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FACTORS CONTRIBUTING TO BONE MINERAL DENSITY AMONG CHINESE WOMEN IN THE KLANG VALLEY, MALAYSIA

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By

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Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the Degree of Master of Science

FACTORS CONTRIBUTING TO BONE MINERAL DENSITY AMONG CHINESE WOMEN IN THE KLANG VALLEY, MALAYSIA

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LAU LEE TING

January 2016

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Osteoporosis and its related fractures have become epidemic health problem over the years. However, the studies on bone mineral density (BMD) and its related factors were limited in Malaysia. The purpose of this study was to determine the bone health status and examine the contribution of sociodemographic background, family history of fracture, reproductive history, biochemical measures, dietary intake, lifestyle practices as well as anthropometric measurements towards BMDs among healthy Chinese women residing in the Klang Valley. Subjects were participants from a 12-month milk supplementation study conducted from 2012 to 2014. There were 263 women, of which 137 were premenopausal and 126 were postmenopausal women.

A pre-tested questionnaire and three validated questionnaires, namely International Physical Activity Questionnaire (IPAQ), Weekly Sun Exposure Questionnaire and Food Frequency Questionnaire (FFQ), were administered through interview to collect details of all variables, except biochemical measures which were collected through fasting blood and urine samples. Dual-energy X-ray absorptiometry (DXA) scan examined BMD at total body, L1-L4 spine and total hip. All variables that were significant at bivariate analysis were selected into respective models of BMDs in stepwise multiple linear regression (MLR).

The mean age of the subjects was 50.0 ± 10.3 years. Prevalence of osteoporosis was 1% and 4% at total body and lumbar spine BMD in postmenopausal subjects. There were 1% of premenopausal subjects who had L1-L4 spine and total hip BMD below the expected range for age. Postmenopausal subjects presented significant lower mean BMD at all sites ($p<0.05$). Older age, lower education level and lower monthly household income as well as higher parity, bone turnover rate [Procollagen Type 1 N-Terminal Propeptide (P1NP), osteocalcin (OC) and C-telopeptide of type I collagen crosslinks (CTX)], energy and nutrients intake, physical activity measure, body mass index (BMI), fat mass, measures of central obesity were observed among postmenopausal women ($p<0.05$). Vitamin D deficiency (<50 nmol/L) was presented in 42.5%, of which 2/3 was contributed by premenopausal subjects. Mean serum 25-

hydroxyvitamin D, physical activity measure, habitual and current calcium intake were reported as 56 ± 20 nmol/L, 1040 MET-minutes/week, 499 ± 202 mg/day and 330 mg/day, respectively.

Among the variables, menopausal status had shown to develop the strongest correlation with BMDs, especially at L1-L4 spine BMD ($r = -0.570$, $p<0.01$). Age and biochemical measures, particularly urinary CTX also demonstrated moderate and negative association with BMDs ($p<0.01$). Besides, weight and lean mass presented higher magnitude than BMI and fat mass, respectively, in positive relation with BMDs. Despite weaker associations, lower BMDs were associated with lower education level, presence of family history of fractures, multiparous, higher physical activity measure, smoking and higher central obesity measures.

Stepwise multiple linear regression analyses on three skeletal sites showed 40.1%, 42.1% and 17.2% variances in the regulation of BMD at total body, L1-L4 spine and total hip, respectively. Significant contributors of BMDs were as following: urinary CTX towards all BMD sites; menopausal status and lean mass towards total body and L1-L4 spine BMD; weight towards total hip BMD.

In conclusion, this study presented the bone heath status and identified risk of low bone mass significantly contributed by high CTX, being postmenopausal, low anthropometric measurements of lean mass and weight among Chinese women throughout middle-aged and senior adulthood. Where low physical activity level, low dietary calcium intake and vitamin D deficiency were prevalent, appropriate health promotion programs should be carefully planned to optimize bone health status among Chinese women in Malaysia.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk Ijazah Master Sains

FAKTOR-FAKTOR MENYUMBANG KEPADA KEPADATAN MINERAL TULANG DALAM KALANGAN WANITA CINA DI LEMBAH KLANG, MALAYSIA

Oleh

LAU LEE TING

Januari 2016

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Osteoporosis dan keretakan tulang telah membawa masalah kesihatan secara epidemik selama ini. Walaubagaimanapun, kajian tentang faktor berkaitan dengan kepadatan mineral tulang (KMT) masih terhad di Malaysia. Kajian ini bertujuan untuk menentukan status kesihatan tulang dan menguji sumbangan latar belakang sosiodemografik, sejarah retak tulang keluarga, sejarah reproduktif, ukuran biokimia, pengambilan makanan, amalan gaya hidup dan ukuran anthropometrik terhadap KMT dalam kalangan wanita cina yang sihat di Lembah Klang. Responden kajian ini terdiri daripada 263 wanita yang menyertai kajian suplementasi susu selama 12 bulan bermula tahun 2012 hingga 2014. Antaranya, terdapat 137 wanita pra-menopaus dan 126 wanita pos-menopaus.

