Nutrition Education and Cardiometabolic Risk

Dimitrios Chaniotis[1] and **Leto Papagiannakopoulou**[2]

[1]Technological Educational Institution (TEI) of Athens,
[2]Health Visitor, Children's Hospital Agia Sofia,
First Department of Paediatrics, University Medical School

Abstract

Metabolic Syndrome (MS) is constituted from a sum of risk factors and it is one of the most important diseases that contribute greatly to the morbidity and mortality caused by atherosclerosis and other cardiovascular disorders. Every disturbance in the MS constitutes an independent risk factor; however they can accumulate in the same person and as a result there is an increase of complications. Simple measures like the loss of weight, physical exercise, smoking cessation and (when needed) drug treatment may have a great effect in decreasing the risk of these complications. The research effort for the understanding of the causes that provoke resistance to insulin and the appearance of MS, still presents a great scientific interest. Among the causes that contribute to the development of MS are genetic and environmental factors. Recent studies have shown that MS increases even in children due to the appearance of their obesity. Children however, present all the characteristics of MS, like adults, therefore more case studies are needed in order to define the factors of MS for children.

Key words: Nutrition Education, Metabolic Syndrome, Cardiometabolic Risk, central obesity, diabetes mellitus, atherogenic dyslipidemia

Introduction

An important clinical syndrome of the modern era related with metabolic abnormalities and cardiovascular disease burden is the Metabolic Syndrome (MS). The MS, also known as syndrome X or the insulin resistance syndrome, is characterized by the clustering of metabolically interrelated cardiovascular risk factors such as central obesity, atherogenic dyslipidemia, hyperglycemia, elevated blood pressure, prothrombotic and proinflammatory states. Most of these modifiable risk factors of cardiovascular diseases are influenced by diet and nutrition.
The untreated MS places individuals at risk for coronary artery disease, stroke, peripheral arterial disease, advanced vascular damage, type 2 diabetes mellitus (t2DM), and mortality [1, 2].

Address for correspondence:
Dimitrios I. Chaniotis, MD, PhD
Ag. Spyridonos, 112 43 Egaleo, Athens, Greece
Tel. +30 6973049444
E-mail: dchaniotis@teiath.gr

If more than one of these parameters are present in the same person, the hazard is not only doubled, but multiple. This destructive course of MS ending in the risk of prime cardiovascular disease appearance is characterized as Cardiometabolic Risk and it defines the coexistence of multiple and correlated metabolic disorders of utmost importance to the pathogenesis of atherosclerosis.

The MS is characterized by a combination of abnormalities that cause increased risk for the appearance of cardiovascular disorders, heart attack and t2DM [3, 4, 5, 6].
The World Health Organisation (WHO) accepting the resistance to insulin as a main disorder of the syndrome, has recommended as mandatory criteria one of the following (Table 1): resistance to insulin, DMII, resistance to fasting glucose, abnormal glucose curve and two of the following: resistance o insulin or pathological resistance to glucose (or DM), hypertension, increased triglycerides, low HDL, increased ratio of waste perimeter to the hips perimeter and microleukomatinurea [7].
Among the recent data, International Federation for Diabetes (IDF) and the AHA/NHLBI joined by the World Heart Federation, International Atherosclerosis Society, and International Association for the Study of Obesity have resulted in an acceptable unified definition, which has now been published to attempt to resolve the remaining diagnosis differences of metabolic syndrome. (Table 2) [8]. MS is considered an important risk factor for cardiovascular disease (CVD) [9]. However, this correlation with the risk for CVD depends on the definition used for the diagnosis of MS.

