Identifying nutritional and life-style risk factors associated with the development of osteoporosis in women of Asian origin at the Aga Khan University Hospital, Nairobi, Kenya

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Tauseef Chaudhri

Study Leader: **Dr R Blaauw**
Co- Study Leader: **Professor D Labadarios**
Statistician: **Prof DG Nel**
Confidentiality: **Grade A**

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DECLARATION OF AUTHENTICITY

I, the undersigned, hereby declare that the work contained in this thesis is my own original work and that I have not previously, in its entirety or in part, submitted it at any university for a degree.

Signature Date: 21 November 2006

ABSTRACT

INTRODUCTION: Postmenopausal osteoporosis is associated with significant morbidity, mortality, reduction in quality of life, and increasing health care costs

OBJECTIVE: The study objective was to identify the risk factors associated with the occurrence of osteoporosis, in Kenyan Asian women seen at the Aga Khan University Hospital, Nairobi, Kenya since there is no literature on the prevalence of all these risk factors for osteoporosis in a similar middle aged population sample of Kenyan Asian women.

METHOD: The study was of a retrospective design and used recall as a basis of data collection. A socio-demographic questionnaire was completed and anthropometric measurements, of height, weight, waist and hip circumference taken. Bone mineral density (BMD) had been measured previously using Quantitative Computed Tomography (QCT) at the lumbar spine, T11 to L4. Nutrient intake was assessed using a validated food frequency questionnaire (FFQ) and physical activity was determined using the Epic Physical Activity Questionnaire 2 (EPAQ2). BMD scans had been done on all study participants from January 2004 to December 2004 and the subjects were aware of their bone status.

RESULTS: Risk factors that were identified by being associated with the development of osteoporosis in Asian women were age ($p<0.001$), waist size ($p<0.001$), hip size ($p<0.001$) and BMI ($p<0.001$), low physical activity ($p=0.001$) and use of prescription drugs. Seventy two percent of the study sample was using prescription drugs and the effect on bone mass was most likely detrimental. Anti-hypertensive ($p=0.002$), non steroidal anti inflammatory drugs ($p=0.003$) and anti-diabetic drugs ($p=0.033$) had a significant negative association with bone health. Energy, protein, fat and carbohydrate intake in all the groups was above the EAR and comparatively similar. The intake of all the micronutrients in the study group was above the DRI. There were no statistical significant differences in most of the trace element intake between the two groups, apart from iodine, biotin and manganese. No dietary risk factors were identified which impacted adversely on bone health in this group. The impact of gynaecologic history (parity, oral contraceptive use, age of menarche) on BMD was uncertain. The

educational level of the study sample was high as 50% of the subjects were graduates and had a relatively better diet.

CONCLUSION: As Kenyan Asian women age they experience the menopausal transition and the risk of developing osteoporosis increases. No nutritional factors were identified that were adversely associated with BMD. Low level of physical activity, prescription drugs for chronic diseases like hypertension, asthma, diabetes and arthritis, age, weight and body mass index were identified and found to be adversely associated with bone mineral density. Early detection, and implementation of patient education, physical activity, and a diet rich in all nutrients, will help to slow down the progression of osteoporosis.

OPSOMMING

INLEIDING: Postmenopousale osteoporose word geassosieer met beduidende morbiditeit, mortaliteit, verlaagde lewenskwaliteit en verhoogde gesondheidsorg koste.

DOELWITTE: Die hoofdoelwit was om risikofaktore wat aanleiding gee tot die ontwikkeling van osteoporose in Keniaanse vroue van Asiatiese oorsprong, gesien by die Aga Khan Universiteit Hospitaal, Nairobi, Kenya te bepaal, aangesien daar geen literatuur bestaan oor die prevalensie van hierdie risikofaktore vir osteoporose in ‘n soortgelyke populasie van middeljarige Keniaanse vroue van Asiatiese oorsprong nie.

METODE: Die studie het ‘n retrospektiewe ontwerp gevolg en herroep is gebruik as metode vir data insameling. ‘n Sosio-demografiese vraelys is voltooi en antropometriese meetings (gewig, lengte, middel- en heup omtrekke) is geneem. Beenmineraaldigtheid (BMD) is vroëer bepaal deur middel van Gekwantifiseerde Rekenaar Tomografie (QCT) van die lumbale werwels, T11 tot L4. Nutriëntinname is bepaal deur middel van ‘n gevalideerde voedselfrekwensie vraelys (VFV) en fisiese aktiwiteit is bepaal deur gebruik te maak van die Epic Fisiese Aktiwiteitvraelys 2 (EPAQ2). BMD bepalings is uitgevoer op al die studie deelnemers gedurende die periode Januarie 2004 tot Desember 2004 en die studie deelnemers was bewus van die uitslae.

RESULTATE: Die volgende risikofaktore is identifiseer om ‘n verband te hê met die ontwikkeling van osteoporose in vroue van Asiatiese oorsprong: ouderdom ($p<0.001$), middelomtrek ($p<0.001$), heupomtrek ($p<0.001$), liggaamsmassa indeks ($p<0.001$), lae fisiese aktiwiteit ($p=0.001$) en die gebruik van voorskrif medisyne. Twee en sewentig persent van die studiegroep het voorskrif medisyne gebruik, met ‘n negatiewe effek op beenmassa. Anti-hipertensiewe ($p=0.002$), nie-steroïed anti-inflammatoriese ($p=0.003$) en anti-diabetiese middels ($p=0.033$) het ‘n beduidende negatiewe verband getoon met beenmassa. Energie, proteïen, vet en koolhidraatinname in al die groepe was bo die berekende gemiddelde behoeftes en vergelykbaar tussen die groepe. Die inname van al die makronutriënte in die studiegroep was bo die aanbevole inname vlakke. Daar was geen statisties beduidende verskille tussen die twee groepe vir die meerderheid van die spoorelemente nie, behalwe vir jodium, biotien en mangaan. Daar was ook geen dieetfaktore geïdentifiseer as risikofaktore om ‘n negatiewe invloed te hê op beenmassa nie. Die impak van die ginekologiese geskiedenis (pariteit, gebruik van orale

kontraseptiewe middels en ouderdom van menargie) op BMD was onduidelik. Die opvoedkundige vlak van die studiegroep was hoog, deurdat 50% van die studiegroep gegradueerdes was met ‘n beter dieet.

GEVOLGTREKKING: Met veroudering ervaar Keniaanse vroue van Asiatiese oorsprong menopousale oorgang en die risiko vir die ontwikkeling van osteoporose verhoog. Geen nutrisionele faktore wat ‘n negatiewe impak op BMD het is gevind nie. ‘n Lae vlak van fisiese aktiwiteit, voorskrif medisyne vir kroniese siektes, soos hipertensie, asma, diabetes en arthritis, ouderdom, gewig en liggaamsmassa indeks het ‘n negatiewe impak gehad op BMD. Vroegtydige opsporing en implementering van pasiëntonderrig, fisiese aktiwiteit en ‘n diet ryk in alle nutriënte, sal help om die verloop van osteoporose te vertraag.

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LIST OF ABBREVIATIONS

AI	Adequate Intake
ANOVA	Analysis of variance
BMD	Bone Mineral Density
BMI	Body mass index
CHO	Carbohydrates
cm	Centimeter
CT	Computed Tomography
DEXA	Dual Energy X-ray Absorptiometry
DRI	Dietary Reference Intake
EAR	Estimated Average Requirement
EPAQ2	European Physical Activity Questionnaire
ERT	Estrogen Replacement Therapy
FDA	Food and Drug Agency
FFQ	Food Frequency Questionnaire
gm	Gram
HRT	Hormone Replacement Therapy
kg	Kilogram
kJ	Kilo Joules
m	Metre
mcg	microgram
mg	Milligram
Mj	Mega joules
MUFA	Monounsaturated fatty acids
OCP	Oral Contraceptive Pills
PUFA	Polyunsaturated fatty acids
QCT	Quantitative Computed Tomography
QFFQ	Quantitative Food Frequency Questionnaire
QUS	Quantitative ultrasound
SD	Standard deviation
SERM	Selective Estrogen Receptor Modulators

SFA	Saturated fatty acids
SPSS	Statistical Packages for Social Sciences©
T-score	Number of standard deviations below the mean for young normal adults
WHO	World Health organization
WHR	Waist hip ratio
Z-score	Expected BMD score for same age and sex

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CHAPTER 1: INTRODUCTION AND PROBLEM STATEMENT

1.1 Introduction

Osteoporosis is as old as human civilization. Its impact has not been felt in the third world countries until now, because women and men had a shorter life span. As the life span gets longer scientific research has begun to shed light on the nature of the disease and found that bone loss is nearly universal with age, although differences exist dependent on ethnicity, genetic markers, nutritional habits, life style, body size, hip geometry and gender. Osteoporosis is a major worldwide health problem causing substantial morbidity and costs particularly for elderly women[1, 2,3,4,5].

The age-adjusted prevalence of osteoporosis and the rate of hip fracture are lower in Black women than in White women in the United States. The prevalence of osteoporosis in Hispanic and Asian women is similar to that found in White women.

In April 1993 the Consensus Development Conference defined osteoporosis as: “Osteoporosis is a systemic skeletal disease characterized by a low bone mass and micro architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture[6]. New findings related to the prevention and treatment of osteoporosis, have increased consumer awareness of this “silent disease”, and the best defense against developing osteoporosis is to increase peak bone mass to its genetic potential from preconception through pregnancy, infancy, childhood, adolescence and young adulthood and beyond. Life long attention to proper diet, healthy habits and exercise to maintain bone health offers the greatest potential for reducing the prevalence and severity of osteoporosis. The problem is worsening the world over and prevention is the gold standard in the treatment of this disease. Our major challenge is to identify attitudes, beliefs and behaviors that interfere with the adoption of healthy life style practices to promote and maintain bone health. As women age and experience the menopausal transition, the risk of developing osteoporosis increases. There are a number of factors that have been reported to increase the risk of osteoporosis and may contribute to the heterogeneity in the rates of bone loss experienced by mid life women of all races and communities. There are many misconceptions about osteoporosis, for example that it is "an old woman's disease". In fact, bone loss in women can begin as

early as age 25. Worldwide, the lifetime risk for a woman to have an osteoporotic fracture is 30-40%. In men the risk is about 20% as reported by the World Health Organization.

Anthropometric measures of body size and composition, lifestyle and gynaecological factors have all been shown to be associated with bone mineral density (BMD) and may contribute to the risk of developing osteoporosis. There is also evidence that genetic factors may influence rates of bone loss.

1.2 Incidence

Approximately 28 million Americans have or are at risk of developing Osteoporosis. Eighty percent of them are women[7]. The number of osteoporosis related fractures is rapidly increasing in the United States of America to the extent that 1 in 3 women and 1 in 10 men over the age of 65 will be affected. The consequences of these fractures can be devastating with 6% to 37% hip fractures resulting in death and at least 40% with permanent disability [8]. Osteoporotic fractures cost the U.S health care system $14 billion in 1997, with a projected annual cost of $50 billion by 2040, which is more than the projected annual cost of stroke, breast cancer, diabetes, or chronic lung disease[9]. There are no figures available for the developing countries as population studies have not been done and also the technology to assess bone status may not be available or affordable.

Large scale studies from developing countries are not available; however, there is substantial evidence that musculoskeletal disease prevalence is at least similar in western countries and the developing world[10, 11, 12]. A small study that looked at 289 Indian women from low-income groups showed that they consume diets that have inadequate calcium coupled with too few calories, proteins and micronutrients. Hospital based data suggest that these women have osteoporotic hip fractures at a much earlier age than Western women. Studies reporting bone parameters of the Indian population involving large sample sizes are not available[13].

Another study revealed a high prevalence of vitamin D deficiency among healthy, urban north Indian hospital staff. Low vitamin D concentrations may be attributed to inadequate sun exposure, skin pigmentation and poor dietary intake. Vitamin D deficiency may lead to low BMD and conceivably increase the risk of fractures [14].

The reference values of bone mineral density (BMD) were determined in healthy Saudis of both sexes and compared with US / northern European and other reference data. Age-related changes in BMD were similar to those described in US / northern European and Lebanese reference data [15].

In a Kuwaiti community cross-sectional sample the rates were 35.7% for women and 20.2% for men[16]. A cross-sectional study of Jordanian women found 29.6% osteoporotic and 43.8% osteopenic[17]. A Saudi Arabian study found high levels of radiographic osteoarthritis, 53.3% amongst men and 60.9% amongst women over 40 years old [16, 18.]

The first normative reference database of bone mineral density in the Indian women and men was established using digital x-ray radiogrammetry. Further analysis of this database revealed that 29.9% of women and 24.3% of men between the age of 20 and 79 years had low bone mass. About 50% women and 36% of men over 50 years of age were noted to have low bone mass. The observations of this study suggest that there is higher prevalence of low bone mass in the Indian population compared to the western populations[19].

1.3 Determinants of Peak Bone Mass

Bone is a living growing tissue. The main components are collagen, which provide the soft framework of the bone, and calcium phosphate, which hardens and adds strength to it. Peak bone mass is attained between the ages of 25 years and 35 years, following the cessation of longitudinal growth. Cortical bone is dense, has a low surface area and forms an envelope around the marrow cavity. Trabecular bone is spongy and has a lower density. Almost 80% of bone in the skeleton is cortical. The distal portion of the long bones, the vertebral bodies and the calcaneus comprise predominantly trabecular

bone whereas cortical bone predominates in the shafts of the long bones and the femoral neck. These differences are relevant clinically because trabecular bone is remodeled more rapidly than cortical bone as a result of its high surface area. Thus bone is lost more rapidly from sites rich in trabecular bone under conditions of increased bone turnover[20].

The human skeleton is a dynamic entity as considerable alterations occur throughout an individual's life. The process of bone resorption releases stored calcium into the systemic circulation and is an important process in regulating calcium balance. As bone formation actively fixes circulating calcium in its mineral form, resorption actively unfixes it thereby increasing circulating calcium levels. These processes occur in tandem at site-specific locations and are known as bone turnover or remodeling. Osteoblasts and osteoclasts, coupled together via paracrine cell signaling, are referred to as bone remodeling units. The iteration of remodeling events at the cellular level is influential on shaping and sculpting the skeleton both during growth as well as after. The amount of bone formed during each remodeling cycle decreases with age in both sexes. This is indicated by a consistent histological feature of the osteopaenia that occurs during aging, namely a decrease in wall thickness, especially in trabecular bone[21, 22]. Maximum attainment of peak bone mass is achieved during growth and early adulthood. The development of peak bone mass and the rate of bone loss in postmenopausal women and the elderly are determined by a combination of genetic, endocrine, mechanical and nutritional factors[23, 24].

1.4 Risk Factors for Osteoporosis

Risk factors are characteristics that increase the chances of developing a certain condition or disease. Some risk factors are modifiable and others are genetic and non modifiable (Table 1.1). Some women are at greater risk for developing osteoporosis than others[25].

Pregnancy could also be a risk factor as a Saudi study indicated that women who had borne >6 children were less osteoporotic and of low fracture risk as compared to those

women who had <5 children. The BMD of the women with >6 children was statistically higher than their counterparts, and they sustain this after prolonged lactation.[26]

The same may not hold true for other populations as shown in an American study. In this group of women with their multiple cycles of pregnancy and lactation do not appear to increase the risk of osteoporosis.[27]

Adolescence is a critical time for skeletal growth and mineralization. Exposure to protective or detrimental factors during this period may influence peak bone mass attainment and subsequent development of osteoporosis. The later the menarche and the earlier the menopause, the higher the degree of osteoporosis[28].

Table 1.1: Risk factors that contribute to osteoporosis

Non-Modifiable	Modifiable
Age	Sedentary lifestyle
Caucasian or Asian race	Smoking
Low body weight	Excessive alcohol intake
Family history of osteoporosis	Estrogen-deficient states
Nulliparity	Calcium deficient diet
	Use of certain drugs and medications

1.4.1 Genetics

Heredity has an important role to play as it has been estimated that genetic factors account for 60% to 85% of variance in bone mass. The strong association between body mass and peak bone mass may partly result from shared genetic influences. Vitamin D receptor gene and its alleles are shown to be associated with small differences in bone mineral density, but there is no evidence that mutations in this gene are responsible for development of osteoporosis [29].

In premenopausal women, more than 95% of serum estradiol (E_2) and most of serum estrone (E_1) is derived from ovarian secretion. Estrogen has specific functions at the organ, tissue, and cellular levels of the skeleton. At the organ level, estrogen acts to conserve bone mass. Indeed, the actions of estrogen and those of biomechanical strain are the major physiological mechanisms for bone mass conservation. In fact, with a few exceptions, such as states of corticosteroid excess, major decreases in bone mass do not occur unless one of these two homeostatic mechanisms is affected. At the tissue level, estrogen tonically suppresses bone turnover and maintains balanced rates of bone formation and bone resorption[30.] During the 2- or 4-yr menopausal transition, serum estradoil levels fall to 10–15% of the premenopausal level, although levels of serum estrone, a 4 fold weaker estrogens, and fall to about 25–35% of the premenopausal level [31].

The late, slow phase of bone loss is also associated with progressive increases in levels of serum PTH and in biochemical markers, serum osteocalcin, a marker for bone formation, and urine N-telopeptide of type I collagen a marker for bone resorption, and these increases correlate with each other [32].

Osteoporotic abnormalities generally have been attributed to age-related factors, particularly to decreases in paracrine production of growth factors or to decreases in circulating levels of GH and IGF [33, 34, 35,36,37,38].

Functional analysis has shown that the osteoporosis-associated T allele ("s") of the Sp1 polymorphism is associated with increased DNA-protein binding, increased transcription, and abnormally increased production of the collagen type I α1 mRNA and protein [39]. It is thought that the resulting imbalance between the type I collagen αI and α2 chains contributes to impairment of bone strength and reduced bone mass in carriers of the T allele by subtly affecting bone mineralization [40].

1.4.2 Nutrition

The influence of nutrient intake on bone mineral status from birth onwards is largely undefined[41]. A larger number of dietary components have been proposed as determinants of peak bone mass. The majority of work examining the effect of nutrition on bone has focused on calcium and phosphorus, due to them being major constituents of bone tissue. However some trace elements such as zinc, manganese and copper are necessary for growth, development and maintenance of healthy bones.

Dietary components such as magnesium, fluoride, ascorbic acid and Vitamin K work biologically at the level of bone itself. Vitamin A, B6 and D are also necessary for healthy bone formation [42]. Long term intake of a diet high in Vitamin A may promote the development of osteoporotic hip fractures in women. The amounts of Vitamin A in fortified foods and vitamin supplements may need to be reassessed in the developed world[43]. However; foods in Kenya are not fortified with Vitamin A, apart from margarine, which is not used on a large scale by the study population.

1.4.2.1 Calcium

Calcium is the fifth most abundant mineral in the human body accounting for 1 – 2% of adult body weight. Over 99% of total body calcium is found in the inorganic phase of bones and teeth. Calcium is absorbed depending on its interaction with other dietary constituents and physiological factors such as calcium regulating parathormone and the stage of the life span. Calcium intake must be sufficient to meet biological requirements if optimal bone development is to be achieved. Therefore the calcium in the diet must be sufficient to provide an adequate amount once absorption, efficiency, obligatory, excretory, and dermal losses have been rationalized[44].

1.4.2.2 Calcium: foundation of skeletal strength

The Food and Nutrition Board, Institute of Medicine set calcium intake recommendations at different levels for the various life stages (Table 1.2). These recommendations are intended to promote bone strength, maximize peak bone mass during growth and to minimize bone loss in mature adults[45].

A national survey conducted in 1994 by the US department of Agriculture determined that the average American consumes approximately 800mg of calcium per day[46]. The survey indicated that milk supplies 40% of the calcium requirements. During the teen and early adult years however, there is a dramatic reduction in milk consumption, which is replaced by soft drinks, coffee, tea and alcohol. Non-dairy foods contribute 9% of calcium from fruit and vegetable; 95% from sardines and salmon with bones, perch, almonds and fortified tofu and 5% from grains[47].

1.4.2.3 Calcium absorption and excretion.

Dietary calcium absorption in adults with the usual intake is approximately 25% to 35%. Calcium absorption is dependent on several factors, including age, Vitamin D, and exposure of food to gastric acids. During pregnancy, lactation and growth, there is an increase in calcium absorption. Women retain 21% calcium after ingesting 1330 mg of calcium[48] Elderly women have an impaired intestinal response to 1, 25(OH) 2D. This defect may contribute to the negative calcium balance, secondary hyperparathyroidism, and bone loss in aging women[49].

