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DIETARY GLYCEMIC INDEX AND LOAD: ASSOCIATIONS WITH CARDIOMETABOLIC ABNORMALITIES AMONGST HEALTHY LEBANESE ADULTS

by
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AN ABSTRACT OF THE THESIS OF

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The Metabolic Syndrome (MetS) is a major health concern, putting individuals at an increased risk of cardiovascular diseases, diabetes mellitus and mortality. Preventive strategies mainly focus on diet as a modifiable risk factor. Recently, carbohydrates and their glycemic response are being recognized as potential MetS drivers. The glycemic response is dictated by both the glycemic index (GI) and glycemic load (GL). The objectives of this study were to: (1) determine the GI of Lebanese food items based on pertinent literature, (2) estimate dietary GL for a sample of healthy Lebanese adults, (3) examine the association of dietary GI and GL with fasting blood lipid levels, fasting glycemia and blood pressure and (4) investigate the association between dietary GI and GL and the MetS in a sample of healthy Lebanese adults.

This is a cross-sectional study of healthy Lebanese adults aged ≥18 years (n=283) residing in the Greater Beirut area. Using standardized techniques, anthropometric measurements and biochemical analyses were performed. A multi-component questionnaire was administered to study participants, tackling family history, medical history, and sociodemographic and lifestyle characteristics. Physical activity was assessed using the International Physical Activity Questionnaire. Dietary habits were assessed in an interview setting by trained dietitians by means of an 86-item, semi-quantitative, and culture specific food frequency questionnaire (FFQ). GI and GL values were assigned for each food based on the International GI table and other pertinent literature. Total dietary GI and GL were calculated for study participants. The MetS was diagnosed based on the Harmonized IDF definition.

Average dietary GI and GL were estimated at 59.87 ± 7.99 and 209.75 ± 100.26, respectively with significantly higher values in those having MetS compared to their non-MetS counterparts (61.16 ± 8.19 vs 59.25 ± 7.77 and 225.8 ± 106.2 vs 201.54 ± 95.79). Logistic regression analysis showed that participants belonging to the highest quartile of GI were at increased risk of having MetS (OR= 2.251, 95% CI: 1.120-4.525). These participants also had significantly higher odds of having elevated Triglyceride levels (OR: 2.157, 95% CI: 1.022-4.552). However, these associations were only observed in the crude model and lost significance after adjusting for confounders. Participants belonging to the second quartile of GI had significantly lower odds of having elevated fasting blood glucose (OR: 0.464, 95% CI: 0.225-0.957) in the crude model. This association remained significant after adjustment

for confounders (OR: 0.380, 95% CI: 0.174-0.833). No significant associations were detected between GL and MetS. A significant association was found for Triglycerides with the second quartile of GL (OR: 0.425, 95% CI: 0.181-0.995).

The developed GI/GL database for Lebanese foods will be a useful tool for similar research studies investigating diet-disease relationships. More studies are warranted to clarify the association between GI, GL and cardiometabolic abnormalities. Such studies can serve to develop public health strategies for awareness and disease prevention in Lebanon.

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To My Wonderful Parents

Nadia & Joseph

CHAPTER I

INTRODUCTION

The metabolic syndrome (MetS) refers to a constellation of cardiometabolic risk factors that identifies individuals at particularly high risk for cardiovascular disease and diabetes mellitus (G. M. Reaven, 1988). These risk factors include elevated fasting blood glucose, raised blood pressure, elevated serum triacylglycerols (TAG) levels, low high-density lipoprotein (HDL) cholesterol levels, and obesity, particularly central adiposity (K. G. M. M. Alberti et al., 2009). MetS is a major health concern putting more than a billion people in the world at increased risk of morbidity and mortality (Saklayen, 2018; Zimmet, Magliano, Matsuzawa, Alberti, & Shaw, 2005). The Eastern Mediterranean region is no exception. In the past few years, the prevalence of MetS has dramatically increased in Middle Eastern countries, with Lebanon in the lead (Chedid, Gannagé-Yared, Khalifé, Halaby, & Zoghbi, 2009; Sibai et al., 2008). A study by Naja et al. (2013) reported a MetS prevalence of 34.7% among Lebanese adults (Naja et al., 2013).Several genetic and environmental factors have been proposed as potential drivers for MetS development (Branth et al., 2006; Mirmiran, Noori, & Azizi, 2007). Among those, diet has gained great attention for being a modifiable risk factor in MetS etiology. A plethora of studies have investigated the effect of single food times and nutrients on MetS risk (Saklayen, 2018). In this context, clinical approaches to the prevention and management of MetS have always focused on dietary fat (Grundy, 2006). However, since 2017, attention started shifting towards carbohydrate intake, especially from refined grains and sugars (Dehghan et al., 2017). The resulting glycemic response, expressed as the postprandial change in blood glucose level, was recognized as a crucial determinant of cardiometabolic risk in an International scientific consensus held by the International

Carbohydrate Quality Consortium (ICQC) (Augustin et al., 2015). The glycemic response is dictated by both the quantity of carbohydrates ingested and the rate of absorption. In order to better assess it, the glycemic index (GI) and the glycemic load (GL) were proposed as measures of quality and quantity, respectively (D. J. Jenkins et al., 1981; Salmerón et al., 1997). Few studies have examined the association between dietary GI, GL and MetS in various populations, yielding conflicting results (Culberson, Kafai, & Ganji, 2009; de Mello Fontanelli, Sales, Carioca, Marchioni, & Fisberg, 2018; Finley, Barlow, Halton, & Haskell, 2010; Juanola-Falgarona et al., 2015; McKeown et al., 2004; Song, Lee, Song, Paik, & Song, 2014). However, such studies are lacking in the EMR and Lebanon. The overall aim of the present study is to evaluate the association between dietary GI, GL and cardiometabolic abnormalities in healthy Lebanese adults, based on a cross-sectional survey conducted in 2014. The specific objectives are to: 1) Determine the GI of Lebanese food items based on pertinent literature. 2) Estimate the GL of healthy Lebanese adults. 3) Examine the association between dietary GI and GL and fasting blood lipid levels, fasting glycemia and blood pressure in healthy Lebanese adults. 4) Investigate the association between dietary GI and GL and the MetS in a sample of healthy Lebanese adults.

Findings of this study can be used to develop culture-specific, evidence-based intervention strategies that contribute to better cardiometabolic health among Lebanese adults.

CHAPTER II

LITERATURE REVIEW

A. The Metabolic Syndrome (MetS)

1. History

Although what we now call the "Metabolic Syndrome" seems to be relatively modern, its components have been identified two hundred and fifty years ago (Crepaldi, 2006). Our current knowledge of its definition and complex pathophysiology is the result of the cumulative contributions of several researchers throughout history:

In the 18th century, JB Morgagni first introduced the "mechanistic concept" in human physiology and pathology. Enzi, Busetto, Inelmen, Coin, & Sergi (2003) note that using only an anatomical dissection knife, he was able to detect intra-abdominal fat accumulation in android obesity and study its clinical manifestations. In two medical letters (*epistola anatomo clinica*), the Italian physician and anatomist described a correlation between visceral obesity and several pathological findings including: atherosclerotic vascular disease, arterial hypertension, obstructive sleep apnea syndrome and hyperuricemia (Enzi, Busetto, Inelmen, Coin, & Sergi, 2003). The descriptions of clustering metabolic abnormalities go back almost one hundred years ago to the discovery of insulin by Banting and Best (Banting & Best, 1922). According to Sarafidis & Nilsson (2006), the discovery of MetS is marked by the following historical milestones:

During World War I when clinical observations in patients with metabolic abnormalities were recorded by Karl Hitzenberger and Martin Richter-Quittner. The Austrian physicians investigated the interdependence of diabetes mellitus and blood pressure (K Hitzenberger, 1921; K Hitzenberger & Richter-Quittner, 1921). Simultaneously, a Swedish (Eskil Kylin)

and a Spaniard (Gregorio Marañon) physicians independently discussed the usual coexistence of these two conditions and proposed common mechanisms for their development (Kylin, 1921; Marañon, 1922). A year later, in 1923, Kylin expanded this observation by introducing a triad of metabolic disturbances known as the "hypertension–hyperglycaemia–hyperuricaemia syndrome" (Hypertoni–Hyperglycemi–Hyperurikemi syndrom) (Kylin, 1923). This was considered as the earliest attempt to combine several metabolic abnormalities as one condition. A decade later, Vague first introduced gender differences in body fat distribution (Vague, 1956). He distinguished the gynoid from the android type of obesity, linking the latter to the development of dangerous metabolic abnormalities and eventually, cardiovascular disease. This was in line with the findings of Albrink and Meigs (1946) who also highlighted this relationship between acquired obesity in adulthood and hypertriglyceridemia and impaired glucose tolerance. Starting the 1960s, the definition began to evolve as researchers from different parts of the world independently investigated the clustering of the MetS components each from their own perspective (Albrink & Meigs, 1964; Sarafidis et al., 2006). The various nomenclatures are displayed in Table 1.

Table 1: The different nomenclatures assigned to MetS throughout history

Author	Year	Proposed nomenclature
Kylin	1923	Hypertension–Hyperglycaemia–Hyperuricaemia Syndrome (Hypertoni–Hyperglycemi–Hyperurikemi syndrom)
Camus	1966	Metabolic trisyndrome (Trisyndrome metabolique)
Avogaro & Crepaldi	1967	Plurimetabolic syndrome
Mehnert & Kuhlmann	1968	Syndrome of affluence (Wohlstandssyndrom)
Hanefeld & Leonhardt	1981	Metabolic syndrome (metabolische syndrom)
Reaven	1988	Syndrome X
Kaplan	1989	Deadly quartet
DeFronzo & Ferrannini	1991	Insulin resistance syndrome
Haffner	1992	

Adapted from Sarafidis & Nilsson (2006)

In 1966, the French Camus grouped gout, diabetes and hyperlipidemia together creating a "metabolic trisyndrome" (trisyndrome metabolique) (Camus, 1966). A year later, the Italians Avogaro and Crepaldi named this condition "plurimetabolic syndrome". This was based on the fact that hyperlipidemia, obesity and diabetes constantly occur together, often coupled with hypertension and coronary artery disease (Avogaro & Crepaldi, 1967). In 1968, the Germans Mehnert and Kuhlmann associated the increased prevalence of this condition with the nutrition and lifestyle habits of the developed Western communities during that era. According to the authors, this led them to label it as the "syndrome of affluence" (wohlstandssyndrom) (Mehnert & Kuhlmann, 1968).

A very important milestone in the comprehension of MetS during that era was the "glucose-fatty acid cycle", also known as the "Randle cycle". This finding highlighted the role of non-esterified fatty acids (NEFAs) in causing insulin resistance at the level of the muscle and the adipose tissue (Randle, Garland, Hales, & Newsholme, 1963). This came to reinforce the findings of Himsworth (1936) who was the first to differentiate between insulin-resistant and

insulin-sensitive diabetics (Himsworth, 1936). This later contributed to a better understanding of the pathophysiology of MetS, where insulin resistance plays a key role.

In the early 1970s, Hanefeld pointed out the high risk of atherosclerosis in individuals carrying these abnormalities (M Hanefeld, 1973). Eleven years later, Hanefeld and Leonhardt described the "metabolic syndrome" (metabolisches syndrom), a state which combines type 2 diabetes mellitus, hyperinsulinemia, gout and thrombophilia, leading to atherosclerosis. They noted the role of genetic predisposition and environmental factors in the development of this condition (M Hanefeld & Leonhardt, 1981). It was not until 1988 that Gerald M. Reaven, the most popular pioneer, joined the efforts to define MetS. Through his expertise in studying the resistance of insulin-mediated glucose uptake, he hypothesized that insulin resistance is the common aetiological factor for a group of disorders including: "impaired glucose tolerance (IGT), hyperinsulinemia, high levels of low-density lipoprotein (VLDL)-triglycerides, low levels of high-density lipoprotein (HDL) cholesterol and hypertension" (G. Reaven, 1993). The American endocrinologist called this combination "Syndrome X" to highlight its unknown aspect. He also mentioned the increased risk of atherosclerosis in individuals with the syndrome, in addition to the role of genetic and environmental factors in aggravating insulin resistance, as reported by Sarafidis & Nilsson (2006). A year later, Kaplan (1989) found that individuals with excess central body fat were more likely to suffer from glucose intolerance, high blood pressure and raised triglycerides levels. Therefore, he added central adiposity as an essential feature to Reaven's previous findings. Kaplan reintroduced the syndrome as having 4 components (central adiposity, IGT, hypertriglyceridemia and hypertension) and called it "the deadly quartet" due to its detrimental cardiovascular risk (Kaplan, 1989). In the early 1990s a big body of evidence, mostly by DeFronzo and Ferrannini, and Haffner, accused insulin resistance to be the main

culprit behind MetS, even calling it “insulin resistance syndrome” (Sarafidis & Nilsson, 2006).

2. Definition

Currently, MetS has numerous definitions (Tsai, Chu, Chen, & Chu, 2018). Many international organizations and expert groups, such as the World Health Organization (WHO), the European Group for the study of Insulin Resistance (EGIR), the National Cholesterol Education Program Adult Treatment Panel III (NCEP:ATPIII), the American Association of Clinical Endocrinology (AACE), the International Diabetes Federation (IDF), and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), have attempted to define MetS (Kassi, Pervanidou, Kaltsas, & Chrousos, 2011). In 1998, the WHO initiated the attempts to define MetS as part of their report on the definition and classification of diabetes mellitus (K. G. Alberti, Zimmet, & Consultation, 1998). In this report, insulin resistance was identified as the major underlying risk factor and was required for the diagnosis. It was identified by the presence of type 2 diabetes, IGT, or for individuals with normal blood glucose levels, by a glucose uptake below the lowest quartile of the values of the population. Thus, according to the first formalized definition of MetS, diagnosis of the syndrome could be made on the basis of several markers of insulin resistance in addition to two additional risk factors of the following: obesity (elevated Waist to Hip Ratio: > 0.90 for males and > 0.85 for females or elevated Body Mass Index), high blood pressure (> 160/90 mmHg), high triglyceride level (> 150 mg/dl), reduced HDL cholesterol level (< 35 mg/dl for men and > 21 mg/dl for women), or microalbuminuria (moderate increase in the level of urine albumin), which was a new component. Alberti & Zimmet’s working model received a lot of criticism, especially on the use of the euglycemic clamp to measure insulin sensitivity, making it unpractical in both the clinical and epidemiological setting (Alberti & Zimmet, 1998). A year later, Balkau & Charles, experts

from the EGIR proposed an alternative set of criteria. They suggested that diagnosing MetS required the presence of insulin resistance in addition to two or more of the following factors: central obesity, dyslipidemia (high triglycerides or low HDL), hypertension and fasting blood glucose ≥ 6.1 mmol/l. The authors defined insulin resistant individuals as the 25% of the representative population with the highest insulin resistance or the highest fasting insulin concentrations. During that time, fasting insulin was considered the best available simple proxy for insulin resistance (B. Balkau & Charles, 1999). In spite of these efforts, the EGIR definition did not reach international significance. In 2002, the Adult Treatment Panel (ATP III) of the NCEP proposed an approach that differs greatly from the one previously released by the WHO ("Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III)," 2001). No single factor was needed for diagnosis. Instead, the basis of diagnosis became the presence of 3 of the 5 following risk factors: abdominal obesity, elevated triglyceride, reduced HDL cholesterol, elevated blood pressure (≥ 130/85 mmHg), and elevated fasting glucose (Cleeman, 2001). Interestingly, criteria did not require demonstration of insulin resistance per se, assuming that those who fulfill 3 of the 5 criteria will most probably be already insulin resistant. Even though hypercoagulability, inflammation, and insulin resistance are common characteristics of MetS, the ATPIII/NCEP (2001) panel acknowledged that they cannot be routinely screened. Another remarkable characteristic is the emphasis on central obesity as a key component in the development of MetS. It was assessed by a waist circumference (WC) exceeding 102 cm for men and 88 cm for women. However, microalbuminuria was omitted. It is noticeable that the four main characteristics of the syndrome (hyperglycemia, dyslipidemia, hypertension and central obesity) are common between the two previously mentioned definitions, making both approaches very similar (Sarafidis & Nilsson, 2006).

Another attempt to define MetS was led by the American Association of Clinical Endocrinologists. They adopted the term “insulin resistance syndrome” and proposed four underlying abnormalities (elevated triglycerides, low HDL, high blood pressure and high fasting/postload blood glucose levels) without specifying how many are needed for diagnosis. It is important to note that those who fulfill type 2 diabetes criteria were excluded (Einhorn et al., 2003). A major limitation of this approach was that it was left to clinical judgement; therefore, it was not a useful tool for epidemiological studies (Sarafidis & Nilsson, 2006). Despite all of these attempts, there was still a need for a single, clear and universally-accepted diagnostic tool for MetS. In 2005, a consensus by the International Diabetes Federation (IDF) emerged to fill this gap in the literature. Similarly to the ATPIII recommendations, the IDF dropped the WHO requirement for insulin resistance. The main focus was placed on abdominal obesity, particularly waist circumference, which was considered crucial for MetS diagnosis when combined with two other risk factors. The IDF recommended that the threshold for waist circumference to define abdominal obesity should be ethinic-specific and suggested that it should be ≥94 cm for men and ≥80 cm for women in Europids (Zimmet et al., 2005). This was accompanied by the introduction of Metabolically Obese Normal Weight. MONW individuals are those who, despite their normal BMI, suffer from unfavorable metabolic abnormalities and are prospective MetS candidates. This novel concept came to further support the use of WC in MetS diagnosis (St-Onge, Janssen, & Heymsfield, 2004). The different criteria proposed by each of these associations are summarized in Table 2

Table 2: MetS diagnosis criteria as proposed by different organizations

WHO	EGIR	NCEP:ATPIII	AACE	IDF
High insulin level	High fasting insulin concentrations – insulin resistance	*Any three of the following:*	Impaired glucose tolerance	Central obesity = WC (ethnicity and gender specific)
+	+		+	+
Two of the following:	*Two of the following:*		*Two of the following:*	*Two of the following:*
1. Abdominal obesity WC > 37″, BMI > 30 kg m^{-2}	1. WC ≥ 94 cm (male) ≥80 cm (female)	1. WC > 40″ (male) >35″ (female)	1. Triglycerides ≥150 mg dL^{-1} Cholesterol – HDL <40 mg dL^{-1} (male) <50 mg dL^{-1} (female)	1. Triglycerides ≥150 mg dL^{-1} Cholesterol – HDL <40 mg dL^{-1} (male) <50 mg dL^{-1} (female)
2. Triglycerides >150 mg dL^{-1} Cholesterol – HDL <35 mg dL^{-1} (male) <39 mg dL^{-1} (female)	2. Triglycerides >2 mmol L^{-1} Cholesterol – HDL <1 mg dL^{-1}	2. Triglycerides ≥150 mg dL^{-1} Cholesterol – HDL <40 mg dL^{-1} (male) <50 mg dL^{-1} (female)	2. BP ≥ $\frac{130}{85}$ mm Hg	2. BP ≥ $\frac{130}{85}$ mm Hg
3. BP ≥ $\frac{140}{90}$ mm Hg	3. BP ≥ $\frac{140}{90}$ mm Hg or hypertensive medication	3. BP $\frac{130}{85}$ mm Hg		3. Fasting plasma glucose ≥5.6 mmol L^{-1} or T2DM
4. Microalbuminuria >30 mg g^{-1}	4. Fasting glucose ≥6.1 mmol L^{-1}	4. Fasting plasma glucose ≥110 mg dL^{-1}		

Criteria set out for the diagnosis of MetS according to a number of influential associations.
AACE, American Association of Clinical Endocrinology; BMI, body mass index; BP, blood pressure; EGIR, European Group for the Study of Insulin Resistance; HDL, high-density lipoprotein; IDF, International Diabetes Federation; MetS, metabolic syndrome; NCEP:ATPIII, National Cholesterol Education Program – Third Adult Treatment Panel; T2DM, type 2 diabetes mellitus; WC, waist circumference; WHO, World Health Organization.

Adapted from (O'Neill & O'Driscoll, 2015)

Finally, in 2009, the IDF and AHA/NHLBI representatives held discussions to resolve the remaining contradictions between definitions of MetS. There was a mutual agreement that abdominal obesity should not be a prerequisite for diagnosis but that it is 1 out of 5 criteria. That way, the presence of any 3 out of the 5 risk factors constitutes a diagnosis of MetS (Alberti et al., 2009). This joint scientific statement produced a harmonized definition of MetS, displayed in Table 3. When it comes to WC, ethnic-specific thresholds are summarized by population, organization and gender in Table 4.

Table 3 Criteria for clinical diagnosis of MetS

Measure	Cut point
Elevated waist circumference	Population- and country-specific definitions
Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator)	≥150 mg/dL (1.7 mmol/L)
Reduced HDL-C (drug treatment for reduced HDL-C is an alternate indicator)	<40 mg/dL (1.0 mmol/L) in males; <50 mg/dL (1.3 mmol/L) in females
Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)	Systolic ≥130 and/or diastolic ≥85 mm Hg
Elevated fasting glucose (drug treatment of elevated glucose is an alternate indicator)	≥100 mg/dL

Adapted from (Alberti et al., 2009)

Table 4: Current recommended waist circumference thresholds for abdominal obesity

Population	Organization (reference)	Men	Women
Europid	IDF	≥94 cm	≥80 cm
Caucasian	WHO	≥94 cm (increased risk)	≥80 cm (increased risk)
		≥102 cm (still higher risk)	≥88 cm (still higher risk)
United States	AHA/NHLBI (ATP III)	≥102 cm	≥88 cm
Canada	Health Canada	≥102 cm	≥88 cm
European	European Cardiovascular Societies	≥102 cm	≥88 cm
Asian (including Japanese)	IDF	≥90 cm	≥80 cm
Asian	WHO	≥90 cm	≥80 cm
Japanese	Japanese Obesity Society	≥85 cm	≥90 cm
China	Cooperative Task Force	≥85 cm	≥80 cm
Middle East, Mediterranean	IDF	≥94 cm	≥80 cm
Sub-Saharan African	IDF	≥94 cm	≥80 cm
Ethnic Central and South American	IDF	≥90 cm	≥80 cm

Adapted from: Alberti et al. (2009)

3. Epidemiology of MetS

Worldwide, MetS is a major health concern associated with increased morbidity and mortality (Zimmet et al., 2005). Over the last fifty years, there has been a dramatic change in the human environment, lifestyle and behaviors. This resulted in escalating rates of both obesity and type 2 diabetes coupled with an increase in MetS prevalence. Knowing that MetS is about 3 times more common than diabetes, it is estimated to affect about one quarter of the world population. In other words, more than a billion people in the world are currently affected by MetS (Saklayen, 2018). The prevalence of MetS in the world's adult population is estimated to range between 20 and 25%, according to the International Diabetes Federation (IDF, 2006). Prevalence estimates vary based on the population and diagnostic criteria used (Kassi et al., 2011). In the United States, MetS affects an estimated 64 million adults based on the NHANES survey (Ford, Giles, & Mokdad, 2004). The survey reveals an increase in MetS prevalence from 32.9% in 2003-2004 to 34.7% in 2011-2012. It was noticed that the

prevalence of MetS increased dramatically as BMI increased (Ervin, 2009). However, starting 2007, it remained stable as a result of the stabilization of obesity rates in the country (Aguilar, Bhuket, Torres, Liu, & Wong, 2015). After significantly increasing from 1988 to 2012 for every sociodemographic group, MetS prevalence affected a third of all US adults by the year 2012 (Moore, Chaudhary, & Akinyemiju, 2017). In Canada, representative data from the Health Measures Survey revealed that about one in every five Canadian adults suffered from MetS. Age was the strongest predictor of the syndrome, in addition to lower education and income levels. Among the MetS risk factors, abdominal obesity was the most common, mostly in women. Meanwhile, men were more likely to have hypertriglyceridemia and elevated fasting glucose levels (Riediger & Clara, 2011). Moving to Latin America, a systematic review revealed a general MetS prevalence ranging from a minimum of 18.8% in Arequipa to a maximum of 43.3% in San Juan. The syndrome was shown to be slightly more frequent in women and in those over 50 years of age, with low HDL cholesterol levels (62·9 %) and abdominal obesity (45·8 %) being the most common components (Márquez-Sandoval et al., 2011). In Brazil, for instance, a systematic review from 2013 reported a high MetS prevalence of 29.6%. Values varied depending on the location: highest in an indigenous population (65.3%) and lowest in a rural area (14.9%). Hypertension and low HDL were ranked as the leading risk factors there (de Carvalho Vidigal, Bressan, Babio, & Salas-Salvadó, 2013). Subsequently, in 2018, a MetS prevalence of 30.3% was detected among adult and older adults of Sao Paulo (de Mello Fontanelli et al., 2018).