Epidemiology

One complete health research that was performed on a representative sample of population in the USA showed that MS, is particularly high in the American population and it is observed in a ratio ¼ [10]. The appearance of MS in a total of about 24%, is similar for men and women. However, the individuality of its appearance, depending on gender, has shown that a few metabolic characteristics were observed more often in men (high levels of triglycerides, hypertension, and high levels of fasting glucose) than in women.
Moreover the appearance of MS increases considerably with age and is observed at a percentage of more than 40% in people that are more 60 years old [11]. Nowadays MS affects many people from different races in the entire world, including the populations of SouthEastern Asia. The most recent data concerning obesity are [11]:

- 1.000.000.000 overweight people include 300.000.000 obese people globally
- Greece is first in EU in adult obesity and second (after Italy) in juvenile
- Cardiovascular diseases are the first cause of death in the west world
- Hypertension, obesity, increased levels of cholesterol, t2DM and smoking answer 75% and more of cardiovascular episodes
- Decrease of weight by 30% prevents or cures t2DM
- After 25, for every year, the human body needs 1% less calories
- In order to burn ½ of fat, 3.500 less calories must be taken
- Quick walking for 4-5 hours per day has the same effect on weight as the decrease of calories taken by food (750-1.000)
- Obese children have 2-5 times more possibilities to suffer a stroke or myocardial infarction before they reach the age of 65.

Table 1. Definition of MS according to WHO (1999) [7]

- **Resistance to insulin (DMII, resistance to fasting glucose disorder, glucose pathology curve)**
- **Combination of 2 of the following**
  - Arterial pressure (≥ 140/90 or hypertension treatment)
  - Triglycerides ≥ 150 mg/dl
  - HDL-C <35 mg/dl (male), <40 mg/dl (female)
  - BMI >30 and /or WC/HC >0,90(male), >0,85 (female)
  - Microalbuminuria, i.e., urinary albumin excretion rate ≥ 20 μgm/minute or albumin/creatine ratio ≥ 30 μgm/mg..

BMI= body mass index, WC= Waist circumference, HC=Hip circumference, WC/HC =Waist to Hip ratio.

Table 2. Definition and Criteria for clinical diagnosis of MS according to JIS 2009 [8]

Abdominal obesity should not be a prerequisite for MS diagnosis. MS = 3 of 5 from the following risk factors.	
Risk factors	**Level**
Abdominal obesity: (Increased waist circumference)	**Categorical cutpoints** (Population and country-specific definitions)
It is recommended that the IDF cutpoints be used for non-Europeans and either the IDF or AHA/NHLBI cutpoints used for people of European origin until more data are available [next Table 2].	
Triglycerides	**≥150mg/dl**
HDL-C	
	Male **<40mg/dl**
	Female<**50mg/dl**
Blood arterial pressure	**Systolic≥130/ and or diastolic≥85mmHg**
Fasting glucose	**≥100mg/dl**

In Greece the risk from MS is real. The epidemiological evidence of the Attica research [12] from the University Cardiology Clinic of Hippocratio Hospital, are alarming for the appearance of MS in the future. According to the results of the research:

- 1 out of 5 (19,8%) presented risk factors. Men had double percentages.
- Very few men and women with risk factors followed the Mediterranean diet, while they had reduced percentages of physical exercise
- The frequency of MS appearance presented increase with age (38% to people older than 65).

Table 2. Current Recommended Waist Circumference Thresholds for Abdominal Obesity by Organization

		Recommended Waist Circumference Threshold for Abdominal Obesity	
Population	Organization (Reference)	Men	Women
Europid	IDF (4)	≥94 cm	≥80 cm
Caucasian	WHO (7)	≥94 cm (increased risk)	≥80 cm (increased risk)
		≥102 cm (still higher risk)	≥88 cm (still higher risk)
United States	AHA/NHLBI (ATP III)* (5)	≥102 cm	≥88 cm
Canada	Health Canada (8,9)	≥102 cm	≥88 cm
European	European Cardiovascular Societies (10)	≥102 cm	≥88 cm
Asian (including Japanese)	IDF (4)	≥90 cm	≥80 cm
Asian	WHO (11)	≥90 cm	≥80 cm
Japanese	Japanese Obesity Society (12)	≥85 cm	≥90 cm
China	Cooperative Task Force (13)	≥85 cm	≥80 cm
Middle East, Mediterranean	IDF (4)	≥94 cm	≥80 cm
Sub-Saharan African	IDF (4)	≥94 cm	≥80 cm
Ethnic Central and South American	IDF (4)	≥90 cm	≥80 cm

*Recent AHA/NHLBI guidelines for metabolic syndrome recognize an increased risk for CVD and diabetes at waist-circumference thresholds of ≥94 cm in men and ≥80 cm in women and identify these as optional cut points for individuals or populations with increased insulin resistance.