Table 1.2: Recommended Calcium Intake through the life stages[45]

Life Stage/Age group	Mg per Day
0 – 6 months	210
7 – 12 months	270
1 – 3 years	500
4 – 8 years	800
9 – 18 years	1300
19 – 50 years	1000
51 – 70 years	1200

Decreased calcium absorption occurs during menopause and maturity, when Vitamin D is insufficient. As women go through menopause, their bodies produce less estrogen.

This loss of estrogen is the major cause of bone loss in women later in life, according to the National Institute of Arthritis and Musculoskeletal and Skin Disease as this may create poor calcium absorption Calcium absorption is also decreased when the gastric acidity is low and in the presence of liver, pancreatic, small bowel disease and mental and physical stress[49].

1.4.3.4 Calcium supplementation

Most experts recommend obtaining as much calcium as possible from foods because calcium in foods is accompanied by other nutrients that assist the body in utilizing calcium. Numerous clinical trials of calcium supplementation showed that it can reduce bone loss[50, 51, 52]. Other studies showed that the risk of bone fractures is lower with supplementation[53 54, 55]. However, concomitant treatment with Vitamin D makes it difficult to attribute benefits to calcium per se, and the increment in bone density in the first year or two of calcium supplementation may not substantially increase with continued treatment [56, 57, 58].

A recent meta-analysis of 15 calcium intervention trials involving healthy women and postmenopausal women with osteoporosis demonstrated an increase of nearly 2 percent in spine bone mineral density after two years, although the risk of vertebral and nonvertebral fracture was not reduced to a statistically significant level[59]. A very recent study done in York, England found no evidence of a benefit on fractures in older community dwelling women given calcium and Vitamin D supplementation[52]. A total calcium intake of 1200 to 1500 mg per day (through diet, supplements, or both) is recommended for all postmenopausal women[60].

Recent results from the Women Health Initiative study among healthy postmenopausal women, calcium with vitamin D supplementation resulted in a small but significant improvement in hip bone density, did not significantly reduce hip fracture, and increased the risk of kidney stones[61].

1.4.3.5 Oxalates

Oxalic acid inhibits calcium absorption. Oxalates are found in many plant sources. Foods high in oxalate include spinach, beets, rhubarb, carrots, snap peas, lettuce, peanuts, cocoa, chocolate and tea[62].

1.4.3.6 Phytates

High fibre foods have little effect on calcium absorption. However, only concentrated sources of phytates such as wheat bran or dried beans substantially reduce calcium absorption. Phytates and calcium combine and produce insoluble salts in the small intestines[63].

1.4.3.7 Phosphorus

Phosphorus regulates bone formation, inhibits bone resorption, and also affects the regulation of calcium metabolism. Although there are few studies on the direct effect of phosphorus on bone mineral density, it is important to maintain a proper phosphorus-to-calcium intake because of the effect phosphorus has on calcium metabolism[57]. One researcher recommended a daily intake of 1000 mg calcium, with three-quarters as much (750 mg) phosphorus, as this intake was associated with higher bone mineral density among young women[64]. It is also a good idea to reduce the consumption of soft drinks since they are high in phosphorus and can unfavorably alter the calcium/phosphorus balance. The role of phosphoric acid on bone loss requires additional investigation. Intake of cola, but not of other carbonated soft drinks, is associated with low BMD in women. In a recent study cola intake was associated with significantly lower BMD at the hip site, but not the spine, in women but not in men. The mean BMD of those with daily cola intake was 3.7% lower at the femoral neck and 5.4% lower at Ward's area than of those who consumed <1 serving cola per month[65]. No evidence exists that occasional use of carbonated beverages, including cola, is detrimental to bone. However, unless additional evidence rules out an effect, women who are concerned about osteoporosis may want to avoid the regular use of cola.

1.4.3.8 Protein

Protein plays an important and complex role in bone growth, development and maintenance throughout the life span of human beings. The Framingham Osteoporosis Study found that no adverse effects on bone health were observed from higher intakes of animal protein consumption[66]. In contrast, another study showed that a higher consumption of animal to vegetable protein ratio experienced a higher rate of femoral bone loss and a higher risk of fractures[67].

However, results of epidemiological studies have been conflicting. Heaney argues that the actual effect of protein intake on bone is complicated and dependent on other components in the diet. Nutrients such as calcium, potassium, phosphorus and vitamin D, isoflavones, antioxidants, salt, oxalate, phytates and caffeine can influence the effects of protein. Thus, it is important to consider the entire dietary intake when delineating the role that dietary protein plays on bone health[68].

Protein is an important component of bone. Protein supplementation improves the medical outcome in elderly hip fracture patients[69]. However, the role of protein intake remains controversial as several population based studies have examined the relationship between protein intake and hip fractures risk and the results have been conflictive[63]. One previous study has shown a positive and protective link between protein intake and osteoporosis[70]. At the other end of the spectrum inadequate dietary protein intake is harmful to bone health, especially among elderly individuals. A low protein intake is associated with a poor general overall nutritional status, compromised recovery from osteoporotic fractures and increased bone loss in elderly individuals[71].

Recent research suggests those advanced glycation end products, maybe implicated in bone loss. These are formed when proteins interact with glucose molecules to form damaged structures in the body. One study examined the proteins in osteoporotic bones to determine if there was damage by advanced glycation products. More advanced glycation products present resulted in fewer bone-building osteoblasts[72].

1.4.3.9 Vitamin D

Vitamin D has a clear role in the absorption of calcium from the gut and after metabolism to its active metabolite 1, 25 $(OH)_2$ D3 in the regulation of bone turnover. It arises both from the diet by metabolism of ergocalciferol and also by metabolism from its precursors 7- dehydrocholesteral in the skin in response to ultraviolet light[43]. International studies demonstrate that even in hot, sunny climates substantial proportions of the population can have low exposure to sunlight and suboptimal vitamin D intake as reported from Kuwait, the United Arab Emirates, Turkey and Bangladesh and subsequently the rising incidence of osteoporosis [73, 74,76 76].

There is a diverse elderly Asian women population in Kenya and avoid direct exposure to sunshine.. They wear either long or short sleeves when outside and therefore may also be inadequately exposed to sunshine like in Middle Eastern or Muslim countries but they are not covered from head to toes.

Conversion of vitamin D to the metabolically active 25(OH) D_3 and 1, 25 $(OH)_2$ D3 takes place in the liver and kidney respectively. The conversion factor becomes less effective in the elderly leading to secondary hyperparathyroidism, bone loss and consequent risk of osteoporosis especially in the northerly latitudes during wintertime[77].

1.4.3.10 Vitamin D supplementation

Vitamin D_3 plays an important role in calcium absorption and in normal mineralization of new bone. It increases intestinal calcium absorption, enhances renal tubular calcium reabsorption, stimulates osteoblastic synthesis of osteocalcin but decreases osteoblast synthesis of collagen, and only a high dose augments bone resorption. Because of decreased calcium absorption and reduced circulating levels of 1, 25(OH) 2D3 in patients with postmenopausal osteoporosis, the hormone has been used in the treatment of disease. The value of 1-alpha-OHD and 1, 25(OH) 2D3 in the treatment of osteoporosis is controversial. Some, but not all, studies have shown that low-dose $1,25(OH)_2D_3$ or its analogues increase bone mass or reduce fracture frequency in patients with established osteoporosis[78].

Excessive Vitamin D intake causes toxicity producing hypercalcaemia, soft tissue calcification, anorexia, weakness and weight loss, and stiffness, In severe cases, hypercalcaemia may lead to irreversible renal and heart failure and death[79]. Hypercalcaemia is a contraindication for the administration of vitamin D.

Due to concerns that individuals do not get enough vitamin D through sunlight, recommendations for intake are set at a level to be adequate for individuals having no sun exposure. The most accurate way to tell if an individual or population group is getting enough Vitamin D is by measuring levels of serum 25-hydroxy Vitamin D. These levels have been measured in various populations, and they indicate a high prevalence of Vitamin D insufficiency in nursing home residents, hospitalized patients, and adults with hip fractures[80,81, 82]. Vitamin D levels commonly deteriorate in older adults, and thus the requirement for Vitamin D increases with age.

1.4.3.11 Vitamin A

The results of a recent prospective study suggest that long term intakes of retinol in excess of 1500 mcg/day are associated with increased risk of osteoporotic fracture and decreased bone mineral density (BMD) in postmenopausal women. Women with intakes of 500 mcg of Vitamin A and below had the lowest rate of hip fractures[83]. Excess Vitamin A seems to stimulate osteoclasts, scavenger cells that break down bone, and suppress osteoblasts that build up bone and also interfere with vitamin D, which is crucial for calcium absorption and metabolism[84]. Retinol comes primarily from animal sources and from the supplements added to margarine.

Beta carotene is the other source, from brightly coloured fruit and vegetables, which gets converted to retinol in the body. Feskanich did not find a similar effect with beta carotene. It can be postulated that an intake of 500 mcg of Vitamin A and the rest from beta-carotene would reduce the risk of hip fractures in postmenopausal women.

1.4.3.12 Vitamin K

Vitamin K mediates the gamma- carboxylation of glutamyl residues on several different bone proteins, notably osteocalcin, which is involved in mineralization of bone matrix[85]. Many elderly people have a low intake of Vitamin K primarily, because they eat fewer green vegetables, may be taking antibiotics, which reduce the formation of Vitamin K by the gut flora, or anticoagulants[86]. Increased vitamin K is associated with a decreased loss of calcium in the urine. A prospective analysis of the Nurses Health Study Cohort found that a low intake of Vitamin K was associated with an increased fracture risk[87]. More research needs to be done to determine the optimal intake of Vitamin K for older people to help slow down bone loss. In these modern times, it seems likely that, a diet rich in refined foods may result in low enough intakes of micronutrients to undermine the formation and remodeling of healthy bones.

More research is needed to determine the amount of various trace elements necessary for optimal bone health.

1.4.3.13 Vitamin B12

Recent evidence has implicated elevated homocysteine as a possible risk factor for osteoporosis, especially in women [88, 89]. Vitamin B12, together with folic acid and vitamin B6, can help lower homocysteine. Before the evidence connecting elevated homocysteine to osteoporosis emerged, vitamin B12 had already been identified as a possible strategy to reduce the risk of osteoporotic fracture, primarily because vitamin B12 deficiency has been associated with decreased bone-mineral density in the hip[90]. Vitamin B12 and Folate have been shown to reduce the risk of hip fracture in elderly Japanese people who have suffered stroke[91].

1.4.3.14 Trace Elements

Apart from calcium and phosphates other minerals like magnesium aid in the absorption and metabolism of Vitamin D with 50% of the magnesium in the body being stored in the bones. Research continues on other trace elements like boron and manganese as boron appears to increase the body's absorption of calcium, magnesium and phosphorus[92].

Boron appears to be used by osteoblasts in bone formation and seems to mimic some of the effects of oestrogen. A supplement of 3mg of boron was shown to increase beta-estradoil and testosterone levels in older subjects[93]. Boron's function in bone formation appears to be related to magnesium metabolism[94]. Whether or not boron is absolutely required for healthy bone formation in humans is still a matter for debate.

A low serum magnesium level, which is often seen with chronic alcoholism, diabetes mellitus and malabsorption syndromes, like coeliac and crohns disease appear to be risk factors for the development of osteoporosis and osteomalacia. Inadequate serum magnesium levels are known to result in low serum calcium levels, resistance to parathyroid hormone, and resistance to some of the effects of vitamin D, all of which can lead to increased bone loss[95, 96]. Magnesium comprises about 1% of bone mineral and is known to influence both bone matrix and bone mineral metabolism. The bone crystals become larger and more brittle as the magnesium content of bone mineral decreases[97].

Diets low in copper may contribute to osteoporosis by interfering with the formation of the protein support structure for new bone[98]. Copper plays an essential role in bone metabolism and turnover. It modulates the differentiation and proliferation of osteoblast precursors, namely the mesenchymal stem cells[99]. Women taking copper supplementation have shown improved bone density, while copper deficiency can produce osteoporosis in animal models of the disease[100].

Iron is another micronutrient involved in bone metabolism. It serves as a catalytic cofactor for ascorbic acid in the hydroxylation of proline and lysine which is essential for the maturation of the collagen matrix. In theory a deficiency of either iron or vitamin C, could lead to a weaker bone matrix, but there are no studies which suggest that a lack of either plays a role in the development of osteoporosis. Iron accumulation in tissues is believed to be a risk factor for some chronic diseases. However, it is not known whether age-associated iron accumulation is part of the pathogenesis of postmenopausal osteoporosis.

Zinc, manganese and fluoride are all involved in the formation of healthy bone. Mega doses of fluoride do increase bone mineral density, however there is evidence that excessive fluoride content is more susceptible to micro fractures because of alterations in the structure of hydroxyapatite and is not likely to reduce the overall fracture risk in osteoporosis[101].

The role of zinc in osteoporosis is less well understood, but it is increasingly apparent that zinc deficiency is a risk factor for osteoporosis. It has been theorized that zinc deficiency may lead to the increase of natural anticoagulants in the blood[102]. In alcoholics, zinc has also been shown to limit the damaging effects of alcohol on bone[103],

A diet rich in refined fats, oils, sugar, white flour and other refined carbohydrates will be much lower in many essential trace elements than the diet consumed by our ancient ancestors during the evolution of man. An increased consumption of fruits and vegetables, which are excellent sources of both potassium, Vitamin K, magnesium and trace elements involved in bone metabolism, was shown to have a beneficial effect on the maintenance of BMD in a 4 year longitudinal study[104].

1.4.3.15 Sodium

Urinary sodium excretion and urinary calcium excretion occur together in the kidneys. Therefore increasing the level of dietary sodium triggers urinary calcium losses[105]. Data regarding the long term effects of sodium on bone health are sparse[106]. Several studies report correlations between sodium intake and biomarkers of bone turnover and hipbone loss[107]. Other studies find no correlations with bone density in elderly men and women or in prepubertal children[108, 109]. The National Research Council of the National Academy of Sciences in Washington D.C. has determined that the recommended safe minimum daily amount is about 500mg of sodium with an upper limit of 2400mg. However, the council has said that lowering it to1800mg would be healthier and beneficial.

1.4.4 Menopause

Many conditions that affect different organ systems can cause osteoporosis. One of the more common etiologies is hypogonadism. In women, menopause signals the end point of the perimenopause, a process that started 10 to 12 years earlier, where the number of follicular units capable of producing estradiol within the ovary starts to decline until it is completely exhausted. Amenorrhoea and systemic hypoestrogenism follows. As a result of low levels of oestrogen there is an accelerated rate of bone loss particularly in the spine.

A similar clinical picture is seen in cases where both ovaries are surgically removed or when ovaries are not appropriately stimulated by gonadotropins to produce estradiol. This can occur in younger women as a result of excessive exercise, low body fat or as sequelae to eating disorders such as anorexia nervosa and bulimia.
In terms of bone remodeling the lack of estrogen enhances the ability of osteoblasts to absorb bone. Since the osteoblasts are not encouraged to lay down more bone they start losing their mineral density[110].

1.4.5 Body weight

Body weight is an important determinant of bone density. The skeleton of heavy individuals tends to benefit from its increased load-carrying role. Studies have demonstrated that body weight is positively correlated with BMD and that weight loss is associated with bone loss. Weight loss in older individuals has been linked to an increase in fracture risk. Maintaining weight in later life may have a protective effect on bone[111].

The endocrine effect of fat mass on bone may be minimal before menopause. After the menopause, fat mass and weight increase, while lean mass decreases[112]. Hormonal contribution of the fat mass may explain the association between fat mass and BMD[113]. Adipose tissue contains aromatase and this enzyme is responsible for the conversion of androgenic steroids into estrogens. The greater the fat mass, the greater the amount of estrogen synthesized. The association of BMD with lean mass in elderly twins supports

the need for further study of the relationship between body composition and bone strength in the elderly[114].

1.5 Bone Protecting and Building Strategies

While risk factors such as genetics, aging, gender or ethnicity are unchangeable, there are several lifestyle and nutrition strategies to maintain healthy bones. If the following factors are modified early or stopped, bone health can still stand to benefit.

1.5.1 Cigarette smoking

Smoking cigarettes increases the risk of heart disease, hypertension, emphysema, lung cancer and osteoporosis. The nicotine and cadmium found in cigarettes can have a direct toxic effect on bone cells[115 116]. Smoking may also harm bone indirectly by lowering the amount of calcium absorbed from the intestine, altering the body's handling of vitamin D and various hormones needed for bone health or lowering body weight[117, 118,119,120]. Smokers may also be less physically active.

A recent meta-analysis, using data from 10 different observational studies from around the world, found that smoking was associated with an increased risk of hip and other fractures in both men and women[121]. Although the lower BMD and body mass index (BMI) of smokers were found to contribute to the increased risk of fracture, these factors did not completely explain the increased risk. After adjustment for BMD, BMI, and age, the risk of hip fracture was 55% higher in smokers than in non-smokers.

Smoking reduces the amount of estrogen produced by the ovaries in pre-menopausal women. In general, the onset of menopause is two years earlier in smokers than non-smokers. This also applies to women who are exposed to passive smoking. Women, to protect their health and bones should adopt the policy of no smoking[122].

1.5.2 Alcohol

Excessive alcohol intake is a major cause of osteoporosis, particularly in men. Research indicates that alcohol decreases the ability of osteoblasts to make new bone.

Alcohol also suppresses the appetite and heavy drinkers tend to eat less nutritious meals. In addition alcohol reduces the ability of liver cells to activate Vitamin D causing reduced calcium absorption. The amount of alcohol that affects bone status is not known. Therefore, moderate alcohol intake, if any, is recommended. The National Institute of Alcohol Abuse and Alcoholism recommends women have no more than one drink a day and men limit their drinks to two a day[123].

1.5.3 Caffeine

Excessive intake of caffeine increases urinary calcium excretion. A study at the University of California, San Diego of 980 post-menopausal women showed a lifetime intake of caffeinated coffee was associated with reduced bone mineral density. When the participants supplemented their coffee intake with one glass of milk for most of their adult lives their bone mineral density was not affected[124].

A study conducted in 1994 at the Calcium and Bone Metabolism laboratory at Tufts University found accelerated bone loss from the spine and total body with daily consumption of two to three cups of coffee and calcium intake of less than 744 mg/day of calcium[125]. Caffeine intake should be limited to no more than three cups per day of coffee, tea or soft drinks as long as there is adequate calcium in the diet.

1.5.4 Phytoestrogens

Phytoestrogens are plant-derived compounds (isoflavones) that have a similar chemical structure to endogenous estrogen with the potential to act like estrogen on bone tissue[116]. Soy protein and flaxseed are the most commonly used plant sources. The protective effect of phytoestrogen, genistein has been reported from a very recent study where data suggest that through attenuation of bone loss, isoflavones have a potentially protective effect on the lumbar spine of women[126].

The collective data from all the clinical studies thus far performed suggest that diets rich in phytoestrogens have bone sparing effects in the long term, although the magnitude of the effect and exact mechanisms of action are presently elusive or speculative[127]. There

are no studies on fracture risk. Therefore longer and larger randomized trials are required prospectively to establish whether consuming a diet rich in phytoestrogens prevents bone loss and reduces fracture risk.

The value of soy protein as a substitute for oestrogen pills was questioned by Dutch researchers who found that soy did not increase bone density in postmenopausal women, and did not improve their memory or cholesterol levels[128]. In this study, Dr Yvonne van der Schouw of the Julius Center for Health Sciences and Primary Care at the University Medical Center, Utrecht, the Netherlands, and colleagues randomly assigned 202 healthy postmenopausal women aged 60 to 75 years to receive daily, either 25.6 g of soy protein (containing 99 mg of isoflavones) or a placebo for 12 months. They were recruited from a population based sample in the Netherlands between April 2000 and September 2001.

Another recent study showed that loss of bone mineral content at the hip over one year was lower in Taiwanese women who took 80 mg/day of isolated soy isoflavones compared to placebo. The difference was significant only in those women who were at least 4 years past menopause, had lower body weights or lower calcium intakes[129]. While there is some evidence that isoflavones-rich diets have bone-sparing effects, it is not known whether increasing soy isoflavones intake appreciably decreases the risk of osteoporosis or osteoporotic fracture.