Sesi temubual dijalankan berpandukan satu borang soal selidik yang dipra-uji dan tiga borang soal selidik yang disahkan, iaitu borang soal selidik aktiviti fizikal antarabangsa (IPAQ), borang soal selidik pendedahan cahaya matahari mingguan dan kekerapan pengambilan makanan (FFQ) untuk mengumpul semua butiran pembolehubah kajian kecuali ukuran biokimia yang dikumpul melalui sampel darah dan kencing puasa. Imbasan dual-energy X-ray absorptiometry (DXA) dijalankan untuk mengukur KMT pada bahagian keseluruhan tubuh, lumbar dan pangkal pinggul. Semua pembolehubah yang signifikan pada ujian pekali dipilih untuk model KMT dalam analisis regresi linear berganda.

Min umur responden ialah 50.0 ± 10.3 tahun. Seramai 1% dan 4% responden pos-menopaus dikategorikan sebagai osteoporosis pada bahagian keseluruhan tubuh dan lumbar manakala 1% responden pra-menopaus mempunyai KMT di bawah jangkaan umur. Kepadatan mineral tulang dalam kalangan responden pos-menopaus adalah lebih rendah ($p<0.05$). Secara keseluruhannya, responden pos-menopaus adalah lebih berumur, berpendidikan lebih rendah, pendapatan isi rumah lebih rendah, lebih pariti, mempunyai kadar pertukaran tulang [Procollagen Type 1 N-Terminal Propeptide (P1NP), osteocalcin (OC) dan C-telopeptide of type I collagen crosslinks (CTX)] yang lebih tinggi, mempunyai pengambilan tenaga dan nutrien makanan yang lebih tinggi,

lebih aktif secara fizikal dan mempunyai ukuran antropometrik [indek jisim badan (IJT), jisim lemak badan, obesiti abdomen] yang lebih tinggi berbanding dengan responden pra-menopaus ($p<0.05$). Seramai 42.5% responden menghidapi kekurangan vitamin D (<50 nmol/mL) dan kira-kira 2/3 disumbangkan daripada responden pra-menopaus. Min serum 25-hydroxyvitamin D, ukuran aktiviti fizikal, pengambilan kalsium lazim dan semasa ialah 56 ± 20 nmol/L, 1040 MET-minit/minggu, 499 ± 202 mg/hari and 330 mg/hari masing-masing.

Antara pembolehubah-pembolehubah, ujian pekali menunjukkan kolelasi yang paling kuat di antara status menopaus dengan KMT pada bahagian lumbar ($r= -0.570$, $p<0.01$). Umur dan ukuran biokimia, terutamanya CTX mempunyai perkaitan negatif yang serderhana dengan KMT pada semua bahagian ($p<0.01$). Selain itu, berat badan dan jisim otot menunjukkan magnitud korelasi yang lebih tinggi daripada IJT dan jisim lemak dalam perkaitan positif dengan KMT pada semua bahagian. Walaupun berkorelasi lemah, KMT menurun secara signifikan dengan tahap pendidikan, mempunyai sejarah retak tulang keluarga, lebih pariti, lebih aktif secara fizikal, merokok dan lebih tinggi ukuran obesiti abdomen.

Analisis regresi linear berganda menjelaskan 40.1%, 42.1% dan 17.2% varians KMT pada bahagian keseluruhan tubuh, lumbar dan pangkal pinggul masing-masing. Penyumbang KMT yang signifikan adalah seperti berikut: CTX terhadap semua bahagian KMT; status menopaus dan jisim otot terhadap KMT pada bahagian keseluruhan tubuh dan lumbar; berat badan terhadap KMT pada bahagian pangkal pinggul.