Cardiovascular risk evaluation

Epidemiological and clinical data verify that CVD is a disease of "multiple etiologies"; it is apparent that a series of valid and rising factors are the complex cause of the disease. Among these, some factors like age, sex and family history cannot be affected. Others, like smoking, hypertension, lipid metabolism disorders, glycaemia regulation and obesity can be modified (Fig. 1). Also there is evidence to prove the significant decrease of CVD and mortality by using anti-hypertensive, hypolipidaemic and anti-diabetic treatment [13].
Often, some of the above factors coexist in a person and act in a synergy, playing an important role in the pathogenesis of atherosclerosis. The accumulation of risk factors may have multiple effects and a particular person with more than one, but only medium increased risk factors may be under more significant risk, than a person with only one risk factor highly increased. The right therapeutic approach of the patient makes necessary the need to evaluate the total cardiovascular risk for the possibility of CVD development.

The evaluation of cardiovascular risk in people with MS is connected its the strategic treatment. The presence of MS does not suggest that the patient automatically belongs to the high risk category, similar to the one of patients with diagnosed coronary artery disease (CAD) or DMII. The cardiovascular risk in MS varies and some patients have only moderate or low risk.

DM is related to the increased risk for CVD, even from the resistance to glucose phase. The special (unfavorable) profile of cardiovascular factors in DMII (increased level of triglycerides, low HDL cholesterol levels, low-density LDL, central type obesity and hyperinsulinaemia) explains greatly the development of CAD or atherosclerosis. People with DM, without CAD, are placed in a risk level equal to CAD and therefore the intensity of risk therapy should be proportional to the person's total risk.