1.5.5 Physical activity

Physical activity is important for bone health. In long-term studies, researchers have found that, regular participation in weight bearing exercise leads to a significant increase in bone mineral content. Bone mass is higher in athletes than in non athletes as the more active we are the thicker and stronger the bones grow. There is a connection between muscle strength and bone density. When muscles are moved the pull on bones and the jolting of exercise, encourage the bones to absorb more calcium. Physical inactivity and muscle weakness are both associated, independent of other influences, with an increased risk of fractures of the femur in the elderly[130].

Some exercises have been associated with reduced bone loss, although few studies have directly evaluated their effect on bone mineral density[131]. A meta-analysis of clinical trials published from 1966 to 1996 showed that exercise training programs prevented or reversed almost 1% of bone loss per year in the lumber spine and femoral neck for both pre and postmenopausal women[132].

The type of exercise is important. Weight bearing exercises like walking, jogging, stair climbing, dancing and running have a beneficial effect on bones and muscle as they work against gravity. Strength training or resistance exercises like free weights and weight machines improve muscle mass through muscle resistance[133].

Hormone levels may also influence the amount of bone gained during this period. In a trial with prepubertal and early pubertal girls, greater gains in bone mass with physical activity were seen in the girls in early puberty, possibly because of their increasing estrogen levels [134].

The recommended minimum exercise for healthy midlife women is 30 minutes of moderate intensity physical activity performed on preferably all days of the week. Strength training can be performed as little as twice a week and need not involve specialized equipment other than simple weights or elastic bands[135].

The elderly Asian woman, due to cultural mores, has not been very active physically, however, this trend is changing. It has been observed that the younger women are now more aware of the benefits of high impact physical activity and are exercising more.

1.6 Osteoporosis

1.6.1 Pathophysiology of Osteoporosis

Basic mechanisms responsible for the development of primary osteoporosis are poor bone mass acquisition during growth and development and accelerated bone loss in the period after peak bone mass is acquired. Both processes are modulated by

environmental and genetic factors. Loss of gonadal function and aging are the two most important factors contributing to the development of this condition coupled with the Caucasian and Asian race and a low body mass index.

About two thirds of the risk for fractures in postmenopausal women is determined by pre menopausal peak bone mass. Peak bone mass is higher in Africans than in Asians or Caucasians and higher in men than in women, resulting in a lower incidence of hip fractures in these populations[122].

Increase in bone mineral mass during growth and development in all individuals is the result of longitudinal bone growth and changing bone thickness and shape. Approximately half the bone mass is accumulated during pubertal development[123]. This is associated with an increase in oestrogen, progesterone and testosterone levels and is almost completed with closure of the end plates. There is only minimal additional accumulation of bone minerals during the next five to fifteen years, which results in achievement of peak bone mass during the third decade of life.

1.6.2 Clinical features

Clinical features of osteoporosis include chronic or recurrent backaches and episodes of severe back pain associated with acute vertebral compression. Typically these symptoms follow an episode of acute pain that develops after ordinary activities such as lifting a sack of groceries or raising a window. Pain may become chronic with recurrent fractures whereas more than a third of the fractures may be asymptomatic and painless.

Physical findings include progressive kyphosis and shortened stature. Significant pain need not be a feature of the dorsal kyphosis and lordosis characteristic of a dowager's hump that occurs in elderly women[137]. Laboratory findings are usually normal in osteoporosis. Transient elevations of alkaline phosphatase produced by the osteoblasts and associated with increased bone turnover, may be seen at times in some individuals[138].

1.6.3 Diagnosis

Diagnosis of clinical osteoporosis is made from history of fractures or radiological evidence of the same. A simple plain film sometimes shows demineralized bone. However, osteopaenia as a radiological diagnosis on a plain film usually implies a bone loss of 30% or more and as such is a very insensitive test[139]. In the vertebral column loss of horizontal trabeculation, ballooning of discs and the classic anterior wedge fracture are commonly seen.

BMD is the single best predictor of osteoporotic fracture risk and is used to follow therapeutic interventions[140]. Both peripheral and central bone sites can be measured to assess BMD. Three major imaging modalities are commonly used in the clinical setting.

1.6.4 Bone Mineral Density

1.6.4.1 Dual energy x-ray absorptiometry

Dual energy x-ray absorptiometry (DEXA) is widely accepted as a gold standard technique for BMD measurement[140]. Measurements can be obtained in any site of the body, but the standard sites consist of spine and hip imaging in anterior-posterior projection and the distal forearm. Approximately 15% of patients may have high bone density at one site and low at another site and measurements at multiple sites may be desirable. Measurements of total body bone mineral content and density are also possible with DEXA and are useful for assessment of bone mineral accumulation during growth and development. The high level of precision of this technique allows not only for diagnosis but also for monitoring response to therap[140].

1.6.4.2 Quantitative ultrasound

Quantitative ultrasound (QUS) measures the speed of sound and attenuation of the ultra sonic beam in the bone. Results of these measurements correlate with bone density and strength and can predict hip fracture[141]. QUS is an attractive alternative to DEXA because of its portability, lower cost and lack of exposure to radiation. However DEXA is required to confirm the diagnosis. QUS measurements are limited to peripheral bone,

usually the calcaneous and are usually very precise with a coefficient variation of less than 1%. Currently, however the measurements are being confirmed by DEXA. The above methods measure apparent bone density (gm/cm^2) calculated as bone mineral content per unit of projected area rather than true volumetric bone density (gm/cm^3).

1.6.4.3 Quantitative computed tomography

Quantitative computed tomography (QCT) can determine the true volumetric density (mg/cc) of trabecular bone at any skeletal site. QCT has been principally employed to determine trabecular bone density in the vertebral column. Spinal QCT is performed on standard clinical CT scanners. It employs an external bone mineral reference phantom as well as special software to place regions of interest inside the vertebral bodies, typically L1-L3. QCT allows for selective assessment of both cortical and trabecular bone and metabolic changes in trabecular bone are picked earlier as its turnover is higher than cortical bone[142]. Longitudinal and cross-sectional bone mass measurements have been obtained at the University of California at San Francisco (UCSF) in over 3,000 patients to make the standards used all over the world. These are used and the scanner is regularly calibrated and standardized according to their scale every month.

QCT`s ability to measure bone loss is significantly better than projectional methods such as DEXA, as QCT selectively assesses the structurally important trabecular bone in the vertebral body. As osteoporosis is a generalized process and since BMD shows at least modest correlation across sites, BMD at one site is predictive of fracture at another site. The results of QCT are reported as T-scores as the number of standard deviations below the mean for young normals. The BMD scan is painless requiring a brief low dose radiation lasting 12 minutes.

QCT is the method that is available and used to perform BMD scans at the Aga Khan Hospital, Nairobi. The equipment used is a Light speed 16 slice CT scanner with a QCTPRO module. The serial number is 306290CN8 and is made by General Electric. This is a specific program which does 2D axial scans through the centres of 3 or 4 vertebral bodies between T11 through to L4. A phantom is used to calibrate CT numbers

as measured within a patient relative to those measured in regions of a phantom with a known equivalent BMD. This information is relayed to a computer and printed. Change in BMD is reflected by changes in the peak bone mass after 40 years of age when the pre-menopause period sets in. To assess the normality or otherwise of the measurements made in individual patients, results are interpreted in relation to appropriate sex and ethnic match reference data which is part of the installed software.

BMD measurements are expressed relative to two norms: 1) the expected BMD for persons of the same sex and age (Z score) and 2) the expected BMD for young healthy adults of the same sex (T score). The difference between the patient's score and the norm is expressed as standard deviation (SD) above or below the mean, with 1 SD indicating about 10% to 12% difference in BMD.

The World Health Organization (WHO) has established diagnostic guidelines for interpretation of T –score values based on BMD measurements in white women[142]. It defines normal BMD as within 1 SD above or below the T score in young healthy adults. T scores between -1.0 and -2.5, indicate osteopaenia whereas T scores lower than -2.5 indicate osteoporosis. Severe osteoporosis is considered to be present when the value for bone mineral content is more than 2.5 SD below the mean for young adults.

1.7 Biochemical Markers of Bone Turnover

A combination of markers of bone turnover can be used in a variety of ways in the clinical investigation of osteoporosis. Growing evidence suggests that the rate of postmenopausal bone loss may be determined by biochemical markers such that a single biochemical marker shortly after menopause, in conjunction with a bone mass measurement, may be used to identify women with high bone turnover and who are therefore likely to sustain a high rate of bone loss. In osteoporotic patients, markers may be used to identify the subgroup of patients with high bone turnover, who may benefit from a different therapeutic strategy from that used in patients with low turnover. Markers can also be used in the clinical investigation of new therapeutic agents to monitor their effect and mechanism of action[143]

Osteocalcin is a bone-specific protein secreted by osteoblasts and its serum level is a sensitive marker of the rate of bone formation. Other markers of bone formation include serum levels of total and bone specific alkaline phosphate and serum type 1 collagen propeptide[61]. Pyridinoline and deoxypyridinoline are collagens cross links that are released into the blood and urine during the degeneration of type 1 collagen in the process of osteoclastic bone resorption[144]. Urinary excretion of pyridinoline such as hydroxylysylpyridinoline and lysylpyridinoline has been shown to be a more sensitive and specific marker of bone resorption than conventional markers such as urinary hydroxyproline[144]. Its use should be valuable in the clinical investigation of metabolic bone disease specially osteoporosis[144].

1.8 Medication and illnesses

Several medications show clear association with osteoporosis (Table1.3). Glucocorticoids are used in the treatment of a number of chronic diseases and are the most important cause of loss of mostly trabecular bone. Consequently fractures occur most commonly in vertebrae, ribs and ends of long bones. Bone loss occurs very rapidly and maybe as high as 20% during the first year of steroid use. Dose of steroids that is detrimental to BMD in most people appears to be more than 7.5 mg of prednisone daily, but risk for fracture may be seen with lower doses[145]. Mechanisms for steroid induced bone loss include decreased intestinal calcium absorption, decreased renal reabsorption, decreased levels of gonadal hormone secretion, decreased osteoblastic activity, increased rate of osteoclastic activation and secondary hyperparathyroidism.

Patients using antiepileptic drugs for more than 2 years, in particular those taking enzyme-inducing anti epileptic drugs and those older than 40 years, have significantly lower bone mineral density at clinically relevant fracture risk sites [146].

In cross-sectional analysis of NHANES III, anticonvulsants and opioids (but not benzodiazepines or antidepressants) were associated with significantly reduced bone mineral density. These findings have implications for fracture-prevention strategies[147].The pathophysiology of osteoporosis in the setting of HIV infection is

unclear. In some studies osteoporosis occurred in conjunction with antiretroviral-associated lactic acidosis, a situation in which phosphate may act as a buffer[148]. Others have postulated that PIs may inhibit new bone formation by stimulating osteoclasts activity or inhibiting osteoblast activity[149]. The PIs are metabolized by cytochrome P450 enzymes, and inhibition of 2 cytochrome P450 mixed function oxygenases that mediate vitamin D activation has been suggested as a possible mechanism for development of osteoporosis. Dusso and associates found that all the protease inhibitors inhibited conversion of 25-hydroxy vitamin D to 1, 25-dihydroxy vitamin D in vitro[150].

Table 1.3: Chronic diseases, medications and surgical factors that affect bone health

Chronic Diseases	**Medications**
Cushing's syndrome	Glucocorticoid
Anorexia nervosa	Prednisone
Hyperthyroidism	Cyclosporine
Hyperparathyroidism	Excess thyroid hormones
Marfan syndrome	Methotrexate
Type 1 Diabetes	Phenobarbital
Chronic renal insufficiency	Phenytoin
Hypercalciuria	Phenothiazines
Chronic liver disease	GnRH agonists
Osteogenesis imperfecta	Heparin
Haemochromatosis	Aluminum antacid
Malabsorption	Isoniazid
Hyperprolactinaemia	Lasix
Any malignancy including solid tumours	
Hypogonadism	
Surgical Factors	
Gastrectomy	
Intestinal bypass	

1.9 Pharmacotherapy for bone health

There are several medications that have been approved by the United States food and drug administration (FDA) for the prevention and treatment of postmenopausal osteoporosis. Treatments for osteoporosis may be classified into antisorptive and anabolic agents. Antisorptive agents like selective estrogen receptor modulators (SERM) cause a transient uncoupling of resorption and formation leading to a modest increase in bone density of 5%- 10%. Anabolic agents lead to a larger increase in bone density.

1.9.1 Bisphosphonates

Bisphosphonates are stable analogues of naturally occurring pyrophosphate, which are poorly absorbed from the bowel, localize preferentially in bone where they bind to hydroxyapatite. Alendronate has been shown to increase bone density in the spine by 7%-10% and the hip by 6% over three years resulting in 63% fewer vertebral fractures[151].

Risedronate is a newer bisphosphonate that binds to hydroxyapatite. In individuals treated with 5mg for two years bone mineral density increased by 5% - 7%[152].

Bisphosphonates are also effective in preventing bone loss in men and women on long term corticosteroids[153]. Side effects are uncommon but may include abdominal or musculo skeletal pain, nausea, heartburn or oesophageal irritation.

More recently, bisphosphonates have been linked to osteonecrosis (death of the bone) in the jaw. In one study of women being treated with alendronate, pamidronate, or zolendronate, researchers reviewed records from a referral center. They identified 23 patients with osteonecrosis of the jaw in the 100 patients tested. They had all been on bisphosphonates for the previous twelve months[154].

1.9.2 Selective estrogen receptor modulators

Raloxifene is a SERM which has oestrogen agonist actions on the skeleton and lipid profile but act as an oestrogen antoginist on the breast and endrometrium. It has been shown to decrease bone resorption and increase bone density by 2% -2.5 % in two years as well as decreasing low density lipoproteins[155]. It does not, however protect against hip fracture. Raloxifene cannot be used to treat menopausal symptoms and it does not stimulate endometrial growth but it may provide an alternative to hormone replacement therapy (HRT) for treatment of osteoporosis. It should not be used for premenopausal women as it may be teratogenic[156].

1.9.3 Salmon Calcitonin

Calcitonin is a naturally occurring polypeptide hormone involved in calcium regulation and bone metabolism. It is a potent antisorptive agent with a rapid but short lived effect on osteoclastic function. In women who are at least five years beyond menopause, calcitonin slows bone loss, increases spinal bone density and relieves the pain associated with bone fractures[157].

Calcitonin reduces the risk of spinal fractures and may reduce hip fracture risk as well. It is currently available as an injection or nasal spray. It does not affect the other organs or systems in the body but may cause side effects including nausea, urinary frequency, flushing of hands and face and skin rash. The side effects reported with nasal calcitonin are a runny nose.

1.9.4 Teriparatide

Teriparatide is the first anabolic treatment that has been shown to decrease fracture incidence. Treatment with Teriparatide, an injectable form of human parathyroid hormone, for a median 20 months increased bone mineral density by 9%- 13% in the lumbar spine and 3% -6% in the femoral neck than the placebo preparation[158]. There was also a 53% reduction in non vertebral and 63% reduction in new vertebral fractures. The anti fracture efficacy is independent of age, initial bone mineral density and the absence or prevalence of fractures[159, 160, 161].

1.9.5 Hormone/estrogen replacement therapy

HRT reduces bone breakdown, increases bone density in the hip and spine and reduces the risk of hip and spinal fractures[113]. Estrogen replacement therapy (ERT) is a FDA approved drug but only for the prevention and not for the treatment of osteoporosis. ERT can increase the risk of endometrial cancer but adding progesterone reduces this risk. Long-term use of HRT/ERT may increase the risk of breast cancer[162].

Perhaps more disturbing are the results of the large Women's Health Initiative study. This study found that conventional hormone replacement therapy, with either estrogen alone or estrogen and synthetic progestin, was associated with an increased risk of stroke [163]. Additionally, in the first one to two years of therapy, women experience an increased risk of coronary heart disease, stroke, deep vein thrombosis, or pulmonary embolism. Moreover, the risk of fracture does not decline until the fifth year of treatment[164]. These findings had a dramatic effect on the number of women taking conventional hormone replacement therapy: some studies report that as many as 80 percent discontinued their treatment after the results were made public[165].

1.10 Education for Osteoporosis Prevention

Age is not a drawback to start osteoporosis preventive strategies. Healthcare professionals have to educate themselves in order to assess and counsel their clients on the risk factors, nutrition recommendations, physical activity needs and pharmacological options as well as other life style modifications required to obtaining and maintaining optimum bone density and health. The ones already diagnosed with osteoporosis can also benefit from employing the same assessment and educational principles to reduce or halt further bone loss.

1.11 Study Justification

As women age and experience the menopausal transition, the risk of developing osteoporosis increases. There are a number of factors that have been reported to increase the risk of osteoporosis and may contribute to the heterogeneity in the rates of bone loss experienced by mid life women of all races and communities. There are many misconceptions about osteoporosis, for example that it is "an old woman's disease". In

fact, bone loss in women can begin as early as age 25. Worldwide, the lifetime risk for a woman to have an osteoporotic fracture is 30-40%. In men the risk is about 13%.

Anthropometric measures of body size and composition, lifestyle and gynaecological factors have all been shown to be associated with bone mineral density (BMD) and may contribute to the risk of developing osteoporosis. There is also evidence that genetic factors may influence rates of bone loss.

The prevalence of risk factors in a Kenyan born Asian sample of mid life women and the changes, beneficial or otherwise, that occur in these risk factors as women pass through the menopause have yet to be documented.

The prevalence of osteoporosis needs to be documented too, in this population and also whether there are any differences in comparison to other Asian women in other adopted countries of their choice or other races.

It is hoped that the results compiled in this study will improve the awareness of this silent killer among the health care providers. It will also assist in improving their knowledge about calcium intake, activity levels and lifestyles so that they can assist their patient population in reducing the risk of developing osteoporosis and fractures.

CHAPTER 2: METHODOLOGY

2. 1 Study Aims and Objectives

The study aim was to identify the risk factors associated with the occurrence of osteoporosis in Asian women as seen at the Aga Khan University Hospital, Nairobi, who had previously had BMD scans done from January 2004 to December 2004.

2.1.1 Primary objective.

The primary objective of this study was to identify the risk factors that are associated with the development of osteoporosis in Asian women.

2.1.2 Secondary objectives

The secondary aims were to document:

- BMD values of Asian women in Kenya with osteoporosis
- Dietary intake of Asian women in Kenya with osteoporosis
- Physical activity of Asian women in Kenya with osteoporosis

2.2 Study Design

2.2.1 Study type

This was a cross sectional, descriptive and observational study which describes the bone mineral density, socio-demographics, dietary intake and physical activity of Kenyan Asian women of same ethnic parentage. The study was designed such that data was collected after women had received their BMD scans and were aware of the results. The study samples with normal bone scans were used as the control group for comparison with the abnormal sample scans, which formed the osteoporosis group to identify the risk factors associated with osteoporosis.

2.2.2 Study population

The sample population was women above 40 years of age, of Asian origin living in Kenya who had been referred for bone mineral density scans and had BMD scans done at The Aga Khan University Hospital, Nairobi from January 2004 to December 2004.

2.2.2.1 Inclusion criteria

- All female clients of Asian origin who had already had BMD scans done at Aga Khan University Hospital, Nairobi during the period January 2004 to December 2004
- Female clients older than 40 years
- Clients who consented to take part in the study after counseling

2.2.2.2 Exclusion criteria

- Clients who declined consent
- Clients younger than 40 years of age.
- Pregnant women
- Clients of mixed race parents

2.2.2.3 Sample selection and size

Asian women living in Kenya are descendents of immigrants who came from India and Pakistan in the late 19th and early 20th century. They speak and read English fluently, although it is their second language.

According to the records of the Radiology Department of the Aga Khan Hospital, a total of 180 BMD scans were done on Asian women and men, from January 2004 to December 2004. The women had scans done on the recommendation of their gynaecologists as routine tests because of age or other gynaecological issues. Medical practitioners asked for them because of other chronic diseases like diabetes and rheumatoid arthritis. Since the study sample consisted only of females, the total number of scans for women was reduced to 150. The latter was further reduced to 100 women as 30 women were younger than 40 years and did not meet the selection criteria; another 10 had immigrated to other countries, 5 were of mixed race parentage and 5 had been visitors from abroad. Therefore the total number of women who met the selection criteria was 100.

These women were identified and the investigator collected the telephone numbers of the participants from the Radiology Department. Each participant was contacted by

telephone and if the selected participant was willing to take part in the study, a suitable appointment was scheduled.

The total number who agreed to take part was 64 (n=64). The reasons for the ones who were unwilling to participate were as follows, 8 were busy; 12 were out of town; 3 felt that they did not want to share information and 13 did not come for their appointment despite rescheduling twice.