Kesimpulannya, kajian ini menunjukkan status kesihatan tulang dan mengenalpasti risiko KMT yang rendah disumbang secara signifikan oleh CTX yang tinggi, pos-menopaus, ukuran anthropometrik yang rendah (jisim otot dan berat badan) dalam kalangan dewasa dan warga emas. Program kesihatan yang mengutamakan pengamalan gaya hidup yang aktif, pengambilan cukup kalsium dari makanan dan peningkatan status vitamin D hendaklah dirancangkan untuk mengoptimumkan status kesihatan tulang dalam kalangan wanita cina di Malaysia.

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I certify that a Thesis Examination Committee has met on 28 January 2016 to conduct the final examination of Lau Lee Ting on her thesis entitled "Factors Contributing to Bone Mineral Density among Chinese Women in the Klang Valley, Malaysia" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Master of Science.

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This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in Rule 41 in Rules 2003 (Revision 2012-2013) were adhered to

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Name of Member of Supervisory Committee: Professor Dato' Dr. Lye Munn Sann

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Name of Member of Supervisory Committee: Dr. Chin Yit Siew

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LIST OF ABBREVIATIONS

AFM	Appendicular fat mass
AOI	Android-to-gynoid ratio
ASEAN	Association of Southeast Asian Nations
BMD	Bone mineral density
BMI	Body mass index
BTM	Bone turnover markers
CSDH	Commission on Social Determinants of Health
CT	Computed tomography
CTX	C-telopeptide of type I collagen crosslinks
DBP	Vitamin D binding protein
DOSM	Department of Statistics Malaysia
DXA	Dual-energy X-ray Absorptiometry
eGFR	Estimated glomerular filtration rate
FFQ	Food Frequency Questionnaire
GDP	Gross Domestic Product
HRQoL	Health-related quality of life
IGF	Insulin-like growth factor
IGF-1	Insulin like growth factor I
IOF	International Osteoporosis Foundation
IOM	Institute of Medicine
IPAQ	International Physical Activity Questionnaire
IPH	Institute for Public Health
ISAK	International Society for the Advancement of Kinanthropometry
ISCD	International Society for Clinical Densitometry
KNHANES	Korean National Health and Nutrition Examination Survey
MANS	National Malaysian Adult Nutrition Survey
MET	Multiples of the resting metabolic rate
MOH	Ministry of Health Malaysia
MRI	Magnetic resonance imaging
NCCFN	National Coordinating Committee for Food and Nutrition Malaysia
NHANES III	The Third National Health and Nutrition Examination Survey
NHMS III	The Third National Health and Morbidity Survey
NHWS	National Health and Wellness Surveys
NIH	National Institute of Health
NOF	National Osteoporosis Foundation
PBM	Peak bone mass
PLI	Poverty Line Income
PPAR	Peroxisome proliferator activated receptor
PTH	Parathyroid hormone
P1NP	Procollagen Type 1 N-Terminal Propeptide
QALYs	Quality-adjusted life years
RNI	Recommended Nutrient Intakes
SD	Standard deviation
SES	Socioeconomic status
SPSS	Statistical Package for Social Sciences
SWAN	Study of Women's Health Across the Nation

TEM	Technical Error of Measurement
UKMMC	Universiti Kebangsaan Malaysia Medical Centre
WHO	World Health Organization
WHO/IOTF/IASO	World Health Organization, the International Association for the Study of Obesity and the International Obesity Task Force
WHR	Waist-to-hip ratio

GLOSSARY OF TERMS

Bone mineral density	Bone mineral density is a globally recognized surrogate measurement of bone strength that could be most accurately measured by Dual-energy Absorptiometry. It is expressed in absolute terms of grams of mineral per square centimetre scanned (g/cm^2) and its relationship to two norms, namely Z-score and T-score (National Osteoporosis Foudation, 2010).
Dual-energy X-ray Absorptiometry (DXA)	Dual-energy X-ray Absorptiometry is the most highly developed technique that is thoroughly validated biologically to assess bone mass, which is regarded as "gold standard" for the assessment of osteoporosis and for the evaluation of therapies (Blake & Fogelman, 2009; World Health Organization, 2003b).
Osteoporosis	Osteoporosis is a bone disease characterized by porous and brittle bone, which increase the susceptibility of the individual towards fractures (NIH Consensus Development Panel on Osteoporosis Prevention and Therapy, 2001).
Fracture	Fracture in this thesis are referring to osteoporotic fracture that is contributed from low energy traumas which may occur during a fall from a standing height, or less, or traumas that would not cause fracture in healthy individual (Melton et al., 1997).

