AMERICAN UNIVERSITY OF BEIRUT

ADHERENCE TO THE MEDITERRANEAN DIET AND DIETARY COMPOSITION AMONG BREAST CANCER FEMALE PATIENTS IN BEIRUT, LEBANON: A CROSS-SECTIONAL STUDY

By
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Education is a lifelong and never-ending process

AN ABSTRACT OF THE THESIS OF

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Breast cancer is the most commonly diagnosed cancer site among women worldwide, and the second most common cause of cancer mortality. Breast cancer rates differ vastly between geographical areas, countries, and within the same country. In Lebanon, the proportion of breast cancer to all other sites of tumor is 38.2%; these rates are still lower than those observed worldwide, but remain the highest among Arab countries. Studies and evidence based reviews show a strong association between breast cancer development and prognosis and dietary habits, specifically the Mediterranean diet (MD). As such, the aim of this study is to examine dietary composition and adherence to the MD among a sample of 182 breast cancer female patients in Beirut, Lebanon. Subjects were recruited from two major hospitals; a private medical center and a philanthropic hospital; all subjects were administered two questionnaires: socio-demographics and dietary intake evaluation. Five Mediterranean scores were calculated from the dietary questionnaire: MS, MSDPS, PMDI, PREDIMED and DDS. The mean age of the participants was 53.78 years, and overall adherence to the Mediterranean diet (MD) was low since the sample means of 3 out of the 5 calculated scores were less than the scores' median values. Given that 4 out of the 5 Mediterranean scores significantly varied between the recruitment sites, women in the private medical center were found to adhere more to the MD. Our results also show that the majority of the sample population's intakes are exceeding the recommendations for total and saturated fat, while meeting the requirements for fiber, EPA, DHA and Linolenic Acid. Participants in the private medical center were consuming significantly more calories, carbohydrates, fiber, sugar, Lycopene, Calcium, Iron and Folate and less fat. After conducting multivariate linear regression analyses, the following statistically significant results were observed: positive associations between MD (CPMDI, PREDIMED) and monthly income & current state of health, while negative associations between MD (MSDPS, PREDIMED) and age & employment status. Our findings indicated a low overall adherence to the MD and identified factors associated with it; which suggests a need to address dietary habits among BC patients in Lebanon, specifically encouraging them to adhere to their traditional Mediterranean diet.

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LIST OF ABBREVIATIONS

AMDR	Acceptable Macronutrient Distribution Range
BC	Breast Cancer
BF	Breastfeeding
BMI	Body Mass Index
Ca	Calcium
CHO	Carbohydrate
COX-2	Cyclooxygenase-2
CPMDI	Cardio- Protective Mediterranean Diet Index
DDS	Dietary Diversity Score
DHA	Docosa-Hexaenoic Acid
DM2	Diabetes Mellitus Type 2
EPA	Eicosa-Pentaenoic Acid
EPIC	European Prospective Investigation into Cancer and Nutrition
ER	Estrogen Receptor
ER+	Estrogen Receptor Positive
ERPR-	Estrogen Receptor Progesterone Receptor Negative
ERPR+	Estrogen Receptor Progesterone Receptor Positive
EVOO	Extra Virgin Olive Oil
F&V	Fruits and Vegetables
FAOSTAT	Food and Agricultural Organization Statistical Databases
GI	Glycemic Index
GL	Glycemic Load
HR	Hazard Ratio
HSE	High Socio-Economic
IGF	Insulin- like Growth Factor
IU	International Unit

LSE	Low Socio-Economic
MAI	Mediterranean Adequacy Index
MD	Mediterranean Diet
MDS	Mediterranean Diet Score
MS	Mediterranean Score
MSDPS	Mediterranean Style Dietary Pattern Score
MUFA	Mono- Unsaturated Fatty Acids
NF- ƙ β	Nuclear Factor-ƙ β
OR	Odds Ratio
OW	Overweight
PA	Physical Activity
PMC	Private Medical Center
PR+	Progesterone Receptor Positive
PREDIMED	PREvención con DIeta MEDiterránea
PUFA	Poly- Unsaturated Fatty Acids
rMED	relative Mediterranean Diet Score
ROS	Reactive Oxygen Species
RR	Relative Risk
SENECA	Survey in Europe on Nutrition and the Elderly: a Concerted Action
SFA	Saturated Fatty Acids
TFA	Trans Fatty Acids
UK	United Kingdom
US	United States
VDR	Vitamin D Receptor

CHAPTER I

LITERATURE REVIEW

A. Breast Cancer

1. Prevalence of Breast Cancer

Breast cancer is the most commonly diagnosed site of cancer among women worldwide. In the year 2012, it accounted for 25% of newly diagnosed cancer cases in women (Ferlay et al, 2012). One in 8 women, who will live more than 70 years, will develop breast cancer in their lifetime (American cancer society, 2006). The highest incidences of breast cancer occur in the US and some European regions, with Belgium being the first, followed by Denmark and France (Ferlay et al, 2012). On the other hand, Africa, South America, and Asia ranked the lowest incidence rates (CDC, 2013). According to the CDC, breast cancer is also the most common cause of mortality due to cancer among Hispanic women, and the second most common cause among women from other races, the first being lung cancer. In the year 2010, 40,996 females in the United States died due to breast cancer (CDC, 2013). Some common reasons for the high prevalence of breast cancer in the US may be, low number of pregnancies, delayed child bearing age, hormonal replacement therapy, and increased awareness about mammography screening (Jemal et al, 2010). However, studies show a decreasing trend in breast cancer rates in the US, UK, France and Australia, and an increase in some European countries, Asia and Africa. This increase might be due to unsuitable lifestyle habits, low number of children per family, decreased physical activity and obesity (Jemal et al, 2010). Even though Belgium, Denmark and France had the highest rates of BC, when assessing the 5-years post diagnosis survival rate they also ranked the top 3;

whereas, Africa and Asia ranked last. This discrepancy might be due to early detection of the BC, and different management techniques used in various countries; as well as, the availability and accessibility of primary health care (Ferlay et al, 2013).

Rates of total deaths due to cancer vary vastly from one country to the other in the Mediterranean region (**Fig.1**). Countries in the low to middle income category seem to have the lowest rates of percentage total deaths due to cancer; rates in Egypt and Morocco are 14% and 11% respectively. On the other hand, countries that fall in the highest category of income also have the highest rates; rates in France, Italy, Malta and Spain are 31%, 29%, 31% and 28% respectively. Percentage to total death due to cancer in Algeria, a country in the upper middle category of income, was the lowest, 10%; in the contrary, rates in Lebanon (same income category as Algeria) are similar to those observed in high income countries, 22% (WHO, Non-communicable Diseases Country Profiles, 2014).

Breast cancer rates also differ even within the same region, for example, the Mediterranean region shows vast differences as well. Southern Europe exhibits the highest rates of BC incidence among this region, with rates up to 75/100,000 adult female. On the other hand, North Africa and West Asia have relatively lower rates, around 40/100,000 adult female. France and Italy have the highest rates of BC incidence in the Mediterranean region, and the best 5 year post diagnosis survival rates. In contrast, Turkey, Morocco and Syrian Arabic Republic have incidence rates between 38- 40/100,000 female, the lowest in the region (WHO, Cancer Country Profiles, 2014). However, the mortality rates due to breast cancer are somehow similar between these three areas, mortality rate around 18-20/100,000 female; Spain had the lowest rate in the European regions, 12/100,000 (Globocan, 2013). Spain and Turkey had the lowest rates

of BC mortality, around 16%; whereas, Morocco had the highest rate, 27.6% (WHO, Cancer Country Profiles, 2014).

2. Breast Cancer Rates in Lebanon

Lebanon, a country on the Eastern Mediterranean coast, has a BC incidence rate of 79.1/100,000 female, this number falls in between other rates observed in the Mediterranean region. However, rate of BC mortality in Lebanon is 26.2%, similar to that observed in Morocco, noting one of the highest rates in the region. In 2014, 1, 934 Lebanese women developed BC, of which, 550 died (WHO, 2014). Studies show that about 49% of Lebanese females diagnosed with BC are less than 50 years old, as compared to a 25- 30% in the US and Europe (El Saghir et al, 2007). One reason could be the age distribution in Lebanon is skewed towards the younger age groups (Lakkis et al, 2010). Therefore, the Lebanese Ministry of Public Health started a screening campaign in 2002 in which discounts were offered on mammography for women aged more than 40 years (Lakkis et al, 2010). The life expectancy and median age of the population in Lebanon is expected to increase to 78.7 and 41.7 years respectively in 2050, which will lead to an increased prevalence of different types of cancers (Shamseddine et al, 2014). This 10 year projection study expects an increased incidence of cancer to 339.5 cases/ 100,000 female in Lebanon in 2018, of which breast cancer will be the most prevalent 137 cases/ 100,000 (Shamseddine et al, 2014).

3. Risk Factors for BC

The risk factors for breast cancer are many; some of them are factors that can be avoided or changed; whereas, other factors are predetermined. Some of the predetermined factors include, age, race, breast density, family history and genetic mutations. For example, age is directly proportional to BC risk; women above the age of 50 years and have went through menopause have the highest risk of developing BC. As for race, white women, compared to African-Americans, also have an increased risk of developing BC. Likewise, higher breast density, denoting more gland tissue rather than fat cells, is a risk factor for BC. Lastly, women who have a family history of BC or have mutations in the BRCA 1 and 2 genes, tumor suppressor genes, also have an increased risk of developing BC (NHS, Breast Cancer-Causes, 2014; Breastcancer.org, 2014).

Risk factors that can be avoided included women's age at first pregnancy, usage of hormone replacement therapy or contraceptive pills; as well as, some nutrition and lifestyle related factors. Women who have their first child when they are above 30 years are at risk of developing BC; being pregnant at a young age exerts a protective effect against BC. Estrogen and progesterone exposure through birth control pills and hormone replacement therapy increases the risk of BC; however, upon stopping their usage, BC risk diminishes (NHS, Breast Cancer-Causes, 2014; Breastcancer.org, 2014).

B. Nutrition and Lifestyle Related Risk Factors of Breast Cancer

1. Over-weight and Obesity

Overweight and obesity are responsible for 44% of diabetes burden, 23% of ischemic heart disease burden, and 7%- 41% of certain cancer burdens (WHO, Obesity and Overweight, 2014). The most common sites of cancers that result from excessive

body weight and obesity are: esophagus, pancreas, colon and rectum, breast, endometrium, kidney, thyroid, and gallbladder (National Cancer Institute, 2012).

Overweight and obesity are a major health issue, even in the traditionally healthy Mediterranean countries, with increasing yearly incidence rates. More than half of the adult population in the majority of countries residing on the Mediterranean Sea are either OW or obese. The North African region holds the highest prevalence of OW and obesity; 2014 rates in Egypt, Libya and Morocco are 66%, 68% and 58.4% respectively (**Fig.2**). Whereas the Southern European region had the lowest rates, prevalence in Greece, France and Italy is 54%, 52.6% and 52%. Prevalence of OW and obesity in Lebanon is similar to that in the North African region, which is relatively high, 67.4% (WHO, Cancer Country Profiles, 2014). Worldwide, specifically among people aged 20 years and above, the rates of overweight and obesity are 35% and 11% respectively; of which more than half are women.

In pre-menopausal women, obesity has been linked to breast cancer mainly by increased anovulation which in turn may lead to breast cancer (Vecchia et al., 2011). In relation to post-menopausal breast cancer risk, overweight and obese women have low levels of sex-hormone binding globulin, and high levels of circulating estrogen since the main source of estrogen after menopause is the adipose tissue (Vecchia et al., 2011). As a result, obesity has been strongly linked to Estrogen Receptor positive (ER+) breast cancer (Cleary et al., 2009). Obesity has been also shown to increase levels of circulating insulin and insulin resistance both of which play a role in increased risk of breast cancer (Xue et al., 2007). Moreover, obesity is linked to elevated leptin synthesis which is a risk factor for breast cancer development.

Overweight and obese pre-menopausal women, as compared to women with BMI < 25 Kg/ m^2, were at a 59% and 70% increased risk of developing breast cancer respectively (Cecchini et al., 2012). Women with increasing leptin levels (5.6- 10.9 ng/ ml) had a significantly increased risk of developing breast cancer, P trend =0.039 (Wu et al., 2009). Compared to pre-menopausal women with BMI< 25 Kg/ m^2, overweight and obese women have HR of 1.59 (1.05–2.42) and 1.70 (1.10–2.63) respectively of developing breast cancer (Cecchini et al., 2012).

Nichols et al. (2009) showed that BC women who were obese prior to their diagnosis, compared to women with normal BMI, were about 50% more likely to die due to any cause, 95% CI (1.17-1.98). On the other hand, obese women post-diagnostically had a 2 times higher risk of BC mortality, 95% CI (1.43-3.64). In another cohort study, a significant association was also found between pre-diagnostic BMI and BC related mortality; obese premenopausal women were 2 times more likely to die compared to those with a BMI= 21-22, 95% CI (1.13-3.61). Moreover, BC women who gained 0.5- <2 Kg/m^2 and 2 Kg/m^2 or more had a RR= 1.40 95% CI (1.02-1.92) and 1.53 95% CI (1.04-2.24) of BC recurrence, P-trend=0.03. On the contrary, only women who gained 2 Kg/m^2 or more were 78% more likely to have an elevated tumor size with a 95% CI (1.20-2.64), compared to those who maintained their BMI (Kroenke et al., 2005).

2. Diabetes Type 2

Overweight and obesity can in-turn lead to diabetes type 2, another factor associated to an elevated risk of developing BC. Excess body weight, specifically in the abdominal area causes insulin resistance, which, in turn, advances to cause diabetes. Women that are at greater risk of developing DM2 are those whose waist circumference is 80 cm or more (NHS, 2014). Diabetes type 2 is a growing concern since, according to a CDC report, 95% of all diabetics are diagnosed with type 2 DM (CDC, 2011).

According to the WHO, the global prevalence of DM2 among adults was 9% in 2014. In 2012, 1.5 million people died as a direct consequence of DM2; as a result, researchers predict that DM2 will be the 7th global leading cause of death in 2030 (WHO, 2015). In 2014, Morocco exhibits the highest percentage of total deaths due to diabetes; 12%; Algeria and Cyprus followed with rates equal to 7% (**Fig.1**). On the other hand, Egypt and Greece had the lowest rates in the Mediterranean region, with only 1% of the countries' total death due to diabetes. Malta, France and turkey also had low rates, 2%; followed by Spain 3%. Finally, diabetes accounted for 4% of the total deaths in Lebanon (WHO, Non-communicable Diseases Country Profiles, 2014).

Patients with DM2 usually suffer from hyper-insulinemia, increased body mass index, and insulin resistance, all of which have been linked to breast cancer. DM2 is related to increased risk for BC by 2 pathways; either directly or indirectly. An increased insulin level by its own has direct effects on breast tissue and through inducing hyper-insulinemia (Vona- Davis, L, 2007). Indirectly, through the inhibition of SHBG which will in turn lead to an increase in sex steroid; in addition, to an increase in IGF1. All the mentioned changes in the hormonal level will result in abnormal or imbalanced growth at the cellular level (Lawlor, DA, 2004). Moreover, insulin or

secretogogues administered by diabetic patients can further increase the risk of BC (Bowker, SL, 2006). On the other hand, Metformin was shown to decrease the risk of breast cancer among diabetic patients; diabetics taking Metformin for > 5 years had an OR= 0.44 95% CI 0.24–0.82 of developing BC as compared to diabetics not taking this medication (Bodmer, M, 2010).

A recent study done by Cleveland et al. (2012) showed a borderline significant association between diabetes and risk of developing breast cancer, specifically among post-menopausal women, OR= 1.35. However, white women did not show this significant association, but women of other races had about a 4 times increased risk of developing breast cancer with diabetes.

Diabetes might also affect BC prognosis, not only by the same mechanisms mentioned above, but also by the fact that diabetics are usually diagnosed at a later stage of BC since they are screened less, they don't receive aggressive treatment, and have many other comorbidities (Lipscombe et al., 2007). After collecting breast cancer treatment techniques of 56,367 non-diabetics and 14,414 diabetics, Srokowski et al. (2009), observed significant differences among the two groups; diabetics, compared to non-diabetics, were significantly less likely to receive radiotherapy. Another study showed similar results, diabetic BC patients, compared to non-diabetics, had an OR=0.73 (0.60-0.88) of receiving radiotherapy and OR=0.52 (0.36-0.75) of receiving chemotherapy (Van de Poll-Franse et al., 2007). On the other hand, diabetics were more likely to receive hormonal therapy and undergo surgery, OR=1.66 (1.18-2.31) and 2.32 (1.01-5.38) respectively (Van de Poll-Franse et al., 2007). Specifically, diabetics were significantly more likely to undergo mastectomy surgery, rates among DM 53.8% and non-DM 51.8%; whereas, non-diabetics were more likely to undergo breast-conserving

surgery. On another matter, the rates of chemotherapy toxicity, infections/fever and anemia were higher among diabetics, P-value <0.001 (Srokowski et al., 2009). Upon following up 6,107 BC women over 5 years, a significantly increased risk of over-all mortality was observed in the diabetics group; compared to non-diabetics, BC women with DM had around a 40% increased risk of mortality 95% CI (1.22-1.59), P-value<0.0001 (Lipscombe et al., 2007). A meta-analysis by Peairs et al. showed that, upon analysing 8 studies, women with pre-existing DM had around a 50% increased risk of over-all mortality compared to non-diabetics, 95% CI (1.35-1.65) (Peairs et al., 2011). In a cohort study, this time taking BC women at an early stage of BC, HbA1C was significantly associated with over-all mortality. Over-all mortality in women with HbA1C=7% or more, versus, those with HbA1C less than 6.5%, were more than 2 folds more likely to die, HR=2.35 95% CI (1.56-3.54). Moreover, per 1 unit increase in HbA1C levels, over-all mortality in diabetic women with BC had a HR=1.20 95% CI (1.07-1.34) (Erickson et al., 2011). Moreover, Srokowski et al. (2009) also showed that diabetic BC patients taking chemotherapy, compared to non-DM BC patients taking chemotherapy, had a higher risk of BC related mortality, HR=1.20; 95% CI (1.07-1.35).

3. Vitamin D

On another matter, the sunny weather that shelters the countries surrounding the Mediterranean Sea also bestows on this population a protective effect against BC. Studies have linked vitamin D and breast cancer, this relationship started out in the early 1990s. Garland et al. (1990) depicted an inverse association between sunlight exposure and breast cancer risk; for states that received more annual sunlight had about a 1.8 fold decreased risk of mortality due to breast cancer.

Many studies started investigating the mechanism by which vitamin D and breast cancer are related. The breast tissue contains all the signalling components of vitamin D: 1, 25 vitamin D, 24, 25 vitamin D, 1, 24, 25 vitamin D, Vitamin D receptor (VDR), and 24- hydroxylase enzyme (Shao et al., 2014). The active form of vitamin D increases cell-cycle arrest, particularly in MCF- 7 breast cancer cells (Jensen et al., 2001); moreover, it regulates oncogenes expression, specifically IGF-1 and several growth factors (Colston et al., 2002). 1, 25 dihydroxy-vitamin D down-regulates prostaglandin synthesis in breast tissue by two mechanisms; it decreases synthesis of COX-2 and increases expression of 15- hydroxyprostaglandin dehydrogenase (Krishnan et al., 2010).

An NHANES cohort study done between 1975- 1992 showed that women who had frequent sun exposure over 17 years were at a 33% lower risk of developing breast cancer as compared to women who never or rarely exposed themselves to the sun (John EM et al., 1999). To further advocate the role of vitamin D on breast cancer, some studies examined vitamin D intake and serum levels in relation to breast cancer. Women with a vitamin D intake of > 190 IU, as compared to women with an intake of < 60IU, had a 34% lower risk of developing breast cancer (Rossi et al., 2009). Results were similar to two other cohort studies that investigated the same issue. In the Nurse's Health study and Women's Health cohort Study, women with high vitamin D intake (>500 IU/ day as compared to those of < 150) had lower risk of developing pre-menopausal breast cancer, OR= 0.72, 95% CI=0.55-0.94; however, no significant results were observed for post- menopausal women (Shin et al., 2002, Lin et al., 2007). Chen et al. (2010), showed that women with the highest versus lowest serum levels of 25- hydroxyl vitamin D (52 ng/ml and 13 ng/ml respectively) had a 45%; 95% CI=0.3-

0.8 lower risk of developing breast cancer, with no variation in results between pre and post- menopausal women.

Two good sources of vitamin D are breast milk and dairy products. Breastfeeding is a practice that has been linked to various anti-carcinogenic characteristics; moreover, the consumption of dairy products in moderation also exhibits a similar effect (to be discussed later).

4. Breastfeeding

The association between breastfeeding and cancer risk dates back to the 1920s; Claypon et al. (1926) showed that if the breast doesn't function its purpose, it will be at a higher risk of developing cancerous tumors.

To explain this association, several hypotheses were proposed. One explanation is that BF decreases the menstrual cycle, which in turn decreases hormonal levels, specifically progesterone (Butt et al., 2014). When looking at the literature, we can see that different studies examined different aspects of this relation; such as, any history of BF, number of children breastfed, cumulative duration of breastfeeding, or average duration of BF per child.

Upon reviewing various studies, Lipworth et al. (2000) deduced that women who breastfed, versus women who never breastfed, had a protective effect against developing breast cancer, with a RR ranging from 0.54 to 1. Moreover, even in women who have first-degree relatives with breast cancer, having ever breastfed decreased the risk of developing breast cancer with an OR= 0.41 95% CI (0.22-0.75) (Stuebe et al., 2009). Women who breastfed 1 or 2 children, in contrast to women that never breastfed, had a 43%, 95% CI (0.34-0.96) decrease in breast cancer risk; in addition, women who

breastfed 4 or more children had a 60%, 95% CI (0.21-0.70) reduced risk (Romieu et al., 1996). There is an increasing inverse relation between cumulative duration of breastfeeding and risk of developing breast cancer; women who breastfed for 5 and 30 months had a reduced risk of breast cancer, RR= 0.97 and 0.64 respectively (the LANCET, 2002). Women with a mean duration of BF per child of more than 12 months, as compared to those with < 12 months, had an OR= 0.52 95% CI = 0.28, 0.94.of developing breast cancer (De Silva et al., 2010).

