THE ASSOCIATION OF LIFESTYLE PHYSICAL ACTIVITY, SMOKING AND ALCOHOL CONSUMPTION PRACTICES ON BONE HEALTH STATUS OF POSTMENOPAUSAL CHINESE WOMEN IN KELANTAN

By

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ABSTRAK

Sungguhpun penyertaan tinggi dalam aktiviti fizikal yang kuat dan mempunyai muatan mekanikal memberi kesan osteogenik dalam memaksimumkan pertumbuhan jisim tulang sepanjang hayat, tetapi jenis, intensiti, dan kekerapan aktiviti fizikal yang khusus bagi mengurangkan kehilangan tulang yang pesat dalam kalangan wanita yang sudah menopaus adalah masih terhad, terutama dalam kalangan populasi tua di Asia. Objektif kajian ini adalah untuk mengkaji pengaruh aktiviti fizikal harian dan amalan gaya hidup yang lain terhadap status kesihatan tulang dalam kalangan wanita menopaus berbangsa Cina di Kota Bharu, Kelantan. Seramai 73 wanita yang berusia di antara 51 dan 78 tahun telah dipilih melalui pensampelan bertujuan dalam kajian ini. Beberapa metodologi kajian telah digunakan seperti borang soal selidik mengenai ciri-ciri umum, status kesihatan umum, amalan aktiviti fizikal, tabiat pengamalan merokok, pengambilan minuman alkohol, dan juga amalan pemakanan. Borang soal selidik aktiviti fizikal bagi setahun lepas yang telah diujipakai telah digunakan di mana borang tersebut dibahagikan kepada 2 aktiviti utama, iaitu aktiviti riadah dan aktiviti kerja rumah. Ketumpatan tulang pada bahagian seluruh badan, tulang belakang lumbar (L2-L4) dan tulang paha proksimal telah diukur dengan menggunakan alat absorptometri X-ray dua sinar (DXA), sebagai kaedah kriteria penilaian status kesihatan tulang. Purata umur peserta ialah 57.3 tahun, dengan purata tahun sejak menopaus selama 7.6 tahun. Analisis kovarians multivariate (ANCOVA) telah dijalankan untuk menilai tahap pengaruh aktiviti fizikal terhadap jisim tulang, setelah mengambil kira faktor-faktor membaurkan yang berpotensi seperti umur, umur menopaus, jenis menopaus, sejarah

risiko penyakit osteoporosis dalam kalangan ahli keluarga, indeks jisim badan, lilitan pinggang, dan amalan gaya hidup pemakanan yang lain. Hàsil analisa telah menunjukkan bahawa wanita dengan tahap aktiviti fizikal harian (mengandungi aktiviti riadah dan kerja rumah) yang tinggi mempunyai tahap kepadatan tulang bagi seluruh badan, paha proksimal dan tulang belakang lumbar yang lebih tinggi berbanding dengan wanita yang mempunyai tahap aktiviti fizikal yang lebih rendah. Sebaliknya, mengamalan merokok dan tahap pengambilan alkohol tidak menunjukkan kesan yang ketara dan signifikan terhadap nilai ketumpatan tulang yang diuji. Hasil kajian ini telah menunjukkan bahawa, penyertaan aktiviti fizikal yang tinggi dengan tahap loading mekanikal yang mencukupi akan memberikan bermanfaat dalam pemeliharaan jisim tulang dalam kalangan wanita menopaus berbangsa Cina. Oleh itu, penyertaan aktitivi fizikal aktif yang berterusan sebanyak 2jam setiap hari harus digalakkan untuk mengelakkan penghakisan tulang dalam process penuaan.

Kata Kunci: aktiviti fizikal harian, aktiviti riadah, kesihatan tulang, wanita menopaus berbangsa Cina

ABSTRACT

Although higher participation of intense and mechanical-loading physical activity (PA) yields significant osteogenic effects in maximizing bone mass development throughout lifespans, but specific types, intensity and frequency of PA that could help to prevent an excessive bone loss during adulthood and aging is still limited, in particular among older populations in Asia. The aim of the present study was to examine the influence of habitual PA and other lifestyle practices on bone health status among postmenopausal Chinese women aged between 51 and 78 years in Kota Bharu, Kelantan. Several method assessments were used namely, a piloted questionnaires pertaining to general characteristics, general health status, lifestyle PA, smoking and alcohol consumption practices, as well as dietary behavioral practices were gathered. A piloted PA questionnaire for the past one-year was used to assess the habitual PA levels of two domains of leisure-based and household-based activities. Bone health profiles of these participants were measured at various skeletal sites of the total body, lumbar spine (L2-L4) and proximal femur using a dual energy *X*-ray absorptiometry device (DXA), as a criteria reference method for bone health assessment. The mean age of the participants was 57.3 years, with mean age since menopause of 7.6 years. Multivariate analysis of co-variance (ANCOVA) was carried-out to examine these lifestyle practices on bone health profiles, after taking into account for other potential confounding factors such as age, age of menopause, types of menopause, and family history of osteoporosis, BMI, waist circumferences, and other dietary lifestyle practices. The findings found that postmenopausal Chinese women with higher daily PA levels both in leisure-time and

household-time physical activity were significantly associated with higher BMD levels of the total body, proximal femur and lumbar spine (L2-L4) than that of those women of lower daily PA practices. In contrary, there was not significant association found between smoking status and alcohol consumption level on any bone health indices measured. The present findings showing that higher participation in daily PA with sufficient mechanical loading exerts significant beneficial impacts on bone health among postmenopausal Chinese women. Therefore, continuous encouragement of active lifestyle practices such as daily PA levels for at least 2 hours of moderate to high-intense physical activity in a day should be highly encouraged among older populations in order to prevent an excessive bone loss during the late adulthood.

Key Words: habitual physical activity, leisure-time physical activity, Bone health, postmenopausal Chinese women

DECLARATION

I hereby declare that the thesis is my original work except for the quotations and citations which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently submitted for any other degree or purposes in Universiti Sains Malaysia or at any other institutions.