Several observation studies were carried out across Europe. Data from Switzerland, Spain, Netherlands, Italy, France, Denmark and the United Kingdom reported a MetS frequency of 7% - 36% for men and 5% - 22% for women aged 40 to 55 years (Beverley Balkau et al., 2002). In Norway, the age-specific prevalence of MetS using the IDF criteria was 29.0% for men and 30.3% for women (Hildrum, Mykletun, Hole, Midthjell, & Dahl, 2007). In 2014, the

Healthy Obese Project of BioSHaRE-EU gathered data from several cohort studies across Europe: Estonia, Finland, Germany, Italy, Netherlands, Norway and the United Kingdom. For women, the age-standardized percentage of obese subjects with MetS ranged from 24% in the Italian CHRIS cohort to 65% in the Finnish Health2000 cohort. In men, it ranged from 43% in CHRIS to 78% in the Finnish DILGOM cohort. Elevated blood pressure was the most frequently occurring factor (van Vliet-Ostaptchouk et al., 2014). Meanwhile in Spain, results from a cross-sectional, population-based health survey in Catalonia showed a MetS prevalence of 28.5 % and 24.8 % according to IDF and ATP III criteria, respectively in 2002-2003. It was significantly positively associated with male gender, age, BMI, physical inactivity and lower socioeconomic status (Buckland, Salas-Salvadó, Roure, Bulló, & Serra-Majem, 2008). A more recent study showed a MetS prevalence of 21.39% (using ATPIII criteria) and 16.46% (using IDF criteria) in Spanish men. Surprisingly, the prevalence was much lower in Spanish women who scored 6.94% (using ATPIII criteria) and 10.07% (using IDF criteria) (Tauler et al., 2014). A study in Greece revealed a high MetS prevalence of 45.7% based on the IDF criteria (V. Athyros et al., 2010). Only 5 years earlier, the MetS-Greece Multicentre Study had reported a prevalence of 23.6% according to NCEP ATP- III criteria (V. G. Athyros et al., 2005).

Moving to Asia, studies generated remarkable results following the rapid socioenvironmental changes in that part of the world. Very recently, a nationally representative study in China reported an overall standardized MetS prevalence of 24.2% (24.6% in men and 23.8% in women). A positive association was shown with age. However, it was negatively associated with physical activity level in men and inversely associated with education level in women (Li, Zhao, Yu, Wang, & Ding, 2018). In Korea, another Asian country, the National Health and Nutrition Examination Surveys from different years were compared. The age-adjusted

prevalence of MetS increased significantly with time. It shifted from 24.9% in 1998 to 29.2% in 2001 to 30.4% in 2005, to finally reach 31.3% in 2007 (Lim et al., 2011).

Similarly to western communities, the prevalence of MetS is on the rise in developing countries as well. It started as a characteristic of westernized societies but is now emerging in developing countries and countries of the Eastern Mediterranean Region (Chedid, Gannage-Yared, Khalife, Halaby & Zoghbi, 2009). This increase is witnessed regardless of the diagnostic tool used and is highly attributed to the transition from a traditional to a western-like diet and lifestyle. It is also important to mention the significant demographic and epidemiological transitions that occurred as these countries started becoming more economically resourceful. This has resulted in an increased BMI, general and abdominal obesity, in addition to metabolic abnormalities (Kassi et al., 2011). Recorded values of MetS prevalence in these countries range from as low as 9.8% in males of urban India to as high as 42% in females of urban Iran (Kassi et al., 2011). In fact, MetS was shown to affect more than 11 million Iranians. In 2009, a national survey revealed that MetS prevalence was about 34.7% (ATPIII criteria), 37.4% (IDF criteria) and 41.6% (ATPIII/AHA/NHLBI criteria) (Delavari, Forouzanfar, Alikhani, Sharifian, & Kelishadi, 2009). The same pattern was observed with all definitions: higher levels in women, urban settings and older age groups, in comparison to their counterparts. A study conducted about the migration of Iranians to Sweden provides further confirmatory evidence of the ethnic predisposition to low HDL cholesterol (Koochek et al., 2008). A recent study in Kazakhstan reported a low MetS score of 14.74% of study population. Interestingly, it was noticed to occur more frequently among women than men. Among men, MetS manifested itself earlier in life (Sorokina et al., 2017). In Turkey, MetS prevalence was found to be high: 36.6% according to ATP III and 44.0% according to IDF criteria. MetS risk was 1.62-fold higher in females compared to males. Increased BMI and age were also independent risk factors for MetS development (Gundogan

et al., 2013). Similarly, a study in Tunisia recorded a MetS prevalence of 55.8% in women and 30.0% in men using the IDF criteria. The prevalence was higher in women than in men using all definitions. This was mostly because of significant differences in central obesity, HDL cholesterol and, to a lesser extent, hypertension (Harzallah, Alberti, & Ben Khalifa, 2006). A study of female Saudi Arabian subjects found the MetS prevalence to be 16.1% (IDF criteria) and 13.6% (ATPIII criteria) respectively (Al-Qahtani, Imtiaz, Saad, & Hussein, 2006). In a population in Northern Jordan, the prevalence of MetS was reported to be 36.3%, with a significantly higher prevalence in women than in men. The most common abnormality was low HDL cholesterol in men (62.7%) and increased waist circumference in women (69.1%) (Khader, Bateiha, El-Khateeb, Al-Shaikh, & Ajlouni, 2007). A study using data from the population-based program 'Weqaya', suggested that almost half of the studied population in Abu Dhabi was diagnosed with MetS, using IDF criteria. Also, 78.6% of them were found to be diabetic (Hajat & Shather, 2012).

Among these countries, Lebanon—a small middle-income country on the Eastern shore of the Mediterranean Sea—has unique features that make the health of its population a complex challenge: "a high urbanization rate (87%), fast decline in fertility and mortality rates and a growing trend toward survival in later life, coupled with westernization and changes in lifestyle". In fact, one of the highest estimated prevalences of MetS in the region (31.2%) was observed in Lebanese adults (Sibai et al., 2008). The study identified central obesity and low HDL-cholesterol as the leading risk factors and males as more likely to develop MetS than their female counterparts. These findings were in line with those of Naja et al. (2013) where the prevalence of MetS in Lebanese adults was found to be around 34.7%.

4. Pathophysiology of MetS

During the last three decades, as the prevalence of MetS increased, so did our understanding of the biology behind this complex and multifactorial syndrome (Saklayen, 2018).

As mentioned previously, central obesity is unanimously recognized for its primary role in the pathophysiology of MetS. This was evidenced by the attention given to this risk factor, especially in the first IDF diagnostic criteria (K. George M. M. Alberti, Zimmet, Shaw, & Group, 2005). What differentiates this android obesity from the gynoid one is its detrimental health effect due to an increased release of free fatty acids (FFAs) that are delivered directly and at high rates to the liver via the portal vein (Miles & Jensen, 2005). FFAs will stimulate the secretion of harmful substances including plasminogen activator inhibitor-1 (PAI-1). PAI-1 further affects adipogenesis and disturbs the insulin signaling cascade (Alessi & Juhan-Vague, 2006). Additionally, this can lead to endothelial dysfunction, a double burden that increases the likelihood of developing MetS (Miles & Jensen, 2005). Endothelial dysfunction is accompanied by impaired nitric oxide-mediated vasodilation, increasing arterial stiffness and leading hypertension and abnormalities of the lipid profile (Aizawa, Shoemaker, Overend, & Petrella, 2009; Emanuela et al., 2012; Ferrari & Weidmann, 1990). Once enlarged, adipocytes lack adequate oxygen supply, leading to the stimulation of macrophages. The major involvement of residing macrophages in energy metabolism is a growing research interest (Jing et al., 2018). This will subsequently encourage the release of several adipocytokines: TNF alpha, IL-6 and Angiotensin II which will decrease insulin sensitivity and promote insulin resistance (Esser, Legrand-Poels, Piette, Scheen, & Paquot, 2014). Moreover, subjects with excess visceral fat are characterized by lower levels of plasma Adiponectin (Di Chiara, Argano, Corrao, Scaglione, & Licata, 2012). This anti-inflammatory adipokine possesses insulin sensitizing properties (Klöting & Blüher, 2014), as well as effects on beta cell functioning and survival (Adamczak & Wiecek, 2013). This proposes that it may

be involved and causally related to the etiology of MetS (Okamoto, Kihara, Funahashi, Matsuzawa, & Libby, 2006). In fact, Adiponectin showed effective protective effects against MetS in a rat model with polycystic ovary syndrome (Benrick et al., 2017).

Moreover, other newly recognized adipocytokines like Visfatin may be involved in the complex etiology of MetS (J.-H. Kim, Kim, Im, & Lee, 2010). This is mostly due to its proposed insulin-mimicking effects and contribution to the body's inflammatory processes (Stofkova, 2010). Neprilysin, an adipose tissue enzyme, is also under investigation. In addition to fibroblast growth factor 21 for its role in glucose and lipid metabolism regulation (Xu et al., 2009).

Even though obesity and insulin resistance are the core of the etiology of MetS, several factors are being studied as potential contributors to its pathogenesis, such as: chronic stress and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and autonomic nervous system (ANS), increases in cellular oxidative stress, renin-angiotensin-aldosterone system activity, and intrinsic tissue glucocorticoid actions (Kassi et al., 2011). Also, a novel hypothesis emphasizes the importance of the gut microbiome and its effect on overall health and possibly features of MetS (Saklayen, 2018). These hypotheses are still not fully convincing and require further epidemiological confirmation.

Recently, a new role has been proposed for discovered molecules such as micro RNAs that may also play a role in insulin resistance and development of MetS by regulating cellular gene expression at the transcriptional or post-transcriptional level. However, the pathway remains unclear and further studies are needed to elucidate this novel agent in MetS development (Kassi et al., 2011). Epigenetics is a growing field of research that may explain several health conditions, including MetS, through exposures and effects on gene expression in the human genome. Studies have shown strong associations between adulthood MetS and

intrauterine nutrition, postnatal nutrition, and growth. By examining mothers and children from the 1944 – 1945 Dutch famine, it was observed that low birthweight (LBW) infants, who had rapid catch up growth as infants, had the highest risk of developing obesity and MetS in adult life. Similarly, the same observation was seen in China after the 1959 – 1961 famine. This phenomenon can be explained by decreased DNA methylation of the imprinted IGF2 gene in the offspring and hypermethylation of Leptin and TNF. It is proposed that this may be a driver of the newly increased prevalence of obesity and MetS in developing countries (Heijmans et al., 2008). However, further investigation is required in this field.

Finally, it is important to add that susceptibility and age of onset of MetS are highly influenced by genetic and environmental factors, even in individuals with identical risk profiles (Kassi et al., 2011).

5. Associated health risks

Because it is a multi-risk factor condition, MetS carries a greater risk for adverse clinical outcomes. The syndrome feeds into the spread of diseases like diabetes, cardiovascular diseases, strokes, and other disabilities (Saklayen, 2018).

A systematic review and meta-analysis of 87 studies revealed that the MetS is associated with a twofold increase in the risk of developing CVD (Mottillo et al., 2010). This is mostly attributed to the development of atherogenic dyslipidemia, which is defined by elevated levels of triglycerides (TG) and small-dense low-density lipoprotein (LDL) cholesterol and low levels of high-density lipoprotein (HDL) cholesterol. This detrimental lipid triad compromises heart health (Grundy, 2006). According to Mottillo et al. (2010), women were found to be affected more than men, most probably due to menopause and polycystic ovary syndrome.

Although ATPIII identified CVD as the main clinical outcome of MetS, most people with the syndrome are insulin resistant, therefore, at an increased risk for type 2 diabetes. In fact,

regardless of the diagnostic criteria used, MetS predicts an increased risk of diabetes mellitus type 2 with a relative risk between 3.5 and 5.2 (Ford et al., 2004). The effect of abdominal obesity on fasting plasma glucose levels is behind this phenomenon. In a cohort of the Framingham Offspring Study, MetS patients having impaired fasting glucose (IFG) were at higher risk of developing type 2 diabetes mellitus (RR = 11). On the contrary, subjects without IFG manifested a lower type 2 diabetes risk (RR = 5) (Wilson, D'Agostino, Parise, Sullivan, & Meigs, 2005). Studies have revealed that MetS is correlated with a fivefold increased risk of newly diagnosed type 2 diabetes (Tsai et al., 2018).

Additionally, through the combined effects of dyslipidemia, diabetes, hypertension and sleep apnea, CVD risk is further increased (Kassi et al., 2011). The Framingham risk equations actually reinforce this concept because they incorporate many of the components of MetS (Grundy et al., 2004).

It is also important to mention the hepatic component of MetS. As explained by (McCullough, 2011), this includes several liver-related pathologies with nonalcoholic steatohepatitis (NASH) being the most prominent feature. In fact, 88% of patients diagnosed with NASH were found to be carrying MetS, as evidenced by biopsy testing, with an adjusted odds ratio of 3.2 (Marchesini et al., 2003). The obesity-related cycle of hyperglycemia, insulin resistance and compensatory hyperinsulinemia is the main culprit behind this phenomenon.

Moreover, elevated insulin levels were proven to induce obesity-related tumorigenesis. This is caused by free insulin growth factor-1 (IGF-1), a molecule which once accumulated, can exert this carcinogenic effect (Renehan, Frystyk, & Flyvbjerg, 2006). This implies that MetS can even increase the risk of having cancer. A meta-analysis of cohort studies revealed an association with liver cancer in men with a risk ratio of 1.43. For postmenopausal women with MetS, breast cancer was in the lead with an RR of 1.61 (Esposito, Chiodini, Colao,

Lenzi, & Giugliano, 2012). Other potential consequences of MetS include: cholesterol gallstones, asthma, polycystic ovary syndrome and sleep disturbances (Grundy et al., 2004).

6. Diet as a risk factor for MetS

MetS and its components are the result of the interaction between several genetic and environmental factors (Mirmiran, Noori, & Azizi, 2008; Branth et al., 2007). The main culprit seems to be the modern lifestyle and its associated physical inactivity and unhealthy diet. (Juanola-Falgarona et al., 2015). Extensive investigations have been conducted to define the role of diet in influencing MetS status. According to (Saklayen, 2018), some dietary items (olive oil, capsaicin, luteolin, curcumin, cinnamon, rosemary, polyphenols, green tea, soy, citrus, cocoa…) have been associated with lower risk of MetS or its components, with varying levels of evidence. Other research have studied the effect of the diet as a whole, rather than focusing on a single nutrient. A plethora of studies support the Mediterranean diet for being protective against MetS due to its rich and nutritious components (Esposito, Kastorini, Panagiotakos, & Giugliano, 2013).

On the contrary, the western diet is associated with an increased risk of MetS. Evidence from the "Atherosclerosis Risk in Communities" study links the western diet consisting of processed and fried foods, refined grains, and red meat with an 18% increase in MetS risk In Lebanon, a study on dietary patterns by Naja et al. (2013) revealed that the "fast food/dessert" dietary pattern is positively associated with impaired glucose metabolism and MetS in a sample of Lebanese adults.

While clinical approaches to the prevention and management of MetS vary, the most popular one is adopting a diet that is low in saturated fat and total fat (Grundy et al., 2006). It has been shown that saturated fat plays an essential role in the development of insulin resistance. In fact, it indirectly stimulates the toll-like receptor (TLR) 4 signaling pathway which

activates c-Jun N-terminal kinase (JNK) and IκB kinase (IKK). In turn, this will lead to an inhibition of insulin signaling by the phosphorylation of insulin receptor substrate-1 (IRS-1) and the production of inflammatory cytokines (Glass & Olefsky, 2012).

While dietary fat is given most of the attention, it has also been suggested to consider the glycemic response induced by increased carbohydrate intake from refined grains and sugars. In 2017, the Prospective Urban Rural Epidemiology (PURE), a cohort study of more than 135,000 subjects from 18 countries, shattered all beliefs about dietary fat. The study, published in the prestigious "Lancet", clearly stated that fats, including saturated fats, were associated with lower risk of total mortality and stroke. The thought-provoking article placed all the blame on a high carbohydrate intake, which was associated with an adverse effect on total mortality (Dehghan et al., 2017). In this context, replacing saturated fat with carbohydrates could be a 2-edged sword. While it would improve insulin sensitivity and glucose tolerance on one hand, it can on the other hand, increase postprandial hyperglycemia and insulin demand on the other (Jennie C. Brand-Miller, 2004). In this respect, carbohydrate quality plays a crucial role.

B. Dietary Glycemic Response

The importance of postprandial glycemia in overall health was recognized in a scientific consensus (Augustin et al., 2015). It was acknowledged as a valid and reproducible tool for this purpose. Over the course of history, carbohydrates were divided into two major forms: simple (monosaccharides and disaccharides) and complex (polysaccharides including starch, cellulose, fiber and their related compounds). A major flaw of this classification was its inability to predict plasma glucose and insulin trends, which are key elements in the genesis of several health outcomes (Crapo, Reaven, & Olefsky, 1976). However, this is only the tip of the iceberg. Glycemic response is actually dictated by both: the amount of carbohydrates

consumed (quantity) and the rate of absorption (quality). Hence, some advocates are highlighting the importance of studying the glycemic index and the glycemic load of the diet (Brand-Miller, 2004). Although it is still controversial, there is a growing interest in using glycemic index and glycemic load as potentially important exposures in the investigation of risk for a variety of chronic diseases (Augustin et al., 2015; Flood et al., 2006).

1. Glycemic Index (GI)

In 1981, Jenkins and co-workers were the first to introduce the term "glycemic index" (GI). This concept was created as a measure of carbohydrate quality. It allows for the comparison of foods based on their physiological effects rather than their chemical composition only (D. J. Jenkins et al., 1981). Foods having the same carbohydrate content can, in fact, produce a wide range of glycemic responses in comparison with the average blood glucose response following the ingestion of a referent food. In 1998, the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) released a report on carbohydrates in human nutrition emphasizing the importance of GI testing standardization. The joint expert statement was coupled with a detailed protocol for GI measurement: Ten healthy subjects, at least, are fed 50 grams of available (digestible) carbohydrates from the test food. Over the following 2 hours, the effect on their capillary blood glucose levels is measured. Then, the incremental area under the curve (AUC) of blood glucose response for each person is derived. On a separate occasion, the same subjects are instructed to consume a 50 gram portion of a reference food. Glucose or white bread are usually adopted as reference, having a GI of 100. Once again, by checking the AUC, their 2 hour capillary blood glucose response is recorded. By dividing the glucose AUC for the test food by that of the reference food and multiplying by 100, the GI value of the studied food is obtained. Then, an average for all subjects is calculated (FAO/WHO, 1998). This method was originally created to serve as a guide for individuals with diabetes, relying on food's immediate effect on blood glucose

levels. In their food selection, diabetics were advised to choose foods with a lower GI to benefit from their relatively low glycemic response following ingestion. This was a remarkable milestone in the evolution of the diabetic diet (Jenkins et al., 1983).

Subsequently, in 2002, the International GI Table was created by Foster-Powell and colleagues. By also including unpublished data from labs including Sydney University's Glycemic Index Research Service, the table gathered more than 1,300 GI values corresponding to more than 750 food items (Foster-Powell, Holt, & Brand-Miller, 2002). The foods were classified and divided into 22 food groups:

Table 5: Food groups adopted by Foster-Powell and colleagues' international GI table

1. Bakery Products	2. Legumes and Nuts
3. Beverages	4. Meal-Replacement Products
5. Breads	6. Mixed Meals and Convenience Foods
7. Breakfast Cereals and Related Products	8. Nutritional Support Products
9. Breakfast Cereal Bars	10. Pasta and Noodles
11. Cereal Grains	12. Snack Foods and Confectionery
13. Cookies	14. Sports Bars
15. Crackers	16. Soups
17. Dairy Products and Alternatives	18. Sugars and Sugar Alcohols
19. Fruit and Fruit Products	20. Vegetables
21. Infant Formula and Weaning Foods	22. Traditional Foods

For a food to be eligible for classification, it must contain enough available carbohydrates per serving (25 to 50g) to allow the clinical determination of GI. For this reason, foods with little or no carbohydrates (meat, poultry, fish, avocados, salad vegetables, cheese, eggs…) were assigned a value of zero (Flood et al., 2006). This table became a reliable reference for carbohydrate classification globally. In such classification, foods are categorized as having low (less than 55), medium (55 to 69) or high GI (above 70), respectively (Brand-Miller, 2004). Since its formulation, the concept of GI served as a useful tool for the assessment of

carbohydrate quality used for research on the etiology and prevention of several chronic diseases (Olendzki et al., 2006).

2. Glycemic Load (GL)

Although the quality of carbohydrates is very important, the quantity is an essential factor to be taken into account. For example, watermelon (a high GI food) would typically be avoided in a low GI diet. However, this fruit only contains 5 grams of carbohydrates per 100 grams. Therefore, it would actually have a minimal effect on glycemia.This observation sheds the light on the importance of a quantitative assessment tool (Venn & Green, 2007).

It was not until 1997, when researchers from Harvard were seeking a way to derive estimates of postprandial glycemia and insulin demand, that the glycemic load (GL) was created. GL aims to quantify the overall glycemic effect of food with respect to its specific carbohydrate content in typically consumed quantities (Salmerón et al., 1997). GL can be obtained by two different methods: an indirect and a direct one. The indirect method consists of multiplying the GI of a food (divided by 100) by its available carbohydrate content (in grams) in the portion consumed. On the other hand, the "glycemic equivalence" is a more direct approach for GL calculation. For each subject, a range of doses of the reference food are tested over the course of several days while recording the AUC responses. For each individual, a standard curve is plotted with the increasing quantity of reference on the x axis and its corresponding blood glucose AUC on the y axis (Venn & Green, 2007). The authors suggest that both methods are coherent, at least when food is frequently consumed on a regular basis. The GL classification system categorizes food as being low (less or equal to 10), medium (between 10 and 20) or high (greater or equal to 20). In some cases GI and GL can have a positive association. This applies to the comparison of cornflakes to porridge: where cornflakes, having the higher the GI, also has the higher the GL. However, the relationship between GI and GL is not that simple. A high GI food, if eaten in low quantities, can have a low GL.

Alternatively, if the portion size is big, a food with a low GI can have a high GL. Another example given by the authors is that of macaroni and mashed potato. Although macaroni has the lower GI between the two foods, it is actually the one with the higher GL per serving. It is also important to take into consideration the nutrient profile. For example, foods varying as much as a chocolate bar and paraboiled rice can actually have very similar GI and GL values.As different as they may seem, these two measures are actually two sides of the same coin. GL, however, combines the qualitative and the quantitative aspects together. It came to reinforce the concept of GI by specifying the joint effect of both quality and quantity per serving of carbohydrate ingested from a food item (Venn & Green, 2007).