5. Physical Activity and BC

People residing the coast of the Mediterranean Sea were traditionally known to physically active. Nevertheless, the rates of insufficient physical activity in the Mediterranean region vary between different countries (Fig.4). Libya and Malta score the highest percentages in this region, prevalence of insufficient PA are 43.3% and 47.2% respectively. On the other hand, Greece and France have the lowest rates, 15.7% and 28.5% respectively. Lebanon falls between these two extremes; with a prevalence of insufficient PA= 33.8% (WHO, Global Status Report, 2014).

In 2012, the fraction of breast cancer attributed to physical inactivity was 10% worldwide (Lee et al., 2012). Physical activity lowers body fat (Donnelly et al., 2009), and by decreasing body fat levels, PA decreases a major contributor to estrogen production (Cleary et al., 2009). Physical activity also affects estrogen levels by delaying menarche, increasing amenorrhea, and decreasing ovulation (Bernstein, 2009). Additionally, physical activity helps improve insulin resistance (Klein et al., 2004), and insulin resistance is associated with an increased risk of BC since insulin acts as an anti-apoptotic and pro- mitotic factor in BC cells (Lann et al., 2008). Finally, physical

activity decreases oxidative stress (Schmitz et al., 2008) and methylation of tumor suppressor genes (Coyle, 2006).

After analysing 31 prospective studies linking breast cancer risk to physical activity, Wu et al. (2013) showed that the RR for developing BC for physical activities < 10 years and > 10 years are 0.89 (0.84–0.94) and 0.88 (0.84–0.91) respectively. The highest decrease in risk of breast cancer was among vigorously active women, 26%, versus a 22% among moderately active women (Friedenreich et al., 2008). When researching the link between physical activity and breast cancer risk in relation to other factors, the results were conflicting between prospective and epidemiological reviews. In prospective studies, the association was highest among pre-menopausal RR= 0.77 (0.72–0.84) women and activities done at >50 years old with a RR= 0.88 (0.83–0.92) (Wu et al., 2013). Epidemiological studies show the highest association in post-menopausal women (31% risk reduction), and physical activities done when women are > 50 years old with a reduction of 17% versus an 8% in women< 20 years old (Friedenreich, 2010). When adding BMI to the equation, the data was more consistent, the strongest association between PA and risk of BC was among women with BMI <22 Kg/ m2 27% decreased risk, and less than 1% decreased risk among obese women (Friedenreich, 2010).

PA was also not `only related to BC risk, but also to BC mortality and recurrence. A meta-analysis showed that pre-diagnosis and post-diagnosis PA were inversely associated with all-cause mortality, HR= 0.82 (0.67-0.99) and 0.59 (0.53-0.65) respectively. On the other hand, only pre-diagnosis PA was associated with BC specific mortality, HR= 0.66 (0.57-0.77), and post-diagnosis PA was associated with 24% decreased risk of BC recurrence, 95% CI (0.66-0.87) (Ibrahim et al., 2011). When 2,987

women were followed up in a prospective observational study from 1986 till their death or till 2002, a negative association was also established between post-diagnostic physical activity and BC related/over-all mortality rates. All intensities of PA, MET-h/ week ranged from 3 till more than 24, were significantly related to a 29-44% decreased risk of over-all mortality among BC female patients, compared to women with < 3 MET-h/ week, P-trend= 0.003. These results were similar in relation to BC deaths, RR ranged from 20-50% decreased risk, P-trend= 0.004. This same study also showed that women with a PA of 9- 23.9 MET-h/ week had a significantly lower risk of BC recurrence RR between 0.57 and 0.66; 95% CI (0.38-0.93) (Holmes et al., 2005). Contrary to Friedenreich's findings on PA and BC risk (mentioned earlier); overweight and obese women, compared to those with BMI< 25 Kg/m2, benefited more from PA in relation to BC related deaths, P-trend= 0.01. While pre-menopausal women failed to show a significant association between PA and BC related deaths, post-menopausal women with a PA level of >= 9 MET-h per week had a RR= 0.73 95% CI (0.54-0.98) of BC death (Holmes et al., 2005). Another prospective study showed similar results, BC women with moderate intensity PA had a RR of 0.47 95% CI (0.26-0.86) and 0.47 95% CI (0.34-0.65) of BC related deaths and over-all mortality respectively. Moreover, as levels of PA increased from 2 till more than 10 MET-h/ week a significant linear trend was also observed between moderate intensity PA and both BC related deaths/over-all mortality, P-trend= 0.03 and < 0.001 respectively (Holick et al., 2008).

C. The Mediterranean Diet

Historically, the Mediterranean region had the lowest rates of over-all cancer incidences, specifically breast cancer. One possible reason might be the Mediterranean diet; this diet was first described in the literature in the 1960s. Keys et al. (1980) were the first to relate this diet to the scientific field, particularly stating the benefits of the MD on human health. In 2010, the UNESCO declared the MD as an 'intangible cultural heritage' (UNESCO, 2011).

1. Definition

Rather than just being a healthy eating pattern, the MD is a lifestyle that population living in the Mediterranean region traditionally follow (Sofi et al., 2010). There is no unified definition of the MD, as some minor aspects of this diet differ from one country to the other, and even within the same country. These discrepancies are due to environmental factors; such as, food availability and cultural traditions; however, the key points of this diet are somehow the same across all countries residing the Mediterranean Sea (Gracia-Meseguer et al., 2014). The MD is mainly characterised by high content of fruits, vegetables, legumes, nuts, fish and olive oil; low to moderate content of dairy products, poultry and eggs; low in SFA, red and processed meats; as well as, regular moderate intake of red wine with foods (Couto et al., 2011, Bach-Faig et al., 2010).

2. The Mediterranean food pyramid

The Mediterranean food pyramid, adapted from the Greek food intake in the 1960s, summarizes these main points and helps put things into perspective. Carbohydrate rich foods (preferably whole grains) such as, breads, pasta, cereals, bulgur, rice, potatoes and legumes are at the base of this pyramid. As well as daily consumptions of not less than 5 servings of fruits and vegetables, not more than 2 servings of dairy products, and 2 servings of nuts, seeds, and olives. Weekly, one should consume around 2 servings of poultry, no more than 4 eggs, at least 2 serving of each, fish/ seafood and legumes and no more than 2 servings of sweets. Red meats were at the very top of the pyramid, with a consumption of no more than a few times per month (Willett et al., 1995, Giacosa et al., 2013). People in the Mediterranean region were considered a population that is highly active, enjoyed nutritious foods and were regular moderate wine drinkers, 1 glass/day for women and 2 glasses/day for men (Willett et al., 1995). Due to its low animal protein content, the MD is low in SFA; however, it is not low in total fat content. MD has a total fat content ranging from as low as 28% in Italy to as high as 40% in Greece; nevertheless, the major contributor to this amount is olive oil (Giacosa et al., 2013).

3. Health Benefits of the MD

a. Life expectancies in this region

The MD has various health benefits; populations in this region have the highest life expectancies and the lowest rates of cardiovascular diseases. Worldwide, Sierra Leone has the lowest life expectancy at birth among both sexes and among women, both= 46 years (**Fig.3**). On the other hand, Japan has the highest rates; life expectancies

among both sexes and among females are 84 and 87 years respectively. When examining the life expectancy rates among various areas, a difference is observed between countries that reside the Mediterranean Sea versus other countries within the same continent. For example, in Africa, life expectancies (both sexes and female) were higher within countries in the Northern region versus other areas. Female life expectancies in Tunisia and Egypt are 78 and 74 respectively; whereas, the Central African Republic and Liberia had rates of 52 and 53 years respectively (close to rates seen at Sierra Leone). In Europe, the over-all life expectancies were close to the rates observed in Japan; most countries in Europe had life expectancies between 83 and 85 years. Moreover, no difference in life expectancy was observed between counties in the Mediterranean coast and countries in the Northern area. Countries in Western Asia showed some variation, but to a large extent. In Lebanon, life expectancies among both sexes and among females were 80 and 82 years respectively; whereas, life expectancies among females in Bahrain and Iraq were 78 and 74 years respectively (WHO, World Health Statistics, 2014).

b. MD and Mortality

A meta-analysis of 18 studies resulted in a RR= 0.91; 95% CI (0.89-0.93) of over-all mortality and adherence to the Mediterranean diet. This same study resulted another significant finding, upon a 2-point increment in the MD adherence score, subjects had a RR= 0.90; 95% CI (0.87-0.92) of CVD risk and/or mortality (Sofi et al., 2013). Another study that followed-up 166,012 women for 10 year showed that those with the highest compliance to the MD, as compared to those with the lowest, had a HR= 0.80; 95% CI (0.75-0.85) of all-cause mortality, P-trend <0.001, and a HR= 0.81; 95% CI (0.68-0.97) of CVD mortality , P-trend =0.01 (Mitrou et al., 2007).

4. MD and Breast Cancer

The MD also protects against cancer since it is low in refined sugar sources and very rich in fiber, thus affects insulin sensitivity, IGF and tumor growth (Giacosa et al., 2013). The MD has an excellent ratio of omega 6/ omega 3; moreover, it is low in SFA and high in MUFA, specifically olive oil, that is an excellent source of anti-oxidants, such as vitamin E, rarely causes LDL peroxidation, may increase HDL, and can be used as a food condiment to improve foods' taste (Willett et al., 1995).

A study done by Trichopoulou et al. (2000) showed that if women living in developed western regions of the world followed the MD, 15% of BC cases will be prevented. Upon analysing the dietary habits of 335,873 women recruited in the EPIC cohort study between 1992 and 2000, Couto et al. (2011) showed a dose-responsive association between the MD and risk of developing all types of cancers since women who adhered most to the MD, as compared to those with the lowest adherence, had a HR= 0.93; 95% CI (0.89-0.96) with a P-trend of 0.0001. Upon analysing the dietary habits of 65,374 post-menopausal women for 9.7 years, the results reveal an increased risk of developing invasive breast cancer among those following a Western diet, HR= 1.20; 95% CI (1.03-1.38); whereas, the healthy Mediterranean diet decreased the risk, HR= 0.85; 95% CI (0.75-0.95) (Cottet et al., 2009). Another meta-analysis showed that upon a 2-point increment in the MD adherence score, subject had a RR= 0.95; 95% CI (0.93-0.97) of cancer risk and/or mortality (Sofi et al., 2013). When comparing women with the highest adherence to the MD to those with the lowest; a 10 year follow-up study resulted in a HR=0.86 95% CI (0.76-0.97), P-trend =0.01 of cancer specific mortality (Mitrou et al., 2007).

D Specific foods within the Mediterranean food pyramid in relation to BC

1. Dairy Products

Data in the literature on the relation between dairy products consumption and BC show different results; for instance, high fat dairy consumption might increase the risk/worsen the prognosis of BC, but low fat dairy might decrease the risk/improve prognosis. Dairy products affect vitamin D and calcium levels, both of which have a role in BC cells by affecting BC cells differentiation and proliferation (mentioned earlier). Calcium intake helps stabilize intracellular calcium levels which, in turn, decrease fat-induced cellular proliferation.

In a 16 year cohort study, Shin et al. (2002) showed that pre-menopausal women with a cumulative dietary calcium intake of more than 1000 mg/day, compared to women who consumed 500mg or less/day had around a 30% lower risk of developing BC. Vitamin D also acts as a catalyst for cell-cycle arrest (Shin et al., 2002). Estrogen, another factor that exerts effect of BC wells, is mainly found in the fat of the cow's milk, so by varying fat content, the effect of dairy on cancer cells varies as well (Kroenke et al., 2013). Estrogen content of dairy products in the Mediterranean region is lower than values observed in the West; in most Western countries cows' milk content of estrogen and progesterone are differentially elevated due to the way of raising cows (Ganmaa et al., 2010).

Around 830 pre-menopausal women were followed from 1980-1996; women who consumed more than 3 servings of dairy per day had a 30% lower risk of developing BC, compared to those who ate 1 or less servings, P-trend 0.009. However, after adjusting for total Ca and vitamin D intake, this relation was no longer significant. Similarly women who consumed more than 1 serving of low-fay dairy, compared to

those who consumed 3 or less servings per month, had a significantly lower risk of developing BC, RR=0.68 (0.55-0.86), P-trend=0.003. Moreover, this effect remained significant even after adjusting for total Ca and vitamin D intake (Shin et al., 2002). Yoghurt intake was also shown to decrease the risk of developing BC; women who consumed 365 servings of yoghurt per day, versus those who consumed 24, had a 60% lower risk of developing BC, 95% CI (0.22-0.79), P-trend=0.008 (Ronco et al., 2002). In contrary, a case-control study done by Ronco et al. (2002) in Uruguay showed that women with the highest consumption whole-fat milk, 730 servings/year, compared to those who didn't consume whole milk at all, had about a 3 fold increased risk of developing BC, 95% CI (1.38-5.84), P-trend= 0.0007. Upon analysing dietary intake of 90,655 pre-menopausal women, Cho et al. (2003) concluded that women who consumed 1 and 2 serving of high-fat dairy per day were 40% more likely to develop BC, RR=1.37; 95% CI (1.07-1.75). Similar results were shown among those who had 2 servings per day, RR=1.36 95% CI (1.06-1.75), and there was a positive dose dependant association was well, P-trend=0.02 (Cho et al., 2003). Kroenke et al. followed up 1,893 female BC patients over a period of around 12 years, and showed that high-fat dairy product consumption was significantly associated with elevated risk of over-all mortality. BC women who consumed 1 or more servings of high-fat dairy products per day were 64% more likely to die than those who consumed less than 0.5 servings per day, 95% CI (1.24-2.17); moreover, a dose dependent association was also establishes, P-trend<0.001 (Kroenke et al., 2013).

2. Lycopene

Another micro-nutrient that has been proposed to exhibit a protective effect against the risk of developing BC and improving BC prognosis is Lycopene. Lycopene is a carotenoid found in apricots, watermelon, grapefruit and papaya; however, the major sources of Lycopene in the diet are tomatoes and tomato products (Clinton et al., 1998). Upon heating and processing, the total content of lycopene in tomatoes decreases, but its bioavailability increases due to cell wall breakdown (Grosso et al., 2013).The interest in Lycopene was due to various epidemiological studies that showed that tomato consumption decreased the risk of developing cancer (Franceschi et al., 1994).

Studies show that Lycopene affects breast cancer cells not only by being an anti-oxidant, but also by inducing apoptosis and cell cycle arrest at the G1 phase, affecting DNA synthesis and decreasing IGF1 signalling and mammary cell proliferation (Wertz et al., 2004, Karas et al., 2000).

Sesso et al. (2005) showed that, after 9.9 years of follow-up, women with the highest intake of tomato sauce, 2-4 servings/ week, compared to those who didn't consume tomato sauce at all, had a significantly lower risk of developing BC, P trend= 0.046 . Teodoro et al. (2012) showed that upon injection with Lycopene (1-5 μM), cancer cells significantly decreased in viability, increased apoptosis and cell cycle arrest. When Hu et al. (2010) pooled 9 case-control studies, linking Lycopene to breast cancer, they deduced that Lycopene significantly the risk of developing breast cancer OR= 0.71 (0.56- 0.92).

McEligot et al. (2006) showed that the risk of over-all mortality was reduced to half among post-menopausal women who consumed the highest versus the lowest

amounts of β-carotene prior to their diagnosis, 95% CI (0.29-0.85). Results from the same study also showed that women who consumed around 835µg of lycopene per day, had a 40% decreased risk of over-all mortality, 95% CI (0.35-0.96) (McEligot et al., 2006).

3. Fruits/Vegetables

Lycopene is not the only component of fruits that is linked to BC; in fact, over-all intake of fruits and vegetables has an anti-carcinogenic effect on BC cells.

Fruits and vegetables differ immensely in their nutrient composition; however, they are excellent sources of anti-oxidants that play a protective role against breast cancer cells by decreasing DNA damage (Brian et al., 2006). They also contain high amounts of fiber, and fiber is known to bind to estrogen thus further inducing an anti-carcinogenic effect (Maskarinec et al., 2006). Studies show that F&V are associated with ER+ and PR+ tumors rather than ERPR-; usually ERPR+ tumors are associated with better overall cancer prognosis (Gaudet et al., 2004).

Upon reviewing 7 cohort studies, with more than 233,036 participants, linking BC to F&V intake, Aune et al. (2012) calculated an OR= 0.89 (0.80-0.99) of developing BC for high versus low intake. Similar results were shown when they examined the association between fruit intake and risk of developing BC, 10 cohort studies resulted in an OR= 0.92 (0.86-0.98) (Aune et al., 2012). Results from another study also showed that women with the highest quartile of vegetable intake, 5.6 standard servings/ day, compared to women who consumed 2.6 standard servings had a significantly lower risk of developing BC. Vegetable intake seemed to improve BC prognosis, for instance, pre-diagnostic vegetable intake was associated with around a 50% decreased risk of over-all

mortality among post-menopausal women; those who consumed around 3 serving per day had a HR= 0.57; 95% CI (0.35-0.95) (McEligot et al., 2006).

4. Carbohydrates

Macro-nutrient distribution of the diet also plays a major role in either increasing or decreasing the risk of developing BC; as well as, affecting over-all prognosis and survival rate. For example, carbohydrate rich foods differ from each other by various factors; such as, glycemic index (GI) to measure carbohydrate quality, glycemic load (GL) to measure the quantity, and fiber content. High carbohydrate intake has been hypothesized to be inked to increased risk of breast cancer, and various studies investigated this linked by looking at different aspects of a carbohydrate rich diet. The link between glycemic load and increased risk of breast cancer appears to be stronger than the link between the BC and glycemic index, since higher GL results in higher blood insulin levels (Brand-Miller et al., 2009).

In their study, Sieri et al. (2012) showed that increasing dietary carbohydrate intake and food glycemic index did not have an effect on breast cancer risk; however, glycemic load showed to significantly increase the risk with a P-trend value of 0.029 when increasing the intake from the 120g/day to 190g/ day. Another study investigated the same link; however, they added dietary fiber intake to the connection. Women with dietary fiber intake of less than 22g/ day had a significantly increased risk of developing breast cancer when increasing GI, GL and CHO intake from <52.7 units/ day to >58.9 units/day, <101.8units/ day to >137.8 units/day, and <185.3 g/day to > 244.1g/day respectively (Romieu et al., 2012).

5. Fiber

A diet rich in fiber has been shown to have a protective effect against breast cancer. Fiber decreases serum levels of various inflammatory markers such as, interleukins and tumor necrosis factor-α (Ma et al., 2004). Dietary fiber also helps lower blood glucose and insulin levels by slowing down glucose absorption. Moreover, fiber decreases estrogen levels by two pathways: it helps decrease estrogen reabsorption at the intestinal level and increases its excretion through the biliary system into the feces (Park et al., 2009).

Upon analysing dietary fiber intake, from the UK women's cohort study, of 35,792 females, of which 257 developed pre-menopausal BC, a significantly inverse associated was depicted among fiber intake and risk of BC. A dose dependant association was established; the more fiber pre-menopausal women ingested, the lower their risk of developing BC, P-trend=0.01. However, the greatest protective effect was among those who consumed more than 30g of fiber per day, RR=0.48 (0.24-0.96) compared to those eating less than 20g/day (Cade et al., 2007). Another study done on post-menopausal women showed similar results; Park et al. collected and analysed usual dietary fiber intake of 185,598 post-menopausal women, of which 5,461 developed BC over the course of the 7 year follow up. Women with the highest quintile to fiber intake, 26g/day, compared to the lowest, 11g/day, had the lowest risk of developing BC, RR=0.87 (0.77-0.98). a dose responsive associated was established between post-menopausal dietary fiber intake and risk of developing BC, P-trend=0.02 (Park et al., 2009).

When pre-diagnostic dietary habits of 516 post-menopausal BC women were analysed, a significant linear inverse association was established between dietary fiber

and over-all mortality in BC patients. Women with the highest, versus the lowest, intake of fiber had a 52%; 95% CI (0.27-0.86) decreased risk of over-all mortality, P-trend= 0.01 (McEligot et al., 2006).

6. Animal Proteins

A tool used for weight-loss and diabetes control usually involves following a low carbohydrate/ high protein diet; however, caution should be given when advising such diets, since protein intake has been linked to breast cancer risk mainly due to the fact that protein intake increases levels of IGF-1 which promotes tumor growth (Levine et al. 2014). Moreover, red meat contains high amounts of heme iron which in turn has been linked to increased risk of tumor formation though estrogen levels (Liehr et al., 2001). Studies did not show a significant association between protein sources such as, eggs, legumes, nuts and fish and increased risk of developing breast cancer (Pala et al., 2009). The relation between red meat and breast cancer is mainly due to the presence of heterocyclic amines and poly-aromatic hydrocarbons that result from meat processing mechanisms (Taylor et al., 2009).

In their study, Egeberg et al. (2008) showed that postmenopausal women who ate more than 50g/day of red meat, as compared to those whose intake was < 50g/day, had a higher risk of developing breast cancer, P- Trend= 0.03; furthermore, every additional serving of red meat (25g) per day increased breast cancer risk by 15%.

7. Dietary fat

Westernized diets are associated with an increased risk of breast cancer and breast cancer mortality (Kroenke et al., 2005); one possible explanation for this association is because of the fact that the Western diet is high in total fats, SFA, TFA and low in PUFA and MUFA.