AGNES WONG

23TH JUNE 2013

I certify that Ms. AGNES WONG has carried out her study entitled The Association Of Lifestyle Physical Activity, Smoking And Alcohol Consumption Practices On Bone Health Status Of Postmenopausal Chinese Women In Kelantan as a final year research project in nutrition under my supervision. She has complied with the ethical standard and regulations in conducting her study and has completed writing her thesis. I am satisfied with her work and have no objection for the thesis to be examined by the appointed examiners by the School of Health Sciences, Universiti Sains Malaysia.

Thank you

DR FOO LENG HUAT

Supervisor

23TH JUNE 2013

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LIST OF ABBREVIATIONS

BMD	:	Bone mineral density
BMC	:	Bone mineral content
BA	:	Bone area
BMI	:	Body mass index
WHR	:	Waist hip ratio
MET	:	Metabolic equivalent
PTH	:	Parathyroid hormone
HRT	:	Hormone replacement therapy
PA	:	Physical activity
SHS	:	Second hand smoke
DXA	:	Dual energy *X*-ray absorptiometry
WHO	:	World Health Organization

CHAPTER 1

INTRODUCTION

1.0 Background of osteoporosis

Osteoporosis is defined as "*a progressive systemic skeletal disease characterized by low bone mass and micro- architectural deterioration of bone tissue, with a consequent increase in risk of skeletal fragility and susceptibility to osteoporotic fractures*" (WHO, 1994), in which the osteoporotic fractures is commonly occurs at skeletal sites of the hip, the vertebral and the wrist (Johnell & Kanis, 2006). Based on the WHO's diagnosis criteria (WHO, 1994), osteoporosis is defined as a BMD that assessed by a dual-energy *X*-ray absorptiometry (DXA) of *t*-score less than -2.5 standard deviations of an average value for reference values for young women, whereas, normal and osteopenia are defined by a BMD *t*-score of more than -1.0, and ranging between -2.5 and -1.0, respectively.

Worldwide prevalence of osteoporotic fractures has been estimated to be approximately 9.0 million in 2000, in which about 61% of these fractures attributed to osteoporosis is occurred among women, especially those after postmenopausal, with is 6-times higher than their men counterparts (Johnell & Kanis, 2006). Clinical consequences of osteoporotic fracture are huge. For instance, the risk of mortality after a hip fracture estimated to be the high (around 25 mortality per 100000 cases), in which high proportion of mortality as compared with other skeletal site fractures (Johnell & Kanis, 2006). In Malaysia, it was reported that the incidence of hip fracture among individuals

aged 50 years and above was 90 per 100,000 (Lee & Khir, 2007), and it is expecting to rise dramatically due to changing of aging populations.

Osteoporosis has been considered as an emerging major public health concerns and challenges in both developed and developing countries, including in Malaysia. It causes significant health problems that result in substantial morbidity and mortality risks, which leading to significant higher expenses and utilization of health-care related cost and resources. For instance, it is estimated that the lifetime risk associated with osteoporotic fracture at any skeletal site is high, which is ranging from 40 to 50 % in women and 13 to 22 % for men, both at the age of 50 years old (Johnell & Kanis, 2005). Similar findings was also found by a study conducted by Ioannidis and his colleagues (2009), in which there was significant increase of risk of death among those who had a vertebral and hip fracture in the first and second year compared to those who had no fracture during follow-up. According to Sànchez-Riera and his colleague (2010), it was about 20% increase risk of premature death following the hip fracture. Furthermore, osteoporotic fractures of spine, vertebrae and hips were significantly associated with higher risk of morbidity such as long term chronic pain, deformity and disability to those affected individuals (Loh & Shong, 2007).

Apart from the negative effects to affected individuals, it contributes huge costs on health care and health-care resources utilization. For instance, approximately 30% of hip fracture patients were required a long-term rehabilitation, 18% excessive long term healthcare and over 65% received long-term home-care assistance, with an estimated

cost during the first year after fracture is ranging from CAD$35,000 (RM 104,368.57) to CAD$40,000 (RM 119,278.37) annually in the subsequent years in Canada (Nikitovic *et al.*, 2013). Most of the health care resources were attributed to long term hospitalizations, costs-related to surgery, emergency visits, continuing healthcare, rehabilitation, long-term care, home care, physician services, and prescription medications. Apart from healthcare costs, it is also reported that osteoporotic fractures involve long term hospitalization. For instance, it is reported that clinical vertebral fractures resulted in 617days of hospitalization and 512 days of rehabilitation and/or long term nursing home care; hip fractures accounted for 1,306 days of hospitalization and 1,650 days of rehabilitation/nursing home care; non-hip, non-spine fractures accounted for 3,805 days of hospitalization and 5,186 days of rehabilitation/nursing home care (Ioannidis *et al.*, 2013).

It is generally-agreed that osteoporosis is attributed to a multifactorial risk factors, which generally can be classified as non-modifiable and modifiable environmental factors (WHO, 2003). Non-modifiable risk factors associated with osteoporosis are genetic factors, sex differences, hormonal status, and body composition, whereas modifiable risk factors that is include dietary and lifestyle practices. For non-modifiable factors, genetic factor plays a significant factor associated with higher risk of osteoporosis. Person with family history of osteoporosis have greater predisposition risk of osteoporosis (Fox *et al.*, 1998). In particular, parental history of hip fracture increases the daughter's risk of hip fracture by about 50% while a parental history of wrist fracture increases the risk of wrist fracture by 64%. Apart from the genetic factors,

sexes differences is also profoundly found in the prevalence of osteoporosis, whereby older women is significantly increase risk for 2-folds of getting osteoporosis than that of their men counterparts (Adam, 2005).