Although GI and GL have been widely used for commercial and research purposes, their validity in clinical and research settings remains controversial (Eleazu, 2016).

Recently, Vega-Lopez, Venn and Slavin (2018) gathered randomized controlled trials and observational studies published between 2006 and 2018 testing the short-term (satiety) and long-term (weight, cardiovascular disease, and type 2 diabetes) effects of GI and GL in humans. The review yielded limited evidence on the relationship between glycemic response and disease risk. Thus, GI and GL were found to be weak predictors of health and disease outcome when compared to other dietary factors (Vega-Lopez, Venn, & Slavin, 2018). This was in line with Matthan, Ausman, Meng, Tighiouart and Lichtenstein (2016) who do not encourage GI and GL as ideal food choice guides. In their study, the authors aimed to examine the intra- and inter-individual variability in glycemic response. They found that the GI of a food can vary by a mean of 20% within an individual and 25% among individuals despite increasing sample size, replication of reference and test foods, length of blood sampling and AUC calculation method. This affects the clinical and public health applicability of GI and GL, in relation to their associations with chronic disease risk (Matthan, Ausman, Meng, Tighiouart, & Lichtenstein, 2016). Over time, GI and GL have

also been criticized for their reproducibility and variation according health status, race, and gender and degree of insulin resistance. In light of these inconsistent findings, the American Diabetes Association (ADA) has not fully endorsed the use of GI for food guidance yet (Eleazu, 2016).

3. GI, GL and MetS

a. Association of GI, GL and MetS risk

Several studies have evaluated the association between GI and GL with MetS and its components, yielding conflicting results. In this context, prospective studies have been limited and inconsistent:

GI & MetS: While McKeown et al. (2004) found a positive association between GI and the prevalence of MetS in the Framingham Offspring Cohort, other studies were only able to detect an association in subsets of the population. The PERIMED study conducted by Juanola-Falgarona et al. (2015) revealed that a 5-point higher GI was associated with a greater risk of prevalence of MetS in the first two age groups, but not in those aged 75 and older. On the other hand, the Cooper Center Longitudinal Study found a positive association across quintiles of GI and MetS, however, this was observed exclusively in men (Finley, Barlow, Halton & Haskell, 2010).

GL & MetS: In the Cooper Center Longitudinal Study, no significant association was observed between GL and MetS in women. Surprisingly, in men, the highest quintile of GL had decreased odds of having MetS (Finley, Barlow, Halton & Haskell, 2010). More recently, the PERIMED study found an association between 10-point higher dietary GL and greater risk of developing MetS in all age groups. However, it was not significant (Juanola-Falgarona et al., 2015).

In the 3rd National Health and Nutrition Examination Survey, although GL was associated with HDL (a component of MetS), Culberson et al. (2009) failed to detect any association between GL and prevalence of MetS. Cross-sectional studies assessing this association have also had their share of controversy: In Korea, researchers identified an increased risk of MetS across quintiles of GI and GL only in females out of the 910 participants enrolled. Years later, another cross-sectional study on a bigger sample of 6,845 Korean adults did not detect any association between GI, GL and MetS (K. Kim, Yun, Choi, & Kim, 2008; Song et al., 2014). Similarly, a recent cross-sectional, population-based study conducted by de Mello Fontanelli et al. (2018) found no association between GI, GL and MetS in 591 adult residents of São Paulo.

Trials presented mixed results as well. A study carried out on 15 overweight subjects over a period of 11 weeks found no effect of diets with identical macronutrient content but with differences in GI and GL on MetS biomarkers (Vrolix & Mensink, 2010). During the same year, Klemsdal and colleagues compared the effect of a low-GL diet and a reduced total fat diet in 202 individuals with varying degrees of MetS over a one year intervention. They observed significant improvements in MetS risk factors in both diets, however, the low-GL diet appeared more effective in individuals with MetS rather than healthy ones (Klemsdal, Holme, Nerland, Pedersen, & Tonstad, 2009).

b. ***Pathophysiology of the link between GI, GL and MetS***

The GI and GL of the standard US diet have risen in the past years. Modern food processing technologies and increased carbohydrate intakes are major drivers for this increase (Ludwig, 2002). Since then, the hormonal and metabolic events following the ingestion of high GI/GL foods became a topic of interest (Du, Van Der & Feskens, 2006). Glucose homeostasis is tightly regulated by insulin and counterregulatory hormones (glucagon, epinephrine, cortisol and growth hormone). The fast absorption and spike in blood glucose level after a high GI

meal disturb these mechanisms, which will complicate the achievement of normoglycemia. According to Ludwig (2002), when comparing the body's acute response after consumption of a high GI versus a low GI meal with identical energy and nutrient content, several differences were noted:

In the early postprandial stage (0-2h after meal), carbohydrates are rapidly absorbed leading to hyperglycemia (Vrolix, van Meijl, & Mensink, 2007). This increase in blood glucose (at least double) is coupled with elevated concentrations of the gut hormones glucagon-like-peptide-1 and glucose-dependent insulinotropic polypeptide, stimulating insulin release from pancreatic beta cells and inhibiting glucagon release from alpha cells. Therefore, high insulin, low glucagon and high incretins are observed, explains Ludwig (2002). The resulting high insulin to glucagon ratio amplifies the body's usual anabolic response to eating: uptake of nutrients by insulin-responsive tissues, stimulation of glycogenesis and lipogenesis and suppression of gluconeogenesis and lipolysis. Accordingly, the expression of enzymes involved in lipid synthesis, such as ACC mRNA, is up-regulated, whereas the expression of those involved in lipid oxidation, such as CPT1 mRNA, are down-regulated (J. C. Brand-Miller, Holt, Pawlak, & McMillan, 2002). Therefore, low free fatty acid levels are observed (Du, Van der, & Feskens, 2006).

In the middle postprandial stage (2-4h after meal), the nutrient absorption from the gastrointestinal tract decreases but the previously mentioned biological changes (high insulin and high glucagon) persist. As a result, blood glucose drops rapidly, often leading to hypoglycemia. Physiologically, this is exacerbated by a decrease in glucose oxidation rate (Vrolix, van Meijl & Mensink, 2007). Free fatty acid, the other metabolic fuel, is suppressed further in this case (Ritz, Krempf, Cloarec, Champ, & Charbonnel, 1991). The decrease in metabolic fuels urges the body to restore energy homeostasis by provoking hunger and potentially, food intake. It was found that hyperinsulinemia and hypoglycemia after

consumption of a high GI meal preferentially stimulate cravings for more high GI foods, while also encouraging overconsumption. This traps the body in an ongoing cycle of hyperglycemia, hypoglycemia and hyperphagia (Ludwig, 2002; Brand-Miller, Holt, Pawlak & McMillan, 2002). Finally, during the late postprandial stage (4-6h after meal), low circulating levels of metabolic fuels are observed. This will trigger a counter-regulatory hormone response in order to restore euglycemia. Similarly to fasting, glycogenolysis and gluconeogenesis are stimulated, followed by a marked increase in free fatty acid levels (Du et al., 2006). The aforementioned metabolic disturbances following a high GI consumption pose the individual at a higher risk of developing obesity, diabetes and cardiovascular disease, all associated with the metabolic syndrome. In fact, it was found that calorie for calorie, high GI stimulates more insulin secretion than low GI carbohydrate intake because of postprandial hyperglycemia and increased insulin levels (Ludwig, 2002). Therefore, a habitual high GI may have several health implications:

First, studies provide the hypothesis that a high GI diet promotes excessive weight gain (Augustin et al., 2015). The faster digestion and absorption and higher insulin levels after high GI meals dictate differences in satiety and energy partitioning that, over the long term, promote the expansion of body fat stores (Brand-Miller, Holt, Pawlak & McMillan, 2002). This includes the rapid activation of key rate-limiting enzymes. For example, malonyl-CoA, an intermediate of glucose oxidation, strongly inhibits fatty acid transport into the mitochondria, resulting in decreased fatty acid oxidation (Wolfe, 1998). Over a chronic exposure, this can result in decreased expression of crucial enzymes and eventually alter the potential for fat oxidation (Brand-Miller, Holt, Pawlak & McMillan, 2002).

Second, this state of primary hyperinsulinemia may in turn decrease insulin sensitivity and cause insulin resistance. Other drivers include the direct effects of hyperglycemia, counter-regulatory hormone secretion and high late postprandial fatty acid levels. Eventually, a

habitual high GI intake initiates a cycle of hyperinsulinemia and insulin resistance that places Beta cells under higher demand. On the long term, this can lead to impaired Beta cell function through both glucotoxicity (resulting from hyperglycemia) and lipotoxicity (resulting from increased fatty acid concentrations) (Ludwig, 2002).

Third, a high GI consumption has been acknowledged as a significant cardiovascular risk factor. Recent studies have been focusing on postprandial lipemia, based on the thought that increased triglycerides and triglyceride-rich lipoproteins after a meal are highly atherogenic (Augustin et al., 2015). The biological mechanisms behind this phenomenon are thought to be through increased oxidative stress induced by high levels of blood glucose (Liu et al., 2002). Several lines of evidence have shown that high blood glucose levels could increase reactive oxygen species (ROS), which may in turn lead to the oxidation of membrane lipids, proteins, lipoproteins and DNA, damage endothelial function and activate inflammation (Ludwig, 2002; Liu et al., 2002). In fact, high insulin levels and insulin resistance could cause hypertension. This alteration in blood pressure is achieved by inducing arterial stiffness and by the generation, availability and application of ROS (Westerbacka & Yki-Jarvinen, 2002). Hyperinsulinemia itself mediates the increased risk for heart disease through independent effects on blood pressure, serum lipids, coagulation factors, inflammatory mediators and endothelial function, states Ludwig (2002). In addition, hypoglycemia, which occurs in the middle postprandial stage following a high GI meal, is one of the most important risk factors. This is due to the fact that it stimulates the release of counterregulatory hormones. As explained previously, this will lead to a marked rise in free fatty acids at the late postprandial stage, which promotes the incidence and progression of cardiovascular risk (Du et al., 2006; Kabir et al., 1998).

In contrast, a low GI meal causes lower peaks and less fluctuation in postprandial blood glucose levels than foods with higher GI (Du, Van Der & Feskens, 2006). Also,

hypoglycemia and its hormonal sequelae do not occur in the postprandial period (Ludwig, 2002). This is because low GI foods are digested and absorbed slowly, which may decrease the postprandial rise in gut hormones and insulin. Insulin plays an important role in postprandial lipid metabolism by stimulating the activity of lipoprotein lipase and thereby enhancing the postprandial clearance of chylomicrons from the blood (Vrolix, van Meijl & Mensink, 2007). In addition to promoting fat oxidation at the expense of carbohydrate oxidation, low GI food consumption is characterized by better satiety through the stimulation of nutrient receptors of the gastrointestinal tract. This leads to a prolonged feedback, via satiety signals such as cholecystokinin (CCK) and glucagon-like peptide-1 (GLP-1) to the satiety center in the hypothalamus (Brand-Miller, Holt, Pawlak & McMillan, 2002). It was reported that while high GI carbohydrates may suppress short term food intake (at 1h), low GI carbohydrates are more effective on the long term (at 6h) (Anderson & Woodend, 2003; Venn & Green, 2007). Similarly, mixed meals with low GIs were found to induce greater CCK secretion and greater satiety over a 180-min period, according to Holt, Brand, Soveny & Hansky (1992). Even with identical appearance and nutrient content, low GI foods not only induce higher satiety than do their high-GI counterparts, but also delay hunger and decrease energy intake at subsequent meals. This was supported by several studies (Du, Van Der & Feskens, 2006).

In brief, the consumption of lower GI foods results in lower but more sustained increases in blood glucose, more satiety, less load on pancreatic beta-cells and mild changes in blood free fatty acid levels Du, Van Der & Feskens (2006). Therefore, the postprandial sequence of physiological events is highly dependent on the GI of the food consumed. Unlike low GI, a high GI consumption seems to alter metabolic processes and increase the risk of developing cardiometabolic abnormalities. The proposed mechanism illustrates the importance of the rate of glucose entry into blood and the duration of elevated blood glucose concentrations in

inducing many hormonal and metabolic changes that may compromise health and increase the risk of several diseases, including MetS (Ludwig, 2002).

CHAPTER III

MATERIALS AND METHODS

A. Study Population

This study is based on a population-based cross-sectional study ("*Assessment of BPA levels and their association with the health status among the Lebanese population*") that was conducted in 2014 in Beirut, Lebanon. A representative sample of 501 adult Lebanese subjects residing in Greater Beirut was selected. The inclusion and exclusion criteria adopted for this study were as follows:

- Inclusion: Lebanese, residing in Greater Beirut , age > 18 years
- Exclusion: Plastic/chemical factory workers, pregnant women, dialysis patients and individuals with mental disabilities

The random selection of the study participants was based on a multistage probability sampling, where the strata were the districts of Central Administrative Beirut in addition to areas in the districts of Chouf, Aley, Baabda, Metn and Keserwan. The second stage included the selection of neighborhoods within each of the selected areas in a way to represent the make-up of the areas, then selecting households based on a systematic random sample in each selected neighborhood according to the estimated number of buildings in the neighborhood, and finally sampling a primary respondent within each household based on the most recent birthday.

After asking for the total number of adults aged 18 years and above living in the household, a primary correspondent having the most recent birthday was chosen. If the selected person was absent, one follow-up was conducted before declaring a non-response. The name, date of

birth, availability on week days and telephone number of the potential participant were recorded for further follow up. This method was used in order to eliminate self-selection and ensure an equal chance of inclusion for all members of the family.

The initial study population included 501 participants. Since the main interest of the research study was healthy individuals, all participants having diabetes, dyslipidemia or hypertension were excluded, yielding 314 participants. Ethical aspects were also taken into consideration. The study protocol was approved by the Institutional Review Board (IRB) of the American University of Beirut (AUB). A written informed consent was filled out by all participants (Appendix I and Appendix II) prior to the initiation of the study. Participants were given the right for withdrawal at any given time.

B. Data Collection

A total of 501 participants participated in the parent study. They presented to the American University of Beirut (AUB), Department of Nutrition and Food Sciences (NFSC) for data collection. On the assigned date, subjects were asked to show up after an overnight fast and to bring their medications, if any. Data collection included: a physical examination, blood tests and exhaustive data collection forms that were completed in an interview setting (Appendix III and Appendix IV).

1. Demographic, Socio-Economic Status and Lifestyle Information

Using a sociodemographic and lifestyle questionnaire, information about the following criteria were collected: age (in years), gender, monthly income (expressed in U.S dollars), marital status, education, smoking status and pattern, sleeping difficulties, alcohol and coffee intake, physical activity (using the International Physical Activity Questionnaire IPAQ to measure activities belonging to different levels of physical activity), family and personal

medical history (coronary artery disease, hypertension, diabetes mellitus, dyslipidemia, thyroid disease, cancer).

2. Anthropometric Measurements

Measurement of weight, height, waist circumference (WC) and percent body fat were obtained for participants who had to be wearing light clothing and barefoot or in stocking feet. All measures were taken by trained personnel and according to standardized procedures (Lee & Nieman, 2009).

- Weight and height:

Participants were weighed to the nearest 0.1 Kg using calibrated equipment (Inbody 3.0, Biospace Co. Ltd, Korea). Standing body height (in cm) was measured to the nearest 0.5 cm with a portable wall stadiometer (Seca 213, Germany). The candidates were completely aligned and flat against the measuring board, their shoulders were relaxed and their upper arms were hanging freely on both sides. BMI was calculated as weight divided by height squared (Kg/m2).

- Waist circumference:

A plastic, inelastic measuring tape (Seca 201, Germany) was used to measure WC to the nearest 0.5cm. After locating the upper hip bone and the right superior border of the ilium, the tape was placed around the abdomen, parallel to the ground, at the level of the iliac crest, and without exerting pressure on the skin. A mean of two measurements, following normal expiration was recorded.

- Percent body fat:

Percent body fat was estimated using the Bioelectrical Impedance Analysis (BIA) technique (Inbody 3.0, Biospace Co. Ltd, Alpha-Tec s.a.r.l.).

3. Dietary Intake Assessment

Interviews were conducted by trained dietitians, using an 86-item, semi-quantitative, and culture specific food frequency questionnaire (FFQ) (Appendix III). The FFQ collected dietary data reflecting the food intake of the last 12 months before the interview.

For each food item, one serving represented a standard household serving measure (cups, spoons and plates) and/or a customary packing size. A standard two-dimensional food portion visual chart was also used in order to simplify and assist in the portion estimation process. This chart has been developed by Nutrition Consulting Enterprises and validated for use amongst adult men and women aged 20 to 70+ years as part of the Framingham Heart Study (Posner, 1992). For data entry, a database application using Microsoft Access (Microsoft Corp., Redmond, WA, USA) was developed. This helped in grouping food items into 16 categories and determining mean consumption values per food item and per food group (g/day), average daily intake per individual, per sex group (g/day) and per age group (g/day), and the percentage of consumers per food item and per food group.

The Nutritionist Pro software, version 1.2, was used for the estimation of energy and macronutrient intakes of the study participants. For culture-specific/traditional food items not included in the database, recipes were added based on “Alef Baa Al Tabkh”, a local cookbook (Kamal & Osman, 1995). For composite dishes, this allowed to account for added oil, fat or other ingredients constitutive of the composite food. Energy, carbohydrates and total fiber per gram were calculated for each food item included in the FFQ. Individual daily

energy intake was then computed by multiplying the energy per gram of each food item by the quantity consumed (Flegal, Larkin, Metzner, Thompson, & Guire, 1988). The same concept was applied to determine the daily intake of macronutrients (Flegal & Larkin, 1990). Moreover, over-reporters and under-reporters (based on caloric interquartile range) were excluded, leaving us with 283 participants.

4. Physical Activity Assessment

The short version of the International Physical Activity Questionnaire (IPAQ) was adopted as an interviewer-administered tool for physical activity assessment. Three categories of physical activity were assigned based on METS-min per week (low: <600, moderate: at least 600 or high: at least 3,000) (IPAQ, 2005).

5. Biochemical Measurements and Blood Pressure Data

For each subject, 10 milliliters of blood were withdrawn and divided into EDTA and chemistry tubes. EDTA tubes were stored at -20 ºC whereas chemistry tubes were centrifuged and then stored at -80 ºC. All tubes were kept frozen until analysis.

At the NFSC Department, an enzymatic spectrophotometric technique using Vitros 350 analyzer (Ortho-Clinical Diagnostics, Johnson and Johnson, 50–100 Holmers Farm Way, High Wycombe, Buckinghamshire, HP12 4DP, United Kingdom) was used for Serum triglycerides, HDL-C, LDL-C, CRP, and glucose. When it comes to blood pressure, it was measured twice in a seated position after a ten-minute rest with a standard digital sphygmomanometer. The mean of both values was recorded.

C. Diagnostic Criteria for MetS

The Harmonized Definition of the International Diabetes Federation (K. G. M. M. Alberti et al., 2009) was used to assess the cardiometabolic abnormalities, based on the following cut-off points:

- Elevated Triglycerides ≥150 mg/dL
- Low HDL cholesterol level: < 40mg /dL for men and < 50 mg/dL for women
- Elevated blood pressure: systolic ≥ 130 mmHg and/ or diastolic ≥ 85 mm Hg
- Elevated fasting glucose level ≥100 mg/dL
- Elevated WC: ≥94 cm for men and ≥ 80 cm for women (based on the Europids cut-offs, which are recommended for the Middle Eastern population)

Participants were classified as having the metabolic syndrome if they have 3 out of the 5 risk factors mentioned above.

D. Calculation of GI & GL values

For the purpose of the present study, it was required to generate the glycemic index and glycemic load of each food item in the adopted FFQ. Since it is the only and most reliable reference, the International Table (Foster-Powell, Holt & Brand-Miller, 2002) was used. One by one, food items were manually matched to their corresponding equivalent. While the process was simple and straightforward for some foods, it was more difficult for others. For this reason, special considerations were adopted:

In the case of multiple entries (a single food having several values in the table), a mean of the listed values was calculated. If the food lacked a direct match, a closely related/identical match was chosen from the table. If the food item was a mixed meal, a standardized recipe from the previously mentioned Lebanese cookbook was used. With the help of the Nutritionist Pro software at the NFSC department, recipes were broken down into single ingredients, which were assigned GI values from the table. Then, a mean GI for the whole

dish was calculated depending on each ingredient's weighted value by its contribution to total carbohydrates.

A classical approach was created. This first approach, as per International Table, assumes that low carbohydrate foods do not contribute to GI. It covered several food categories like Breads and Cereals, Fruits and Fruit juices, Sweets and Deserts… Therefore, as expected, it lacked GI/GL values for several items, including: cheese, vegetables, fish, eggs, olives, butter, ketchup, alcohol… For this reason, a second approach was created to take these food items into account. In this approach, available GI values suggested in the literature were adopted. Few items with incomplete data remained unassigned. The majority of the values were from the CSFII USDA data (U.S. Department of Agriculture, 1998), while others were proposed by studies (Schulz et al., 2005; van Bakel et al., 2009) . For most of them, GL values were not provided and had to be calculated. Using Nutritionist Pro, the available carbohydrate content of the food item, defined as the carbohydrate that is digested, absorbed and metabolized, was calculated (Augustin et al., 2015). This was done by subtracting total fiber from total carbohydrate content. The CHO value was then multiplied by the corresponding GI and divided by 100, to yield the food's GL value.

Therefore, each food item from the FFQ was assigned a food match, GI 1/GL 1 (Approach 1) and GI 2/GL 2 (Approach 2). The next step was to calculate the overall dietary GI and GL values for each individual.

Overall Dietary GI and GL were calculated as follows:

$$\text{Overall Dietary GL} = \sum_{i=1}^{n} \text{GI}_i \times \text{CHO}_i$$

$$\text{Overall Dietary GI} = \sum_{i=1}^{n} \text{GI}_i \times \text{CHO}_i / \sum_{i=1}^{n} \text{CHO}_i$$

Based on the method adapted by Olendzki et al. (2006) , where:

- GI_i is the GI for food i
- CHO_i is the CHO content in food i (grams per day)
- n is the number of foods eaten per day

Overall dietary GI is the sum of the GI of foods consumed per day, multiplied by the corresponding carbohydrate content per serving, divided by the total daily carbohydrates consumed. Similarly, overall dietary GL is the same, however, without dividing by total carbohydrates. This calculation was done for both approaches, providing each participant with an overall dietary GI 1, overall dietary GL1 (from the first approach) and an overall dietary GI 2, overall dietary GL 2 (from the second approach).

E. Statistical Analysis

Frequencies, means, and standard deviations (SD) for socio-demographic and lifestyle characteristics, anthropometric measurements, biochemical indices, cardiometabolic risk factors and dietary intake were calculated for the study sample across categories of MetS status based on the IDF definition criteria (Alberti et al., 2009).

Independent student t-tests were used to compare continuous variables while Chi-square and Fisher exact tests were used to compare categorical variables.

Daily dietary GI and GL were grouped into quartiles. Logistic regression models were used to estimate odds ratios (OR) and 95% confidence intervals (CI) to evaluate the association between GI, GL and prevalent MetS and its components, while adjusting for potential confounders. The models were created with MetS/MetS components as dependent variables and GI/GL quartiles as independent variables. A crude model for the total sample was created. Then, variables found to be significantly associated with MetS in both the univariate analyses and the literature were included in the analysis.

Statistical analysis was performed using the Statistical Analysis Package for Social Sciences IBM SPSS Statistics 20 (SPSS Inc., Chicago, IL, USA). All analyses were two tailed, and a p value < 0.05 was considered statistically significant.

CHAPTER IV

RESULTS

A. GI and GL values of Lebanese food items:

For the first time, the present study aimed to determine the GI of Lebanese food items based on pertinent literature. Foods from the adopted semi-quantitative FFQ were assigned GI and GL values using Approach 1 and Approach 2 (Table 6).