Dietary fat is not only associated with BC incidence, but also with BC reoccurrence and mortality (Makarem et al., 2013). Increased intake of dietary fats is associated with elevated body fat levels mainly due to their high caloric content (Austin et al., 2011). This increase in body adiposity, in turn, leads to hyper- insulinemia, insulin resistance, increase in ROS, adipokine secretion, and tumor growth (Sung et al., 2011). The produced ROS are associated with mutations in the p53 gene causing an increased DNA damage and imbalanced cellular proliferation thus promoting carcinogenesis (Gasco et al., 2002). Moreover, fats play a role in regulating transcription factors related to breast cancer; they affect cellular survival, death and differentiation (Jump et al., 2004). Fatty acids also affect cell signalling pathways, enzyme activity, activation/deactivation of tumor suppressor genes and oncogenes (Escrich et al., 2011). Dietary fatty acids also manipulate cell membranes' lipid profiles, thus inducing lipid peroxidation in these membranes (Hulbert et al., 2005). In addition, a high-fat diet significantly advances sexual maturation, a risk factor for BC (Escrich et al., 2014). Various types of fatty acids seem to exert diverse effects of human breast cancer cells. For example, omega 3 derived eicosanoids are anti- inflammatory agents; whereas, omega 6 derived eicosanoids are pro- inflammatory agents. Eicosanoids, in general, affect hormonal levels, signalling pathways, immunity, inflammation and carcinogenesis (Rose et al., 2000). Moreover, after analysing 16 experimental laboratory

series, Escrich et al. (2014) noted that a diet rich in omega 6 PUFAs increased mammary tumors' aggressiveness and stimulated carcinogenesis. EPA and DHA, also called marine fatty acid, not only inhibit tumor growth and induce cell death in breast cancer cells, but also inhibit metastasis and the production of Arachidonic acid, estrogen and prostaglandin E2 (Schley et al., 2005, Larsson et al., 2004). The major dietary source of EPA and DHA are fatty fish.

a. Total fat intake

A cohort study that followed up 90,655 pre-menopausal women over a course of 8 years depicted a significant association between the risk of developing BC and animal fat. As percentage of total energy derived from animal fat increased from 17 to 20 and 23, the RR for developing BC also increased, 1.37 95% CI (1.07-1.75), 1.54 95% CI (1.20-1.97) and 1.33 95% CI (1.02-1.73) respectively, and a dose related association was establishes, P-trend= 0.002. A meta-analysis done by Boyd et al. (2003) included both case-control studies and cohort studies, and resulted in analogous findings; a significance was established in the cohort studies between increased total fat intake and BC risk, RR= 1.13 95% CI (1.04-1.23).

Studies have also linked fat intake to BC prognosis, for instance, McEligot et al. (2006) showed that BC women that pre-diagnostically consumed around 38% of their total energy from fat, had more than a 3 times higher risk of over-all mortality, compared with those taking the AMDR, P-value <0.0001. A study showed that women with the highest tertile of pre-diagnostic dietary fat intake (56-76g/ day) had more than a 2 fold CI (1.1-4.3) increased risk of breast cancer specific mortality (P-trend of total fat and % total energy= 0.016 and 0.044) (Zhang et al., 1995). A randomized clinical trial

done between 1994 and 2001 also showed comparable results; women taking a low fat diet, 20% of total Kcal, had a 24% with a CI (0.60-0.98) reduced risk of BC reoccurrence (Chlebowski et al., 2006).

b. SFA and TFA

A significant association was also observed between the risk of developing BC and SFA; when SFA accounted for 12% of total energy intake, the RR was 1.41 95% CI (1.12-1.78) (Cho et al., 2003). Upon analysing 12 cohort studies, the over-all relative risk of developing BC with increased SFA intake was 1.15 95% CI (1.02-1.30); similar results were observed in 23 case-control studies, RR= 1.23 95% CI (1.03-1.46) (Boyd et al., 2003).

SFA and TFA also played a role in worsening prognosis among BC patients. Results from a study show that women who consumed on average 13% of their total calories from SFA, as compared to those who consumed 7%, had a HR of 1.41 (1.06-1.87) of mortality; moreover, women with the highest intake of TFA, versus the lowest, had a 78% (1.35- 2.32) increased risk of dying (Beasley et al., 2011). Another study showed similar results, women that pre-diagnostically consumed around 19% of their total energy from SFA had a HR=4.45; 95% CI (2.26-8.78) of over-all mortality, compared to those taking <7% (McEligot et al., 2006).

c. EPA/DHA and MUFA

A cohort study done over a course of 7.3 years showed that women who consumed >= 153 mg/ day of EPA and DHA, as compared to those who consumed <= 36.7 mg/ day, had a 28% decreased risk of additional breast cancer complication 95% CI 0.57- 0.90, and a 41% decreased risk of all- cause mortality 95% CI 0.43- 0.82 (Patterson et al., 2010). Likewise, MUFAs also seemed to play a protective role against BC; women consuming the highest amount of MUFAs, >47g/ day, as compared to those consuming <33g/day, had a significantly lower risk of developing BC, OR= 0.52 CI (0.30–0.92) P trend= 0.02 (Garcia-Segovia, 2006).

8. Olive Oil

The major contributor to dietary fat content in the Mediterranean region is olive oil. When researchers reviewed experimental studies linking olive oil to breast cancer, they deduced that a diet rich in EVOO had a protective effect since it decreased the incidence of BC, and decreased the progression of already existing tumor cells (Escrich et al., 2014). EVOO decreased the expression of IGF-1, unlike omega-6 that up-regulated its expression (Escrich et al., 2011). Olive has also affects cancer prognosis by decreasing the expression of COX-2, GSH and NF- ƙ β; as well as, inducing apoptosis (Grosso et al., 2013).

In a case control study, women consuming > 8.8g of olive oil/day also had a protective effect against developing BC, OR= 0.27 CI (0.17–0.42), and each additional gram further decreased the risk by 2-4% (Garcia-Segovia, 2006). After reviewing 19 observational studies with 1380 and 23340 cases and controls, Psaltopoulou et al. (2011) showed similar results. Olive oil consumption significantly decreased all-cancer

risk and BC risk, log OR= -0.41; 95% CI (-0.53,-0.29) and log OR= -0.45; 95% CI (-0.78,-0.12) respectively.

9. Alcoholic Beverages

Williams et al. (1977) reported the first positive association between alcohol and BC in 1977. The proposed mechanisms of how alcohol affects BC cells are many; some of them may be due to nutrient interactions, hormonal imbalances and DNA damages. Acetaldehyde, a metabolite of ethanol, interferes with the pathways of folate and methionine, thus inducing changes in DNA methylation, and disrupting gene expression. Ethanol stimulates carcinogen initiation and DNA damage by converting inactive carcinogens to active ones, and it decreases carcinogen detoxification by impairing liver clearance of carcinogens (Singletary et al., 2001). Additionally, alcohol consumption decreases serum anti-oxidant levels, such as β- carotene and vitamin C (Singletary et al., 2001). In pre-menopausal women, alcohol increases estrogen exposure by interfering with menstrual cycles' frequency and duration (Sarkola et al., 2000).

A study done in the US between 1992 and 2004 showed that women who consumed >30g of alcohol/ day, as compared to those with no alcohol consumption, had a 43% with CI (2%-202%) increased risk of developing invasive BC (Zhang et al., 2007). A meta-analysis done by Key et al. (2006) showed that alcohol drinkers, versus non-drinkers, had an OR= 1.16, 95% CI (1.10-1.24) of developing BC.

Alcohol intake was also associated to BC prognosis; BC women consuming >= 6g of alcohol per day, compared to non-drinkers, had a 1.6 increased risk of BC recurrence CI (1.08-2.38), and HR= 1.72 (1.05-2.81) of BC related mortality (Kwan et

al., 2010). In contrast, another study showed that consuming 3-6 alcoholic drinks per week, compared to non-drinkers, prior to BC diagnosis decreases BC related mortality and over-all mortality, HR= 0.85, 95% CI (0.75-0.95) and HR= 0.80, 95% CI (0.74-0.86) respectively (Newcomb et al., 2013).

10. Wine

The specific type of alcohol included in the Mediterranean dietary requirements is regular intake of moderate amounts of red wine, a potent anti-carcinogenic drink. The anti-carcinogenic characteristic of red wine is mainly attributed to its polyphenol, resveratrol. Resveratrol is not only linked to cancer, but it is also associated with diabetes, CVD, arthritis, and pulmonary diseases (Saiko et al., 2008). Plants such as, peanuts, plums, berries and grapes, usually produce resveratrol to stop cellular growth and proliferation when they are stressed, and it acts as a natural antibiotic (Harikumar et al., 2008).

Resveratrol induces cells cycle arrest and apoptosis, decreases inflammation, and boosts the immune system. It also affects breast cancer prognosis by interfering in signalling pathways, preventing metastasis, cellular attacks and angiogenesis (Kundu et al., 2008). Studies done on mice show that resveratrol affects BC cells by decreasing the production and activation of COX-2 and NF-ƙ β thus improving mammary gland maturation and apoptosis (Bishayee et al., 2009). Signalling pathways play a major role is the progression of BC; intracellular calcium levels affect cancer cells by affecting these signalling pathways, regulating cell cycle, and inducing apoptosis. Resveratrol inhibits calcium secondary messenger, thus inhibits the further development breast cancer (Berridge et al., 2000).

A case–control study done between 1993 and 2003 showed that women consuming the highest dietary tertile of resveratrol >160.7 µg/day, as compared to those consuming the lowest < 73.0 µg/day, had a significantly lower risk of developing BC, OR= 0.39 (0.25-0.62), P value <0.001 (Levi et al., 2005). Not only does wine effect BC risk, but it also improve the prognosis of BC patients; after 11.3 years of follow up, pre-diagnosis wine intake (3-6 drinks/week) significantly reduced the risk all-cause mortality, HR= 0.75 (0.67-0.84); however, post-diagnosis wine intake was not related to mortality risk (Newcomb et al., 2013).

E. Summary

As a conclusion, dietary habits play an important role in the risk of developing breast cancer, and affect rates of recurrence and mortality among patients. Studies have shown that the Mediterranean diet, specifically, decreases the risk of developing BC and improves over-all prognosis of BC patients. Over-all adherence to the MD has decreased worldwide, specifically among populations in the Mediterranean region. For example, a study that was published in 2009 examined adherence to the MD from 1961-2003, used a Mediterranean Adequacy Index (MAI) ratio; this MAI is calculated by dividing the energy coming from Mediterranean foods by an individual's energy intake from non-Mediterranean foods. The worldwide between the years 1961 and 2003 of MAI were 2.86 and 2.03 respectively. The MAI among non-Mediterranean countries were 1.55 and 1.14 respectively also indicating a decreased adherence to the MD; however, in the Mediterranean region, a sharper decrease in adherence to the MD was observed since the MAI were 3.44 and 1.98 respectively between 1961 and 2003 (De Silva et al., 2009). Countries in the Mediterranean region, mostly in Southern Europe,

have published various studies about adherence to the MD among their general population; however, data on BC patients remain very low. In Lebanon, a country on the Eastern Mediterranean coast, dietary intake among BC patients is minimally studied.

F. Aim of this Study

For the following reasons, the primary aim of this study is to examine the prevalence and determinates of the adherence to the Mediterranean diet among breast cancer patients in Beirut, Lebanon. A secondary aim of our study is to examine the over-all dietary composition among these patients. Results from this study can be used to assess dietary adequacy among this population, and can also encourage healthcare providers to recommend the MD to their BC patients as a form of an alternative medicine. Not only can this study be a foundation for other researchers in Lebanon to build their future studies, but it can also inspire other researchers in the Mediterranean region to do some more in-depth cohort studies to assess the exact impact of MD on BC patients' prognosis and survival rates.

CHAPTER II

METHODOLOGY

A. Study design

This is a cross-sectional study done in Beirut, Lebanon in order to assess dietary composition and adherence to the Mediterranean diet among female breast cancer patients. The study was conducted between October 2013 and August 2014.

B. Subjects

Subjects were recruited from two major health care facilities in Beirut, Makassed General Hospital (MGH) and American University of Beirut Medical center (AUBMC). Both, the hospital and the medical center, are accredited by the Lebanese Ministry of Public Health and attract the largest proportion of the patient population in Beirut, Lebanon. The philanthropic hospital generally serves patients belonging to a lower socioeconomic status as compared to the private medical center. The pool of participants in this study included patients followed for breast cancer at the outpatient clinics in both health care facilities, as well as breast cancer patients presented for chemotherapy administration. For patients to be included in the study they had to be females, aged 18 years or older, Lebanese, conversant in either the English or Arabic language, diagnosed with breast cancer for at least 2 months. The 2 month duration was preferred in order to assess participants' dietary intake during breast cancer rather than before diagnosis. Subjects were excluded if they were unable or unwilling to give

consent for the study. Recruitment of breast cancer patients took place at the waiting room in the clinics.

C. Ethical approval

Ethical approval for this study was obtained from the Institutional Review Board (IRB) of the Social and Behavioural Sciences at the American University of Beirut Medical Center (AUBMC), as well as from the ethics committee review at Makassed General Hospital (MGH).

IRB study approval can be found in Appendix A

All research assistants/interviewers involved in this study have successfully completed the Collaborative Institutional Training Initiative (CITI) course as per the requirements of the IRB. They approached patients and obtained written consent from those agreeing to participate.

Written consent forms can be found in Appendix B

D. Protocol

The nurse in the doctor's clinic or in the chemotherapy department was charge of introducing the study to the patients. Research assistants underwent standardized training sessions and where well knowledgeable in the field of research and nutrition. In a face-to-face interview, patients completed two multi-component questionnaires. The interviewer emphasized that patients' answers are confidential and will not be shared with their health care providers. Moreover, the study collaborators and research assistants did not have access to the medical records of any of the patients. To ensure a representative cross-sectional sample of patients from the two participating medical centers, interviews were conducted on different days of the week and at varying times.

E. Data Collection

For the purpose of this study, 2 questionnaires were administered. The first questionnaire consisted of three sections; the first section included questions assessing socio-demographic and lifestyle characteristics of the study participants such as age, marital status, educational level, employment status, and health insurance. The second section included questions specific to breast cancer and general health, such as the age of diagnosis, history of cancer in family, and perception of health status. And lastly, we conducted a 24-hr recall in order to assess macro and micro nutrient intakes of our sample population.

The second questionnaire was a dietary questionnaire that was composed of 26 questions. Questions included frequencies and quantities of specific foods that are mainly related to the Mediterranean diet.

The content validity of the multi-component questionnaire was confirmed by a panel of experts consisting of an oncologist, nutrition epidemiologist and health policy expert. The questionnaire was originally written in English and then translated to Arabic by a professional translator. The translated Arabic version was back translated by a professional translator to ensure the parallel-form reliability of the questionnaire. The original and the back translated versions were reviewed for consistency in meaning by two bilingual experts. A pilot study was conducted with 15 selected breast cancer patients to ensure that the target population understood the questions and that the answers yielded the required data. The findings of the pilot study were included in the analysis of the data for the present study.

Both questionnaires can be found in Appendix C

F. Calculation of the Mediterranean Scores

The dietary questionnaire did not only include the quantities eaten of a specific food, but also the frequency. Answers from this questionnaire were used to calculate 5 different Mediterranean diet adherence scores:

1. MS: Mediterranean Score

Questions are mainly related to portions and frequencies of consumption of: whole grains, fruits, vegetables, legumes, nuts, olives, olive oil, dairy, milk, animal protein sources, eggs and sweets. This score is composed of 11 questions, and each question is allocated a score from 0 to 4 (0 noting the lowest adherence). The individual scores from each question are then added up the produce the over-all Mediterranean Score that ranges from 0- 44; the higher the score, the better adherence to the traditional MD.

2. MSDPS: Mediterranean Style Dietary Pattern Score

The Mediterranean-Style Dietary Pattern Score was developed by a research group in Boston, USA in 2009 in order to assess an individual's adherence to the traditional MD. This questionnaire constitutes of 13 food groups taken from the Mediterranean pyramid. This- score ranges from 0- 100; it is composed of 13 components, 11 of them being the same as those in the MS, in addition to 2 others: wine and starchy roots intake. Each group is allocated a score from 0-10, and the total, being over 130, is converted to a total over 100. Similar to the previous score, as the scoring increases, the adherence to the MD increases as well. This score was the first to account for over-consumption of the specified foods, since over-consumption leads to a

deduction of the over-all scoring. Since people in the US eat a `mixture of Mediterranean and non-Mediterranean foods this questionnaire included some foods that are not interpreted as a part of the MD and the results of the 13 component score is weighed against energy that is derived from non-Mediterranean foods.

3. PREDIMED: PREvención con DIeta MEDiterránea (Prevention with Mediterranean Diet)

PREDIMED is a study that took place at various locations in Spain between the years 2003 and 2011. The study included around 7, 000 men and women aged between 55 and 80 years old. Participants were divided into 3 groups: MD supplemented with mixed nuts (30g/day), MD supplemented with EVOO (50ml/day), and a low-fat control group. The main objective of this study was to assess that effect of the Mediterranean diet on cardiovascular diseases. The questionnaire that assesses the adherence to the MD is composed of 14 questions. Each question is given a score of 0 or 1, depending on whether a person met the criteria or not. This score ranges from 0- 14; 0 indicating low adherence and 14 indicating full adherence to the MD. In addition to assessing intakes of specific food groups, it assesses the intake of carbonated beverages, differential intake of white meat over red meat, and the consumption of tomato sauce cooked with onion, garlic and olive oil.

4. CPMDI: Cardio- Protective Mediterranean Diet Index

This short questionnaire was established in Spain in 2004. The aim of this score is to assess an individual's adherence to the cardio protective aspects of the Mediterranean diet. This score ranges from 0- 9; it is composed 9 main questions, and each question is either scored 0 or 1. Questions are mainly related to the intake of fruits, vegetables, olive oil, legumes, fish, meat, wine and breads. Data from this score was compared to data from other case-control studies in order to assess a person's risk of myocardial infarctions. For example, people who scored between 7 and 9, as compared to those who scored 0-2, had a RR= 0.18; 95% CI (0.03–0.97) of developing myocardial infarctions.

5. DDS: Dietary Diversity Score

DDS is used to evaluate the individual's adherence to the USDA food guide. This score ranges from 0- 10; it includes the 5 food groups from MyPlate food guide, and each food group is divided into various subgroups. If a person consumed more than or equal to the recommended number of subgroups per group, he/ she is given a score of 2. However, if the amount consumed is less than the recommendation, another equation is used. The number of subgroups consumed is divided by the recommended amount, and the result is then multiplied by 2. The resulting score in this case is between 0 and 1, so the over-all score of DDS ranges from 0 and 2. A score of 2 indicates that the person's dietary intake is fully compliant to the USDA's food pyramid guide.

Detailed explanation and calculations for all the dietary scores can be found in Appendix D

G. Statistical analysis

The data was checked for completeness, and responses were coded and entered into the Statistical Package for the Social Sciences (SPSS) software version 21.0 for Windows. As for the 24 hr. recalls, they were entered into the Nutrition Pro software; this software allows us to analyse an individual's detailed dietary intake and composition. Frequencies and percentages as well as means and standard deviations were used to describe categorical and continuous variables, respectively. Dietary composition and adherence to the Mediterranean diet were main outcomes in this study. Dietary composition were both categorical and continuous outcomes; whereas, the MD scores were continuous. Chi-square and independent t-tests were used to chart comparisons of categorical and continuous variables between the philanthropic hospital and the private medical center. Univariate and multivariate linear regression analyses were applied to determine which factors are associated with the adherence to the Mediterranean dietary scores. The effect of each variable on the model was assessed, and the variable was kept if it significantly contributed to a better fit of the model. β and 95% confidence intervals were calculated. A p-value of 0.05 was used to determine statistical significance.

CHAPTER III

RESULTS

A. Socio- demographics and disease-related characteristics of the sample population

Table 1 shows that the mean age of the participants was 53.78 ± 9.93 years, and participants at the private medical center were significantly younger than those at the philanthropic hospital. The majority of participants were married, 80.2%, and the philanthropic hospital had significantly more single women. In both health care centers, women mainly had a high school or lower educational level. About 29% of the sample population were unemployed. Crowding index did not show any significant variation between the two sites, and more than half of the participants had a crowding index of less than 1. Most women had public insurance, about 76%, with a significant difference between study sites. The minority of women had monthly incomes of less than 500$; moreover, the philanthropic hospital housed more than two third of this group. Most of the enrolled participants had breast cancer for less than 1 year at the recruitment time, and more than half of the sample population had no family history of breast cancer and were at early stages of the disease. About 90% of participants adhered to their doctors' recommendations; in addition, participants at the philanthropic hospital had a significantly better reported current health status than those at the private medical center, 67.2% of them were in the good/ very good category.

B. Mediterranean dietary adherence scores in the sample population, and across recruitment sites

Our sample population means for MS, MSDPS and CPMDI are less than the median of the full scores, indicating very low adherence to the Mediterranean diet (**Table 2**). For example, over-all scoring of the Mediterranean score was around 24.7 ± 5.55 out of the full score, 44, and over-all scoring of the Mediterranean Style Dietary composition Score was 31.34 ± 8.49 out of the full score, 100. On the other hand, participants scored higher given the two other scores, PREDIMED and DDS, 6.06 and 9.09 out of 9 and 10 respectively. All of the examined scores significantly varied between the philanthropic hospital and the private medical center, except for the MSDPS, P value > 0.05. When compared to the philanthropic hospital, the private medical center had an overall higher adherence to the Mediterranean diet. However, the mean scores of the over-all sample population remain very low.

C. Dietary intakes of specific foods that are usually included in the Mediterranean pyramid

Table 3 shows that the serving sizes and portions were determined in the study and they included foods that are frequently consumed in the Lebanese population. We can see that breast cancer patients in our study consumed around 1.4, around servings of whole grain products per day. Intakes of fruits and vegetables were significantly different across the recruitment areas. For example, patients at the private MC seemed to eat more F&V as compared to their fellow participants at the philanthropic hospital. Even though most of the total participants stated that they used olive oil as their major dietary fat source (data not shown); patients at the philanthropic hospital only consumed

0.95±0.91 Tbsp., less than half the amount patients at the private MC ate 2.67 ±1.73Tbsp. Another finding is that participants seemed to consume more red meat and poultry over fish and seafood products. In both sites, BC patients consumed about 240 grams of each red meat and poultry per week; while they consumed less than 2 servings of fish/seafood. As for the intake of eggs, both sites consumed less than 2 eggs per week; however, participants at the private MC were significantly more likely to consume higher amounts.