On the other hand, lifestyle practices such as physical activity practices have significantly associated with the risk of osteoporosis. It is generally agreed that higher participation of physical activity is important in attainment and maintaining higher bone mass throughout the lifespan (Kagan, 2002). Other lifestyle practices such as smoking and excessive alcohol consumption are also found to exert adverse effects on bone, such as increase the risk of excessive bone loss, consequently increase risk of osteoporotic fracture (Sloan *et al.*, 2010; Jin *et al.*, 2011). Another important modifiable factor is dietary intake, in which higher and adequate dietary intakes such as calcium, vitamin D, other micronutrients intake are also significantly associated with higher bone mass since they are the basic unit of bone composition.

1.1 Problem statement of the study

Osteoporosis affects approximately 200 million people and causes more than 8.9 million fracture annually worldwide (WHO, 2004). It was estimated that osteoporotic fractures occur every 3 seconds where this amounts to almost 25 000 fractures per day or 9 million globally per annual and it is affecting for every 1 in 2 women and every 1 in 5 men aged 50 years-old and above (International Osteoporosis Foundation, 2012). Elderly population is the fastest growing population in the world. With great number of population, Asia was estimated to have the most dramatic demographical changes along

with similar trends found in most western countries nowadays, in which the proportions of older people aged 50 years-old and above was projected to increase to almost 5-folds from 438million in 1990 to 1867 million in 2050, where the incidence of hip fracture was also expected to rise from 0.56million fractures reported in 1990 to 3.22million fractures by year 2050 among people aged 50 years old and above (Cooper *et al.*, 1992). Moreover, populations of Asian-origin are generally found to have lower levels of BMD as compared to their Caucasian populations, especially in women (Russell-Aulet *et al.*, 1991; Russell-Aulet *et al.*, 1993). These differences in the BMD in both men and women are mainly due to differences in the height, weight and hormonal factors. Therefore, Asian older populations are higher risk of osteoporosis. Malaysia is a multiracial country with three main ethnic groups, comprising Malays, Chinese and Indians. Several diseases have shown that certain illnesses, including osteoporosis will affect certain ethnic group more than the others due to their different genetic, environmental factors, cultures and diet practices. A marked difference in ethnicity was also found in the prevalence of osteoporotic hip fracture reported in 1996 and 1997. Older Chinese adults aged 50 years and above were found to be highest rate of hip fractures, followed by Indian and Malay (Lee & Khir, 2007).

Lifestyle practices in Malaysian populations are generally physically inactive, as indicated by a nationwide study of 6926 adults aged between 19 and 59 years showing that about three-quarters of them were travelled by passive modes of transportation (75%), with only one third were reported to have ever-exercise in past two weeks' time, and very small proportion (14.2%) had reported to have adequate exercise (at least 3

times a week for 20 minutes each session). Furthermore, majority of adults (74.0%) were engaged in sedentary activities, such as sitting, sleeping or lying down (Poh *et al.*, 200). Bringing this inactive lifestyle may increase risk of osteoporosis risk in population especially in elderly populations.

Smoking is another important risk factors of bone loss because cigarettes itself contains thousands of chemicals which is detrimental to living organisms, as well as to bone cells. They distract bone remodeling process and cause bone loss. Study carried-out by Tamaki and his colleagues (2011) found that BMD for ever-smoker either current smoker or former smoker, was significantly decreased with increasing number of smoking duration. In addition, a secondhand smoke (SHS) exposure is also possesses an adverse effect on bone health. Kim and Lee (2013) found that SHS exposure was positively associated with increased risk of osteoporosis. For example, those who cohabitant with smokers who smoked ≥20 cigarettes/day showed increased occurrences for lumbar (adjusted odd ratio of 5.4) and femoral neck (adjusted odd ratio of 4.35) osteoporosis as compared to non-exposed group, regardless of how many numbers of cigarettes/day they smoked. In year 1996, Malaysia's primary tobacco growing state, Kelantan had the highest smoking rate among other states in Malaysia, which is 31.7% (by National Health and Morbidity Survey *1996*), which may predisposition them to higher risk of osteoporosis.

Another lifestyle practice of alcohol consumption is also associated with lower bone mass. Higher consumption of alcohol consumption is associated with higher parathyroid

hormone (PTH) secretion, distracts calcitonin levels, decrease activated vitamin D, affects the level of testosterone and estrogen level, and also decrease growth hormone levels in body (Sampson, 1998). Alcohol itself decreases the bone formation cells of osteocalcin, impaired osteoblast activity, which subsequently decrease the osteoblastic activity (Sampson, 1998; Chakkalakala *et al.*, 2005).

1.2 Significant of study

Beneficial effects of healthy lifestyle practices on non-communicable diseases prevention have been well-documented throughout the lifespan. Although it is well-established that higher participation of habitual physical activity levels exert higher bone mass that could help to prevent the risk of osteoporotic fractures in postmenopausal women and elderly. However, the magnitude and intensity of habitually physical activity levels on bone health are still not precisely documented especially among older populations in Asian. For example huge cultural and lifestyle differences is found in different ethnicity, where habitual physical activity, dietary lifestyle practices may be different across the populations in Malaysia.

Understanding such lifestyle practices is important especially among older Chinese women that has highest incidence of osteoporosis compared to their Indian and Malay in Malaysia. Although several studies and interventions related to physical activity had been performed in older populations mainly from western countries (Bolton *et al.*, 2012; Marques *et al.*, 2012), there is no exact study that specifically focus on older Chinese women in Malaysia, In addition, the detailed information on magnitude, intensity, and

frequency of habitual physical activity associated with bone health status is still limited, especially among those older Chinese women after postmenopausal .

Other lifestyle practices such as smoking and alcohol consumption that are known to be common lifestyle practice among Chinese population that associated with bone health are still unknown. Such comprehensive understanding of habitual physical activity and other lifestyle practices among older Chinese women is crucial in order to tackle the osteoporosis problem among Chinese women in Malaysia. An effective lifestyle intervention can be formulated through these understanding of the magnitude, intensity, and frequency of habitual physical activity that will be beneficial to their bone health.

1.3 Objective of the study

1.3.1 General objective

To examine the influence of habitual physical activity, cigarette smoking and alcohol consumption on bone health status among postmenopausal Chinese women in Kota Bharu, Kelantan.