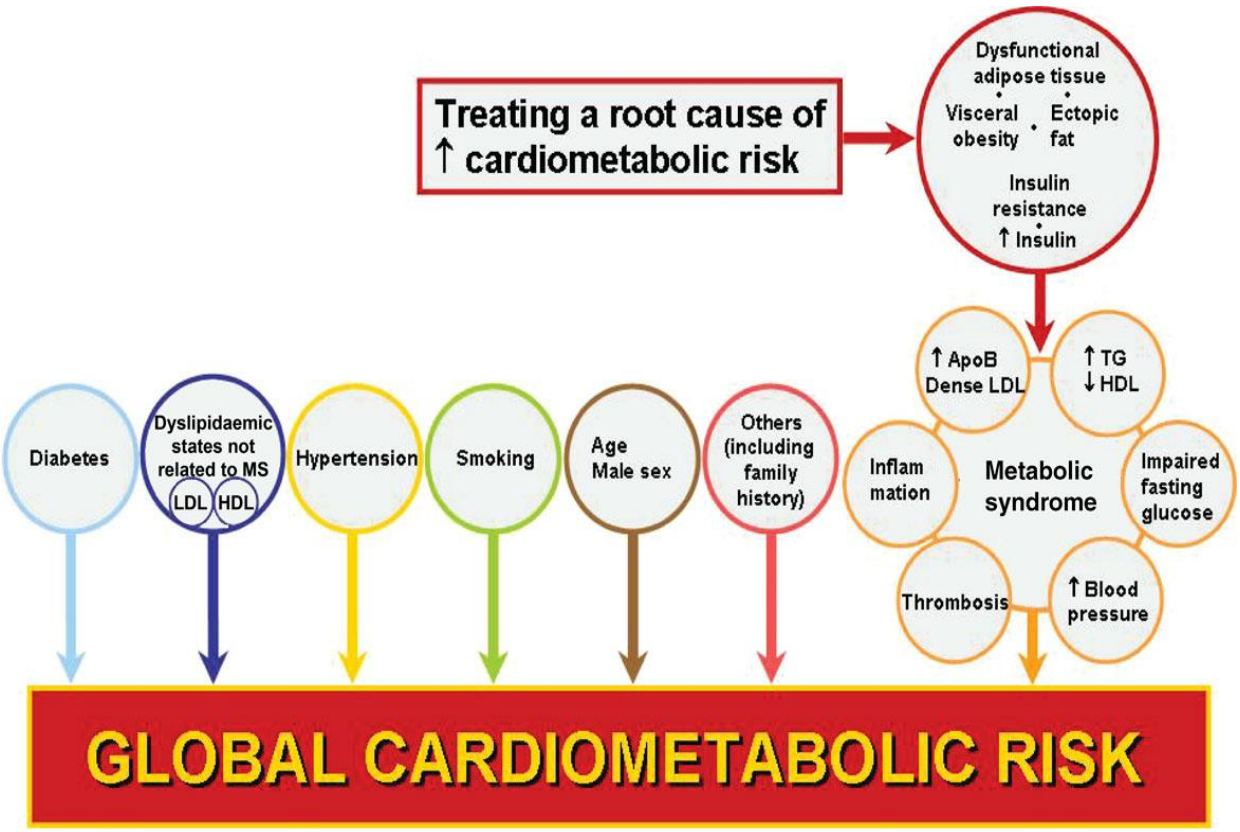

***Figure 1**. Assessment and management of global cardiometabolic risk. Eur Heart J Suppl 2008:10,B1–B3.*

Table 3: The guidelines of USA: NCEP-ATP III Targets and periods for hypolipidaemic therapy [14].

Risk Category	Target LDL	LDL levels to which a change of lifestyle is recommended	LDL levels to which drug treatment is recommended
CAD or equal to CAD (10 year risk > 20%)	<2,6mmol/L <100mg/dL Optional target <70mg/dl	≥2,6mmol/L ≥100mg/dL	≥3,3mmol/L (≥130mg/dl) (2,6-3,3mmol/L: optional drug
Risk factors ≥2 (10 year risk ≤20%)	<3,3mmol/L <130mg/dL optional target <100mg/dl	≥3,3mmol/L ≥130mg/dL	10 year risk 10-20%: ≥3,3mmol/L (≥130mg/dL) 10 year risk -<10%: ≥4,2mmol/L (≥160mg/dL)
0 -1 Risk factors	<4,2mmol/L <160mg/dL	≥4,2mmol/L ≥160mg/dL	≥4,9mmol/L (≥190mg/dL) (4,2-4,9mmol/L: optional drug)
Almost all the people with 0-1 risk factors have a 10 year risk <10%, so the evaluation of the 10 year risk in people with 0-1 risk factors, is not necessary			

National Cholesterol Education Program Adult Treatment Panel III. JAMA 2001; 285: 2486-2497.

Causes

Most doctors believe that the main cause of MS is the resistance to insulin (a hormone produced by pancreas that helps the regulation of glucose levels in the blood) [10].
Usually the digestive system breaks down the food we consume to glucose particles. People that suffer from resistance to insulin, have cells that do not correspond to insulin, therefore glucose cannot diffuse in them [15]. The body reacts by producing higher and higher levels of insulin to help glucose diffuse.
This leads to simultaneous increase of insulin and glucose in the bloodstream. The low glucose levels that are not caused by DM have serious impact on health. The increased levels of insulin cause an increase in the triglyceride and other lipids levels in the blood and affect renal function, leading to arterial hypertension. The combination of these phenomena caused by resistance to insulin, leads to the appearance of cardiovascular diseases, heart attack and DM [10]. The cells become resistant to insulin and to DMII.
Resistance to insulin that has a genetic basis, but may worsen due to the modern way of life (couch potato, obesity, increased fat intake) leading to repercussions of all the disorders that constitute MS [16]. Resistance to insulin can be inherited and it is closely connected with the function, the size and the number of mitochondria in the muscle tissue. Genes that relate to the biogenesis of mitochondria have decreased expression in children of diabetic parents with normal Body Mass Indicator (BMI).
Decreased oxidization of fatty acids in skeletal muscles leads to higher triglyceride concentration in the muscle fibers and causes resistance to insulin. This means that the fat layer is increased causing obesity and DM expression. Therefore, resistances to insulin together with insulin excretion disorder are the two main causes for the appearance of DMII [17]. The decreased excretion of insulin may also be associated to the deficient mitochondrial function of β-cells in pancreas, since the stimulus for insulin excretion is the production of ATP from the mitochondria.
Resistance to insulin also leads to chronic hyperfunction of β-cells and to other disorders like the high levels of free fatty acids (FFA) in the blood circulation due to increased lipolysis, triglyceride concentration in pancreas, amplified production of cytokines, increased oxidative stress and others, leading to augmented apoptosis of β-cells [17].
Hepatic resistance to insulin and increased production of FFA in the liver causes hepatic production of VLDL rich in triglycerides, resulting to higher levels of triglycerides, low levels of HDL and increase of small and dense LDL. Finally resistance to insulin is connected to the causes of hypertension. It contributes to the dysfunction of the endothelial, the reduced NO production that causes vasodilatation and the increased production of endothelin (vasoconstrictor). This resistance is responsible for the loss of vasodilatation and natriuria that are normally regulated by insulin.
People presenting resistance to insulin and obesity have increased myocardial production, periphery resistance and sympathetic system tone. All the above, including augmented activity of the rennin-ngiotensin system (which is normally also present) and the imbalanced hyperinsulinemia (leading to increased reuptake of $N\alpha^+$ and water) cause hypertension [18].
Disorders related to resistance to insulin and hyperinsulinemia are [19]:

- Glucose intolerance
- Uric acid metabolic disorders
- Dyslipidaemia

- Hemodynamic disorders
- Hemostasis disorders

Risk factors

The risk factors contributing in MS appearance are [20]:

- Age
- Race
- Obesity
- Diabetes history
- Other disorders

Symptoms

MS is apparent when there are simultaneously various disorders connected to the metabolism of a person. These include the following as shown in Fig. 2 [8]:

- Obesity, especially around the waist (apple form)
- High levels of blood pressure
- High levels of fat in the blood (triglycerides)
- Low levels of HDL cholesterol (high density lipoproteins) – "good" cholesterol
- Resistance to insulin

When somebody presents one symptom of MS, it is very likely that the rest of the symptoms are there. The more symptoms apparent, the graver is the health risk.
People that present three symptoms of MS have double the possibility to suffer a heart attack or arrest and triple the possibility to present a cardiovascular disorder, than the people that suffer from no symptoms.
The appearance of an MS symptom, like high arterial pressure, high levels of cholesterol or abdominal obesity, may be followed by the other symptoms. This is when a person should visit a doctor, as the rest of the syndrome's symptoms must be checked out.
Various organisations have adopted criteria for the diagnosis of MS, all of which have been accepted by the American Heart Association [21]. According to these, someone suffers from MS when three or more symptoms are present:

- Increased abdominal periphery
- Increased levels of triglycerides
- Decreased HDL cholesterol
- Increased arterial pressure
- Increased levels of blood sugar