CHAPTER 1

INTRODUCTION

1.1 Introduction

Bone is essential for growth, mobility, protection, storage of mineral and support to human body (Boskey & Coleman, 2010). Since last century, bone health had received much concern from the healthcare professions and public. National bone health related bodies and organizations such as International Osteoporosis Foundation (IOF), National Osteoporosis Foundation (NOF), Malaysian Osteoporosis Society and Malaysian Orthopaedic Association were established with mission to serve as connection platform to resources and information on bone health. Of which, many were dedicated to create awareness, spread the knowledge and increase understanding among health professionals, patients, populations at risk of bone related diseases and general public. These bodies were passionate about communicating disease prevention, early detection and appropriate treatment of bone related diseases including osteoporosis.

Osteoporosis is a bone disease characterized by porous and brittle bone, which increase the susceptibility of fractures. In the past, osteoporosis was perceived as an inevitable condition along with ageing for an individual lost bone mass as they aged (Holroyd, Cooper, & Dennison, 2008). Susceptibility to fracture was described as the most devastating outcome of osteoporosis. Thus, the incidence of osteoporosis is best measured by incidence of fractures (Handa, Kalla, & Maalouf, 2008). Osteoporosis causes more than 8.9 million fractures every year, of which majority of these incidences were reported in Europe, Western Pacific and Southern Asia. These regions collectively contributed to 96% of all fractures worldwide. Astonishingly, Southeast Asia accounted for 15.3% of the statistic (Johnell & Kanis, 2006).

Osteoporosis is a relevant socioeconomic burden at individual, family, health service and societal level. It is a major public health concern that may bring major implications into future (Guillemin et al., 2013; Harvey, Matthews, Collins, & Cooper, 2013; Qu et al., 2014). In Europe, osteoporotic fractures were estimated to cost €37.4 billion in year 2010. The first year post fracture, subsequent year of long term fracture care, pharmacological costs accounted for 66%, 29% and 6% of the total costs, respectively (Hernlund et al., 2013). In Malaysia, the direct hospitalization cost for hip fractures was estimated at USD6 million in year 1997 (IOF, 2009). Such estimation however did not take into account the costs incurred in rehabilitation and long term nursing care. Quality-adjusted life years (QALYs) lost associated with osteoporosis incorporate both the health-related quality of life (HRQoL) and life years lost due to fracture (Hernlund et al., 2013). In European Union, there were approximately €1.2 million QALYs lost due to osteoporosis in 2010 with women experienced most of the QALYs lost as compare to men. Fractures, especially hip and vertebral fractures that associated with increased mortality, were estimated to cause 2/3 life years lost. When the cost and

QALYs lost were combined and valued at 2 times of Gross Domestic Product (GDP), the cost of osteoporosis in European Union was amounted to €98 billion in 2010 (Hernlund et al., 2013).

Over the past three decades, the incidence of hip fracture incidence has raised two- to three-fold in most Asian countries (IOF, 2009). Recent finding also suggested that 30% of the hip fractures occurred worldwide aroused from Asian population (Cooper et al., 2011). With rapid urbanization happening parallel to the rising fracture rate, it was suggested that urbanization could be the main contributors through decreased physical activity, increased in prevalence of vitamin D deficiency, calcium intake inadequacy and other lifestyle factors (Alves, Castiglione, Oliveira, Sousa, & Pina, 2014; Ballane et al., 2014; Lau et al., 2001). In the Malaysian context, Chinese presented the highest rates of hip fractures compared to Malays and Indians, which constituted 63% of all cases. Race and gender-specific incidence data illustrated that Chinese females reported the highest incidences of hip fractures (220 per 100,000). Female were twice more vulnerable to fractures compared to males (Lee & Khir, 2007), which was in concordance with the findings worldwide (Kanis et al., 2012). The plausible explanation might be due to smaller bone size, weaker bone structure and strength with accelerated loss during advancing age in female comparing to males (Havill, Mahaney, Binkley, & Specker, 2007; Yates, Karasik, Beck, Cupples, & Kiel, 2007).

1.2 Problem statement

Despite the magnitude of fracture were widely reported, the epidemiology of osteoporosis was still underrated, underdiagnosed and undertreated (IOF, 2009) as it is a "silent disease" with symptomless nature during disease progression (Barling, 2013; Iacono, 2007). Advance technologies are invented nowadays to assist in the assessment of bone health, but many individuals who have osteoporosis are still unaware of their condition until a fracture occurs [Iacono, 2007; Ministry of Health Malaysia (MOH), 2012; NOF, 2010].