Table 6: GI and GL values of food items in the FFQ

Food item	GI 1[a]	GI 2[b]	Serving(g)	GL 1[a]/svg	GL 2[b]/svg
Bread, white	95	95	30	15	15
Bread, brown	68	68	30	9	9
Traditional (markouk/tannour)	97	97	30	15	15
BF cereals (reg, sugar c., choc, bran)	66.6	66.6	30	16	16
Kaak	81	81	25	15	15
Rice, W, cooked	64	64	150	23	23
Pasta/Noodles, plain, cooked	45.5	45.5	180	20	20
Wheat/Bulgur, cooked	48	48	150	12	12
Whole grain Rice/Pasta/Cereals	37	37	180	16	16
Milk, skim/lowfat (0-2%)	32	32	250	4	4
Milk, whole-fat	27	27	250	3	3
Yogurt, fat-free/low fat	27	27	200	7	7
Yogurt, whole-fat	36	36	200	3	3
Cheese, regular/yellow	x	27	250	x	3
Cheese, low fat, white	x	32	250	x	4
Labneh, regular	36	36	200	3	3
Labneh, low fat	27	27	200	7	7
Citrus orange/ grapefruit	33.5	33.5	120	4	4
Peach, plum, prunes	40.5	40.5	120	5	5
Strawberries	40	40	120	1	1
Grapes	46	46	120	8	8
Banana, Apples	45	45	120	9	9
Dried Fruits	66	66	60	26	26
Fruit juice, fresh	45	45	250	13	13
Fruit juice canned/bottle	66	66	250	13	13
Fruits, canned	50.5	50.5	120	7	7
Salad green	x	32	138	x	0.5
Dark green or deep yellow	x	37	138	x	1.9
Tomatoes, fresh	x	38	123	x	1.2
Corn/green peas, fresh	51	51	80	6	6
Corn/green peas, canned	46	46	80	7	7
Potatoes, baked/boiled/mashed	50	50	150	14	14
Zucchini/eggplants cooked	28.3	44.3	65	1.9	2.5
Cauliflower, cabbage, broccoli	x	32	123	x	1
Other canned veg (mushroom, palmetto, asparagus)	x	32	123	x	3.3
Veg juice, fresh	40	40	250	7	7

Legumes: Lentils, beans, chickpeas dried, cooked	28	28	150	7	7
Legumes canned	52	52	150	9	9
Nuts & seeds	18	18	55	2	2
Red meat	x	x	x	x	x
Poultry	x	x	x	x	x
Fish/seafood	x	50	100	x	4
Fish (canned)	x	50	x	x	x
Eggs	x	50	44	x	0.3
Organ meats	x	50	100	x	3.2
Luncheon meats	x	50	30	x	0.3
Sausages, uncanned	28	28	100	1	1
Sausages, hotdogs, canned	x	28	100	x	0.1
Veg oil, corn/sunflower/soya	x	x	x	x	x
Olive Oil (inc w thyme)	x	x	x	x	x
Olives	x	50	22	x	0.3
Butter	x	50	15	x	0.0045
Ghee	x	50	15	x	0.06
Mayonnaise	x	50	13.8	x	0.04
Tahini	x	x	x	x	x
Cakes/Cookies/Donuts/Muffins/Croissants/Biscuits	66	66	51	16	16
Ice cream	61	61	50	8	8
Chocolate bar	50	50	60	18	18
Sugar, honey, jam, choc	44	44	22	7	7
Arabic Sweets (baklava, maamoul, knefe)	59	59	x	x	21
Soft drink	63	63	250	16	16
Soft drink, diet	x	x	x	x	x
Turkish Coffee	x	x	x	x	x
Instant coffee/ tea	x	50	240	x	0.4
Cocoa / Hot chocolate	51	51	250	12	12
Beer	66	66	250	5	5
Wine	x	61	104	x	1.65
Liquor, whiskey, vodka, rum	x	61	45	x	x
Water	x	x	x	x	x
Manaeesh, zaatar/cheese	36	36	100	9	9
French Fries	75	75	150	22	22
Potato chips/tortilla	57	57	150	26.5	26.5
Falafel, without bread	15.6	29.5	27	0.5	0.9
Shawarma	70	70	x	x	23.8
Burgers	66	66	95	17	17
Pizza	36	36	100	9	9
Canned/pre-packed soups	58	58	250	11	11
Ketchup	x	60	15	x	2.4
Mustard	x	x	x	x	x

[a] Values based on Approach 1(International table): considering only carbohydrate-rich foods (Foster-Powell, Holt & Brand-Miller, 2002)

[b] Values based on Approach 2: same as Approach 1 in addition to GI and GL values proposed by studies (Schulz et al., 2005; van Bakel et al., 2009) and USDA CSFII 94-96 food codes with the help of NutritionistPro records at the American University of Beirut (AUB)

B. Socio-demographic and lifestyle characteristics:

The socio-demographic and lifestyle characteristics of the study sample are presented by MetS status in Table 7. Participants' mean age was 40.9 ± 13.7 years, with those having MetS being significantly older ($p<0.05$). The study sample consisted of 93 (32.5%) males and 193 (67.5%) females. Within the MetS groups, the proportion of females was significantly higher (54.9%) as compared to males (45.1%). Interestingly, more than half of the study population had an education level up to intermediate, with only 13.7% attaining university level. A significant difference was observed between the MetS groups, where those having MetS seemed less likely to reach higher levels of education. However, marital status, income and crowding index (an indicator of socioeconomic status) did not show any significant difference between the two groups.

For the lifestyle characteristics, smoking, alcohol and sleep difficulties, no significant differences were observed across MetS groups. The case is similar for engagement and levels of physical activity, however, a significant difference was observed between the two groups for sedentary behavior. Participants with MetS spent 307.43 ± 166.785 minutes per day being sedentary as compared to 263.62 ± 176.58 for participants without MetS ($p< 0.05$).

Table 7: Socio-demographic and lifestyle characteristics of participants with and without MetS (n=283)

	Total (n=283)	**Participants without MetS (n=181)**	**Participants with MetS (n=102)**	**P value**
Age (years) (Mean ±SD)	40.9 ± 13.7	38.8 ± 12.7	44.8 ± 14.6	p< 0.001
Gender			p=0.001	
Male	92 (32.5)	46 (25.4)	46 (45.1)	
Female	191 (67.5)	135 (74.6)	56 (54.9)	
Marital Status			p=0.063	
Married	193 (68.2)	127 (70.2)	66 (64.7)	
Single	66 (23.3)	44 (24.3)	22 (21.6)	
Widow	14 (4.9)	5 (2.8)	9 (8.8)	
Divorced	8 (2.8)	3 (1.7)	5 (4.9)	
Engaged	2 (0.7)	2 (1.1)	-	
Income/Month			p=0.232	
< 600$	75 (26.5)	42 (23.5)	33 (32.4)	
600$ - 999.9$	104 (36.7)	65 (36.3)	39 (38.2)	
1000$ - 2000$	61 (21.5)	40 (22.3)	21 (20.6)	
> 2000$	24 (8.5)	17 (9.5)	7 (6.9)	
Education			p=0.021	
No schooling	20 (7.1)	10 (5.6)	10 (9.8)	
Primary school	69 (24.4)	41 (22.8)	28 (27.5)	
Intermediate school	77 (27.2)	46 (25.6)	31 (30.4)	
Secondary school	55 (19.4)	36 (20)	19 (18.6)	
Technical diploma	22 (7.8)	13 (7.2)	9 (8.8)	
University degree	39 (13.8)	34 (18.9)	5 (4.9)	
Crowding Index			p=0.384	
< 1 person/room	42 (14.8)	24 (13.3)	18 (17.6)	
≥ 1 person/room	241(85.1)	157 (86.7)	84 (82.4)	
Physical Activity				
Total minutes per day (from all three)	110.3 ± 81.5	113.9 ± 85.8	103 ± 73.3	0.327
Met-minutes of heavy work per week	304.6 ± 1369.5	298.3 ± 1300	324.7 ± 1509	0.877
Met-minutes of Moderate work per week	164.4 ± 573.7	220.2 ± 694.8	70.2 ± 230.4	0.035
Met-minutes of Walking per week	1334.2 ± 1412.4	1393.9 ± 1424	1187.9 ± 1374	0.238
Total Met-minutes from all three categories per week	2113.6 ± 2291.5	2177 ± 2357.8	1968.9 ± 2193.9	0.507
Sedentary (minutes/day)	279.3 ± 174.8	263.62 ± 176.58	307.4 ± 166.8	0.043
Levels of physical activity			p=0.202	
Low-intensity activity	131 (46.3)	80 (44.2)	51 (50)	
Moderate-intensity activity	88 (31.1)	54 (29.8)	34 (33.3)	
High-intensity activity	64 (22.6)	47 (26)	17 (16.7)	
Engagement in Physical Activity			p=0.116	

None	42 (14.8)	22 (12.2)	20 (19.6)	
Any	241 (85.1)	159 (87.8)	82 (80.4)	
Smoking			p=0.657	
No	63 (22.3)	42 (23.2)	21 (20.6)	
Yes	220 (77.7)	139 (76.8)	81 (79.4)	
Alcohol consumption			p=0.187	
No	196 (69.3)	115 (85.6)	81 (79.4)	
Yes	47 (16.6)	26 (14.4)	21 (20.6)	
Sleeping difficulties			p=0.259	
No	168 (59.4)	112 (61.9)	56 (54.9)	
Yes	115 (40.6)	69 (38.1)	46 (45.1)	

C. Anthropometric Characteristics, Biochemical and Blood Pressure Data:

Anthropometric characteristics, biochemical and blood pressure data of the study sample are shown in Table 8. BMI was significantly higher in subjects having MetS as compared to those without MetS (31.04 ± 5.4 vs 26.379 ± 5). As expected, this was also the case of percent body fat and waist circumference (38.748 ± 10.1 vs 34.51 ± 10.08 and 100.65 ± 11.39 vs 87.1 ± 12, respectively). Biochemical values (including total cholesterol, LDL cholesterol, insulin and HbA1c) and both systolic and diastolic blood pressure were significantly higher in the MetS group ($p < 0.05$).

Table 8: Anthropometric characteristics, biochemical and blood pressure data of participants with and without MetS

	Total (n=283)	**Participants without MetS (n=181)**	**Participants with MetS (n=102)**	**Significance**
Anthropometric Characteristics				
BMI (Kg/m2) (Mean ± SD)	28 ± 5.61	26.379 ± 5	31.04 ± 5.4	p< 0.001
BMI categories			p < 0.0001	
Underweight (BMI < 18.50)	4 (1.4)	4 (2.2)	-	
Normal weight (BMI = 18.50 - 24.99)	86 (30.4)	74 (40.9)	12 (11.9)	
Overweight (BMI = 25.00 – 29.99)	99 (35)	65 (35.9)	34 (33.7)	
Obese (BMI = 30 – 39.99)	85 (30)	36 (19.9)	49 (48.5)	
Morbidly obese (BMI ≥ 40)	8 (2.8)	2 (1.1)	6 (5.9)	
Percent Body Fat (%) (Mean ± SD)	36 ± 10.3	34.51 ± 10.1	38.748 ± 10.1	0.001
Waist circumference (cm) (Mean ± SD)	91.9 ± 13.5	87.1 ± 12	100.65 ± 11.4	p< 0.001
Biochemical and blood pressure data				
Total Cholesterol (mg/dL) (Mean ± SD)	172.5 ± 13.4	178.06 ± 36.5	192.72 ± 43.2	0.003
LDL-C (mg/dL) (Mean ± SD)	99.5 ± 14.8	101.78 ± 31.4	116.23 ± 38.3	0.001
Triglycerides (mg/dL) (Mean ± SD)	115 ± 60.8	96.07 ± 50.9	164.39 ± 80	p< 0.001
HDL-C (mg/dL) (Mean ± SD)	50.5 ± 10.6	56.98 ± 16	42.87 ± 10.9	p< 0.001
Blood Pressure				
SBP (mmHg) (Mean ± SD)	101.25 ± 12.4	111.7 ± 13.2	125.5 ± 18.4	p< 0.001
DBP (mmHg) (Mean ± SD)	65 ± 7	70.35 ± 8.2	77.41 ± 10.3	p< 0.001
Measures of Glycemia				
FBG (mg/dL) (Mean ± SD)	87	93.99 ± 7.2	105.7 ± 17.7	p< 0.001
HbA1c (%) (Mean ± SD)	5.3	5.35 ± 0.4	5.7 ± 0.6	p< 0.001
Insulin (mU/mL) (Mean ± SD)	17.5	23.4 ± 8.8	31.37 ± 22.1	p< 0.001

D. Prevalence of MetS components:

The prevalence rates of the metabolic abnormalities of MetS are displayed in Table 9. In the study sample, prevalence rates were as follows: 70.6% for elevated waist circumference, 34.2% for elevated blood glucose, 27.7% for elevated blood pressure, 27.7% for elevated triglycerides and 37.9% for reduced HDL levels. When compared between the two groups, all of these risk factors were significantly higher among the MetS group (94.1%, 68.6%, 55.9%, 55.9% and 63.7, respectively).

Table 9: Cardiometabolic risk factors of participants with and without MetS

	Total (n=283)	**Participants without MetS (n=181)**	**Participants with MetS (n=102)**	**Significance**
Elevated WC	200 (70.7)	104 (57.5)	96 (94.1)	$p < 0.0001$
Elevated FBG	97 (34.3)	27 (14.9)	70 (68.6)	$p < 0.0001$
Elevated BP	79 (27.9)	22 (12.2)	57 (55.9)	$p < 0.0001$
Elevated serum TG	78 (27.6)	21 (11.6)	57 (55.9)	$p < 0.0001$
Low serum HDL	107 (37.8)	42 (23.2)	65 (63.7)	$p < 0.0001$

E. Dietary energy and macronutrient intakes:

Dietary intake data of the study participants are displayed in Table 10. Participants with MetS had a higher intake in terms of energy (sum of calories), carbohydrate (grams per day and percent calories) and fat (grams per day and percent calories) while the other group consumed more protein (grams per day and percent calories) and fiber (grams per day and percent calories). However, none of these differences reached statistical significance.

Table 10: Dietary energy and macronutrient intakes of participants with and without MetS

	Total (n=286)	**Participants without MetS (n=181)**	**Participants with MetS (n=102)**	**Significance**
Mean ± SD				
Energy (Kcal/day)	3131.2 ± 1302.6	3080.2 ± 1281.6	3232.1 ± 1337.9	0.347
Protein (g/day) (Mean ± SD)	102.7 ± 3.6	103.3 ± 65.8	101.9 ± 50.4	0.854
Protein (% of energy)	13 ± 3.6	13.2 ±3.9	12.7 ± 3.2	0.224
Fat (g/day)	131.8 ± 64.8	130.1 ± 63.8	134.8± 67.3	0.560
Fat (% of energy)	39.1 ± 7.9	39.4 ± 7.7	38.6 ± 8.1	0.385
Carbohydrates (g/day)	387.55± 158.4	377.4 ± 150.4	407.4 ± 170.2	0.126
Carbohydrate (% of energy)	50.3 ± 8.3	50 ± 8.2	51 ± 8.4	0.360
Dietary Fibers (g/day)	28.1 ± 11.8	28.7 ± 13.5	27.8 ± 10.7	0.563

F. Total dietary GI and GL:

Table 11 displays total dietary GI (1,2) and GL (1,2) of participants with and without MetS. Although not statistically significant, the results of the conducted t tests show higher GI and GL values for participants with MetS in both models. P values were found to be borderline significant (0.053, 0.050 and 0.058) for GI 1, GL 1 and GL 2, respectively.

Table 11: Total dietary GI and GL intake of participants with and without MetS

	Participants without MetS (n=181)	**Participants with MetS (n=102)**	Significance
Mean ± SD			
GI 1[a]	59.25 ± 7.77	61.16 ± 8.19	0.053
GI 2[b]	60.63 ± 7.63	62.34 ± 7.94	0.076
GL 1[a]	201.54 ± 95.79	225.8 ± 106.2	0.050
GL 2[b]	205.89 ± 97.05	229.6 ± 106.83	0.058

[a] Values based on Approach 1(International table): considering only carbohydrate-rich foods (Foster-Powell, Holt & Brand-Miller, 2002)

[b] Values based on Approach 2: same as Approach 1 in addition to GI and GL values proposed by studies (Schulz et al., 2005; van Bakel et al., 2009) and USDA CSFII 94-96 food codes with the help of NutritionistPro records at the American University of Beirut (AUB)

G. Association between dietary GI, GL and MetS and its components:

The association between GI 1, GL1 and MetS and its components were examined using logistic regression models. The results of several models are displayed in Table 12 and Table 13:

- Crude model for the total sample
- Model 1: Adjusted for age and gender
- Model 2: Adjusted for age, gender, BMI, smoking status. alcohol intake, energy intake, total fiber intake, sedentary behavior and education level
- Model 3: Adjusted for all variables in Model 2, in addition to percentage of energy from both protein and fat (for GI only)

In the crude model, participants belonging to the highest quartile of GI had significantly higher odds of developing MetS (OR: 2.251, 95% CI: 1.120-4.525). In the same model, participants in the highest quartile of GI had significantly higher odds of having elevated Triglyceride levels (OR: 2.157, 95% CI: 1.022-4.552). However, these associations lost significance with further adjustments. In contrast, it was shown that participants belonging to

the second quartile of GI had significantly lower odds of having elevated fasting blood glucose (OR: 0.464, 95% CI: 0.225-0.957) in the crude model. This association remained significant with additional adjustments in model 1 (OR: 0.377, 95% CI: 0.175-0.810), model 2 (OR: 0.380, 95% CI: 0.174-0.833) and model 3 (OR: 0.380, 95% CI: 0.174-0.833). When it comes to GL, no significant association was detected with MetS in all models. Interestingly, subjects belonging to the highest quartile of total GL had significantly higher odds of developing high blood pressure (OR: 2.498, 95% CI: 1.173-5.320) in the crude model. This significance did not persist after adjustments.

When it comes to triglycerides, a significant association was found with the second quartile of GL in Model 2, with an OR of 0.425 and 95% CI of 0.181-0.995. However, no other associations were detected between GL and any of the MetS risk factors.

The same regression analyses were conducted for overall dietary GI 2, GL 2 and MetS and its components (data not shown). Results showed no significant associations.

Table 12: Multivariable logistic regression analyses of MetS and its components by dietary GI 1 quartiles

	Daily Glycemic Index 1			
	Quartile 1 (n=71)	**Quartile 2** (n=72)	**Quartile 3** (n=72)	**Quartile 4** (n=71)
	OR (95% CI)			
Metabolic Syndrome				
Crude model	1	1.225 (0.600-2.503)	1.251 (0.612-2.559)	**2.251 (1.120-4.525)**
Model 1	1	1.093 (0.517-2.311)	1.138 (0.539-2.402)	1.483 (0.702-3.134)
Model 2	1	1.258 (0.547-2.891)	1.090 (0.473-2.512)	1.269 (0.546-2.945)
Model 3	1	1.195 (0.518-2.756)	0.973 (0.414-2.289)	1.215 (0.518-2.847)
Elevated triglycerides				
Crude model	1	1.338 (0.617-2.903)	1.364 (0.628-2.961)	**2.157 (1.022-4.552)**
Model 1	1	1.193 (0.539-2.642)	1.251 (0.565-2.769)	1.788 (0.827-3.867)
Model 2	1	1.340 (0.582-3.086)	1.297 (0.564-2.986)	1.672 (0.739-3.783)
Model 3	1	1.340 (0.582-3.086)	1.297 (0.564-2.986)	1.672 (0.739-3.783)
Elevated waist circumference				
Crude model	1	0.958 (0.477-1.926)	1.021 (0.506-2.059)	1.951 (0.906-4.202)
Model 1	1	0.888 (0.430-1.833)	0.915 (0.442-1.893)	1.347 (0.599-3.028)
Model 2	1	1.329 (0.452-3.907)	1.212 (0.416-3.526)	3.008 (0.835-10.841)
Model 3	1	1.329 (0.452-3.907)	1.212 (0.416-3.526)	3.008 (0.835-10.841)
Elevated fasting blood glucose				
Crude model	1	**0.464 (0.225-0.957)**	0.673 (0.336-1.348)	1.098 (0.561-2.147)
Model 1	1	**0.377 (0.175-0.810)**	0.572 (0.276-1.185)	0.655 (0.312-1.373)
Model 2	1	**0.380 (0.174-0.833)**	0.550 (0.260-1.167)	0.598 (0.277-1.288)
Model 3	1	**0.380 (0.174-0.833)**	0.550 (0.260-1.167)	0.598 (0.277-1.288)
Elevated blood pressure				
Crude model	1	1.721 (0.808-3.665)	1.222 (0.560-2.670)	1.757 (0.824-3.745)
Model 1	1	1.517 (0.672-3.423)	1.047 (0.452-2.421)	1.014 (0.437-2.351)
Model 2	1	1.560 (0.659-3.690)	0.938 (0.387-2.272)	0.803 (0.328-1.961)
Model 3	1	1.560 (0.659-3.690)	0.938 (0.387-2.272)	0.803 (0.328-1.961)
Reduced HDL				
Crude model	1	0.868 (0.441-1.708)	0.887 (0.450-1.748)	1 (0.510-1.960)
Model 1	1	0.868 (0.441-1.708)	0.887 (0.450-1.748)	1 (0.510-1.960)
Model 2	1	0.894 (0.450-1.779)	0.880 (0.442-1.754)	0.938 (0.469-1.876)
Model 3	1	0.894 (0.450-1.779)	0.880 (0.442-1.754)	0.938 (0.469-1.876)

Table 13 Multivariable logistic regression analyses of MetS and its components by dietary GL 1 quartiles

	Daily Glycemic Load 1			
	Quartile 1 (n=71)	**Quartile 2** (n=72)	**Quartile 3** (n=72)	**Quartile 4** (n=71)
	OR (95% CI)			
Metabolic Syndrome				
Crude model	1	1.432 (0.711-2.885)	1.027 (0.502-2.101)	1.965 (0.981-3.936)
Model 1	1	1.330 (0.638-2.774)	0.672 (0.304-1.485)	1.572 (0.710-3.480)
Model 2	1	0.941 (0.407-2.173)	0.579 (0.236-1.421)	1.595 (0.657-3.875)
Elevated triglycerides				
Crude model	1	0.671 (0.311-1.447)	0.788 (0.372-1.669)	1.601 (0.790-3.245)
Model 1	1	0.579 (0.263-1.276)	0.532 (0.237-1.192)	0.869 (0.389-1.938)
Model 2	1	**0.425 (0.181-0.995)**	0.460 (0.198-1.067)	0.810 (0.351-1.871)
Elevated waist circumference				
Crude model	1	1.279 (0.595-2.747)	0.731 (0.356-1.499)	0.672 (0.328-1.376)
Model 1	1	1.307 (0.594-2.877)	0.653 (0.309-1.380)	0.842 (0.398-1.779)
Model 2	1	1.559 (0.481-5.058)	0.525 (0.187-1.477)	0.831 (0.278-2.486)
Elevated fasting blood glucose				
Crude model	1	1.233 (0.614-2.476)	1.091 (0.540-2.204)	1.212 (0.600-2.447)
Model 1	1	1.159 (0.561-2.397)	0.763 (0.354-1.645)	0.974 (0.438-2.168)
Model 2	1	1.025 (0.484-2.169)	0.755 (0.344-1.657)	0.973 (0.430-2.201)
Elevated blood pressure				
Crude model	1	1.488 (0.678-3.265)	1.460 (0.666-3.200)	**2.498 (1.173-5.320)**
Model 1	1	1.285 (0.559-2.956)	0.779 (0.321-1.890)	1.392 (0.578-3.351)
Model 2	1	1.116 (0.464-2.686)	0.773 (0.305-1.956)	1.441 (0.574-3.618)
Reduced HDL				
Crude model	1	0.815 (0.411-1.617)	1.099 (0.561-2.152)	1.086 (0.552-2.138)
Model 1	1	0.815 (0.411-1.617)	1.099 (0.561-2.152)	1.086 (0.552-2.138)
Model 2	1	0.729 (0.360-1.477)	1.112 (0.563-2.195)	1.122 (0.565-2.226)

CHAPTER V

DISCUSSION

To our knowledge, this is the first study to determine dietary GI and GL in the EMR. Because Gl and GL are not components of the standard output provided by nutrient analysis softwares, the developed GI/GL database for Lebanese foods will be useful for studies investigating diet-disease associations using similar FFQs. In our study, the link between GI, GL and metabolic abnormalities was investigated amongst Lebanese adults, and the results did not show any significant association with the MetS. Studies investigating such associations are completely lacking in the EMR, but previous studies conducted in other parts of the world yielded equivocal results. In Korea, a study conducted by Song et al. (2014) on 6,845 adults found no association between GI, GL and MetS. Similarly, in Brazil, de Mello Fontanelli et al. (2018) did not detect an association in a study on 591 adult residents of Sao Paulo.