1.3.2 Specific objectives:

i. To determine the influence of the frequency and intensity of habitual physical activity status on bone health status among postmenopausal Chinese women in Kota Bharu, Kelantan.

ii. To determine the influence of smoking status on bone health status in postmenopausal Chinese women in Kota Bharu, Kelantan.

iii. To determine the influence of alcohol consumption on bone health status in postmenopausal Chinese women in Kota Bharu, Kelantan.

iv. To identify the lifestyle practices, bone health status, knowledge and attitude on osteoporosis of postmenopausal Chinese women in Kota Bharu, Kelantan.

1.4 Null hypothesis of the study

i. There was association between habitual physical activity and bone health status in postmenopausal Chinese women in Kota Bharu, Kelantan.

ii. There was association between smoking status and bone health status in postmenopausal Chinese women in Kota Bharu, Kelantan.

iii. There was association between alcohol consumption and bone health status in postmenopausal Chinese women in Kota Bharu, Kelantan.

iv. The lifestyle practices, bone health status, knowledge and attitude on osteoporosis of postmenopausal Chinese women in Kota Bharu, Kelantan were same as other postmenopausal women in Malaysia.

1.5 Conceptual framework of the study

Bone health is affected by a complicated multifactorial model. In this research, the main focus were on physical activity, smoking status and alcohol consumption of participant, which taken into account the confounding factors such as age, age of menopause, type of menopause, years since menopause, body mass index (BMI), waist circumferences, waist hip ratio (WHR), and some other dietary practices like caffeinated beverages intakes and calcium and/or vitamin D supplements intake (**Figure 1.1**). Physical activity was measured through MET-min/weeks of the participant. The smoking status was measured by determining whether one is a passive smoker or not since none of them was a smoker. Alcohol consumption was assessed through the identification of whether the participant drinks alcohol on weekly basis. Pearson correlation coefficient test and multivariate (ANCOVA) test were used to test whether the hypothesis.

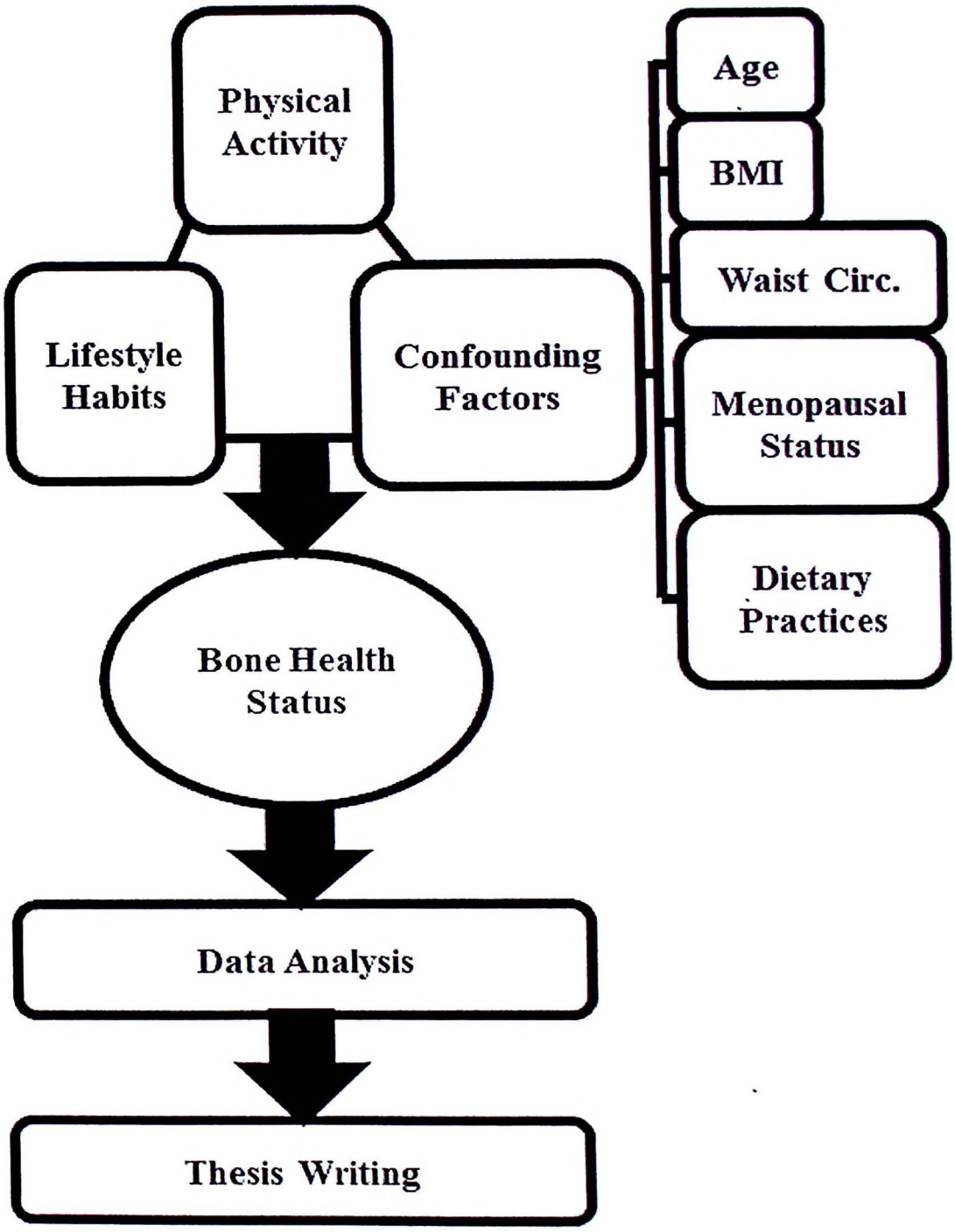

Figure 1.1. Conceptual framework of research study

CHAPTER 2

LITERATURE REVIEW

2.0 Osteoporosis overview

Osteoporosis is considered as a silent disease because most of people are not aware they have such condition until they have osteoporotic fractures. The most common skeletal site of having fractures are hip, vertebral and forearm fractures as well as other peripheral fractures related to low density or poor quality of bone mass such as proximal humeral, pelvic, rib, proximal tibia or ankle fractures (Johnell and Kanis, 2006). The consequences of an osteoporotic fracture for an individual vary from short-term pain to chronic disability and premature death.