Low bone mineral density is multifactorial. Given that osteoporotic fracture can be predicted from low bone mineral density (BMD) (Kanis, 2002), some available evidence revealed systematically lower BMD being observed among Asian comparing to the White counterparts (Mehta et al., 2004; Roy et al., 2005). Several physical, nutritional and lifestyle aspects were proposed to be responsible for such variations. With smaller body size than the European, Asian was found to have smaller bone size and different rate of bone accrual therefore resulted in lower BMD (Roy et al., 2005). Low calcium intake and greater prevalence of vitamin D deficiency in this region was also been proposed to contribute to the phenomena (Handa et al., 2008; Harinarayan, 2005; Malhotra & Mithal, 2008). Surprisingly, tropical countries also experienced deficiency in vitamin D and the prevalence rate could be as high to 85% as that was observed in Western populations (Chee et al., 2010; Hawkins, 2013; Nguyen et al., 2012; Wat, Leung, Tam, & Kung, 2007).

On the other hand, the pandemic trend in the rising of overweight and obesity over the past three decades predicted a continuous rise in the developing world in near future (Ng et al., 2014). Available evidence showed there were large gap existed between actual and ideal participation in the lifestyle behaviours, including eating a healthy diet and undertaking physical activity. Indeed, the prevalence of healthy lifestyle behaviours was low globally, with lower levels in the lower-income countries as compare to high-income countries. Less than half of the world population has good diet quality while high levels of physical activity related to recreational or leisure activity were more prevalent in high-income countries. The observed lifestyle practices deposed the population especially whom resided in developing countries of middle-income status to overweight and obesity (Teo et al., 2013).

The pandemic issue on overweight and obesity cultivated the interest of many researchers on the relationship between anthropometric measures and BMD in recent years (Fu et al., 2011; Gonnelli, Caffarelli, & Nuti, 2014; Montazerifar et al., 2014; Shao et al., 2014). Till date, there are many investigations from epidemiological, clinical and basic research point of view performed actively, demonstrating that osteoporosis and obesity is no longer opposing in their standings but may present connection (Gonnelli et al., 2014; Hsu et al., 2006; Wang et al., 2013). Malaysia, being one of the nations that has been reported with rapid increase in overweight and obesity rate and rated as having the highest obesity rate among Association of Southeast Asian Nations (ASEAN), has brought to greater concern in healthcare aspect [Dans et al., 2011; World Health Organization (WHO), 2011]. The Third National Health and Morbidity Survey (NHMS III) reported a prevalence of 29.1% overweight and 14.0% obesity among Malaysian which was further increase to 33.3% preobese and 27.2% obese in 2011 [Institute for Public Health (IPH), 2011b]. A similar increasing trend of abdominal obesity was also documented among Malaysian (MOH, 2006). Such unhealthy norm among Malaysian could bring deleterious yet undesired impact in the future.

Acknowledging the magnitude of the bone health related risk factors, related studies in examining the associations between many of the life aspects and BMD were however limited in the Malaysian context with majority of such studies were confined to bivariate analysis where possible interaction between multiple factors are not able to be ascertained (Chan et al., 2014; Chee et al., 2010; Lim et al., 2005; Yee, Zaitun, Chan, & Norhaizan, 2013). The limited studies and national reports called up the needs to initiate study in exploring the contribution of bone health related risk factors towards BMDs using multifactorial analysis approach.

Realizing the epidemic and pandemic trend that would most likely to affect bone health deleteriously, this study proposed the following research questions:

i. What are the sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, anthropometric measurements and bone health status among premenopausal and postmenopausal Chinese women residing in the Klang Valley?

ii. Is there any significant difference on sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, anthropometric measurements and BMD measurements between premenopausal and postmenopausal Chinese women residing in the Klang Valley?
iii. What is the relationship between sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, anthropometric measurements and BMDs among premenopausal and postmenopausal Chinese women residing in the Klang Valley?
iv. What is the contribution of sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, and anthropometric measurements towards BMDs?

1.3 Significance of study

Chinese female, being the most vulnerable group towards low bone mass and hip fracture, has been identified as the study population of this study. Since osteoporosis and its related fractures mostly affected postmenopausal individuals, many studies have been focused on them. Similarly, this study also intends to investigate the bone status and the relevant determinants of BMD among postmenopausal Chinese women from wider perspectives than the previous local studies. Additionally, this study commits into determination of bone health status and the mentioned measures among premenopausal Chinese women, of which data is very limited in local sources. Nonetheless, the determination of bone health status in this study is through the use of Dual-energy X-ray Absorptiometry (DXA), which is the gold standard for BMD measurements.

