QATAR UNIVERSITY

COLLEGE OF HEALTH SCIENCES

THE ASSOCIATION BETWEEN SOFT DRINK CONSUMPTION AND BONE MINERAL DENSITY AMONG QATARI WOMEN: ANALYSIS OF QATAR BIOBANK DATA

BY

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ABSTRACT

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Title: The Association between Soft Drink Consumption and Bone Mineral Density Among Qatari Women: Analysis of Qatar Biobank Data

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With the rapid increase in longevity, osteoporosis is viewed as a global problem and recognized to be one of the most common diseases in both developed and developing world. It is common in older women, as the bone mineral density (BMD) tends to decrease with age, particularly after menopause. Decrease in BMD increases the risk of osteopenia and osteoporosis. Often the first clinical manifestation of osteoporosis might be a fracture, as the women do not recognize the decreases in BMD levels. Whilst age and hormonal changes are well established risk factors, there are other factors that have been investigated for possible links to increase the risk of osteoporosis. These factors include dietary patterns and lifestyle.

Few studies have examined the soft drinks consumption as a potential risk-factor for lowering BMD levels. Reports from these studies presented conflicting findings. Some suggesting significant decreases in BMD levels due to soft drink consumption, while others find null associations. In the context of the unclear association, we made use of a relatively larger Qatar Bio-Bank (QBB) data to explore the cross-sectional association between soft drink consumption and BMD. The strength of the QBB data include objective and validated measurement of outcome and risk factors. This study included 1000 Qatari women age ≥ 40 years volunteered to take part

in the QBB survey. BMD levels were measured using the Dual-Energy X-ray Absorptiometry (DXA) scan one of the most reliable and valid measures and the soft drink consumption was assessed using validated food frequency questionnaires.

Data were checked for errors and explored using descriptive statistical methods. Multiple regression models were then used to assess the association between bone mineral density and soft drink consumption. The use of multiple regression was essential to adjust for a number of person-centered confounders. Given those with lower BMD levels were considered to have high risk of osteoporosis, quantile regression models were used. This is one of the most sophisticated models that is meant to identify the risk factors associated with high risk population while adjusting for potential confounders. Nutritional epidemiology studies have shown use of quantile regressions can pick up the risk factors much more efficiently.

Our findings suggest that there was a clinically and statistically significant association between BMD and soft drink consumption after adjusting for age, BMI, menopausal status, smoking status, physical activities, milk intake, and fruit and vegetable consumption. Further high-quality studies with long term follow up with specific purpose of testing the hypothesis are warranted before we can comment on potential causal association. If future cohort studies were to confirm such association, it is possible to develop appropriate public health intervention to improve bone health via reduced soft drink consumption.

DEDICATION

I would like to dedicate this work to my parents and my friends Eman Sababa, Fatma Salem, Seham Abdi, and Shaima Ahmed.

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CHAPTER 1: INTRODUCTION

The rapid epidemiological transition resulted from the improvement in sanitation and healthcare led to a global reduction in infectious diseases over the past decades. That, however, was offset by a rapid increase in the non-communicable diseases (NCD). Lifestyle changes with the shift toward sedentary life with nutritional imbalance were among the key reasons for the increase in the NCD in both developed and developing part of the world. (1) A very recent study (2) published in Lancet has highlighted the role of nutrition in mortality via increased NCD. The authors concluded that one in five mortality could be linked improper diet.

The Arabian Gulf countries, in particular, have undergone rapid epidemiological and demographic transitions since the discovery of oil and gas in the '60s. (3, 4) These changes led to a significant increase in the NCD burden, due to unhealthy life style that came with the affluence and oil income. (5) Today Arabian Gulf countries are struggling to control man made disorders like diabetes, hypertension and cardiovascular diseases. These countries also now have most obese populations in the world.(6) Given that the lifestyle and diet are modifiable risk factors, public health workers in the region are aiming to alter the lifestyle and nutrient to prevent and control the NCD burden.

The musculoskeletal disorders are one of the most common NCD's that lead to severe long-term physical disability, pain and decreased quality of life. These disorders affect about hundreds of millions of people around the globe as well as their families. (7) With the rapid increase in longevity, osteoporosis, in particular, is viewed as a global problem and recognized to be the most common disease in old age population. (8)

1.1 The Burden of the Osteoporosis

World Health Organization (WHO) has defined osteoporosis in 1994 for the first time as a "disease characterized by low bone mass and micro-architectural deterioration of bone tissue, enhanced bone fragility and an increase in fracture risk." (9) Since then increasing number of researchers have focused on assessing the burden of osteoporosis and related bone health. Global burden of non-communicable diseases represented by osteoporotic fractures was reported to be around 9 million fractures per year. (10) The most affected individuals are older and menapausal women (11); with about 200 million women are estimated to be affected annually by osteoporosis, worldwide. (12)

One feature of osteoporosis is that it is a silent disease where the first clinical manifestation might be a fracture. Hence, it is frequently under-recognized. (13) Globally, such fractures cause a substantial economic burden on healthcare services. (14) As such, the toll of mortality and morbidity associated with fractures caused by osteoporosis became one of the critical public health concern. (15) Trend analysis reveals that hip fractures are steadily increasing, with projected global estimates to reach as high as 6.3 million cases by 2050. (16) Same reports suggested that the Asian population are at a higher risk of being affected by bone fractures than other populations. (16) Given that the predictor of bone fractures is low bone mineral density (BMD), identifying modifiable factors associated with lower BMD can help develop appropriate public health intervention to prevent and control bone fractures.

1.2 Research Aim

The study aim is to explore the relationship between soft drink consumption and BMD among Qatari women.

1.3 Research Questions

- Is there an association between the soft drinks consumption and low bone mineral density after adjusting for potential confounders?

CHAPTER 2: LITERATURE REVIEW

2.1 Women and Bone Health

Over the past decade most research about osteoporosis has emphasized the role of Menopause and lack of hormone on bone health. Old aged women at post-menopausal stage are the most vulnerable group to be affected by osteoporosis. As with menopause the ovarian activities decrease and the production of sex hormones decreases significantly, and eventually the reproductive capacity ends in a woman's life. Menopause tends to occur naturally in women at around 45 to 54 years. With the increase in the life expectancy, women live longer and live up to 80 years or even more in many parts of the world. This means a woman will live more than one-third of her life lacking bone protection by sex hormones. (17)

2.2 Factors Associate with Low BMD

Researchers have investigated potential risk factors associated with the lower BMD and the increased risk of osteoporosis. The key risk factors suggested include age, gender, adulthood history of fractures, hormonal changes, family history of fracture (relative of first-degree), chronic use of opioid, low body weight and consumption of oral glucocorticosteroids (three months or longer). Additionally, It has been found that about 20%-50% of bone mass changes were associated with the lifestyle such as lack of physical activities, smoking, alcohol consumption, poor nutrition intake such as lower than required calcium and vitamin D intake. (18)

For instance, an early study assessing the possible predictors and risk factors for bone density among 284 British women aged 21 to 68 years, found that BMD measured using dual photon absorptiometry declined steadily among women as they get older. More importantly, they found that the BMD in the proximal femur were also

significantly reduced in the menopausal women. (19) Likewise, a recent study revealed that an increased risk of osteoporosis was independently associated with history of fracture, menopausal duration , and parity. While decreased risk of osteoporosis at each femoral neck and lumbar spine or both sites were independently associated with physical activity, obesity, higher education levels, metabolic syndrome, serum ferritin, and polypharmacy (including calcium and vitamin D supplementation). The authors investigated the relationship between bone mineral density (BMD) and bio-chemical, demographic, and clinical features among 537 postmenopausal Iranian women. They collected the data through questionnaire, clinical, and laboratory examination and BMD measured using Dual Energy X-ray Absorptiometry. (20)

Another study among Arabian Gulf population was conducted by Hammad and Benajiba (21). They found the lifestyle related factors were associated with the bone health among Saudi Arabian women even when they were relatively younger. They quantified the level of osteopenia and osteoporosis in 101 Arabian women using quantitative ultrasonography measurements of the calcaneal region. The life style related factors were measured using a validated questionnaire to assess dietary habits, sun exposure, and exercise.

Additionally, evidences suggested that low BMI, exercises and calcium are vital risk factors for osteoporosis. In a study (22) which set out to determine the relationships between BMI, lean mass, fat mass and BMD levels. The findings after adjusting for relevant covariates, showed that lean mass and fat mass were significant predictors of all BMD measures in both genders. Also, positive relationship between lean or fat mass with BMD among those with higher BMI were absent in males and weaker in females in middle-aged adults. Another systematic review and meta-analysis of randomized controlled trials (23) exploring the effect of exercise among menopausal women, found

that exercises had a significant benefit for menopausal women bone mineral density, waist circumference, body fat, triglyceride. Furthermore, evidence from another systematic review and meta-analysis (24) reveled that increasing calcium intake from either dietary sources or taking calcium supplements produces slight non- progressive increases in BMD levels, that unlikely lead to a clinically significant reduction in fracture risk.

Few studies focused at the relationship between socioeconomic status and bone mineral density in adults. A recent study (25) showed that men with education levels below high school graduate experienced relatively low hip BMD than their counterparts with college or graduate education, after adjusting for other physiological and behavioral factors. In addition, women with personal annual income reported under $20,000 had relatively low BMD at spine and hip than their counterparts with higher income level. This study investigated the relationship by race/ethnicity and gender were the data about 6568 participants from the Louisiana Osteoporosis Study (LOS) was examined, it included 4153 data from non-Hispanic whites, 1907 non-Hispanic blacks, and 508 non-Hispanic Asians.

2.3 Diet, Nutrition and Bone Health

Evidence to suggest diet and nutrition has impact on bone health has been emerging. A scoping review (26) including 49 human studies from 2002 to 2016 looked at the impact of dietary patterns on bone outcomes, including bone mineral status, osteoporosis, bone biomarkers, and fracture risk. This review included studies that used data-driven dietary pattern methods as well as a priori dietary pattern approach, and those assessed both dietary patterns approaches in association with bone health. The review findings suggested that improved bone health was associated with a high intake of fruit, poultry and fish, vegetables nuts and legumes, whole grains, and low-fat dairy

products. Likewise, intake fried foods, processed products, meat, sweets and desserts, soft drinks, and refined grains were inversely associated with bone health.

In another study by Langsetmo et al. (27) showed BMD was associated with dietary patterns in both gender, men and women, after controlling for lifestyle factors and the association was mediated by the body mass index (BMI). This study included 6539 Canadian participants randomly selected from an on-going cohort of Canadian Multicenter Osteoporosis Study (CMOS). They assessed the diet pattern using a validated food frequency questionnaire in the second year of follow-up and measured the BMD by dual x-ray absorptiometry in the fifth year of follow-up to establish the temporal relationship. Diet intake was categorized as nutrient dense (whole grains, vegetables, and fruits) and energy dense (French fries, potato chips, meats, soft drinks, and desserts). They found no positive association between BMD and diet, although dense energy diet was independently associated with BMI and BMI was an independent and a significant predictor of BMD.

2.4 Soft Drink Consumption and Bone Health

There is paucity of studies that focused specifically on testing the hypothesis to evaluate the effect of soft drink consumption on Bone health. Our comprehensive search few studies testing this hypothesis. Most of the studies looked at the soft drink and BMD link as part of the diet, although these studies were not specifically designed to evaluate this research hypothesis per se.

A strong evidence reveled on this link from a well conducted systematic review (28), that reviewed 88 studies assessing the relationship between soft drink consumption and nutrition with health outcomes. Their meta-analysis showed that consumption of soft drink was associated with an increase in energy intake and linked with increases in body weight, also the risk of several medical conditions such as

diabetes. Lower consumption of milk, calcium, and other nutrients were also associated with increased soft drink consumption. They noted also that the study design influenced the results as large effect sizes were seen in studies with superior study designs such as experimental and longitudinal studies. The authors also concluded that moderate effect sizes seen in some studies were affected by various confounders such as age and gender. Likewise, non-industry funded studies reported large effects than studies funded by the food industry. As such authors inclined to suggest that effect of soft drink consumption may in fact be larger than some of the previous studies have shown.