2.1 Prevalence of osteoporosis

It has been projected by Cooper and his colleagues (1992) that the world population of elderly aged 50 years old and above increase dramatically by the year 2050, especially those in Asian countries (**Table 2.1**). As compared to other populations from western countries such as Europe and North America, Asia has reported to have larger number of older population ages 50 years-old and above in year 1990, with a total of 438.394 million people, and it is projected to increase about 4 folds to 1867.398 million by the year 2050. Hence, Asia also leading in the projected numbers of hip fractures as compared to Europe, North America and Africa, due to its increasing with aging society in Asian countries as shown in Table 2.1.

Table 2.1. Projection of the total population age 50 and above and hip fractures in 1990 and 2050 for Asia, Europe, Africa and North America (In Million).

Year/	Asia		Europe		Africa		North America	
Gender	Pop	Frac	Pop	Frac	Pop	Frac	Pop	Frac
1990								
Women	221.535	0.379	84.809	0.307	26.537	0.003	39.550	0.251
Men	216.859	0.178	66.681	0.091	24.813	0.003	31.620	0.097
Total	**438.394**	**0.557**	**151.490**	**0.398**	**51.350**	**0.006**	**71.170**	**0.348**
2050								
Women	979.001	2.273	119.365	0.530	222.018	0.037	75.478	0.531
Men	888.397	0.948	104.113	0.187	197.249	0.028	63.355	0.222
Total	**1867.398**	**3.221**	**223.478**	**0.717**	**419.267**	**0.065**	**138.833**	**0.753**

Abbreviations: Pop, Regional population in million; Frac, Number of hip fractures.

Source: Cooper, *et al.*, 1992

According to Sànchez-Riera *et al.* (2010), Asia appears as the world region with the lowest T-score, which is consitent with the fact that Asian ethnicity is related with lower BMD values compared with other ethnicities (**Figure 2.1**), making Asian is more predisposing to higher risk of osteoporotic fractures as compared with other regions of the world.

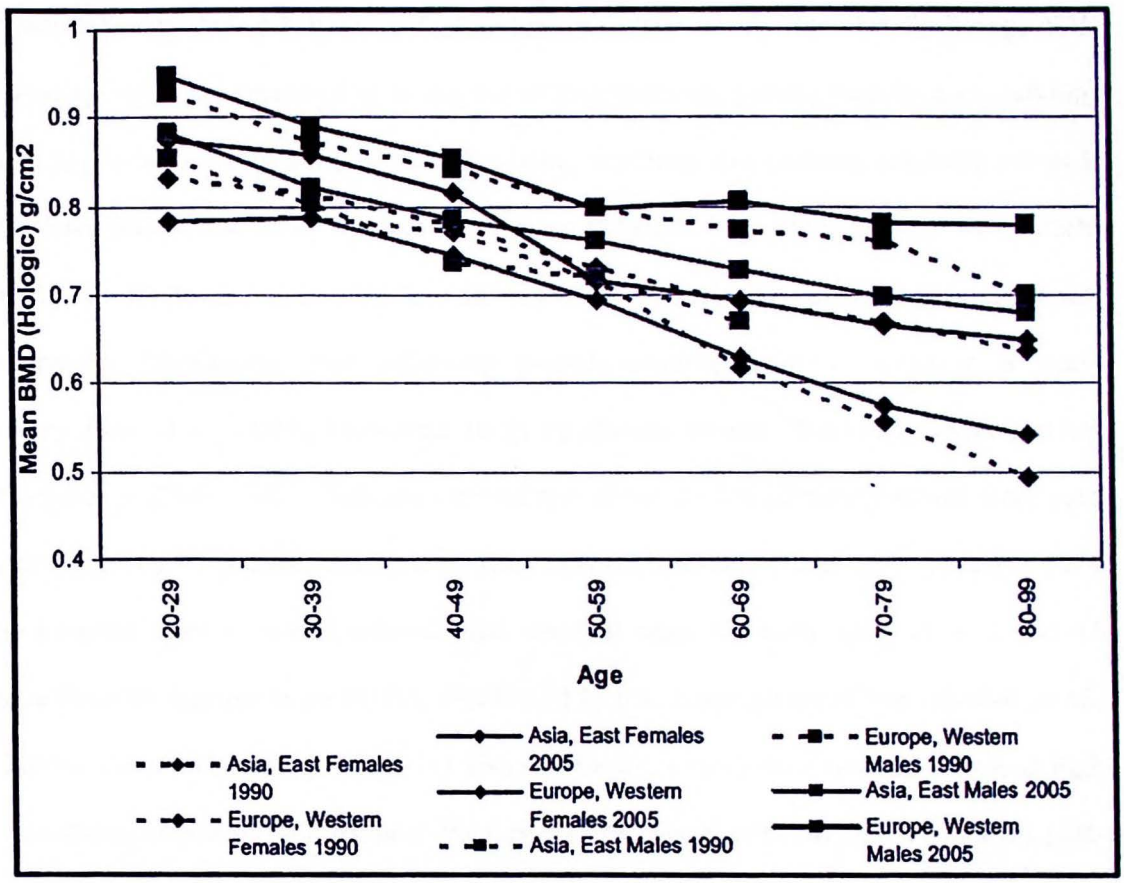

Figure 2.1. Mean BMD (Hologic) for females and males in Asia East and Western Europe for 1990 and 2005 (Sànchez-Riera *et al.*, 2010).