In our study, and in order to estimate the participants' dietary GI and GL, the international GI table was used (Foster-Powell, Holt & Brand-Miller, 2002). The dietary GI was then calculated by summing the GI of foods consumed per day, multiplying them by the corresponding carbohydrate content per serving, then dividing by the total daily carbohydrates consumed. As such, average dietary GI was estimated at 59.87 ± 7.99, which is in line with estimates reported in Australia (57.5 ± 0.3) (Louie, Flood, Turner, Everingham, & Gwynn, 2011) and Mexico (51.8 ± 5.3) (Castro-Quezada et al., 2017). Another study conducted in Spain (Juanola-Falgarona et al., 2015) reported age-specific values for dietary GI in adults, with the estimates being of 57 ± 5 for those aged less than 65), 56.4 ± 4.9 for those between 65 and 74 and 55.9 ± 4.7 for those aged 75 and above. In the present study, the overall GL was calculated as the product of the GI of the consumed foods and the corresponding carbohydrate content per serving. This calculation was adopted by several

studies (Olendzki et al., 2006; Finley, Barlow, Halton & Haskell, 2010; Cluberson et al., 2009). Accordingly, the average dietary GL for Lebanese adults was estimated at 209.75 ± 100.26. Using data from NHANES III, Culberson et al. (2009) divided GL into quartiles, ranging from < 119 (median of 95 for men and 96 for women) to ≥ 204 (median of 244 for men and 245 for women). Our results are slightly higher than those reported by other studies: 143.4 ± 2.6 (Louie, Flood, Turner, Everingham & Gwynn, 2011), 150 ± 27.3 (Castro-Quezada et al., 2017) and 113.2 ± 40.8, 110.8 ± 39.5 and 107.4 ± 37.8 across age groups (Juanola-Falgarona et al., 2015). This could be due to the fact that GL is a quantitative indicator and dietary assessment in our study was conducted using an FFQ, which tends to overestimate dietary intake (Huang et al., 2018; Kowalkowska et al., 2013; Moghames et al., 2016; Steinemann et al., 2017). In our study, the MetS prevalence was estimated at 35.6% among healthy Lebanese adults. This is in line with previous prevalence estimates reported amongst Lebanese adults (34.6% by Naja et al., 2013 and 31.2% by Sibai et al., 2007). Our results showed that individuals with the MetS had a significantly higher dietary GI than their non-MetS counterparts (61.16 ± 8.19 vs. 59.25 ± 7.77). These findings are in agreement with those reported by Finley, Barlow, Halton & Haskell (2010), where values of 54.9 ± 4.6 VS 54.2 ± 4.8 (in men) and 53.4 ± 6.3 VS 53.1 ± 5.9 (in women) were recorded. In the logistic regression analyses, participants belonging to the highest GI quartile had significantly higher odds of developing MetS. However, this was only observed in the crude model and was no longer significant after adjustments. The results provided by the literature are inconsistent. The Framingham Offspring Cohort (n= 5,135) was able to detect an association between GI and MetS in the population as a whole (McKeown et al., 2004), while the Prevención con Dieta Mediterránea (PERIMED) study (Juanola-Falgarona et al, 2015) suggested that this association is age-dependent with an increased MetS risk in younger age groups only, but not in those aged 75 and above. Other studies have suggested that the association between GI and

MetS is gender-specific. The Cooper Center longitudinal study in the United States, detected such an association in men, but not in women (Finley, Barlow, Halton & Haskell, 2010).

For GL, participants with the MetS had significantly higher values (225.8 ± 106.2) compared to their non-MetS counterparts (201.54 ± 95.79). Contrary to our findings, Finley et al. (2010) reported lower GL values in those having MetS as compared to those without MetS (140.5 ± 33.2 VS 145.2 ± 34.3 in men and 114.6 ± 25.5 VS 115.1 ± 26.6 in women) in the United States. The regression analyses performed in our study did not show any significant association between GL and MetS. Similarly to our findings, Culberson et al. (2009) did not detect any association between GL and MetS, using data from NHANES III on 5011 US adults,. The Cooper Center longitudinal study did also not find any significant association in women (n=1,775), but interestingly, among men (n=9,137), those belonging to the highest quintile of GL were at decreased risk of developing MetS (Finley, Barlow, Halton & Haskell, 2010). Trials have also yielded conflicting results. Findings from PERIMED, the largest dietary intervention trial assessing the effects of the Mediterranean diet on cardiovascular disease, found no association between GL and MetS. Vrolix & Mensink (2010), in an intervention on 15 overweight subjects, found no effect of diets identical in macronutrients but different in terms of GI and GL on MetS biomarkers, while Klemsdal et al. (2010) reported that low-GL diet are more effective in individuals with MetS compared to healthy ones. The aforementioned studies all differ in design, sample size, time and geographical area, which may explain the discrepancy in results. Unfortunately, we were not able to investigate subgroups (age/gender) separately due to the small sample size (n=283). This is because subjects having chronic diseases or metabolic abnormalities were excluded to decrease potential reverse causation.

When examining the association between GI, GL and the components of MetS, we found a decreased risk of high fasting blood glucose in those belonging to the second quartile of

dietary GI in all models. In addition, for GL, the second quartile was associated with lower triglycerides in the second model, which is in line with findings reported by Finley, Barlow, Halton & Haskell (2010) and Juanola-Falgarona et al. (2015). These observations shed the light on the importance of nutrient distribution amongst those belonging to the first quartile of GI and GL. It is possible that although they are consuming low GI, their energy intake (especially from fat) is higher. Table 14 (Appendix V) clearly shows that those belonging to Q1 of GI, despite consuming less energy and less carbohydrates, were consuming more percent from total fat and saturated fat. This could lead to increased fasting blood glucose and triglycerides levels (Westman et al., 2007) independently from carbohydrates, which explains the decreased odds in the second quartile in comparison to the first.

Despite the growing interest in GI and GL as markers of risk factors for disease, the methods for assessing these exposures in an epidemiologic context are neither well established nor consistently applied (Flood et al., 2006). Each of the previously mentioned studies used a different dietary assessment tool to assess GI and GL, including: 3-day diet record (Finley, Barlow, Halton & Haskell, 2010), 24-hour recall (Culberson et al., 2009) and FFQ (Castro-Quezada et al., 2017; Juanola-Falgarona et al., 2015), which may affect the results and therefore, the relationship between GI, GL and MetS.

In addition, despite having used the international GI table, which is the most commonly used source of GI values (Foster-Powell, Holt & Brand-Miller, 2002), it is important to acknowledge that this table has its own set of limitations, (restricted food items, broad groupings, multiple entries, missing values, different formulations of brands and laboratory errors) (Flood et al., 2006; Foster-Powell, Holt & Brand-Miller, 2002). In addition, numerous other factors may affect the GI of a specific food. The GI of the same fruit tends to decrease when it becomes ripe (Englyst & Cummings, 1986; Pi-Sunyer, 2002). Also, a whole food has a lower GI than its mashed or pureed form, which in turn has a lower GI than its juice form

(Pi-Sunyer, 2002). When it comes to grains, finely ground ones have a higher GI than those that are roughly ground (Heaton, Marcus, Emmett, & Bolton, 1988). Chemical modification of a food during processing also affects its GI value (Farhat, 2010; Maioli et al., 2008; Sugiyama, Tang, Wakaki, & Koyama, 2003). Also, increasing the acidity of a food significantly lowers its GI. Foster-Powell et al. (2002) suggest that foods should be tested in the geographical area where they are consumed. Dietary fiber may also affect the GI of a food to a certain extent. In our study we have adjusted for total fiber intake in the regressions analyses but the type of fiber was not taken into account. A positive association was fond between insoluble (but not soluble) fiber on GI (Wolever, 1990). Additionally, the more viscous the fiber, the higher its ability to decrease the GI value of a food (Farhat, Moukarzel, El-Said & Daher, 2010).

In our study, GI values of mixed dishes were calculated based on a weighted mean of the GIs of its ingredients (Farhat, Moukarzel, El-Said & Daher, 2010) using standardized recipes (Alef Baa al Tabekh) and a reliable software (Nutritionist Pro) for nutrient analysis.

The issue of whether the glycemic index of an individual food is valid when incorporated in a meal or a mixed recipe is controversial, and there is a debate as to whether summing the individual GIs of foods in a meal can be used to accurately calculate the GI of the meal (Venn & Green, 2007). While Jenkins et al. (1981) and Chew, Brand, Thorburn & Truswell (1988) suggest that the GI of a meal can be calculated by adding the carbohydrate contributions of each constituent food multiplied by its published GI, another school of thought argues that a food is more than just the sum of its nutrients due to several chemical and physical interactions that may occur. Combining macronutrients was found to influence GI, that is positively associated with its carbohydrate content and negatively associated with its protein and fat content, which can significantly reduce the glycemic response (Farhat, Moukarzel, El-Said & Daher, 2010). In our analyses, we have adjusted for the percent contribution of

protein and fat, but this may not account for the physical interactions that may occur between the various components of the meal.

It is also important to note that some GI values are completely missing from international databases. This is the case of food with little or no carbohydrates, which are all assigned a GI value of zero in the international tables. However, some studies (Schulz et al., 2005; van Bakel et al., 2009) and the CSFII 94-96 USDA food codes have proposed GI values for some of these foods. For this reason, two approaches were applied in this study: Approach 1, abiding by the international GI table and Approach 2, taking into account GI values proposed by the literature with the help of Nutritionist Pro and standardized recipes. The results on the associations with metabolic abnormalities were similar using both approaches.

The results of this study ought to be interpreted in light of the following limitations. In our study, dietary assessment was performed using the FFQ. This approach may be limited by the individuals' ability to estimate and describe the frequency and portion sizes of their usual dietary intake (Barclay, Flood, Brand-Miller, & Mitchell, 2008). Despite its limitations, the FFQ approach has been described as one of the most reliable dietary assessment methods in large epidemiological surveys as it assesses the participant's habitual diet over longer periods of time (Nasreddine et al., 2018). Although the FFQ that was used in this study was not previously validated, it has been used in several studies, yielding plausible results (Naja et al., 2013; Naja et al., 2011; Nasreddine et al., 2018). It is also important to note that the FFQ used in this study was not specifically designed to assess dietary GI and GL. When compared to a diet record, FFQ was reported as less accurate in predicting GI (Castro-Quezada et al., 2017). This is because details regarding food groupings, meal preparation or mode of consumption may be omitted in the FFQ which may hinder the estimation of GI and GL for some foods (de Mello Fontanelli et al., 2018). Other studies have, however, reported on the validity and reproducibility of GI/GL from FFQs (Barclay et al., 2008; Levitan, Westgren,

Liu, & Wolk, 2007). The questionnaire for this study was filled in an interview setting. This approach may be associated with social desirability bias, whereby participants may respond in a way that they believe is acceptable or favorable to the interviewer (Nasreddine et al., 2018; Okamoto et al., 2006). In our study, the field workers who performed data collection underwent extensive training to decrease any judgmental verbal or non-verbal communication and thus to minimize social desirability bias. Furthermore, the cross-sectional design adopted in our study can only reflect an association between the exposures (GI and GL) and outcome (MetS), but does not allow for the determination of causality. Finally, this study was restricted to the urban setting of the Greater Beirut area, and hence, findings related to food consumption and lifestyle characteristics may not be representative of less urban areas in the country and future nationally representative studies are needed.

Despite its limitations, the present study contributes to the body of evidence discussing the relationship between GI, GL and MetS, considering that it is the first in the EMR to examine this association. This study is also characterized by a well-planned design and methodology. In the future, large scale studies, especially clinical trials and prospective studies analyzing the possible association are needed.

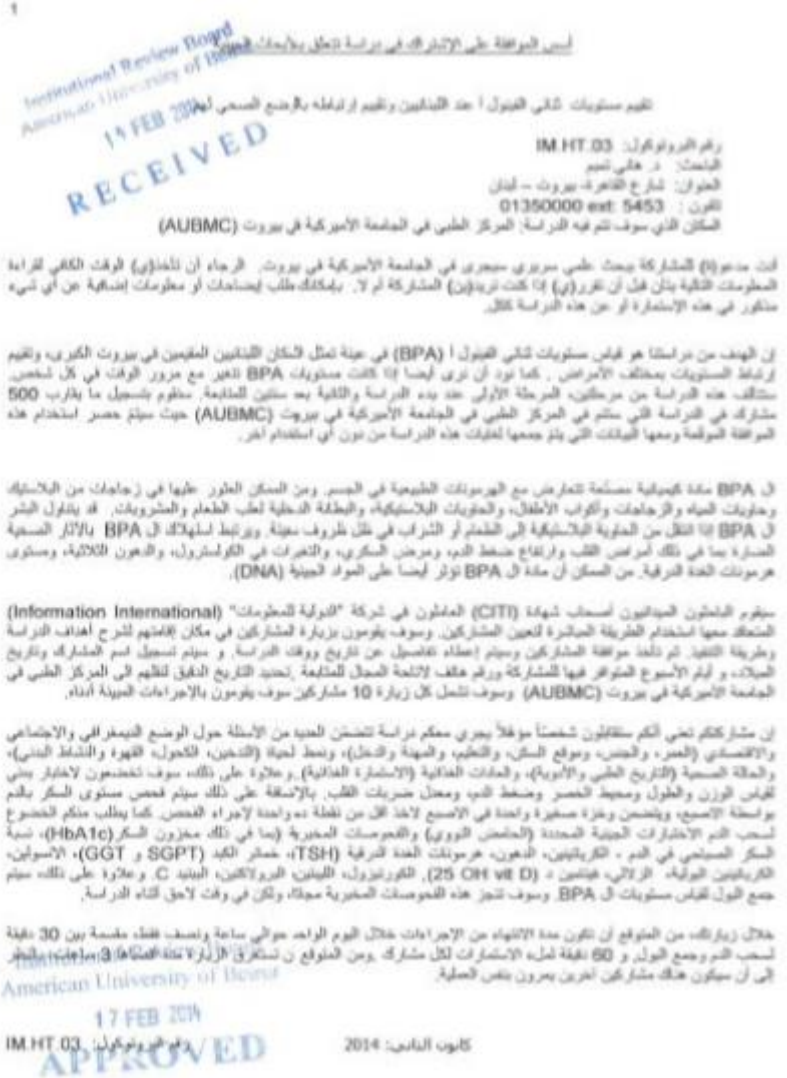
CHAPTER VI

CONCLUSION

This study is the first in the EMR to report dietary GI and GL and examine their association with MetS and its components, using data from a representative sample of healthy Lebanese adults. No significant associations were observed between GI, GL and MetS. Available studies testing the association between GI, GL and MetS are controversial. Until more evidence is available, it is prudent to abide by the dietary guidelines, minimize added sugar and consume a minimum of three servings of whole grains per day (Culberson et al., 2009). In the future, there is an urgent need to clarify the role that GI and GL exert on cardiometabolic health. Future studies may use questionnaires specifically designed to gather GI and GL data (Neuhouser et al., 2006; Flood et al., 2006) to improve the quality of evidence investigating the effect of these dietary factors on health outcomes (Bakel et al., 2009; Barclay, Flood, Brand-Miller & Mitchell, 2007). In addition, more prospective studies and clinical trials testing the association between GI, GL and MetS are required. Findings can later be communicated to the general public in the form of national dietary guidelines, food composition tables and food labels in order to ensure overall health and disease prevention.

APPENDIX I

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY (ARABIC)



أنت مدعو(ة) للمشاركة ببحث علمي سيجري في الجامعة الأميركية في بيروت. الرجاء أن تأخذ(ي) الوقت الكافي لقراءة المعلومات التالية بتأن قبل أن تقرر(ي) إذا كنت تريد(ين) المشاركة أم لا. يمكنك طلب إيضاحات أو معلومات إضافية عن أي شيء مذكور في هذه الاستمارة أو عن هذه الدراسة ككل.

إن الهدف من دراستنا هو قياس مستويات ثنائي الفينول أ (BPA) في عينة تمثل السكان اللبنانيين المقيمين في بيروت الكبرى، وتقييم ارتباط المستويات بمختلف الأمراض . كما نود أن نرى أيضا إذا كانت مستويات BPA تتغير مع مرور الوقت في كل شخص. ستتألف هذه الدراسة من مرحلتين، المرحلة الأولى، حد بدء الدراسة والثانية بعد سنتين للمتابعة. سنقوم بتسجيل ما يقارب 500 مشارك في الدراسة التي ستتم في المركز الطبي في الجامعة الأميركية في بيروت (AUBMC) حيث سيتم حصر استخدام هذه الموافقة الموقعة ومعها البيانات التي يتم جمعها لغايات هذه الدراسة من دون أي استخدام آخر.

ال BPA مادة كيميائية معتمة للتعارض مع الهرمونات الطبيعية في الجسم. ومن المكان العثور عليها في زجاجات من البلاستيك وحاويات المياه والزجاجات وأكواب الأطفال، والحاويات البلاستيكية، والبطانة الداخلية لعلب الطعام والمشروبات. قد يتناول البشر ال BPA إذا انتقل من الحاوية البلاستيكية إلى الطعام أو الشراب في ظل ظروف معينة. ويرتبط استهلاك ال BPA بالآثار الصحية الضارة بما في ذلك أمراض القلب وارتفاع ضغط الدم، ومرض السكري، والتغيرات في الكولسترول، والدهون الثلاثية، ومستوى هرمونات الغدة الدرقية. من الممكن أن مادة ال BPA تؤثر أيضا على المواد الجينية (DNA).

سيقوم الباحثون المبتدئون أصحاب شهادة (CITI) العاملون في شركة "الدولية للمعلومات" (Information International) المتعاقد معها باستخدام الطريقة المباشرة لتعيين المشاركين. وسوف يقومون بزيارة المشاركين في مكان إقامتهم لشرح أهداف الدراسة وطريقة التنفيذ. ثم تأخذ موافقة المشاركين وسيتم إعطاء تفاصيل عن تاريخ ووقت الدراسة. و سيتم تسجيل اسم المشارك وتاريخ الميلاد، و أيام الأسبوع المتوافر فيها للمشاركة ورقم هاتف لاائحة المحال للمتابعة. يحدد التاريخ الدقيق لتقلهم الى المركز الطبي في الجامعة الأميركية في بيروت (AUBMC) وسوف تشمل كل زيارة 10 مشاركين سوف يقومون بالإجراءات المبينة أدناه.

إن مشاركتكم تعني أنكم ستقابلون شخصاً مؤهلاً يجري معكم دراسة تتضمن العديد من الأسئلة حول الوضع الديمغرافي والاجتماعي والاقتصادي (العمر، والجنس، وموقع السكن، والتعليم، والمهنة والدخل)، ونمط الحياة (التدخين، الكحول، القهوة والنشاط البدني)، والحالة الصحية (التاريخ الطبي والأدوية)، والعادات الغذائية (الاستمارة الغذائية). وعلاوة على ذلك، سوف تخضعون لاختبار يشمل لقياس الوزن والطول ومحيط الخصر وضغط الدم ومعدل ضربات القلب. بالإضافة على ذلك سيتم فحص مستوى السكر بالدم بواسطة الاصبع، ويتضمن وخزة صغيرة واحدة في الاصبع لأخذ اقل من نقطة دم واحدة لإجراء الفحص. كما يطلب منكم التضوع لسحب الدم الاختبارات الجينية المحددة (الحامض النووي) والفحوصات المخبرية (بما في ذلك مخزون السكر (HbA1c)، نسبة السكر المتراكم في الدم ، الكرياتينين، الدهون، هرمونات الغدة الدرقية (TSH)، خمائر الكبد (SGPT و GGT)، الانسولين، الكريتينين البوليك، الزلالي، فيتامين د (25 OH vit D)، الكورانيزول، الليبتين، البروتاكتين، البيتيد C. وعلاوة على ذلك، سيتم جمع البول لقياس مستويات ال BPA. وسوف تتجز هذه الفحوصات المخبرية مجانا، ولكن في وقت لاحق اثناء الدراسة.

خلال زيارتك من المتوقع أن تكون مدة الانتهاء من الإجراءات خلال اليوم الواحد حوالي ساعة ونصف فقط، مقسمة بين 30 دقيقة لسحب الدم وجمع البول، و 60 دقيقة لملء الاستمارات لكل مشارك. ومن المتوقع ان تستغرق الزيارة الثانية 3 ساعات، بالنظر إلى أن سيكون هناك مشاركين آخرين يخضعون لنفس العملية.

رقم البروتوكول: IM.HT.03 كانون الثاني 2014

بعد حوالي سنتين من الزيارة الأولى، سيتم الاتصال بكم هاتفياً لدعوتكم إلى استكمال الجزء الثاني من الدراسة وذلك من خلال زيارة المركز الطبي في الجامعة الأميركية في بيروت (AUBMC) والقيام بنفس الإجراءات التي قمتم بها في الزيارة الأولى.

على الرغم من أن أي دراسة قد تترافق مع مخاطر لا يمكن التنبؤ بها، هذه الدراسة تحمل الحد الأدنى من المخاطر. لا تحمل أي من عمليات جمع البيانات أية مخاطر على المدى الطويل، وسوف يتم سحب الدم ضمن ظروف وقاية صحية صارمة وحجم الدم الإجمالي المطلوب هو 20 سم مكعب. ومن الآثار الجانبية المحتملة التي من المحتمل أن تصيبكم: ألم معتدل، نزف محدود، رضة خفيفة في موضع إدخال الإبرة. وقد تحدث في بعض الأحيان حالات إغماء أو دوار خفيف، ولكنها لا تدوم عادة أكثر من دقائق قليلة.

ستقدم نتائج جميع الاختبارات التي أجريت مجاناً للمشاركين وذلك عبر الاتصال بهم وتزويدهم بنتائج الفحوصات المخبرية عند انتهائها. وعلاوة على ذلك، سيتم تعويض المشاركين عن نفقات التنقل بمبلغ 30,000 ليرة لبنانية عند وصولهم إلى المركز الطبي في الجامعة الأميركية في بيروت (AUBMC)، كما سيزود المشاركون بوجبة الفطور في ذات اليوم.

إذا وافقت على الاشتراك بهذا البحث سوف تبقى المعلومات سرية. وحدهم الأطباء بدائرة الأخلاقيات والمحققين في المؤسسات العامة يمكنهم الإطلاع على النتائج بناءً لأمر قانوني فقط.