2.4.1 Soft Drink Consumption and Bone Health in Adult Population

Of the handful studies found that explored the association between soft drink consumption and bone health, one study looked at the association among Arabian women. This study investigated the high consumption of soft drinks, insufficient milk and dairy products intake, low supplementation of vitamin D and calcium, and less exercise among Saudi Arabian participants diagnosed with osteopenia or osteoporosis compared to healthy controls. They found that T-score and Z-score of BMD were inversely associated with soft drink intake and positively with milk, and dairy products consumption, calcium, and vitamin D supplementation use, and exercise. (21)

A more recent study exploring the association between soft drink consumption and multiple morbidity among South Australian adults showed similar negative effect of soft drink consumption on range of health outcome including osteoporosis. They used data collected between 2008 and 2013 from a large sample of 36,663 participants who were adults over 16 years. Participant's multi-morbidity was defined as having two or more of the following nine conditions: asthma, chronic obstructive pulmonary disease, hypertension, high cholesterol, diabetes, arthritis, osteoporosis, cardiovascular disease, and mental health problems. Their estimates showed that about 28.5% of the

participants had multi-morbidity and 10.5% of the participant reported that they consume more than half a liter of soft drink daily. Consumption of soft drink was associated positively with multi-morbidity. However, the relationship existed with all the chronic diseases except osteoporosis. More convincing finding in this study was the dose-response relationship with the increasing level of morbidity with increased the level of soft drink consumption. As the multi-morbidity increased with age, the association between soft drink consumption and morbidity were further evaluated in strata of those below 60 years old. They found significant association even in those below 60 years, indicating the age may not have been a confounder in this relationship. (29)

Another recent study, also in Australia investigated the association between dietary patterns and bone mineral density among adults aged over 50 years. This included a sample of 1182 participants selected from the on-going Australian population-based cohort of North West Adelaide Health Study (NWAHS). They measured the BMD using dual-energy X-ray absorptiometry and gathered the data about the dietary pattern using a validated food frequency questionnaire. Dietary pattern categorized as a prudent pattern versus Western pattern. The prudent pattern comprises of a high intake of vegetables and fruits, high fiber bread, fish, nut-based milk legumes, and sugar; while the Western pattern consisted of high levels of fast foods, white bread, high-fat dairy products eggs, processed and red meat, poultry, snacks, potato with fat, jam, beer, and soft drinks. The results showed that those participants with a prudent dietary pattern had a lower prevalence of decreased BMD compared to those consuming Western diet. As such the prudent diet was positively associated with the level of BMD. On the other hand, their findings suggested that the participants who mainly followed the Western diet had a higher prevalence of decreased BMD compared to their

counterparts. The study included clinical, social, and biochemical data collected in three phases using a computer-assisted telephone interview, a self-completed questionnaire, and clinical assessments. The whole body bone mineral density (BMD) was measured in the second phase, and the participants were classified into two groups and were categorized as having low BMD: T-scores less than -1 were considered as osteopenic and T-scores of less than or equal to -2.5 were considered osteoporotic. (30)

The Framingham osteoporosis study (31) measured bone mineral density in 1413 women and 1125 men at the spine and three other hip sites by using dual-energy X-ray absorptiometry (DXA) and assessed the dietary intake by food-frequency questionnaire. The bone mineral density measure and the frequency of soft drink consumption for men and women analyzed at each level after adjustment for body mass index, height, age, total calcium intake, energy intake, total vitamin D intake, season of measurement, physical activity score, alcohol use, smoking, caffeine from different non-cola sources, and, for women, menopausal status, and estrogen use. The study results revealed that Cola intake associated with significantly lower BMD at each hip site only in women. The results were similar in case of diet cola and weak for decaffeinated cola. A non-significant relationship reported between non-cola carbonated beverage consumption and BMD. The mean BMD was 3.7% lower at the femoral neck for those with daily cola intake and 5.4% lower at ward area than those who consumed <1 serving cola/month. Furthermore, the results indicate that calcium-to-phosphorus ratios were lower although the daily cola consumers total phosphorus intake was not significantly higher than in non-cola consumers.

Sámano et al. (32) explored the association of carbonated beverages consumption with BMD among two groups of Mexican women: reproductive age group and not reproductive age group Diet pattern of a total of 328 women were also assessed

along with the anthropometric measures and the BMD. Participants mean age of not-reproductive and reproductive age group were 47 years and 18.7 years, respectively. The median intake of carbonated beverages was higher in reproductive age women. The reproductive age group who had osteopenia drank 500 mL/day more compared to those who had not. Osteopenia risk was associated with carbonated beverages consumption, drinking no milk, and calcium intake less than 700 mg.

Nurses' Health Study cohort (33) evaluated the association between soda consumption and the risk of hip fracture among postmenopausal women. The participants were 73572 white postmenopausal women were assessed for their diet pattern using a semiquantitative food-frequency questionnaire completed in 1980, 1984, 1986, and then updated every four years. There was an 1873 incident of hip fractures in≤30 years of follow-up. They found that each added serving of total soda per day was associated with a 14% increased risk of hip fracture. In the cohort, the attributable risk for total soda consumption was 12.5%. The risk was significantly increased among consumers of regular soda and diet soda; however, did not significantly differ between sodas with or without caffeine or colas and non-colas. Furthermore, the association between hip fractures and soda did not vary by the diagnosis of diabetes or body mass index of the women.

Kim, Morton, & Barrett-Connor (34) study results showed that BMD levels were not associated with the type of carbonated beverage intake even after adjustment for age, obesity, exercise, calcium intake and current use of the following tobacco, alcohol, thiazides, estrogen, and or thyroid hormone. The authors evaluated the association between carbonated beverage consumption and BMD in older White women using a community-based cohort study. They assessed the bone mineral density at four sites among 1000 women age between 44 to 98 years. Also, collected data on

the medical, behavioral histories, and the type and amount of carbonated beverages consumed.

2.4.2 Soft Drink Consumption and Bone Health in Younger Population

Soft drink consumption and bone health were also investiaged in other populations such as athletes and younger adults. For instance, Wyshak, Frisch, Albright, Albright, Schiff, and Witschi (35) studied the association between bone fractures and the consumption of non-alcoholic carbonated beverage among 5,398 college graduates (2,622 college former athletes, and 2,776 non-athletes). The participant responded to a mail questionnaire that assessed both the outcome and the exposure. Their findings showed a significant association between bone fractures and non-alcoholic carbonated beverage consumption, but only among the former athletes even after controlling for potential confounders including current exercise patterns. Also, they noted a significant dose-response relationship between the number of bone fractures among the athletes and the amount of carbonated beverages consumed daily.

Likewise, one of the early studies with a small sample of 76 females and 51 males used food-frequency questionnaires and medical histories to test this hypothesis among relatively younger population. The study found that consumption of non-alcoholic carbonated beverages, particularly colas, were significantly associated with an increased fracture risk among females. The investigators suggested that the phosphoric acid content of cola beverages might prevent absorption of calcium leading to a loss in bone mass, although, they did not measure the bone mineral density. They also suggested that females may become more susceptible to osteoporosis later in life. (36)

In the same idea of the previous study Libuda et al. (37) wanted to evaluated the association between bone health and soft drink consumption in healthy children and

adolescents. The long-term consumption of soft drinks were recorded from an ongoing open cohort study that assess the relationship between development, nutrition, and metabolism with infancy and early adulthood. The sample included 228 children and adolescent and the bone health was measured using peripheral quantitative computed tomography for the bone modeling and remodeling of the radius. Their finding highlighted a negative association between the consumption of soft drinks and variables of bone modeling and remodeling in this younger low risk population. The effects seen were related to the long-term consumption of caffeinated and un-caffeinated soft drinks and was potentially mediated through an inverse association with total protein intake not primarily based on milk displacement.

Another observational study examined the BMD of 12 and 15-years-old in a large population (1335 boys and girls) of healthy adolescents. They used a relatively improved validated method for the collection of data on regular food and beverage intake. The participants were observed at schools during regular school hours, BMD of the non-dominant forearm and dominant heel were measured using DXA, and the dietary data were collected using an open-ended interview. The authors found that body weight, physical activity, smoking, and drinking habits were strong factors that affected bone health. They reported inverse relationship between BMD and carbonated soft drinks (CSD) consumption. The higher intakes of carbonated soft drinks were significantly associated with lower bone mineral density at the heel, and a weaker relationship was seen at the forearm in girls and no such effect was observed among the boys. There was a possibility of a threshold effect for calcium and physical activity, which boys are better than girls, permitting boys to drink more CSDs without affecting negatively on their bone health as suggested by the authors. (38)

2.4.3 Animal Studies on Soft Drink Consumption and Bone Health

In vitro studies have shown that cola-consuming significantly decreases bone mineral density. A study conducted to test the effect of Coca-Cola consumption on rats findings revealed that both male and female cola-consuming rats had a statistically significant decrease in bone mineral density about 20% lower when compared to the control group rats, while their serum calcium levels were not significantly different. Moreover, female test group rats significantly consume more Coca-Cola than male rats (76.2 ml versus 55.3 ml). While the water consumption decrease by 5.9 times compared to control group and kidneys examination showed general glomerular congestion and inter-tubular bleeding which suggest that the decrease in BMD might be linked to the renal damage produced by cola drinks in addition to other related factors. The results were consistent with other previous studies findings and explained by the theory that both high caffeine in colas and high phosphate may cause an increased acid load in the body, which can influence the calcium to phosphorous ratio and bone mineral density. Even the result cannot be generalized to the human population as always with animal studies; it shades the light to the dangerous effects that worth exploring. (39)

2.5 BMD levels and Osteoporosis among Qatari Women

A recent study determined the reference values for the Qatari female population and compared it with western and other Arab countries counterparts. The study participants were 574 Qatari women aged between 20 and 69 years. The DEXA scan at the proximal femur and lumbar spine were used. The results indicated an expected decline in BMD at spinal sites after peaking with age at 30–39 years age group, and for the femoral site at 40–49 years. Moreover, when comparing the BMD values of the spine of Qatari women with Caucasian and Kuwaiti women, it was lower but higher than the Lebanese and similar to Saudi women. However, the values of the total femur

BMD were higher in Qatari females compared to other Caucasians, Kuwaitis, Lebanese and Saudis females in the age group of 40–59, but lower in the age group 60–69 years. (40)

There is a paucity of high-quality data on prevalence and risk factors associated with osteoporosis in Qatar. Bener, Hammoudeh, and Zirie (41) reported that the prevalence of osteoporosis among Qatari post-menopausal women was 12.3%. They also found the BMI was higher among post-menopausal women compared to pre-menopausal women. Another recent study explored the association of body mass index, menopause status, and nationality, on BMD of the spine and femur among Arab women living in Qatar aged between 40 and 60. Their findings showed that the prevalence of osteopenia and osteoporosis combined was 4% at the femur and 16.2% at the spine. Also, BMI and menstrual status were both independently associated, and as BMI increased BMD increased at both the spine and femur. Nationality was not associated with mean BMD while the premenopausal women had greater BMD at the spine and femur compared to menopause women.

2.6 Significance of the Study

There is an observed increase in the soft drinks, in particular, the carbonated beverage consumption, while the potential effect on human health yet to be uncovered and not clear. Few studies explore the association between soft drink consumption and bone mineral density with controversial findings. Also, to the best of our knowledge, there are no previous studies that explore the association between soft drink and BMD among Qatari women. The current study aims to assess the association between soft drink consumption and bone mineral density among Qatari women.

CHAPTER 3: METHODS

3. 1 Study Design

The study uses secondary data collected by Qatar BioBank (QBB) to explore the association between soft drink consumption and bone mineral density among Qatari women. This is part of the QBB project which aims to collect data for research purposes from Qatari nationals and long-term residents using cross-sectional surveys to build a population-based health data depository.

3.1.1 Sample Size

Given that the study aimed to evaluate the association between BMD and soft drink consumption after adjusting for many potential confounders. A sample size of 1224 was required to achieve a 95% power at 5% significance level to detect a lower level of expected R-squared of 0.01 attributed to one independent variable using linear regression models adjusted for 20 potential confounders.

Given the expected missing values for some variables in the QBB database (has been as high as 50% based on our preliminary discussion) an estimated sample size of about 2500 were required for this study. Additionally, if the quantile regression were to be employed the sample size required will be much higher as such, so we requested 6000 participant data from QBB. However, only data on 1000 Qatari females aged ≥ 40 years were made available by QBB for this study. The sample size computation was determined using NCSS PASS version 14 (NCSS LLC, Kaysville, Utah).

3.1.2 Data Source

Qatar Biobank Center is part of Qatar Foundation, established in collaboration with the Ministry of Public Health and Hamad Medical Corporation. The aim is to enable local scientists and researchers to research common health issues in Qatar. Scientists expert in the field from Imperial College London supported the project in the

pilot phase. (42) The QBB data depository provides an extensive resource for research investigating the role of the different factors like environmental, lifestyle, genetics, and disease occurrence. Moreover, facilitate studying causes of diseases. (43)

3.1.3 Data Collection

The data collected primarily by well-trained QBB personnel using the most validated instruments available. Data collected using questionnaire included lifestyle, clinical information and further biological samples were also obtained from the participants. All individuals who took part in the survey provided written consent to participate. Participants completed a 5-stage interview, physical and clinic measurement. QBB used a computerized clinic-based system for data collection. Various information on socio-demographic factors, diet, lifestyle, anthropometry measurement, body composition, retinal imaging, health conditions, bone health, grip strength, dual-energy X-ray absorptiometry scan for the whole body, cognitive function, and measurements of cardiovascular and respiratory function are collected. Also, blood (a panel of 66 clinical biomarkers routinely measured), saliva, and urine sample were collected and stored for any future studies. (43)

3.1.4 Inclusion and Exclusion Criteria

The inclusion criteria for this study were female Qatari participants, aged ≥ 40 years at the time of recruitment. Participants have been recruited within the last five years with no missing records on the primary outcome bone mineral density or the main predictor soft drink consumption. Any women who were pregnant at the time of the survey were also excluded.

3.1.5 Measures

The variables were measured using validated tools based on the international best practice adopted by QBB. Data were collected by qualified nurses and researches

employed at QBB. In addition to the physical measurements and blood samples on each participant, face to face interviews and questionnaire surveys were used to collect behavioral and lifestyle. The list of variables selected for the study is shown in a table (Appendix A).

3.1.5.1 Outcome Variable

In the current study, the primary outcome of interest is total body BMD values (g/cm2) for each participant obtained using dual-energy x-ray absorptiometry (DXA) GE scan. The dual-energy x-ray absorptiometry (DXA) scanners considered one of the most common diagnostic device to determine BMD. (44) Bone density at forearm, spine, and femur sites was obtained. The overall total body BMD was also measured which was used in the analysis for this project. The process of measuring the outcome by QBB for full body using dual-energy x-ray absorptiometry scan usually takes 5-10 minutes on average. The scanner emits a low level of ionizing radiation and screens the bone density and body composition. (42)

3.1.5.2 Predictor Variable

The primary predictor variable is the frequency of the soft drink consumptions that include regular soft drink, diet soft drink, and energy drink. These data were extracted from QBB food frequency questionnaire which included questions on dietary intake in general, consumption of various types of drinks, and eating habits. Data on soft drink consumption were self-reported and measured as “never or rarely,” “1 to 3 times per month”, “1 to 3 times per week”, “4 to 6 times a week”, “once per day”, and “2 or more times per day”.