D. Dietary intake of the sample population and recruitment sites

According to table 4a, the over-all caloric intake of the sample was 1578.08 ± 42.46 Kcal/day, with patients at the private medical center consuming statistically significant more calories than those at the philanthropic hospital. Our sample population's macro-nutrient intake of CHO, protein and fat were around 47%, 15% and 40% respectively. BC patients at the private medical center were consuming significantly more CHO and less fat than patients at the philanthropic hospital. The subtypes of dietary fats consumed did not differ in between the recruitment sites. Patients consumed around 18g of fiber per day; compared to those from the private medical center, participants from the philanthropic hospital consumed significantly less amounts of fiber, 14.90g/day ± 1.17 versus 19.26g/day ± 1.19. Almost all of the examined mirco-nutrients' intakes differed in between the recruitment sites; BC women in the private medical center were consuming statistically higher amounts than those at the philanthropic hospital, P-value < 0.05.

E. Dietary adequacy in the sample population

The AMDRs for carbohydrates, proteins and fats did not significantly differ across recruitment sites (**Table 4b**). Most participants were within the recommended AMDRs for carbohydrate and protein consumption, 51.7% and 86.1% respectively. In contrast, the majority of participants exceeded the recommendation for total fat intake; 72.2% of them had a fat intake of more than 35% of total Kcal. The different sub- types of fat intake were consistent between the philanthropic hospital and the private medical center. 73.9% of participants were consuming more saturated fats than generally recommended. However, around 70% of the participants were fulfilling the requirements for MUFA and PUFA intake. The majority of women, 53.3%, consumed linoleic acid more than recommended; on the other hand, linolenic acid was mostly consumed at levels lower than recommended, 65%. None of the women in the private medical center met the requirements of EPA and DHA, and only 1 woman in the philanthropic hospital consumed the required amount; in contrast, 78.3% ate less than 200mg of cholesterol per day. Similarly, 72.2% of the participants fell below the recommended intake of fiber, with only 16.1% of them meeting the recommendation. Total amount of added sugar was the only variable to show a significant difference between the two recruitment sites. Most of the sample had added sugar up to 25% of their total Kcal; however, women from the philanthropic hospital adhered more to the recommendation. Likewise, most of the recruited participants abided by the reference intake of sodium, 77% of them had up to 2,300 mg of sodium per day.

F. Univariate linear regression analysis between the Mediterranean scores and the sample population's socio- demographics

Table 5 shows that age was significantly negatively associated with 4 out of the 5 Mediterranean scores, MS, MSDPS, CPMDI and PREDIMED. The higher the age the less likely the participant is to adhere to the MD. Contrary, marital status was only significantly positively associated to the CPMDI score. Married women, versus single women, followed the Cardio- Protective diet more. Educational level was also positively associated to 4 Mediterranean scores. Employment status was only negatively associated PREDIMED. The duration of breast cancer, family history of BC, metastatic versus early stages, adherent to doctor's recommendations versus none adherent and current state of health were not related to any of the scores; on the other hand, the higher the family's monthly income, the more likely the participant is to follow all of the Mediterranean scores.

G. Multivariate linear regression analysis of the Mediterranean scores and the socio-demographics of the sample population

After adjusting for all socio- demographics at the same time, most of the associations observed in the univariate analysis failed to further exist (**Table 6**). Two negatively significant associations remained: age & MSDPS and employment status & PREDIMED. Moreover, two positively significant associations also remained: monthly income & CPMDI and current state of health & PREDIMED.

CHAPTER IV

DISCUSSION

A. Major findings of this study

Many reports have assessed pre-diagnostic food intake among BC patients; however, a few addressed the issue of post-diagnostic food intake. The majority of these studies examined intakes of specific foods/nutrients among BC patients, but none examined adherence to the Mediterranean diet. For the following reasons, this study is considered a pioneer since it is the first to examine dietary composition and adherence to the Mediterranean diet among breast cancer patients.

Results of this study showed that over-all adherence to the MD among breast cancer patients in Lebanon was low; with patients from the private medical center differentially adhering more to the Mediterranean dietary guidelines than patients at the philanthropic hospital. Multivariate linear regressions showed that age and employment were negatively associated with adherence to the Mediterranean diet; whereas, monthly income and better over-all health status were positively associated with the MD. Moreover, breast cancer patients, from both the private MC and the philanthropic hospital, were consuming more than the recommended amounts of red meat, poultry and dairy products; on the other hand, they were consuming less than the recommended amounts of whole grain CHO products, fish and seafood. In terms of nutrients, breast cancer patients in this study met the recommendations for protein, MUFA, cholesterol, added sugar and sodium intake, but they failed to meet other recommendations. For instance, they exceeded the recommended intakes of

total fats and SFA, and fell below the dietary recommendations of carbohydrates, fiber, linolenic acid, EPA and DHA.

B. Adherence to the Mediterranean Diet

Over-all adherence to the Mediterranean diet was low among breast cancer patients in Beirut, Lebanon since the scorings of most of the Mediterranean scores (3 out of 5) were below the median values.

In the scientific literature, little information can be found about adherence to the MD among breast cancer patients. Nevertheless when comparing our results to studies done on patients with other types of cancers, our results are in conformity with their findings. A study by Buckland et al. (2010) included 485,044 gastric adenocarcinoma patients from 10 European countries. Most patients, particularly, in the Netherlands, Germany, Sweden, Denmark and Norway, did not meet the median value for the rMED score (Buckland et al., 2009). In addition, our results are also comparable with results from a study done in Spain. Upon assessing the dietary intake of around 25,600 females from the EPIC cohort study, researchers also used the rMED score to measure adherence to the MD; participants in this Spanish study also did not meet the median value of rMED scoring (Buckland et al., 2009).

However, some results from previous studies show that the general population in other countries are adhering more to the MD than BC patients in our study. For example, after analyzing dietary intake of 4,391 female for 4.4 years, Trichopoulou et al. in 2003 showed that only 33% of Greek women included in the study scored less than the median value of the Mediterranean-Diet scale (Trichopoulou et al., 2003); whereas the majority of

BC patients, >50%, in our sample scored below the median. In another study that took place in Italy, Pelucchi et al. (2010) also assessed the adherence to the MD among the general population between 1991 and 2006. In 1991 women scored 4.61 ±1.77 on the 9 point MDS; in 2006 they scored 4.71 ±1.63. As a result, women in Italy seemed to be scoring, on average, higher than the median value of the MDS (Pelucchi et al., 2010). After recruiting 832 women in the SENECA cohort study from 19 European towns, the mean adherence to the MD among the participants was 4 out of the total 8 (Knoops et al., 2004).

Most countries in the Mediterranean region are developing countries and belong to the middle income socio-economical level, so populations in this area are prone to undergo changes in their dietary pattern (Belahsen et al., 2006). For the following reasons, these countries are undergoing a nutritional transition; Mediterranean nations are experiencing dietary Westernization, thus they are moving away from their traditional diet. The differences in adherence to the Mediterranean diet across countries could be either due to the fact that different studies use different dietary scores in order to assess adherence to the MD, or due to differences in the availability of Mediterranean foods from one country to the other. For example, European Mediterranean countries, as compared to other Mediterranean countries, have an increased availability of cereals, nuts and wine, as well as, lower availability of animal fats (Vareiro et al., 2009). Countries residing the Northern and Eastern Mediterranean coast, compared to other Mediterranean countries, have the lowest supply of F&V, olive oil, and fish/seafood along with the highest supply of meats (Gracia-Closas et al., 2005). In Lebanon, a difference in food availability was observed between the years 1969 and 2005; for instance, energy intake per person has increased from 2,330 Kcal/day to 3,180 Kcal/day, and fat supply has also doubled from 63g/day to 117g/day (Sibai et al., 2009).

The only score that showed relatively high adherence to the MD among BC patients in our study were PREDIMED. PREDIMED has two components that other score do not account for, and these might have caused an increase in the scoring as compared to other scores. It assesses intake of white meat over red meat and the consumption of sofrito, a sauce that includes tomatoes along with onions, garlic and olive oil. Due to cultural habits and beliefs, intake of red meat in Lebanon is low, compared to white meat, and intake of sofrito is high. Tomato sauce is a tradition in the Lebanese heritage, and it is basically used in most Lebanese stews. Moreover, white meat is much more affordable than red meat and more culturally acceptable, so most families differentially consumed white meat over the red one. In compliance to the later, a pricing difference truly exists between red meat and white meat; while 1 Kg of chicken costs around 4,000 LBP (less than 3$), 1 Kg of cow meat costs around 10,000 LBP (more than 6$) (Zaki et al., 2014). For example, when conducting the surveys at the philanthropic hospital, many patients stated that they enjoyed eating red meat over white meats; however, they couldn't afford it, so they ended up eating more white meats, specifically chicken.

As for the DDS, it doesn't measure adherence to the MD, but assesses the compliance to the USDA dietary recommendations. DDS can also be used to assess dietary quality and nutritional adequacy on an individual level. Our sample's mean scoring was 9 on the 10 point dietary score; this shows that BC patients in this study were eating a well-balanced variety of foods. A high DDS score has been linked to a lower risk of developing chronic diseases and over-all mortality. The DDS results of BC women in our study score were higher than results from a study that included women from the general population in Tehran; Tehranian women had a mean score of 6.01 (Mirmiran et al., 2013). Our results were also higher than values observed in the US; dietary diversity has decreased in the

United States; while in 1971-1975 46% of the participants in the National Health and Nutrition Examination Surveys met the median value for DDS, in 1999-2002 only 37% of participants met the median scoring (Kant et al., 2007).

C. Specific Foods from the Mediterranean Food Pyramid

Upon analyzing intakes of specific types of foods included in the Mediterranean dietary pyramid, our sample population only abided by the recommended intakes of fruits, vegetables and eggs. However, they exceeded the recommended intakes of dairy products, red meats and poultry; and consumed below the recommended amounts of fish and seafood.

Dietary results from this study will be compared to two major cohort studies done on breast cancer patients in the United Kingdom and the United states (Velentzis et al., 2011; Kroenke et al., 2013). Results will also be compared to other studies done on women from the general population in Lebanon and other countries in the Mediterranean region, specifically Spain and Greece (Nasreddine et al., 2005; Buckland et al., 2009; Trichopoulou et al., 2003).

Intakes of fruits and vegetables were similar to results from other studies found in the literature. In a study that examined dietary intakes of 1,893 BC patients from the Life After Cancer Epidemiology cohort study in the United states, participants consumed 2.1 servings of fruits per day (Kroenke et al., 2013). Our results were also similar to results published by Velentzis et al. (2011), who examined dietary intake of 1,560 BC patients in the United Kingdom from the year 1998 till 2007; participants in this study were recruited from 56 medical centers across the UK. When comparing our results to a

study done by Nasreddine et al. (2005) that measured food consumption among 234 urban Lebanese women; BC patients seemed to consume the same amount of vegetables, but greater amounts of fruits. As for vegetable intake, our results were also similar to intakes in Spain; however, it was much lower than values observed in Greece (Buckland et al., 2009, Trichopoulou et al., 2003).

Our sample, in both the private MC and the philanthropic hospital, seemed to be consuming more dairy products than BC patients in the US and the UK. While our sample was consuming about 2 servings of dairy per day, BC patients in the US and UK consumed around 1.7 and 1 serving of dairy per day respectively (Kroenke et al., 2013; Velentzis et al., 2011). Dairy products have a mixed effect on BC prognosis; while low-fat dairy consumption improves BC prognosis, high-fat dairy consumption increases mortality risk. However, in our study, the fat content of dairy products consumed by BC patients was not specified.

The Mediterranean dietary recommendations are low in animal protein sources and depend on legumes as the major contributor of dietary protein; a condition that was also not met by the majority of BC patients in this study. Over-all consumption of animal protein sources was >9 servings/week; most of this amount was from red meat and poultry. In comparison to Nasreddine et al. (2005), our sample was consuming more animal proteins, red meats, chicken and fish than other women in Beirut.

Intake of red meat among BC patients in this study was relatively high; for example, our sample consumed more than double the amount of red meat consumed by BC patients in the US (Kroenke et al., 2013). BC patients in the UK consumed even lower amounts; their intake of red and processed meats was 30g/day/1,000 Kcal consumed (Velentzis et al., 2011). Results from Spain also showed low intake of red meats

among the general female population, 56g of red meat per day; likewise, consumption of red meat among women in Greece was as low as 90g/day (Buckland et al., 2009, Trichopoulou et al., 2003). Poultry intake among BC patients is the UK was also lower than values observed among BC patients in this study, both at the private MC and the philanthropic hospital. BC patients in the UK consumed 1.8 servings of poultry per week, given a 1,600Kcal/day diet; a value still lower than half the amount our sample population consumed in a day, around 4 servings/day (Velentzis et al., 2011). Intake of fish and seafood products among our sample fell below the recommended amounts of intake; given than people living on the Mediterranean coast should have access to healthy/nutritious/diverse quantities and types of seafood. Although our sample's intake fell below the recommendations; fish intake in this study was higher than values observed in other countries. While BC patients in our study consumed around 100g of fish/seafood per day; fish intakes in Europe, Spain, and Greece were 23g/day, 27.3g/day and 19g/day respectively (Knoops et al., 2004; Buckland et al., 2009, Trichopoulou et al., 2003). This high fish intake among our sample helps improve their disease prognosis by inducing cell death and inhibiting tumor growth.

D. Detailed Dietary Composition

Our results on macro-nutrient composition are similar to Nasreddine's results; CHO accounted for 47% of total energy intake, proteins for 13.4% and fats for 39% among women residing in Beirut (Nasreddine et al., 2005). However, our sample demonstrated lower intakes of CHO and higher intakes of fats and protein than other Mediterranean countries; in 2007 the Middle Eastern countries' total dietary intake was composed of 63% CHO, 11% protein and 26% fats (Golzarand et al., 2012).

Our over-all sample's mean dietary fiber intake, 17.6g/day, remained lower than fiber intake among BC in the United States, 15g/day (Kroenke et al., 2013). Nevertheless, our sample was consuming amounts very similar to that observed among breast cancer patients in the United Kingdom, 16g of fiber/1,600 Kcal consumed (Velentzis et al., 2011). As a result, BC patients in our sample and the UK have a higher risk of mortality than BC patients in the US given that fiber improves BC prognosis by decreasing estrogen levels.

When comparing our results of MUFA and PUFA intakes to that o BC patients in the UK; our sample was consuming more MUFAs and PUFAs than patients in the United Kingdom (Velentzis et al., 2011). Similarly, our sample consumed more PUFAs than values documented in Spain and Greece, 6 and 12.6g of PUFA/day respectively (Buckland et al., 2009, Trichopoulou et al., 2003). However, intake of MUFA among BC patients in our study remained lower than values measured in Greece, 46.5g/day (Buckland et al., 2009, Trichopoulou et al., 2003).

E. Differences of dietary intake between the private MC and the philanthropic hospital

Dietary intake among breast cancer patients in our sample varied significantly across the recruitment sites. For instance, patients at the private MC seemed to be consuming significantly more fruits and vegetables as compared to patients at the philanthropic hospital. Our results are in conformity to the literature given that there is convincing evidence that people from high socioeconomic (HSE) levels tend to consume more fruits and vegetables than people from low socioeconomic (LSE) levels. After analyzing dietary intakes of more than 13,000 males and females in the US,

Dubowitz et al. (2008) showed that families from HSE levels (as measured by family income and educational attainment) consumed significantly more fruits and vegetables than participants that belonged to lower socioeconomic levels. A review by Irala-Estevez et al. (2000) also showed similar findings; upon reviewing evidence from 11 studies and 7 countries, they found a positive association between education/occupation and F&V intake.

While some studies might show results that are contrary to ours, other studies confirm our findings that there exists a positive association between fiber intake and socioeconomic level. For instance Barquera et al. (2003), and in a study that included on 2,630 women in Mexico, showed that women that belonged to the HSE group consumed less fiber than women that belonged to the LSE group. However, another study that analyzed fiber intake among 322 participants from Palestine showed that those who belonged to the HSE group consumed significantly more fiber, 20.6 g per day, compared to participants from the LSE group, 16.7g/day (Shahar et al., 2005).

Breast cancer patients at the private MC were consuming significantly more calories than patients at the philanthropic hospital. This is in line with other studies; such as Barquera's study; women from the HSE group were consuming 1,511 kcal per day, as compared to an intake of 1456 kcal per day among women from the LSE group (Barquera et al., 2003).

F. Determinants of the Adherence to the MD

This difference in adherence to the Mediterranean diet between the 2 recruitment sites could be due to differences in the characteristics of these distinct groups. BC patients at the private medical center were significantly younger, more likely to be mar-

ried, more educated and employed, and had higher levels of monthly income. All of the factors mentioned above may explain the differential level of adherence to the MD between the private medical center and the philanthropic hospital.

Our results show an increased adherence to the MD as BC patients get more educated and earn a higher monthly income. Education and monthly income were significantly associated with almost all the calculated scores. Similar results were observed in a study that examined adherence to the MD, between the years 1991 and 2006, among 1,969 Italian women. In the later study, education was directly associated with MDS; people with more than 12 years of education were more likely to adhere to the MD, compared to women with less than 7 years of education (Pelucchi et al., 2010). However, a study done on gastric adenocarcinoma patients showed opposite results; women with a lower educational level seemed to adhere more to the rMED scoring (Buckland et al., 2010).

Oppositely, age was inversely associated with all the Mediterranean dietary scores, except with the dietary diversity score, DDS. Similar to our results, older gastric adenocarcinoma patients, compared to younger patients, seemed to adhere less to the rMED dietary score (Buckland et al., 2010). However, Pelucchi et al. (2010) showed that age was directly proportional to adherence to the MD. Italian women between the ages 55 and 64, compared to those aged less than 45 years, scored the highest values on the Mediterranean Dietary Score, MDS.

Another finding of our study showed that employed patients, compared to non-employed patients, were less likely to adhere to the PREDIMED score. Employed people usually work long hours; as a result, people usually have a quick sandwich at work or order delivered foods. These delivered foods could range from something

healthy/Mediterranean such as grilled fish/chicken, to something unhealthy/Westernized such as fast foods. Additionally, people may munch on unhealthy snacks during working hours, such as products from the readily available vending machines (Chips, chocolate, and salted crackers…).

A new association, which did not exist in the univariate analysis, emerged upon applying multivariate linear regressions. Better over-all health status was positively associated with the PREDIMED score. Given that our study is of a cross-sectional design, it cannot be determined whether good health is causing increased adherence to the MD, or, given that patients are adhering to the MD, they have a better health.

CHAPTER V

STRENGTHS, LIMITATIONS AND CONCLUSIONS

A. Strengths and Limitations

A selection bias might have jeopardized the representativeness of the sample population and the external validity of the results. Nevertheless, subjects were recruited from two major healthcare centers in Beirut, Lebanon; one representing patients from the high socio-economic level; whereas the other, representing patients from the low socio-economic level. Characteristics of patients in these two hospitals are similar to all BC patients in the Lebanese capital, Beirut. For example, the mean age of participants in our sample is very similar to the mean age of BC patients in Lebanon, 53 years. To further improve the sample population, participants included BC patients receiving chemotherapy, outpatients; as well as, newly diagnosed cases of BC and patients at advanced stages of the disease.

Information bias in the classification of the exposure, breast cancer, was minimized since diagnosis with BC was determined by the physicians' medical records. However, misclassification of the outcome, adherence to the Mediterranean diet, could result from recall biases in the 24 hr. recalls and dietary questionnaire, data entry biases or interviewer biases. Data entry biases might result if the person in charge of entering the data was differentially entering the information on the software system, SPSS and Nutri-Pro. Interviewer biases could also result, since neither the subjects nor the interviewers were blinded. However, the two researchers who were responsible for

conducting the interviews and entering the data were licensed dietitians, and they underwent standardized and in-depth training sessions in order to avoid any biases that might happen in the process. As a result, interviewer and data entry biases are not likely to exist. On the other hand, usually diseased patients remember more what they eat, this might cause a recall bias in a study; nevertheless, upon interviewing the patients for dietary information, interviewers used the 5-step dietary interview multiple pass in order to aid participants in remembering what they ate. Moreover, this multiple pass has been used by the USDA and validated for accuracy against the gold standard. In addition, 24 hr. recalls are used to estimate an individual's dietary intake of various nutrients since it denoted the actual intake; it also highly specific and of an open ended format. People exhibit day-to-day dietary variation, given that no one eats the same exact foods every day. Even if a person ate the same foods, they don't all prepare/cook the foods in the same manner, and cooking methods affect the food's dietary composition. The positive side is that, true people don't eat the same foods every day, but their over-all dietary intake/composition are somehow consistent from day-to-day. Researchers and dietary experts say that: "A central feature of the dietary intake of free living individuals is variation from day to day superimposed on an underlying consistent pattern". Caloric intake exhibits the least variation from one day to the other, followed by macro-nutrient intake and finally, micro-nutrient intake varies the most.

Given that our study is of a cross-sectional design, the main limitation is that temporality or causality cannot establish; however, in some analysis this was not the case. For example, monthly income was positively associated with adherence to the MD; in this case, one can say that increased monthly income causes an individual to adhere more to the MD, given that the adherence to the MD does not affect monthly

income. Moreover, this study design is the best way to measure the prevalence of adherence to the MD among BC patients in Beirut, Lebanon given that exposure and outcome are measured at the same time.