The present knowledge on bone health and its contributing factors was mostly learnt from abroad research. While research study examining bone health from the above mentioned aspects is scarce in Malaysia, this study may contribute to the pool of local data resources. Conversely, it is important in the study of a disease to take into considerations of cultural, religious, dietary and geographical differences. A broad, racial summarization data would not be more valuable than an ethnic-specific data in bone health studies since variations were reported among Asian ethnic groups (Handa et al., 2008; Lee & Khir, 2007).

With more local data available, the foundation of strategy development in osteoporosis prevention and treatment strategy can be more solid. The findings shall assist healthcare authorities (MOH and non-governmental organizations) in forming strategies targeted to the population to maximize bone formation within the modifiable period, to maintain and to reduce bone loss rate after attainment of peak bone mass. This may result in reducing burden of osteoporosis and fractures while maintaining and improving the quality of life of vulnerable populations and their family members.

Lastly, this study will contribute to the existing body of knowledge academically and can be used as future research reference. It can be served as baseline references for future intervention study as well.

1.4 Objective of study

1.4.1 General objective

To determine factors contributing to bone mineral density among Chinese women in the Klang Valley, Malaysia.

1.4.2 Specific objective

i. To determine sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, anthropometric measurements and bone health status among premenopausal and postmenopausal Chinese women in the Klang Valley.
ii. To compare sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, anthropometric measurements and BMD measurements between premenopausal and postmenopausal Chinese women.
iii. To determine the relationship between sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, anthropometric measurements and BMDs among premenopausal and postmenopausal Chinese women.
iv. To examine the contribution of sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices and anthropometric measurements towards BMDs.

1.5 Hypotheses

i. H_0: There is no significant difference in sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, anthropometric measurements and BMD measurements between premenopausal and postmenopausal Chinese women.
ii. H_0: There is no significant relationship between sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices, anthropometric measurements and BMDs among premenopausal and postmenopausal Chinese women.
iii. H_0: There is no significant contribution of sociodemographic background, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices and anthropometric measurements towards BMDs.

1.6 Conceptual framework

Bone mineral density is an important determinant of bone strength (NOF, 2010). Bone mineral density measurement defines bone health status as normal bone density, low bone mass (named osteopenia) and osteoporosis according to T-score classification (WHO, 1994). Accumulated BMD before peak bone mass (PBM) achieved and loss of bone mass during advancing age determine the BMD in later life (Cashman, 2007b). Evidence has demonstrated relationships between many factors to play as the determinants of BMD. Of which, the factors are categorized into several categories: sociodemographic factors, family history, reproductive history, biochemical measures, dietary intake, lifestyle practices and anthropometric measurements.

Ageing is associated with impaired bone formation and increased bone resorption. Bone mineral density (BMD) reduction in elderly is secondary to physiological and lifestyle changes that causes impaired production of bone stimulatory agents such as insulin-like growth factor (IGF), increased parathyroid hormone secretion and increased muscle loss (Demontiero, Vidal, & Duque, 2012; Lips, 2001). Socioeconomic status is also found to be one of the risk factors associated with poor bone health along with the emerging evidence on socioeconomic gradient relating to all causes of morbidity and mortality (Begg, Vos, Barker, Stanley, & Lopez, 2008; Turrell, Stanley, Looper, & Oldenburg, 2006). Most of the findings suggested a protective role of greater educational attainment and higher income against low BMD and osteoporotic fracture (Peel, McClure, & Hendrikz, 2007; Wang & Dixon, 2006). While genetic factors contributed more than 60% of the total variance in PBM attainment (Rizzoli, Bianchi, Garabédian, McKay, & Moreno, 2010), assessment on family history, especially parental history of fracture provided insight to the relationship between genetic and BMD for the studied population (Kanis, Johansson, et al., 2004).