For the analysis, the data were converted to consumption frequency per week. The consumption recorded as 0 per week, 0.5 per week, two times per week, five times a week, seven times a week, and 14 times per week. Finally, the total consumption of

all soft drink types was calculated per participant by summing up the frequency intake of the three types: regular soft drinks, diet soft drinks, and energy soft drinks. Due to the lack of the variability and the relatively smaller sample size, the total consumption classified into three categories (cutoff as zero per week, less than one per week, and more than one per week) were used for the regression modeling.

3.1.5.3 Potential Confounders Variables

Given the aim of our study was to explore the association between BMD and soft drink consumption, a number of socio-demographic variables, as well as diet, lifestyle, and anthropometry measures were considered to be potential confounders in this study.

3.1.5.3.1 Socio-demographic Variables

Age, education, and income were considered significant based on the literature review. For the data analysis, age was further categorized into four groups: 40-50 years, 51-60 years, 61-70 years and over 70 years. Use of age as a continuous variable would require a larger sample size than what was made available to us, particularly when adjusted along with other variables. These categories also have an epidemiological basis, and previous researchers considered similar cut off values.

Educational levels were recorded in eight categories ("did not attend school," "did not complete primary school", "primary school", "secondary school", "high school, technical/professional school", "university degree", and "postgraduate degree"). For data analysis, they were farther reduced to small categories. Education level was summarized into three categories: up to secondary (no schooling to secondary), post-secondary (trade, certificate, diploma), and a university degree or higher (university degree" and postgraduate degree).

Total monthly income included the salary, rental income, investment and

government transfers in Qatari Riyal. The income data were recorded by the QBB to indicate the closest category from “no income”, “less than 10000 QR”, “between 10000-20000 QR”, and “more than 20,000”.

3.1.5.3.2 Diet-related variables

Diet was assessed using a validated self-administrated food-frequency questionnaire. The amount of the consumed vegetables and fresh fruits per week was recorded similar to the soft drink consumption: zero, 0.5 per week, two times per week, five times a week, seven times a week, and 14 times per week.

The total consumption of the fresh fruits drinks included the fresh fruit juice, smoothies, and preserved fresh juice. The total consumption was computed in a similar way to the total soft drink consumption as described above, while different cutoff point used (less than four times per week, 5-6 times per week, and more than seven times per week).

The total consumption of milk computed in a similar way to the total soft drink consumption as described above, but included cold milk, Milk added to cereals, and milkshakes or flavored milk. The cutoff point used (less than four times per week, 4-5 times per week, and 6 or more times per week).

3.1.5.3.3 Physical activity

Physical activity (PA) collected by staff-administered questionnaires and were reported as average hours spent per week. For the data analysis, the total PA were converted to metabolic equivalent (MET)-hours-per-week to reflect both intensity and time spent on activities. The total leisure time physical activity level was calculated by multiplying the appropriate MET values based on the “Compendium of Physical Activities” by the time spent in each activity. (45) The MET values assigned for PA were: 3 for walking; 4.5 for swimming or bicycling at a regular pace, yoga, double

tennis, and gym; 7 for running, fast bicycling, fast swimming, aerobics, and tennis. For the analysis, the three activities were summed up and categorized based on cutoff points were (zero MET hours/week as no activity, 3-73.5 MET hours/week as low activity, and more than 75 MET hours/week as moderate activity).

3.1.5.3.4 Anthropometry

The weight and height were measured directly by a trained nurse. Participant stand without shoes wearing a light gown and the weight measured reported to the nearest kilogram, while height measured reported to the nearest centimeters. Body mass index (BMI) was then computed using the weight and height and reported as "weight in kilograms by the square of height in meters (kg/m2)". (46) The BMI was further classified : normal (BMI =18.5 and < 25), overweight (BMI =25 < 30), and obese(BMI > 30) based on the WHO (46) cut off values of BMI.

3.1.5.3.5 Smoking status

Information about smoking status was obtained from the questionnaires and recorded as Non-smoker, Smoker, and Ex-Smoker.

3.1.5.3.6 Menopausal status

The question used to assess the menopausal status was "Did your menstrual cycle stopped" and each participant reported either (yes/no or had a hysterectomy before natural menopause).

3.1.5.3.7 Comorbidities

Self-reported rheumatoid arthritis, diabetes, gestational diabetes, thyroid disease, kidney disease, osteoporosis, and asthma were recorded as yes or no.

3.1.5.3.8 Supplements and treatments

Hormone replacement therapy, multivitamins or minerals, vitamin D, or calcium supplements were also obtained using the questionnaire and recorded as yes or

no.

3.1.6 Statistical Analysis

As an initial step in the data analysis, various methods were employed to check for potential errors in the data. The range of values of each of the variable were examined for their validity. Missing values for each variable were also assessed. Descriptive analysis was performed and presented as percentages for categorical variables and mean values with standard deviations for continuous variables. Further bivariate association between the outcome variables and these potential confounders were also assessed as a confounder is associated with both outcome and predictor and potentially distort the relationship. Multiple linear regression was used first to explore the association between soft drink consumption and BMD including the potential confounders, result not shown because we are interested in lower level of BMD. The associated plotting and diagnostic tests were used to check the model assumption and the best fit. The model specification was tested to ensure it include all the required predictors and the tests show that the model correctly specified. Most importantly, the effect of the soft drink consumption on different quantiles of BMD was evaluated using multivariate quantile regression models. As evidence showed that ordinary least squares regression method for statistical inference is ineffective when the distributions are skewed or when the quantity of interest is the upper or lower tail of the distributions. (47) Quantile regression provides a solution and model the relationship between the covariates and the conditional quantiles of the response variable. (48) Also, it provides a flexible framework and models the likely heterogeneous effects of the risk factor through the entire distribution of the outcome. (49)

In the analysis, we were interested in assessing the association between the lowest quantile of BMD with the consumption of soft drinks. The lowest quantile of

BMD is assumed to represent women below the healthy level of BMD. Quantile regression model employed to assess the association between soft drink consumption and BMD. Quantile regression often used in nutritional epidemiology to identify those with the high-risk group based on quantiles and link those high risk individuals to predictors while adjusting for potential confounders. (50)

Multiplicative interaction between soft drink consumption and other covariates tested by adding the product term in the multivariable quantile regression model, but since there was no significant interaction between gender and soft drink and BMI and soft drink in the model the result was not presented in the results as a table. Also, to understand the effect of the fruit drink consumption on BMD, quantile regression modelling with potential confounder was used to analyze the association. Subgroup analysis was conducted to investigate the association between soft drink and BMD in the different levels of the categorical covariates. Sensitivity analysis also carried out to assess the effect of each type of soft drink (regular, diet, and energy) on the BMD.

Finally, a set of four models were used to assess if the effect estimate differs and the association between soft drink and BMD was influenced (mediated) by other covariates. the Models comprise of: model 1 adjusted for age; model 2 farther adjusted for BMI; model 3 farther adjusted for education, income, menopause status, multivitamin or minerals, total consumption fruits drink consumption, smoking status, total consumption of milk, diabetes, and asthma; model 4 adjust for age, BMI, education, income, menopause status, multivitamin or minerals, total consumption fruits drink consumption, smoking status, total consumption of milk, and excluding those already diagnosed with osteoporosis.

The current study takes in to account adjusting for the identified confounders and test for interaction and effect modifier as illustrated in the Directed acyclic graphs

(DAG) to provide a visual representation of causal assumptions as shown in (Figure 1). All statistical analyses were conducted using STATA 15 (Stata Corporation, College Station, TX, USA). Stata codes used for data analyses are presented in the (Appendix B).

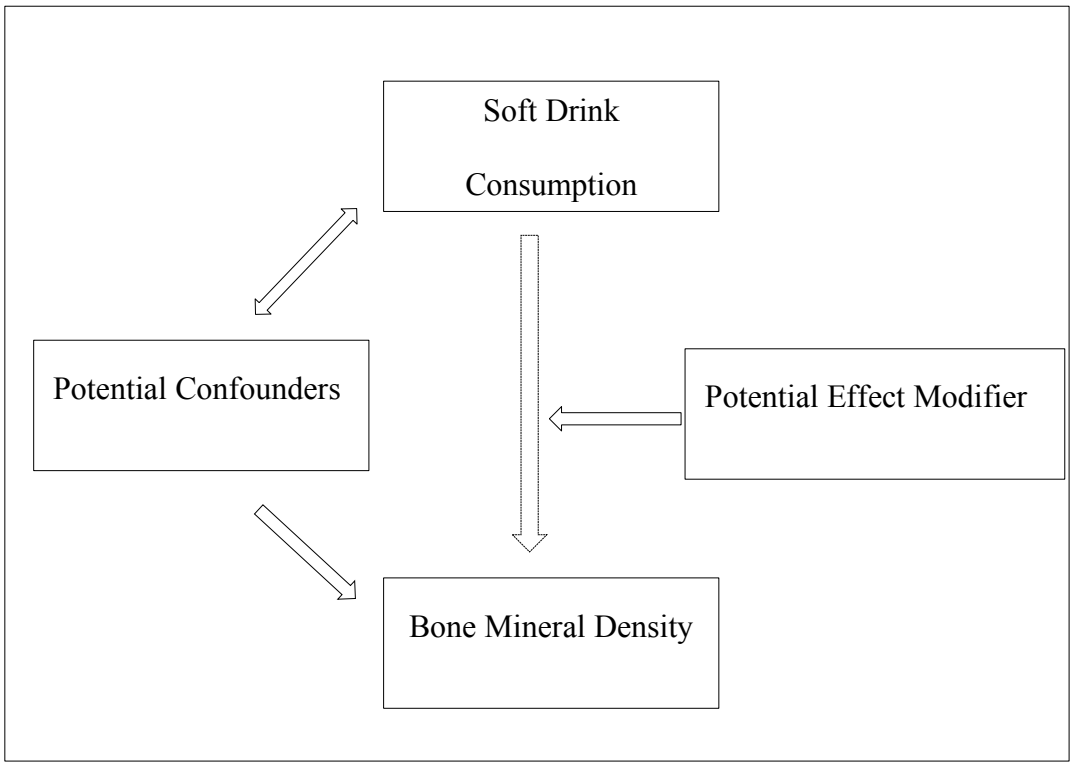

Figure 1. DAG representing a theoretical framework to account to the variability in the primary outcome by the predictor variable while adjusting for potential confounder and taking into consideration the presence of the potential effect modifiers.

3.2 Potential Challenges

Based on the literature review number of variable identified as potential confounders such as biological factors (genetics, age, and BMI), lifestyle (physical

activity, smoking, alcohol use), and type of diet (fruit and vegetable, caffeine intake, and calcium intake).(51) Also, using any of the following medication (steroids, anticonvulsants, Heparin, thyroxine, immunosuppressant, estrogen, vitamin D metabolites, chemotherapeutic drugs and use of thyroid medication); and having any of the following diseases or condition (chronic renal disease, parathyroid, thyroid , adrenal, hypogonadism malignancy, chronic live disease, chronic gastrointestinal disease, diabetes, early oophorectomy, osteomalacia, and rheumatoid arthritis, and hysterectomy). (9, 51, 52) (Appendix C)

3.3 Ethical Consideration

The data used in this study were collected by QBB, and all participants consented. The participation was voluntary. Also, individuals participated have been given the complete right to withdraw at any time from QBB project without consequences. For research purposes, QBB provides the data de-identified in an anonymous electronic form. In order to ensure data security, the dataset was stored in a password protected computer and accessible only by the principal investigator. The data were kept confidential as per the agreement with the QBB, and its privacy was maintained throughout the research process and after. Institutional Review Board (IRB) approval was obtained from the Qatar Biobank Ethics Committee. Additional IRB exemption from Qatar University was also sought.

CHAPTER 4: RESULTS

4.1 Sample Description: distribution of exposure and outcome variables

Figure 2 below shows the distribution of BMD among the 1000 participants. Overall, the BMD was normally distributed. The mean BMD was 1.17 (SD 0.12) $g.cm^3$.