2.3 Study Techniques

A general socio-demographic questionnaire, Food Frequency questionnaire (FFQ) and a physical activity questionnaire were completed for each participant and anthropometric measurements were taken as well. A BMD scan had been done on each of the study participants by the Radiology Department and the results were sourced from there for the purpose of the study (Appendix 1, Appendix 2, Appendix 3, Appendix 4, and Appendix 5).

2.3.1 Socio-Demographic information

The following socio-demographic and life- style related information was obtained:

- Date of birth
- Age
- Marital status
- Medication
- Level of education
- Occupation
- Age at menopause
- Age at menarche
- Contraceptive use
- HRT
- Family size
- Alcohol intake
- Cigarettes

2.3.2 Anthropometric data

The investigator obtained height, weight, waist and hip circumference measurements using standard equipment and standardized techniques.

2.3.2.1 Weight and height

Weight and height were determined using a standardized Seca® beam balance scale with stadiometer. Height to the nearest 0.1 cm and weight to the nearest 0.1 kg were taken and subjects were measured and weighed in one light layer of outer clothing.

The height was measured in centimeters to the nearest 0.1cm. Height measurement was done with the subject standing with feet together, upright and the head placed in the Frankfort plane[166]. The scale was regularly controlled for zero reading between measurements. Weight was measured in kilograms to the nearest 0.1 kg twice and the average weight was recorded. The scale was regularly controlled for zero reading between measurements.

2.3.2.2 Waist and hip circumferences

Waist and hip circumferences were measured in the horizontal plane with the tape pulled tight over light clothing, but not causing indentation. Waist circumference was measured at the midpoint between the lower costal border and iliac crest, arms at side. Hip circumference was measured at the widest point of the posterior (gluteal) protuberance, feet together and gluteal muscle relaxed. An automatically retractable fiberglass tape was used to measure all circumferences[166]. All measurements were taken by the investigator at the time of the interview and measured to the nearest 0.1 cm. To improve the reliability of the measurements all were measured twice and an average measurement was calculated.

2.3.3 Dietary intake

For the purpose of this study, dietary intake of focus included the intake of all macro and micronutrients.

A Food Frequency Questionnaire was modified and tested for use in the study sample. The format and content used were modeled on the FFQ used in South Asian women in

Britain which had been validated in eleven South Asian immigrant women, against a 7 day food dairy. The Pearson correlation coefficients for proportion of total energy from fat, protein and carbohydrates were 0.64, 0.84 and 0.42 respectively.

The population was similar to the Kenyan Asian women as some were immigrants from Kenya[167]. This validated questionnaire which was modified by the investigator to include local foods had an open ended format (i.e. how often per day; week; month; never). This has been found to be better to use in an interview administered setting and provided more accurate information.[168]. The Food Frequency Questionnaire covered the preceding six months prior to data collection in June, July and August 2005, and included 18 sections with a total of 248 food items commonly used by the Asian community. Each food was coded for analysis according to the Food Finder 3 analysis program developed jointly by, Wam Technology and Medical Research Council South Africa, for analysis. There was no previous validated FFQ in Kenya for this sample population and there are no software programs available for food analysis either.

2.3.3.1 Pilot study

Initial pretesting of the FFQ was carried out on 10 Asian women, from different sub ethnic groups, known to the investigator. All the sub ethnic groups, which included Sikh (n=2), Gujarati (n=3), Ismaili (n=3) and Punjabi Muslims (n=2) were represented. The purpose of the pretesting was to test for comprehension of the FFQ, to check for ambiguity and to assess the utility of the different response categories.

The investigator integrated and incorporated all the suggestions made and the revised questionnaire was then returned to all the participants for a second review. All the final suggestions made were used for the improvement of the content and comprehension of the questionnaire and were incorporated in the final questionnaire used in this study.
Portion sizes were determined using the commonly used household measures and crockery, and weighing the portion sizes for the different foods used.

2.3.3.2 Repeatability

A pilot study was carried out on 10 participants to test the questionnaire and get the range of the nutrients ingested. After three weeks the FFQ was repeated in the same. The second FFQ measurement gave a slightly higher median of intake than the first measurement.

The median paired differences between the two measurements were small for all the nutrients examined. The levels of agreement between the two FFQ were high for absolute nutrient intake (Table 2.1). The Pearson's correlation coefficients for energy, protein, fat and carbohydrate were 0.99, 0.99 0.88 and 0.99 respectively. There were no significant differences in the two tabulations, suggesting no significant loss of information.

Table 2.1: Pearson correlation coefficient of nutrients between the two FFQ used for the pilot study

Nutrient	FFQ1(n=10)		FFQ2 (n =10)		Pearson Correlation
	Mean	±SD	Mean	±SD	
Energy (Mj)[1]	9.9	1.37	9.8	1.7	0.997
Protein(gm)[2]	64	11	69	21	0.996
Fat(gm)[2]	115	19	106	12	0.884
Carbohydrates(gm)[2]	233	45	237	63	0.998
Calcium(mg)[3]	885	256	892	359	0.997
Iron(mg)[3]	14	3.6	15	6.5	0.992
Magnesium(mg)[3]	410	108	448	156	0.996
Phosphates(mg)[3]	1304	326	1363	444	0.986
Potassium(mg)[3]	3660	943	4192	1534	0.994
Vitamin A(mcg)[4]	2967	166	2751	277	0.987
Vitamin D(mcg)[4]	1.9	1.2	2.2	2	0.984
Vitamin B12(mcg)[4]	2.9	1.4	4.9	6.2	0.973
Vitamin C(mg)[3]	204	100	263	184	0.985

[1] Mega joules [2] gram [3] milligram [4] microgram

2.3.4 Physical activity

Since there was no validated physical activity questionnaire available for any population in Kenya, EPAQ2 was used. EPAQ2 is a self completed questionnaire that collects self reported physical activity behaviours in a disaggregated way such that the information can be reaggregated according to the dimension of physical activity that is of interest[169]. The recreational section is derived from the previously validated Minnesota leisure time activity questionnaire with activities ordered according to their frequency in the United Kingdom population[170, 171]. Correlation coefficients for the activity indices used in this study ranged from 0.7 to 0.95.

The EPAQ-2 physical activity questionnaire was used to assess daily activity.
This questionnaire elicited information about activity in three sections.

1) Activity at home

    This section asked about physical activity in and around the house.

2) Travel to work and activity at work

    This section asked about activity at work and may be skipped by people who have not worked over the last 12 months.

3) Recreation

    This section was about how leisure time was spent.

This questionnaire was chosen by the investigator as it had been validated in a sedentary population[169]. The middle aged women in the study sample population were fairly sedentary. It had the advantage that any portion that was not relevant to a participant could be omitted.

2.3.5 Bone mineral density measurement

BMD had been measured at the lumbar spine (anterior-posterior position) using QCT to perform BMD scans at the Aga Khan University Hospital, Nairobi previously in the study sample (Appendix 8). The equipment used was a Light speed 16 slice CT scanner with a QCTPRO module which performed axial scans through the centres of 3 or 4 vertebral bodies between T11 through to L4. Areal BMD was expressed in gm/cm^2 and in standard

deviations from the young normal mean (T-score). The scanner is calibrated and standardized every month.

The WHO has determined that a T score of minus 2.5 defines osteoporosis. This level has been set to enable bone density comparisons between populations and is not meant to dictate treatment. However, T scores in this range do define a population at risk for fracture that has been shown to benefit from treatment. Osteopaenia has been defined as a BMD of -1.0 to -2.5. The risks associated with this level and the benefits of treatment are less clear.

2.4 Data Collection Procedure

The investigator contacted each BMD scanned Asian client by telephone, and if she agreed to be a participant in the study, an appointment at a time convenient to the participant, during week days, and weekends, was made.

It was explained that measurements of height, weight and waist and hip circumferences would be done and data collection for the FFQ, the socio demographic and exercise + diet questionnaire would also be collected. Information was also given that it would take approximately $1^{1}/_{2}$ hours for the whole exercise.

The participant was invited to The Aga Khan University Hospital to come to the diet advisory office. On arrival the participant was once again briefed about the study and a consent form given. The consent form was filled with the relevant information, signed and collected after completion. The socio-demographic questionnaire was given to the participant for self completion. The FFQ and physical activity questionnaire were interview administered by the investigator. For completion of all the three questionnaires it took an average time of one hour. A period of three months was allocated for data collection.

BMD scans were downloaded from the Radiology department and printed after the women consented to be part of the study and had filled the questionnaires.

2.5 Ethics

The study was approved (Ref No 04/10/167) by the Committee on Human Research of the Health Sciences Faculty of the University of Stellenbosch, Tygerberg, South Africa.(Appendix 5). The study was also approved by the Ethics Committee, Aga Khan Hospital, Nairobi (Appendix 6). Confidentiality was ensured throughout the study process. Each participant was provided with an informed consent form by the investigator which was completed before data collection (Appendix 7).

2.5.1 Patient confidentiality

Patient identification information was omitted from study related material to ensure participant confidentiality. Each participant received a subject identification number upon entering the study. This number was used on all study related material and documentation. The participant was assured that all information given verbally and on the questionnaires would be confidential and used specifically for the study and would not be shared with anyone for any other project or purpose.

2.6 Data Analysis

The overall data from all the questionnaires was analyzed by Statistical Packages for Social Sciences© (SPSS) version 11.5 program and Stat Soft Inc. (2004) STATISTICA (data analysis software system), version 7. The statistician assisted by the investigator entered all the data in this program and double-checked by checking that the entries on the hard copy questionnaires matched those entered in the software. A qualified statistician carried out the data analysis with the assistance of the investigator.

2.6.1 Analysis of dietary data

The Food Frequency Questionnaire was analyzed using the Food Finder 3 program from South Africa. Food Finder 3 for Windows® is a computer software application developed by the Nutritional Intervention Research Unit and Biomedical Informatics Research Division of the South African Medical Research Council in collaboration with Wam Technology.

There is no database for food analysis or Kenyan foods software available. Hence, Food Finder 3, a South African software program was used as it had the analysis of foods commonly eaten in Kenya and it was suitable due to the similarity of foods. The first edition of the Food Composition Tables of the Nutritional Intervention Research Unit of the Medical Research Council was published in 1981 (1). Updates of these tables appeared in 1986 (2) and 1991(3). These tables have become the standard reference for dietitians and those involved in nutrition research, in South Africa to determine the nutritional intake of people. The program has the advantage of additional food items which can be added to the database. This was done for any foods specific to Kenyan Asians. Food Finder 3 was used to analyze the macronutrients and micronutrients from the food frequency questionnaire.

The food intake was calculated from the amount taken in gram or mg per day. Energy, nutrient and food intake were obtained by summing the reported frequency multiplied by the amount consumed over all reported foods and expressed in grams consumed per day. For example if 100gm bread was consumed 4 times per day, it was tabulated as 400g but If 100g of bread was consumed once per week, it was tabulated as 100/7 = 14 g per day. If 100g of bread was consumed twice per month, it was tabulated as 100x2 / 30 days = 6, 6 = 7 g per day. This was done for each individual food. After entering the data for each participant, it was analyzed and the macronutrients were expressed in grams and the micronutrients were expressed in milligrams or micrograms. Each nutrient was also calculated and given as a percentage of the Daily Recommended Intake (DRI).

2.6.2 Physical activity questionnaire

Estimates of energy expenditure, at home, work and during recreation, from the questionnaire was calculated by multiplying days per week and minutes per day. The sum in each category was given in units of hours per week. Pearson correlation was used to test the significance of relationships between the different characteristics observed in the three categories and the BMD t-score.

2.6.3 BMD analysis

The sample of women was grouped into 2 groups based on the WHO recommended criteria, Normal above – 1.0, Osteopaenia between - 1.0 and -2.5 standard deviations below the normal values and osteoporosis below – 2.5 standard deviation below the normal values with a previous fracture[172]. Women with osteopaenia and osteoporosis were combined together to form the osteoporosis group and the women with normal BMD T-score formed the control group.

2.6.4 Analysis of Anthropometric data

Weight was measured in kilograms and height was measured in centimeters which were converted into Body Mass index. Derived parameters were calculated using the following standard formulas[173].

Body mass index (BMI) (kg/m^2)

$$\frac{\text{Weight}}{\text{Height}^2}$$

17.9= Very Underweight
18 – 19.9 = Underweight
20 – 24.9 = Healthy Weight Range
25 – 29.9 = Overweight
30 + = Excessively Overweigh

Waist: hip ratio (WHR) was derived using the formula below.

$$\frac{\text{Waist circumference}}{\text{Hip circumference}}$$

Waist-hip ratio (WHR) was defined as the waist circumference divided by the hip circumference. WHR is a measure of deposition of abdominal fat leading to central obesity. Unlike BMI there is no consensus to define a cut-off point for WHR. A raised WHR has been taken to be 0.85 or more in women [174].

2.7 Statistical Methods

Descriptive statistics using means and standard deviations were used to describe the sample.

The following components were described using descriptive statistics:

Dietary intake

- Physical activity
- Body mass index (weight and height)
- Waist and hip circumference
- Socio-demographics

The principle statistical procedure used was the general linear model, including repeated measures analysis of variance (ANOVA), as well as Pearson's correlation coefficient to test for significance in relationships.

To establish which risk factors were most associated with osteoporosis in this study group, a p-value < 0.05 was considered as significant.

To compare means for age and anthropometric measurements of the control and osteoporosis group, one way ANOVA test was used.

Kruskal-Wallis test was used to compare nutritional intake at different levels of education.

Since the sample size was larger than 30, we assumed normality in all analysis and a P-value of <0.05 was considered statistically significant*

* Campbell Mj, David M, Medical Statistics; A common sense approach. Third Edition. 1991; 85-89
* Martin Bland. Medical Statistics, Low price Edition, 1993; 241-261
* David SM, George PM. Introduction to the Practice Statistics, Third edition, 1999.

CHAPTER 3: RESULTS

3.1 Sample Characteristics

The study was conducted between September and November 2005, over a three month period. A total of 100 BMD scanned clients were identified and 64 participants consented to the study. These were interviewed representing a 64% response rate and were therefore used for data analysis. The study group comprised of 81% non vegetarians (n=52) and 19% vegetarians (n=12) thus capturing the diverse eating habits and nutrient intake. For results reporting, data was reported for the study sample (n=64), and a comparison of the control group with normal BMD scans (n=24), and the osteoporosis group with abnormal BMD scans (n=40) was done.

3.1.1 Socio- Demographic information

3.1.1.1 Age

Age distribution of the study sample (n=64) ranged from a minimum of 44 years to a maximum of 83 years with a mean of [56.6 (SD 7.9) years]. The majority of the subjects were between 50 and 55 years and two were above 80 years (Figure 3.1). The mean age of the control group was [51.9(4.9) years] with the osteoporosis group at [59.7(7.6) years] and a statistical significant difference $p = 0.001$ in the ages.

3.1.1.2 Marital status and educational level

In the study sample 83% women were married, 9% widowed and 8% single. Fifty percent were university graduates, 39% had a High School Certificate and 11% had schooling up to Primary School Level.

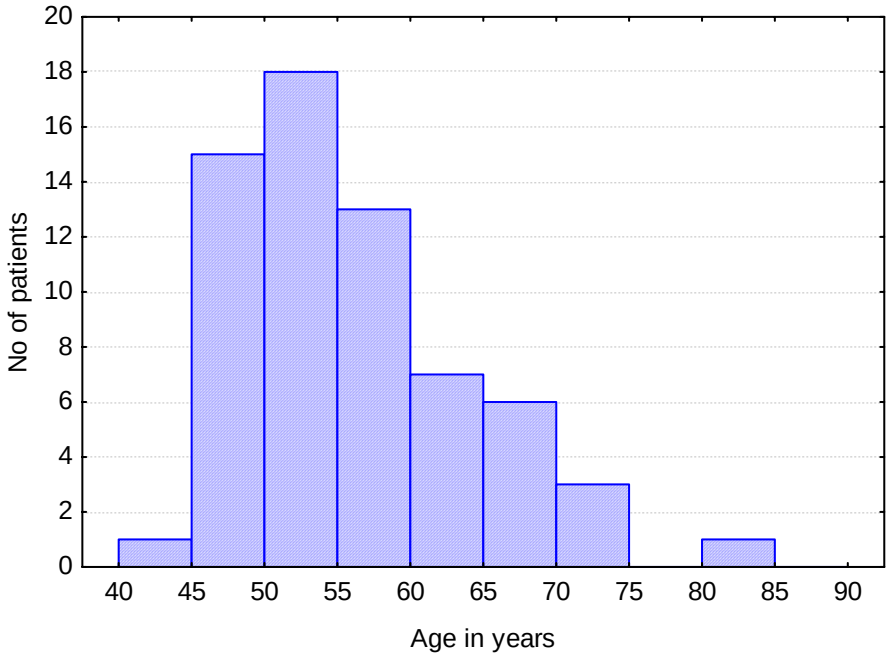


Figure 3.1: Age Distribution of the study sample

3.1.1.3 Employment status

Thirty one percent of the women were housewives and did not work in paid or self-employment, 11% were self-employed in various diverse fields, as business women (n=4), hairdressers (n=1), caterers (n=2). The remainder 58% were employed either in the public or private sector as secretaries (n=9), accountants (n=5), doctors (n=6), pharmacists (n=3), bankers (n=4), teachers (n=8), microbiologist (n=1) and biostatistician (n=1).

3.2 BMD

Thirty eight percent (n=24) had normal BMD scores with a T- score of -0.13 - 1, (control group), 30% (n=19) had a T- score -2.5 - -3.3 with osteoporosis, 30% (n=19) had a T-score -1.43 - -2.5 with osteopaenia and 3% (n=2, both elderly, >80 years) had a T score above -5 with osteoporosis but no fragility fractures (Figure 3.2). The mean T-score for the study sample was [-1.92(-1.20)]. The control group mean BMD T-score was [-0.65 (-0.28)] and the osteoporosis group had a mean T-score [-2.68 (-0.84)]. There was a significance difference p=0.001 between the two groups with ANOVA.

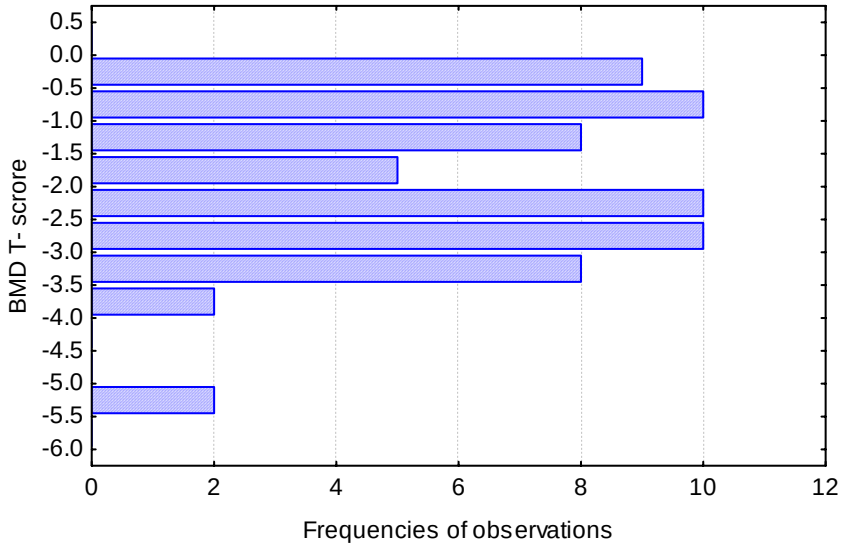


Figure 3.2: Frequencies and distribution of BMD T-score in all study participants

There was a negative correlation between BMD T-score and age as the T-score decreased with advancing age. (Pearson's correlation coefficient R =0. 733) (Figure 3.3).