Changes in reproductive system over lifespan also alter bone metabolism. Estrogen exposure at menarche positively influenced BMD during puberty years (Yilmaz et al., 2005) and across premenopausal years (Sioka et al., 2010). Estrogen prevents substantial bone loss through inhibiting formation of bone-resorbing cell (namely osteoclast) and stimulating cell death on osteoclast (Clarke & Khosla, 2010). Thus, estrogen enables bone mass accumulation during young age and estrogen deficiency leads to accelerated bone loss after menopause (Khosla et al., 2005; Yilmaz et al., 2005). Age of menarche and number of years since menopause as measures of estrogen exposure are therefore played determining roles towards BMD. Besides, pregnancy induced changes in bone metabolism (Oliveri, Parisi, Zeni, & Mautalen, 2004). Parity was shown to influence BMD both positively (Allali et al., 2007; Streeten et al., 2005) and negatively (Ozdemir, Demirbag, & Rodoplu, 2005; Shin et al., 2010) or produced no significant effect (Lenora, Lekamwasam, & Karlsson, 2009; Sioka, Bougias, Papadopoulos, & Fotopoulos, 2007). Lactation induced approximately 5% maternal bone resorption in six months. However, the bone mass was expected to re-establish and restore after weaning (Oliveri et al., 2004). Duration of lactation also showed either negative association or no association with BMD in studies (Dursun, Akin, Dursun, Sade, & Korkusuz, 2006; Kojima, Douchi, Kosha, & Nagata, 2002).

Parathyroid hormone (PTH) and serum vitamin D are important in the maintenance of normal homeostatic regulation of bone mineral content, particularly through the regulation of serum mineral levels (Moe, 2008). Impairment in PTH regulatory mechanism caused impairment in bone metabolism while serum vitamin D positively influenced BMD (Bischoff-Ferrari, Dietrich, Orav, & Dawson-Hughes, 2004; Moe, 2008). Biochemical measures of bone turnover serve as surrogate markers in the assessment of bone metabolism and management of bone diseases (Niimi et al., 2014). The commonly used bone turnover markers are Procollagen Type 1 N-Terminal Propeptide (P1NP), serum osteocalcin and bone resorption markers, namely C-telopeptide of type I collagen crosslinks (CTX) (Penny, Godber, & Lawson, 2007). These markers demonstrated negative associations with BMD at lumbar spine, femoral neck and total hip (Hu et al., 2013).

Dietary factors such as energy, protein, calcium, phosphorus and vitamin D consumed as part of diet potentially influence BMD. Energy and the mentioned nutrients have been widely studied and have shown to play remarkable roles in preserving bone health (Caporaso, Frisch, & Sumida, 2011; Chevalley, Bonjour, Ferrari, Hans, & Rizzoli, 2005; Heaney, 2007; Holm, Dan, Wilbur, Li, & Walker, 2010; Ihle & Loucks, 2004; Lamberg-Allardt, Karp, & Kemi, 2010; Takeda, Yamamoto, Yamanaka-Okumura, & Taketani, 2012; Thorpe & Evans, 2011). While dietary intake of vitamin D through exogenous food sources ingestion played least role as compare to endogenous synthesis of vitamin D, serum vitamin D is well accepted as a biomarker for vitamin D status which accounted for both endogenous and exogenous sources (Adams & Hewison, 2010; Goff, Cavalier, Souberbielle, González-Antuña, & Delvin, 2015).

Lifestyle practices play significant role in influencing bone health. Regular engagement in physical activity exerted mechanical loading to bone and promoted PBM attainment in early life (DiVasta & Gordon, 2013), maintained bone mass in adulthood (Babatunde, Forsyth, & Gidlow, 2012) and reduced bone loss rate in elderly (Pines & Berry, 2007). Besides, literature suggested a positive relationship between sun exposure and BMD through synthesis of serum 25(OH)D and thereby reduced bone loss (Macdonald et al., 2008; Zhen, Liu, Guan, Zhao, & Tang, 2015). On the other hand, long term cigarette smoking substantially increased risk of osteoporotic fracture to nearly two-fold in hip fracture compare with non-smoker (Kanis et al., 2005). Contrary to harmful effect of smoking, moderate alcohol consumption of less than 150 g or 12 drinks weekly was not associated significant harmful effect on BMD (Waugh et al., 2009). However, excessive and prolonged alcohol intake caused compromised BMD and contributed to increased fracture risk (Berg et al., 2009).