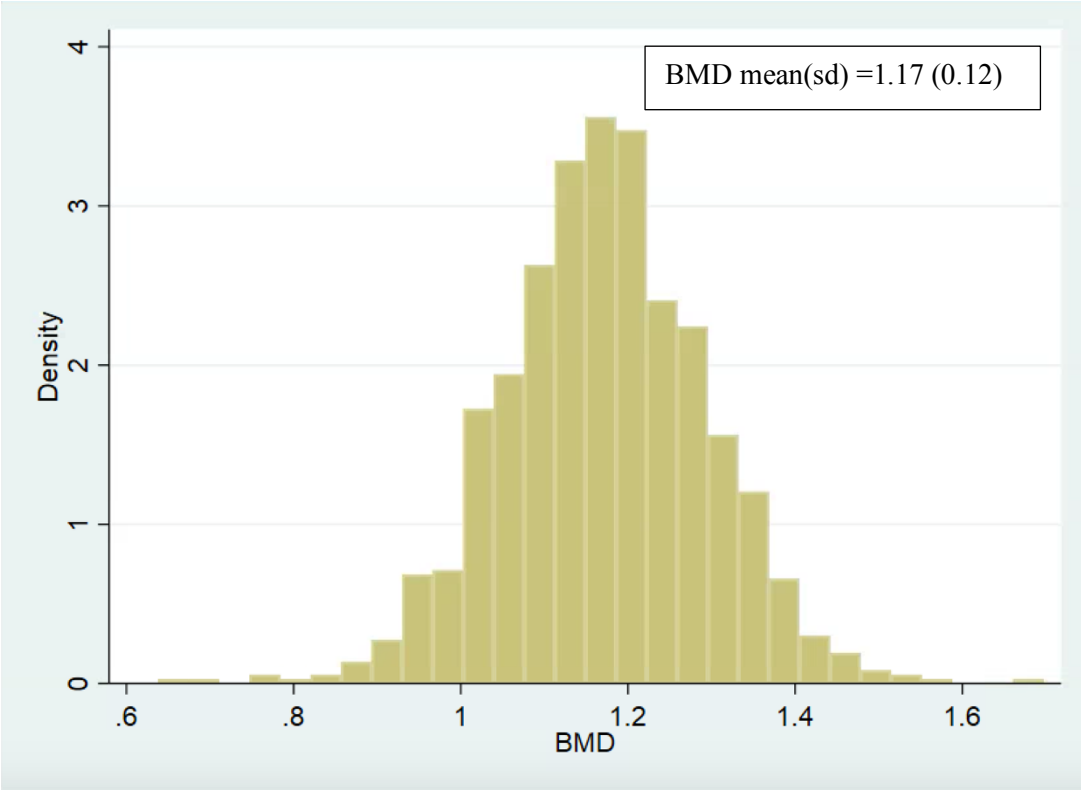

Figure 2. The distribution of the total body BMD in the study population (n=1000)

Figure 3 shows the distribution of the total soft drink consumption of the participants. While most of the participants did not drink soft drink (68%), around one third reported consuming soft drink. A total of 15.6% participants consumed soft drink on a weekly basis.

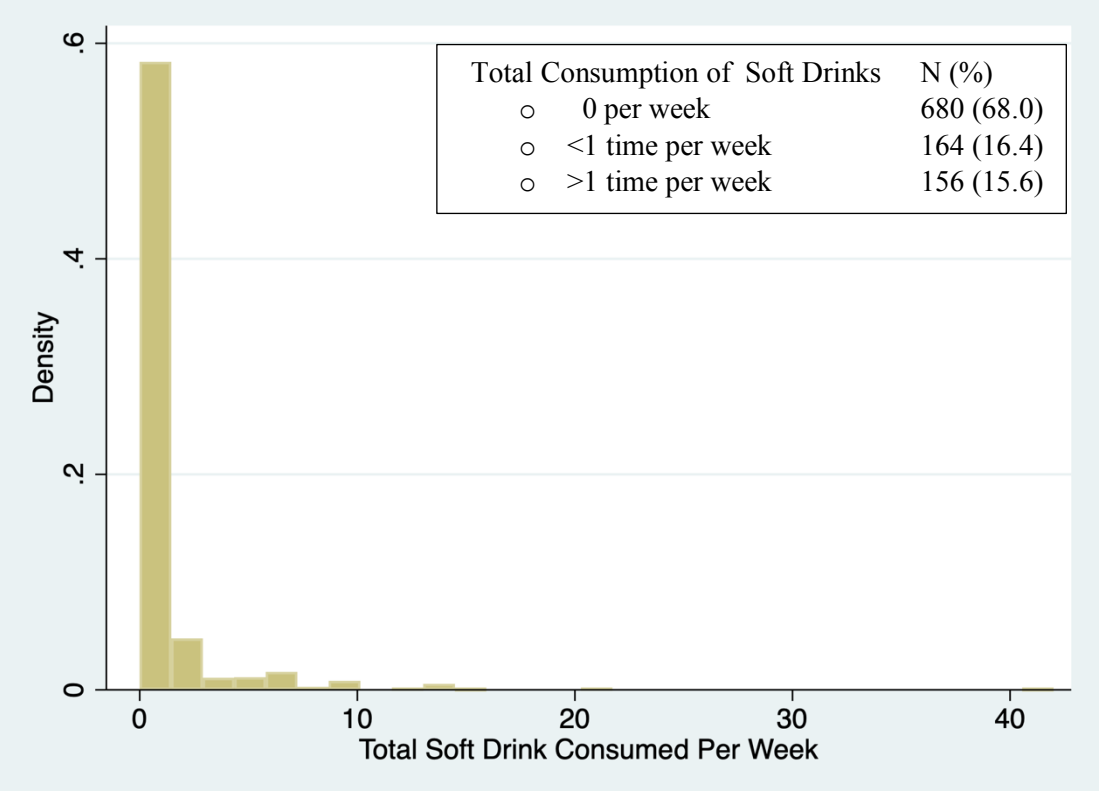

Figure 3. The distribution of the total soft drink consumption in the study population (n=1000)

4.2 Sample Characteristics of the Study Population

Among the 1000 Qatari women aged 40 years or above, the mean age was 51.8 (SD = 8.3) years. For the purpose of analysis, the age was grouped into four categories: 40-50, 51-60, 61-70, >70 years. The majority (48.1%) of the participants were between 40-50 years old, and about 36% were between 51-60 years. The remained 15% were over 60 years old. The study population is fairly well educated with about 60% have either university degrees or post-secondary diplomas. Most of the women also come from a higher socio-economic background with over 2/3rd of the women earning more than 10,000 QAR per month as shown in Table 1.

Table 2 shows the distribution of menopausal status, where about 42% of the

women were at the post-menopausal stage. In total, 5.5% of them uses hormonal replacement therapy (HRT) and 3.4% had hysterectomy carried out at a pre-menopausal stage. Moreover, all the participant reported that they did not use vitamin D and calcium supplements in the past three months. However, 65.4% of the participants reported taking multivitamin or minerals supplements in the past three months.

Table 3 present the distribution of comorbidities including diabetes, gestational diabetes, kidney disease, osteoporosis, asthma, thyroid disease, and rheumatoid disease in the study population. More than 30% of the participants were diabetics. About 36.6% (n=322) had gestational diabetes, 6.5% (n=352) had been diagnosed with kidney diseases, 14.1% (n=383) had osteoporosis, 41.1% (n=559) had thyroid disease, 38.5% (n=535) had rheumatoid disease (e.g. arthritis), 12.0% (n=921) had asthma.

Table 1: Distribution of socio-demographic characteristics of the study sample (n=1000)

Variables	n (%)
Age group	
o 40 _ 50	481 (48.1)
o 51 – 60	364 (36.4)
o 61 – 70	120 (12.0)
o >70	35 (3.5)
Education	
o Up to secondary	405 (40.5)
o Post-secondary	211 (21.1)
o University degree or higher	384 (38.4)
Total monthly income (QR)	
o No income	144 (15.7)
o Less than 10,000	203 (22.1)
o Between 10,000 and 20,000	205 (22.4)
o More than 20,000	365 (39.8)

Table 2: Distribution of menopausal status, HRT, and supplements of the study sample (n=1000)

Variables	n (%)
Menopausal status	
o Pre	548 (54.8)
o Post	418 (41.8)
o Hysterectomy Pre-menopause	34 (3.4)
HRT	
o No	945 (94.5)
o Yes	55 (5.5)
Vitamin D	0 (0.0)
Calcium	0 (0.0)
Multivitamin and Minerals	
o No	654 (65.4)
o Yes	346 (34.6)

Table 3: Distribution of comorbidities of the study sample (n=1000)

Variables	N (%)
Diabetes	
o No	653 (65.3)
o Yes	347 (34.7)
Gestational Diabetes	
o No	204 (63.4)
o Yes	118 (36.6)
Kidney Disease	
o No	329 (93.5)
o Yes	23 (6.5)
Osteoporosis	
o No	329 (85.9)
o Yes	54 (14.1)
Thyroid Disease	
o No	329 (58.9)
o Yes	230 (41.1)
Rheumatoid Diseases	
o No	329 (61.5)
o Yes	206 (38.5)
Asthma	
o No	810 (88.0)
o Yes	111 (12.0)
Variation in the numbers of participants (n) was due to the unequal response to the question related to the comorbidities.	

Table 4 illustrate the distribution of anthropometric variables, physical activity and smoking habits. The mean BMI was 32.8 kg/m^2 (SD= 5.8 kg/m^2). Almost 2/3rd of the participants were obese and an additional 27% were overweight. Only about 5% were normal. The use of tobacco reported by the participants reveals that 2% (n= 20) of the participants were smokers at a point of their lives and 98% (n= 980) never smoked and were classified as non-smokers. The leisure time physical activity among the participant didn't vary as most of the participants were classified to have no activity (zero MTE hours/week) 66.1%, 15.0% were classified having low activities (between 3-73.5 MET hours/ week), and 18.9 classified moderate activities (75 MTE hours/week).

Table 4: Distribution of anthropometry and lifestyle-related variables of the study sample (n=1000)

Variables	N (%)
BMI (kg/m^2)	
o Normal	52 (5.2)
o Overweight	271 (27.1)
o Obese	677 (67.7)
Smoking Status	
o None smoker	980 (98.0)
o Smoker	18 (1.8)
o Ex-smoker	2 (0.2)
Physical Activities **	
o No activity	661 (66.1)
o Low	150 (15.0)
o Moderate	189 (18.9)
** Metabolic equivalent (MET)-hours-per-week, BMD: body mass index	

The main predictor and related dietary intake were described in Table 5. The mean consumption of fruits and vegetables was 9.4 times per week (SD= 6.0).

Participants were classified to be having consuming fruit drinks 3-4 times per week, 5-6 times per week, and 7 or more times per week as 24.7%, 39.2%, and 36.1% respectively.

Table 5: Distribution of diet-related variables of the study sample (n=1000)

Variables	N (%)
Total Consumption of Fruit Drinks	
o 3-4 times per week	247 (24.7)
o 5-6 times per week	392 (39.2)
o 7 or more times per week	361 (36.1)
Total Consumption of Soft Drinks	
o 0 per week	680 (68.0)
o <1 time per week	164 (16.4)
o >1 time per week	156 (15.6)
Total Consumption of Milk	
o Less than 4 times per week	378 (37.8)
o 4-5 times per week	320 (32.0)
o 6 or more times per week	302 (30.2)
Fruit and Vegetable intake*	9.4 (6.0)

*: mean (SD)

4.3 Sample characteristics by soft consumption levels

Prior modelling to test the hypothesis on BMD and its association to soft drink consumption, it was essential to assess soft drink consumption and the characteristics of the participants (Table 6 and continue in Table 7). As shown in Table 6, most of the participants did not consume soft drink and soft drink consumers were younger than non-consumers. The consumption of soft drink as less than one per week or more than one per week decreases with age. The highest consumption was seen among age group 40-50, while the lowest was among participants over 70. Contrarily, as the income increase the soft drink consumption among participants increased and the highest

consumption found among participants with monthly total income of more than 20,000. Soft drink consumption was higher among participants with university degree or higher followed by those below secondary school educations and lower among those with post-secondary (trade, certificate, diploma). Pre-menopause participants consumed soft drinks more than post-menopause participants also lower among those participants undergone hysterectomy.

Table 6: Main characteristics of study participants distribution by soft drink consumption

Main characteristics	Soft Drink Consumption		
	0	<1	>1
Age group			
o 40 _ 50	282 (41.5)	101 (61.6)	98 (62.8)
o 51 – 60	277 (40.7)	45 (27.4)	42 (26.9)
o 61 – 70	92 (13.5)	17 (10.4)	11 (7.1)
o >70	29 (4.26)	1 (0.6)	5 (3.2)
Education			
o Up to secondary	298 (43.8)	50 (30.5)	57 (36.5)
o Post-secondary	135 (19.9)	38 (23.2)	38 (24.4)
o University degree or higher	247 (36.3)	76 (46.3)	61 (39.1)
Total monthly income (QR)			
o No income	98 (15.7)	15 (10.2)	31 (21.5)
o Less than 10,000	153 (24.4)	24 (16.3)	26 (18.0)
o Between 10,000 and 20,000	137 (21.9)	37 (25.2)	31 (21.5)
o More than 20,000	238 (38.0)	71 (48.3)	56 (38.9)
Menopause			
o Pre	335 (49.3)	107 (65.2)	106 (68.1)
o Post	315 (46.3)	56 (34.2)	47 (30.1)
o Hysterectomy	30 (4.4)	1 (0.6)	3 (2.0)
Diabetes			
o No	443 (65.2)	106 (64.6)	104 (66.7)
o Yes	237 (34.9)	58 (35.4)	52 (33.3)

Table 7 : Continue of main characteristics of study participants distribution by soft drink consumption

Main characteristics	Soft Drink Consumption		
	0	<1	>1
Gestational Diabetes			
o No	148 (65.2)	29 (58.0)	27 (60.0)
o Yes	79 (34.8)	21 (42.0)	18 (40.0)
Kidney Disease			
o No	230 (93.1)	54 (94.7)	45 (93.8)
o Yes	17 (6.9)	3 (5.3)	3 (6.3)
Osteoporosis			
o No	230 (84.3)	54 (94.7)	45 (84.9)
o Yes	43 (15.8)	3 (5.3)	3 (15.1)
Thyroid Disease			
o No	230 (59.6)	54 (60.0)	45 (54.2)
o Yes	156 (40.4)	36 (40.0)	38 (45.8)
Rheumatoid Diseases			
o No	230 (61.3)	54 (65.9)	45 (57.7)
o Yes	145 (38.7)	28 (34.2)	33 (42.3)
Asthma			
o No	549 (87.7)	134 (88.2)	127 (88.8)
o Yes	77 (12.3)	18 (11.8)	16 (11.2)
Vitamin D	0 (0.0)	0 (0.0)	0 (0.0)
Calcium	0 (0.0)	0 (0.0)	0 (0.0)
Multivitamin and Minerals			
o No	442 (65.0)	105 (64.0)	107 (68.6)
o Yes	238 (35.0)	59 (36.0)	49 (31.4)
HRT			
o No	643(94.6)	155 (94.5)	147 (94.2)
o Yes	37 (5.4)	9 (5.5)	9 (5.8)
BMI(kg/m^2)			
o Normal	36 (5.3)	7(4.3)	9 (5.8)
o Overweight	183 (26.9)	43 (26.2)	45 (28.9)
o Obese	461 (67.8)	114 (69.5)	102 (65.4)
Smoking Status			
o None smoker	670 (98.5)	159 (97.0)	151 (96.8)
o Smoker	9 (1.3)	5 (3.1)	4 (2.6)
o Ex-smoker	1 (0.2)	0 (0.0)	1 (0.6)
Physical Activities*			
o No activity	456 (67.1)	93 (56.7)	112 (71.8)
o Low	99 (14.5)	31 (18.9)	20 (12.8)
o Moderate	125 (18.4)	40 (24.3)	24 (15.4)
**Bone Mineral Density ** **	680(1.17± 0.1)	164(1.18± 0.1)	156(1.16± 0.1)

HRT: hormonal replacement therapy, BMI: body mass index,*: (MET)-hours-per-week, **: (mean ±standard deviation)

Also, Table 7 show that participants diagnosed with rheumatoid arthritis, diabetes, gestational diabetes, thyroid disease, kidney disease, osteoporosis, and asthma have low consumption of soft drink compare to those free of the disease.