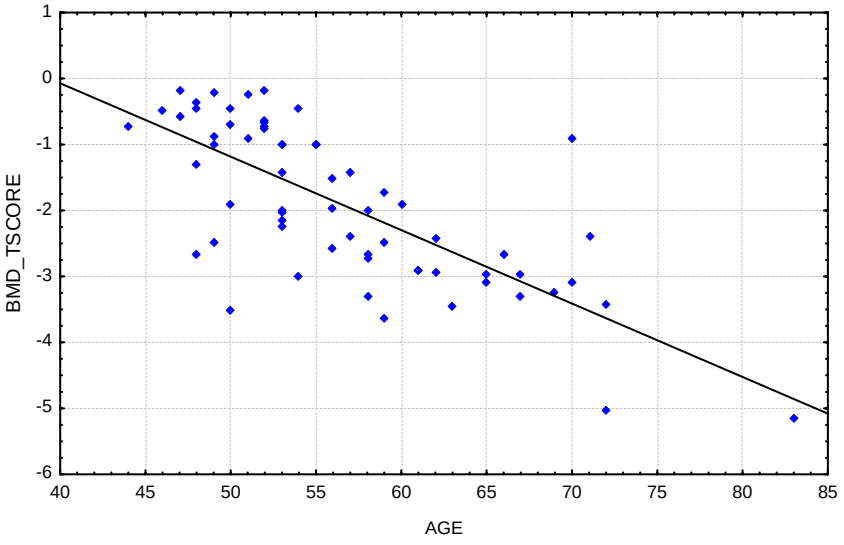


Figure 3.3: Scatter plot of BMD in relation to age distribution in the study sample

3.3 Anthropometry

The study sample had a mean height [158.8 (6.1) cm], a mean weight [68.4(8.3) kg] with a mean BMI [27.2 (3.5) kg/m^2] (Table 3.1). Fifty percent of the study sample was overweight in the range of 25 -29.9 kg/m^2, 30% had a normal BMI in the healthy range of 19 – 24.9 kg/m^2, and 20% were obese in the range of 30 -36 kg/m^2. The mean waist [85.6 (10.2) cm], mean hip circumference [105 (12.24) cm] and the mean waist /hip ratio [0.81(0.06)] of the study sample were within the normal range (Table 3.1).

Table 3.1: Anthropometric characteristics of all study participants

Parameter (unit)	Minimum	Maximum	Mean	SD
Height (cm)[1]	146.00	172.0	158.8	6.1
Weight (kg)[2]	49.00	85.0	68.4	8.3
Body Mass Index (Kg/m^2)	19.7	36.1	27.2	3.5
Waist (cm)[1]	63.00	110.0	85.6	10.2
Hip size (cm)[1]	78.00	131.0	105.1	12.1
Waist-Hip Ratio	0.66	0.94	0.8	0.06

[1]centimeter [2] kilograms

The mean height of the control group was [160 (6.13) cm] with the osteoporosis group having a mean height of [158 (6.14) cm], with a non-significant inter-group difference (p=0.165). The control group had a mean weight of [65 (7.00) kg] with the osteoporosis group at a mean of [70.26 (8.65) kg] and significance p=0.02. The mean BMI of the control group was lower at [25 (2.59)] kg/m^2] and of the osteoporosis group was higher at [28.3 (3.65) kg/m$^{2.}$] with a significance p=0.001(ANOVA) (Table 3.2).

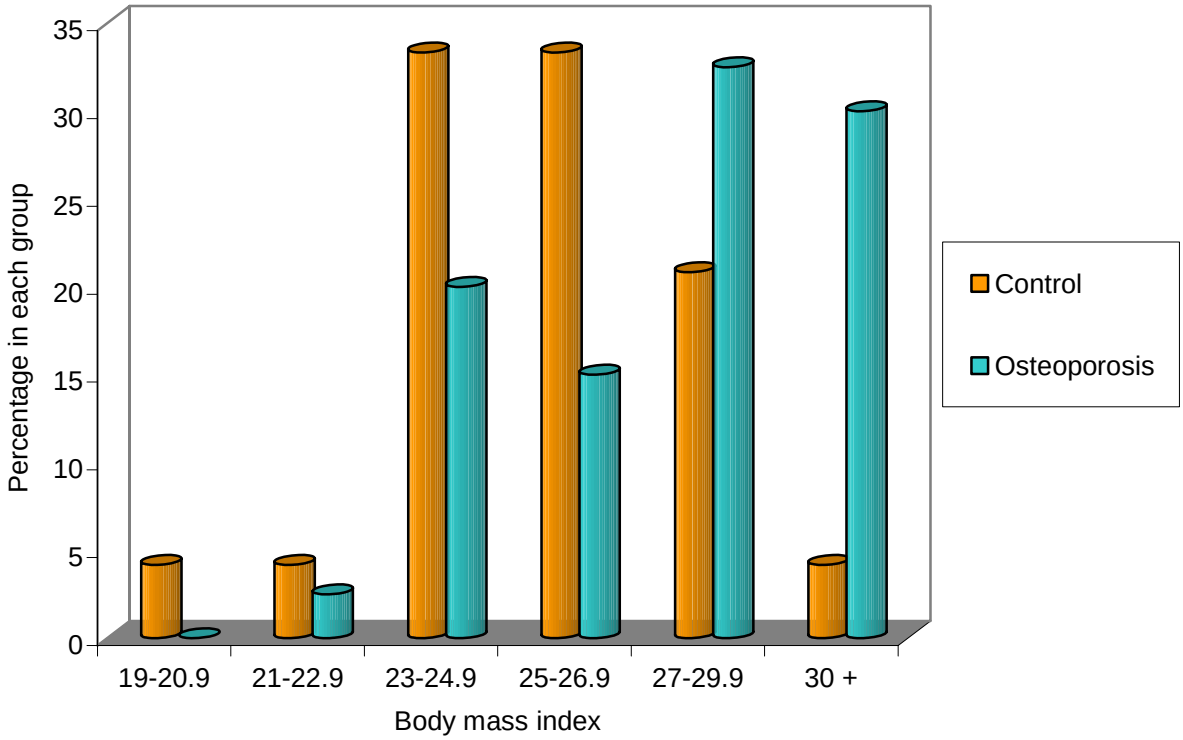


Figure 3.4: The comparative percentage distribution of Body Mass Index (BMI) of the control and osteoporosis groups

Forty five percent of the control group had a normal BMI range between 19 -24.9 versus 23% in the osteoporosis group with a significance p = 0.001. The osteoporosis group was heavier than the control group (Figure 3.4). The control group had a smaller waist size [78.79 (8.19) cm] than the osteoporosis group [89.75 (9.42) cm] with p=0.023. The control group's mean hip size was [97.48 (11.73) cm] whereas the osteoporosis group had a mean hip size of [109.75 (9.98) cm] with a significance p=<0.001 (Table 3.2).

Significant p values with an association with BMD were for age (p=<0.001), waist size (p =<0.001), hip size (p=<0.001) and BMI (p=< 0.001) (Table 3.2).

Table 3.2: Comparison and correlation of anthropometric characteristics between the control and osteoporosis group and BMD

Variables	Control (n=24)		Osteoporosis (n=40)		p-value (ANOVA)	Pearson's correlation	
	Mean	SD	Mean	SD		R^3	p-value
Height (cm)[1]	160.23	6.13	158.00	6.14	0.165	0.235	0.062
Weight (kg)[2]	65.40	7.00	70.26	8.65	0.023	-0.207	0.101
BMI	25.46	2.59	28.36	3.56	<0.001	-0.378	0.002
Waist (cm)[1]	78.79	8.19	89.75	9.24	<0.001	-0.508	<0.001
Hip size (cm)[1]	97.48	11.73	109.75	9.98	<0.001	-0.519	<0.001
WHR	0.81	0.06	0.82	0.07	0.672	-0.013	0.922

P value < 0.05 [1]centimeter [2] kilograms [3] Pearson's correlation coefficient

3.4 Smoking and Alcohol

None of the women had ever smoked and only 3% (n = 2) drank alcohol socially taking on average 6 drinks (wine and/or spirits) a month for the last 10 years.

3.5 Obstetric and Gynaecological Factors

Age at menarche ranged from 11 to 16 years with a mean of 13 years SD. Forty five percent started at 13 years, 22% at 12 years, 16% at 14 years, 11% at 15 years, 3% at 11 years and 3% at 16 years. The family size varied from 1 to 6 children with a mean of 2 children. Fifty percent of women had 2 children, 22% had 3 children, 13% had no children, 8% had 1 child, 5% had 4 children and 1% had 5 children and 6 children each. There were no significant differences between the groups.

The contraceptive methods of choice were the pill and the coil. Fifty six percent of the sample had never used any form of contraception. Forty one percent were on the pill for a maximum of 5 years and a minimum time of 1 year, with a mean of [1.56(2.1) years]. The coil was used by 3% of the subjects. Thirty six percent of the sample (n=23) had been on hormone replacement therapy with a mean duration of [4.6 (4.8) years]. One

respondent had been on HRT for 20 years. Contraceptive usage was higher in the control group with a significant difference of p=0.01 between the two groups. For HRT the significance was p= 0.012 with the osteoporosis group having a higher usage.

3.6 Medications

Twenty eight percent of the women (n=18) were not on any medication, 25% were on one drug (n=16), 23% on two drugs (n=15), 14% were taking three drugs (n=9), 8% were taking four drugs (n=5) with 2% of the sample taking five drugs (n=1} (Figure 3.5).

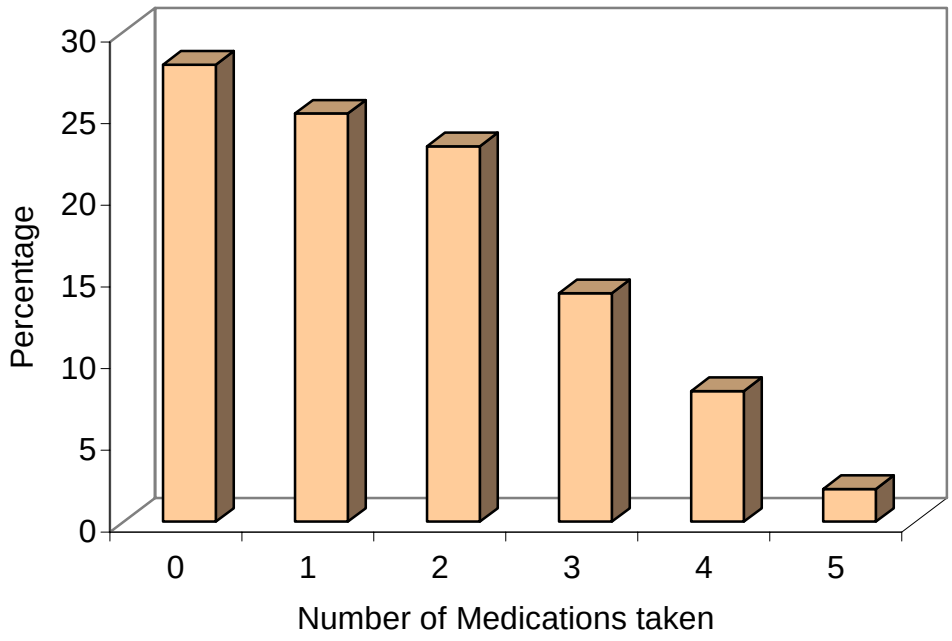


Figure 3.5: The number of different medications taken by the study sample

Seventy two percent (n=46) of the study sample were on regular medication. Statins, antihypertensive drugs, thyroxine replacement, inhaled glucocorticoids for asthma, oral hypoglycaemic agents, insulin and non steroidal anti-inflammatory drugs (NSAID) for pain relief for arthritis were the drugs used. (Figure 3.6)

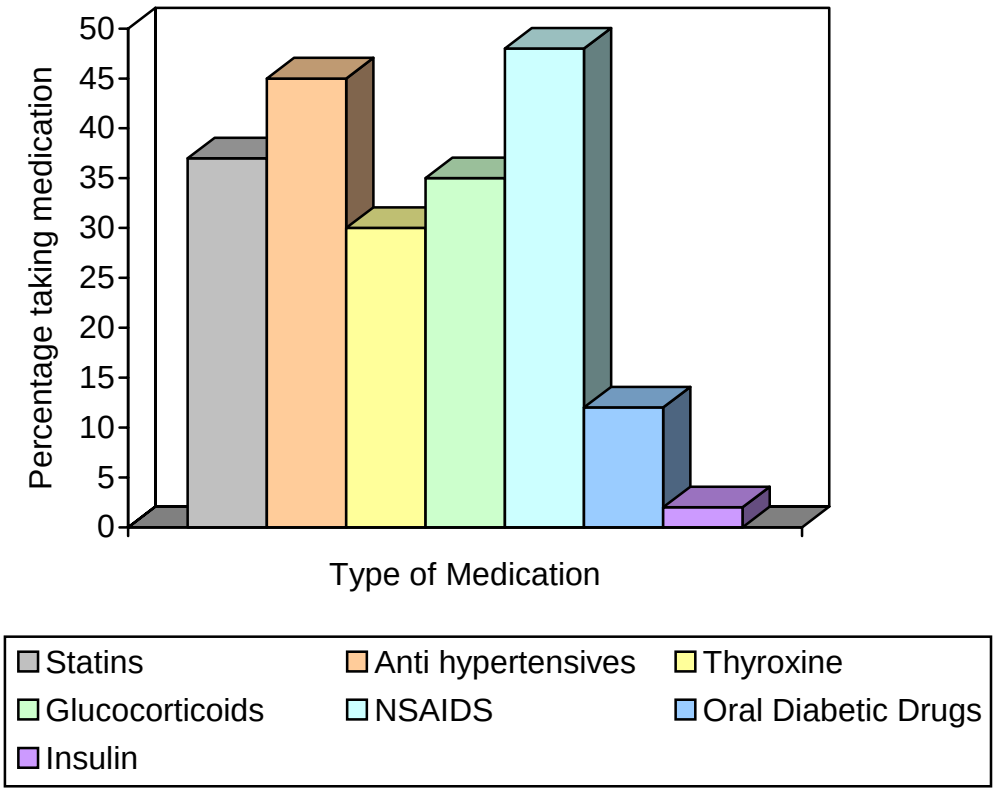


Figure 3.6: Different drugs being taken by the seventy two percent of the subjects in the study who were on medicinal therapy

Anti-hypertensive, NSAID and anti-diabetic drugs had a significant negative association with bone health [p = 0.002, 0.003 and 0.033 respectively (ANOVA)]. There was no such significant association with statins, thyroxine replacement or inhaled glucocorticoids for asthma (Table 3.3).

Table 3.3: ANOVA of medication use between cases and controls

Medications	**p-value**
Statins	0.060
Anti – Hypertensive drugs	0.002
Thyroxine	0.352
Glucocorticoids	0.119
NSAID	0.003
Insulin and Oral Diabetic drugs	0.033

3.7 Dietary Intake

3.7.1 Macronutrients

The nutrient intake analysis did not take into account dietary supplements and the contribution of supplements to the nutrient intake was excluded as only 12.5% of the subjects (n =8) were taking such supplements sporadically.

The reported mean energy intake in the study sample was 9.9 MJ which was significantly higher than the estimated average requirement (EAR) of 8 MJ [9.9 (1.3) MJ]. There was no significant difference in energy consumption between the osteoporosis group [9.9(1.6) MJ] and the control group [9.8(0.94) MJ]. (Table 3.4)

Mean carbohydrate intake of all subjects was [223 (45) gm]. Carbohydrate intake was similar between the two groups. The osteoporosis group had a mean of [234 (52) gm] and the control group [233 (33) gm] and for both the groups intake fell within the DRI guidelines (Table 3.4). Total fat intake, including polyunsaturated fatty acids (PUFA), saturated fatty acids (SFA) and monounsaturated fatty acids (MUFA), had a mean of [115(19)gm]. The mean total fat intake for the osteoporosis group [116 (20) gm] and control group [115 (18) gm] were also similar. There were no differences in the macronutrient intakes between the two groups (Table 3.4).

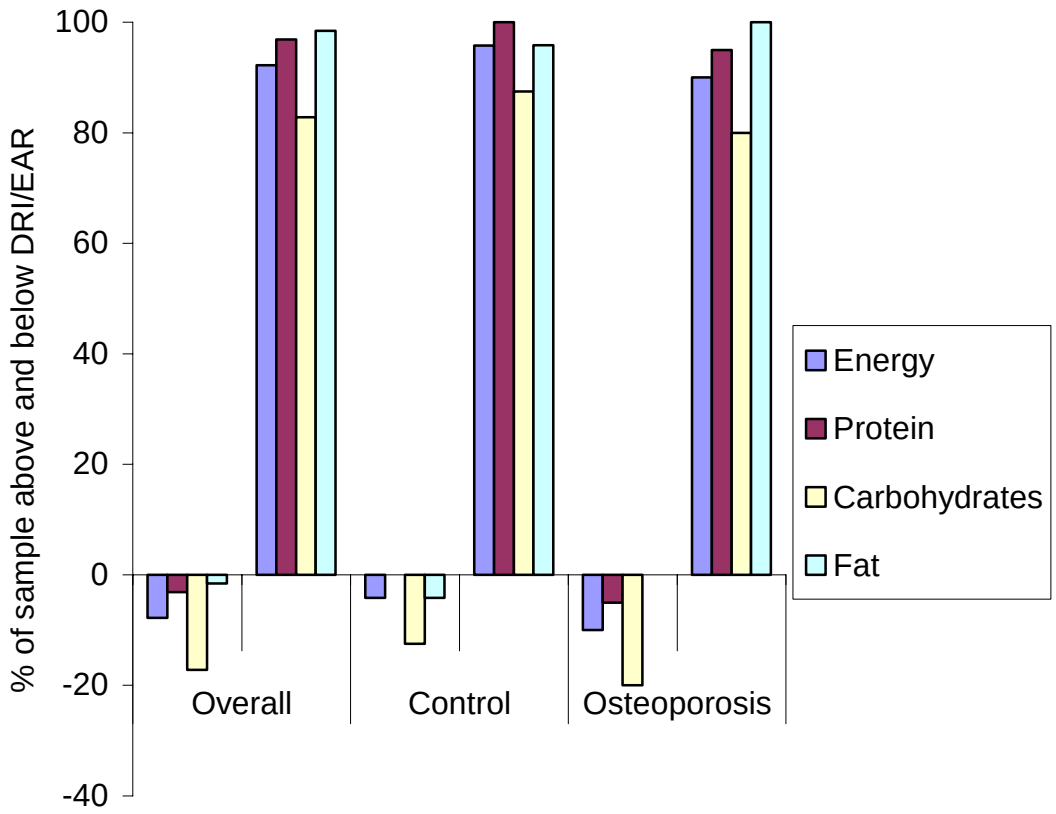
The mean protein intake of the sample was [64(12) gm]. Protein intake was within the DRI guidelines, with a mean for the osteoporosis group [65 (14) gm] being similar to the control group [65 (8) gm] (Table 3.4). Protein intake contributed 11% energy in both the groups, while fat provided 43% of the total energy, resulting in relatively low carbohydrate energy intake of 46%.

Analysis of variance (ANOVA) was used to test for any associations between macronutrients and BMD. The only macronutrient which was significantly associated with BMD was saturated fatty acids ($p < 0.01$) (Table 3.4).

Table 3.4: Distribution and comparison of macronutrients intake for the study sample, control group and the osteoporosis group

Macronutrients	Overall		Control group		Osteoporosis group		EAR/RNI[5]	p-value (ANOVA)
	Mean	SD	Mean	SD	Mean	SD		
Energy (MJ)[1]	9.9	1.3	9.8	0.94	9.9	1.6	8	0.72
Protein (gm)[2]	64	12	65	8	65	14	45	0.96
% energy	11	1.9	11.1	1.4	11.0	2.3	10	0.91
Fat (gm)[2]	115	19	115	18	116	20	73	0.85
% energy	44	4.6	44	4.6	44	4.6	<30	0.91
PUFA (%E)[4]	15	2.8	14	2.4	15	3.0	~10%E	0.21
SFA (%E)[4]	11	2.4	12	2.3	10	2.2	<10%E	0.01
MUFA (%E)[4]	13	2.7	14	2.4	13	2.7	<10%E	0.11
Cholesterol (mg)[3]	173	74	182	52	168	85	300	0.48
Carbohydrates (gm)[2]	233	45	233	33	234	52	193	0.94
% energy	46.	4.6	47	4.6	46	4.6	>55	0.57

[1]megajoules [2] gram [3] milligram [4] Percentage energy [5] EAR =Estimated Average Requirement; RNI = Reference Nutrient Intake
E= energy
p = 0.05
SOURCE: Dietary Reference Intakes for Energy, Carbohydrate. Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (2002/2005). This report may be accessed via www.nap.edu. Copyright 2004 by The National Academies.



X-axis = 100% DRI/EAR

Figure 3.7: The macronutrient intake in all groups above and below the EAR values

Energy, protein, fat and carbohydrate intake in all the groups was above the EAR and comparatively similar, with a small percent below the EAR in each group. The latter was due to having diabetics in each group. In general, a small percentage of subjects were below the EAR for energy (10%) protein (5%) and carbohydrates intake (18%) in the three groups (Figure 3.7).