2.2 Clinical consequences

Osteoporosis causes a lot of disables and consequently declining in body functioning in life following a fracture in especially in old ages. In one Epidemiologic Study in 594 hip fracture elderly cohorts aged 65 and above, carried-out by Magaziner and colleagues (2003) in United States, showed that for every 100 hip fracture cases, about 26 of them were walking disabled, 22 more were transferring disabled, and six more were grooming disabled over 2 years follow by their fractures. Their respondents who

fractured a hip during follow-up declined more in basic Activities of daily living, ADL (bathing, dressing, transferring in and out of bed, toileting, getting outside, and walking) and upper-body functioning (difficulty sitting, reaching up overhead, reaching out as if to shake hands, and using the fingers to grasp objects) . This study showed that elderly with hip fractures have a decline in both lower-extremity functioning and upper-extremity functioning over follow-up periods ranging from 6 weeks to 6 years (Magaziner *et al.*, 2003). In another study conducted among Thai elderly who had hip fractures in Chaing Mai, Thailand showed that about 24.2% of these patients were died after one year: 7 patients during the initial hospitalization, 64 later at home and 9 later in hospital after a second referral. The survival rates for both sexes at 3, 6 and 12 months after fracture were 91.5%, 88.2% and 83.0%, respectively (Chariyalertsak *et al.*, 2001). Yoon and colleagues (2011) also conducted a study in Korea that showed high cumulative mortality rate for post-fracture patient, where over the first 12 months post-fracture was 18.8% (3,166/16,866) in 2005 and 17.8% (3,307/18,610) in 2007.

2.3 Socio-economic consequences

Increase in osteoporotic fractures has led to increase in hospitalization cost due to prolonged bed-stay and long-term care of patients. Osteoporotic fractures in the United States in 1995 led to more than half a million hospitalizations, over 800,000 emergency room encounters, more than 2.6 million physician office visits, and the placement of nearly 180,000 individuals into nursing homes (**Table 2.2**). Hip fractures account for the largest proportion (total of 63 % or $11.3 billion) of medical care costs (Ray *et al.*, 1997).

Table 2.2. Distribution of Health Resources Utilization Attributable to Osteoporotic Fractures among Person ≥ 45 years of age in the United States in 1995, by Type of Service and Fracture.

Type of service	*All fractures*	*Type of fracture (%)*			
		Hip	*Forearm*	*Spine*	*Other sites**
Inpatient hospital					
discharges w/ primary diagnosis	432,448	57.0	3.1	6.8	33.0
discharges w/ secondary diagnosis	114,971	19.8	4.2	13.9	62.1
Nursing home residents	179,221	76.9	0.9	2.7	19.5
Outpatient					
physician visits	2,486,272	14.4	20.5	2.4	62.7
emergency room encounters	807,349	21.3	9.0	3.6	66.2
hospital encounters	147,417	13.7	14.9	4.8	66.6
physical therapy sessions†	193,557	22.9	38.7	0.6	37.8
diagnostic radiology†	1,902,211	18.1	16.8	3.6	61.5
medications†‡	2,358,003	13.3	12.9	3.2	70.6
home health care visits	2,205,026	59.5	2.2	2.9	35.4
ambulance encounters	219,815	35.8	0.0	9.5	54.7
orthopedic and other supplies	491,555	28.4	0.0	8.6	63.0

* Other sites include fractures of the pelvis, humerus, and other sites.
† Services provided during outpatient physician, outpatient hospital, and emergency room encounters.
‡ Includes prescription and nonprescription medications.

Source: Ray *et al.*, 1997.

In Germany, with the sharp increase in OAF, the growing demand on long-term care and hospital care was expected (Bleibler *et al.*, 2012). Indirect costs were expected to increase from 172 million Euros in 2010 to 1.4 billion Euros in 2050. The finding was mainly driven by the loss of productivity due to the inability to engage in unpaid work because of premature death. In total, OAF was expected to cause approximately 88.5 billion Euros aggregated direct (76 %) and indirect (24 %) costs from 2010 to 2050. Women accounted for about 77 % of these costs. The main cost drivers for direct costs will be long-term care costs after hip fractures with 38.5 billion Euros (43.5 %) and hospital care costs with 22.6 billion Euros (25.5 %). Productivity losses of 13.2 billion

Euros (14.8 %) due to osteoporosis-related premature deaths will be the largest share in indirect costs. According to fracture types, hip fractures will account for 66.1 % of all direct and for 55.8 % of all indirect costs. The fracture type with the second largest impact on overall costs will be clinical vertebral fracture with a percentage share of 15.4 %. The lowest impact on overall costs will be wrist fracture with a share of 3.6 %. **Figure 2.2** displays the cumulative direct costs for long-term care due to incident osteoporosis-related hip fractures in between 2010 and 2050.

The cost of hospitalization due to fractures increases with the days of patient's stay in hospital. McGowan and his colleagues (2013) also conducted a study in Ireland, and showed that the number of patient-days per year spent in hospital for all osteoporotic-type fractures in over 50-year age group increased from 97,753 days in 2000 to 132,786 days in 2009 in women with an increase of 36 %, and from 33,131 days in 2000 to 56,380 days in 2009 in men with an increase of 70 %. On the other hand, the annual Diagnosis-Related-Groups (DRGs) cost of hospitalization for all types of fractures also increased by 30% in women and by 31% in men from year 2003 to year 2008 (McGowan *et al.*, 2013).