4.4 Determinants of BMD: linear regression analyses

Univariate analysis was carried out to identify those variables that are clinically and statistically associated with the main predictor and the outcome are identified and were used to adjust for in the main regression modelling.

In the initial univariate analysis, Table 8 shows that there was no significant association between total consumption of soft drinks and BMD, although each increase of soft drinks consumption of more than one time per week was negatively associated with BMD resulting in - 0.004 reduction of the predicted mean value p-value= 0.725, 95%CI (-0.025 0.016). Also, there was no significant association between total consumption of fruit drinks and BMD. The regression coefficients for BMD were 0.011 and 0.012 among consumers of 5-6 times/week, and >=7 times/week, respectively.

Age was inversely associated with BMD on an observed trend. Age between 51-60 decreases BMD predicted mean value by 0.04, p-value= 0.001, 95%CI (-0.060 , -0.029) compare to those age 40-50 years old and age between 51-60 decreases it by 0.02, p-value= 0.001, 95%CI (-0.029, -0.097) compare to those age 40-50 years old. Similarly, those older than seventy decreases BMD predicted mean value by 0.02, p-value= 0.001, 95%CI (-0.097, -0.082) compare to those age 40-50 years old as seen in Table 8.

As illustrated in Table 8, participants education levels were positively associated with the BMD. Participants having post-secondary education increases the predicted BMD mean value by 0.029, p-value= 0.005, 95%CI (0.009,0.049) compare to those below secondary. Likewise, participants with post-graduate degree found to be

increasing the predicted BMD mean value by 0.033, p-value= 0.001, 95%CI (0.016, 0.050).

Total monthly income of the participant was associated with the BMD. The results revealed a negative association between participants having income less than 10,000 or between 10,000 and 20,000 per month and BMD. They decrease the predicted BMD mean value by -0.039, p-value= 0.003, 95%CI (-0.064, -0.013) and -0.002, p-value= 0.908, 95%CI (-0.027, 0.024) respectively compare to those having no income. Whereas the association was positive between participants income more than 20,000 and BMD. The results showed that it increases the predicted BMD mean value by 0.014, p-value= 0.234, 95%CI (-0.009, 0.037) as shown in Table 8.

Menopause status was also negatively associated with BMD. Compared with pre-menopausal women, post-menopause women had a lower BMD (β -0.08, 95%CI -0.098,-0.068). Similarly, hysterectomy decreased the predicted BMD mean value by -0.04, p-value= 0.001, 95%CI (-0.083, -0.003) as compared to those pre-menopausal.

On the other hand, there were no associations between the comorbidities and BMD, while most of the diseases were negatively affecting BMD mean value. Using hormonal therapy, smoking status, fruit and vegetable consumption, and low physical activity were negatively affecting the BMD but insignificant. The moderate physical activity was positively affecting the BMD, but also insignificant as presented in Table 8.

However, BMI and total consumption of milk were found positively associated with BMD; each unit increase in BMI was associated with an BMD increase of 0.004 (95%CI 0.002-0.005). The β (95%CI) for BMD were: 0.00, 0.026 (0.008, 0.044), and 0.022 (0.004, 0.040) among those with milk consumption of <4 times/week, 4-5 times/week, and >=6 times/week, respectively (Table 8)

Table 8: Univariate analysis of main outcome and predictors

Predictors	Coefficient	P-value	95% CI	
Total Consumption of soft drinks				
o <1 time per week	0.010	0.328	-0.011	0.030
o >1 time per week	-0.004	0.725	-0.025	0.016
Total Consumption of fruit drinks				
o 5-6 times per week	0.011	0.274	-0.009	0.030
o 7 or more times per week	0.012	0.231	-0.008	0.032
Age group				
o 51 – 60	-0.045	**0.001**	-0.060	-0.029
o 61 – 70	-0.121	**0.001**	-0.029	-0.097
o >70	-0.122	**0.001**	-0.097	-0.082
Education				
o Post-secondary	0.029	**0.005**	0.009	0.049
o High	0.033	**0.001**	0.016	0.050
Total monthly income (QR)				
o Less than 10,000	-0.039	**0.003**	-0.064	-0.013
o Between 10,000 and 20,000	-0.002	0.908	-0.027	0.024
o More than 20,000	0.014	0.234	-0.009	0.037
Menopause				
o Post	-0.083	**0.001**	-0.098	-0.068
o Hysterectomy	-0.043	**0.035**	-0.083	-0.003
Diabetes	-0.012	0.135	-0.028	0.003
Gestational Diabetes	0.027	0.082	-0.003	0.056
Kidney Disease	0.009	0.732	-0.043	0.061
Thyroid Disease	-0.006	0.552	-0.027	0.014
Rheumatoid Diseases	-0.021	0.052	-0.042	0.000
Asthma	-0.015	0.220	-0.039	0.009
HRT	-0.007	0.678	-0.040	0.026
Multivitamin or Minerals	0.023	**0.005**	0.007	0.039
BMI (kg/m^2)	0.004	**0.001**	0.002	0.005
Smoking Status				
o Smoker	0.054	0.062	-0.002	0.111
o Ex-smoker	0.024	0.778	-0.145	0.194
Physical Activity				
o Low	0.015	0.168	-0.102	0.081
o Moderate	-0.002	0.847	-0.006	0.037
Fruit and Vegetable intake	0.000	0.965	-0.001	0 .001
Total Consumption of Milk				
o 4-5 times per week	0.026	**0.005**	0.008	0.044
o 6 or more times per week	0.022	**0.019**	0.004	0.040

HRT: hormonal replacement therapy, BMI: body mass index

4.5 Soft drink consumption and BMD in quantile regression

In our study, those in the lowest quantile for BMD were assumed to represent

women with low BMD and in turn with high-risk of osteoporosis. Age, BMI, menopausal status, multivitamin or minerals use, consumption of milk and education level were found to be statistically associated with BMD in the univariate analysis and were included in the model building. The main predictor and the other clinically significant variables such as smoking status and fruit and vegetable consumption were also added to adjust for in the model. Also, farther adjustment for consumption of milk and leisure time physical activity to the previous model was made. Even after further adjusting for both total consumption of milk and leisure time physical activity by adding them to the previous model, the results revealed a statistically significant inverse association in the 25th percentiles of the BMD distribution with the total soft drink consumption of more than one time per week. Each increase in soft drink consumption per week was associated with a BMD decrease of -0.034 (95%CI (-0.056, -0.012)) in the 0.25 quantile (Table 9).

In quantile regression model, there was an inverse association with both age group and menopause status with BMD. Across age groups of 40-50, 51-60, 61-70, and > 70 years, the β (95%CI) for BMD were 0.00, -0.025 (-0.048, -0.001), -0.077 (-0.108,-0.044), and -0.053 (-0.102, -0.004) respectively. The β (95%CI) for BMD were: 0.00, -0.062 (-0.085, -0.039), and -0.059 (-0.105, -0.014) among those pre-menopausal, post-menopausal, and those undergo hysterectomy respectively (Table 9).

Additionally, the results showed that BMI was positively associated with the 25th percentiles of the BMD distribution and each unit increase in BMI increases predicted BMD value by 0.006, p-value= 0.001, 95% CI (0.004, 0.07) after adjusting for other variables in the model. However, in the quantile regression model of the BMD distribution, education level, multivitamin or minerals use, smoking status, physical activities, total consumption of milk and fruit and vegetable consumption were not

associated with 25 percentiles of BMD after adjusting for other variables in the model. The analysis revealed that soft drink consumption >1 time/week decrease BMD more than 10 years aging (Table 9).

Table 9: Adjusted Quantile regression testing the association among 0.25 quantiles of BMD and its association to soft drink consumption after adjusting for potential confounders

Predictors	**Bone Mineral Density**			
	Q (0.25)			
	Coefficient	p-value	95% CI	
Total Consumption of Soft Drink				
o <1 time per week	-0.001	0.926	-0.023	0.020
o >1 time per week	-0.034	**0.003**	-0.056	-0.011
Age group				
o 51 – 60	-0.022	**0.057**	-0.045	-0.001
o 61 – 70	-0.077	**0.001**	-0.108	-0.044
o >70	-0.053	**0.033**	-0.102	-0.004
Education				
o Post-secondary	0.012	0.293	-0.010	0.034
o University degree or higher	0.017	0.078	-0.000	0.038
Multivitamin or Minerals	0.009	0.290	-0.008	0.025
Menopause				
o Post	-0.062	**0.001**	-0.085	-0.039
o Hysterectomy	-0.059	**0.011**	-0.105	-0.014
BMI	0.006	**0.001**	0.004	0.007
Smoking Status				
o Smoker	0.052	0.081	-0.007	0.110
o Ex-smoker	0.084	0.324	-0.089	0.257
Physical Activity				
o Low	0.002	0.871	-0.021	0.024
o Moderate	-0.009	0.385	-0.030	0.011
Total Consumption of Milk				
o 4-5 times/week	0.006	0.498	-0.012	0.025
o 6 or more times/week	-0.003	0.685	-0.023	0.015
Fruit &Vegetable intake	0.000	0. 578	-0.001	0.002

BMI: body mass index, CI: confidence interval, Q: quantile

4.6 Fruit drink consumption and BMD in quantile regression

Table 10 showed that there is no significant association at the 0.25 quantile of the BMD distribution with the total fruit drink consumption. Participants age, post-menopause, and BMI found significantly associated with BMD at the 0.25 quantile of the distribution. Both age group and post-menopause decrease the predicted value of the BMD, while BMI increases the predicted value of BMD.

Table 10: Adjusted Quantile regression testing the association among 0.25 quantiles of BMD and its association to fruit drink consumption after adjusting for potential confounders

Predictors	**Bone Mineral Density**		
	Q (0.25)		
	Coefficient	p-value	95% CI
Total Consumption of Fruit Drink			
o 5-6 times per week	0.017	0.111	-0.004 0.037
o 7 or more times per week	0.010	0.335	-0.011 0.032
Age group			
o 51 – 60	-0.028	**0.018**	-0.052 -0.004
o 61 – 70	-0.078	**0.001**	-0.111 -0.046
o >70	-0.062	**0.014**	-0.113 -0.012
Education			
o Post-secondary	-0.009	0.411	-0.013 0.032
o University degree or higher	0.011	0.301	-0.009 0.031
Multivitamin or Minerals	0.011	0.186	0.006 0.028
Menopause			
o Post	-0.052	**0.001**	-0.076 -0.028
o Hysterectomy	-0.053	**0.028**	-0.099 -0.006
BMI	0.005	**0.001**	0.039 0.007
Smoking Status			
o Smoker	0.054	0.080	-0.006 0.113
o Ex-smoker	0.076	0.398	-0.101 0.254
Physical Activity			
o Low	0.001	0.924	-0.022 0.024
o Moderate	-0.000	0.938	-0.023 0.020
Total Consumption of Milk			
o 4-5 times/week	0.008	0.441	-0.012 0.027
o 6 or more times/week	-0.002	0.856	-0.021 0.018
Fruit &Vegetable intake	0.001	0.270	-0.001 0.002

BMI: body mass index, CI: confidence interval, Q: quantile

4.7 Additional Analysis

Sensitivity analysis was conducted, and the association was examined separately for regular soft drinks, diet soft drinks, and energy drinks (used the continuous variables in the model). Table 11 shows that there was a significant inverse association between the regular soft drink consumption and the BMD at 0.25 quantile of the distribution. Each one time per week increase of regular soft drink consumption was associated with -0.005 decrease in the predicted value of BMD at 0.25 quantile of the distribution 95%CI (-0.010, 0.000), p-value= 0.040.

