Cost-effective osteoporosis intervention thresholds for Hong Kong postmenopausal women

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KEY MESSAGES

1. A Markov state-transition model was used to determine osteoporosis treatment thresholds in osteoporotic Hong Kong postmenopausal women, using local data of hip, vertebral, and wrist fracture incidence and mortality.
2. The lifetime costs and quality-adjusted life years (QALYs) for the treated (osteoporosis treatment for 5 years) and untreated cohorts were estimated from a societal perspective.
3. The incremental cost-effectiveness ratio for treatment in women around age 50 years was estimated to be approximately HK$3.6 million per QALY. This decreased with increasing age and fell below the cost-effectiveness threshold of $333 840 from the age of 70 years.
4. Probabilistic sensitivity analysis showed that treatment for those aged ≥70 years had a 75% likelihood of being cost-effective, even at a QALY value of only about $250 000.
5. The cost-effectiveness model can be used together with the World Health Organization fracture risk assessment algorithm to determine whether treatment is likely to be cost-effective at a given QALY value for any individual.

Hong Kong Med J 2015;21(Suppl 6):S13-6
HHSRF project number: 07080711

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Introduction

Osteoporosis is characterised by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.[1] Osteoporosis is more common in older people, and complications of fragility fractures are associated with high morbidity and mortality. Although there was a slight decline in the age-specific incidence of hip fracture from 1995 to 2004 in Hong Kong, the absolute number of hip fractures has increased due to an ageing population.[2] In 1996, the cost of acute hospital care for hip fractures exceeded 1% of the public hospital budget. Sensitive fracture risk assessment tools can improve the prognostication of osteoporotic fracture and result in significant health care savings.

The intervention threshold for osteoporosis should be based on the absolute risk rather than the relative risk of fracture based solely on the bone mineral density (BMD) T-score. Apart from BMD assessment, global evaluation of osteoporotic fracture risk can be enhanced by incorporation of clinical risk factor (CRF) assessment. We have identified eight independent CRFs for osteoporotic fracture in Hong Kong postmenopausal women. Some are related to the risk of fall; others are related to osteoporosis and low BMD.[3] The World Health Organization fracture risk assessment algorithm (FRAX) provides 10-year probabilities of hip fractures and major osteoporotic fractures (of the spine, hip, humerus, and forearm). The FRAX integrates independent CRFs for osteoporotic fracture, including low body mass index, parental history of hip fracture, history of fragility fracture, long-term use of oral glucocorticoids, rheumatoid arthritis, other secondary causes of osteoporosis, current smoking, and an average intake of alcohol ≥3 units per day.[4]

Integration of these CRFs and the BMD T-score in the FRAX model not only increases its sensitivity to detect those at high risk of fracture over the subsequent 10-years, but also provides the basis on which intervention thresholds can be developed. This study aimed to determine intervention thresholds for osteoporotic fractures (based on the absolute 10-year risk) in Hong Kong postmenopausal women, using the local epidemiology and economics (fracture incidence, morbidity, mortality, and costs).

Methods

This study was conducted from October 2009 to November 2011. A cost-effectiveness model was used to simulate the transition between no fracture, fracture, and post-fracture states, and the appropriate costs and quality-adjusted life years (QALYs) over the remaining lifetime in women of different ages. By comparing women with or without osteoporosis treatment, the difference in costs and QALYs gained through treatment was used to estimate the cost-effectiveness of treatment at different ages at different fracture rates. A treatment that gained a QALY at a cost equivalent to under two times the per capita gross domestic product is considered cost-effective.

A Markov cohort state-transition model was used to simulate osteoporosis treatment thresholds in Hong Kong postmenopausal women. The model was based on a Swedish cost-effectiveness model for osteoporosis treatment published in 2004.[5] This model began with women in the no fracture state and simulated the yearly transition from age 50 to 100 years or death. The state transition probabilities were based on local age-specific mortality and estimated fracture incidence.