سيتم تخزين كافة البيانات والعينات البيولوجية التي تم جمعها بطريقة سرية. وستتخذ جميع التدابير لضمان عدم حدوث أي خرق لخصوصية المشتركين. وعلاوة على ذلك، سيتم تخزين ما تبقى من عينات الدم والبول بشكل آمن إلى أجل غير مسمى في مختبر الدكتورة نادالي زغيب خويري في المركز الطبي في الجامعة الأميركية في بيروت (AUBMC). إذا اخترتم سحب موافقتكم من الدراسة، سيتم تدمير العينات الخاصة بكم.

بناءً على طلبكم، سوف نزودكم بنتائج الفحوصات الجينية وشرح أهميتها لكم. سيتم الابقاء على سرية المعلومات.

لقد أن أعرف ما إذا كنت على استعداد للمشاركة في هذه الدراسة. لديك الحق في قبول أو رفض المشاركة. في حال رفض المشاركة، لن يكون هناك أي خسارة للمنافع التي يقدمها المركز الطبي التابع للجامعة الأميركية في بيروت (AUBMC). كما يحق لكم الانسحاب من هذه الدراسة في أي وقت من دون خسارة المنافع التي يقدمها المركز الطبي التابع للجامعة الأميركية في بيروت (AUBMC). أيضاً، يحق للباحث انهاء مشاركتك بهذه الدراسة.

أوافق على المشاركة في هذه الدراسة والإجراءات المحددة أعلاه.
نعم_____ لا_____

أوافق على أن يتم التواصل معي للدراسات المستقبلية
نعم_____ لا_____

أوافق على أن يتم التواصل معي إذا كانت نتائج الفحوصات الجينية ذات أهمية طبية
نعم_____ لا_____

استخدام ما تبقى من عينات الدم والبول للدراسات المستقبلية

نود تخزين ما تبقى من عينات الدم والبول لاستخدام محتمل في دراسات مستقبلية. للقيام بذلك، قد يكون هناك في المستقبل متعاونين في الجامعة الأميركية في بيروت، أو في المؤسسات الأخرى في لبنان وأو خارج بلدنا. لن يتم أي عمليات وخز إضافية وسيتم "ترميز" عينات الدم المخزنة. (تشير عبارة "ترميز" إلى *قابلية التعريف والتعقب. لا يتم تعريف عينات الدم لغايات الأبحاث، ولكن يمكن ربطها بمصدرها عبر استخدام الرموز. إلا أن الباحث المسؤول أو المشرف الأساسي هو الوحيد الذي يحق له الحصول على اللائحة التي تحدد الرمز الخاص بكل مريض.*)

أوافق على أن يتم استخدام ما تبقى من عينات الدم والبول للدراسات المستقبلية
نعم_____ لا_____

يمكن مشاركة عينات دمكم المرمزة مع باحثين آخرين لدراسات ذات صلة. ولن يعرف هؤلاء الباحثون هويتكم.

أوافق على مشاركة عينات دمي المرمزة مع باحثين آخرين لإجراء دراسات ذات صلة.
نعم_____ لا_____

إقرار المريض بالمشاركة في البحث:

أنا الموقع أدناه وبعد أن اطلعت واستوعبت كل جوانب هذا البحث وأجبت عن كل أسئلتي أوافق بملئ إرادتي على المشاركة في هذه الدراسة وأنا على علم تام بأنني أستطيع الإتصال بالدكتور هاني تميم على الرقم 01350000 المقسم 5453 أو بأي من ممثليه المخولين بهذه الدراسة وذلك إذا أردت توجيه أي سؤال، كما أنني أعلم أنه فيما لو أن أسئلتي لم يجاوب عليها بطريقة مقنعة بمكنني الإتصال بأحد أعضاء لجنة الأخلاقيات على المقسم 5445. كما أنني أعلم أنه بمكنني الإنسحاب من المشاركة في هذه الدراسة في أي وقت شئت حتى بعد التوقيع على هذه الوثيقة وإن العناية التي أتلقاها لن تتأثر بهذا الإنسحاب وإنني سوف أزود بنسخة عن هذه الوثيقة.

_____ _____
إسم المريض أو ممثله القانوني/قريبه أو وصيه التوقيع

_____
التاريخ و الساعة

_____ _____
إسم الشاهد التوقيع
التاريخ و الساعة

إقرار الباحث باستلام التعهد بالإشتراك:

لقد أطلعت بالتفصيل على التعهد بالإشتراك في البحث مع_____ (إسم المريض، ممثله القانوني، قريبه، وصيه)، وأفهمت المريض الغاية من هذه الدراسة ومن أخطارها وفوائدها. لقد أجبت المشترك على جميع الأسئلة التي تقدم بها بوضوح تام وتعهدت له بإعلامه عن أي تغيير يطرأ في موضوع هذا البحث.

_____ _____
التوقيع إسم الباحث أو ممثل المشترك

_____
التاريخ و الساعة

Institutional Review Board
American University of Beirut
17 FEB 2014
APPROVED

أسس الموافقة على الإشتراك في دراسة تتعلق بالأبحاث الحيوية

تقييم مستويات ثنائي الفينول أ عند اللبنانيين وتقييم إرتباطه بالوضع الصحي لهم

رقم البروتوكول: IM.HT.03
الباحث: د. هالي تميم
العنوان: شارع القاهرة، بيروت – لبنان
تلفون : 01350000 ext: 5453
المكان الذي سوف تتم فيه الدراسة: المركز الطبي في الجامعة الأميركية في بيروت (AUBMC)

أنت مدعو(ة) للمشاركة ببحث علمي سريري سيجرى في الجامعة الأميركية في بيروت. الرجاء أن تأخذ(ي) الوقت الكافي لقراءة المعلومات التالية بتأن قبل أن تقرر(ي) إذا كنت تريد(ين) المشاركة أم لا. بإمكانك طلب إيضاحات أو معلومات إضافية عن أي شيء مذكور في هذه الإستمارة أو عن هذه الدراسة ككل.

إن الهدف من دراستنا هو قياس مستويات ثنائي الفينول أ (BPA) في عينة تمثل السكان اللبنانيين المقيمين في بيروت الكبرى، وتقييم إرتباط المستويات بمختلف الأمراض . كما نود أن نرى أيضا إذا كانت مستويات BPA تتغير مع مرور الوقت في كل شخص. ستتألف هذه الدراسة من مرحلتين، المرحلة الأولى عند بدء الدراسة والثانية بعد سنتين للمتابعة. سنقوم بتسجيل ما يقارب 500 مشارك في الدراسة التي ستتم في المركز الطبي في الجامعة الأميركية في بيروت (AUBMC) حيث سيتم حصر استخدام هذه الموافقة الموقعة ومعها البيانات التي يتم جمعها لغايات هذه الدراسة من دون أي استخدام آخر.

ال BPA مادة كيميائية مصنّعة تتعارض مع الهرمونات الطبيعية في الجسم. ومن الممكن العثور عليها في زجاجات من البلاستيك وحاويات المياه والزجاجات وأكواب الأطفال، والحاويات البلاستيكية، والبطانة الداخلية لعلب الطعام والمشروبات. قد يتناول البشر ال BPA إذا انتقل من الحاوية البلاستيكية إلى الطعام أو الشراب في ظل ظروف معينة. ويرتبط استهلاك ال BPA بالآثار الصحية الضارة بما في ذلك أمراض القلب وارتفاع ضغط الدم، ومرض السكري، والتغيرات في الكولسترول، والدهون الثلاثية، ومستوى هرمونات الغدة الدرقية. من الممكن أن مادة ال BPA تؤثر أيضا على المواد الجينية (DNA).

سيقوم الباحثون الميدانيون أصحاب شهادة (CITI) العاملون في شركة "الدولية للمعلومات" (Information International) المتعاقد معها استخدام الطريقة المباشرة لتعيين المشاركين. وسوف يقومون بزيارة المشاركين في مكان إقامتهم لشرح أهداف الدراسة وطريقة التنفيذ. ثم تأخذ موافقة المشاركين وسيتم إعطاء تفاصيل عن تاريخ ووقت الدراسة. و سيتم تسجيل اسم المشارك وتاريخ الميلاد، و أيام الأسبوع المتوافر فيها للمشاركة ورقم هاتف لإتاحة المجال للمتابعة وتحديد التاريخ الدقيق لتظهم الى المركز الطبي في الجامعة الأميركية في بيروت (AUBMC) وسوف تشمل كل زيارة 10 مشاركين سوف يقومون بالإجراءات المبينة أدناه.

إن مشاركتكم تعني أنكم ستقابلون شخصياً مؤهلاً يجري معكم دراسة تتضمن العديد من الأسئلة حول الوضع الديمغرافي والاجتماعي والاقتصادي (العمر، والجنس، وموقع السكن، والتعليم، والمهنة والدخل)، ونمط الحياة (التدخين، الكحول، القهوة والنشاط البدني)، والحالة الصحية (التاريخ الطبي والأدوية)، والعادات الغذائية (الاستمارة الغذائية). وعلاوة على ذلك، سوف تخضعون لاختبار بدني لقياس الوزن والطول ومحيط الخصر وضغط الدم، ومعدل ضربات القلب. بالإضافة على ذلك سيتم فحص مستوى السكر بالدم بواسطة الاصبع، ويتضمن وخزة صغيرة واحدة في الاصبع لأخذ أقل من نقطة دم واحدة لإجراء الفحص. كما يطلب منكم الخضوع لسحب الدم الاختبارات الجينية المحددة (الحامض النووي) والفحوصات المخبرية (بما في ذلك مخزون السكر (HbA1c)، نسبة السكر السباعي في الدم ، الكرياتينين، الدهون، هرمونات الغدة الدرقية (TSH)، خمائر الكبد (SGPT و GGT)، الانسولين، الكرياتينين البولية، الزلالي، فيتامين د (25 OH vit D)، الكورتيزول، البيتين، البروتاكتين، البتايد C. وعلاوة على ذلك، سيتم جمع البول لقياس مستويات ال BPA. وسوف تنجز هذه الفحوصات المخبرية مجانا، ولكن في وقت لاحق أثناء الدراسة.

خلال زيارتك، من المتوقع أن تكون مدة الانتهاء من الإجراءات خلال اليوم الواحد حوالي ساعة ونصف فقط، مقسمة بين 30 دقيقة لسحب الدم وجمع البول، و 60 دقيقة لملء الاستمارات لكل مشارك .ومن المتوقع أن تستغرق الزيارة مدة أقصاها 3 ساعات، بانتظر إلى أن سيكون هناك مشاركين آخرين يمرون بنفس العملية.

بعد حوالي سنتين من الزيارة الأولى، سيتم الاتصال بكم هاتفياً لدعوتكم إلى استكمال الجزء الثاني من الدراسة وذلك من خلال زيارة المركز الطبي في الجامعة الأميركية في بيروت (AUBMC) والقيام بنفس الإجراءات التي قمتم بها في الزيارة الأولى.

على الرغم من أن أي دراسة قد تترافق مع مخاطر لا يمكن التنبؤ بها، هذه الدراسة تحمل الحد الأدنى من المخاطر. لا تحمل أي من عمليات جمع البيانات أية مخاطر على المدى الطويل، وسوف يتم سحب الدم ضمن ظروف وقاية صحية صارمة وحجم الدم الإجمالي المطلوب هو 20 سم مكعب. ومن الآثار الجانبية المحتملة التي من المحتمل أن تصيبكم: ألم معتدل، نزف محدود، رضّة خفيفة في موضع إدخال الإبرة. وقد تحدث في بعض الأحيان حالات إغماء أو دوار خفيف، ولكنها لا تدوم عادةً أكثر من دقائق قليلة.

ستقدم نتائج جميع الاختبارات التي أجريت مجاناً للمشاركين وذلك عبر الاتصال بهم وتزويدهم بنتائج الفحوصات المخبرية عند انتهائها. وعلاوة على ذلك، سيتم تعويض المشاركين عن نفقات التنقل بمبلغ 30,000 ليرة لبنانية عند وصولهم إلى المركز الطبي في الجامعة الأميركية في بيروت (AUBMC)، كما سيزود المشتركون بوجبة الفطور في ذات اليوم.

إذا وافقت على الإشتراك بهذا البحث سوف تبقى المعلومات سرية. وحدهم الأطباء ودائرة الأخلاقيات والمحققين في المؤسسات العامة يمكنهم الإطلاع على النتائج بناءً لأمر قانوني فقط.

سيتم تخزين كافة البيانات والعينات البيولوجية التي تم جمعها بطريقة سرية. وستتخذ جميع التدابير لضمان عدم حدوث أي خرق لخصوصية المشاركين. وعلاوة على ذلك، سيتم تخزين ما تبقى من عينات الدم والبول بشكل آمن إلى أجل غير مسمى في مختبر الدكتورة نادالي زغيب خويري في المركز الطبي في الجامعة الأميركية في بيروت (AUBMC). إذا اخترتم سحب موافقتكم من الدراسة، سيتم تدمير العينات الخاصة بك.

بناءً على طلبكم، سوف نزودكم بنتائج الفحوصات الجينية وشرح أهميتها لكم. سيتم الابقاء على سرية المعلومات.

نود أن أعرف ما إذا كنت على استعداد للمشاركة في هذه الدراسة. لديك الحق في قبول أو رفض المشاركة. في حال رفض المشاركة، لن يكون هنالك أي خسارة للمنافع التي يقدمها المركز الطبي التابع للجامعة الأميركية في بيروت (AUBMC). كما يحق لكم الانسحاب من هذه الدراسة في أي وقت من دون خسارة المنافع التي يقدمها المركز الطبي التابع للجامعة الأميركية في بيروت (AUBMC). أيضاً، يحق للباحث انهاء مشاركتك بهذه الدراسة.

أوافق على المشاركة في هذه الدراسة والإجراءات المحددة أعلاه.
نعم_____ لا_____

أوافق على أن يتم التواصل معي للدراسات المستقبلية
نعم_____ لا_____

أوافق على أن يتم التواصل معي إذا كانت نتائج الفحوصات الجينية ذات أهمية طبية
نعم_____ لا_____

استخدام ما تبقى من عينات الدم والبول للدراسات المستقبلية

نود تخزين ما تبقى من عينات الدم والبول لاستخدام محتمل في دراسات مستقبلية. للقيام بذلك، قد يكون هناك في المستقبل متعاونين في الجامعة الأميركية في بيروت، أو في المؤسسات الأخرى في لبنان وأو خارج لبنان. لن يتم أي عمليات وخز إضافية. وسيتم "ترميز" عينات الدم المخزنة. (تشير عبارة "ترميز" إلى قابلية التعريف والتعقب. لا يتم تعريف عينات الدم لغايات الأبحاث، ولكن يمكن ربطها بمصدرها عبر استخدام الرموز. إلا أن الباحث المسؤول أو المشرف الأساسي هو الوحيد الذي يحق له الحصول على اللائحة التي تحدد الرمز الخاص بكل مريض).

أوافق على أن يتم استخدام ما تبقى من عينات الدم والبول للدراسات المستقبلية
نعم_____ لا_____

ل مشاركة عيّنات دمكم المرمّزة مع باحثين آخرين لدراسات ذات صلة. ولن يعرف هؤلاء الباحثون هويتكم.

ق على مشاركة عيّنات دمي المرمّزة مع باحثين آخرين لإجراء دراسات ذات صلة.
_____ نعم _____ لا

إقرار المريض بالمشاركة في البحث:

أنا الموقع أدناه وبعد أن اطلعت واستوعبت كل جوانب هذا البحث وأجبت عن كل أسئلتي أوافق بملئ إرادتي على المشاركة في هذه الدراسة وأنا على علم تام بأنني أستطيع الإتصال بالدكتور هادي نعيم على الرقم 01350000 المقسم 5453 أو بأي من ممثليه المصادقين بهذه الدراسة وذلك إذا أردت توجيه أي سؤال، كما أنني أعلم أنه فيما لو أن أسئلتي لم يجاوب عليها بطريقة مقنعة يمكنني الإتصال بأحد أعضاء لجنة الأخلاقيات على المقسم 5445. كما إنني أعلم أنه يمكنني الإنسحاب من المشاركة في هذه الدراسة في أي وقت شئت حتى بعد التوقيع على هذه الوثيقة وإن العناية التي أتلقاها لن تتأثر بهذا الإنسحاب وإنني سوف أزود بنسخة عن هذه الوثيقة.

_____ _____
إسم المريض أو ممثله القانوني/قريبه أو وصيه — التوقيع

_____
التاريخ و الساعة

_____ _____
إسم الشاهد — التوقيع
التاريخ و الساعة

إقرار الباحث باستلام التعهد بالإشتراك:

لقد أطلعت بالتفصيل على التعهد بالإشتراك في البحث مع _____ (إسم المريض، ممثله القانوني، قريبه، وصيه)، وأفهمت المريض الغاية من هذه الدراسة ومن أخطارها وفوائدها. لقد أجبت المشترك على جميع الأسئلة التي تقدم بها بوضوح تام وتعهدت له بإعلامه عن أي تغيير يطرأ في موضوع هذا البحث.

_____ _____
التوقيع — إسم الباحث أو ممثل المشترك

_____
التاريخ و الساعة

APPENDIX II

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY (ENGLISH)

Consent to participate in a genetic research study

Assessment of BPA levels and their association with the health status among Lebanese population

Protocol number: IM.HT.03
Investigator: Dr. Hani Tamim
Address: American University Hospital
Hamra Street
Beirut, Lebanon
Phone: (01) 350 000 ext: 5453

Site where the study will be conducted: AUBMC

You are being asked to participate in a clinical research study conducted at the American University of Beirut. 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 the representative of the contracted company if you need more information or clarification about what is stated in this form and the study as a whole.

The aim of our study is to measure Bisphenol A (BPA) levels in a representative sample from the Lebanese population residing in Greater Beirut, and to assess if it is related to different diseases. We also would like to see if BPA measures change over time in any person. This study will be composed of 2 stages; at baseline and a 2-year follow up. We will be recruiting approximately 500 subjects and study will be conducted at AUBMC whereby this informed consent along with the data collected will be used for this study only.

BPA is a synthetic chemical that interferes with the natural hormones in the body. It can be found in plastic bottles and water containers, baby bottles and toddler cups, plastic ware, the inner lining of food cans and beverages. Humans may ingest BPA if it leaches from the plastic container into the food or drink under certain conditions. Consumption is associated with adverse health effects including heart disease, high blood pressure, diabetes, changes in cholesterol, triglycerides, and thyroid levels. BPA can also affect the expression of DNA material, called 'epigenetic effect.

The CITI certified field workers employed by the contracted company (Information International) will use the direct approaching method to recruit the cohort. They will visit the respondents in their residence to explain the study aims and method of implementation. Then the respondents will be consented and given the details of the date and time of the study. The name, date of birth, availability on week days and telephone number of the potential participant will be recorded for further follow up to specify the exact date for taking them to AUBMC. Each visit will include 10 participants who will complete the procedures described below.

Participating in this study means that you will sit with a certified research assistant who will conduct a survey which includes multiple questions about the demographic and socioeconomic status (Age, gender, location, education, occupation, income), lifestyle (smoking, alcohol, coffee, physical activity),

health status (medical history and medications), and dietary habits (Food Frequency Questionnaire). Moreover, you will undergo a physical exam to measure weight, height, waist circumference, blood pressure, and heart rate. Moreover, your blood sugar will be checked by a fingerstick, which means a very small prick will be done to your finger to get less than a drop of blood to do the test. You will also be asked to have blood withdrawn for specific genetic testing (DNA methylation) and clinical laboratory tests (including HBA1c, fasting blood sugar, creatinine, lipid profile, TSH, SGPT, GGT, fasting insulin, urinary creatinine, microalbuminuria, 25 OH vit D, Cortisol, leptin, C-peptide, prolactin). Moreover, urine will be collected for measuring BPA levels. These tests will be done free of charge, but will be done at a later time during the study.

During your visit, the duration for completing the procedures is expected to be for around an hour and a half over one day only, divided between 30 minutes for blood withdrawal and urine collection and 60 minutes for filling the surveys for each participant. Your total visit time to AUBMC is expected to be for a maximum of 3 hours, given that there will be other participants undergoing the same process.

After around 2 years from the baseline visit, you will be contacted by phone to be invited to complete the second part of the study (2-year follow-up stage) by visiting the AUBMC and going through the same process as the one described at baseline.

Although any study may be associated with any unforeseeable risk, this proposal has minimal risk. None of the data collection measures have any long term hazards, and all blood withdrawal will be done under sterile hygienic conditions and the total volume required is 20 cc. Possible side effects include mild pain, bleeding, bruising at the site of the needle insertion. Fainting or light-headedness can sometimes occur, but usually last only a few minutes.

The results of all tests conducted will be freely provided to the participants by calling them and providing them with the results of the test upon its completion. Moreover, the participants will be compensated for travel expenses with 30,000 LBP upon arriving to AUBMC. In addition, we will provide the participants with breakfast the same day.

If you agree to participate in this research study, the information will be kept confidential. Unless required by law, only the study doctor and designee, the ethics committee and inspectors from governmental agencies will have direct access to your information collected.

All data and biological samples collected will be stored in a confidential manner. These measures will all be conducted ensuring there is no breach of participants' privacy. Moreover, the remaining blood and urine samples will be stored securely indefinitely in Dr. Nathalie Zgheib Khoueiry's laboratory at the AUBMC. If you elect to withdraw your consent for the study, your samples will be destroyed.

You may ask that we provide you with the genetic results and explain their significance to you. The information will be kept confidential.

I would like to know if you would be willing to participate in this study. You have the right to accept or decline participation. Refusing to participate will not involve any loss of benefits offered in the future by AUBMC. Moreover, you are entitled to withdraw from the study at any time without any loss of benefits offered by AUBMC at any time.

I agree to participate in this study and the procedures explained above.

YES ..... NO.....

I agree to be contacted for future studies

YES ..... NO.....

I would like to be contacted if the genetic test results are significant

YES ..... NO.....

Using remaining blood and urine for other future studies

We would like to keep the remaining blood and urine samples for potential use in other future studies. To do so, there might be future collaborators at AUB, at other institutions in Lebanon and/or outside Lebanon. There will be no extra prick. The stored blood and urine samples will be coded (*"Coded" means identifiable, traceable. Blood* and urine *samples that are unidentified for research purposes but can be linked to their source through the use of codes; however, the principal investigators or VMP will be the only ones to have the list linking patients to the codes assigned.)*

I agree to permit the use of the remaining blood and urine sample for future studies

YES ..... NO.....

Your coded blood and urine samples may be shared with other investigators for related studies. These investigators will not know your identity.

I agree to have my coded blood and urine samples shared with other investigators for related studies.

YES ..... NO.....

Patient's Participation:

I have read and understood all aspects of the research study and all my questions have been answered. voluntarily agree to be a part of this research study and I know that I can contact Dr. Hani Tamim at 01350000 extension: 5453 or any of his/her designee involved in the study in case of any questions. If I felt that my questions have not been answered, I can contact the Institutional Review Board for human rights at 01350000 extension: 5445. 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 the care I might receive at AUBMC. I also understand that my participation may be ended by investigator at anytime. I know that I will receive a copy of this signed informed consent.