Table 11:Association between different types of soft drink consumption at 0.25 quantile of the BMD distribution

Predictors	**Bone Mineral Density**		
	Q (0.25)		
	Coefficient	p-value	95% CI
Regular Soft Drink	-0.005	**0.034**	-0.009 0.000
Diet Soft Drink	-0.006	0.124	-0.013 0.002
Energy Soft Drink	0.006	0.353	-0.007 0.020

Model adjusted for age, BMI, menopause, education, multivitamin or minerals, smoking status, physical activities, fruit and vegetable consumption

In subgroup analyses, soft drink consumption was inversely associated with the BMD at the 0.25 quantile mostly when the consumption was more than one time per week. The findings were observed among age group (40-50) years old and among those (51-60) years old, participants with education below secondary school and participants with postgraduate education, and among those pre-menopause and participants undergone a hysterectomy as shown in Table 12. Additionally, subgroup analysis

showed that soft drink consumption was inversely associated with the BMD at the 0.25 quantile mostly when the consumption was more than one time per week among those without diabetes, osteoporosis, thyroid disease, kidney disease, and rheumatoid disease. Also, among participants who were overweight, not physically active, and non-smokers not taking multivitamin or minerals or on HRT (Table 12 and continue in 13).

Table 12: Subgroup analyses of soft drink consumption at the 0.25 quantiles of BMD distribution

Subgroup	Soft Drink Consumption		
	None Coef.	<1 Coefficient (95% CI)	>1 Coefficient (95% CI)
Age group			
o 40 _ 50	0.00	-0.012 (-0.040, 0.016)	**-0.031*** (-0.060, -0.004)
o 51 – 60	0.00	0.030 (-0.010, 0.071)	**-0.052*** (-0.094, -0.011)
o 61 – 70	0.00	-0.007 (-0.073, 0.059)	-0.004 (-0.081, 0.073)
o >70	0.00	0.272 (-0.063, 0.609)	0.061 (-0.102, 0.225)
Education			
o Up to secondary	0.00	-0.003 (-0.045, 0.039)	**-0.051*** (-0.091, -0.012)
o Post-secondary	0.00	0.007 (-0.030, 0.044)	-0.035 (-0.073, 0.003)
o University degree or higher	0.00	0.003 (-0.024, 0.031)	**-0.030*** (-0.061, -0.000)
Total monthly income (QR)			
o No income	0.00	0.014 (-0.084, 0.111)	-0.019 (-0.093, 0.056)
o Less than 10,000	0.00	0.030 (-0.034, 0.095)	-0.029 (-0.092, 0.034)
o Between 10,000 and 20,000	0.00	-0.049 (-0.105, 0.007)	-0.056 (-0.117, 0.004)
o More than 20,000	0.00	0.007 (-0.028, 0.043)	-0.031 (-0.070, 0.009)
Menopause			
o Pre	0.00	-0.005 (-0.034, 0.022)	**-0.036*** (-0.064, -0.008)
o Post	0.00	0.027 (-0.011, 0.065)	-0.027 (-0.068, 0.014)
o Hysterectomy	0.00	-0.182 (-0.428, 0.062)	**-0.216** (-0.355, -0.078)
Diabetes			
o No	0.00	0.005 (-0.021, 0.032)	**-0.026*** (-0.052, -0.000)
o Yes	0.00	-0.007 (-0.047, 0.033)	-0.022 (-0.064, 0.019)
Gestational Diabetes			
o No	0.00	-0.011 (-0.078, 0.055)	-0.012 (-0.080, 0.055)
o Yes	0.00	0.008 (-0.084, 0.101)	-0.017 (-0.110, 0.075)
Kidney Disease			
o No	0.00	-0.016 (-0.054, 0.022)	**-0.044*** (-0.085, -0.002)
o Yes	0.00	**-0.264*** (-0.310, -0.217)	-0.021 (-0.054, 0.010)

Model adjusted for age, BMI, menopause, education, multivitamin or minerals, smoking status, physical activities, fruit and vegetable consumption. CI: confidence interval, *P-value <0.05

Table 13: Continue subgroup analyses of soft drink consumption at the 0.25 quantiles of BMD distribution

Subgroup	Soft Drink Consumption		
	None Coef.	<1 Coefficient (95% CI)	>1 Coefficient (95% CI)
Osteoporosis			
o No	0.00	-0.016 (-0.055, 0.022)	**-0.043** *(-0.085, -0.002)
o Yes	0.00	0.027 (-0.156, 0.212)	0.080 (-0.033, 0.194)
Thyroid Disease			
o No	0.00	-0.016 (-0.055, 0.022)	**-0.044*** (-0.085, -0.002)
o Yes	0.00	0.045 (-0.014, 0.103)	-0.017 (-0.075, 0.040)
Rheumatoid Diseases			
o No	0.00	-0.016 (-0.054, 0.022)	**-0.043*** (-0.085, -0.002)
o Yes	0.00	0.025 (-0.027, 0.078)	-0.017 (-0.064, 0.031)
Asthma			
o No	0.00	-0.004 (-0.028, 0.019)	**-0.037*** (-0.062, -0.013)
o Yes	0.00	0.036 (-0.055, 0.128)	0.041 (-0.138, 0.054)
Multivitamin & Minerals			
o No	0.00	0.005 (-0.020, 0.029)	**-0.046*** (-0.070, -0.021)
o Yes	0.00	0.005 (-0.038, 0.048)	-0.001 (-0.046, 0.045)
HRT			
o No	0.00	-0.003 (-0.025, 0.019)	**-0.032*** (-0.054, -0.010)
o Yes	0.00	0.033 (-0.089, 0.156)	-0.078 (-0.204, 0.046)
BMI(kg/m^2)			
o Normal	0.00	-0.063 (-0.169, 0.042)	0.049 (-0.059, 0.159)
o Overweight	0.00	-0.002 (-0.054, 0.049)	**-0.050*** (-0.102, -0.000)
o Obese	0.00	0.005 (-0.025, 0.035)	-0.015 (-0.047, 0.016)
Smoking Status			
o None smoker	0.00	0.005 (-0.017, 0.028)	**-0.033*** (-0.056, -0.009)
o Smoker	0.00	-0.013 (-0.672, 0.646)	-0.000 (-0.451, 0.450)
o Ex-smoker	0.00	-	-
Physical Activities*			
o No activity	0.00	0.024 (-0.007, 0.055)	**-0.029*** (-0.057, -0.001)
o Low	0.00	**-0.048** (-0.090, -0.004)	-0.051 (-0.102, 0.001)
o Moderate	0.00	0.011 (-0.039, 0.060)	0.014 (-0.047, 0.075)

Model adjusted for age, BMI, menopause, education, multivitamin or minerals, smoking status, physical activities, fruit and vegetable consumption. HRT: hormonal replacement therapy, BMI: body mass index, *P-value <0.05
*: (MET)-hours-per-week, CI: confidence interval

Table 14 show the soft drink consumption was negatively associated with BMD only after adjusting for age and BMI in model 2. Compared with non-consumers, high consumers (>1 times/week) had BMD β -0.024 (95% CI: -0.048, -0.001). In the fully

adjusted multivariable quantile regression (Model 3), the β (95% CI) for BMD were 0.00, 0.001(-0.020, 0.022), and -0.043(-0.048, -0.001) across non-consumers, <1 time/week, >1 times/week of soft drink consumption, respectively. Compared the models with and without adjustment of BMI, the regression coefficient for BMD among those consume soft drink more than once per week changed slightly (from -0.021 to -0.024). After further excluding those diagnosis with osteoporosis, the association persist almost the same between soft drink consumption and BMD among those consumers of soft drink more than 1 times/week β 0.040 (95% CI: -0.082 , 0.002).

Table 14: Coefficient regression (95% CI) for BMD by soft drink consumption levels*

Predictor	**Bone Mineral Density**		
	Q (0.25)		
	Coefficient	p-value	95% CI
Model 1			
Non-consumers	0.00		
o <1 time per week	-0.001	0.926	-0.031 0.028
o >1 time per week	-0.021	0.162	-0.051 0.009
Model 2			
Non-consumers	0.00		
o <1 time per week	0.003	0.784	-0.020 0.026
o >1 time per week	-0.024	**0.041**	-0.048 -0.001
Model 3			
Non-consumers	0.00		
o <1 time per week	0.001	0.933	-0.020 0.022
o >1 time per week	-0.043	**0.001**	-0.065 -0.022
Model 4			
Non-consumers	0.00		
o <1 time per week	-0.005	0.798	-0.045 0.034
o >1 time per week	-0.040	**0.063**	-0.082 0.002

*Model 1: adjust for age.
*Model 2: further adjust for adjust for BMI.
*Model 3: further adjust for education, income, menopause status, multivitamin or minerals, total consumption fruits drink consumption, smoking status, total consumption of milk, diabetes, and asthma.
*Model 4: adjust for age, BMI, education, income, menopause status, multivitamin or minerals, total consumption fruits drink consumption, smoking status, total consumption of milk, and excluding those already diagnosed with osteoporosis.

CHAPTER 5: DISCUSSION

5.1 Soft Drink and BMD

The purpose of the current study is to investigate the association between soft drink consumption and bone mineral density among Qatari women age 40 years or older. Evidence from previous studies suggested that soft drink consumption has negative consequences on bone mineral density. (33) Our findings were consistent with those results; it indicates a statistically significant negative association between soft drink consumption when all types of soft drink were combined. Compared with non-consumers of soft drink, weekly consumers had a lower bone mineral density. Although a high proportion of the participants did not consume soft drink, more than 15% consumed on a weekly basis.

Similar to our finding the Framingham osteoporosis study found that Cola intake was associated with significantlly lower BMD at hip site among women, while non-Cola-beverages consumption and BMD has a non-significant relationship.(31) Also, another study conducted on Saudi postmenopausal women found an inversed association between soft drink and T-score and Z-score of BMD, while positively associated with milk and dairy products consumption. (21) In our study the result showed that milk consumption independently associated with BMD. Also, no association between fruit drink and BMD was found.

In the univeriate analysis results showed that the association between soft drink consumption and BMD was insignificant. However, using different model adjusting for covariates revealed that both age and BMI confuses the relation between soft drink consumption and BMD. Supplee et. al (53) found a similar finding in their investigation about soda intake and osteoporosis risk in postmenopausal American-Indian women.

The authors highlighted the potential effect of those factors and concluded that the association between soda consumption and bone health might be mediated by the two factors.

Sensitivity analysis showed that there was a significant inverse association between regular soft drink consumption and the BMD at 0.25 quantile of the distribution. That might be due to the adverse effect of the fructose syrup contained in the sweeten carbonated beverages on BMD. (54) Our result is different from the study conducted by Kim, Morton, & Barrett-Connor (34) concluded that there were non-significant association between the type of carbonated beverage intake and BMD levels even after adjustment for age, obesity, exercise, calcium intake and current use of the following tobacco, alcohol, thiazides, estrogen, and or thyroid hormone.

Subgroup analysis revealed that soft drink consumption was inversely associated with the BMD at the 0.25 quantile when the consumption was more than one time per week among participants not having diabetes, osteoporosis, thyroid disease, kidney disease, and rheumatoid disease. That might indicate that there are multiple mechanism and factors yet to be explored in order to explain the effect of the soft drinks on health. (33) Also, maybe those with diseases have changed their food habits and affect the results.

5.2 Factors Associated with BMD

Our study found an independent association between each Age, BMI, menopausal status, multivitamin or minerals use, consumption of milk, and education level with BMD. These findings are relatively consistent with previous studies. (20) Increased BMI was a protective independently. Similar findings were reported in study (22) conducted to determine the relationships between BMI, lean mass, fat mass and BMD levels. The results showed that lean mass and fat mass were significant predictors

of all BMD measures in both genders. Also, there was a positive association in the current study between age, BMI, and menopausal status with BMD in quantile regression and those results were consistent with previous studies. (41) On the other hand, age and menopausal status were negatively associated with BMD independently and after controlling other covariates, which was similar to previous studies. (19)

The current study results indicated non-significant associations for smoking status, physical activities and fruit and vegetable consumption with BMD. That can be due to the limited variability of the data in those covariates. In our study, the prevalence of smoking was very low. Different from our results a systematic review and meta-analysis of randomized controlled trials (23) reported that exercises had a significant benefit for menopausal women bone mineral density. Also, studies about dietary intake found a significant association between consumption of fruit and vegetable and bone health. A scoping review (26) including 49 human studies from 2002 to 2016 suggested that improved bone health was associated with a high intake of fruit and vegetable among other food types.

The finding in the present study showed that there was insignificant association between total fruit drink consumption and BMD. Although, study participants reported high consumption frequency of fruit drinks and milk intake. Contrarily, previous studies reported that dietary pattern with high vegetable and fruit consumption as well as the dairy product positively associated with BMD. (30) A possible explanation for the differences in the results is that the consumption of fresh fruit juice is common among the participants of the study and might be one of the reasons we did not find any association between fruit juice and BMD.

5.3 Potential Mechanisms

There were multiple potential mechanisms proposed to explain the effect of soft

drink consumption effects on BMD. For example, the phosphate content in soft drinks that affect the body acid load and buffering the calcium leading to demineralization of the bone. It was suggested and examined in animal studies to assess the effect of cola (containing phosphoric acid) on BMD which confirmed the risk of hypercalciuria causing a loss in BMD in the femur. (39, 55) In the current study, we didn't investigate that and further studies are needed to confirm and examine the effect of phosphoric acid on BMD. Another mechanism is that soft drink is a major component of western diet. Previous studies found that there is an inverse association between western diet and BMD. (30) Although we have adjusted for the consumption of fruit and vegetable, residual confounding is possible. Also, Phthalates commonly used as plasticizers for soft drink containers are endocrine disruptors with estrogenic activity as seen in urinary phthalate metabolites were associated with decreased BMD and increases the risk of osteoporosis in postmenopausal women. (56) Also, among the possible mechanisms that have been hypothesized to explain the evident relationship between soft drink and BMD decreases include the displacement of milk from the diet. (57) in our case milk consumption was high compared to soft drink among the study population, it is not a possible mechanism explaining our findings. Lastly, results of studies indicate that dietary fructose adversely affects macromineral homeostasis in humans when consuming decaffeinated beverage containing high fructose corn syrup, decreasing calcium balance. (54) These findings may explain why regular soft drink type was associated inversely with BMD.

