for FRAX risk category 6 (average 10-year fracture risk of 7.3%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Risedronic acid	7475.99	10.62569	–11.43	0.00245	–4669	205,038	311,295	NA
Alendronic acid	7478.92	10.62561	–8.50	0.00237	–3590	205,033	311,289	Dominated
Ibandronic acid (oral)	7485.42	10.62525	–2.00	0.00201	–995	205,020	311,272	Dominated
No treatment	7487.42	10.62324	0.00	0.00000	NA	204,977	311,210	Dominated
Ibandronic acid (i.v.)	7682.17	10.62829	194.75	0.00505	38,595	204,884	311,167	Extendedly dominated
Zoledronic acid (i.v.)	7934.82	10.63568	447.40	0.01244	35,970	204,779	311,136	45,934

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 20 Base-case results from 200,000 PSA samples for FRAX risk category 7 (average 10-year fracture risk of 8.8%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	7504.15	9.08546	–15.69	0.00232	–6767	174,205	265,060	NA
Ibandronic acid (oral)	7513.64	9.08514	–6.19	0.00200	–3093	174,189	265,041	Dominated
Risedronic acid	7514.56	9.08528	–5.28	0.00214	–2463	174,191	265,044	Dominated
No treatment	7519.83	9.08314	0.00	0.00000	NA	174,143	264,974	Dominated
Ibandronic acid (i.v.)	7708.61	9.08756	188.78	0.00442	42,735	174,043	264,918	Extendedly dominated
Zoledronic acid (i.v.)	7924.19	9.09571	404.36	0.01257	32,171	173,990	264,947	40,975

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

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TABLE 21 Base-case results from 200,000 PSA samples for FRAX risk category 8 (average 10-year fracture risk of 10.7%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	8095.68	7.90099	–28.85	0.00274	–10,520	149,924	228,934	NA
Ibandronic acid (oral)	8097.00	7.90073	–27.53	0.00248	–11,093	149,918	228,925	Dominated
Risedronic acid	8101.99	7.90062	–22.53	0.00237	–9496	149,910	228,917	Dominated
No treatment	8124.52	7.89825	0.00	0.00000	NA	149,840	228,823	Dominated
Ibandronic acid (i.v.)	8269.02	7.90317	144.50	0.00492	29,347	149,794	228,826	Extendedly dominated
Zoledronic acid (i.v.)	8486.57	7.91257	362.05	0.01432	25,287	149,765	228,890	33,770

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 22 Base-case results from 200,000 PSA samples for FRAX risk category 9 (average 10-year fracture risk of 14.9%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Alendronic acid	11,206.05	6.91190	–36.79	0.00331	–11,121	127,032	196,151	NA
Risedronic acid	11,209.80	6.91143	–33.04	0.00284	–11,627	127,019	196,133	Dominated
Ibandronic acid (oral)	11,213.91	6.91155	–28.93	0.00296	–9785	127,017	196,132	Dominated
No treatment	11,242.84	6.90859	0.00	0.00000	NA	126,929	196,015	Dominated
Ibandronic acid (i.v.)	11,375.26	6.91469	132.42	0.00610	21,693	126,919	196,066	Extendedly dominated
Zoledronic acid (i.v.)	11,527.42	6.92572	284.58	0.01713	16,614	126,987	196,244	23,252

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

TABLE 23 Base-case results from 200,000 PSA samples for FRAX risk category 10 (average 10-year fracture risk of 25.1%)

Treatment strategy	Mean outcomes (discounted)		Incremental outcomes vs. no treatment (discounted)		ICER vs. no treatment (£)	Net benefit at £20,000 per QALY (£)	Net benefit at £30,000 per QALY (£)	Incremental analysis[a] (£)
	Cost (£)	QALYs	Cost (£)	QALYs				
Risedronic acid	18,600.92	4.56909	–85.05	0.00374	–22,721	72,781	118,472	NA
Alendronic acid	18,601.57	4.56947	–84.40	0.00412	–20,491	72,788	118,483	1714
Ibandronic acid (oral)	18,617.90	4.56894	–68.07	0.00359	–18,973	72,761	118,450	Dominated
No treatment	18,685.97	4.56535	0.00	0.00000	NA	72,621	118,275	Dominated
Ibandronic acid (i.v.)	18,754.72	4.57262	68.75	0.00727	9461	72,698	118,424	Extendedly dominated
Zoledronic acid (i.v.)	18,771.96	4.58466	85.99	0.01931	4453	72,921	118,768	11,216

NA, not applicable.
a ICER vs. next least costly non-dominated strategy.

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