Name of patient or Legal Representative or Parent/Guardian _____ Signature _____

Date & Time _____

Witness's Name _____ Signature _____

Date & Time _____

Investigator's Statement:

I have reviewed, in detail, the informed consent document for this research study with _____ _____ (name of patient, legal representative, or parent/guardian) the purpose of the study and its risks and benefits. I have answered all the patient's questions clearly. I will inform the participant in case of any changes to the research

Name of investigator or designee _____ Signature _____

Date & Time _____

APPENDIX III

DATA COLLECTION FORM (ARABIC)

تقييم مستويات الـHP8 وارتباطها بالحالة الصحية بين السكان اللبنانيين

الاسم:	الحروف الأولى للاسم:	رقم المشارك:
رقم الهاتف:		تاريخ:

العوامل الديموغرافية:

تاريخ الميلاد:	الجنس: ذكر ☐ أنثى ☐
الحالة الاجتماعية: ☐ متزوج ☐ أعزب ☐ أرمل ☐ مطلق ☐ خاطب	

الاجتماعية والاقتصادية:

هل كانت مقيم خارج لبنان خلال العام الماضي:	نعم	لا
إذا كانت الإجابة بنعم، المكان _____ المدة _____		
مكان الإقامة _____		
طبيعة العمل _____		
ما هو دخلك في الأسرة		☐ <600$ ☐ 600-999$ ☐ 1000-2000 $ ☐ >2000$ ☐ لا أعلم ☐ رفضت الإجابة
ما هو أعلى مستوى تعليمي أكملته؟		☐ لم أكمل بالمدرسة ☐ المرحلة الإبتدائية ☐ المرحلة المتوسطة ☐ المرحلة الثانوية ☐ دبلوم تعليم تقني/مهني ☐ شهادة جامعية ☐ رفضت الإجابة
ما هو عدد الأشخاص الذين يسكنون في منزلكم (بما في ذلك الأقارب غير المقربة أو الخدم الذين يسكنون معك بشكل مؤقت)؟		
كم عدد الغرف في منزلكم (باستثناء المطبخ والحمامات		

تدريج التدخين			
السجائر	هل تدخن/ي السجائر حاليًا؟	☐ نعم ☐ لا	إذا كان الجواب نعم، كم سيجارة في اليوم؟ _____ منذ متى؟ _____
	إذا لا، هل كنت مدخن/ة سجائر سابقًا؟	☐ نعم ☐ لا	إذا كان الجواب نعم، متى توقفت؟ _____
الرجيلة / الشيشة	هل تدخن/ي الرجيلة حاليًا؟	☐ نعم ☐ لا	إذا كان الجواب نعم، كم مرة في اليوم؟ _____ منذ متى؟ _____
	إذا لا، هل كنت مدخن/ة رجيلة سابقًا؟	☐ نعم ☐ لا	إذا كان الجواب نعم، متى توقفت؟ _____
الكحول			
هل تشرب الكحول حاليًا؟		☐ نعم ☐ لا	إذا كانت الإجابة نعم، منذ النوع _____ كم كوب في اليوم؟ _____ منذ متى؟ _____
هل كنت تشرب الكحول سابقًا		☐ نعم ☐ لا	إذا كان الجواب نعم، متى توقفت؟ _____
القهوة			
هل تشرب القهوة حاليًا؟		☐ نعم ☐ لا	إذا كان الجواب نعم، كم كوب في اليوم؟ _____
النشاط البدني			
خلال السبعة أيام الماضية، كم مرة مارست الأنشطة البدنية القوية مثل رفع الأوزان الثقيلة والتمارين الرياضية أو ركوب الدراجات بسرعة لفترة لا تقل عن 10 دقائق أو أي نشاط يتطلب الجهد البدني الشاق ويسبب سعوبة بالتنفس؟			_____ أيام في الأسبوع ☐ لم أمارس الأنشطة البدنية القوية كم من الوقت قضيت على العمل لممارسة الأنشطة البدنية القوية؟ _____ ساعات _____ دقائق؟ خلال الـ 3 أشهر الماضية، كم عدد الأسابيع التي مارست بها الأنشطة البدنية القوية؟ _____ أسابيع
خلال السبعة أيام الماضية، كم مرة مارست الأنشطة البدنية المعتدلة مثل رفع الأوزان الخفيفة أو ركوب الدراجات أو ممارسة رياضة الغولف أو أي نشاط يتطلب الجهد البدني المعتدل ويسبب سعوبة خفيفة بالتنفس (لا تشمل المشي)؟			_____ أيام في الأسبوع ☐ لم أمارس الأنشطة البدنية المعتدلة كم من الوقت قضيت على العمل لممارسة الأنشطة البدنية المعتدلة؟ _____ ساعات _____ دقائق؟ خلال الـ 3 أشهر الماضية، كم عدد الأسابيع التي مارست بها الأنشطة البدنية المعتدلة؟ _____ أسابيع
خلال السبعة أيام الماضية، كم مرة مارست رياضة المشي لفترة لا تقل عن 10 دقائق؟ وهذا يشمل المشي في المنزل وخلال العمل والمشي للتنقل اليومي أو الرياضة أو التسلية			_____ أيام في الأسبوع ☐ لم أمارس الأنشطة البدنية المعتدلة كم من الوقت قضيت على العمل لممارسة رياضة المشي؟ _____ ساعات _____ دقائق؟ خلال الـ 3 أشهر الماضية، كم عدد الأسابيع التي مارست رياضة المشي؟ _____ أسابيع
خلال السبعة أيام الماضية، ما هي الفترة الزمنية التي أمضيتها جالسة؟ وهذا يشمل الجلوس وراء مكتب أو خلال زيارة الأصدقاء أو الجلوس للقراءة أو مشاهدة التلفاز أو النوم على مقعد			_____ ساعات _____ دقائق؟ خلال الـ 3 أشهر الماضية، كم عدد الأسابيع التي قمت فيها بهذا النشاط من الوقت جالسة؟ _____ أسابيع

التاريخ الطبي:

مرض الشريان التاجي:

هل اصيب أي من أفراد الأسرة الذين تم تشخيصهم بمرض الشريان التاجي أو ماتوا منه؟	□ نعم □ لا إذا كان الجواب نعم عدد من: ____	في أي سن: ____
هل قيل لك من قبل طبيب انك اصبت بنوبة قلبية؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____
هل خضعت لعملية تمييل (قسطرة) الشرايين القلب؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____
هل تم تشخيص [illegible]؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____
هل خضعت لعملية جراحية لتغيير شرايين القلب؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____

ارتفاع ضغط الدم:

هل قيل لك من قبل طبيب أو أحد العاملين في مجال الرعاية الصحية أن لديك ارتفاع في ضغط الدم؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____
هل خضعت لقياس ضغط الدم من قبل الطبيب أو أحد مقدمي الرعاية الصحية؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____ عدد المرات: ____
هل تخضع حاليا لأي علاج لارتفاع ضغط الدم؟	□ نعم □ لا	إذا كان الجواب نعم، حدد النوع: □ تعديل نمط الحياة □ الأدوية: ____

داء السكري:

هل قيل لك من قبل طبيب أو أحد العاملين في مجال الرعاية الصحية أنك تعاني من ارتفاع نسبة السكر في الدم أو من مرض السكري؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____
هل خضعت لقياس نسبة السكر في الدم من قبل طبيب أو العاملين في مجال الرعاية الصحية؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____ عدد المرات: ____
هل تخضع حاليا لأي علاج لارتفاع السكر في الدم أو لمرض السكري؟	□ نعم □ لا	إذا كان الجواب نعم، حدد النوع: □ تعديل نمط الحياة □ الأدوية: ____

ارتفاع مستوى الدهون في الدم:

هل قيل لك من قبل طبيب أو أحد العاملين في مجال الرعاية الصحية أنك تعاني من ارتفاع نسبة الكولسترول أو الدهون الثلاثية؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____
هل خضعت لقياس الكولسترول من قبل طبيب أو العاملين في مجال الرعاية الصحية؟	□ نعم □ لا	إذا كان الجواب نعم، حدد متى: ____ عدد المرات: ____
هل تخضع حاليا لأي علاج لارتفاع مستوى الدهون في الدم؟	□ نعم □ لا	إذا كان الجواب نعم، حدد النوع: □ تعديل نمط الحياة □ الأدوية: ____

3

مرض الغدة الدرقية:

هل قيل لكم من قبل طبيب أو أحد العاملين في مجال الرعاية الصحية أنكم تعانون من مرض الغدة الدرقية؟	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________ حدد طبيعة المرض: ________
هل تم تحديد مستويات غير طبيعية لهرمونات الغدة الدرقية من قبل طبيب أو العاملين في مجال الرعاية الصحية؟	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________ حدد النتيجة: ________
هل تخضعون لأي علاج لأمراض الغدة الدرقية؟	□ نعم □ كلا	إذا كان الجواب نعم حدد النوع □ تعديل نمط الحياة □ الأدوية ________
هل لديك أي من أفراد الأسرة الذين تم تشخيصهم بمرض الغدة الدرقية؟ (والد، أم، أخ، أخت، جد، جدة)	□ نعم □ كلا	إذا كان الجواب نعم حدد من: ________

تاريخ أمراض السرطان:

هل قيل لكم من قبل طبيب أو أحد العاملين في مجال الرعاية الصحية أنكم تعانون من مرض السرطان؟	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________ حدد طبيعة المرض: ________
هل تخضعون لعلاج كيميائي أو أي علاج آخر لمرض السرطان؟	□ نعم □ كلا	إذا كان الجواب نعم حدد النوع ________
هل لديك أي من أفراد الأسرة الذين تم تشخيصهم بمرض السرطان؟ (والد، أم، أخ، أخت، جد، جدة)	□ نعم □ كلا	إذا كان الجواب نعم حدد من: ________ حدد طبيعة المرض: ________

تاريخ الكسور:

هل عانيت من أي كسر في العظام؟	□ نعم □ كلا
إذا كان الجواب نعم	حدد أين: ________ العمر عند حصول الكسر: ________ كيف تم الكسر؟ (الوقوع من ارتفاع، حادث سير) ________

أمراض أخرى:

هل قيل لكم من قبل طبيب أو أحد مقدمي الرعاية الصحية أن لديك أي من التالي:		
الجلطة الدماغية	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________
التهاب المفاصل	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________
التهاب الشعب الهوائية المزمن أو انتفاخ الرئة	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________
أمراض القلب	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________

مرض الغدة الدرقية:

هل قيل لكم من قبل طبيب أو أحد العاملين في مجال الرعاية الصحية أنكم تعانون من مرض الغدة الدرقية؟	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________ حدد طبيعة المرض: ________
هل تستخدمون أدوية أو هرمونات الغدة الدرقية من قبل طبيب أو العاملين في مجال الرعاية الصحية؟	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________ حدد الكمية: ________
هل تخضعون لأي علاج لمرض الغدة الدرقية؟	□ نعم □ كلا	إذا كان الجواب نعم حدد النوع: □ تعديل نمط الحياة □ الأدوية ________
هل لديك أي من أفراد الأسرة الذين تم تشخيصهم بمرض الغدة الدرقية؟ (الأب، الأم، الأخ، أعضاء بيت جدة)	□ نعم □ كلا	إذا كان الجواب نعم حدد من: ________

تاريخ أمراض السرطان:

هل قيل لكم من قبل طبيب أو أحد العاملين في مجال الرعاية الصحية أنكم تعانون من مرض السرطان؟	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________ حدد طبيعة المرض: ________
هل تخضعون لعلاج كيميائي أو أي علاج آخر لمرض السرطان؟	□ نعم □ كلا	إذا كان الجواب نعم حدد النوع: ________
هل لديك أي من أفراد الأسرة الذين تم تشخيصهم بمرض السرطان؟ (الأب، الأم، الأخ، أعضاء بيت جدة)	□ نعم □ كلا	إذا كان الجواب نعم حدد من: ________ حدد طبيعة المرض: ________

تاريخ الكسور:

هل عانيت من أي كسر في العظم؟	□ نعم □ كلا
إذا كان الجواب نعم	حدد أين: ________ العمر عند حصول الكسر: ________ كيف تم الكسر؟ (الوقوع من ارتفاع، حادث سير) ________

أمراض أخرى:

هل قيل لكم من قبل طبيب أو أحد مقدمي الرعاية الصحية أن لديك أي من التالي:		
السكتة الدماغية	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________
التهاب المفاصل	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________
التهاب الشعب الهوائية المزمن أو انتفاخ الرئة	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________
أمراض الكبد	□ نعم □ كلا	إذا كان الجواب نعم حدد متى: ________

4

هل تعاني من أمراض اخرى؟

زيارة طبيب الأسنان:

هل قمت بزيارة طبيب الأسنان في العام الماضي؟	□ نعم □ لا	إذا كان الجواب نعم حدد متى: ________
هل تم وضع الحشوات في العام الماضي ؟	□ نعم □ لا	إذا كان الجواب نعم حدد متى: ________

الأدوية: (إذا لم تتوفر الأدوية الرجاء الاتصال بالمشارك)

الاسم (العلامة التجارية و الاسم العام)	الجرعة	تاريخ بدء الاستعمال

مراجعة عامة

هل شعرت بتغير في الوزن خلال ال 3 أشهر الماضية؟		□ الوزن مستقر □ وزن مفقود ________ كلغ □ وزن مكتسب ________ كلغ
النساء فقط	متى كانت آخر دورة شهرية؟ ________	
	هل أنت في مرحلة: □ قبل انقطاع الطمث □ بعد انقطاع الطمث	إذا في مرحلة قبل انقطاع الطمث: □ الدورة الشهرية منتظمة □ الدورة الشهرية غير منتظمة
هل تعاني من:	□ حب الشباب □ الشعرانية	

5

عادة النوم

1 . كم ساعة تنام في الليل في ايام الأسبوع؟

4 ساعات أو أقل	5 إلى 6 ساعات	6 إلى 7 ساعات	7 إلى 8 ساعات	8 إلى 9 ساعات	9 ساعات أو أكثر

2 . كم ساعة تنام في الليل في ايام عطلة نهاية الأسبوع ؟

4 ساعات أو أقل	5 إلى 6 ساعات	6 إلى 7 ساعات	7 إلى 8 ساعات	8 إلى 9 ساعات	9 ساعات أو أكثر

3 . هل تشعر أنك لا تحصل على قسط كاف من النوم؟

أبدا	نادرا (يوم واحد في الشهر)	أحيانا (2-4 أيام في الشهر)	كثيرا (5-15 يوم في الشهر)	تقريبا دائما (16-30 يوم في الشهر)

4 . هل تواجه او صعوبة خلودك عند مضاجعك للنوم ؟

أبدا	نادرا (يوم واحد في الشهر)	أحيانا (2-4 أيام في الشهر)	كثيرا (5-15 يوم في الشهر)	تقريبا دائما (16-30 يوم في الشهر)

5 . هل تستيقظ خلال الليل وتجد صعوبة في العودة الى النوم؟

أبدا	نادرا (يوم واحد في الشهر)	أحيانا (2-4 أيام في الشهر)	كثيرا (5-15 يوم في الشهر)	تقريبا دائما (16-30 يوم في الشهر)

6 . هل تستيقظ في الصباح الباكر جدا وتكون غير قادر على متابعة النوم؟

أبدا	نادرا (يوم واحد في الشهر)	أحيانا (2-4 أيام في الشهر)	كثيرا (5-15 يوم في الشهر)	تقريبا دائما (16-30 يوم في الشهر)

7 . هل قال لك الطبيب أن لديك حالة توقف التنفس أثناء النوم؟

لا	نعم

8 . هل تشخر؟

لا أعرف	لا	نعم

9 . إذا كنت تشخر, كيف يمكن أن تصف ارتفاع صوت شخيرك؟

د .مرتفع جدا يمكن سماعه من الغرف المجاورة	ج .أعلى من الكلام	ب .بنفس درجة ارتفاع الكلام	أ .أعلى بقليل من صوت التنفس

10 . إذا كنت تشخر, كم مرة يتكرر شخيرك؟

ه .لا يحدث	د .مرة إلى مرتين بالشهر	ج .مرة إلى مرتين بالأسبوع	ب .3- 4 مرات بالأسبوع	أ .تقريبا كل يوم

11 . إذا كنت تشخر, هل سبق وأن سبب شخيرك الإزعاج للآخرين؟

لا أعرف	لا	نعم

12 . هل لاحظ أي شخص انك توقف التنفس أثناء النوم؟

ه .لا يحدث	د .مرة إلى مرتين بالشهر	ج .مرة إلى مرتين بالأسبوع	ب .3- 4 مرات بالأسبوع	أ .تقريبا كل يوم

13 . كم مرة تشعر بالتعب او الإرهاق عند الاستيقاظ من النوم؟

ه .لا يحدث	د .مرة إلى مرتين بالشهر	ج .مرة إلى مرتين بالأسبوع	ب .3- 4 مرات بالأسبوع	أ .تقريبا كل يوم

14 . هل تحس بالتعب أو الإرهاق أثناء ساعات اليقظة؟

ه .لا يحدث	د .مرة إلى مرتين بالشهر	ج .مرة إلى مرتين بالأسبوع	ب .3- 4 مرات بالأسبوع	أ .تقريبا كل يوم

15 . هل سبق أن نعست أو نمت خلال قيادة السيارة أو الانتظار؟

لا	نعم

16 . إذا كانت الإجابة نعم، كم مرة يحدث هذا؟

ه .لا يحدث	د .مرة إلى مرتين بالشهر	ج .مرة إلى مرتين بالأسبوع	ب .3- 4 مرات بالأسبوع	أ .تقريبا كل يوم

APPROVED

Code	الطعام	مرجع حجم الحصة	حجم الحصة	في اليوم	في الأسبوع	في الشهر	نادراً/أبداً
		عيران					
2.5	جبن (عالي بالدسم/صفراء)	حصة واحدة = مثلث/مربع Side A or B					
2.6	جبن (قليل الدسم/لايت/بيضاء)	حصة واحدة = مثلث/مربع Side A or B					
2.7	لبنة، عادي	Side A					
2.8	لبنة، لايت/ خالية الدسم	Side A					
3	الفاكهة والعصائر						
3.1	الحمضيات: برتقال ،غريفون	Side A / حبة واحدة وسط					
3.2	فاكهة ذات اللون الأصفر أو البرتقالي الداكن (دراق، خوخ، الخ)	Side A / حبة واحدة وسط					
3.3	فراولة	Side A /فراولة 10					
3.4	عنب	Side A /عنب 10					
3.5	فاكهة اخرى: موز، / تفاح، طازج	حبة واحدة وسط					
3.6	فاكهة مجففة: زبيب ، تمر مشمش	زبيب (1 ملعقة طعام)، تمر/ مشمش (حبة واحدة)					
3.7	عصير فاكهة طازج	Side A					
3.8	مشروبات بطعم الفاكهة: تنكة/بلاستيك	Side A/تنكة					
3.9	مشروبات بطعم الفاكهة: معبأة في زجاجات /كرتونة	كرتونة / زجاجة صغيرة Side A					
3.10	فاكهة معلبة	Peach/ apricot = ½ fruit, Pineapple = 1 slice					
4	الخضار						
4.1	سلطة خضراء: خس، فقل أخضر، خيار،...	Side A/ Page 8					
4.2	خضار ذات اللون الأخضر أو الأصفر الداكن (سبانخ، هندباء، ملوخية، جزر...)	Side A/ Page 4					
4.3	بندورة طازجة، حجم وسط	10 cherry /حبة واحدة					
4.4	ذرة / بازلاء خضراء، مطبوخة	Side A/ Page 4					
4.5	ذرة / بازلاء خضراء، معلبة	Side A/ Page 4					
4.6	بطاطا مشوية/ مسلوقة/ مهروسة	Side A /حبة واحدة					
4.7	قرع، كوسى، باذنجان/ مطبوخ	Side A/ 1 med. stuffed					
4.8	قرنبيط/ ملفوف/ بروكولي	Side A/ Page 4					
4.9	خضار أخرى معلبة (بازيلا، فطر، زيتون)	Side A/ Page 4					
4.10	عصير خضار طازج: بندورة/ جزر	Side A					
5	اللحوم وبدائلها						
5.1	بقول: عدس، فاصوليا، حمص، مطبوخة/ غير معلبة	Side A/ Page 4					
5.2	بقول معلبة (فول، فاصوليا ...) المكدوجاج	Side A/ Page4					

نادرا/أبدا	في الشهر	في الأسبوع	في اليوم	حجم الحصة	مرجع حجم الحصة	الطعام	Code
					Side A/ small bag Page 4	مكسرات وبذور: فول سوداني، لوز/جوز ، بذور دوار الشمس	5.3
					مفروم –Side A Steak -Side B/ Thickness	لحم أحمر (بقر، عجل، غنم)	5.4
					ساق/فخذ/صدر/جوانح Thickness/Side B	دواجن	5.5
					Side B/Thickness فريدس: 1 وسط كالماري: 1 وسط كراب: 1 أصبع	سمك/ ثمار البحر طازج	5.6
					علبة كبيرة/ علبة صغيرة 1 Page 19	سمك معلب (تونا، سردين)	5.7
					1 بيضة	بيضة، كاملة	5.8
					Side B/ Thickness	لحوم الأعضاء (كبد، كلاوي، نخاع)	5.9
					شريحة واحدة Side B/ Thickness	لحوم باردة: مرتديلا، جامبون، سلامي، حبش، الخ	5.10
					Side B/ Thickness-حجم مقانق	سجق، مقانق، غير معلب	5.11
					Side B/ Thickness-حجم مقانق حجم هوت دوغ	سجق، مقانق، هوت دوغ ، معلب	5.12
						الدهون والزيوت	6
					Side A	زيت نباتي: ذرة/ دوار الشمس/ صويا	6.1
					Side A	زيت زيتون (يلطمس مع الزعتر)	6.2
					1 حبة	زيتون	6.3
					Side A	زبدة	6.4
					Side A	سمن	6.5
					Side A	مايونيز	6.6
					Side A	طحينة	6.7
						الحلويات	7
					Page 14, 15, 16 Side B/ Thickness	كيك، كوكيز ، دونتس، مافن، كرواسان	7.1
					1 scoop/ Page 9 /1 stick	بوظة	7.2
					1 شوكولا وسط	لوح شوكولا	7.3
					Side A	سكر ، عسل، مربى، دبس، كريمة شوكولا chocolate spread	7.4
					Thickness /Side B كنافه مع كعك	حلويات عربيّة، بقلاوة، معمول، كنافه	7.5
						المشروبات	8
					Side A/ 1 can (330 mL)	مشروبات غازيّة، عادي	8.1

9

Code	الطعام	مرجع حجم الحصة	حجم الحصة	في اليوم	في الأسبوع	في الشهر	نادراً/أبداً
8.2	مشروبات غازية ، دايت	Side A/ 1 can (330 mL)					
8.3	قهوة تركية	Side A					
8.4	قهوة/نسكافيه أو شاي	Side A					
8.5	شراب الشوكولا أو الكاكاو الساخن	Side A					
8.6	بيرة، عادي	Side A/ 1 bottle					
8.7	نبيذ: أحمر، أبيض، أو وردي	Side A					
8.8	الخمور: ويسكي، فودكا، جين، رم	Side A					
8.9	مياه	Side A/ bottle (0.5 L)					
9	مأكولات أخرى						
9.1	مناقيش، زعتر، جبنة	منقوشة كبيرة / bouchee صغيرة					
9.2	بطاطا مقلية	Side A / Page 4					
9.3	رقائق البطاطا	XS/S/M/L/XL Page 20					
9.4	فلافل دون خبز	1 فلافل، حجم وسط					
9.5	سندويش شاورما	سندويش، حجم وسط					
9.6	برغر (لحمة، دجاج، سمك)	Side B /1 medium					
9.7	بيتزا	Side B/ Thickness					
9.8	حساء معلب	Side A/ Page 3					
9.9	كاتشب	Side A					
9.10	خردل	Side A					

10.1. كم مرة تتبل طعامك مع صلصة الطماطم المكونة من **الطماطم والبصل والثوم مع زيت الزيتون**؟
------------------------------- عدد مرات باليوم / الأسبوع / الشهر؟

10.2. هل تستهلك لحوم الدجاج أو الديك الرومي بدلاً من اللحم الأحمر: البقر، العجل، لحم الخنزير، همبرغر، أو السجق؟
------ نعم ------ لا

هل هناك أي أطعمة أخرى غير تلك المذكورة أعلاه تتناولها **عادةً مرة في الأسبوع على الأقل**؟

مثال: يانيه، صلصة الكريمة، كرواسان، ***coffee creamer, energy drink*** الخ (لا تشمل التوابل الجافة). لا تسجل الأطعمة التي تم ذكرها في القسم السابق.