B. Conclusion

This is the first study to describe adherence to the Mediterranean diet and its determinants among breast cancer patients. Most BC patients in this study were married, educated, and of middle income families. Our results show that BC patients are moving away from their traditional MD and following a more Westernized diet; however, patients from the high socio-economic level (private MC) seem to be better health aware and adhere more to the MD. A possible reason for this low over-all adherence could be due to low public awareness concerning the health benefits of the Mediterranean diet. Another reason could be dietary globalization and the westernized effect; as well as, climate changes that may cause a decrease in the availability of the traditional Mediterranean foods. This low adherence to the MD could put BC patients in Beirut, Lebanon at various risks; such as, developing comorbidities and increasing the risk of BC related/over-all mortality. Physicians and health care providers could play a role in increasing adherence to the MD by recommending the Mediterranean diet as a form of a complementary alternative medicine for their BC patients to improve disease prognosis. Although many publications show that adherence to the healthy/Mediterranean diet improves the prognosis of BC patients, most published studies investigate dietary habits pre-diagnostically rather than post-diagnostically. This study could fill the following gap in literature, and may be a corner stone for future studies to build on. Additionally, this study could alert physicians, decisions makes, the

Lebanese Ministry of Public Health and dietitians to develop awareness campaigns in order to encourage the community as a whole to back to eating their traditional/healthy Mediterranean diet.

TABLES

Table 1: Socio-demographic and disease-related characteristics of the study population (n=182)

Characteristics	Overall	Private Medical Center n (%)*	Philanthropic hospital n (%)	P- Value
Age (years)	53.78 ± 9.93	51.3 ± 9.70	58.1 ± 8.85	**0.000**
Marital status				
Single	36 (19.8)	14 (12.1)	22 (33.3)	**0.001**
Married	146 (80.2)	102 (87.9)	44 (66.6)	
Educational level				
High school or less	129 (70.9)	76 (65.5)	53 (80.3)	**0.035**
University degree	53 (29.1)	40 (34.5)	13 (24.2)	
Employment status				
Unemployed	130 (71.4)	75 (64.7)	55 (42.3)	**0.007**
Employed	52 (28.6)	41 (35.3)	11 (16.7)	
Crowding index				
<1	95 (52.5)	60 (51.7)	35 (53.0)	0.865
≥1	87 (47.8)	56 (48.3)	31 (47.0)	
Type of health insurance				
Private	44 (24.2)	40 (34.5)	4 (6.1)	**0.000**
Public	138 (75.8)	76 (65.5)	62 (93.9)	
Monthly income				
<500$	36 (19.9)	8 (7.0)	28 (43.1)	**0.000**
500-1000$	74 (40.9)	52 (44.8)	22 (33.8)	
>1000$	71 (39.2)	56 (48.2)	15 (23.1)	
Duration of breast cancer				
< 1 year	71 (39.4)	51 (44.0)	20 (31.2)	0.239
1-5 years	66 (36.7)	40 (34.5)	26 (40.6)	
>5 years	43 (23.9)	25 (21.5)	18 (28.1)	
Family history of breast cancer				
No	105 (58.3)	67 (57.8)	38 (59.4)	0.833
Yes	75 (41.7)	49 (42.2)	26 (40.6)	
State of breast cancer				
Early stage	99 (55.0)	62 (53.4)	37 (57.8)	**0.002**
Locally advanced	44 (24.4)	22 (19.0)	22 (34.4)	
Metastatic	37 (20.6)	32 (27.6)	5 (7.8)	
Adherence to doctor's recommendations				
No	12 (6.7)	9 (7.8)	3 (4.7)	0.429
Yes	168 (93.3)	107 (92.2)	61 (95.3)	
Current state of health				
Poor/very poor	31 (17.2)	21 (18.1)	10 (15.6)	
Fair	65 (36.1)	54 (46.6)	11 (17.2)	**0.000**
Good/ very good	84 (46.7)	41 (35.3)	43 (67.2)	

Table 2: Adherence to the Mediterranean diet in the sample population (n= 164)

Mediterranean Scores	**Overall mean ±sd.**	**Private Medical Center mean ±sd.**	**Philanthropic hospital mean ± sd.**	**P- Value**
MS	24.69 ± 5.55	25.95 ± 5.69	22.86 ± 4.81	**0.001**
MSDPS	31.34 ± 8.49	32.26 ± 8.32	30.09 ± 8.63	0.123
CPMDI	5.67 ± 1.31	5.96 ± 1.25	5.22 ± 1.29	**0.000**
PREDIMED	6.06 ± 1.81	6.62 ±1.87	5.27 ± 1.38	**0.000**
DDS	9.09 ± 1.19	9.38 ± 0.95	8.68 ± 1.38	**0.000**

Table 3: Dietary intake of various foods (Mediterranean pyramid) by site in the study population (n=166)

	Overall mean ±sd	Private Medical Center mean ±sd	Philanthropic hospital mean ±sd	P- Value
Servings per day				
Whole grains (1 serving=30g)	1.38 ±2.63	1.28 ±2.58	1.56 ±2.74	0.489
Fruits (1 serving= 1 medium)	3.72 ±2.32	4.44 ±2.37	2.51 ±1.62	**0.000**
Vegetables (1 serving= ½ cup)	2.88 ±1.58	3.32 ±1.59	2.15 ±1.28	**0.000**
Dairy (1 serving=1 cup milk, ½ cup yoghurt, 50g cheese)	2.52 ±1.39	2.62 ±1.42	2.34 ±1.31	0.189
Olive oil (1 serving=1 Tbsp.)	2.02 ±1.69	2.67 ±1.73	0.95 ±0.91	**0.000**
Servings per week				
Red Meat (1 serving=60g)	3.97 ±3.87	3.98 ±3.79	3.96 ±4.03	0.989
Poultry (1 serving=60g)	3.93 ±2.81	4.09 ±2.41	3.67 ±3.40	0.373
Fish and seafood (1 serving=60g)	1.68 ±2.49	1.89 ±2.26	1.32 ±2.83	0.142
Eggs (1 serving=1 egg)	1.27 ±1.38	1.41 ±1.54	1.03 ±1.00	**0.046**

Table 4a: Energy and nutrient intake by site in the study population (n= 180)

	Overall mean ±SE.	**Private Medical-Center mean ±SE.**	**Philanthropic Hospital mean ±SE.**	**P- Value**
Kcalories (kcal)	1578.08 ± 42.46	1658.0 ± 50.91	1440.04 ± 72.77	**0.013**
Carbohydrate (% of total Kcal)	47.08 ± 0.78	48.56 ± 0.92	44.52 ± 1.35	**0.012**
Protein (% of total Kcal)	14.81 ± 0.35	14.87 ± 0.40	14.71 ± 0.66	0.818
Total Fat (% of total Kcal)	40.09 ± 0.74	38.66 ± 0.86	42.56 ± 1.31	**0.010**
SFA (% of total Kcal)	9.71 ± 0.31	9.41 ± 0.38	10.23 ± 0.53	0.200
TFA (% of total Kcal)	0.31 ± 0.03	0.30 ± 0.03	0.32 ± 0.05	0.668
MUFA (g/ day)	26.91± 0.54	28.85 ± 1.97	27.00 ± 2.46	0.964
PUFA (g/ day)	15.84± 0.33	15.85 ± 0.98	15.82 ± 1.38	0.986
PUFA, Linoleic Acid (g/day)	14.70 ± 0.78	14.63 ± 0.96	14.82 ± 1.35	0.908
PUFA, Linolenic Acid (g/day)	0.74± 0.03	0.75 ± 0.04	0.72 ± 0.05	0.654
PUFA, EPA and DHA (g/day)	0.074 ± 0.02	0.10 ± 0.04	0.03 ± 0.01	0.089
Cholesterol (mg/day)	151.50 ± 11.14	162.7 ± 15.07	132.16 ± 15.54	0.187
Dietary Fiber (g/day)	17.66 ± 0.88	19.26 ± 1.19	14.90 ± 1.17	**0.016**
Added Sugar (g/day)	63.54± 2.63	72.49 ± 3.28	48.08 ± 3.72	**0.000**
Added Sugar (% of total Kcal)	16.29 ± 0.58	18.00 ± 0.77	13.32 ± 0.74	**0.000**
Sodium (mg/day)	1748.04 ± 71.07	1872 ± 89.50	1611.58 ± 115.90	0.145
Lycopene (µg/ day)	2884.36 ± 288.94	3435.11 ± 382.37	1933.08 ± 407.43	**0.008**
Calcium (mg/ day)	582.63 ± 23.09	638.56 ± 28.64	486.03 ± 36.26	**0.001**
Iron (mg/ day)	9.56 ± 0.46	10.53 ± 0.62	7.88 ± 0.63	**0.006**
Folate (µg/ day)	265.52 ± 14.65	300.62 ± 20.27	204.88 ± 16.95	**0.000**

Table 4b: Dietary adequacy in the study population (n= 180)

	Overall n (%)	Private Medical-Center n (%)	Philanthropic Hospital n (%)	P-Value
Carbohydrate (% of total Kcal)				0.326
Lower than AMDR	77 (42.8)	44 (38.6)	33 (50.0)	
Within AMDR	93 (51.7)	63 (55.3)	30 (45.5)	
Exceeds AMDR	10 (5.6)	7 (6.1)	3 (4.5)	
Protein (% of total Kcal)				0.165
Lower than AMDR	23 (12.8)	14 (12.3)	9 (13.6)	
Within AMDR	155 (86.1)	100 (87.7)	55 (83.3)	
Exceeds AMDR	2 (1.1)	0 (0.0)	2 (3.0)	
Total fat (% of total Kcal)				0.324
Lower than AMDR	4 (2.2)	3 (2.6)	1 (1.5)	
Within AMDR	46 (25.6)	33 (28.9)	13 (19.7)	
Exceeds AMDR	130 (72.2)	78 (68.4)	52 (78.8)	
SFA				0.136
<= 7% of total energy intake	47 (26.1)	34 (29.8)	13 (19.7)	
>7% of total energy intake	133 (73.9)	80 (70.2)	53 (80.3)	
MUFA				0.090
<= 20% of total energy intake	143 (79.4)	95 (83.3)	48 (72.7)	
> 20% of total energy intake	37 (20.6)	19 (16.7)	18 (27.3)	
PUFA				0.068
<= 10% of total energy intake	124 (68.9)	84 (73.7)	40 (60.6)	
>10% of total energy intake	56 (31.1)	30 (26.3)	26 (39.4)	
PUFA, Linoleic Acid				0.960
Lower than recommendation	72 (40.0)	45 (39.5)	27 (40.9)	
Within recommendation (10-12g/day)	12 (6.7)	8 (7.0)	4 (6.1)	
Higher than recommendation	96 (53.3)	61 (53.5)	35 (53.0)	
PUFA, Linolenic Acid				0.746
Lower than recommendation	117 (65.0)	72 (63.2)	45 (68.2)	
Within recommendation (0.8-1.1g/day)	35 (19.4)	24 (21.1)	11 (16.7)	
Higher than recommendation	28 (15.6)	18 (15.8)	10 (15.2)	
PUFA, EPA and DHA				0.196
Lower than recommendation	172 (95.6)	108 (94.7)	64 (97.0)	
Within recommendation (0.3-0.5g/day)	1 (0.6)	0 (0.0)	1 (1.5)	
Higher than recommendation	7 (3.9)	6 (5.3)	1 (1.5)	
Cholesterol				0.910
<= 200 mg/ day	141 (78.3)	89 (78.1)	52 (78.8)	
>200 mg/ day	39 (21.7)	25 (21.9)	14 (21.2)	
Total Fiber				0.400
Lower than recommendation	130 (72.2)	81 (71.1)	49 (74.2)	
Within recommendation 20-30 g/ day	29 (16.1)	17 (14.9)	12 (18.2)	
Exceeds recommendation	21 (11.7)	16 (14.0)	5 (7.6)	
Total added sugar				**0.002**
<= 25% of total Kcal	160 (88.9)	95 (83.3)	65 (98.5)	
> 25% of total Kcal	20 (11.1)	19 (16.7)	1 (1.1)	
Sodium				0.137
<= 2,300 mg/day	139 (77.2)	84 (73.7)	55 (83.3)	
> 2,300 mg/day	41 (22.8)	30 (26.3)	11 (16.7)	

Table 5: Univariate linear regression analysis of Mediterranean scores and the socio- demographics of the sample population (n= 164)

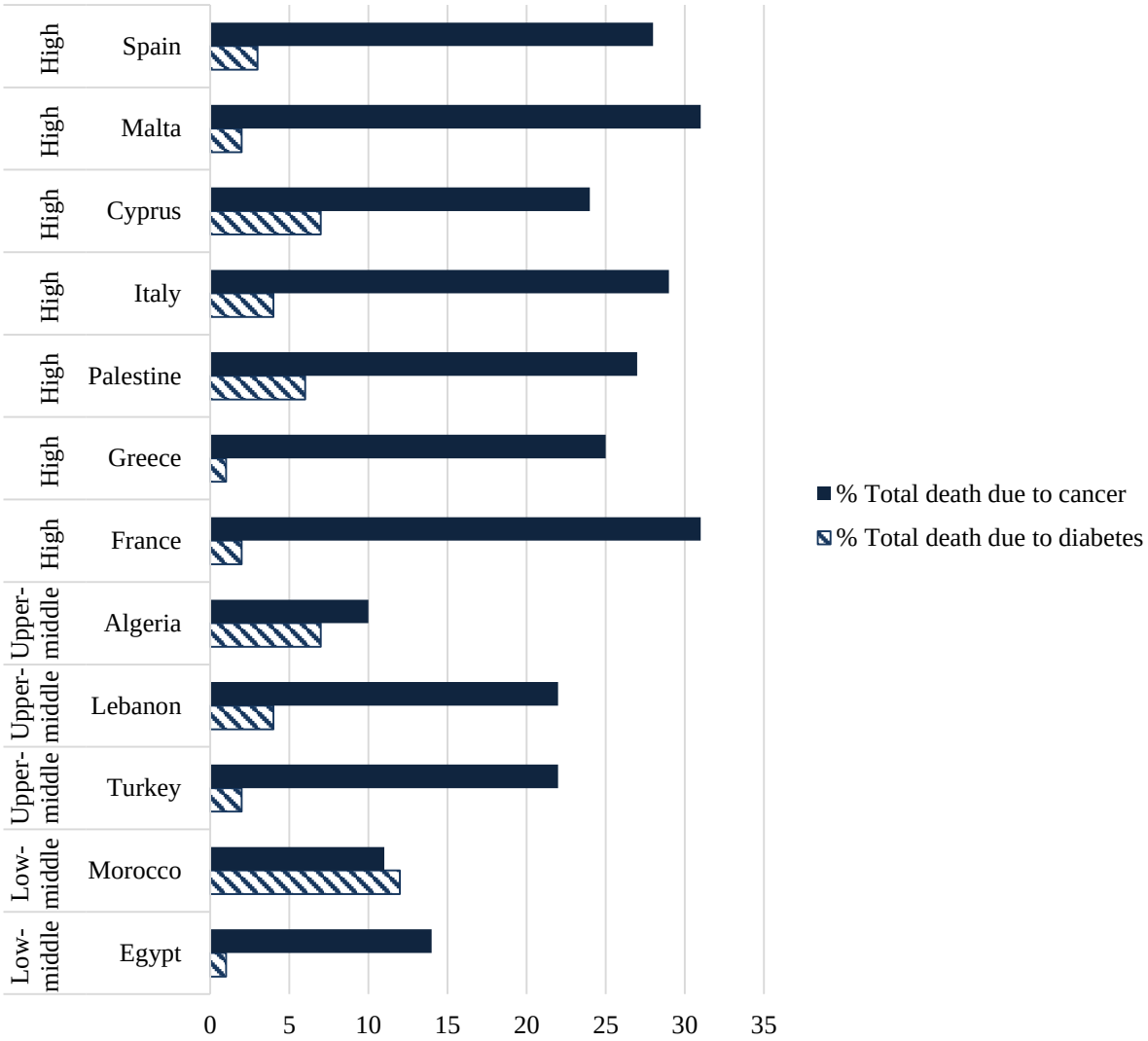
Socio- demographics	MS, β 95% CI	MSDPS, β 95% CI	CPMDI, β 95% CI	PREDIMED, β 95% CI	DDS, β 95% CI
Increasing age	**-0.184 (-0.008, -0.001)**	**-0.307 (-0.014, -0.005)**	**-0.221 (-0.010, -0.002)**	**-0.265 (-0.013, -0.003)**	-0.140 (-0.007, 0.000)
Married versus single	0.129 (-0.017, 0.168)	0.040 (-0.094, 0.154)	**0.156 (0.002, 0.205)**	0.146 (-0.009, 0.231)	0.059 (-0.065, 0.139)
Increasing educational level	**0.182 (0.013, 0.176)**	**0.193 (0.023, 0.238)**	**0.211 (0.035, 0.216)**	**0.218 (0.043, 0.260)**	0.027 (-0.076, 0.107)
Employed versus non- employed	-0.096 (-0.134, 0.033)	-0.139 (-0.210, 0.015)	-0.078 (-0.138, 0.045)	**-0.256 (-0.283, -0.069)**	-0.016 (-0.103, 0.084)
Increasing crowding index	0.097 (-0.029, 0.120)	**0.171 (0.007, 0.202)**	**0.163 (0.005, 0.170)**	0.114 (-0.028, 0.170)	0.147 (-0.006, 0.156)
Public versus private insurance	-0.126 (-0.158, 0.018)	0.059 (-0.161, 0.075)	-0.128 (-0.180, 0.017)	-0.077 (-0.180, 0.062)	-0.116 (-0.173, 0.027)
Increasing monthly income	**0.195 (0.012, 0.111)**	**0.249 (0.037, 0.167)**	**0.277 (0.046, 0.154)**	**0.207 (0.021, 0.153)**	**0.184 (0.009, 0.116)**
Increasing duration of BC	0.051 (-0.032, 0.062)	0.009 (-0.060, 0.067)	0.076 (-0.027, 0.080)	-0.048 (-0.081, 0.044)	0.103 (-0.019, 0.087)
Family history of BC versus no history	0.065 (-0.045, 0.108)	0.112 (-0.032, 0.173)	0.042 (-0.063, 0.109)	0.081 (-0.050, 0.152)	-0.045 (-0.109, 0.061)
Metastatic versus early stages	-0.020 (-0.053, 0.041)	-0.033 (-0.076, 0.050)	-0.067 (-0.075, 0.030)	0.043 (-0.046, 0.079)	-0.113 (-0.089, 0.016)
Adherent to doctor's recommendations versus none adherent	0.076 (-0.075, 0.213)	0.034 (-0.152, 0.230)	0.034 (-0.125, 0.195)	0.066 (-0.112, 0.266)	0.026 (-0.134, 0.185)
Better overall health status	0.027 (-0.042, 0.059)	0.002 (-0.067, 0.069)	0.103 (-0.019. 0.093)	0.130 (-0.012, 0.120)	-0.027 (-0.064, 0.046)

Table 6: Multivariate linear regression analysis of Mediterranean scores and the socio-demographics of the sample population (n= 164)

Socio- demographics	MS, β 95% CI	MSDPS, β 95% CI	CPMDI, β 95% CI	PREDIMED, β 95% CI	DDS, β 95% CI
Increasing age	-0.082 (-0.006, 0.002)	**-0.207 (-0.012, -0.001)**	-0.097 (-0.007, 0.002)	-0.124 (-0.009, 0.002)	-0.077 (-0.007, 0.003)
Married versus single	0.029 (-0.090, 0.125)	-0.142 (-0.250, 0.031)	0.010 (-0.106, 0.120)	0.068 (-0.082, 0.183)	-0.069 (-0.164, 0.074)
Increasing educational level	0.090 (-0.053, 0.147)	0.058 (-0.091, 0.170)	0.098 (-0.049, 0.167)	0.085 (-0.069, 0.184)	-0.084 (-0.161, 0.064)
Employed versus non- employed	-0.054 (-0.130, 0.074)	-0.033 (-0.158, 0.112)	-0.006 (-0.112, 0.105)	**-0.197(-0.259, -0.007)**	-0.025 (-0.130, 0.100)
Increasing crowding index	0.092 (-0.042, (0.128)	0.147 (-0.020, 0.201)	0.141 (-0.015, 0.168)	0.084 (-0.055, 0.158)	0.144 (-0.021, 0.169)
Public versus private insurance	-0.103 (-0.151, 0.038)	-0.013 (-0.134, 0.116)	-0.085 (-0.157, 0.048)	-0.035 (-0.147, 0.096)	-0.119 (-0.185, 0.035)
Increasing monthly income	0.122 (-0.026, 0.102)	0.235 (0.013, 0.181)	**0.219 (0.012, 0.148)**	0.106 (-0.037, 0.124)	0.191 (-0.004, 0.136)
Increasing duration of BC	0.115 (-0.019, 0.087)	0.090 (-0.033, 0.103)	0.125 (-0.014, 0.099)	0.043 (-0.048, 0.082)	0.137 (-0.014, 0.105)
Family history of BC versus no history	0.093 (-0.034, 0.124)	0.107 (-0.035, 0.171)	0.059 (-0.051, 0.117)	0.101 (-0.036, 0.164)	-0.034 (-0.106, 0.070)
Metastatic versus early stages	0.076 (-0.029, 0.073)	0.043 (-0.051, 0.084)	0.003 (-0.054, 0.056)	0.111 (-0.022, 0.108)	-0.047 (-0.074, 0.043)
Adherent to doctor's recommendations versus none adherent	0.073 (-0.082, 0.214)	0.031 (-0.153, 0.225)	0.013 (-0.145, 0.172)	0.100 (-0.069, 0.302)	-0.004 (-0.169, 0.162)
Better overall health status	0.035 (-0.40, 0.062)	0.036 (-0.051, 0.081)	0.123 (-0.011, 0.099)	**0.164 (0.003, 0.132)**	-0.018 (-0.062, 0.050)