3.7.2 Micronutrients

The intake of all the micronutrients in the study group was either within or above the DRI guidelines. There were no significant differences between the two groups.

3.7.2.1 Minerals and trace elements

The intake of all the micronutrients in the study group was above the DRI. There were no statistical significant differences in most of the trace element intake between the two groups (Tables 3.5 and 3.6). However, there was a significant (p =0.05) difference in manganese intake with a mean of [3.4 (7.7) mg] in the control group and a mean of [4.0 (1.1) mg] in the osteoporosis group, but there was no association with BMD. Iodine mean intake in the control group was [165 (20) mg], the osteoporosis group [154 (19) mg] and a significance p = 0.03 with analysis of variance (ANOVA) (Table 3.6). Iodine had a positive correlation with BMD with a significance p=0.01 (Table 3.6).

Ninety two percent in both groups were below the DRI (1200 mg) in their calcium intake. In the osteoporosis group 20% were below the DRI for iron, magnesium 8%, phosphates 3%, potassium 35%, sodium 13% and chloride 97%. Three percent were above the DRI for calcium, 32% for iron, 37% for magnesium, and 39% for phosphates, 26% potassium, 35% sodium and 1% chloride (Table 3.8). In the control group 33% were below the DRI for iron, 71% for potassium, 8% for sodium and 100% for chloride.
Two percent were above the DRI for calcium, 16% iron, 100% for magnesium and phosphates, 29% potassium and 92% sodium (Table 3.7).

Ninety two percent in the control group were below the DRI for zinc, 79% copper, 100% chromium, selenium and fluoride, manganese 71% and 21% iodine. Eight percent were above the DRI for zinc, 21% copper, 29% manganese, and 79% iodine. Eighty three percent in the osteoporosis were below the DRI for zinc, 68% for copper, 100% for chromium, selenium and fluoride, 38% manganese and 43% iodine. Seventeen percent were above the DRI for zinc, 32% copper, 62% manganese and 57% iodine (Table 3.7).

Table 3.5: Distribution and comparison of minerals intake for the study sample, control and osteoporosis group

Minerals	Overall (n=64)		Control group (n=25)		Osteoporosis group (n=39)		Dietary Reference Intakes[2]	p-value (ANOVA)
	Mean	SD	Mean	SD	Mean	SD		
Calcium (mg)[1]	885.5	256.4	943.0	177.0	851.1	290.7	1200	0.17
Iron (mg)[1]	14.7	3.7	14.1	2.6	15	4.2	8	0.37
Magnesium (mg)[1]	410.4	108.5	391.2	97.83	421.9	114.0	320	0.28
Phosphates (mg)[1]	1304.4	326.1	1269.5	176.9	1325.3	390.0	700	0.51
Potassium (mg)[1]	3660.3	943.1	3428.9	586.7	3799.2	1086.7	3500	0.13
Sodium (mg)[1]	3109.7	1054.7	3054.9	823.8	3142.5	1180.5	1600	0.75
Chloride (mg)[1]	985.8	422.4	962.9	276.9	999.6	492.4	2500	0.74

[1] milligram

[2] SOURCE: Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate. This report may be accessed via www.nap.edu. Copyright 2004 by The National Academies.

Table 3.6: Comparison and correlation of trace elements intake between the groups and BMD

Trace elements	Overall		Control group		Osteoporosis group		DRI/AI[4]	p-value (ANOVA)	Pearson's correlation	
	Mean	SD	Mean	SD	Mean	SD			R^3	p-value
Zinc (mg)[1]	9.6	2.0	9.6	1.5	9.6	2.3	8	0.94	0.01	0.92
Copper (mg)[1]	1.9	0.6	1.8	0.5	2.0	0.6	3	0.22	-0.13	0.28
Chromium (mcg)[2]	52.8	18.6	47.0	14.2	56.2	20.1	20	0.06	-0.22	0.09
Selenium (mcg)[2]	30.9	8.6	31.4	7.5	30.6	9.3	55	0.70	0.14	0.29
Manganese (mg)[1]	3.8	1.1	3.4	7.8	4.0	1.1	2.3	0.05	-0.18	0.16
Iodine (mcg)[2]	158	20	165	21	154	19	150	0.03	0.35	0.01
Boron (mcg)[2]	2693.1	1466.9	2552.5	1748.2	2777.5	1286.2	ND	0.56	-0.11	0.41
Fluoride (mg)[1]	1.8	5.7	1.6	3.0	1.9	6.7	4	0.10	-0.15	0.25
Silicon (mcg)[2]	7247.6	3902.6	6056.0	2732.0	7962.5	4336.3	ND	0.06	-0.22	0.09

[1] milligram [2] microgram [3] Pearson's correlation coefficient

[4]SOURCES: Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride (1997); Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6,Folate, Vitamin B12, Panthothenic Acid, Biotin, and Choline (1998); Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids (2000); and Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc This report may be accessed via www.nap.edu. Copyright 2004 by The National Academies

ND = Not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts. Source of intake should be from food only to prevent high levels of intake. (2001).

Table 3.7: Frequency and percentage of minerals and trace elements intake above and below the DRI in the control and osteoporosis groups

Minerals	Control (n=24)				Osteoporosis (n=40)			
	below DRI		above DRI		below DRI		above DRI	
	no	%	no	%	no	%	no	%
Calcium	22	92	2	8	37	92	3	8
iron	8	33	16	67	8	20	32	80
magnesium	0	0	24	100	3	8	37	92
Phosphates	0	0	24	100	1	3	39	97
Potassium	17	71	7	29	14	35	26	65
Sodium	2	8	22	92	5	13	35	87
Chloride	24	100	0	0	39	97	1	3
Trace elements								
Zinc	22	92	2	8	33	83	7	17
Copper	19	79	5	21	27	68	13	32
Chromium	24	100	0	0	40	100	0	0
Selenium	24	100	0	0	40	100	0	0
Manganese	17	71	7	29	15	38	25	62
Iodine	5	21	19	79	17	43	23	57
Fluoride	24	100	0	0	40	100	0	0

3.7.2.2 Vitamins

The reported Vitamin D intake in the osteoporosis group [1.97(1.26) mcg] and the control group with a mean of [2.02(1.19) mcg] were below the DRI but there was no statistical significant association with BMD (p= 0.86). Both groups were below the DRI of 15mcg (13% DRI) (Table 3.8).

Vitamin A, was above the DRI (700mcg) with osteoporosis group [3266.5 (1791.7) mcg] and control group [2469.5 (1307.5) mcg] with a weak significance p=0.06. (Table 3.8)

The fat soluble Vitamin K intake mean in the osteoporosis group was [194.6(122.6] mcg] and the control group [128 (54.3) mcg] with a significance p =0.01 between the two groups (Table 3.8). There was no significant association found between Vitamin K and BMD.

The control group was 4% below the DRI for Vitamin A , 100% Vitamin D, 21% Vitamin K. Ninety six percent were above the DRI for Vitamin A, 100% Vitamin E and 79% Vitamin K (Table 3.9). The osteoporosis group had 5% of the sample for Vitamin A below the DRI,100% Vitamin D, 15% Vitamin K. Ninety five percent were above the DRI for Vitamin A, 100% Vitamin E and 39% Vitamin K (Table 3.9).

The water soluble vitamins of note were biotin and Vitamin C. Biotin mean intake in the control group was [41.7 (8.2) mcg] and in the osteoporosis group was [50.4 (18.27) mcg] with a significant difference p= 0.03 between the two groups (Table 3.8). There was a significant correlation between biotin and BMD with p=0.04. Vitamin C intake was above the DRI in all groups with the mean [172.9 (55.1) mg] in the control group and [223.3(116.6) mg] in the osteoporosis group with a significance p=0.03. However, there was no association between Vitamin C and BMD (Table 3.8). Thiamine intake, in the control group, 29% were below the DRI with Riboflavine at 8%, Niacin and Vitamin B6 both at 58%, Folate at 96%, Vitamin B12 at 8%, and Panthothenic Acid at 71% and Biotin at 96%. Vitamin C had 100% below the DRI in the control group.

Thiamine intake, in the control group, 71% were above the DRI with Riboflavin at 92%, Niacin and Vitamin both at 42%, Folate at 4%, Vitamin B12 at 92%, and Panthothenic Acid at 29% and Biotin at 4% (Table 3.9).

For thiamine intake, in the osteoporosis group, 30% were below the DRI with Riboflavine at 15%, Niacin at 25% and Vitamin B6 at 38%, Folate at 82%, Vitamin B12 at 28%, and Panthothenic Acid at 52% and Biotin at 82% (Table 3.9). Vitamin C had 3% below the DRI in the osteoporosis group. Thiamine intake, in the osteoporosis group, 70% were above the DRI with Riboflavine at 85%, Niacin at 75% and Vitamin B6 at 62%, Folate at

18%, Vitamin B12 at 72%, and Panthothenic Acid at 48% and Biotin at 18%. For Vitamin C 97% was above the DRI (Table 3.9).

Table 3.8: Comparison of fat and water soluble vitamins intake for all the groups and correlation with BMD

Fat and water soluble vitamins	Overall		Control group		Osteoporosis group		DRI/AI[4]	p-value (ANOVA)	Pearson's correlation	
	Mean	SD	Mean	SD	Mean	SD			R^3	p-value
Vitamin A (mcg)[1]	2967.6	1662.1	2469.5	1307.5	3266.5	1791.7	700	0.06	-0.24	0.06
Vitamin D (mcg)[1]	2.0	1.2	2.0	1.2	1.9	1.3	15	0.86	-0.03	0.80
Vitamin E (mg)[2]	35.5	11.2	33.8	12.3	36.6	10.5	15	0.35	-0.19	0.13
Vitamin K (mcg)[1]	169.6	106.9	128.0	54.3	194.6	122.6	90	0.01	-0.18	0.15
Thiamine (mg)[2]	1.2	0.3	1.1	0.2	1.2	0.3	1.1	0.18	-0.16	0.21
Riboflavine (mg)[2]	2.1	1.1	1.8	0.7	2.2	1.3	1.1	0.21	-0.09	0.48
Niacin (mg)[2]	15.1	4.0	14.2	3.5	15.7	4.2	14	0.12	-0.17	0.17
Vitamin B6 (mg)[2]	1.7	0.5	1.6	0.4	1.8	0.5	1.5	0.20	-0.17	0.19
Folate (mcg)[1]	314.6	94.2	298.9	64.4	324.0	107.9	400	0.31	-0.09	0.49
Vitamin B12 (mcg)[1]	3.2	2.7	2.9	0.9	3.3	3.3	2.4	0.57	-0.09	0.50
Panthothenic acid (mg)[2]	5.4	1.4	5.2	1.1	5.6	1.5	5	0.23	-0.09	0.50
Biotin (mcg)[1]	47.15	15.78	41.70	8.17	50.42	18.27	30	0.03	-0.26	0.04
Vitamin C (mg)[2]	204.42	100.63	172.92	55.12	223.33	116.58	75	0.05	-0.23	0.06

[1] microgram [2] milligram [3] Pearson's correlation coefficient; [4]SOURCES: Dietary Reference Intakes for Calcium, Phosphorous, Magnesium, Vitamin D, and Fluoride (1997); Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6,Folate, Vitamin B12, Panthothenic Acid, Biotin, and Choline (1998); Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids (2000); and Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc (2001) . This report may be accessed via www.nap.edu. Copyright 2004 by The National Academies

Table 3.9: Frequency and percentage of fat and water soluble vitamins intake above and below the DRI in the two groups

Vitamins	Control				Osteoporosis			
	below DRI		above DRI		below DRI		above DRI	
Fat soluble vitamins	no	%	no	%	no	%	no	%
Vitamin A	1	4	23	96	2	5	38	95
Vitamin D	24	100	0	0	40	100	0	0
Vitamin E	0	0	24	100	0	0	40	100
Vitamin K	5	21	19	79	6	15	34	85
Water soluble vitamins								
Thiamine	7	29	17	71	12	30	28	70
Riboflavine	2	8	22	92	6	15	34	85
Niacin	14	58	10	42	10	25	30	75
Vitamin B6	14	58	10	42	15	38	25	62
Folate	23	96	1	4	33	82	7	18
Vitamin B12	2	8	22	92	11	28	29	72
Panthothenic acid	17	71	7	29	21	52	19	48
Biotin	23	96	1	4	33	82	7	18
Vitamin C	24	100	0	0	1	3	39	97

3.8 Education Level and Nutritional Intake

Comparatively better micronutrient intake was seen in the graduates with significant p values, copper p=0.009, boron p=0.005, fluoride p=0.005, vitamin D p=0.022, thiamine p=0.015, Folate p=0.017, biotin p=0.008 and vitamin C p=0.018 using the Kruskal Wallis test. However there was no statistical significance with BMD.

3.9 Physical Activity

Physical activity was classified into three groups, work activity, house activity and recreational activity.

The study sample spent a mean of [29.4(11.2) hours], [15.2 (12.6) hours], [9.6 (2.8] hours], and [4.5 (2.3) hours] on total activity. The control group spent a mean [34.2 (8.9) hours] in total activity with a mean of [18.9 and another (10.6) hours] in work activity, a mean of [8.(23.6) hours] in house activity and a mean of [6.6 (1.5) hours] in recreational activity (Table3.10). The osteoporosis group spent a mean [26.5 (11.5) hours in total activity with a mean of [13 (13.3) hours] in work activity, a mean of [10.3 (2.9) hours] in house activity and a mean of [3.2 (1.7) hours] in recreational activity (Table3.10).

Significant correlations were found for all activities and BMD. The highest was for recreational activity (r =0.77). House activity had the least impact on BMD (r =-0.29) (Table3.10). On comparing the control and osteoporosis groups, on average the control group spent 35 hours in all activities compared to the osteoporosis group which spent only 26.5 hours (p=0.01) (Figure 3.8).

Table 3.10: Descriptive Statistics of Physical Activity Questionnaire and Pearson correlation coefficients between the different forms of activity and BMD

Type of activities (hours/week)	Whole study sample (n = 64)		Control (n = 25)		Osteoporosis (n = 39)		(Pearson's correlation)	
	Mean	SD	Mean	SD	Mean	SD	r[1]	p – value
Work Activity	15.2	12.6	18.9	10.6	13.0	13.4	0.327*	0.01
House Activity	9.7	2.9	8.7	2.6	10.3	2.9	-0.287*	0.02
Recreational activity	4.5	2.3	6.6	1.5	3.2	1.7	0.770*	0.01
Total activity	29.4	11.2	34.2	8.9	26.5	11.5	0.453*	0.01

* Correlation is significant at the 0.05 level [1] Correlation coefficient

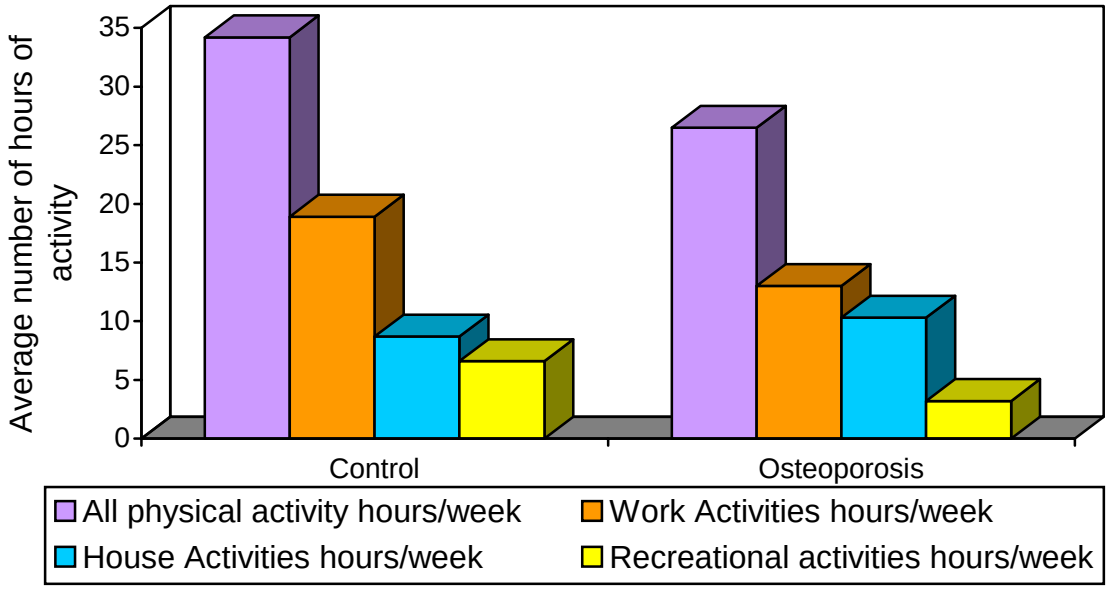


Figure 3.8: A comparison of average time spent doing different types of activities by the control and osteoporosis groups

CHAPTER 4: DISCUSSION

Osteoporosis, the most common disease of bone, affects about 30 million people in the United States and as many as 100 million people worldwide. As the elderly population grows, the prevalence is expected to increase in the 21st century. Osteoporosis is not an inevitable part of growing old but rather a degenerative disease resulting from insufficient physical activity, and improper nutritional intake during our younger formative years.

This study was the first cross sectional, retrospective study of its kind to evaluate and to report on the nutritional intake and physical activity of middle aged Asian women in Kenya. The association between dietary intake and bone mineral density, at the clinically important site of the lumbar spine, by using a purpose designed tool for assessment of dietary intake namely the FFQ, was determined. Despite the relatively small sample size, this simple baseline information is the very initial data on the nutritional intake and bone mineral density of Asian women living in Kenya.

The food frequency questionnaire comprised of a list of foods and beverages on which respondents reported their usual frequency of food consumption over a given period. The quantitative food frequency questionnaire was used for this study as it includes more precise food portion size estimations such as weight, volume or household measures [175, 176, 177]. Energy, nutrient and food intake were obtained by summing the reported frequency multiplied by the amount consumed over all reported foods and expressed in grams consumed per day. In contrast to the 24-hour recall that does not characterize an individual's usual diet and underestimates intakes, the food frequency method provides an estimate of the usual intake of an individual over a given period and may be used to rank individuals according to usual intake within the population The food frequency method does, however, have the following limitations:

1. Estimation of food quantities may not be as accurate as the recall method as FFQ may over or underestimate dietary intakes.
2. Detailed information on the daily variation in the diet cannot be collected and results may be influenced by the foods included in the lists.

3. A food frequency questionnaire developed for one group may not be suitable for use in other groups.

In the present study, the investigator, who interviewed, the study sample had the same ethnic background and was familiar with the dietary habits of the study participants and documented their responses. However, reporting errors may have occurred. It is therefore important to view the reported nutrient intake data as the best estimate of a group's mean nutrient intake and to keep in mind that some individuals may have over or under estimated their intakes. Additionally, most commercially available databases are limited in the extent to which ethnic foods are included. For the present study, the investigator created supplemental data, which included nutrient information for ethnic food recipes based on the available nutritive value of Indian foods[178]. These inherent limitations in the available methodologies should be kept in mind when interpreting. The study results showed a significant association between biotin and BMD (p= 0.04) in the study group. Whether this is of any clinical significance or not needs further research

4.1 Physical Activity

In the study sample significant correlations were found for all activities and BMD. The correlation for recreational activity was (r =0.77) and had a greater impact compared to house activity which had the least impact on BMD (r=-0.29). Women who exercised had a higher BMD and were younger in age.

There was very minimal activity at home involving house work as home help is easily available and all the women had home help. All study participants travelled by car, even short distances, and none of the working women walked to work or used public transport.

The women in the osteoporosis group reported ongoing bone or joint pain of a long duration, and many said it limited or detrimentally affected their daily activities. Hence they had minimal activity and little movement on a daily basis which also had an impact on their weight.

The effect of physical activity on bone mass has been studied extensively and has been recognized as influencing the attainment of peak bone mass in childhood and adolescence[179].

The role of physical activity in maintaining BMD during the menopausal transition and in the postmenopausal years is still a subject of contention.[180]. The best evidence that exercise can slow bone loss or add bone mass to the postmenopausal skeleton comes from prospective intervention studies, although the amounts are site specific and relatively modest, and the activity must consist of high-load resistance exercise.[179, 180, 181]. This evidence, however, comes from trials in which small numbers were involved, and the studies were short in duration and thus have the potential for selection and other biases

A study by Grove and Londeree compared a control no exercising group with low- and high-impact exercise groups. All the women were postmenopausal. Both exercise groups maintained BMD, whereas the control groups experienced a significant decrease in BMD. There was no difference between the low- and high-impact groups, and the researchers concluded that a low-impact exercise, such as walking, was as effective as high-impact regimens in maintaining BMD, with less chance of injury[182].