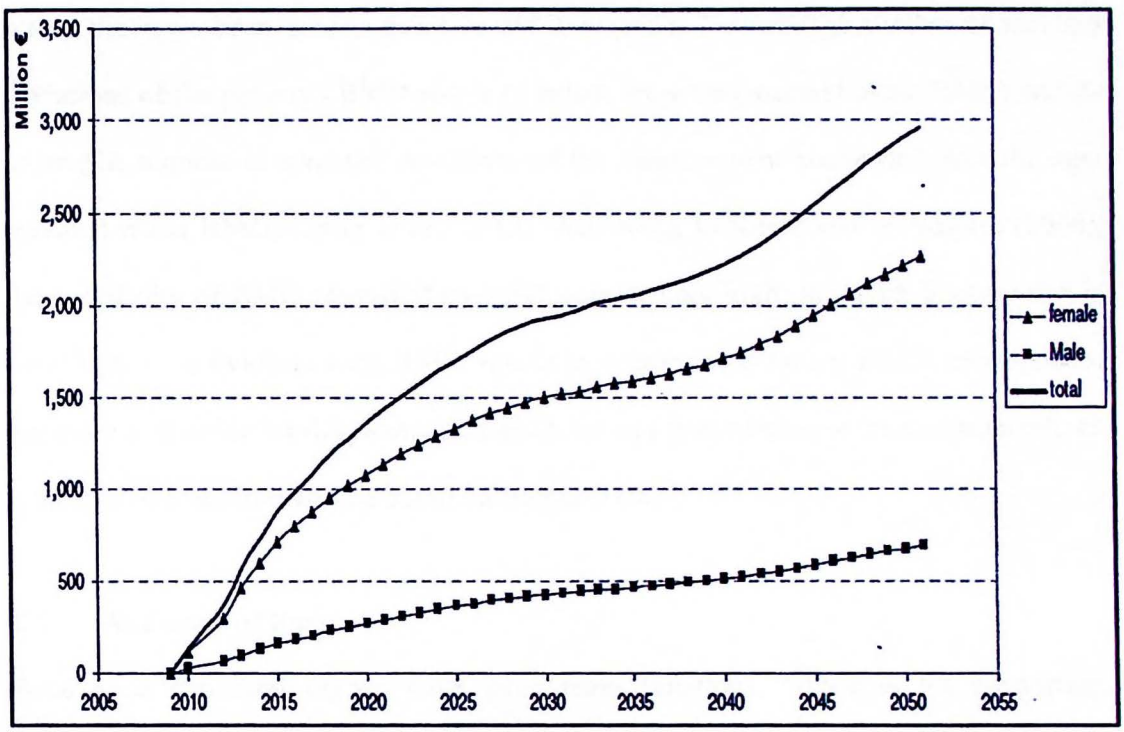

Figure 2.2. Direct long-term care cost estimation due to incident osteoporosis attributed hip fractures by gender within the years 2010 and 2050 (Bleibler *et al.*, 2012).

2.4 Assessment of bone mass

Adams (2005) stated that low bone mineral density (BMD) can be the result of either low peak bone mass or accelerated bone loss. Measuring bone mineral density is important in investigating bone-losing disorders. BMD is expressed in grams per unit area. The Gold standard for measuring BMD is Dual-energy X-ray absorptiometry (DXA). Other instruments for BMD measurement are radiography absorptiometry, Single-energy X-ray absorptiometry (SXA) and Quantitative computed tomography (QCT). Quantitative Ultrasound (QUS) has also been used to assess skeletal status in osteoporosis where the methods evaluated are broad-band ultrasound attenuation (BUA) and speed of sound (SOS) at the heel (WHO, 2003). Traditionally, there is two types of

scores that have been used to quantify BMD, which is T-score (the number of standard deviations of the patient's BMD above or below the young-normal mean BMD) and Z-score (the number of standard deviations of the measurement above or below the age-matched mean BMD) (Saag *et al.,* 2010). According to Kanis and colleagues (2008), the specificity of BMD measured by DXA scan is very high, in which fracture risk is very high in individuals with BMD values in osteoporosis range. BMD measurement therefore is suitable for diagnostic threshold, but not intervention or treatment threshold. Intervention threshold will be based on fracture risk.

2.5 Anatomy of Bone

Bone as a structural organs have three main functions, which is for supporting, protecting and leveraging. It supports every part of the body in a wide variety of positions and load-bearing; it protects important soft tissue and also acts as jointed levers that facilitate a range of movements. Bone also act as reservoir in body composition regulation. Bone consists of largely collagenous matrix (type 1 collagen fibres, numbers of growth factors, non-collagenous proteins, and bone morphogenetic protein) impregnated with mineral salts and populated by bone cells (Berg *et al.*, 2009). The mineral matters of bone are mainly calcium and phosphate in the form of crystalline hydroxyapatite which laid down in osteoid at the calcification front (Solomon *et al.*, 2010).

There are three types of bone cells. The first type is osteoblast, which is responsible for bone formation and osteoclast activation. Their number will decrease during advanced ageing. The second type is osteocytes, which is referred as spent osteoblasts. The third

type is osteoclast, which is the principal mediator of bone resorption. The mature bone tissue is known as lamellar bone, which exist in two structurally forms, the compact (cortical) bone and the cancellous (trabecular) bone (Adams, 2005). The compact bone is the outer walls of all bones and the cancellous bone, which lies in the middle part of the bone, is more porous than cortical bones.

2.5.1 Bone remodeling processes

Bone develops in two different ways, which are ossification of a prior cartilage model or framework (endochondral ossification) and by direct intramembranous ossification. Bone remodeling is the sequential process of bone resorption and formation. Prompted by osteoblasts, osteoclasts carry out bone resorption for 2 to 4 weeks. After resorption ceased, the excavated surface is covered with osteoblast and new bone is formed by the mineralization of osteoid that laid down on the bone surface. The entire remodeling cycle takes 4 to 6 months to complete. Bone remodeling is influenced continuously by an array of hormones, cytokines systems, dietary elements, medication and signals form mechanical stresses that impinge on any part of the Receptor activator of nuclear factor kappa-B ligand (RANKL)/ Receptor activator of nuclear factor kappa-B (RANK)/ osteoprotegerin (OPG) traid (Solomon *et al.*, 2010).