Age-specific hip fracture incidence for postmenopausal women in Hong Kong in 2004 was obtained from the Clinical Data Analysis Reporting System of the Hospital Authority. Age-specific mortality was obtained from the Hong Kong Government Census and Statistics Department. Estimated excess mortality in the first year following hip fracture was based on the mortality risk ratio for hip fracture in Swedish women and Hong Kong mortality. For treatment effect, we assumed that 5 years of drug treatment would reduce the risk of all osteoporotic fracture by 35%. This treatment effect was assumed to decline linearly over 5 years after the end of treatment.

The long-term outcome of treatment was determined using QALYs. The age-related health state for females from a US study and the utility scores for different types of fracture from a Swedish study were used to estimate the disutility of a fracture at a specific age by multiplying the associated health state value of the age group by 1 minus the disutility from the fracture. Using the same assumption to the US study, we assumed that disutility from a fracture would decline linearly over 5 years after the fracture event and that there would be no further disutility in the post-fracture state thereafter.

Costs were based on a societal perspective and adjusted to the year 2009 level. The cost of a fracture included the direct medical costs in the first year and, where relevant, the cost of a nursing home in subsequent years, and the indirect costs of productivity loss due to the fracture. The mean length of stay in hospital in those with a fracture was estimated using the admission data for 2004 from the Hospital Authority. We assumed that 50% of hip fracture patients would be admitted to a nursing home. Productivity loss in the first year was calculated by multiplying the recovery time by the median monthly income. The cost of the treatment included the costs of drugs and monitoring.

To estimate the cost-effectiveness of osteoporosis treatment, we first estimated the lifetime costs and QALYs for women with or without 5 years of drug treatment. All future costs and health effects were discounted at 3% per year. Incremental cost-effectiveness ratios (ICER) between the treated and untreated cohorts were calculated by dividing the difference in cost by the difference in QALYs. The ICERs were compared with the willingness-to-pay threshold for a QALY. Treatment was considered cost-effective if the ICER was below the willingness-to-pay threshold.

One-way sensitivity analyses were conducted to identify the parameters with the strongest effect on cost-effectiveness. In each analysis, one parameter was tested with different values while the other parameters remained unchanged. Probabilistic sensitivity analysis was conducted using second-order Monte Carlo simulation that selected random

TABLE 1. Cost-effectiveness analysis

Age (years)	Mean 10-year fracture risk (%)			Mean cost (HK$)		Incremental cost (HK$)	Mean quality-adjusted life years (QALYs)		QALY gain	Incremental cost-effectiveness ratio (cost/QALY) [HK$]*
	Hip	Vertebral	Wrist	Untreated	Treated		Untreated	Treated		
50	0.18	0.09	0.72	17 299	26 066	8767	17.231	17.234	0.002	3 580 206
55	0.47	0.10	1.02	19 861	28 370	8509	15.583	15.587	0.005	1 881 507
60	1.06	0.12	1.26	22 496	30 683	8188	13.731	13.738	0.008	1 055 436
65	2.47	0.18	1.37	25 003	3731	7728	11.812	11.827	0.015	518 322
70	5.44	0.30	1.55	28 070	34 529	6459	9.780	9.808	0.028	232 705
75	9.90	0.38	1.84	30 595	35 182	4587	7.904	7.949	0.045	101 200
80	16.14	0.36	1.96	30 915	33 315	2400	6.062	6.124	0.063	38 229
85	19.01	0.32	1.74	29 845	30 043	198	4.630	4.696	0.067	2974

* The extra cost to gain one extra QALY after treatment, compared with no treatment

values from the distribution of each parameter. Results are presented as cost-effectiveness acceptability curves.

Results

The ICER for drug treatment for women around age 50 years was estimated to be around HK$3.6 million per QALY. This decreased with increasing age and fell below the cost-effectiveness threshold of $333 840 from the age of 70 years (Table 1).

Table 2 shows the relative risk and the absolute 10-year risk of fracture for each age at which treatment becomes cost-effective. For example, the absolute 10-year risk of hip fracture at which it would be cost-effective to treat a 50-year-old woman would be 1.79, which is derived from a relative risk of 10.09, compared with the average risk in her age group of 0.18%. It is still cost-effective to treat a woman aged ≥85 years who has a relative risk of only 0.26 compared with her peers, which is 74% less than the average risk for that age group. This woman would have an absolute 10-year risk of hip fracture of 5.07%, compared with the average risk of 19.01% for this age group.

