



Using health-economic evidence to support policy-level decision-making in Singapore—sensitivity analysis that provides further confidence in fracture probability-based cost-effective intervention thresholds

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FRAX®-based intervention thresholds (ITs) were identified in Singapore in 2018 [1]. Subsequently, in a separate study, the impact of age-dependent ITs was determined on a population-based sample [2]. The mean-weighted age-dependent thresholds identified in the two studies were mostly similar with a minor difference noted at older ages (e.g. at the age of 75 years, major osteoporotic fracture (MOF) IT being 24% for the former study vs 25.7% for the latter). The clinical impact of these minor differences noted at extremely old ages is unlikely to be significant and is presumed secondary to the small methodological differences between the two studies.

Using the intervention thresholds derived from the first study, and a previously validated economic model adapted to the Singaporean context, we had shown that treating with generic alendronate in post-menopausal Singaporean women was cost-effective at age-dependent FRAX®-based major osteoporotic fracture (MOF) ITs only above the age of 65 years and at hip fracture (HF) ITs only above

the age of 60 years [3]. The corresponding fixed ITs that were found to be cost-effective at any age over 50 years in Singapore were 14% and 3.5%, respectively [3]. In that analysis, we used a very conservative cost-effectiveness threshold that was less than $1 \times$ Singapore's GDP per capita (i.e. $0.7 \times$ GDP). We had also based our analysis on the assumption that bone densitometry was performed annually on patients being treated for osteoporosis and that they had follow-up visits with their health care providers once yearly after being initiated on treatment.

Performing sensitivity analyses can help to increase the level of confidence in health economic models. To test the impact of a more generous and realistic cost-effectiveness threshold of $1 \times$ GDP (SGD 89,000) (as recommended by the WHO [4]) and the more realistic clinical practice scenario of bone density scans and follow-up visits for osteoporosis care once in 2 years that is becoming the norm in Singapore, we conducted an additional sensitivity analysis combining these two parameters. This sensitivity analysis shows that both age-dependent FRAX®-based MOF and HF ITs are cost-effective only in those Singaporean women who are 60 years and over treated with generic alendronate (Table 1). The corresponding fixed thresholds that are now found to be cost-effective are MOF and HF probabilities of 9% and 2%, respectively.

Stakeholders in osteoporosis cannot function in silos, and communication between clinicians, researchers, and health care policy makers is vital. These cost-effective osteoporosis treatment thresholds derived using fracture epidemiology, health care costs, and clinical practice settings specific to Singapore will be used for discussions with policy makers at government level so that clinically useful, economically supported, and pragmatic management guidance for osteoporosis can be provided to clinicians in Singapore. The findings from

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Table 1 Incremental cost-effectiveness ratio (expressed in costs (SGD) per QALY gained) of alendronate compared to no treatment at different MOF and HF ITs in Singapore

Age-MOF IT	Alendronate Real World Adherence Costs (SGD) per QALY gained (BMD monitoring and follow-up visits yearly and cost effectiveness threshold of 0.7 x GDP)	Alendronate Real World Adherence Costs (SGD) per QALY gained (BMD monitoring and follow-up visits once in 2 years and cost effectiveness threshold of 1 x GDP): Sensitivity analysis
50 years-2.86%	392,553	260,905
55 years-4.84%	338,025	219,248
60 years-8.09%	113,431	70,263
65 years-13.01%	57,251	31,881
70 years-18.37%	27,396	12,145
75 years-23.98%	11,745	2,583
80 years-26.07%	10,117	155
85 years-28.39 %	8,922	Cost-saving
Age-HF IT		
50 years-0.61%	252,565	162,417
55 years-1.16%	162,051	102,333
60 years-2.32%	69,560	42,207
65 years-4.27%	43,911	23,918
70 years-6.79%	22,322	9,039
75 years-9.46%	8,456	Cost-saving
80 years-12.65%	3,858	Cost-saving
85 years-15.74%	Cost-saving	Cost-saving

Colour code: white, cost-saving; light grey, below cost-effectiveness threshold (SGD 89,000/QALY gained); dark grey, not cost-effective (i.e. above cost-effectiveness threshold)

MOF IT major osteoporotic fracture intervention threshold, *HF IT* hip fracture intervention threshold, *BMD* bone mineral density, *GDP* gross domestic product

our original study and the subsequent sensitivity analysis also highlight the importance of deriving cost-effective and clinically appropriate intervention thresholds unique to each country.

Declarations

Disclosures The authors declare no competing interests.

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