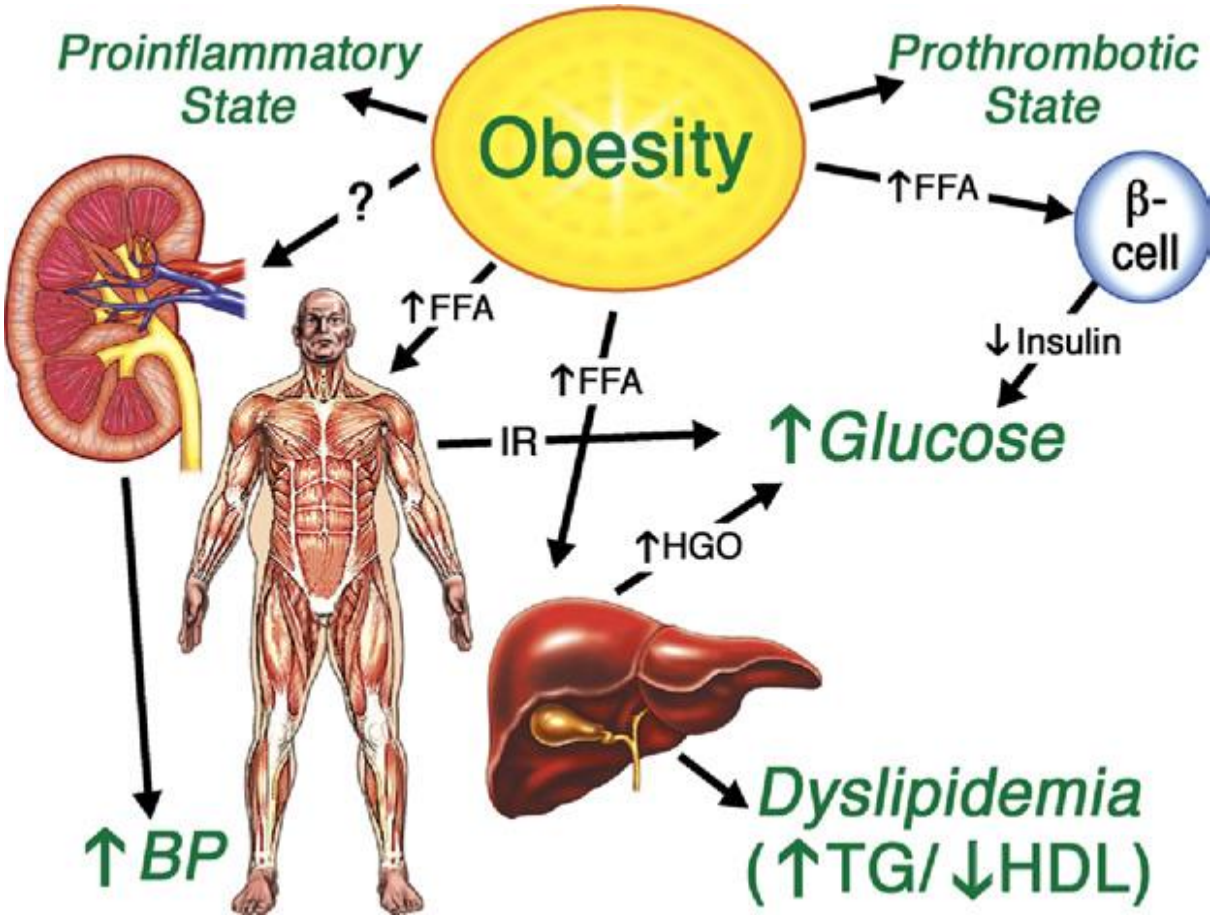

Figure 2. Metabolic Pathways Underlying Pre-Diabetes and Metabolic Syndrome [Hepatic glucose output (HGO), Free fatty acids (FFA), Insulin resistance (IR), Blood pressure (BP), plasma Triglycerides (TG), High-Density lipoprotein (HDL). J Am Coll Cardiol 2012;59:635–643.

Treating MS

Treating one of the risk factors in MS is hard, while treating all of its symptoms seems impossible. Drastic changes in lifestyle and in some cases medication may improve the symptoms of MS and improve the cholesterol and sugar levels in the bloodstream. These actions are vital for the risk factor reduction [22, 23].

- Physical exercise
- Weight loss
- Smoking cessation

A person has to observe the changes in weight, glucose and cholesterol levels and arterial pressure in order to ascertain the repercussions from the change of lifestyle. If someone cannot achieve these goals by changing their lifestyle, medication must follow for the reduction of arterial pressure and weight and for the regulation of cholesterol. Administration of substances sensitive to insulin may aid in more effective insulin use. The use of aspirin may also aid to minimize the heart attack and stroke risk.

Treating Dyslipidemia

Since the primary target of hypolipid treatment is the reduction of LDL-C, statins constitute the first option of medication. Statins not only reduce significantly the concentration of atherosclerotic LDL, but possible also affect favourably the carbohydrates metabolism. Indeed, the analysis of the results in the WOSCOPS case-study has shown that patients who received pravastatin had smaller risk in presenting DM compared to patients that received placebo [23, 24].

Treating Hypertension

According to the recent guidelines for hypertension treatment, the goal of anti-hypertensive medication is the reduction of arterial pressure to <140/90mmHg. Diuretics in high dosages cause unbalanced trigger of the sympathetic and the rennin-angiotensin system, while their chronic use is related to dyslipidaemia and resistance to insulin activity. However, diuretics in small quantities are useful and effective anti-hypertensives and their administration is followed by a few and non-severe metabolic side-effects [25].
β-blockers reduce the heart production and the activity of rennin-angiotensin system. In addition they reduce the cardiovascular morbidity and mortality in hypertensive patients. Moreover β-blockers are the first choice medication in patients with ischemic heart disease. However, these drugs affect harmfully the carbohydrate and lipid metabolism.
Many studies have shown that the antagonists for the angiotensin receptors also increase the sensitivity of tissues in insulin action and reduce the possibility of DM development. Therefore these drugs constitute alternative medication in hypertensive patients presenting resistance to insulin activity to which administration of MAO inhibitors is not advised.