Research studies on the activity levels beneficial for the development of peak bone mass in this ethnic group need to be undertaken.

4.2 Medication

Seventy two percent (n=46) of the study sample were on regular medication. Statins, antihypertensive drugs, thyroxine replacement, inhaled glucocorticoids for asthma, oral hypoglycaemic agents, insulin and non steroidal anti-inflammatory drugs (NSAID) for pain relief for arthritis were the drugs used. On direct questioning many of them did not take their drugs regularly or the correct dosage and the reasons for this were forgetfulness and the expense of medications. Therefore compliance was an issue.

Some of the women in the study group were on one or more medications simultaneously, and several medications were associated with osteoporosis. There was no statistical significance seen with glucocorticoids. This could be so because of irregular use or doses smaller than 7.5 mg as dosage of drugs taken were not illicited[183]. The latter class of medicines is the most important in relation to the development of osteoporosis and cause a loss of mostly trabecular bone; consequently fractures occur most commonly in vertebrae, ribs, and ends of the long bones. Bone loss occurs very rapidly and may be as high as 20-40% during the first year of steroid use. Dose of steroid that is detrimental to BMD in most people appears to be more than 7.5 mg of prednisone daily [145]. However in this study group the steroid preparations were taken short term or were inhaled and these are considered safe. There are few long-term, controlled studies on the use of inhaled glucocorticosteroids and the resulting impact on bone mineral density in the asthmatic population. Furthermore, the results of these studies are difficult to interpret. Some studies have shown decreases in bone mineral density in asthmatics using inhaled glucocorticosteroids compared to controls while others have shown no significant differences[183, 184, 185, 186]. Most of the study sample on glucocorticoids did not take their medication regularly. They took them as the need arose and the dose prescribed was 5mg in most of the cases which may not adversely affect bone mass [145]. This needs further research with a larger sample.

There was no record of the different classes of antihypertensive drugs taken as the women could not remember which specific drugs were being taken. They had not been informed to carry their drugs to the interview. Therefore all the antihypertensive drugs were looked at collectively as one group.

The relationship between osteoporosis and hypertension has not been clearly established, although many alterations in extra cellular metabolism of calcium, which could determine the level of bone mineral density (BMD) in these patients, have been associated to hypertension. Despite these alterations, the lack of studies relating these two important diseases is surprising, and hypertension is not identified as a risk factor

for osteoporosis. There was a significant (p=0.002) correlation found in the study sample on antihypertensive medications and the effect on BMD. Therefore use of antihypertensive drugs is a risk factor in this group.

In this study group no significant correlation was found with statins or thyroxine. Some of the present studies are showing a beneficial effect of statins on bone mass. Although the mechanism of action is not certain, studies continue to find a favorable association between statins and fracture reduction[187, 188, 189 190]. Most observational studies support this finding, whereas limited post hoc analyses of randomized clinical trials of statins failed to find an association[191, 192].

4.3 Education Level and Dietary Intake

An incidental finding was better micronutrient intake in the graduates with significant p values, copper p=0.009, boron p=0.005, fluoride p=0.005, Vitamin D p=0.022, Thiamine p=0.015, Folate p=0.017, Biotin p=0.008 and Vitamin C p=0.018. This could be due to awareness and knowledge about a healthy diet. However no significance was seen between the mentioned micronutrients and BMD.

The education level in the study sample was high and the graduates had a BMD T-score which was higher than the primary and high school level. Most likely this could be due to their education and more awareness about bone health and the need for BMD scans as they became peri or post menopausal. The study samples who were graduates had better bone health. This was an incidental correlation that was seen and needs further investigation in a larger sample.

4.4 Saturated Fats

In general, the dietary fat intake of this study population was higher than that observed to be consumed by Indians living in India (>30% energy *vs.* <30% energy) [193]. These differences in intake suggest that these immigrants have made some changes in their dietary patterns as they adjusted to their new environment and acculturated into the

culture of their host country and at the same time preserved and modified their normal food habits over time and generations with improved socioeconomic status.

The only macronutrient which was significantly associated with BMD was saturated fatty acids ($p < 0.01$). Mounting evidence indicates that the amount and type of fat in the diet can have important effects on bone health. Most of this evidence is derived from animal studies. Of the few human studies that have been conducted, relatively small numbers of subjects and/or primarily female subjects were included. The NHANES III study assessed the relation of dietary fat to hip bone mineral density (BMD) in men and women and found a negative correlation with saturated fatty acids but more so in men[194]. More studies are warranted examining the relationship between dietary fats and BMD.

4.5 Anthropometric Variables

In the present study sample, 30% had a normal BMI 50%of the women were overweight and 20% were obese. It appears that there is an association between fat mass and BMD as conversion of androgens to estrogens becomes a major source of estrogen only after the menopause[194]. Looking at weight in relation to age was not significant but there was a significance of p=0.049 with a coefficient of r =0.247 between BMI and age. As the women got older the weight increased most likely due to inactivity as a result of pain and a fear of falling. The literature shows high BMI and weight significantly augment osteoarthritis risk and some studies suggest also that osteoporosis risk is increased[195 196].

As the populations from India and the Indian sub continent have migrated the eating habits have changed and the incidence of chronic degenerative diseases and obesity is high, as also seen in the present study population, compared to the host population as shown by studies done in the US[197, 198].

Significant p values with an impact on BMD were for age (p=<0.001), weight (p=0.023), waist size (p =<0.001), hip size (p=<0.001) and BMI (p=< 0.001) in this study sample.

Various measures of body size have been shown to be associated with BMD, in particular body weight and height, which have been positively associated with BMD, but there is controversy as to which features of body size are the most important for women going through the menopause transition[199, 200]. Cross-sectional data have found that both total body fat and lean tissue mass explain a large percentage of the variation in BMD in postmenopausal women[201]. Reid and colleagues, in a 2-year prospective study of 122 normal postmenopausal women, reported that the rate of total body bone loss was significantly and directly related to fat mass and the rate of change in fat mass[202]. The positive relationship between increased fat and lean mass and increased BMD is probably the result of increased mechanical forces on the bone[203].

The findings suggest that substantial numbers of Kenyan Asian women aged >50 years are overweight and thereby are at elevated risk for degenerative bone and joint health problems. This study's findings suggest that the issue of overweight and high BMI particularly amongst middle-aged adults requires greater attention, which could be achieved through linking bone/joint health with prevention of other non-communicable diseases such as diabetes and cardiovascular disease.

4.6 Gynaecologic Variables

The oral contraceptive pill (OCP) was used by 41% of the study sample for a mean period of 1 year and OCP use has been associated with no effect on BMD, so it is not a risk factor for osteoporosis. Women with late onset of menarche have been reported to have significantly reduced peak bone mass and increased fracture risk[204, 205]. The majority of women (45%) in the study started menarche at the age of 13 years followed by 22% at 12 years, 16% at 14 years,11% at 15 years, 3% at 11 years and 3% at 16 years. The minimum age at menarche was 11 years; maximum was 16 years. Ito and colleagues showed that BMD of the lumbar spine in postmenopausal women was strongly associated with the length of reproductive years, so those women who had an early menarche and late menopause were advantaged[206]. Women with high BMD and early menarche usually have higher body weight, so it is difficult to separate the effects of anthropometric factors and age of menarche on BMD.

All the study sample women breastfed except for the 13% who had no children. The average time spent breast feeding per child in the osteoporosis group was one to one and a half year, and in the control group was six to nine months. Fifty percent of women had 2 children, 22% had 3 children, 8% had 1 child, 5% had 4 children and 1% had 5 children and 6 children each. There were no significant differences between the groups in family size.

A recent Turkish study showed significant associations between total duration of breast-feeding and BMD as total duration of breast-feeding might be an important risk factor besides age, weight, and years since menopause in postmenopausal osteoporosis [207]. The osteoporosis risk factors of longer duration of lactation and higher number of pregnancies appear to be present for few women in this study and could be a possible risk factor.

CHAPTER 5: CONCLUSIONS AND RECOMMENDATIONS

The present study described the nutrient intake of a select group of Asian women in Kenya, who were second and third generation descendents of the initial immigrants who came to Kenya in the late 19th and early 20th century.

5.1 Conclusions

As a pilot study, the sample was not intended to be representative of the Kenyan middle aged female population. The sample size was small and the conclusions are applicable only to the sample population.

Risk factors for osteoporosis, which could be associated with osteoporosis in this study sample, were the use of prescription drugs and low physical activity levels. The use of prescription drugs likely to affect bone metabolism was high as 72% of the sample were on them and the effect on bone mass could have been detrimental. There were no nutrients identified which had a negative association with BMD apart from biotin with $p=0.037$. The nutritional intake in the two groups was within the specific DRI. The simultaneous occurrence of risk factors within 1 individual has important risk implications because of possible additive effects and interaction between factors. The educational level was high as 50% of the sample were graduates and had a better nutrient intake. There is no literature on the prevalence of all these risk factors for osteoporosis in a similar middle aged population sample of Kenyan Asian women.

5.2 Recommendations

Additional research is required on a larger sample, to study the effects of nutrition and physical activity in a sample adequately representing the diverse Kenyan population. Further studies are also required to evaluate the individual effects of the various food groups on BMD. Any further studies should preferably include a strong clinical component, like biological bone markers to identify the women at risk. Studies done in clinical settings will allow for more improved sampling and sample stratification, particularly in terms of disease progression.

There is a need to document the nutritional status of elderly, to better determine nutrient requirements, and to identify factors affecting dietary intake and nutrient absorption in differing cultural and environmental settings.

It should also be recognized that international dietary guidelines for older individuals are lacking, and that these are needed to guide community awareness and support of nutrition for the elderly and for the development of community-based interventions.

While this study focused on socio-demographic, anthropometric parameters, nutritional intake and physical activity questionnaires, it will be most useful for future research to include assessments of fracture risk, clinical outcomes and evaluation of quality of life.

The findings of this study contribute to the development of evidence-based nutritional messages, which are required to educate health professionals and the general public on the importance of healthy eating and a physically active life style.

School milk projects and well balanced food intake should be encouraged in schools together with the importance of physical activity to achieve a good peak bone mass right from the start.

Nutrition should become an integral part of the teaching curriculum in medical and nursing schools to bring about awareness of good feeding practices and therefore a prevention and reduction in chronic lifestyle diseases.

5.3 Limitations

The sampling strategy used in this exploratory study was non-random and thus the generalizability of the findings is limited to the Asian women represented in this study sample. Other limitations of the study were that the study sample was small (n= 64) and the use of FFQ, to determine nutrient intakes. Any form of self-reported data has limitations, as they relate to dietary assessment, as instances of under and over reporting are prevalent. Since the sample women were already aware of their BMD results, as it was a retrospective study, theoretically it could have had an impact on the

self reported data. The controls were significantly younger than the osteoporotic group. Age matched controls were not possible because of small numbers and the expense of the scan. A large proportion of the whole sample was on prescription drugs for various chronic ailments. Biochemical measurements such as calcitonin, vitamin D, ALP, and hydroxyproxiline are not available in Kenya; therefore the understanding of the pathophysiology of osteoporosis in this group is limited. However, the strength of this study is that it allows for an in-depth examination of the nutrient intakes of this select group of Asian women and the factors influencing the group's nutrient intakes. The diversity among the study participants is reflective of the diversity observed in the Asian community in Kenya. Similar studies are needed with larger samples and more diverse groups of Kenyan Asian immigrants to increase our understanding of the nutritional status of this immigrant group's diet-related risk of chronic diseases.

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APPENDICES

Appendix 1 : Socio- demographic Questionnaire

Socio- Demographic Questionnaire

Patient Code No: _____

Date of Birth_____/_____/19_____ Age_____(yrs)

Please tick appropriate box

1) Marital status:

Married ☐ Single ☐ Widowed ☐ Divorced ☐

2) Level of education:

Primary School Certificate ☐

High School Certificate ☐

Graduate ☐

No Education ☐

3) Employment

Regular Employment ☐
Self-Employment ☐
Not Employed ☐

Specify Occupation_____

4) Habits

1. Do You Smoke? Yes ☐ No ☐

If Yes: How long have you been smoking? _____Years

How many cigarettes per day? _____Sticks

If you smoked in the past:

For how many years _____years

How many sticks per day _____sticks

2. Do you drink alcohol? Yes ☐ No☐

If Yes: What do you drink? Wine ☐ Sprits ☐ Beer ☐

Specify number of drinks _____ per day _____ per week

If you took alcohol in the past:

1) For how many years? _____Years

2) Specify type of drink _____

3) How many drinks at a time _____ Drinks

5) Are You a Strict Vegetarian ☐ Non-Vegetarian? ☐

6) Obs and Gynae History

1. At what age did you begin your first period? (Menarche) _____ (years)

2. How many children do you have? _____ (children)

3. At what age did you stop having your periods? (Menopause) _____ (years)

4) Have you ever been oral on contraceptives Yes ☐ ☐ No

If yes for how many years _____ Years

5) Have you ever been on any hormonal therapy? Yes ☐
No ☐

If yes for how long _____

7) Illnesses and Medication

Do you suffer from any chronic illness? Yes ☐ No ☐

Please specify _____

Are you on any regular medications? Yes ☐ No ☐

If yes please specify

1)

2)

Appendix 2: Food Frequency Questionnaire

Food Frequency Questionnaire

Appendix 3: Physical Activity Questionnaire

Epaq2

Appendix 4: Anthropometry Form

Anthropometry

Height :_____(cm)

Weight: _____ (kg)

BMI: _____ (kg/M^2

Waist Circumference: _____ (cm)

Hip Circumference _____ (cm)

Appendix 5: BMD Scan

QCT Bone Mineral Densitometry

Patient Information

Date: 16/06/2004
Sex: Female
DOB: 19/04/1949
Age: 55
Exam: 4236
Radiologist:
Referring Physician: DR. S. MALIK
Comments:

Analysis Results

BMD in mg/cc K_2HPO_4

T11:	-
T12:	-
L1:	147.0
L2:	132.5
L3:	110.9
L4:	126.5
Average:	129.2
Age Matched Normal (UCSF):	119.4 ± 26
Z-Score:	0.38
T-Score:	-1.51

Comparison with Previous Examinations

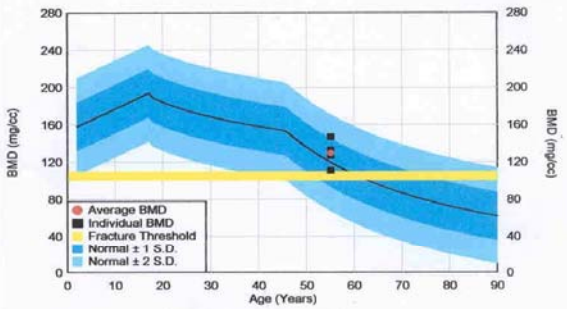
Date	Avg. BMD	Change (mg/cc)
16/06/2004	129.2	-

Change per year: -

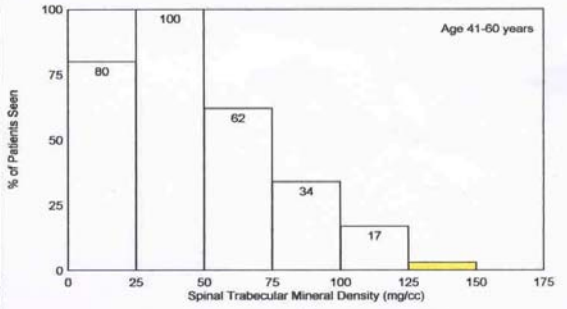
The above analysis based on BMD results for L1 and L2 and L3 and L4 from each exam.

Results do not include a correction for variations in bone marrow fat.

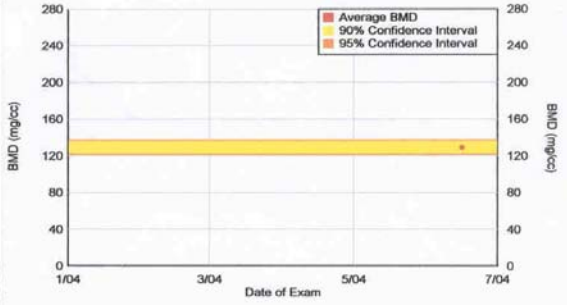
Confidence intervals based on a precision of 3.0 mg/cc.



Patient BMD Value Compared to Age and Sex Matched Control Data (UCSF)



Prevalence of Vertebral Compression Fractures in Untreated Postmenopausal Women Scanned at UCSF



Comparison with Previous Examinations

Interpretation: This is a LOW DOSE Quantitative CT Bone Mineral Densitometry study done through 4 Lumbar vertebrae. This patient's average BMD value of 129.24 mg/cc K2HPO4 falls ONE standard deviation below the normal range according to age and gender.

The T score of - 1.51 indicates moderate osteopaenia.

Aga Khan Hospital • Nairobi • Radiology Department • Telephone: 3740000 Ext. 2294

Appendix 6: Approval from Stellenbosch

UNIVERSITEIT·STELLENBOSCH·UNIVERSITY
jou kennisvennoot • your knowledge partner

15 July 2005

Ms TF Chaudhri
Department of Human Nutrition

Dear Ms Chaudhri

RESEARCH PROJECT: **"IDENTIFYING NUTRITIONAL AND LIFE-STYLE RISK FACTORS FOR THE DEVELOPMENT OF OSTEOPOROSIS IN WOMEN OF ASIAN ORIGIN WHO HAVE BONE MINERAL SCANS AT AGA KHAN HOSPITAL, NAIROBI"**
PROJECT NUMBER : N04/10/167

My letter dated 8 February 2005 refers.

At a meeting that was held on 9 March 2005 the Committee for Human Research ratified the provisional approval of the above-mentioned project.

Yours faithfully

CJ VAN TONDER
RESEARCH DEVELOPMENT AND SUPPORT (TYGERBERG)

CJVT/ev

Copy to: Prof D Labadarios

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Fakulteit Gesondheidswetenskappe • Faculty of Health Sciences

Verbind tot optimale gesondheid • Committed to optimal health
Afdeling Navorsingsontwikkeling en -steun • Division of Research Development and Support
Posbus/PO Box 19063 • 7505 Tygerberg • Suid-Afrika/South Africa
Tel: +27 21 938 9054 • Faks/Fax: +27 21 933 6330
E-pos/E-mail: jdevl@sun.ac.za

Appendix 7: Approval from Aga Khan University Hospital, Nairobi

The Aga Khan Hospital, Nairobi
An Institution of the Aga Khan Health Service, Kenya

P. O. Box 30270 - 00100 GPO Nairobi, Kenya
Telephone : 3740000 / 3742531/ 353999
Fax: 3741749

November 9, 2004

Ms. Tauseef Chaudhri
P O Box 30270-00100
Nairobi

Dear Ms. Chaudhri

Re: **Identifying nutrition and lifestyle risk factors for the development of Osteoporosis in women of Asian origin at the Aga Khan Hospital, Nairobi**

I am in receipt of your request to carry out research in this hospital.

Please note that your request has been approved and permission granted to carry out the study under the supervision of Dr. S. Malik, Consultant Radiologist.

The following are the terms and conditions of the study: -

1. This hospital will in no way be responsible for funding of this project.
2. No material belonging to the hospital e.g. files, diskettes, etc may be taken out of the hospital premises.
3. On completion of the study, a copy of the report will be presented to the Hospital or the result of the study may be given in a lecture form to the medical fraternity in the hospital.
4. No part of the study may be published without written permission from The Aga Khan Health Service, Kenya.

Yours sincerely

Mr. M. M. Qureshi
Medical Director

AK 133

Appendix 8: Informed consent Form

INFORMATION AND INFORMED CONSENT DOCUMENT

TITLE OF THE RESEARCH PROJECT

Identifying nutritional and life-style risk factors for the development of osteoporosis in women of Asian origin the at Aga Khan Hospital, Nairobi

REFERENCE NUMBER: ----------

PRINCIPAL INVESTIGATOR: TAUSEEF CHAUDHRI

Address: C/O AGA KHAN HOSPITAL,
P.O BOX 30270,
NAIROBI, 00100
KENYA.