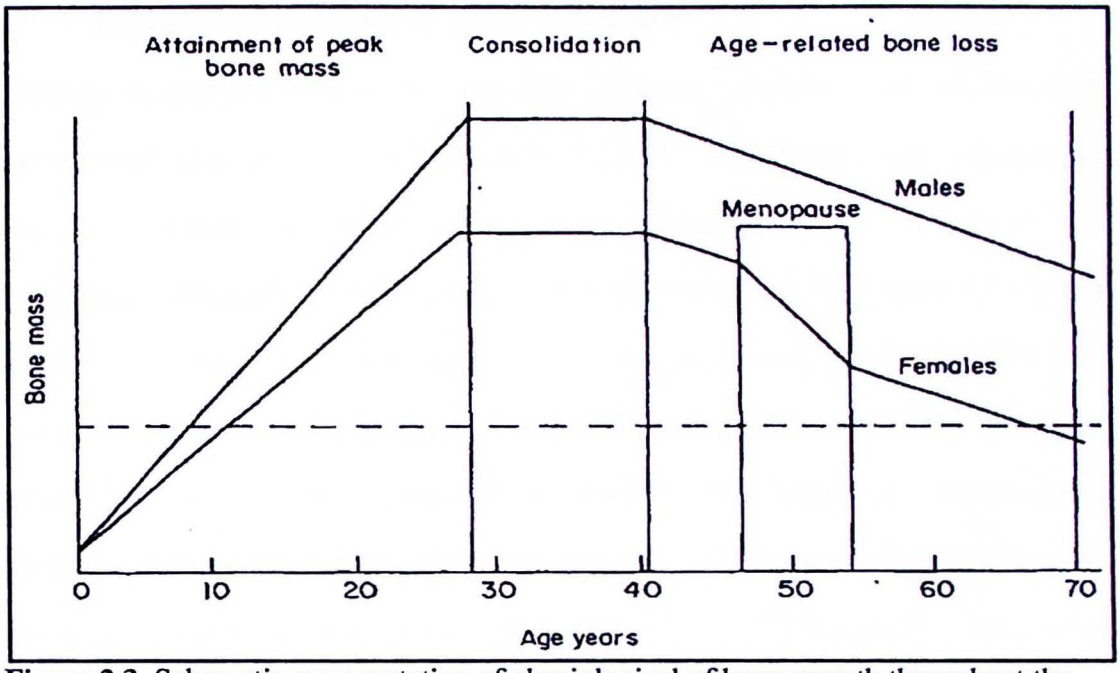

Figure 2.3. Schematic representation of physiological of bone growth throughout the lifespan (Compston, 1990). (- - - Fracture threshold)

2.6 Physiology of bone growth and maintenance in populations throughout the lifespans

Peak bone mass and size is achieved around the age of 15–20 years in women and later in men. After achieving peak bone mass, the bone remodeling process continues at a slower rate with bone resorption predominant over bone formation (Raisz & Seeman, 2001). In the fourth decade or early fifth decade of life, the age-related bone loss begins (**Figure 2.3**) (Compston, 1990). There will be an excessive bone loss with a significant increase in bone resorption over bone formation in women after age of 50 as a consequence of cessation of estrogens production due to menopause (Demontiero *et al.*, 2012). This will indirectly increase the susceptibility to have low bone mass and consequently will increase the risk of osteoporotic fractures.

2.7 Etiology of osteoporosis in adults and elderly

Etiology of primary osteoporosis includes Idiopathic juvenile osteoporosis, post-menopausal (type 1) osteoporosis, senile (type 2) osteoporosis and osteogenesis imperfect. Postmenopausal osteoporosis is the physiological bone depletion that normally accompanies ageing and loss of hormonal gonadal activity. From the starting and the following 10 years of menopause, bone loss accelerates to around 3% per year compared to 0.3% per year during preceding two decades. Senile osteoporosis, the age-related bone loss happens because the impaired in bone formation associated with secondary hyperparathyroidism due to reduced calcium absorption from the intestine secondary to decreased renal production of the active for of vitamin D. Osteogenesis imperfect is congenital disorders due to gene mutation associated with osteoporosis of variable severity (Berg *et al.*, 2009).

2.8 Risk factors associated with osteoporosis

As a multifactorial disease, the risk factors for osteoporosis includes low BMD, age, gender, Caucasian, Asiatic ethnicity, loss in body weight, low body weight, earlier fragility fracture, family history of hip fractures, smoking, glucocorticoid therapy, premature menopause, primary or secondary hypogonadism, primary or secondary amenorrhea, excessive alcohol abuse, high turnover rate of bone, deficient vitamin D, diminished sun exposure, long immobilization, low calcium intake, poor visual acuity, and neuromuscular diseases (Kanis, 2002). However, each factor has different effects on different part of bone. Some might be protected factors while some are risk factors. WHO technical report series 921 has summarized the

Table 2.3. Risk factors (-) and protective factors (+) for axial and appendicular bone mineral density in women at age 65 years and above [a].

Variable	Skeletal site		
	Lumbar spine (DXA)	Femoral neck (DXA)	Distal radius (SPA)
Age		−−	−−
Weight	+++	+++	+++
Fracture in mother	−−	−−	−−
Age at menopause	+	+	++
Estrogen use	+++	+++	+++
Quadriceps strength		++	
Grip strength			+++
Thiazide use	+++	++	+++
Non-thiazide diuretic use	++		
Current smoker			−−
Number of alcoholic drinks in lifetime	+		
Dietary calcium intake		++	+
Lifetime caffeine intake			−
Non-insulin-dependent diabetes mellitus		+++	+++
Gastric surgery			−−
Recent or past physical activity	+	+	

DXA, dual-energy X-ray absorptiometry; SPA, single-energy photon absorptiometry.
[a] The strength of the correlations from multivariate analyses is indicated by the number of symbols: three symbols indicate 3% or greater change in bone mineral density per unit change in the variable; two symbols, a 1–3% change; and one symbol, a change of less than 1%.

Reference: Orwoll *et al.*, 1996

related findings based on a cross-sectional study by Orwoll and his colleagues (1996) in **Table 2.3.** These factors are further divided into modifiable and non-modifiable factors. Those non-modifiable factors including those risk factors that cannot be manipulated or changed, such as ageing, menopause, being as a female, with family history, small body size, etc. The modifiable factors are mostly resulted from our lifestyle practices which can be modified or change depending on the person that practices it, such as smoking, sedentary lifestyle, malnutrition, very thin, low calcium intake, vitamin D intake, and sunlight exposure. In addition, greater weight, older age at menopause, greater physical activity, moderate consumption of alcoholic beverages, treatment with diuretics and