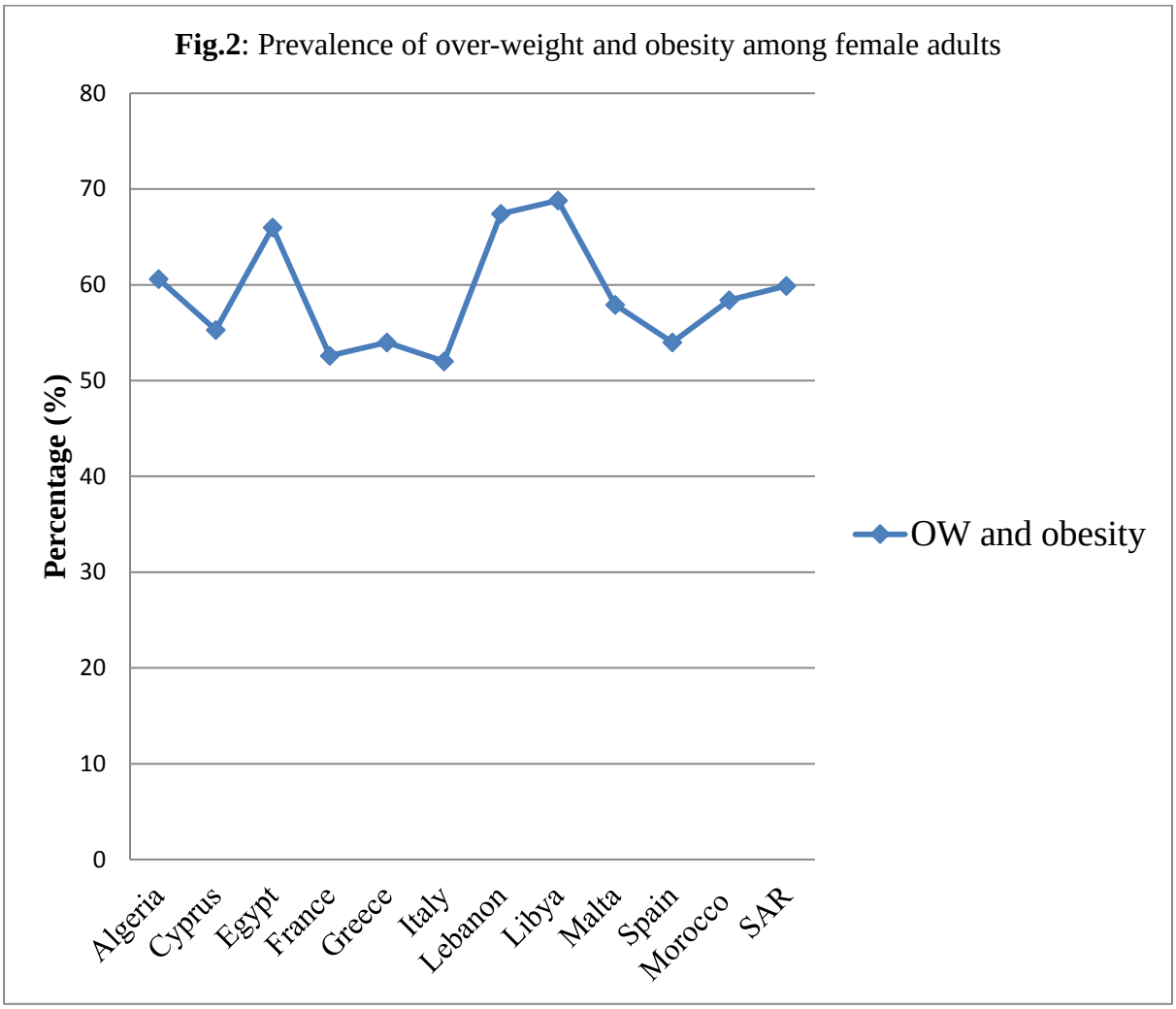
FIGURES

Fig. 1: Percentages of total deaths due to diabetes and cancer among Mediteranean countries according to income groups-2014



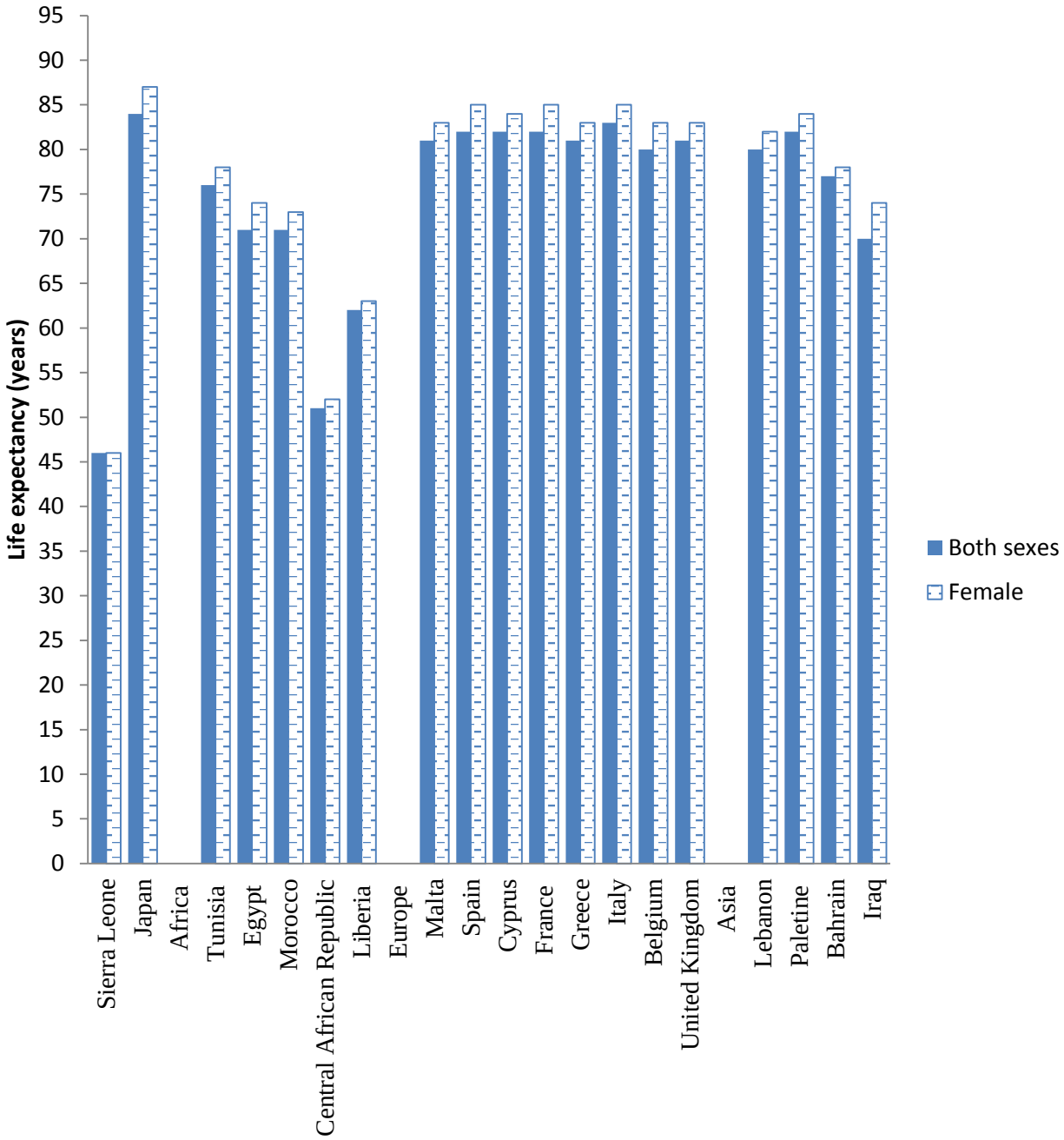
Reference: WHO. (2014). *Noncommunicable diseases country profiles 2014*. Geneva, Switzerland: World Health Organization.

Fig.2: Prevalence of over-weight and obesity among female adults



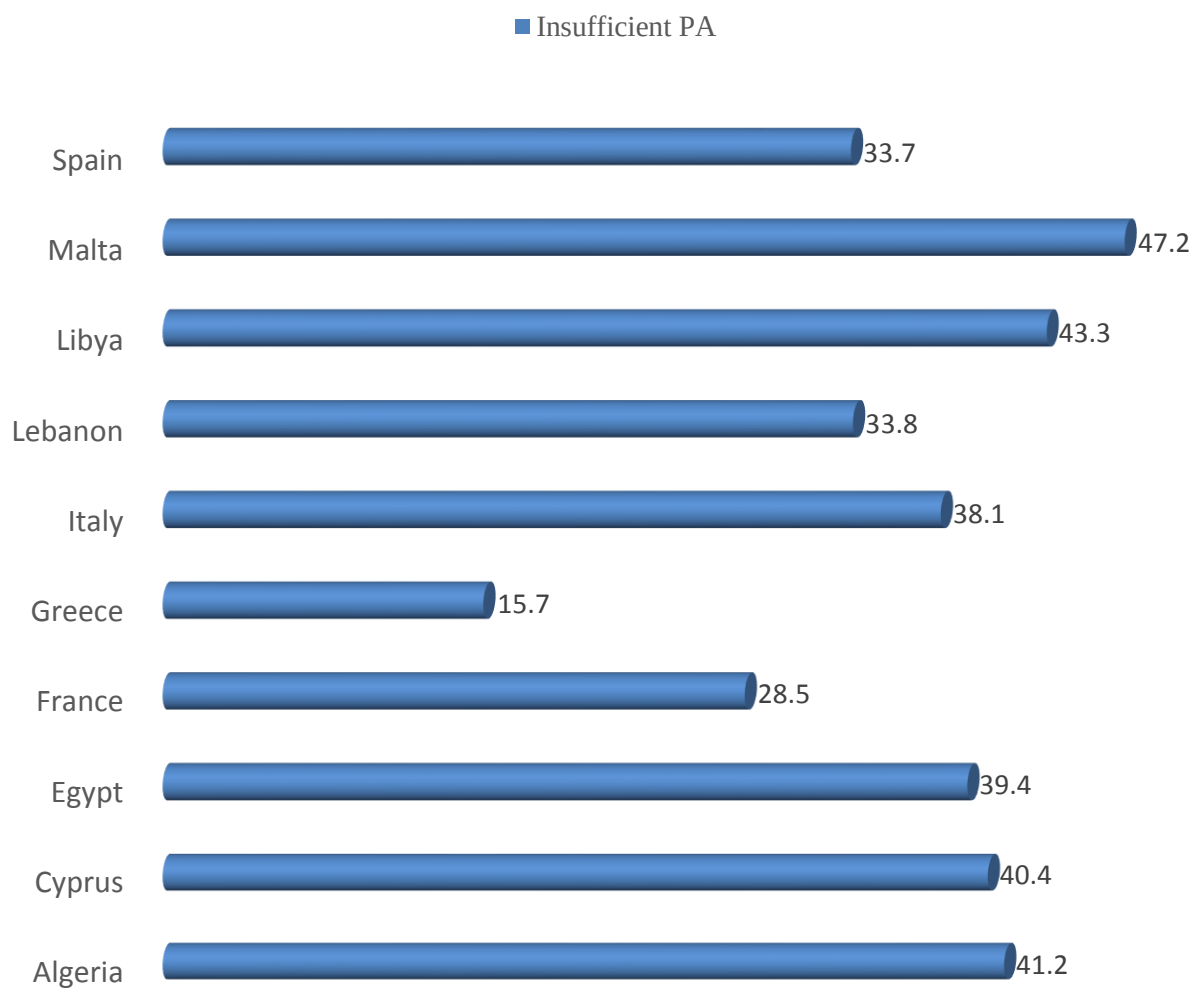
Reference: WHO. (2014). *Obesity and overweight.* Retrieved July/21, 2014, from http://www.who.int/mediacentre/factsheets/fs311/en/

Fig. 3: Life expectancy at birth for both sexes and females among various countries- 2012



Reference: WHO. (2014). *World health statistics 2014- Part3: Global health indicators*.

Fig.4: Prevalence of age-adjusted insufficient physical activity among female adults (%)



Reference: WHO. (2014). *Global status report on non-communicable diseases 2014*. Switzerland

APPENDIX A
ETHICAL APPROVAL LETTER FORM FROM THE INSTITUTIONAL REVIEW BOARD – SOCIAL AND BEHAVIORAL SCIENCES AT THE AMERICAN UNIVERSITY OF BEIRUT

APPROVAL OF RESEARCH AMMENDMENT

September 11, 2013

Dr. Farah Naja
American University of Beirut
01-350000 ext 4504
fn14@aub.edu.lb

Dear Dr. Naja,

On September 11, 2013, the IRB reviewed the following protocol:

Type of Review:	Modification, Expedited
Project Title:	Prevalence and determinants of the use of complementary and alternative medicine among breast cancer patients
Investigator:	Farah Naja
IRB ID:	NUT.FN.11
Funding source:	None
Documents reviewed:	Letter received September 9, 2013, amended: IRB application, proposal, English and Arabic versions of the consent documents (versions received September 9, 2013), diet questionnaire (English and Arabic versions received September 9, 2013), 24 hour dietary recall (English and Arabic versions received September 9, 2013), and the manual for calculation of diet adherences scores.

The IRB approved adding a secondary objective to this study to investigate the adherence to the Mediterranean diet in breast cancer patients from September 11, 2013 to June 13, 2014 inclusive. Before April 13,2014 or within 30 days of study close, whichever is earlier, you are to submit a completed "FORM: Continuing Review Progress Report" and required attachments to request continuing approval or study closure.

If continuing review approval is not granted before the expiration date of June 13, 2014 approval of this research expires on that date.

Please find attached the stamped approved documents:

1. Proposal (version received September 9, 2013),
2. English and Arabic versions of the consent documents (version received September 9, 2013),
3. Diet questionnaire (English and Arabic versions received September 9, 2013),
4. 24 hour dietary recall (English and Arabic versions received September 9, 2013),
5. The manual for calculation of diet adherences scores (version received September 9, 2013).

Kindly, use copies of these documents to document consent.

Thank you

The American University of Beirut and its Institutional Review Board, under the institution's Federal Wide Assurance with OHRP, comply with the Department of Health and Human Services (DHHS) Code of Federal Regulations for the Protection of Human Subjects ("The Common Rule") 45CFR46, subparts A, B, C, and D, with 21CFR56; and operate in a manner consistent with the Belmont report, FDA guidance, Good Clinical Practices under the ICH guidelines, and applicable national/local regulations.

Sincerely,

Michael Clinton, PhD
IRB Vice Chairperson
Social & Behavioral Sciences

Cc: Fuad Ziyadeh, MD, FACP, FASN
Professor of Medicine and Biochemistry
Chairperson of the IRB

Ali K. Abu-Alfa, MD, FASN
Professor of Medicine
Director, Human Research Protection Program

Template Revision: September 11, 2013

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APPENDIX B
CONSENT FORM

Prevalence and Determinants of the use of complementary and alternative medicine (CAM) among Breast Cancer Patients in Lebanon

Consent Form

Investigator: Dr. Farah Naja
Address: American University of Beirut (AUB)- Hamra-Beirut, Lebanon
Phone: 01-350000 (ext. 4504)
Setting: Basile Cancer Institute at AUBMC

You are being asked to participate in a research study conducted at the American University of Beirut-Medical Center. Please take time to read the following information carefully before you decide whether you want to take part in this study or not. Feel free to ask us if you need more information or clarification about what is stated in this form and the study as a whole.
The main objective of this study is to assess the prevalence, determinants, modes of use and disclosure to physicians of Complementary and Alternative Medicine (CAM) among breast cancer patients in Lebanon and to assess the adherence of your dietary intake to the Mediterranean diet.

You are eligible for our research study only if you are of Lebanese nationality, report a diagnosis of breast cancer for a minimum of 2 months prior to the study, and are attending the Basile Cancer Institute at AUBMC for breast cancer treatment or the Makassed General Hospital (MGH). The charge nurse will introduce the study for the patients, after which the research assistant will approach the patients, further explain the study and obtain consent from interested participants for the interview and data collection to follow.
If you are eligible for this study and agree to be a participant, you are asked to complete a survey questionnaire about socio demographic factors such as age, sex, marital status, household income, educational level, symptoms and treatment of of breast cancer, and the type and frequency of complementary and alternative medicine use as well as a diet questionnaire and one a 24-hour recall. A total of 377 breast cancer patients will be recruited for inclusion in this study. The survey needs around 15 minutes to be conducted. The timing of the interview (whether before, after or during the treatment) will be decided by the patient, in a way not to compromise nor delay the medical care and to ensure that the patient is not in a state of discomfort because of the medical treatment.

Your participation in this survey questionnaire is completely voluntary but it is very important to us. If you agree to be part of our study you will be helping us find out the prevalence and the determinants of complementary and alternative medicine use among Lebanese breast cancer patients.

There are no other expected risks to you for helping us with this study. There are also no expected benefits for you either. There will be no loss in health services benefits in case patient refuses to participate and that the participant can stop answering questions at any point in time or refuse to answer any question.

If you agree to participate in this research study, the information will be kept confidential under lock and key. The researcher will not share the patient information with the health care provider. Also, the researcher will not have access to the participant medical records. All information will be collected

anonymously (i.e.: with no name); however, a code on the questionnaire could be linked to the consent form and only the principal investigator has access to that link.

In case of any adverse event as a result of the study, there will be no compensation to cover such expenses.

Investigator's Statement:

I have reviewed, in detail, the informed consent document for this research study with _____ _____ (name of patient) the purpose of the study and its risks and benefits. I have answered to all the patient's questions clearly.

I will inform the participant in case of any changes to the research study.

_____ _____
Name of Investigator or designee Signature

_____ _____
Date Time

Patient's Participation:

I have read and understood all aspects of the research study and all my questions have been answered. I voluntarily agree to be a part of this research study and I know that I can contact Dr. Farah Naja at 01-350 000 ext. 4504 or any of his/her designee involved in the study in case of any questions. If I feel that my questions have not been answered, I can contact the Institutional Review Board for human rights at 01-350 000 ext. 5443. I understand that I am free to withdraw this consent and discontinue participation in this project at any time, even after signing this form, and it will not affect my care or benefits. I know that I will receive a copy of this signed informed consent.

_____ _____
Name of Patient Signature

_____ _____
Date Time

_____ _____
Witness's Name Witness's Signature
(If patient, representative or parent do not read or is visually impaired)

_____ _____
Date Time

Would you allow us to contact you for future research?
□ Yes □ No
If yes, please provide us with your phone number: _____

انتشار استخدام المتممات والبدائل الطبية لدى مرضى سرطان الثدي في لبنان

وثيقة موافقة المشاركة في الدراسة

الباحث: د. فرح نجا
العنوان: الجامعة الاميركية في بيروت- حمرا - بيروت- لبنان
هاتف: 01-350000 (قسم 4504)
مقر إجراء البحث: مركز باسيل للأورام السرطانية في مستشفى الجامعة الاميركية في بيروت

المطلوب منكم المشاركة بدراسة في المركز الطبي في الجامعة الاميركية في بيروت. يرجى أخذ الوقت الكافي لقراءة المعلومات التالية بعناية قبل أن تقرر ما إذا كنت ترغب في المشاركة في هذه الدراسة أم لا .لا تتردد في الطلب اذا كنت بحاجة الى مزيد من المعلومات أو توضيح حول ما ورد في هذا النموذج وهذه الدراسة ككل.

تهدف هذه الدراسة إلى معرفة مدى انتشار واستخدام المتممات والبدائل الطبية لدى مرضى سرطان الثدي في لبنان وتقييم نسبة الالتزام بحميات البحر الأبيض المتوسط (Mediterranean Diet).

يحق لك المشاركة في هذه الدراسة إن كنت لبنانيا، وتشتكي/ن من مرض سرطان الثدي منذ مدة لا تقل عن الشهرين قبل هذه الدراسة وتعالج حاليا في مركز باسيل للأورام السرطانية في مستشفى الجامعة الاميركية لعلاج سرطان الثـــدي أو مستشفى المقاصد في بيروت.

لقد أطلعتـــك الممرضة المسؤولةعلى هذه الدراسة مما سمح الباحث بالإقتراب منك لمناقشة ما إذا كنت مهتم بالمشاركة في هذه الدراسة. في حال الموافقة على المشاركة، سوف تملأ استمارة عن وضعك الاجتماعي مثل العمر، الجنس، الوضع العائلي، الدخل السنوي، المستوى التعليمي الخ ،عوارض وعلاج مرض سرطان الثدي، ونوع المتممات والبدائل الطبية وتواتر استخدامها وكذلك عن استهلاكك الغذائي من خلال إستمارة ومراجعة المحصول الغذائي خلال ال٢٤ الساعة الماضية.

. سيتم ادراج مجموع 377 من مرضى سرطان الثدي لادخالهم في هذه الدراسة. يتطلّب ملء الاستمارة حوالي ال15دقائق. سيتم تحديد وقت المقابلة (سواء قبل، بعد أو أثناء فترة العلاج) من قبل المريض، بطريقة لا تؤثر أو تؤخر الرعاية الطبية و للتأكد أن المريض ليس في حالة من الانزعاج جراء العلاج.

إن مشاركتكم في هذه الدراسة طوعية تماما، ولكنها مهمة جدا بالنسبة لنا .اذا كنت توافق على أن تكون جزءا من دراستنا سوف تساعدنا على معرفة مدى انتشار واستخدام المتممات والبدائل الطبية لدى مرضى سرطان الثدي في لبنان.

إن مشاركتكم في هذا البحث خالية من المخاطر والمكتسبات الشخصية. الرجاء أخذ العلم بأن عدم المشاركة لن يؤثر سلباً على منافعك الشخصية. في حل رفض المريض المشاركة في هذه الدراسة، لن يفقد أي من الخدمات الصحية. بالاضافة. يمكن للمشارك التوقف عن الإجابة على الأسئلة في أي وقت وكذلك يمكنه رفض إجابة أي سؤال.

نريد أن نؤكد على السرية التامة في الدراسة وأن جميع المعلومات و إمضاء كل من المشارك والشاهد في هذه الدراسة ستحفظ في خزانة مقفلة بالمفتاح وستستعمل لهدف علمي فقط. إن الباحث لا يشارك أو يكشف أية معلومات عن المريض مع الطبيب. أيضا، إن الباحث لا يستطيع الحصول على سجلات المريض الطبية. بالإضافة، سيتم جمع جميع المعلومات بشكل مجهول (أي عدم وجود الاسم على الإستمارة). ومع ذلك، يمكن ربط رقم المشترك على الاستمارة بوثيقة الموافقة للمشاركة في هذه الدراسة مع العلم أن الباحث الرئيسي فقط يملك هذا الرابط.