5.4 Study Strengths

Our study had several strengths. First, the study assessed the association of the soft drink at the lowest quantile of BMD distribution which provides essential information about people at high risk of having low BMD. Second, the association

found is reliable since they were controlled for a number of established confounders.

5.5 Study Limitations

The main limitation of our study is its cross-sectional nature making it difficult to assess causality. The residual confounding cannot be eliminated even after using a multivariable regression model adjusting for known confounders. Also, the sample was not population-based and participants were chosen by a convenience sample that depends on voluntary participation. That might introduce potential selection bias resulting in overestimating or underestimating the association between soft drinks and BMD.

Moreover, the participant may have been different from a random sample of the population of interest, and that might limit our ability to generalize the results. Also, the limited sample size affected the study, which if increased could strengthen the results. The absolute intake amount of the soft drink and content data was not collected, only the frequency per week using the food frequency questionnaire (FFQ). Soft drink consumption was not divided into those containing phosphoric acid in the original questionnaire and no information provided on its phosphoric acid content. Besides, it depends on the participant ability to recall and report the intake, which might introduce recall and reporting bias.

Moreover, there was no validation done in the study population for the FFQ. Furthermore, although we had the medication taken by the participants it was not included in the analysis since it was self-reported and didn't provide the medication coded by current procedural terminology (CPT). Lastly, C-reactive protein (CRP) data were not requested from QBB initial so we could not include it in the analysis.

5.6 Research Implication

Many risk factors cannot be prevented or modified; however, dietary and drinks choice can be modified to prevent many non-communicable diseases. Soft drink consumption is high among young people and the contribution of soft drink to BMD might become substantial in the future. Our study findings provide evidence that if confirmed by longitudinal studies and causality affirmed can guide public health promotion and prevention programs. Also, for the management of Low BMD among women and control. Moreover, might provide evidence that can support public health policy and decision making.

CHAPTER 6: CONCLUSIONS

The controversy as to whether there is a causal role between high consumption of soft drink consumption and high rates of fracture and low bone mineral density has been carefully debated over several decades. Support for link and an association between the two came from observational studies (31), however demonstrating causation, a step which debatably provided by cross-sectional study design is required in order to bring sufficient strength of evidence to promote major national and international public policy initiatives, has been more difficult and the argument remains ongoing.

This study emphasized on the possible consequences of soft drink consumption on the overall bone health by exploring the associations between soft drink consumption and BMD. The results showed that about 16.4 percent of participants reported consuming soft drinks less than one time per week, while 15.6 percent of participants reported consuming soft drinks more than one time per week. Our findings suggest that there was a clinically and statistically significant association between BMD and soft drink consumption after adjusting for age, BMI, menopausal status, smoking status, physical activities, milk intake, and fruit and vegetable consumption.

Additionally, the results revealed that soft drink consumption >1 time/week decrease BMD more than 10 years aging (getting older from 40-50 to 51-60). The findings highlight the magnitude and direction of the association between soft drink and BMD. Also, in our attempt to understand the relation between type of soft drink consumption and BMD, we found that BMD was significantly negatively associated with regular soft drink, but not with diet and energy soft drink. Which might be due to the sugar content of the regular soft drinks.

Further high-quality studies with long term follow up with specific purpose of testing the hypothesis are warranted before we can comment on potential causal association. If future cohort studies were to confirm such association, it is possible to develop appropriate public health intervention to improve bone health via reduced soft drink consumption. Lastly, our finding suggests that promoting healthy fluid drinking behavior among women might be considered in the prevention of low bone mineral density and management of related diseases or consequences.

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APPENDIX A

The list of the selected variables

Heath & Lifestyle Questionnaire	Diet Questionnaire	Nurse Interview Questionnaire	Anthropometry	Bone Health
- Age - Education - Income - Current and past smoking habits. - Activity levels & leisure time - Current and past health conditions.	- Information on diet (consumption of fast food) - How often they consumed various foods (vegetable and fruits), beverages (regular soft drink, diet soft drink, energy drink), and (other fruit drinks)	- Previous or prevalent health conditions they have (Asthma, diabetes, arthritis, osteoporosis) - Information on over-the-counter and prescription (Vitamin D, Calcium) - Medications used (glucocorticosteroids, opioid) - Women reproductive factors (menopausal status, on hormonal replacement treatment)	- BMI	- Full body dual-energy X-ray absorptiometry (iDXA GE scan)

APPENDIX B

Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

```
*************************************
* Datasheet preparation and merge  *
*************************************

 cd "\\Client\C$\Users\aamnahamid\Desktop\Datasheets"
\\Client\C$\Users\aamnahamid\Desktop\Datasheets
log using "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\Data_Analysis_Thesis.smcl"
cmdlog using Thesis_CMD.log, replace
 import excel "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\QF_QBB_RES_ACC_0124.xlsx", sheet("Total") firstrow
  save "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\QF_QBB_RES_ACC_0124.dta"
file \\Client\C$\Users\aamnahamid\Desktop\Datasheets\QF_QBB_RES_ACC_0124.dta saved
import excel "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\IDXA_Densitometry_0124_BMD.xlsx", sheet("bmd") firstrow clear
save "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\IDXA_Densitometry_0124_BMD.dta"
file \\Client\C$\Users\aamnahamid\Desktop\Datasheets\IDXA_Densitometry_0124_BMD.dta saved
use "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\QF_QBB_RES_ACC_0124.dta"
merge 1:1 DummyID using  "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\IDXA_Densitometry_0124_BMD.dta"
save "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\dta\QF_QBB_RES_ACC_0124_IDXA_Densitometry_0124_BMD.dta", replace
 destring, replace dpcomma
 destring ARMS , ignore("NULL") replace
 destring HEAD , ignore("NULL") replace
 destring L1 , ignore("NULL") replace
 destring L1_L2 , ignore("NULL") replace
 destring L1_L3 , ignore("NULL") replace
 destring L1_L4 , ignore("NULL") replace
 destring L2_L4 , ignore("NULL") replace
 destring L3_L4 , ignore("NULL") replace
 destring L4 , ignore("NULL") replace
 destring LEGS , ignore("NULL") replace
 destring PELVIS , ignore("NULL") replace
 destring RIBS , ignore("NULL") replace
 destring SPINE , ignore("NULL") replace
 destring T12 , ignore("NULL") replace
 destring TRUNK , ignore("NULL") replace

***********************************************
//Main characteristics of study participants//
***********************************************
**Generating new variable (Agegroup)
recode Age (40/50 = 0 from_40_to_50) (51/60 = 1 from_51_to_60 ) (61/70=2 from_61_to_70) (71/max=3 over_70) , gen(Agegroup)
//Generating new variable(Education)
gen Education=MQ_EDU
recode Education (2 3 4= 1)(5 6 = 2 )(7 8 = 3 )
lab define label9 1 "Low (No schooling to secondary)" 2 "Medium (Trade, certificate, diploma)" 3 "High (University degree or higher)"
label values Education label9
*Generating new variable(Income)
gen Income=MQ_F11
label var Income " Total monthly income"
recode Income (6=0)(5 4 = 3 )
label define Incomelab 0 "No income" 1 "Less than 10,000 per month" 2 "Between 10,000 and 20,000 per month" 3 " More than 20,000 "
label values Income Incomelab
recode Income (7777=.)(9999=.)
*********************************
// consumption of Suplements //
*********************************
```

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Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

```
*********************************
// consumption of Suplements //
*********************************
**Generating new variable (Multivit_Minerals)
gen Multivit_Minerals= MQ_H33_1
label var Multivit_Minerals "Multivitamins and or Minerals"
recode Multivit_Minerals (8888=0)
lab define label 0 "No" 1 "Yes"
lab val Multivit_Minerals label
// to create a new variable assuming that non respondant are non consumers of Multivitamins and or Minerals
egen MM= anymatch(Multivit_Minerals), values(1)
**Generating new variable (Vit_D)
gen Vit_D = MQ_H33_17
label var  Vit_D  "In the last 3 months Taken Vitamin D"
recode Vit_D (8888=0)
lab val Vit_D label
**Generating new variable(Calcium)
gen Calc = MQ_H33_3
label var Calc  "Calcium"
recode Calc (8888=0)
lab val Calc label

************
// Outcome//
************
*Generating new variable  (BMD)
 gen BMD = TOTAL
 label var TotalBMD "Total Body Bone Mineral Density"
*Generating new variable (BMDquart)
//find out how to create qurtiles
*(BMDquart) not created yet since not sure
  sort BMD
  xtile BMDQ = BMD, nq(4)
  lab var BMDQ "Total Body Bone Mineral Density Quantiles"
  lab define BMDQ 1 "Q1" 2 "Q2" 3 "Q3" 4 "Q4"
  lab val BMDQ BMDQ
  tabstat BMD, stat(n mean sd min max p50) by (BMDQ)

 ***********************************
 // lifestyle and other riskfactors//
 ***********************************
**Generating new variable(Smoking_status)
gen Smoking=MQ_S1
recode Smoking (1 5 = 0) (2 3 = 1 ) (4 = 2)
lab define label8 0 "Non-smoker" 1 " Smoker" 2 "Ex-Smoker"
label values Smoking label8
*Generating new variable (W_BMI)
 gen W_BMI=BMI
 label var W_BMI "Body Mass Index"
//Generating new variable (Weight_status)
gen Weight_status =.
replace Weight_status =1 if W_BMI >= 18.5 & W_BMI < 25
replace Weight_status =2 if W_BMI >= 25 & W_BMI < 30
replace Weight_status =3 if W_BMI >= 30
```

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Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

```
//Generating new variable (Weight_status)
gen Weight_status =.
replace Weight_status =1 if W_BMI >= 18.5 & W_BMI < 25
replace Weight_status =2 if W_BMI >= 25 & W_BMI < 30
replace Weight_status =3 if W_BMI >= 30
lab define label10 1 "Normal" 2 "Overweight" 3 "Obese"
label values Weight_status label10

*Generating new variable (lpa)
//Physical Activity, Days, hours, minutes intensitive PA
 mvencode MQ_H3PM_D MQ_H3PM_H MQ_H3PM_M MQ_H3W_D MQ_H3W_H MQ_H3W_M MQ_H3P_D MQ_H3P_H MQ_H3P_M, mv(0)
gen lpa1=MQ_H3W_D*(MQ_H3W_H+MQ_H3W_M/60)*3
gen lpa2=MQ_H3PM_D*(MQ_H3PM_H+MQ_H3PM_M/60)*4.5
gen lpa3=MQ_H3P_D*(MQ_H3P_H+MQ_H3P_M/60)*7.5
egen lpa=rowtotal(lpa1 lpa2 lpa3)
lab var lpa "Leisure time physical activity (MET hours/week)"
recode lpa (0=1)(3/73.5=2) (75/max=3), gen(lpa3c)
lab var lpa3c "Leisure time PA (MET hours/week)"
lab define lpa3c 1 "No activity" 2 "Low" 3 "Moderate ",replace
lab val lpa3c lpa3c
 *Generating new variable Menoupouse status(Menst_C)
gen Menst_C= MQ_L18
label var Menst_C "Has your menstrual cycle stopped?"
lab define label4 0 "No" 1 "Yes" 2 "had a hysterectomy before natural menopause"
lab val Menst_C label4
**Generating new variable  (HRT)
gen HRT= MQ_L19
label var HRT  "Have you ever used hormone replacement therapy (HRT)?"
lab val HRT label

************
//Diseases//
************
**Generating new variable (Dx_DM)
 gen Dx_DM= MQ_H34
 label var Dx_DM  "Diagnosed having Diabetes"
 lab val Dx_DM label
**Generating new variable (Dx_GDM)
gen Dx_GDM= MQ_H35
label var Dx_GDM  "Diagnosed having Gestational Diabetes only"
recode Dx_GDM (7777=.)
lab val Dx_GDM label
**Generating new variable (Dx_Asthma)
gen Dx_Asthma= MQ_H45_1
label var Dx_Asthm  "Diagnosed having Asthma"
recode Dx_Asthm (8888=0)
lab val Dx_Asthm label
*Generating new variable  (Kidney_D)
gen Kidney_D = NQ_A10_F_27
label var Kidney_D "diagnosed with Kidney diseases other than stones"
recode Kidney_D (5555=0)
lab val Kidney_D label
*Generating new variable (Arthritis)
gen Arthritis= NQ_A10_F_29
```

