AN OPTIMAL AND COST-EFFECTIVE APPROACH TO MANAGING OSTEOPOROSIS AND PREVENTING FRACTURES IN SINGAPORE

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I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision. The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo.

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ACKNOWLEDGEMENT OF AUTHORSHIP

I hereby certify that this thesis is in the form of a series of published papers of which I am a joint author. I have included as part of the thesis a written statement from each co-author, endorsed by the Faculty Assistant Dean (Research Training), attesting to my contribution to the joint publications

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GLOSSARY OF ABBREVIATIONS AND ACRONYMS

AAPC	Average Annual Percentage Change
AP	Asia-Pacific
AUC	Area Under ROC curve
BMD	Bone Mineral Density
BOD	Burden of Disease
CBA	Cost-Benefit Analysis
CEA	Cost-Effectiveness Analysis
COI	Cost-of-Illness
CP	Chronic Prostatitis
CPI	Consumer Price Index
CUA	Cost-Utility Analysis
CI	Confidence Interval
DALY	Disability Adjusted Life Years
DALE	Disability-Adjusted Life Expectancy
DFLE	Disability-Free Life Expectancy
DXA	Dual Energy X-ray Absorptiometry
EQ-5D	EuroQol
FCA	Friction Cost Approach
GDP	Gross Domestic Product
HALE	Health Life Expectancy
HCA	Human Capital Approach
HRQoL	Health-Related Quality of Life
HTA	Health Technology Assessment
ICER	Incremental Cost-Effectiveness Ratio
IOF	International Osteoporosis Foundation
IQR	Interquartile Range
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
MID	Minimally Important Difference
MLR	Multiple Linear Regression
NIH	National Institutes of Health
OPTIMAL	Osteoporosis Patient Targeted and Integrated Management for Active Living
QoL	Quality of Life
QALY	Quality Adjusted Life Year
RCT	Randomized Controlled Trial
ROC	Receiver Operating Characteristic
SD	Standard Deviation
SGD	Singapore Dollar
SF-6D	Short Form 6D
SF-36	Short Form 36
WTP	Willingness-to-Pay
YHL	Years of Healthy Life

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EXECUTIVE SUMMARY

In Singapore, as in the rest of Asia, osteoporosis will become an increasingly important public health problem. In the next 50 years, more than half of all hip fractures are projected to occur in Asia (1, 2). Osteoporosis is likely to increase as the population of Singapore is aging rapidly (3-5). In 1990, only 6% of the population in Singapore was above the age of 65, but by 2030, this figure is projected to rise to 25%(6). Osteoporotic fractures at the hip, wrist and spine are increasingly common. In Singaporean men and women above the age of 50 years, hip fracture incidence rates have risen 1.5-fold and 5-fold respectively since the 1960s (7). Our age-adjusted rates among women over the age of 50 years are currently among the highest in Asia, and approaching those of the West. The rise in hip fracture incidence is consistent with secular trends seen in many other countries.

A previous study from Singapore reported a steady increase in age-adjusted hip fracture rates of around 1–1.5% per year in both men and women from 1991 to 1998. Based on these trends, we predicted a further 30–50% increase in hip fracture incidence rates over the ensuing 30 years in Singapore (7). This will result in a great financial burden to the healthcare system of Singapore. We therefore conducted a study to have a better understanding of the direct and indirect costs of osteoporotic fractures in Singapore. The findings were that hospitalization was associated with the highest cost borne by both the hospital and the patients, and informal care dominated indirect costs. With an aging population, the prevalence of osteoporosis-related fractures in Singapore will continue to grow in the years to come, generating what is expected to be a heavy burden on health budgets. Better knowledge of the financial consequences of fragility fractures could enable proactive and preventive measures to be undertaken, especially at sites of care with high cost drivers. This would also provide valuable information for health administrators in healthcare resource and budget allocation planning.

We then undertook a study to examine the incidence of hip fracture In Singapore from 2000 to 2017. We observed several important trends in the occurrence of hip fractures in this study. During the period 2000-2017, absolute numbers of hip fractures continued to increase, with a mean annual increase of 71 fractures per 100,000 and an Average Annual Percentage Change (AAPC) of 3.5% (95% CI: 3.3, 3.8). Nevertheless, the crude fracture rate per 100,000 declined in both men and women, indicating that the increase in absolute number of hip fractures was due to an increase in the numbers of women and men at risk for hip fracture. When crude rates per 100,000 were age-adjusted, fractures trends declined even more steeply, indicating the major contribution of the aging Singapore population to the increase in total number of fractures.

With the available information on patients' knowledge, attitude and practice, as well as the cost burden of fracture management in Singapore obtained from the studies as

conducted in the thesis, we therefore undertook a fracture liaison service program (OPTIMAL) to prevent recurrent fractures from 2008 to 2016. The OPTIMAL program is a clinician champion-driven, case coordinator-run secondary prevention program for osteoporotic fractures. The program strives to narrow the prevalent care gap in osteoporosis care through a judicious combination of fracture case finding, appropriate assessment and evaluation, patient education on osteoporosis and risk factor management, education on nutrition, fall prevention and exercises for muscle strengthening, balance and coordination, in addition to the use of effective anti-osteoporosis pharmacological agents.

The most important finding of this study was the reduction in all sites fracture risk by 41% and hip fracture risk by 47.1% of patients enrolled into the OPTIMAL program when compared with non-enrolees after two years. The absolute risk reduction in hip fracture rate was 7.67% (15.58% in non-enrolees versus 7.93% in OPTIMAL enrolled patients). The absolute reduction in fracture risk was 9% at 5 years. The OPTIMAL program prevented 77 hip fractures for every 1000 participants and reduce mortality by 40% over five years. This led to significant gains of 228 QALYs per 1000 patients. Patients in the program incurred higher costs due to costs of the intervention, BMD test, and osteoporosis treatment, but preventing subsequent hip fractures also saved costs. Discounting costs and benefits at 5 % per year, the program cost $5,607 more and gained 0.228 QALYs per patient, with an incremental cost-effectiveness ratio (ICER) of $24,636 per QALY gained. These results compared favourably with other observational studies and randomised controlled trials of similar fracture liaison service program (8). Taking together with the reduction in fracture, this projected good return of investment would support the cost-effectiveness of implementing such program in Singapore.

Therefore, the overall results from the studies as presented in the thesis would indicate that with the aging population, there is a likelihood of increased osteoporosis-related fractures. This projected increase is expected to impose heavy financial burden to the health care system in Singapore. However, with a coordinated approach in managing osteoporosis as shown by the OPTIMAL program implemented in Singapore, it may be possible at least to damper the clinical and financial impact of osteoporosis-related fractures. The results from the studies in this thesis would also provide an example of tackling the problem of increased osteoporosis-related fractures faced by other countries, particularly in the Asia-Pacific region.