أطعمة أخرى تتناولها عادةً مرة في الأسبوع على الأقل	حجم الحصة الإعتيادي	حصة في الأسبوع

إستفتاء حول العادات الغذائية

1- هل تعلم ما هو ثنائي الفينول أ (BPA) ؟	□ نعم □ كلا
2- هل أنت على علم بوجود زجاجات بلاستيكية/تابروير خالية من BPA؟	□ نعم □ كلا

		دائما 6-7 x/week	معظم الوقت 4- 5x/week	مرات قليلة 2-3 x/week	نادرا 1x/week to 2x/month	أبدا/ كلا	لا أعرف
3	هل تخزن الأطعمة في حاويات بلاستيكية؟						
4	هل تسخن الأطعمة في حاويات بلاستيكية؟						
5	هل تتأكد من أن الحاويات البلاستيكية التي تستخدمها خالية من مادة ال BPA؟						
6	هل تسخن الأطعمة المغلفة بنايلون لاصق؟						
7	هل تشرب المياه المعبأة في قناني بلاستيكية؟						
	7.1 من المياه المعبأة في زجاجات البلاستيك: ---------------- أكواب / يوم 7.2 من مبرد المياه: ---------------- أكواب / يوم						
8	هل تعيد إستخدام قناني المياه البلاستيكية؟						
9	هل تشرب من قناني مياه قد تركتها في سيارتك؟						
10	هل تتناول الطعام خارج المنزل؟ (في المطاعم، في الحالات التي تقدم وجبات خفيفة، الخ)						
11	كم مرة في الأسبوع تقوم بشراء الوجبات السريعة والجاهزة (delivery)؟						
12	هل تشتري المشروبات الغازية المعبأة في علب تنك و في قناني بلاستيكية؟						
13	هل تستهلك معجون الطماطم/ رب البندورة المعلبة؟						


هل كان الأحى يوما عاقلا؟
نعم
لا
متى كانت آخر مرة تذرفت فيها الدموع؟
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Physical Exam Form

Name of the participant: ---------- Initials:---------- Study ID number: ----------

		Results النتائج	Healthy ranges النطاقات الصحية
Body weight (kg	الوزن		
Height (cm):	الطول		
BMI:	مؤشر الكتلة		*18.5-24.9 kg/m²*
Waist circumference (cm):	قياس دائرة الخصر		*نساء <80 cm, رجال <94 cm*
Body fat (kg):	نسبة الدهون في الجسم		*نساء <32%; رجال <25%*
Muscle mass (kg):	نسبة العضل في الجسم		*نساء 24-30 %; رجال 33-40%*
Waist to hip ratio:	قياس محيط الأورك		*نساء <0.9, رجال <0.85*
Heart rate:	قياس نبض القلب		*60-100 bpm*
Blood Pressure – Measurement # 1	قياس ضغط الدم 1		
Systolic blood pressure (mmHg):	العالي		*120 mmHg*
Diastolic blood pressure(mmHg):	الواطي		*80 mmHg*
Blood Pressure – Measurement # 2	قياس ضغط الدم 2		
Systolic blood pressure (mmHg):	العالي		*120 mmHg*
Diastolic blood pressure(mmHg):	الواطي		*80 mmHg*

Time of urine collection	
Time of blood withdrawal	

APPENDIX IV

DATA COLLECTION FORM (ENGLISH)

Assessment of BPA levels and their association with the health status among Lebanese population

Name:	Initials:	Study ID number:
Tel number:		Date:

Demographic Factors:

Date of birth:	Gender: □ Males □ Females
Marital status: □ Married □ Single □ Widow □ Divorced	□ Engaged

Socioeconomic:

Have you lived outside Lebanon for the past year: □ No □ Yes If yes, where_____ and for how long	
Which area do you live?	
What do you work?	
What is your income per family:	□ <600$ □ 600- 999.9$ □ 1000-2000$ □ >2000$ □ I don't know/ Not sure □ I prefer not to answer
What is your highest level of education?	□ No schooling □ Primary school □ Intermediate school □ Secondary school □ Technical diploma □ University degree □ I prefer not to answer
What is the total number of individuals living in your house? (Including relatives, family members and maids that frequently live with you on a semi-permanent basis)	
How many rooms are there in your house? (Excluding kitchens, bathrooms, hallways, balconies, and garage)	

Lifestyle:

Smoking history			
Cigarette	Do you currently smoke cigarettes?	□ No □ Yes	If yes, how many cigarettes/day? Since when?
	If no, are you a previous cigarette smoker?	□ No □ Yes	If yes, when did you stop?
Narghileh	Do you currently smoke narghileh?	□ No □ Yes	If yes, how many narghileh/day? Since when?
	If no, are you a previous narghileh smoker?	□ No □ Yes	If yes, when did you stop?
Alcohol			
Do you currently drink alcohol?		□ No □ Yes	
		If yes specify type? Since when?	How many glasses/week?
Previous drinker?		□ No □ Yes	If yes, when did you stop?
Coffee			
Do you currently drink coffee?		□ No □ Yes If yes how many cups/day?	
Physical activity			
During the last 7 days, on how many days did you do **vigorous** physical activities like heavy lifting, aerobics, or fast bicycling for at least 10 minutes (or any activity that take hard physical effort and make you breathe harder than normal)?		---------- days/week □ None - How much time in total did you usually spend on one of those days doing vigorous physical activities? _____ hours _____ minutes? - How many weeks did you spend doing vigorous physical activities during the last 3 months? ----------weeks	
During the last 7 days, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or tennis or any activity that take hard physical effort and make you breath harder than normal)? Do not include walking.		---------- days/week □ None - How much time in total did you usually spend on one of those days doing moderate physical activities? _____ hours _____ minutes? -How many weeks did you spend doing moderate physical activities during the last 3 months? ----------weeks	
During the last 7 days, on how many days did you **walk** for at least 10 minutes at a time? This includes walking at work and at home, walking to travel from place to place, and any other walking that you did solely for sport, exercise or leisure.		---------- days/week □None - How much time in total did you usually spend walking on one of those days? _____ hours _____ minutes? -How many weeks did you spend walking during the last 3 months? ----------weeks	
During the last 7 days, how much time in total did you usually spend sitting on a week day? This includes time spent sitting at a desk, visiting friends, reading traveling on a bus or sitting or lying down to watch television.		_____ hours _____ minutes? -How many weeks have you been spending the same time in terms of sitting during the last 3 months? ----------weeks	

Medical History:

Coronary artery disease:

Do you have any family member who has been diagnosed with coronary artery disease or died suddenly?	□ No □ Yes If yes: specify who	At what age:
Have you been told by a doctor that you had a heart attack?	□ No □ Yes If yes when:	
Did you undergo cardiac catheterization?	□ No □ Yes If yes when:	
Was a stent placed?	□ No □ Yes If yes when:	
Did you have coronary heart bypass surgery?	□ No □ Yes If yes when:	

Hypertension:

Have you been told by a doctor or a health care worker that you have high blood pressure?	□ No □ Yes If yes when:
Have you had your blood pressure measured by a doctor or a health care worker?	□ No □ Yes If yes when? What was it?
Are you taking any treatment for high blood pressure?	□ No □ Yes If yes specify: □ Life style modifications □ Drugs:

Diabetes Mellitus:

Have you been told by a doctor or a health care worker that you have raised blood sugar or diabetes?	□ No □ Yes If yes when:
Have you had your blood sugar measured by a doctor or a health care worker?	□ No □ Yes If yes when? What was it?
Are you taking any treatment for high blood sugar or diabetes?	□ No □ Yes If yes specify: □ Life style modifications □ Drugs:

Dyslipidemia:

Have you been told by a doctor or a health care worker that you have raised cholesterol or triglycerides?	□ No □ Yes If yes when:
Have you had your cholesterol measured by a doctor or a health care worker?	□ No □ Yes If yes when? What was it?
Are you taking any treatment for dyslipidemia?	□ No □ Yes If yes specify: □ Life style modifications □ Drugs:

Thyroid disease:

Have you ever been told by a doctor or ahealth care worker that you have thyroid disease?	□ No □ Yes If yes when? What was the disease?
Have you had your thyroid hormones measured by a doctor or a health care worker?	□ No □ Yes If yes when? What was it?
Are you taking any thyroid drug?	□ No □ Yes If yes specify:
Do you have any family history of thyroid disease? (Parents, siblings and grandparents)	□ No □ Yes If yes specify who:

Cancer history:

Have you ever been told by a doctor or ahealth care worker that you have cancer?	□ No □ Yes If yes when? What was the disease?
Are you taking any chemotherapy or other drug for cancer?	□ No □ Yes If yes specify
Do you have any family history of cancer? (Parents, siblings and grandparents)	□ No □ Yes If yes specify the disease: Specify who:

Fracture history:

Did you ever sustain a fracture?	□No □Yes
If yes:	Where? Age at onset? How did it happen? (fall from height, accident…)?

Other diseases:

Have you been told by a doctor or a health care worker that you have any?	
Stroke?	□No □Yes If yes when:
Arthritis?	□No □Yes If yes when:
Chronic bronchitis or emphysema?	□No □Yes If yes when:
Liver disease?	□No □Yes If yes when:

Do you have any other illnesses?

Dentist visits:

Have you visited any dentist in the past year?	□ No □ Yes If yes when:
Did you have any fillings done in the past year?	□ No □ Yes If yes when:

Medications (if not brought, call the participant later)

Name (brand and generic)	Dose	Date started

Review of system:

Do you have any weight changes during the last 3 months?		□ Stable weight □ Lost weight How many Kgs? □ Gained weight How many Kgs?
For women:	When was your last menstrual period?	
	Are you: □ premenopausal □ postmenopausal	If premenopausal do you have □ Regular menses □ Irregular menses
	Do you have? □ Acne □ Hirsutism	

Sleep Habits and Berlin questionnaires

1- How many hours do you sleep per night on weekdays?					
4 hrs or less	5 to 6 hrs	5 to 7 hrs	7 to 8 hrs	8 to 9 hrs	9 hrs or more
2- How many hours do you sleep per night on weekends?					
4 hrs or less	5 to 6 hrs	5 to 7 hrs	7 to 8 hrs	8 to 9 hrs	9 hrs or more
3- Do you feel that you are not getting enough sleep?					
Never	Rarely (1 / month)	Sometimes (2-4 / month)	Frequently (5-15 /month)	Almost Always (16-30 / month)	
4- Do you have Trouble falling asleep?					
Never	Rarely (1 / month)	Sometimes (2-4 / month)	Frequently (5-15 /month)	Almost Always (16-30 / month)	
5- Do you wake up during the night and have difficulty resuming sleep?					
Never	Rarely (1 / month)	Sometimes (2-4 / month)	Frequently (5-15 /month)	Almost Always (16-30 / month)	
6- Do you wake up too early in the morning and be unable to resume sleep?					
Never	Rarely (1 / month)	Sometimes (2-4 / month)	Frequently (5-15 /month)	Almost Always (16-30 / month)	
7- Did your doctor tell you that you have sleep apnea?					
Yes	No				
8- Do you snore?					
Yes	No	Don't Know			
9- If you snore, your snoring is?					
a. Slightly louder than breathing	b. As loud as talking	c. Louder than talking	d. Very loud-can be heard in adjacent rooms		
10- If you snore, how often do you snore?					
a. Nearly every day	b. 3-4 times a week	c. 1-2 times a week	d. 1-2 times a month	e. Never or nearly never	
11- If you snore, has your snoring ever bothered other people?					
Yes	No	Don't Know			
12- Has anyone noticed that you quit breathing during sleep?					
a. Nearly every day	b. 3-4 times a week	c. 1-2 times a week	d. 1-2 times a month	e. Never or nearly never	
13- How often do you feel tired or fatigued after you sleep?					
a. Nearly every day	b. 3-4 times a week	c. 1-2 times a week	d. 1-2 times a month	e. Never or nearly never	
14- During your waking time do you fee tired, fatigued or not up to par?					
a. Nearly every day	b. 3-4 times a week	c. 1-2 times a week	d. 1-2 times a month	e. Never or nearly never	
15-Have you ever nodded off or fallen asleep while driving a vehicle?					
Yes	No				
16- If yes, how often does this occur?					
a. Nearly every day	b. 3-4 times a week	c. 1-2 times a week	d. 1-2 times a month	e. Never or nearly never	

FOOD FREQUENCY QUESTIONNAIRE

Name of the participant: ---------- Initials:---------- Study ID number: ----------

Please think about your eating patterns during the past year. Please indicate your usual intake of each of the following food items per day, week, or month. Please be as precise as you can in your recall.

Code	Food item	Reference Portion	Serving Size	Day	Week	Month	Rarely/Never
	Examples:						
	Rice, white, cooked	*A ride*	*½ A 11*		*3*		
	Cheese, regular	*B side/ Thickness*	*B1 / Th 2*	*4*			
	Legumes, canned (beans, peas)	*Side A/ Page 4*	*1.5 cups*		*2*		
1	**Bread and Cereals**						
1.1	Bread, white	1 large Arabic loaf					
		1 medium Arabic loaf					
		1 French baguette					
		1 pain de mie/ toast					
1.2	Bread, brown	1 large Arabic loaf					
		1 medium Arabic loaf					
		1 French baguette					
		1 pain de mie/ toast					
1.3	Traditional breads(markouk/tannour)	1 loaf					
1.4	Breakfast cereals, regular/ sugar coated/ chocolate/ bran	Side A					
		Carton (35 g)					
1.5	Kaak	Finger size Small round / Page 13					
1.6	Rice, white, cooked	Side A/ Page 5					
1.7	Pasta/ Noodles, plain, cooked	Side A/ Page 5					
1.8	Wheat/ Bulgur, cooked	Side A/ Page 5					
1.9	Rice/Pasta/Cereals, whole grain	Side A / Page 5					
2	**Dairy Products**						
2.1	Milk, skim/low-fat (0-2%)	Side A					
2.2	Milk, whole-fat	Side A					
2.3	Yogurt, fat-free/low-fat	Side A					
		Bottled ayran					
2.4	Yogurt, whole-fat	Side A					
		Bottled ayran					

2.5	Cheese, regular / yellow	Side A Side B / Thickness Cube/ triangular portion							
2.6	Cheese, low fat / white	Side A Side B / Thickness Cube/ triangular portion							
2.7	Labneh, regular	Side A							
2.8	Labneh, low fat	Side A							
3.	**Fruits and Fruit Juices**								
3.1	Citrus orange/ grapefruit	Side A / 1 medium							
3.2	Peach, plum, prunes	Side A / 1 medium							
3.3	Strawberries	Side A / 10 strawberries							
3.4	Grapes	Side A / 10 grapes							
3.5	Banana/ Apples	Side A / 1 medium							
3.6	Dried Fruits	Khishis* 1 tbsp Dates: 1 portion Apricots: 1 portion							
3.7	Fruit juice, fresh	Side A							
3.8	Fruit juice, canned	1 can							
3.9	Fruit juice, bottled	1 bottle/ carton							
3.10	Fruits, canned	Peach/ apricot = ½ fruit Pineapple = 1 slice							
4.	**Vegetables**								
4.1	Salad, green lettuce, mint, cucumber, green pepper, rocket, purslane, etc.	Side A/ Page 8							
4.2	Dark green or deep yellow (spinach, Swiss Chard, Jew's mallow, carrots…)	Side A/ Page 4							
4.3	Tomatoes, fresh	1 medium / 10 cherry							
4.4	Corn / Green peas, fresh	Side A/ Page 4							
4.5	Corn/ Green peas, canned	Side A/ Page 4							
4.6	Potatoes, baked / boiled/ mashed	Side A / 1 medium							
4.7	Zucchini/ Eggplants, cooked	Side A/3 med. stuffed							
4.8	Cauliflower/ Cabbage/ Broccoli	Side A/ Page 4							
4.9	Other canned vegetables (Mushroom, palmettis, asparagus, etc.)	Side A/ Page 4							
4.10	Vegetable juice, fresh	Side A							
5.	**Meat and Meat Alternatives**								
5.1	Legumes/ lentils, beans, chickpeas, etc., dried, cooked	Side A/ Page 4							
5.2	Legumes, canned (beans, peas)	Side A/ Page 4							

5.3	Nuts & seeds: walnuts, peanuts, almonds, sunflower seeds, etc.	Side A/ Page 4 Pre-packed small bag								
5.4	Red meat, beef/ lamb/ goat	Side A/ Ground Steak - Side B/ Thickness								
5.5	Poultry	Leg/thigh/breast/wings Side B								
5.6	Fish/ Seafood, fresh	Side B/ Thickness Shrimp: 1 medium Calamari: 1 medium Crab: 1 medium								
5.7	Fish, canned (tuna, sardines)	1 large can/ 1 small can Page 19								
5.8	Eggs	1 medium								
5.9	Organ meats (liver, kidneys, brains)	Side B/ Thickness								
5.10	Luncheon meats (mortadella, turkey, salami, ham, etc.)	Side B/ Thickness Regular slice								
5.11	Sausages, makanek, uncanned	Side B/ Thickness Makanek size								
5.12	Sausages, makanek, hotdogs, canned	Hotdog size Makanek size Side B/ Thickness								
6	**Added Fats and Oils – Salads/ Cooking / Fries**									
6.1	Vegetable oil, corn/ sunflower/ soya	Side A								
6.2	Olive oil (including with thyme)	Side A								
6.3	Olives	5 olives								
6.4	Butter	Side A								
6.5	Ghee	Side A								
6.6	Mayonnaise	Side A								
6.7	Tahini	Side A								
7	**Sweets and Desserts**									
7.1	Cakes / Cookies/ Doughnuts / Muffins/ Croissant / Biscuits	Side B / Thickness Page 14-15-16								
7.2	Ice cream	1 scoop / stick/ Page 9								
7.3	Chocolate bar	1 medium								
7.4	Sugar, honey, jam, molasses, chocolate spread	Side A								
7.5	Arabic sweets Baklava, maamoul, kaeffe	Side B								

8	**Beverages**								
8.1	Soft drink, regular	Side A / 1 can (330 mL)							
8.2	Soft drink, diet	Side A / 1 can (330 mL)							
8.3	Turkish coffee	Side A							
8.4	Instant coffee / Tea	Side A							
8.5	Cocoa / Hot chocolate	Side A							
8.6	Beer	Side A / 1 bottle							
8.7	Wine, red / white/ blush	Side A							
8.8	Liquor, whiskey/ vodka/ gin/ rum	Side A							
8.9	Water	Side A / Bottle (0.5 L)							
9	**Miscellaneous**								
9.1	Manaeish, zaatar/ cheese	1 regular / 1 household Page 17- 18							
9.2	French fries	Side A Plate 4							
9.3	Potato chips / Tortilla	XS/ S/ M/ L/ XL bag Page 20							
9.4	Falafel, without bread	1 medium falafel							
9.5	Shawarma	1 medium sandwich							
9.6	Burgers (beef, chicken, fish)	1 medium burger							
9.7	Pizza	Side B / Thickness							
9.8	Canned/ Pre-packed soups	Side A / Page 3							
9.9	Ketchup	Side A							
9.10	Mustard	Side A							

9.1. How many times do you **season your food with a tomato-based sauce** (tomato, onion, garlic and simmered with olive oil)?
_____ number of times per day / week / month?

9.2 Do you actually consume chicken or turkey meat **instead of** veal, pork, hamburger, or sausage?
____ Yes ____ No

9.3 Are there any other foods/supplements that you regularly consume **(at least once per week)** and that were not mentioned in the FFQ list above?

Food Item	Usual serving size	Frequency of intake per week

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Dietary Habits Questionnaire

1. Do you know what Bisphenol A (BPA) is? ---- No ---- Yes
2. Are you aware of BPA free bottles / plastic containers (Tupperware)? ---- No ---- Yes

		Always (6-7 times/week)	Most of the times (4-5 times/week)	Few times (2-3 times/week)	Rarely (1x/week to 3x/month)	Never	Don't know
3	Do you store foods in plastic containers?						
4	Do you heat foods in plastic containers?						
5	Do you make sure that the plastic containers you use are BPA-free?						
6	Do you heat foods that are wrapped in cling film?						
7	Do you drink bottled water?						
	7.1 From plastic- bottled water: ---------- cups/day 7.2 From water cooler: ---------- cups/day						
8	Do you reuse bottled water?						
9	Do you drink from bottles you left in your car?						
10	Do you eat outside home (snacks, restaurants, bars)?						
11	Do you order delivery foods?						
12	Do you purchase soft drinks in cans and/or plastic bottles?						
13	Do you consume canned tomato paste?						

24-Hours Dietary Recalls

Date: (dd/mm/yyyy) ---/---/---------

Day of the week: ----------

Time	Food eaten	Amount	Method of preparation

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Was yesterday a usual eating day?

- Yes
- No, please specify _____

When was the last meal taken?

-

Lab work data collection

Name of the participant: ---------- Initials:---------- Study ID number:----------

Test	Unit	Result
Hba1c		
LDL		
SGPT		
Urinary creat		
FBS		
HDL		
GGT		
Spot microalbumin		
Fasting insulin		
Triglycerides		
CRP		
Creatinine		
Total cholesterol		
TSH		
25OHvit D		
Cortisol		
C-peptide		
Prolactin		
Leptin		

Physical Exam Form

Name of the participant: ---------- Initials:---------- Study ID number: ----------

	Results النتائج	Healthy ranges النطاقات الصحية
Body weight (kg الوزن		
Height (cm): الطول		
BMI: مؤشر الكتلة		*18.5-24.9 kg/m²*
Waist circumference (cm): قياس دائرة الخصر		*نساء <80 cm, رجال <94 cm*
Body fat (kg): نسبة الدهون في الجسم		*نساء <25%; رجال <25%*
Muscle mass (kg): نسبة العضل في الجسم		*نساء 24-30 %; رجال 33-40%*
Waist to hip ratio: قياس محيط الأورك		*نساء <0.9, رجال <0.85*
Heart rate: قياس نبض القلب		*50-100 bpm*
Blood Pressure – Measurement # 1 قياس ضغط الدم 1		
Systolic blood pressure (mmHg): العالي		*120 mmHg*
Diastolic blood pressure(mmHg): الواطي		*90 mmHg*
Blood Pressure – Measurement # 2 قياس ضغط الدم 2		
Systolic blood pressure (mmHg): العالي		*120 mmHg*
Diastolic blood pressure(mmHg): الواطي		*90 mmHg*

Time of urine collection	
Time of blood withdrawal	

APPENDIX V

Table 13: Energy & nutrient intake of participants across quartiles of GI

	Q1	Q2	Q3	Q4	Significance
Energy (w/o outliers)	2772.767	3238.423	3322.471	3186.811	p= 0.056
Carbohydrates	332.361	397	400	420.5	**p= 0.006**
%Kcal CHO	48.46%	49.7%	49.47%	53.62%	**p= 0.001**
Protein	88.638	103	110.996	108	p= 0.125
%Kcal Prot	13%	12.7&	12.97%	13.27%	p= 0.876
Total Fat	124.5	140.5	144.091	117.623	**p= 0.042**
%Kcal total fat	41.9%	40.52%	39.65%	34.63%	**p= 0.000**
SFA	36.8	39.43	40.1	32	p= 0.073
%Kcal SFA	11.36%	10.84%	10.19%	9%	**p= 0.000**
MUFA	45.69	51.36	53.46	44.28	p= 2.135
%MUFA	14.78%	14.1%	14.34%	12.3%	p= 5.272
PUFA	31.9	38.08	38.97	31.38	p= 2.862
%PUFA	10.53%	10.47%	10.46%	9%	p= 2.641
Sum of Chol	291.72	310.62	386.01	273.5	p= 2.901
Fiber	28.04	29.66	27.71	26.79	p= 0.531

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