في حال حدوث اي شيء سلبي جراء هذه الدراسة، لن يكون هناك تعويضات لتغطية هذه النفقات.

وثيقة الباحث:

لقد راجعت وبالتفصيل مع ----------(اسم المشترك) وثيقة المشاركة في الدراسة هذه واهدافها والمكاسب و المخاطر التي قد تنتج عنها. قمت بالاجابة على كافة الاسئلة و سوف ابلغ المشترك باي تغيير قد يطرأ على هذا البحث العلمي.

الإسم الباحث: ..... الإمضاء: .....

التّاريخ: ..... الوقت : .....

وثيقة الموافقة:

لقد قرأت كل المعلومات التي قدمت عن هذه الدّراسة و تمت الإجابة عن جميع أسئلتي المتعلّقة بها. انا اوافق طوعا للمشاركة في هذه الدراسة و أفهم أنّه بإمكاني التوجّه مباشرة بأي سؤال أواستفسار حيال أي جانب من هذا البحث إلى د. فرح نجا على 01-350000 مقسم 4504 او اي شخص متعلق بالدراسة. أفهم تماما أنّه بإمكاني اكتساب معلومات إضافيّة حيال حقوقي في هذه الدراسة من قبل مجلس المراجعة المؤسسية لحقوق الانسان على الرقم 01-350000 مقسم 5443.

الإسم: ..... الإمضاء: .....

التّاريخ: ..... الوقت : .....

الشاهد: ..... الإمضاء: .....

(اذا المريض، او ممثل المريض او والد/ة المريض لا يقرأ/تقرأ أو ضعيف البصر)

التّاريخ: ..... الوقت : .....

☒ هل تسمح لنا بالاتصال بك للبحوث المستقبلية؟

☐ نعم ☐ لا

اذا كانت الاجابة نعم، يرجى تزويدنا برقم هاتفك

مع الشكر الجزيل،

APPENDIX C
ENGLISH AND ARABIC VERSIONS OF THE QUESTIONNAIRE

Prevalence and Determinants of Complementary and Alternative Medicine Use among Breast Cancer Patients in Lebanon

Date (dd/mm/yy) ___/___/___
Subject ID:_____

Section A: Socio-demographics

1- **Age (years):**_____

2- **Place of residence:** _____

3- **Marital status:**

a- Single (not married, separated, widowed, divorced)
b- Married/living with a partner

4- **Monthly household income**

a-<500$
b-500- 1000$
c-1000-2000 $
d->2000$

5- **Highest education level attained**

a- Illiterate
b- Primary
c- Secondary School
d- Diploma; Bachelor Degree
e- Masters, Doctoral

6- **Employment status**

a- Employed
b- Retired
c- Housewife
d- Unemployed
e- Other: _____

7- **Current occupation:** _____

8- **Number of rooms (except for toilet, kitchen, balcony& garage) in the household: _____**

9- **Number of persons (except for newborns) in the household: _____**

10- **Health insurance by type**
- a- Public (Ministry of Health)
- b- Social (NSSF, COOP, Army, Public Security)
- c- Private
- d- Self-paying

Section B: Breast Cancer

11- How long have you been diagnosed with breast cancer? _____ 1 year.

12- What is your current status of breast Cancer?
- a- Metastatic
- b- Locally advanced
- c- Early stage

13- Site of metastasis (if present):_____

14- Do you have a Family history of breast cancer?
- a- Yes, relation to patient:_____
- b- No

15- Do you have a Family history of other Cancers?
- a- Yes, please specify _____
- b-No

16- Do you suffer from any other health condition?
- a- Hypertension
- b- Cardiovascular disease
- c- Obstructive pulmonary disease
- d- Others:

17- Do you adhere to your doctor's recommendations?
- a- Yes
- b- No

18- What are the main barriers to your adherence to the recommendations?

- a- Unaffordable medication

b- Intolerance of drug side effects
c- others, please specify _____

19- Have you received any dietary advice since you have been diagnosed?
a- Yes
b- No

20- If yes, from whom did you receive the dietary advice?
a- Doctor
b- Nurse
c- Dietitian
i. Referral
ii. Personal decision

21- What symptoms do you have? (circle all that applies)
a- Fatigue
b- Pain
c- Appetite loss
d- Early satiety
e- Weight loss
f- Dry mouth
g- Constipation
h- Taste changes
i- Dysphagia
j- Nausea
k- Vomiting
l- Urinary symptoms
m- Bleeding
n- Hoarseness
o- Skin symptoms
p- Cough
q- Sore mouth
r- Dyspnea
s- Other: _____

22- What is the most distressing symptom among those you have? _____

23- Your current state of health
a- Very poor
b- Poor
c- Fair

d- Good
e- Excellent

Section C: CAM use

24- Have you used CAM since your diagnosis with breast cancer?
a- Yes
b- No

25- Have you used CAM in the previous year?
a- Yes
b- No

26- Are you using CAM as alternative or as complementary to the conventional treatment?
a- Alternative
b- Complementary

27- Are you using CAM as treatment or relief from symptoms?
a- Treatment of breast cancer
b- As relief of symptoms and prevention of suffering

28- If you have not used CAM, would you consider using it in the future?
a- Yes
b- No

29- If you have not used CAM, why not?
a- I never heard of it
b- I'm afraid of the side effects
c- I don't believe in it
d- The doctor didn't prescribe it
e- Not to have additional burden
f- Other, please specify.....

30- Have you asked your doctor about the CAM product you used?
a- Yes
b- No

31- If YES, what was his reaction?
a- Encouraging
b- Discouraging
c- Neutral

32- What type of CAM product have you used?
- a- Vitamins/Minerals
- b- Dietary supplements or (Special foods)
- c- Herbal remedies/Herbal preparations, specify:
- d- Spiritual healing
- e- Folk medicine
- f- Other, please specify……:

33- How did you choose your CAM?
- a- Personal choice
- b- Friends
- c- Media (Internet, magazines, TV)
- d- Health practitioner
- e- Family beliefs
- f- Health food shop
- g- alternative therapist

34- How often do you use CAM?
- a- One time
- b- Regular (2 or more per week for a minimum of a month)
- c- Once per month
- d- Other

35- Who provided you with the CAM treatment?
- a- Massage therapist
- b- Acupuncturist
- c- Practitioner of traditional medicine
- d- Naturopath
- e- Homeopath
- f- Got it from a local store or pharmacy.

36- If the use of CAM was regular, what is the estimated cost per month?
- a- < $10
- b- $11 – 20
- c- $21 – 30
- d- $31 – 40
- e- $41 – 50
- f- >$50

37- Why have you used CAM? (circle all that applies)
- a- To manage cancer complications/progression
- b- To reduce the side effects/symptoms of conventional treatment
- c- To help in relaxation and feeling better psychologically

d- To improve your general health and ensure long term survival
e- To feel more in control over your health care
f- To get relieved from sorcery spell
g- To provide energy
h- Disappointment from conventional medical therapy
i- Feeling of having no alternative
j- Belief in advantages of CAM practices
k- Family tradition/ Culture
l- It is more natural
m- Curiosity
n- Other, please specify:_____

38- In general, how much did CAM help you?
a- Not at all
b- Some
c- A lot, very satisfied
d- You can't tell

39- Have you suffered from any side effect from CAM?
a- Yes
b- No
c- undecided

if yes please specify _____

40- Would you use CAM again?
a- Yes
b- No
c- undecided

41- Will you recommend the use of this CAM to other breast cancer patients?
a- Yes
b- No
c- Undecided

Thank you very much

A. Adherence to the Mediterranean Diet Questionnaire

Section I: Code	Diet Questionnaire	Serving size	Per Day (a)	Per week (b)	Never
1	How many **servings** of whole grains do you consume?	1 slice of brown bread (30g), ½ cup cereals, brown pasta, brown rice			
2	How many **times** do you consume whole grains?				
3	How many **servings** of refined grains do you consume?	1 slice of white bread (30g), ½ cup cereals, white pasta, white rice			
4	How many **times** do you consume white bread?				
5	How many **times** do you consume white rice?				
6	How many **times** do you consume potato & other starchy roots?				
7	How many **servings** of dairy do you consume?	1 cup milk/yogurt 30 g cheese			
8	How many **times** do you consume olive oil?				
9	How many **servings** of olive oil do you consume?	1 teaspoon			
10	How many **servings** of olive do you consume?	5 olives			
11	How many **servings** of nuts do you consume?	½ cup			
12	How many **servings** of vegetables do you consume?	½ cup Medium-sized vegetable			
13	How many **servings** of legumes do you consume?	½ cup			
14	How many **servings** of fruits do you consume?	½ cup 1 Medium-sized fruit			
15	How many **servings** of red meat do you consume?	60 g			

16	How many **servings** of poultry do you consume?	60 g			
17	How many **times** do you consume eggs?				
18	How many **servings** of eggs do you consume?	1 medium egg			
19	How many **servings** of fish/seafood do you consume?	60 g			
20	How many **servings** of butter/margarine/cream do you consume?	1 teaspoon			
21	How many **times** do you consume commercial sweets or pastries (not homemade)?				
22	How many **servings** of commercial sweets or pastries (not homemade) do you consume?	1 chocolate bar (50g)			
23	How many **servings** of sweetened beverages do you consume?	1 cup			
24	How many **servings** of wine do you consume?	1 glass (150ml)			
25	How many **times** do you season your food with a tomato-based sauce (tomato, onion, garlic and simmered with olive oil)?				

Section 2			
		Yes	**No**
26	Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage?		

B. 24-Hour Dietary Recall.

Please recall what you ate and drank the previous day from the time you woke up until the next morning.

Time	Food eaten	Amount	Method of Preparation

Time	Food eaten	Amount	Method of Preparation

** **Was yesterday a usual day?**

1. Yes
2. No, *please specify*: _____

العوامل المؤثرة لاستعمال المتممات والبدائل الطبية والعادات الغذائية لدى المصابين بسرطان الثدي في لبنان
استمارة

تاريخ: (يوم/شهر/سنة): _____
رقم المشترك: _____

SECTION A: DEMOGRAGHICS

1. العمر (سنة):_____

2. مكان الاقامة:_____

3. الوضع العائلي:
❑ أعزب (غير متزوج، منفصل ، مطلق ، أرمل)
❑ متأهل، مقيم مع الشريك

4. الدخل الشهري:
❑ $500 >
❑ $1000-$500
❑ $2000-$1000
❑ $2000 <

5. المستوى العلمي:
❑ أمي
❑ مدرسي-ابتدائي
❑ مدرسي-ثانوي
❑ جامعي- بكالوريوس
❑ جامعي: دراسات عليا

6. الوضع المهني:
❑ موظفة
❑ متقاعدة
❑ ربة منزل
❑ عاطلة عن العمل
❑ غيره:_____

7. المهنة الحالية: _____

8. عدد الغرف في المنزل(باستثناء الحمام، المطبخ، الشرفة،الكاراج): _____

9. عدد أفراد الأسرة (باستثناء حديثي الولادة): _____

10. نوع التأمين:

❑ وزارة الصحة
❑ ضمان/تعاونية/الجيش/الأمن العام
❑ خاص
❑ حساب خاص

SECTION B: Breast Cancer

11. كم مضى على معرفتك بأنك مصاب بسرطان الثدي ؟ _____

12. ما هي مرحلة مرض سرطان الثدي؟
- ❑ منتشر
- ❑ موضعي
- ❑ في المرحلة الأولى

13. موضع انتشار الورم،اذا وجد ؟ _____

14. هل لديك تاريخ عائلي لمرض سرطان الثدي؟
- ❑ نعم ،صلة القرابة للمريض:_____
- ❑ لا

15. هل لديك تاريخ عائلي لأمراض سرطانية أخرى؟
- ❑ نعم، حدد:_____
- ❑ لا

16. هل تعاني من أي عوارض صحية أخرى؟
- ❑ ضغط الدم المرتفع
- ❑ أمراض القلب و الشرايين
- ❑ مرض رئوي
- ❑ غيره حدد: _____

17. هل تتبع تعاليم/نصائح الطبيب؟
- ❑ نعم
- ❑ لا

18. ما هي العوائق الرئيسية التي تحول دون اتباع نصائح الطبيب؟
- ❑ علاج مكلف ماديا
- ❑ عدم القدرة على تحمل العوارض الجانبية
- ❑ غيره. حدد:_____

19. هل حصلت على نصائح غذائية منذ تشخيصك بسرطان الثدي؟
- ❑ نعم
- ❑ لا

20. اذا نعم ، ممن حصلت على هذه النصائح الغذائية؟
- ❑ الطبيب
- ❑ الممرضة
- ❑ أخصائية التغذية
  - o تم تحويلك
  - o قرار شخصي

21. أي من هذه العوارض تعاني؟

- ❑ التعب/ الارهاق
- ❑ الألم
- ❑ خسارة الشهية
- ❑ الشبع المبكر
- ❑ خسارة الوزن
- ❑ جفاف في الفم
- ❑ تغييرات في حاسة التذوق
- ❑ صعوبة في البلع
- ❑ الامساك
- ❑ الغثيان
- ❑ تقيؤ
- ❑ اسهال
- ❑ عوارض في المسالك البولية
- ❑ نزيف
- ❑ بحة في الصوت
- ❑ عوارض في الجلد
- ❑ سعال
- ❑ فم ملتهب
- ❑ ضيق التنفس

22. ما هو العارض الأكثر ازعاجا؟_____

23. كيف تصف حالتك الصحية الآن؟

- ❑رديئة جدا
- ❑ رديئة
- ❑ وسط
- ❑جيدة
- ❑ ممتازة

SECTION C: CAM Use

24. هل استخدمت المتممات والبدائل الطبية بعد تشخيصك بسرطان الثدي؟

- ❑ نعم
- ❑لا

لا

25. هل استخدمت المتممات والبدائل الطبية خلال السنة الماضية؟

- ❑ نعم
- ❑لا

26. هل تستخدم المتممات و البدائل الطبية كعلاج بديل أو كمكمل للعلاج التقليدي؟

- ❑ علاج بديل
- ❑ مكمل للعلاج التقليدي

27. هل تستخدم المتممات و البدائل الطبية لعلاج سرطان الثدي أو لتخفيف العوارض؟

- ❑ علاج لسرطان الثدي

❑ لتخفيف العوارض

28. اذا لم تستخدم المتممات و البدائل الطبية بعد، هل تفكر في استخدامها في المستقبل؟
❑ نعم
❑ لا

29. اذا لم تستخدم المتممات و البدائل الطبية ، ما هو السبب؟
1. لم أسمع بها
2. أخشى من العوارض السلبية
3. لا أؤمن بها
4. لم يصفها الطبيب
5. لنها تشكل عباً اضافياً
6. اخرى، حدد _____

30. هل استشرت الطبيب عن استخدام المتممات و البدائل الطبية؟
❑ نعم
❑ لا

31. اذا كان الجواب نعم، ما كانت ردة فعله؟
❑ مشجعة
❑ غير مشجعة
❑ لم يبد رأياً

32. ما هو نوع المتمم/البديل الطبي الذي استخدمته؟
❑ الفيتامينات و المعادن
❑ متممات غذائية
❑ أعشاب، حدد _____
❑ علاج روحي
❑ علاج شعبي
❑ غيره. حدد _____

33. كيف اخترت المتممات والبدائل الطبية؟ (أشر الى كل الإجابات المناسبة)
❑ خيار شخصي
❑ صديق
❑ وسائل الاعلام (التلفزيون/المجلة/الانترنت)
❑ معتقدات عائلية
❑ متاجر الأغذية الصحية
❑ معالج بالطب البديل
❑ اخرى، حدد _____

34. كم مرة تستخدم المتممات و البدائل الطبية؟
❑ مرة
❑ بانتظام (مرتين أو أكثر في الأسبوع لمدة شهر على الأقل)
❑ مرة في الشهر
❑ غيره، حدد _____

35. من أين حصلت على المتمم والبديل الطبي؟

- ❑ أخصائي تدليك
- ❑ أخصائي في العلاج بالوخز
- ❑ معالج في الطب التقليدي
- ❑ معالج طبيعي
- ❑ متجر أو صيدلية

36. بالمعدل كم تصرف شهرياً على استعمال المتممات والبدائل الطبية؟

- ❑ $10<
- ❑ $20-11
- ❑ $30-21
- ❑ $40-31
- ❑ $50-41
- ❑ $50<

37. لماذا لجأت الى المتممات والبدائل الطبية ؟ (أشر الى كل الإجابات المناسبة)

- ❑ للتحكم في سرطان الثدي
- ❑ للتخفيف من العوارض الجانبية للعلاج التقليدي
- ❑ لتحسين الوضع النفسي
- ❑ لتحسين الوضع الصحي العام واطالة البقاء
- ❑ للاحساس في السيطرة على حالتي الصحية
- ❑ للتخلص من الشعوذة
- ❑ خيبة أمل من العلاج التقليدي
- ❑ لا خيار اخر
- ❑ لمنافع المتممات والبدائل الطبية
- ❑ تقاليد عائلية
- ❑ لأنها مكونات طبيعية
- ❑ بدافع الحشرية
- ❑ اخرى، حدد_____

38. ما هو شعورك بعد استخدام المتممات والبدائل الطبية؟

- ❑ زيادة في الطاقة
- ❑ تحسن في الوضع النفسي
- ❑ تخفيف من العوارض
- ❑ تحسن في الوضع الجسدي
- ❑ تدهور في الوضع النفسي
- ❑ زيادة في العوارض
- ❑ لا تغيير
- ❑ غيره. حدد_____

39. بشكل عام، الى أي مدى ساعدك استخدام المتممات والبدائل الطبية؟

- ❑ أبدا
- ❑ قليلا

❑ كثيرا
❑ لا أعرف

40. هل واجهت أى عوارض سلبية بعد استخدام المتممات و البدائل الطبية؟
❑ نعم
❑ لا
❑ لا أعرف
❑ اذا نعم ، حدد _____

41. هل تعيد استخدام المتممات و البدائل الطبية مرة أخرى؟
❑ نعم
❑ لا
❑ لا أعرف

42. هل تنصح باستخدام المتممات و البدائل الطبية لمرضى سرطان الثدي؟

❑ نعم
❑ لا
❑ لا أعرف

شكراً لتعاونكم ووقتكم

AUB
American University of Beirut
الجامعة الأميركية في بيروت

A - إتباع النظام الغذائي التابع لمنطقة البحر الأبيض المتوسط

القسم الأول					
Code		حجم الحصة	في اليوم ()	في الأسبوع (ب)	أبدا
1	كم حصة من الحبوب الكاملة تستهلك؟	قطعة خبز (30 غ)، ½ كوب حبوب الفطور، الأرز الأسمر ، المعكرونة السمراء			
2	كم مرة تستهلك من الحبوب الكاملة؟				
3	كم حصة من الحبوب المكررة تستهلك؟	قطعة خبز (30 غ)، ½ كوب حبوب الفطور، الأرز الأبيض ، المعكرونة البيضاء			
4	كم مرة تستهلك الخبز الأبيض؟				
5	كم مرة تستهلك الأرز الأبيض؟				
6	كم مرة تستهلك البطاطا و الخضار النشوية؟				
7	كم حصة من الحليب و مشتقاته تستهلك؟	1 كوب حليب/لبن ، 30 غ جبنة			
8	كم مرة تستهلك زيت الزيتون؟				
9	كم حصة من زيت الزيتون تستهلك؟	ملعقة شاي			
10	كم حصة من الزيتون تستهلك؟	5 حبات زيتون			
11	كم حصة من المكسرات تستهلك؟	½ كوب			
12	كم حصة من الخضار تستهلك؟	½ كوب، قطعة حجم وسط			
13	كم حصة من البقول تستهلك؟				
14	كم حصة من الفاكهة تستهلك؟	½ كوب، قطعة حجم وسط			
15	كم حصة من اللحوم الحمراء تستهلك؟	60 غ			
16	كم حصة من الدجاج تستهلك؟	60 غ			
17	كم مرة تستهلك البيض؟				
18	كم حصة من البيض تستهلك؟	1 بيضة وسط			
19	كم حصة من السمك/الأسماك البحرية تستهلك؟	60غ			
20	كم حصة من الزبدة/زبدة المارجرين/ الكريما تستهلك؟	ملعقة شاي			
21	كم مرة تستهلك الحلويات المصنعة أو المعجنات الجاهزة؟				
22	كم حصة من الحلويات المصنعة أو المعجنات الجاهزة تستهلك ؟	لوح شوكولا (50 غ)			
23	كم حصة من العصير المصنع تستهلك ؟	1 كوب			
24	كم حصة من النبيذ تستهلك ؟	كأس (150 مل)			
25	كم مرة تستهلك صوص البندورة المتبل مع البصل، و الثوم، زيت الزيتون؟				

القسم الثاني			
		نعم	لا
26	هل تستهلك الدجاج،و الحبش،و لحم الأرنب أكثر من اللحوم الحمراء كالهمبرغر ،و المقانق؟		

1866
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B -المأخوذ الغذائي خلال الأربع وعشرين ساعة الأخيرة.

نرجو منك أن تتذكري ما تناولتِه من طعام أو شراب في الأمس منذ نهوضك في الصباح وحتى اليوم التالي.

الوقت	الطعام الذي تناولتِه	الكمية	طريقة التحضير

** هل كان الأمس يوماً عادياً؟

1. نعم
2. لا، حددي: _____

APPENDIX D
DIETARY QUESTIONNAIRE MANUAL FOR CALCULATION OF DIET ADHERENCE SCORES

Diet Questionnaire Manual for Calculation of Diet Adherence Scores

The diet questionnaire is a list of 26 questions (Appendix I).

It will allow the collection of data needed to calculate 5 different scores (based on Mediterranean diet pyramid, and USDA food guide pyramid).

It will allow the collection of dietary intake in commonly used serving sizes (per day/ per week); that may need to be converted to other units specific to each score.

1- Mediterranean Score

The score is based on the 11 components of the Mediterranean pyramid.