Self-Treatment

A person may be protected by the MS risk and its complications, diabetes mellitus, heart attack and cardiovascular diseases [15]. Resistance to insulin may be reduced by following the lifestyle changes below:

- Weight loss
- Physical activity
- Smoking cessation
- Diet rich in vegetable fibers

Table 4. Main dietary components in health-diet treatment [14]

- Saturated fat <7% of total calories
- Multi-unsaturated fat up to 10% of total calories
- Unsaturated fat up to 20% of total calories
- Total fat 25-35% of total calories
- Carbohydrates 50-60% of total calories
- Vegetable fibers 20-30gr/day
- Leukocytes approximately 15% of total calories
- Cholesterol <200mgr/day
- Total calories: Balance between taken and burnt calories for the obtaining and retaining of desired body weight. Avoidance of excess body weight.

For an average person, if the body weight is in ordinary levels, the BMI (body mass indicator) should be between 18,5 – 25 kg/m^2. If the weight is between this limit and has to be retained, then the energy taken for the food consumed daily, must be balanced by the energy burnt in physical activity. However, if the person is overweight, the number of mini-portions daily consumed must be reduced, while preserving at the same time the variety in its diet (Fig. 3).

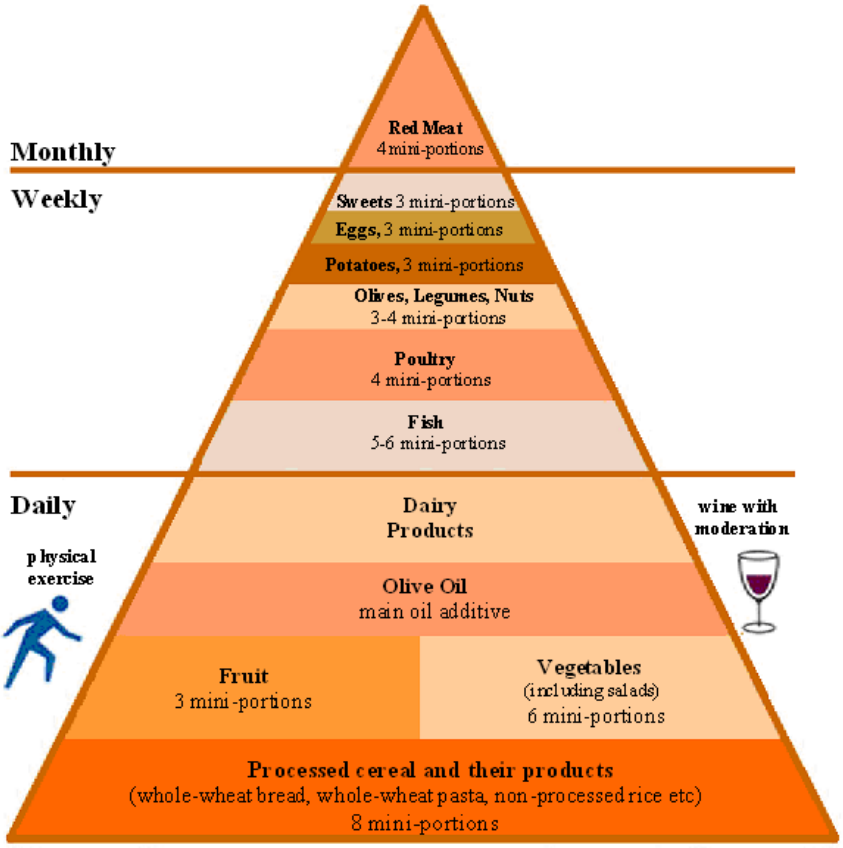

Figure 3. *Pyramid of the Mediterranean diet [26].*

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