DECLARATION BY OR ON BEHALF OF PARTICIPANT:

I, THE UNDERSIGNED, *(name)*

[ID No: _____] the participant/or in my capacity as _____ of the participant [ID No: _____.] of _____

(address)

A. HEREBY CONFIRM AS FOLLOWS:

1. I was invited to participate in the abovementioned research project which is being undertaken by the Department of
Human Nutrition Faculty of Health Sciences, Stellenbosch University, at the Aga Khan Hospital, Nairobi

2. The following aspects have been explained to me.

2.1 Aim

- To identify the nutritional and life-style risk factors contributing to the incidence of osteoporosis in Asian women

- The purpose of the project is to make recommendations on the women's needs for education for the successful management of osteoporosis and to maintain a healthy life-style.

2.2 Procedures

In order to collect this information, I have been told that, a number of questions regarding my food habits, activity patterns and life- style factors will be asked

There will be three questionnaires to fill:

- Socio demographic and life-style Questionnaire
- Food Frequency Questionnaire
- Physical Activity Questionnaire

The questionnaires will take approximately 1 ½ hours to answer

I have also been told that this information will be collected from 120 other participants

2.3 Your participation in this study will help:

- To identify the activity and food factors, which have a beneficial effect on bone health.
- Help us in our efforts to design effective interventions to maintain good bone health.

2.4 Confidentiality

- It has been explained to me that my name does not have to appear on any of the questionnaires and any information that I provide will be kept confidential.
- Information given will be used anonymously for making known the findings to other scientists.

2.5 I will have access to the findings after it has been presented to the department of Human Nutrition, University of Stellenbosch, and published in peer reviewed journals.

2.6 It has been clearly explained to me that I can refuse to participate in this research survey or can stop answering the questions at any time during the interview. If this was to happen, I will not be penalized in any way nor will I be refused any treatment by the institution.

.**3.**The information above was explained to me, by _____ in English and I, am in command of this language. I, was given the opportunity to ask questions and all these questions were answered satisfactorily.

4. No pressure was exerted on me, to consent to participation and I, understand that I, may withdraw at any stage without any penalization.

5. Participation in this study will not result in any additional costs to me.

B.I, HEREBY CONSENT VOLUNTARILY TO PARTICIPATE IN THE ABOVE - MENTIONED STUDY

Signed/confirmed at _____. On

_____20_____*(place)* *(date)*

_____

_____

Signature or right thumb print of representative/ participant

Signature of witness

STATEMENT BY OR ON BEHALF OF INVESTIGATOR(S):

I, _____, declare that

I explained the information given in this document to _____

and/or her representative _____ *;*

she was encouraged and given ample time to ask me any questions;

- This conversation was conducted in English and no translator was used.

Signed at_____ On_____.20___

Signature of investigator/representative _____

Signature of witness_____

Signed at (place) _____ on _____20_____

- .

Signed at …… on

……20……

(Place) (Date)

IMPORTANT MESSAGE TO PARTICIPANT:

Dear participant,

Thank you for your participation in this study. Should, at any time during the study,

- an emergency arise or
- you require any further information with regard to the study, kindly contact

_Tauseef Chaudhri__ telephone number Office 3662042

Mobile no 0733221712

PLEASE PUT A TICK (√) ON EVERY LINE

FOODS AND AMOUNTS	AVERAGE USE LAST YEAR								
	Never or less than once a month	1-3 per Month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6 + per day
BREAD/SAVOURY BISCUITS									
Breads & Rolls									
Chapatti, flour with/without oil									
Paratha ghee/oil									
Paratha stuffed with Pitta Bread, Naan Bread									
Poories									
Bhakri									
Biscuits savoury									
Crackers or Crisp breads									
Sweet biscuits									
BREAKFAST CEREALS									
Porridge, Oatmeal									
Sugar coated cereals e.g. Sugar puffs									
Cereals e.g. Cornflakes, Rice Krispies									
All Bran, Bran Flakes, Fruit & Fiber Muesli, Special K									
Weetabix, Shredded wheat									
Other Breakfast Cereals									
White bread, rolls or toast									
Whole-wheat or rye bread, Rolls or toast									
Fruit bread									
POTATOES, RICE, ETC									
Potato boiled or baked									
Chips									
Jacket Potatoes									
Potato Salad									
Couscous/Tabouleh									
White rice boiled									
Brown Rice boiled									
DIARY & NON DIARY PRODUCTS									
Fresh milk									
Evaporated Milk/Condensed Milk									
Yogurt (incl. Low fat varieties)									
Raita bundi/ cucumber									
Milk Pudding e.g. Rice pudding, Sevian									
Dairy or ice cream desserts, mousse									
Cheese e.g. Brie, Edam									

	Never or less than once a month	1-3 per Month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6 + per day
Cottage Cheese, Paneer									
Feta Cheese									
Hard grating cheeses e.g. Parmesan									
Cream Cheese, Happy cow									
Cheddar Cheeses									
Custard									
Butter Milk									
Fresh or sour cream									
SPREADS									
Peanut butter									
Jam/Honey/Marmalade									
Marmite/Bovril									
SAUCES & SOUP									
Salad Cream/Mayonnaise									
Salad dressing									
Sauces e.g. White/Cheese									
Tomato Ketchup									
Pickles/Chutney									
Packet Soups									
Fresh vegetable Soups									
Fresh Meat Soups									
EGGS/EGG DISHES									
Eggs, boiled or poached									
Eggs, fried or scrambled or Omelette									
Mixed dishes with egg									
Egg desserts									
VEGETABLE DISHES									
Cauliflower									
Aubergine									
Okra or Lady's Fingers or bindi									
Methi, Palak									
Red, Green Peppers									
Cabbage, Chinese									
Karela (Bitter gourds)									
Brussels Spouts									
Pickled vegetables									
Tomatoes									
Lettuce, endive or other salad greens									
Courgette Marrow, Squash, tinda									
Cucumber									
Celery or fennel									
Beetroot									

FOODS AND AMOUNTS	Never or less than once a month	1-3 per Month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6 + per day
Coleslaw									
Carrots									
Broccoli, Spring Greens, Kale									
Spinach or other leafy greens									
Green beans									
Pumpkin									
Onion or Leeks, spring onions									
Mushrooms									
Sweet corn									
Zucchini, squash or courgettes									
Guar									
Ghisoda									
Valor									
Watercress Mustard									
Peas, Mushy peas, Snow peas									
Radish red/white									
Toms-raw/ cooked									
Swedes/turnips/parsnips									
Fried/Spring Onions									
Mixed Vegetables									
Cooked mixed vegetable dish									
LENTILS 'curry' DAHL, and BEANS									
Channas, chick pea									
Masoor - red & brown lentils									
Soya Beans									
Butter Beans/Broad Beans, Red Kidney Beans, Baked Beans									
Bean Sprouts									
Yellow split peas/cholay									
Dahl Mash (urad dahl)									
Whole moong, green gram									
Khadhi & Pakoras									
BEEF DISHES									
Beef Curry									
Beef roast									
Beef steak									
Minced beef									
Beef Biryiani									
Sausages or frankfurters									
Meat pie									
Corned beef									
Manufactured Luncheon meat									

FOODS AND AMOUNTS	Never or less than once a month	1-3 per Month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6 + per day
MUTTON DISHES									
Mutton Curry									
Mutton Kebabs									
Mutton Chops									
Mutton Roast									
Mutton Biryiani									
Liver (Goat)									
Kidney									
Mincemeat Curry									
Kofta/ minced meat curry									
Paey (Goats' feet)									
CHICKEN 'MEAT' DISHES									
Chicken Curry									
Chicken Tikka, Masala									
Chicken Kebabs									
Mixed dishes with chicken (e.g. casseroles, stir fry)									
Roast Chicken									
Bread crumbed e.g. Chicken nuggets/Kiev's									
Chicken Biryiani									
Pies/pastries									
Chicken Sausages									
FISH									
Fish Curry, Grilled									
Fish Tikka, Tilapia, Nile Perch									
Canned fish (incl. Tuna, salmon & Sardines)									
Fried Fish, Coated									
Seafood (Prawns Lobsters, Crabs)									
SNACKS									
Samosa - Meat or Vegetable									
Pakora/bhajia									
Mandazi, Doughnuts									
Pizza									
Vegetable Burger in bun									
Cashew/almonds, macadamia nuts									
Peanuts/pistachio									
Chevda, Sevvian									
Crisps									
Sweets									
Fancy Chocolates									
Mini Chocolate snack bars									

FOODS AND AMOUNTS	Never or less than once a month	1-3 per Month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6 + per day
Chocolate bars									
Spring rolls									
Dhokra									
Bhel									
Corn chips									
Roasted Maize cob									
Roast cassava									
FRUIT, FRESH & TINNED									
Fruit salad									
Oranges or Mandarins									
Apples									
Bananas, Sweet, Kampala									
Peaches, nectarines									
Pears									
Cantaloupe or honeydew melon									
Watermelon									
Strawberries									
Pineapples									
Tree tomatoes									
Grapes									
Mangoes									
Passion Fruit									
Avocado									
Plums									
Pomegranate									
Raspberries									
DRIED FRUIT									
Dates, Figs, Prunes									
Currants, Raisins, Sultanas									
Other dried Fruits									
BEVERAGES									
Tea - Black									
Tea with milk									
Herbal Tea									
Coffee with milk									
Coffee - black									
Hot Chocolate with milk									
Horlicks, Ovaltine with milk									
Orange Juice (Pure fruit)									
Passion Juice									
Other Fruit Juice (100%)									
Fizzy, soft Drinks e.g. Coke, Fanta									

FOODS AND AMOUNTS	Never or less than once a month	1-3 per Month	1 per week	2-4 per week	5-6 per week	1 per day	2-3 per day	4-5 per day	6 + per day
Diet Coke									
Mineral water									
Plain water									
Squashes									
Lucozade									
ASIAN SWEETS/MITHAI									
Milk or Milk powder based									
Wheat or semolina based									
Lentil flour based									
Halwa									
Others please specify									
Other Asian desserts, Specify									
BISCUITS AND CAKES									
Plain Biscuits e.g. Nice, Digestive									
Chocolate Biscuits									
Sandwich Cream Biscuits									
Fruit cake									
Sponge cake									
Buns/sweet Pastries									
Scones/Pancakes/Crumpets									
Fruit Pies, Tarts, Crumbles									
CHUTNEYS & PICKLES									
Onion, mooli, mint, garlic Chutney									
Mixed pickle, e.g. Mango, Lemon etc									
Others									
FATS & OILS									
Sunflower oil									
Corn oil, Elianto									
Palm oil, Golden Fry									
Ghee									
Butter									
Margarine									

PLEASE PUT A TICK (√) ON EVERY LINE

ID Number | | | | | | | | |

PHYSICAL ACTIVITY QUESTIONNAIRE

This questionnaire is designed to find out about your physical activity in your everyday life.

Please try to answer every question, except when there is a specific request to skip a section.

Your answers will be treated as strictly confidential and will be used only for medical research

THE QUESTIONNAIRE IS DIVIDED INTO 3 SECTIONS

- **Section A** asks about your physical activity patterns in and around the house.
- **Section B** is about travel to work and your activity at work.
  It may be skipped by people who have not worked at any stage during the last 12 months.
- **Section C** asks about recreations that you may have engaged in during the last 12 months.

What is your date of birth?

		/			/				
day			month			year			

What is today's date?

		/			/				
day			month			year			

Your sex *(Please tick (✓) appropriate box)*? Male ☐ Female ☐

Section A HOME ACTIVITIES

GETTING UP AND GOING TO BED

*Please put a time in **each** box*

	Average over the past year	
	At what time do you normally get up?	At what time do you normally go to bed?
On a weekday		
On a weekend day		

GETTING ABOUT — Apart from going to work

Which form of transport do you use **most often** apart from your journey to and from work?

*Please tick (✓) one box **ONLY** per line*

Distance of journeys	Usual mode of transport			
	Car	Walk	Public transport	Cycle
less than one mile				
1–5 mile(s)				
More than 5 miles				

TV OR VIDEO VIEWING

*Please put a tick (✓) on **every** line*

Hours of TV or Video watched per day	Average over the last 12 months					
	None	less than 1 hour a day	1 to 2 hours a day	2 to 3 hours a day	3 to 4 hours a day	More than 4 hours a day
On a weekday before 6 pm						
On a weekday after 6 pm						
On a weekend day before 6 pm						
On a weekend day after 6 pm						

STAIR CLIMBING AT HOME

*Please put a tick (✓) on **every** line*

Number of times you climbed up a flight of stairs (approx 10 steps) each day at home	Average over the last 12 months					
	None	1 to 5 times a day	6 to 10 times a day	11 to 15 times a day	16 to 20 times a day	More than 20 times a day
On a weekday						
On a weekend day						

ACTIVITIES IN AND AROUND THE HOME

*Please put a tick (✓) on **every** line*

Approximate number of hours each week	Average over the last 12 months						
	None	Less than 1 hour a week	1 to 3 hours a week	3 to 6 hours a week	6 to 10 hours a week	10 to 15 hours a week	More than 15 hours a week
Preparing food, cooking and washing up							
Shopping for food and groceries							
Shopping and browsing in shops for other items (e.g. clothes,toys)							
Cleaning the house							
Doing the laundry and ironing							
Caring for pre-school children or babies at home (not as paid employment)							
Caring for handicapped, elderly or disabled people at home (not as paid employment)							

Section B ACTIVITY AT WORK

Please answer this section **only** if you have been in paid employment at any time during the last 12 months or you have done regular, organised voluntary work.

If not please go to page 9

TYPES OF WORK DURING THE LAST TWELVE MONTHS

- We would like to know what full or part-time jobs you have done in the last 12 months.
- You may have held a single job or have held two jobs at once.
- If you have changed jobs with the same employer, you should enter it as a change of job **only** if it entailed a substantial change in physical effort.

EXAMPLE

Someone who worked full-time for 6 months, then retired, rested for 3 months and then started a voluntary job for 6 hours a week, would complete the questions as follows.

	Job 1	Job 2
Name of occupation	*nurse*	*shop work*
How many hours **per week** did you usually work?	*38*	*6*
For how many months in the last 12 months did you do this work?	*6*	*3*

ACTIVITY LEVELS AT YOUR WORK

Now we would like you to take the total number of hours you worked per week in each job and divide them up according to your activity level.

Please complete EACH line

	Job 1			Job 2		
	No	Yes	Hours per week	No	Yes	Hours per week
Sitting — light work e.g. desk work, or driving a car or truck		✓	*6*	✓		
Sitting — moderate work e.g. working heavy levers or riding a mower or forklift truck	✓				✓	*2*
Standing — light work e.g. lab technician work or working at a shop counter		✓	*30*		✓	*4*
Standing — light/moderate work e.g. light welding or stocking shelves		✓	*2*	✓		

The number of hours in each activity should add up to the number of hours that you worked in each job e.g. 6+30+2=38 (nurse)

What jobs have you held in the last 12 months, and how many months in the year did you do them?

Please complete EACH line

	Job 1	Job 2
Name of occupation		
How many hours **per week** did you usually work?		
For how many months in the last 12 months did you do this work?		

ACTIVITY LEVELS AT YOUR WORK

Now we would like you to take the total number of hours you worked per week in each job and divide them up according to your activity level.

Please complete EACH line

	Job 1			Job 2		
	No	Yes	Hours per week	No	Yes	Hours per week
Sitting — light work e.g. desk work, or driving a car or truck						
Sitting — moderate work e.g. working heavy levers or riding a mower or forklift truck						
Standing — light work e.g. lab technician work or working at a shop counter						
Standing — light/moderate work e.g. light welding or stocking shelves						
Standing — moderate work e.g. fast rate assembly line work or lifting up to 50 lbs every 5 minutes for a few seconds at a time						
Standing — moderate/heavy work e.g. masonry/painting or lifting more than 50 lbs every 5 minutes for a few seconds at a time						
Walking at work — carrying nothing heavier than a briefcase e.g. moving about a shop						
Walking — carrying something heavy						
Moving, pushing heavy objects objects weighing over 75lbs						

STAIR OR STEP CLIMBING AT WORK

Please put a tick (✓) on EACH line where appropriate

Number of times you climbed up a flight of stairs (10 steps) at work	AVERAGE OVER THE LAST 12 MONTHS					
	None	1 to 5 times a day	6 to 10 times a day	11 to 15 times a day	16 to 20 times a day	More than 20 times a day
Job 1						
Job 2						

Please put a tick (✓) on EACH line where appropriate

Number of times you climbed up a ladder at work	AVERAGE OVER THE LAST 12 MONTHS					
	None	1 to 5 times a day	6 to 10 times a day	11 to 15 times a day	16 to 20 times a day	More than 20 times a day
Job 1						
Job 2						

KNEELING AND SQUATTING AT WORK IN JOB 1

In an average working day in Job 1 did you

kneel for more than one hour in total? No ☐ Yes ☐ Don't know ☐

squat for more than one hour in total? No ☐ Yes ☐ Don't know ☐

get up from kneeling or squatting more than 30 times? No ☐ Yes ☐ Don't know ☐

KNEELING AND SQUATTING AT WORK IN JOB 2

In an average working day in Job 2 did you

kneel for more than one hour in total? No ☐ Yes ☐ Don't know ☐

squat for more than one hour in total? No ☐ Yes ☐ Don't know ☐

get up from kneeling or squatting more than 30 times? No ☐ Yes ☐ Don't know ☐

TRAVEL TO AND FROM WORK

JOB 1

Please complete EVERY line

Roughly how many miles was it from home to Job 1?	
How many times a week did you travel from home to Job 1?	

Please tick (✓) one box ONLY per line

How did you normally travel to Job 1?	Always	Usually	Occasionally	Never or rarely
By car				
By works or public transport				
By bicycle				
Walking				

JOB 2 *(if appropriate)*

Please complete EVERY line

Roughly how many miles was it from home to Job 2?	
How many times a week did you travel from home to Job 2?	

Please tick (✓) one box ONLY per line

How did you normally travel to Job 2?	Always	Usually	Occasionally	Never or rarely
By car				
By works or public transport				
By bicycle				
Walking				

Section C RECREATION

The following questions ask about how you spent your leisure time.

Please indicate how often you did each activity on average over the last 12 months.

For activities that are seasonal, e.g. cricket or mowing the lawn, please put the average frequency during the season when you did the activity.

Please indicate the average length of time that you spent doing the activity on each occasion.

EXAMPLE

If you had mowed the lawn every fortnight in the grass cutting season and took 1 hour and 10 minutes on each occasion.

If you went walking for pleasure for 40 minutes once a week.

You would complete the table below as follows:

Please give an answer for the AVERAGE TIME you spent on each activity and the NUMBER OF TIMES you did that activity in the past year.

	Number of times you did the activity in the last 12 months								Average time per episode	
	None	Less than once a month	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 5 times a week	Every day	Hours	Mins
Mowing the lawn				✓					1	10
Walking for pleasure					✓					40

Now please complete the table on pages 10 and 11

Please give an answer for the NUMBER OF TIMES you did the following activities in the last 12 months and the AVERAGE TIME you spent on each activity.

Please complete EACH line

	Number of times you did the activity in the last 12 months								Average time per episode	
	None	Less than once a month	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 5 times a week	6 times a week or more	Hours	Mins
Swimming — competitive										
Swimming — leisurely										
Backpacking or mountain climbing										
Walking for pleasure — you should not include walking as a means of transportation as this was included in Sections A & B										
Racing or rough terrain cycling										
Cycling for pleasure — you should not include cycling as a means of transportation										
Mowing the lawn — during the grass cutting season										
Watering the lawn or garden in the summer										
Digging, shovelling or chopping wood										
Weeding or pruning										
DIY e.g. carpentry, home or car maintenance										
High impact aerobics or step aerobics										
Other types of aerobics										
Exercises with weights										
Conditioning exercises e.g. using an exercise bike or rowing machine										

Please continue on the next page

Please complete EACH line

	Number of times you did the activity in the last 12 months								Average time per episode	
	None	Less than once a month	Once a month	2 to 3 times a month	Once a week	2 to 3 times a week	4 to 5 times a week	6 times a week or more	Hours	Mins
Floor exercises e.g. stretching, bending, keep fit or yoga										
Dancing e.g. ballroom or disco										
Competitive running										
Jogging										
Bowling — indoor, lawn or 10 pin										
Tennis or badminton										
Squash										
Table tennis										
Golf										
Football, rugby or hockey (during the season)										
Cricket (during the season)										
Rowing										
Netball, volleyball or basketball										
Fishing										
Horse-riding										
Snooker, billiards or darts										
Musical instrument playing or singing										
Ice-skating										
Sailing, wind-surfing or boating										
Martial arts, boxing or wrestling										

You have finished the questionnaire — *Thank you*