37:2

Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

```
recode Kidney_D (5555=0)
lab val Kidney_D label
*Generating new variable (Arthritis)
gen Arthritis= NQ_A10_F_29
label var Arthritis "diagnosed with Arthritis, Osteoarthritis, and Rheumatoid Arthritis)"
recode Arthritis (5555=0)
lab val Arthritis label
*Generating new variable  (Osteoprosis)
gen Osteoprosis= NQ_A10_F_30
label var Osteoprosis "diagnosed with Osteoprosis"
recode Osteoprosis (5555=0)
lab val Osteoprosis label
*Generating new variable  (Thyroid)
 gen Thyroid= NQ_A10_F_4
 label var Thyroid "diagnosed with Thyroid Disease"
 recode Thyroid (5555=0)
 lab val Thyroid label

******************
// Main Predictor//
******************
*Generating new variable 26(R_SoftDrink)
 gen R_SoftDrink= DT_21D
 label var R_SoftDrink "Regular Softdrink"
*Generating new variable 27(D_SoftDrink)
 gen D_SoftDrink= DT_21E
 label var D_SoftDrink "Diet Softdrink"
*Generating new variable 28(Energy_Drink)
 gen Energy_Drink= DT_21F
 label var Energy_Drink " Energy Drink"
*Generating new variable 29(TotalSoftD)
   recode R_SoftDrink D_SoftDrink Energy_Drink (1=0)(2=0.5)(3=2)(4=5)(5=7)(6=14), pre(ffq)
  egen TotalSoftD=rowtotal( ffqR_SoftDrink ffqD_SoftDrink ffqEnergy_Drink )
  lab var TotalSoftD "Total softdrink consumed per week)"
  recode TotalSoftD (0=1)(0.5/1=2) (1/max=3), gen(TSD)

********************************
// Other Fruit and suger drink//
********************************
*Generating new variable (FF_Juice)
 gen FF_Juice= DT_21A
 label var  FF_Juice "Fresh Fruit Juice"
*Generating new variable(Smoothies)
 gen Smoothies= DT_21B
 label var  Smoothies "Smoothies"
*Generating new variable(PF_Juice)
 gen PF_Juice= DT_21C
 label var  PF_Juice "Preserved Fruit Juice (canned/botteld"
*Generating new variable 34(Totalfruitd)
   recode FF_Juice Smoothies PF_Juice (1=0)(2=0.5)(3=2)(4=5)(5=7)(6=14), pre(ffq)
  egen TotalfruitD=rowtotal( FF_Juice Smoothies PF_Juice )
  lab var TotalfruitD "Total Fruit drink consumed per week)"
  recode TotalfruitD (0/4=1)(5/6=2) (7/max=3), gen(TFD)
```

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Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

```
  recode TotalSoftD (0=1)(0.5/1=2) (1/max=3), gen(TSD)

*********************************
// Other Fruit and suger drink//
*********************************
*Generating new variable (FF_Juice)
 gen FF_Juice= DT_21A
 label var  FF_Juice "Fresh Fruit Juice"
*Generating new variable(Smoothies)
 gen Smoothies= DT_21B
 label var  Smoothies "Smoothies"
*Generating new variable(PF_Juice)
 gen PF_Juice= DT_21C
 label var  PF_Juice "Preserved Fruit Juice (canned/botteld"
*Generating new variable 34(TotalfruitD)
  recode FF_Juice Smoothies PF_Juice (1=0)(2=0.5)(3=2)(4=5)(5=7)(6=14), pre(ffq)
  egen TotalfruitD=rowtotal( FF_Juice Smoothies PF_Juice )
  lab var TotalfruitD "Total Fruit drink consumed per week)"
  recode TotalfruitD (0/4=1)(5/6=2) (7/max=3), gen(TFD)

*************************************************
 // Fruit and Vegetable Consumptions           //
*************************************************
*Generating new variable (eat_FF)
 gen Eat_FF= DT_19A
 label var  Eat_FF "Eat Fresh Fruit per week"
*Generating new variable (eat_RV)
 gen Eat_RV= DT14A
 label var  Eat_RV "Eat Row Vegetables  per week"
*Generating new variable (T_Fruit_veg)
  recode  Eat_FF Eat_RV(1=0)(2=0.5)(3=2)(4=5)(5=7)(6=14), pre(ffq)
  egen T_Fruit_Veg=rowtotal( ffqEat_FF ffqEat_RV )
  lab var T_Fruit_Veg "Total Fruit & Vegetables per week)"

***********************************************
 // Total consumption of Milk Consumptions          //
***********************************************
*Generating new variable (cold Milk)
 gen Milk=DT9A
 label var Milk "cold Milk"
*Generating new variable (add milk to cereal)
 gen AddedMilk=DT9B
 label var AddedMilk "Milk added to cereals"
*Generating new variable (Milk shakes  or flavoured milk)
 gen Milkshake=DT9C
 label var Milkshake " Milk shakes  or flavoured milk"
*Generating new variable 29(TotalMilk)
  recode Milk  AddedMilk Milkshake (1=0)(2=0.5)(3=2)(4=5)(5=7)(6=14), pre(ffq)
  egen TotalMilk=rowtotal( Milk  AddedMilk  Milkshake )
  lab var TotalMilk "Total Milkdrink consumed per week)"
  recode TotalMilk (0/3=1)(4/5=2) (5/max=3), gen(TMD)
```

37:2

Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

```

**Thesis Commands:study the association between soft drink consumption and bone
 //mineral density among Qatari women age 40 years or older
**Public Health Master student: Aamna Hamid
log using "\\Client\C$\Users\aamnahamid\Desktop\Datasheets\log\Analysisfinal.smcl",replace
use "/Users/aamnahamid/Desktop/Desktop/Datasheets/dta/QF_QBB_RES_ACC_0124_IDXA_Densitometry_0124_BMD.dta"
histogram BMD
histogram TotalSoftD

//Distribution of socio-demographic characteristics of study population
tab Agegroup
tab Education
tab Income
//Distribution of menopausal status, HRT, and supplements of study population
tab Menst_C
tab HRT
tab Calc
tab MM
tab Vit_D
//Distribution of comorbidities of study population
tab Dx_DM
tab Dx_GDM
tab Kidney_D
tab Arthritis
tab Osteoprosis
tab Thyroid
tab Dx_Asthma
//Distribution of anthropometry and life style related variables of study population
tab Weight_status
tab Smoking
tab lpa3c
//Distribution of diet related variables of study population
tab TSD
tab  TFD
tab  TMD
summarize  T_Fruit_Veg

//Main characteristics of study particpants distribution by Soft Drink Consumption
summarize Age BMD W_BMI T_Fruit_Veg
tab Agegroup TSD , chi2 col
tab Education TSD , chi2 col
tab Income TSD , chi2 col
tab Menst_C TSD , chi2 col
tab Dx_DM TSD , chi2 col
tab Dx_GDM TSD , chi2 col
tab Kidney_D TSD , chi2 col
tab Osteoprosis TSD , chi2 col
tab Thyroid TSD , chi2 col
tab Arthritis TSD , chi2 col
tab Dx_Asthma TSD , chi2 col
tab Vit_D TSD , chi2 col
tab Calc TSD , chi2 col
tab MM TSD , chi2 col
tab HRT TSD , chi2 col
```

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Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

```
tab Arthritis TSD , chi2 col
tab Dx_Asthma TSD , chi2 col
tab Vit_D TSD , chi2 col
tab Calc TSD , chi2 col
tab MM TSD , chi2 col
tab HRT TSD , chi2 col
tab Weight_status TSD , chi2 col
tab Smoking TSD , chi2 col
tab lpa3c TSD , chi2 col

//Univariate analysis (assessed all but reported the linear regression)
reg BMD i.TSD
reg BMD i.TFD
reg BMD i.Agegroup
reg BMD i.Education
reg BMD i.Income
reg BMD i.Menst_C
reg BMD i.Dx_DM
reg BMD i.Dx_GDM
reg BMD i.Kidney_D
reg BMD i.Thyroid
reg BMD i.Arthritis
reg BMD i.Dx_Asthma
reg BMD i.HRT
reg BMD i.MM
reg BMD W_BMI
reg BMD i.Smoking
reg BMD i.lpa3c
reg BMD T_Fruit_Veg
reg BMD i.TMD

//Multiple Quantile regression at (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C W_BMI i.Smoking i.lpa3c i.TMD T_Fruit_Veg , quantile (.25)

 //test interaction (both not sig.)
qreg BMD i.TSD##i.Agegroup i.Education i.MM i.Menst_C W_BMI i.Smoking i.lpa3c i.TMD T_Fruit_Veg , quantile (.25)
qreg BMD i.TSD##c.W_BMI i.Agegroup i.Education i.MM i.Menst_C i.Smoking i.lpa3c i.TMD T_Fruit_Veg , quantile (.25)

//final model
 qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c i.TMD T_Fruit_Veg , quantile (.25)
 qreg BMD i.TFD i.Agegroup i.Education i.MM i.Menst_C W_BMI i.Smoking i.lpa3c i.TMD T_Fruit_Veg , quantile (.25)

//Subgroup analysis
tab Agegroup,nol
qreg BMD i.TSD i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Agegroup==0, quantile (.25)
qreg BMD i.TSD i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Agegroup==1, quantile (.25)
qreg BMD i.TSD i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Agegroup==2, quantile (.25)
qreg BMD i.TSD i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Agegroup==3, quantile (.25)

tab Education, nol
qreg BMD i.TSD i.Agegroup i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Education==1 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Education==2 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Education==3 , quantile (.25)
```

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Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

```
tab Income,nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Income==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Income==1 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Income==2 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Income==3 , quantile (.25)

tab Menst_C, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Menst_C==0, quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Menst_C==1, quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Menst_C==2, quantile (.25)

tab Dx_DM, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Dx_DM==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Dx_DM==1 , quantile (.25)

tab Dx_GDM, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Dx_GDM==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Dx_GDM==1 , quantile (.25)

tab Kidney_D, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Kidney_D==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Kidney_D==1 , quantile (.25)

tab Osteoprosis, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Osteoprosis==0, quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Osteoprosis==1, quantile (.25)


tab Thyroid, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Thyroid==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Thyroid==1 , quantile (.25)

tab Arthritis, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Arthritis==0, quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Arthritis==1, quantile (.25)

tab Dx_Asthma,nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Dx_Asthma==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Dx_Asthma==1 , quantile (.25)

tab MM, nol
qreg BMD i.TSD i.Agegroup i.Education i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if MM==0, quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if MM==1, quantile (.25)

tab HRT, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if HRT==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if HRT==1 , quantile (.25)

tab Weight_status, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking i.lpa3c T_Fruit_Veg if Weight_status==1 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking i.lpa3c T_Fruit_Veg if Weight_status==2 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking i.lpa3c T_Fruit_Veg if Weight_status==3 , quantile (.25)
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Data_Analysis_Thesis_cleaning_fin | Data_Analysis_Thesis_analysis_fin

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tab Thyroid, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Thyroid==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Thyroid==1 , quantile (.25)

tab Arthritis, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Arthritis==0, quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Arthritis==1, quantile (.25)

tab Dx_Asthma,nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Dx_Asthma==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Dx_Asthma==1 , quantile (.25)

tab MM, nol
qreg BMD i.TSD i.Agegroup i.Education i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if MM==0, quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if MM==1, quantile (.25)

tab HRT, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if HRT==0 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if HRT==1 , quantile (.25)

tab Weight_status, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking i.lpa3c T_Fruit_Veg if Weight_status==1 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking i.lpa3c T_Fruit_Veg if Weight_status==2 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking i.lpa3c T_Fruit_Veg if Weight_status==3 , quantile (.25)


tab Smoking, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Smoking==0 , quantile (.25)
bsqreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Smoking==1 , quantile (.25)
bsqreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg if Smoking==2 , quantile (.25)

tab lpa3c, nol
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI T_Fruit_Veg if lpa3c==1 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI T_Fruit_Veg if lpa3c==2 , quantile (.25)
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI T_Fruit_Veg if lpa3c==3 , quantile (.25)

//sensitivity analysis
qreg BMD ffqR_SoftDrink i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg , quantile (.25)
qreg BMD ffqD_SoftDrink i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg , quantile (.25)
qreg BMD ffqEnergy_Drink i.Agegroup i.Education i.MM i.Menst_C i.Smoking W_BMI i.lpa3c T_Fruit_Veg , quantile (.25)


//Multiple Models of Quantile regression at (.25)
  // Model 1
qreg BMD i.TSD i.Agegroup, quantile (.25)
 // Model 2
qreg BMD i.TSD i.Agegroup  W_BMI, quantile (.25)
 // Model 3
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C W_BMI i.Smoking i.lpa3c i.TMD T_Fruit_Veg i.Dx_Asthma i.Dx_DM i.Arthritis, quantile (.25)
 // Model 4
qreg BMD i.TSD i.Agegroup i.Education i.MM i.Menst_C W_BMI i.Smoking i.lpa3c i.TMD T_Fruit_Veg  if Osteoprosis==0, quantile (.25)

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APPENDIX C

Potential causes of low peak bone mass	
Heritability/Genetic syndrome (51, 52)	Genetic polymorphisms Turner syndrome
Hypogonadism(51, 52)	Hypogonadotropic hypogonadism Permanent, e.g. Kallman's syndrome idiopathic Delayed, e.g., constitutional delay, anorexia nervosa Hypergonadotropic hypogonadism Gonadal dysgenesis Gonadal failure, e.g., autoimmunity, chemotherapy, radiation exposure Estrogen receptor defect
Other endocrine disorders(51, 52)	Growth hormone deficiency Hyperthyroidism Cushing's disease Diabetes mellitus Rickets/Osteomalacia
Nutritional(51, 52)	Chronic dietary calcium/vitamin D Deficiency Malnutrition Nutritional disorders Anorexia nervosa Inflammatory bowel disease Celiac disease Cystic fibrosis
Chronic diseases of childhood and adolescence (51, 52)	Chronic kidney disease Chronic liver disease Cancer Rheumatologic disorders
Connective tissue diseases(51, 52)	Osteogenesis imperfecta Marfan syndrome Ehlers-Danlos syndrome
Medications(51, 52)	Glucocorticoids Depot medroxyprogesterone Aromatase inhibitors GnRH analogues Immunosuppressants (e.g. Cyclosporine) Antiepileptic drugs (particularly cytochrome P450 inducers, such as phenytoin and carbamazepine) Chemotherapeutic drugs
Other Medication(51)	Lithium Methotrexate Thyroxin
Lifestyle (51, 52)	Physical activity Smoking Type of diet Alcohol consumption