Majority of the literature suggested a positive relationship between body weight, BMI and BMD. Low BMI was associated with increased risk of fracture whereas higher BMI was protective against osteoporotic fracture (Laet et al., 2005). It was generally accepted that larger BMI imposed greater mechanical loading that bone mass increased to accommodate the load. Recent studies, however, challenge the existing findings and demonstrated negative association between body fat and BMD when the mechanical loading effect was controlled for (Zhao et al., 2007). The relative effect of the two major components of body weight, lean mass and fat mass, is still under dispute. Some

studies proposed stronger effect from fat mass towards BMD while others suggested lean mass being more closely related to BMD. Besides, studies also indicated central obesity imposed detrimental effect towards BMD (Fu et al., 2011; Shao et al., 2014) due to increased production of inflammatory cytokines in obesity (Goodpaster et al., 2003). The conceptual framework of this study is illustrated in Figure 1.1.

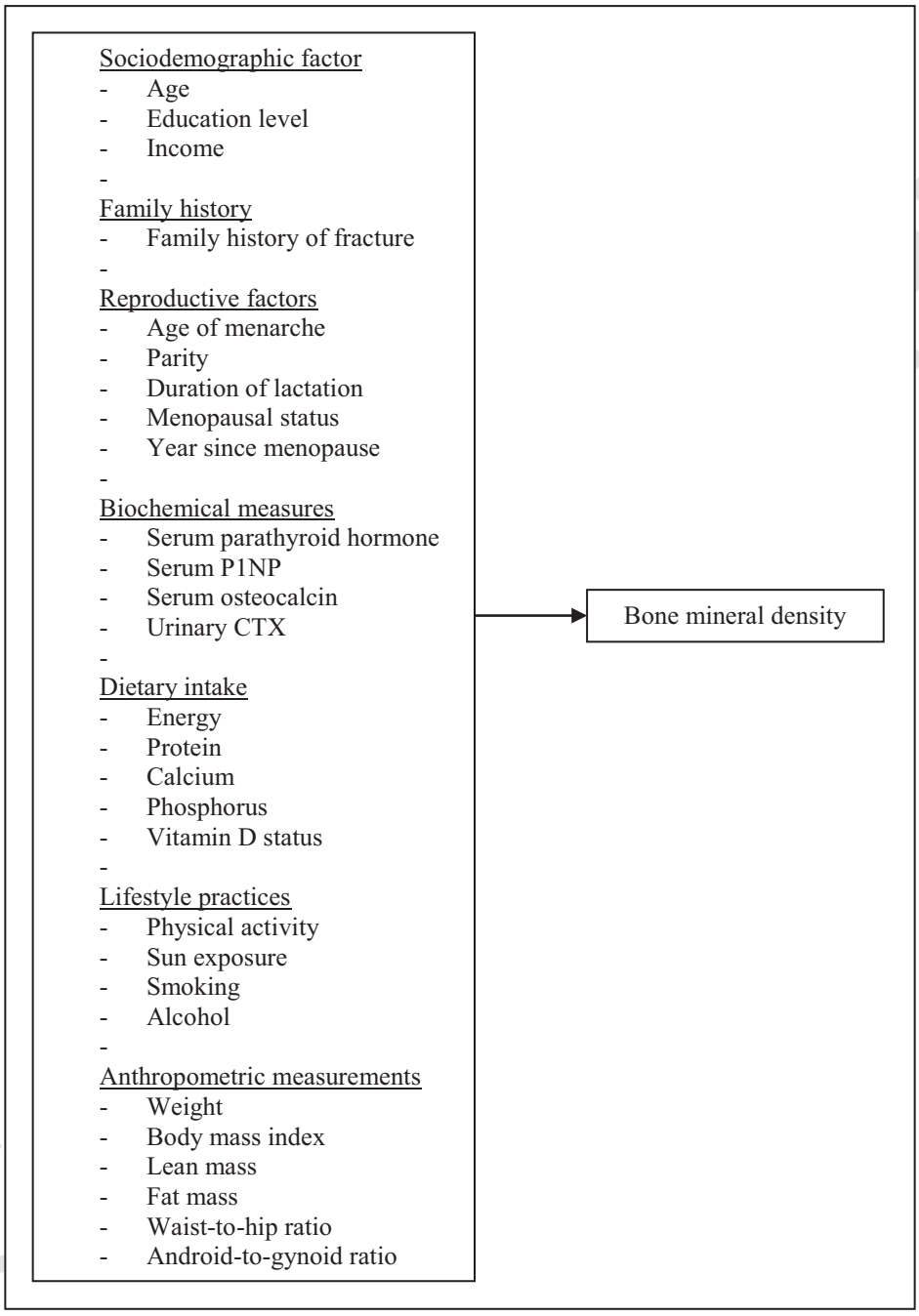

Figure 1.1. Conceptual framework of the study

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