The probabilistic sensitivity analysis showed that at the cost-effectiveness threshold of HK$334 000, treatment for women aged ≥70 had a 75% likelihood of being cost-effective. This high likelihood of cost-effectiveness remained even at a QALY value of only about $250 000 (Fig). In addition, treatment for those aged 50 to 59 years was unlikely to be cost-effective on average, and for those aged 65 years it only reached a 50% or higher chance of being cost-effective if the value of a QALY gained exceeded HK$540 000.

TABLE 2. Estimated relative risk (RR) and absolute risk of fracture at which treatment becomes cost-effective

Age (years)	RR of fracture	10-year absolute risk of fracture (%)		
		Hip	Vertebral	Wrist
50	10.09	1.79	0.87	7.18
55	5.06	2.35	0.49	5.11
60	2.88	3.06	0.33	3.59
65	1.49	3.68	0.27	2.04
70	0.75	4.09	0.23	1.17
75	0.43	4.29	0.17	0.81
80	0.30	4.95	0.12	0.62
85	0.26	5.07	0.09	0.49

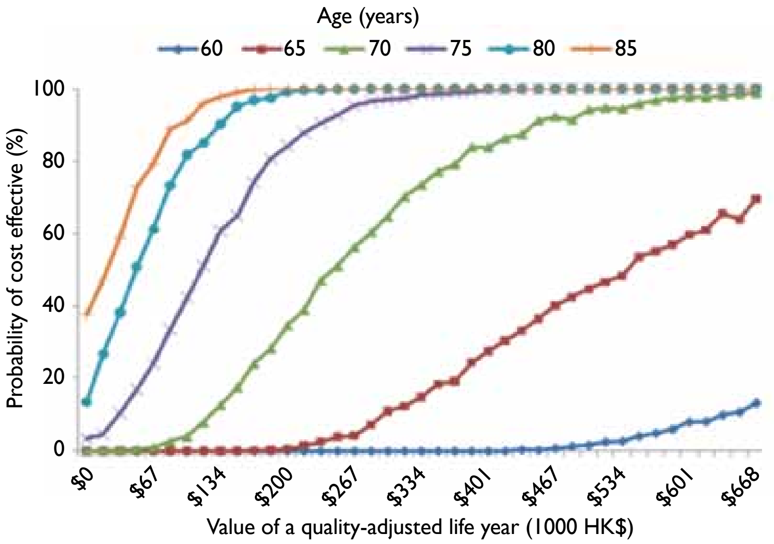

FIG. Cost-acceptability curves

Discussion

This cost-effectiveness model was used to determine the cut-off point for treatment based on treatment efficacy, impact on utility and hence QALYs gained, cost of treatment, and risks in the population. When used with the FRAX algorithm, it can determine whether a treatment is cost-effective at a given QALY value for any individual. This QALY value is open to debate. The cost-acceptability curve shows how the likelihood of cost-effectiveness varies according to the value of the outcome, and the model can be updated with new data and estimates when available.

There were some limitations in the present study. The data on incidence of fracture in Hong Kong were limited, especially those for vertebral and wrist fractures. The base case used estimates from Sweden, but in Asians vertebral fractures may be more common than hip fractures, and the ratio of vertebral to hip fractures was not known. Therefore, more solid data on vertebral fracture rates should have been obtained. The model only simulated hip, vertebral, and wrist fractures and ignored any other fractures. It was assumed that only one fracture would occur in any year. These may have led to underestimation of benefits. When a fracture was treated, the model assumed the subject would be 100% compliant with the treatment regimen. The utility scores used in the model were taken from overseas because of a lack of local data. Nonetheless, in the sensitivity analysis, substituting the utility scores from a systematic review made almost no difference to the results. This model was applied to women only. To adapt it to men, male data on fracture rates, mortality rates, and utility scores are required.

Conclusion

The cost-effectiveness model can be used with estimates of absolute risk of hip fracture from the

FRAX algorithm to determine the cost-effectiveness of drug treatment for women at different ages.

Acknowledgement

This study was supported by the Health and Health Services Research Fund, Food and Health Bureau, Hong Kong SAR Government (#07080711).

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