The score ranges from 0 to 44 points. A score of 44 implies that an individual's food pattern is fully compatible with the typical Mediterranean diet. Mediterranean food pattern promotes whole grains over refined ones, promotes fresh fruits and vegetables over its juices, and olive oil over other visible fat. A partial score from 0 to 4 is attributed to each of the 11 components of the pyramid. A high partial score reflects a high consumption for food groups at the bottom of the pyramid such as fruits and legumes, however; reflects a lower frequency of intake for food groups at the top of the pyramid such as red meat/processed meat (Table 1).

Table 1: Mediterranean Score- scoring method

Score	0	1	2	3	4
Whole grain products[1]	<1 portion/day	1–2 portions/day	3–4 portions/day	5–6 portions/day	≥7 portions/day
Vegetable consumption[2]	<1 portion/day	1 portion/day	2 portions/day	3 portions/day	≥4 portions/day
Fruit consumption[3]	<1 portion/day	1 portion/day	2 portions/day	3 portions/day	≥4 portions/day
Legumes, nuts and seed consumption[4]	<0.5 portion/day	0.5 portion/day	1 portion/day	2 portions/day	>2 portions/day
Olive oil, olives and margarine made of olive oil consumption[5]	<1 time/day	1 time/day	2 times/day	3 times/day	≥4 times/day
Milk and dairy products consumption[6]	<1 portion/day or >4 portions/day	4 portions/day		1 portion/day	2–3 portions/day
Fish and seafood (other than breaded)[7]	Never	<1 portion/week	1 portion/week	2 portions/week	≥3 portions/week
Poultry (other than breaded)[7]	Never	<1 portion/week	1 portion/week or ≥4 portions/week	2 portions/week	3 portions/week
Eggs	≥7/week		5–6/week		0–4/week
Sweets[8]	≥7 times/week	5–6 times/week	3–4 times/week	1–2 times/week	<1/week
Red meat/processed meat[7]	≥7 portions/week	5–6 portions/week	3–4 portions/week	1–2 portions/week	<1 portion/week

Portion size of each food component is defined as follows

Grain products: 1 slice of bread, ½ cup of pasta, rice or couscous, 30 g of cereals.

Vegetables: ½ cup or one medium vegetable, ½ cup of vegetable juice

Fruits: ½ cup or one medium fruit, ½ cup fruit juice.

Legumes, nuts and seeds: ½ cup of legumes, ¼ cup of nuts/seeds or 100 g of tofu.

Dairy products: 1 cup of milk/enrich soy beverages, 50 g of cheese or 175 g of yoghurt.

Red meat/processed meat, poultry, or fish: 50-100 g.

Sweets: equivalent to 1/12 of cake, 1/6 of pie or 1 regular chocolate bar.

Calculation of the score from the diet questionnaire

Questions number 1, 3, 7, 8, 12-17, 19- 21 from the diet questionnaire covers the 11 components of the Mediterranean score.

- Serving size of the nuts differs between the scoring method (¼ cup) and the diet questionnaire (½ cup). Conversion of units is needed to compare similar units of intake from the diet questionnaire and the recommendation from the scoring method, to be able to attribute a score (Table 1). Therefore, multiply the answer in 11a by 2, to obtain the number of ¼ cup servings of nuts.
- Food component 4 (consumption of legumes and nuts) in the scoring method is covered by questions 11a (nuts) and 13a (legumes) in the diet questionnaire. Add the number of servings consumed of 11a and 13a, to obtain number of servings for food component 4.
- A partial score from 0 to 4 is attributed to each of the 11 components of the pyramid (Table 1).

A maximum of 1 point is attributed for: the consumption of refined grain products, for the total number of vegetable juice portions, and for the total number of fruit juice portions.

The **Mediterranean score** is the sum of the 11 partial scores.

Reference: Goulet J, Lamarche B, Nadeau G, Lemieux S. Effect of a nutritional intervention promoting the Mediterranean food pattern on plasma lipids, lipoproteins and body weight in healthy French-Canadian women. *Atherosclerosis*. 2003 Sep; 170(1):115-24. PubMed PMID: 12957689.

2- Mediterranean Style Dietary Pattern Score (MSDPS)

The score is based on 13 components of the Mediterranean diet pyramid (Table 2).
The score ranges from 0-100. A score of 100 implies that an individual's food pattern is fully compatible with the typical Mediterranean diet. Each group is scored from 0 to 10, with the exception of olive oil (Table 2). A higher score reflects more adherences to the recommendation.

Overconsumption incurs a penalty by subtracting a point proportionally to the number of servings consumed that exceeded the recommended intake for that group. Therefore, the score of a food group can be negative. Any negative score is considered a zero (by default).

Table 2: MSDPS-scoring method

Food group components	Criteria for maximum score of 10[1]	Score[2]
	servings/d	*points/serving*
Whole grains	8	1.25
Fruits	3	3.33
Vegetables	6	1.67
Dairy	2	5.0
Wine		
Men	3	3.33
Women	1.5	6.67
	servings/wk	
Fish and other seafood	6	1.67
Poultry	4	2.5
Olives, legumes, and nuts	4	2.5
Potatoes and other starchy roots	3	3.33
Eggs	3	3.33
Sweets	3	3.33
Meat	1	10.0
Olive oil	Use only olive oil	0 (for no use of olive oil) 5 (for use of olive + other vegetable oils)

One serving size of each food component is defined as follows *:

Bread: 25 g

Potatoes: 100g

Cooked rice/pasta: ½ cup or 50-60g

Vegetables: ½ cup of raw/cooked or 100g

Fruits: apple (80 g), banana (60 g), orange (100g), 200g of watermelon/melon, 30g grapes

Dairy: 1 cup of milk/yogurt, 30g of cheese

Eggs: 1 egg

Meat & Fish: 60 g of lean meat/fish

Dry beans: 1 cup or 100g

*Dietary guidelines for adults in Greece, Ministry of Health and Welfare: Supreme Scientific Health Council. Archives of Hellenic Medicine 1999, 16 (5):516-524

Calculation of the score from the diet questionnaire

Questions number 1, 6-7, 8, 10-13, 14-16, 18-19, 20, 22, 24 from the diet questionnaire covers the 13 components of the MSDPS.

The score of each food component is calculated as follows:

- If number of servings consumed *don't exceed* the number of recommended servings, then Score of food group component = Number of servings consumed multiplied by the reference score for each group (Table 2)

- If the number of servings consumed *exceed* the number of recommended servings of the corresponding food group component (overconsumption), then
Score of food group component = 10- [(Number of servings consumed - Number of recommended servings) multiplied by the reference score for each group]

- If the score of food group component is negative, report it as zero.

-For the olive oil food component (Table 2), attribute a
Score of 10 if the diet questionnaire shows a consumption >0 for question 8b and zero for 20b (meaning consumption of olive oil only)
Score of zero if the diet questionnaire shows a consumption equal to 0 for question 8b (meaning no consumption of olive oil)
Score of 5 if the diet questionnaire shows a consumption >0 for question 8b, and >0 for 20b (meaning a consumption of olive oil and other oils)

"Questions in diet questionnaire
8b: How many **times** do you consume olive oil? Per week
20b: How many **servings** of butter/margarine/cream do you consume? Per week"

-For the olives, legumes & nuts food component: Calculate the sum of servings consumed (questions 10b +11b +13b), then calculate the score.

"Questions in diet questionnaire
10b: How many **servings** of olive do you consume? Per week
11b: How many **servings** of nuts do you consume? Per week
13b: How many **servings** of legumes do you consume? Per week"

The **MSDPS score** is: (sum of the 13 food component scores/ theoretical maximum sum of 130)* 100.

Reference: Rumawas ME, Dwyer JT, McKeown NM, Meigs JB, Rogers G, Jacques PF. The development of the Mediterranean-style dietary pattern score and its application to the American diet in the Framingham Offspring Cohort. J Nutr. 2009 Jun;139(6):1150-6. doi: 10.3945/jn.108.103424. Epub 2009 Apr 8. PubMed PMID: 19357215; PubMed Central PMCID: PMC2682986.

3- PREDIMED

The score is based on 14 components of the Mediterranean diet.

The score ranges from 0-14. A score of 14 implies that an individual's food pattern is fully compatible with the typical Mediterranean diet.

Table 3: PREDIMED score- Scoring Method

Foods and Frequency of Consumption	Criteria for 1 Point*
1. Do you use olive oil as main culinary fat?	Yes
2. How much olive oil do you consume in a given day (including oil used for frying, salads, out-of-house meals, etc.)?	≥4 tbsp
3. How many vegetable servings do you consume per day? (1 serving = 200 g [consider side dishes as half a serving])	≥2 (≥1 portion raw or as salad)
4. How many fruit units (including natural fruit juices) do you consume per day?	≥3
5. How many servings of red meat, hamburger, or meat products (ham, sausage, etc.) do you consume per day? (1 serving = 100–150 g)	<1
6. How many servings of butter, margarine, or cream do you consume per day? (1 serving = 12 g)	<1
7. How many sweet or carbonated beverages do you drink per day?	<1
8. How much wine do you drink per week?	≥3 glasses
9. How many servings of legumes do you consume per week? (1 serving = 150 g)	≥3
10. How many servings of fish or shellfish do you consume per week? (1 serving = 100–150 g of fish or 4–5 units or 200 g of shellfish)	≥3
11. How many times per week do you consume commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits, or custard?	<3
12. How many servings of nuts (including peanuts) do you consume per week? (1 serving = 30 g)	≥1
13. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage?	Yes
14. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with *sofrito* (sauce made with tomato and onion, leek, or garlic and simmered with olive oil)?	≥2

Serving size of each food component is defined as follows:

Vegetable: 200g

Red Meat: 100-150 g of hamburger/ham/sausages

Butter/margarine/cream: 12 g

Legumes: 150 g

Fish/shellfish: 100-150 g of fish, 200g of shellfish

Nuts: 30 g

Calculation of the score from the diet questionnaire

Questions number 8, 9, 11-16, 19-21, 23-26 from the diet questionnaire covers the 14 components of the PREDIMED score.

-Attribute a score of 1 for meeting the recommendation for each food component (Table 3).

-Attribute a score of zero for not meeting the recommendation for each food component (Table 3).

- Food component 1 (use of olive oil) in the scoring method is covered by questions 9 and 20 in the diet questionnaire. Compare the answer in question 9 in the diet questionnaire to that of 20. If the number in question 9 > 20, then the answer is "yes", and attribute a score of 1 for meeting the recommendation.

"Food component 1: Do you use olive oil as main culinary fat? Yes/No

Diet questionnaire 9: How many **servings** of olive oil do you consume?

Diet questionnaire 20: How many **servings** of butter/margarine/cream do you consume?"

-Some serving sizes differ between the food components in the scoring method and the diet questionnaire. Conversion of units is needed to compare similar units of intake from the diet questionnaire and the recommendation from the scoring method, to be able to attribute a score (Table 3).

Table 4. Calculating serving sizes, according to PREDIMED definitions.

PREDIMED Scoring	Diet questionnaire	Conversion
2:olive oil consumption in tablespoon	9a: olive oil consumption in teaspoon	Divide the answer of 9a by 3, to obtain intake in tablespoons.
3:Vegetable serving size= 200g	12a:Vegetable serving size= ½ cup =100g	Divide the answer of 12a by 2, to obtain number of 200g servings

5: red meat serving size =100-150 g; 120 g on average.	15a: red meat serving size = 60 g	Divide the answer of 15a by 2, to obtain number of 120g servings
6:butter/margarine/cream serving size = 12g	20a: butter/margarine /cream serving size = 1 teaspoon= 5 g	Multiply the answer in 20a by 5, then divide by 12; to obtain the number of 12g servings
10:fish serving size= 100-150; 120 g on average	19b: fish serving size= 60 g	Divide the answer of 19b by 2, to obtain number of 120g servings
10: shellfish serving size= 200g	19b: shellfish serving size= 60 g	Multiply the answer in 19b by 60, then divide by 200; to obtain the number of 200g servings
12: nuts serving size=30 g	11b: nuts serving size=½ cup= 50g	Multiply the answer in 11b by 50, then divide by 30; to obtain the number of 30g servings

The **PREDIMED score** is the sum of the 14 food component scores.

Reference: Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Ruiz-Gutiérrez V,Covas MI, Fiol M, Gómez-Gracia E, López-Sabater MC, Vinyoles E, Arós F, Conde M, Lahoz C, Lapetra J, Sáez G, Ros E; PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med.* 2006 Jul 4;145(1):1-11. PubMed PMID: 16818923.

4- Cardio-protective Mediterranean diet index

The score is based on 9 components of the Mediterranean diet.

The score ranges from 0-9. A score of 9 implies that an individual's food pattern is fully compatible with the cardio-protective Mediterranean diet.

Table 5: Cardio-protective Mediterranean diet index-Scoring Method

	Yes
1. Olive oil (≥1 spoon/day)	+1
2. Fruit (≥1 serving/day)	+1
3. Vegetables or salad (≥1 serving/day)	+1
4. Fruit (≥1 serving/day) *and* vegetables (≥1 serving/day)[a]	+1
5. Legumes (≥2 servings/week)	+1
6. Fish (≥3 servings/week)	+1
7. Wine (≥1 glass/day)	+1
8. Meat (<1 serving/day)	+1
9. [White bread (<1/day) *and* rice (<1/week)] *or* whole-grain bread (>5/week)[b]	+1

Serving size of each food component

Serving sizes are not identified. Therefore, serving sizes will be adopted as mentioned in the diet questionnaire.

Calculation of the score from the diet questionnaire

Questions number 2, 4, 5, 9, 12-15, 19, 24 from the diet questionnaire covers the 9 components of the Cardio-protective Mediterranean diet index score.

-Attribute a score of 1 for meeting the recommendation for each food component (Table 4).

-Attribute a score of zero for not meeting the recommendation for each food component (Table 4).

The **Cardio-protective Mediterranean diet index score** is the sum of the 9 food component scores.

Reference: Martínez-González MA, Fernández-Jarne E, Serrano-Martínez M, Wright M, Gomez-Gracia E. Development of a short dietary intake questionnaire for the quantitative estimation of adherence to a cardioprotective Mediterranean diet. Eur J Clin Nutr. 2004 Nov;58(11):1550-2. PubMed PMID: 15162136.

5- Dietary Diversity Score (DDS)

The score is based on the 5 food groups of the USDA food guide pyramid (Appendix II). Each food group has a specified number of subgroups.

The DDS ranges from 0 to 10. A score of 10 implies that an individual's food pattern is fully compatible with the recommendations of the USDA food guide pyramid. The score range of each group is 0-2.

Table 6: DDS- Groups and subgroups

Group	Grains	Vegetables	Fruits	Meat	Dairy
Nb Subgroups	7	7	2	4	3
Subgroups	Refined bread Biscuits Macaroni Whole bread Corn flakes Rice Refined flour	vegetables Potatoes Tomatoes Starchy vegetables Legumes Yellow vegetables Green vegetables	Fruits and fruit juices Berries and citrus	Red meat Poultry Fish Eggs	Milk Yogurt Cheese

Serving size of each food component is defined as follows:

Grains: 1 oz eq

Vegetables: ½ cup

Fruits: ½ cup

Meat: 1 oz eq

Dairy: 1cup

Calculation of the score from the diet questionnaire

Questions number 1, 3, 6- 7, 12-15, 18-19 from the diet questionnaire covers the 5 food groups of the DDS.

-Each DDS food group includes several food components from the diet questionnaire. For example, the DDS Grains group includes refined and whole grains, while the diet questionnaire includes each separately. Therefore, the amount of servings consumed from the diet questionnaire should be adjusted to include all DDS food components (Table 7)

Table 7. Calculating number of servings consumed per day, according to DDS food grouping.

DDS Scoring	Diet questionnaire	Conversion
Grains group includes refined and whole grains	1a and 3a	Add the answers in 1a and 3a, to obtain the number of servings consumed in Grains group.
Vegetable Group includes vegetables, legumes, starchy vegetables, potatoes.	12a, 13a	Add the answers in 6a, 12a and 13a, to obtain the number of servings consumed in vegetable group.
Dairy Group includes milk, yogurt and cheese	7a	NA
Fruits Group includes fruits and fruit juices	14a	NA
Meat Group includes red meat, poultry, fish and eggs in oz eq (30g)	15a-19a in 60g	Add the answers in 15a to19a to obtain the number of servings consumed in Meat group. Multiply number of servings consumed by 60, and divide by 30 to obtain number of 1 oz- servings

- The calculation of the DDS requires the number of subgroups consumed per group per day by the individual. This will allow the calculation of the score of each group, and then sum them up to obtain the DDS.

-Calculate the number of subgroups consumed per group.

By definition, the number of subgroups consumed per group= the number of ½ servings consumed per group.

Number of ½ servings consumed per group = Nb of servings consumed per group/ ½ serving size of the group. The ½ serving size of each group is as follows: Grains, ½ oz eq-Vegetables, ¼ cup- Fruits, ¼ cup- Meat, ½ oz eq- Dairy, ½ cup.

For example, Nb of ½ servings of Grains group= Nb of servings of Grains consumed per day/ 0.5

-Calculate the score of each group

If the number of subgroups consumed per group ≥ the number of subgroups defined by DDS, then the score of the group = 2.

If the number of subgroups consumed per group < the number of subgroups defined by DDS, then the score of the group is calculated based on the following formulas.

Score of Grains group= (Nb of subgroups of grains consumed/7)*2

Score of Vegetable group= (Nb of subgroups of vegetables consumed/7)*2

Score of Fruits group= (Nb of subgroups of fruits consumed/2)*2

Score of Meat group= (Nb of subgroups of meat consumed/4)*2

Score of Dairy group= (Nb of subgroups of dairy consumed/3)*2

The **Dietary Diversity Score** is the sum of the 5 group scores. Total DDS = sum of scores (Grains+ vegetables +fruits +meat +dairy)

Reference: Azadbakht L, Haghighatdoost F, Feizi A, Esmaillzadeh A. Breakfast eating pattern and its association with dietary quality indices and anthropometric measurements in young women in Isfahan. Nutrition 2013 Feb;29(2):420-5. doi: 10.1016/j.nut.2012.07.008.

Appendix I

Section 1					
Code	**Diet Questionnaire**	**Serving size**	**Per Day (a)**	**Per week (b)**	**Never**
1	How many **servings** of whole grains do you consume?	1 slice of brown bread (30g), ½ cup cereals, brown pasta, brown rice			
2	How many **times** do you consume whole grains?				
3	How many **servings** of refined grains do you consume?	1 slice of white bread (30g), ½ cup cereals, white pasta, white rice			
4	How many **times** do you consume white bread?				
5	How many **times** do you consume white rice?				
6	How many **times** do you consume potato & other starchy roots?				
7	How many **servings** of dairy do you consume?	1 cup milk/yogurt 30 g cheese			
8	How many **times** do you consume olive oil?				
9	How many **servings** of olive oil do you consume?	1 teaspoon			
10	How many **servings** of olive do you consume?	5 olives			
11	How many **servings** of nuts do you consume?	½ cup			
12	How many **servings** of vegetables do you consume?	½ cup Medium-sized vegetable			
13	How many **servings** of legumes do you consume?	½ cup			
14	How many **servings** of fruits do you consume?	½ cup 1 Medium-sized fruit			
15	How many **servings** of red meat do you consume?	60 g			
16	How many **servings** of poultry do you consume?	60 g			

17	How many **times** do you consume eggs?				
18	How many **servings** of eggs do you consume?	1 medium egg			
19	How many **servings** of fish/seafood do you consume?	60 g			
20	How many **servings** of butter/margarine/cream do you consume?	1 teaspoon			
21	How many **times** do you consume commercial sweets or pastries (not homemade)?				
22	How many **servings** of commercial sweets or pastries (not homemade) do you consume?	1 chocolate bar (50g)			
23	How many **servings** of sweetened beverages do you consume?	1 cup			
24	How many **servings** of wine do you consume?	1 glass (150ml)			
25	How many **times** do you season your food with a tomato-based sauce (tomato, onion, garlic and simmered with olive oil)?				

Section 2			
		Yes	**No**
26	Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage?		

Appendix II

TABLE 5-2. USDA Food Patterns—Food Groups and Subgroups

Food Group	Subgroups and Examples
Vegetables	**Dark-green vegetables:** All fresh, frozen, and canned dark-green leafy vegetables and broccoli, cooked or raw: for example, broccoli; spinach; romaine; collard, turnip, and mustard greens.
	Red and orange vegetables: All fresh, frozen, and canned red and orange vegetables, cooked or raw: for example, tomatoes, red peppers, carrots, sweet potatoes, winter squash, and pumpkin.
	Beans and peas: All cooked and canned beans and peas: for example, kidney beans, lentils, chickpeas, and pinto beans. Does not include green beans or green peas. (See additional comment under protein foods group.)
	Starchy vegetables: All fresh, frozen, and canned starchy vegetables: for example, white potatoes, corn, and green peas.
	Other vegetables: All fresh, frozen, and canned other vegetables, cooked or raw: for example, iceberg lettuce, green beans, and onions.
Fruits	All fresh, frozen, canned, and dried fruits and fruit juices: for example, oranges and orange juice, apples and apple juice, bananas, grapes, melons, berries, and raisins.
Grains	**Whole grains:** All whole-grain products and whole grains used as ingredients: for example, whole-wheat bread, whole-grain cereals and crackers, oatmeal, and brown rice.
	Enriched grains: All enriched refined-grain products and enriched refined grains used as ingredients: for example, white breads, enriched grain cereals and crackers, enriched pasta, and white rice.
Dairy products	All milks, including lactose-free and lactose-reduced products and fortified soy beverages; yogurts; frozen yogurts; dairy desserts; and cheeses. Most choices should be fat-free or low-fat. Cream, sour cream, and cream cheese are not included due to their low calcium content.
Protein foods	All meat, poultry, seafood, eggs, nuts, seeds, and processed soy products. Meat and poultry should be lean or low-fat. Beans and peas are considered part of this group, as well as the vegetable group, but should be counted in one group only.

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